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#### Platform Session: Basic Science Sunday, 6th September 2015

0001

##### SODIUM SELENATE RETARDS EPILEPTOGENESIS VIA ACTIVATING PROTEIN PHOSPHATASE 2A

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**Purpose:** Epileptogenesis describes the neurobiological processes that convert a healthy brain into an epileptic brain. There are no treatments available to mitigate epileptogenesis in clinical practice. Down-regulation of protein phosphatase 2A (PP2A) activity increases phosphorylated tau (p-tau), which is implicated in acquired epilepsy. To investigate the role of PP2A in epileptogenesis, and the effects of a specific PP2A activator – sodium selenate – we utilized three well-characterised rat models of epilepsy: electrical amygdala kindling, post-kainic acid status epilepticus (post-SE) and post-traumatic epilepsy (PTE).

**Method:** For amygdala kindling, rats were implanted with subcutaneous osmotic pumps that delivered selenate (1 mg/kg/day) or vehicle continuously for 4 weeks. Rats received 30 electrical stimulations over the final 3 weeks of treatment. For post-SE experiments, SE was induced by kainic acid injections. Rats were then implanted with subcutaneous osmotic pumps that continuously released selenate or vehicle for 8 weeks. After 5 weeks of treatment, rats underwent MRI followed by continuous video-EEG monitoring. Rats were then given a drug washout period and then underwent additional video-EEG monitoring. For PTE, rats randomly suffered sham surgery or lateral fluid percussion injury and saline vehicle or selenate treatment. After 3-month recovery, all rats underwent video-EEG monitoring during and after the treatment.

**Results:** PP2A activity and expression of the PR55 regulatory subunit B were significantly decreased, and phosphorylation of tau was increased, in all three models. Selenate treatment slowed the progression of epileptogenesis in three models (delayed kindling and reduced spontaneous seizures post-SE and PTE), reversed the biochemical abnormalities, and reduced hippocampal atrophy in the post-SE model. In post-SE and PTE model, this effect was sustained after drug washout, which indicated an anti-epileptogenic effect.

**Conclusion:** Epileptogenesis is associated with down-regulation of PP2A activity and an increase in phosphorylated tau, and enhancing PP2A activity with selenate is a potential anti-epileptogenic therapy.

0002

##### MORPHOLOGICAL CHANGES IN EEG, AQUAPORIN-4, C-FOS AND THE HIPPOCAMPUS OF ANIMAL MODELS WITH TEMPORAL LOBE EPILEPSY INDUCED BY KAINIC ACID

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**Purpose:** Temporal lobe epilepsy (TLE) is the most frequent type of localization-related focal epilepsy seen in humans. It has a frequency rate of 30–35% among all epilepsies, and comprises 70% of intractable epilepsies. With hippocampal sclerosis as the most often observed histopathological finding, its epileptogenesis is still researched.

**Method:** We investigated alterations in EEG findings during epileptogenesis, and the immunohistochemical correlation of AQP4 and c-fos levels to hippocampal morphology in TLE induced by kainic acid (KA) models. Sixty four young adult (220–270 gr) Wistar albino rats were divided into EEG and immunohistochemistry subgroups of sham, acute and chronic KA groups. Following the implantation of depth electrodes, rats were administered 5–15 mg/kg KA. In addition to observing AQP4 and c-fos proteins at the end of the first 24 hours and 60th day, continuous video EEG monitoring (VEM) was carried out for 60 days. Seizure patterns and interictal (II) epileptiform activities on VEM were investigated.

**Results:** All rats in the acute KA group had status epilepticus (SE). While no spontaneous convulsive seizures were observed in the chronic KA group, electrophysiologically rhythmic slow waves were seen during the clinical staring episodes. Interictally, spike/sharp waves were observed. II activity tended to increase gradually during the 60 days. As c-fos immune dying intensified in the hippocampal CA1 and amygdala, an increased rate of AQP4 immune dying in the endothelial cells in the brain capillaries (in the endothelial cells as well as the cytoplasm and feet of the astrocytes) were observed. We determined a correlation between the increased intensity of c-fos and AQP4 proteins in hippocampus and amygdala with the electrophysiological finding of increased number of spikes.

**Conclusion:** Based on our findings, it is possible to suggest that impaired blood brain barrier (BBB) and increased AQP4 immunoreactivity contribute to the development of epileptogenesis.

0003

### SHARED PATHOPHYSIOLOGY OF TEMPORAL LOBE EPILEPSY AND ALZHEIMER'S DISEASE – A DIFFERENTIAL PROTEOMICS APPROACH IN A POST-STATUS EPILEPTICUS MODEL

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**Introduction:** Clinical evidence points to a bidirectional link between temporal lobe epilepsy (TLE) and Alzheimer's disease (AD). However, clear-cut conclusions about a functional link between the pathophysiologicals are clinically difficult. Therefore, we performed a large-scale differential proteome analysis in a rat TLE model of epileptogenesis and compared these data sets with available information about differential protein expression in AD models.

**Materials and Methods:** Following an electrically-induced status epilepticus in female Sprague Dawley rats, hippocampal (HC) and parahippocampal cortex (PHC) tissues were individually subjected to a label-free liquid chromatography tandem mass spectrometry analysis at three time points reflecting the early insult phase (2 days, n = 5), latency phase (10 days, n = 5), and the chronic phase with spontaneous recurrent seizures (8 weeks, n = 5). Control animals (n = 5 per timepoint) were handled in parallel.

**Results:** We identified proteins associated with amyloid-beta processing, deposition, plaque formation, and amyloid-beta-associated pathology (ApoE and  $\alpha$ -synuclein) being regulated in the time course of epileptogenesis.

Moreover, the analysis pointed to an epileptogenesis-associated down-regulation of the microtubule-associated protein Tau in the PHC, whereas Tau exhibited an up-regulation in the HC in the latency phase.

Furthermore, our data sets reveal a prominent dysregulation of mitochondrial expression patterns, which is a typical feature of AD pathophysiology, in the PHC and a less pronounced dysregulation in the HC associated with epileptogenesis.

**Conclusion:** Altogether, our findings provide comprehensive information about the time course of epileptogenesis-associated alterations in the expression patterns of proteins functionally linked with AD pathophysiology, pointing towards a shared pathophysiology of both diseases and further providing information about potential biomarkers. These proteins require immunohistological validation in future studies.

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0005

### SYSTEMIC DELIVERY OF ANTAGOMIRS TARGETING MICRORNA-134 AFTER STATUS EPILEPTICUS REDUCE SPONTANEOUS RECURRENT SEIZURES IN MICE

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**Purpose:** Acquired epilepsy is associated with large-scale changes in gene expression which underlie the cell and network-level changes during epileptogenesis. Despite various efforts we still have no treatments to

prevent the emergence of epilepsy following brain injury. Evidence has emerged that microRNAs, a family of small non-coding RNAs, are important regulators of gene expression in epilepsy. Recent work showed that miRNA-134 is overexpressed in the temporal lobe of patients with pharmacoresistant seizures and in experimental models of epilepsy. Silencing miR-134 using intracerebroventricular injections of antagomirs (Ant) potently suppressed evoked and spontaneous seizures in mice. Here we explored a more clinically relevant route of delivery of these macromolecules, timing injection of antagomirs with blood-brain barrier (BBB) opening after status epilepticus in mice.

**Method:** Status epilepticus (SE) was induced in C57BL/6 adult mice by an intra-amygdala microinjection of kainic acid. Timing of BBB opening was assessed by Evans blue and FITC-dextran injections, and confirmed by extravasation of serum albumin and mouse IgG levels into the brain parenchyma. Antagomirs were locked nucleic acid- and cholesterol-modified. Injections were then timed accordingly and mice subject to continuous long-term video-telemetry EEG recording.

**Results:** BBB opening in this model was apparent 2 h after status epilepticus. Systemic injection of Ant-134 at this time point did not alter the duration or severity of status epilepticus in mice but significantly reduced the number of spontaneous seizures recorded in mice compared with scrambled-sequence and vehicle-injected status epilepticus controls. These seizure-suppressive effects persisted at 1 and 2 months after the SE.

**Conclusion:** The present study provides evidence that macromolecule targeting of an epilepsy-associated microRNA is effective using a clinically-relevant delivery route, supporting the potential translation of this anti-epileptogenic treatment for epilepsy.

## Platform Session: Drug Therapy Sunday, 6th September 2015

0006

### ASSESSING BIOEQUIVALENCE OF GENERIC MODIFIED RELEASE ANTI-EPILEPSY DRUGS

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**Purpose:** To determine how closely generic modified-release anti-epileptic drugs (MR-AEDs) resemble brand formulations, we compared bioequivalence (BE) data for United States Food and Drug Administration (FDA)-approved MR-AEDs. We compared peak concentrations (C<sub>max</sub>), total absorption (AUC), time to C<sub>max</sub> (T<sub>max</sub>), intersubject variability, and food effects between generic/reference products.

**Method:** We collected C<sub>max</sub> and AUC data from the BE studies used to support the approvals of 42 generic MR-AED formulations. We compared the upper and lower limits of 90% confidence intervals (CI) of the generic/brand AUC and C<sub>max</sub> geometric mean ratios (GMRs), and intersubject variability, T<sub>max</sub>, and fasting/fed differences for MR formulations of: phenytoin (8 products), carbamazepine (5 products), divalproex sodium (7 products), levetiracetam (15 products), and lamotrigine (7 products).

**Results:** Forty-two MR-AED formulations were studied with 3175 non-epilepsy subjects in 97 fasting or fed BE studies. BE ratios for AUC and C<sub>max</sub> were similar for most products: AUC ratios varied by >15% in 11.4% of BE studies; C<sub>max</sub> varied by >15% in 25.8% of studies. T<sub>max</sub> was more variable, with >30% difference in 13 studies. T<sub>max</sub> was usually

delayed in the fed BE studies compared to fasting studies. Generic and brand products had similar intersubject variability, suggesting either could be used for initial therapy. MR products did not generally reduce intersubject variability in AUC and Cmax compared to immediate release (IR) products; IR and MR lamotrigine provided variable concentrations across subjects while the IR and MR carbamazepine products had less variability.

**Conclusion:** Most generic and brand MR-AED formulations have similar AUC and Cmax values; a small number of products had 90% CI near acceptance limits which could potentially be clinically significant. Food effects are common with MR-AED products; most MR brand products do not provide advantages with reduced variability across subjects compared to generic products or when compared to IR products.

0007

### DISEASE-MODIFICATION BY A COMBINATORIAL TREATMENT OF ANTI-INFLAMMATORY DRUGS IN TWO RODENT MODELS OF EPILEPSY

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**Purpose:** Neuroinflammation is induced in epileptogenic foci after an inciting event in epilepsy models; this phenomenon was validated in brain specimens from pharmacoresistant patients. Specific anti-inflammatory treatments greatly reduce provoked or spontaneous seizures in experimental models. We studied whether a combination of drugs targeting the ictogenic IL-1 $\beta$ /HMGB1 pro-inflammatory signaling affects the disease onset or its progression in two rodent models of symptomatic epilepsy.

**Method:** Status epilepticus (SE) was induced in adult male rodents by electrical stimulation of the hippocampus (Sprague-Dawley rats) or by intra-amygdala injection of kainate (C57BL6 mice). In rats, a combination of anakinra (IL-1 receptor antagonist), BoxA (HMGB1 antagonist) and ifenprodil (NR2B antagonist) was given 1 h post-SE for 6 consecutive days. In mice, a combination of VX-765 (IL-1<sup>®</sup> biosynthesis inhibitor) and Cyanobacterial LPS (TLR4 antagonist) was given at the onset of epilepsy for 7 days. Controls were vehicle-injected animals exposed to SE. EEG recording (24/7) was done from SE induction until the onset of spontaneous seizures, and for additional 2 weeks in the chronic epilepsy phases. At the end of recording, the Morris Water Maze or the Novel Object Recognition test was performed to assess cognitive performance, then animals were fixative-perfused for brain histology.

**Results:** The combined treatments reduced by 2-fold the proportion of animals with a progressive increase in seizure frequency: progression occurred in 40% of treated animals vs 80% in the vehicle group. Moreover, the progression index was decreased by 2-fold in treated animals. The treatment reduced by 3-fold seizure frequency in animals with a non-progressive disease. Finally, treatment reduced neurodegeneration in forebrain and improved non-spatial memory deficits in epileptic animals while spatial memory was unaffected.

**Conclusion:** Pharmacological targeting of IL-1 $\beta$ /HMGB1 signaling either before or after epilepsy onset, specifically interferes with disease progression, suggesting that anti-inflammatory treatments modify the disease course.

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0008

### PHARMACOLOGICAL OUTCOMES IN JUVENILE MYOCLONIC EPILEPSY OVER 30 YEARS

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**Purpose:** To investigate the long-term outcomes in patients with Juvenile Myoclonic Epilepsy (JME) at a single centre over 30 years.

**Method:** A retrospective analysis was undertaken in 186 patients (male: n = 78; female: n = 108) diagnosed with JME at the Epilepsy Unit in the Western Infirmary, Glasgow, Scotland between July 1982 and 2012.

**Results:** Median age at treatment start was 16 years (range 12–44 years) with a median duration of follow-up of 14 years (range 2–32 years). Overall 171 patients (92%) achieved terminal remission on antiepileptic drug (AED) therapy with a mean seizure-free period of 9.5 years (range 1–31 years). Fifteen patients (5 male, 10 female) continued to have seizures despite taking up to 8 AED regimens, 7 of whom had psychiatric comorbidities. Most commonly prescribed AEDs included sodium valproate (VPA; n = 142), lamotrigine (LTG; n = 66) and levetiracetam (LEV; n = 22). Overall, VPA represented 44% of all AEDs prescribed to male patients compared with 31% in females. Fewer males received LTG (n = 17; 26% vs. n = 49; 74%) and LEV (n = 4; 18% vs. n = 18; 82%). Terminal remission was achieved more often using monotherapy with VPA (n = 74, 52%) and LEV (n = 12, 55%) than with LTG (n = 21; 32%). More males than females attained terminal remission on their first or second AED (n = 69; 88% vs. n = 60; 56%). AED monotherapy resulted in intolerable side-effects in 76 patients.

**Conclusion:** JME is a benign syndrome with high rates of seizure freedom. Female patients had a worse outcome than males, since they were less likely to receive VPA because of concerns regarding teratogenicity. Patients with psychiatric comorbidities were also less likely to achieve optimal seizure control.

0009

### EFFICACY AND SAFETY OF ANTI-TUMOR NECROSIS FACTOR ALPHA THERAPY IN RASMUSSEN'S ENCEPHALITIS: AN OPEN STUDY

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**Purpose:** Rasmussen's encephalitis (RE) is a severe chronic inflammatory brain disorder affecting one cerebral hemisphere, leading to drug-resistant epilepsy, progressive neurological deficit and unilateral brain atrophy. Some immunomodulatory therapies have been tried with varied efficacy, but there is no standardized treatment strategy. TNF  $\alpha$  seems to play an important role in RE pathophysiology including pro-inflammatory, pro-epileptogenic and pro-excitotoxicity effects.

**Method:** We report an open study evaluating the effect of anti-TNF- $\alpha$  therapy (Adalimumab) in 10 patients with RE. The main outcome criterion was the decrease by 50% of monthly number of days with seizure.

**Results:** Adalimumab was started with a median delay of 4.8 years after first seizures (range: 1 month-16 years) and followed-up a median period after initiation of 18.4 months (range: 12–36 months). Four patients (40%) were found to be responders experiencing a rapid and prolonged effect after Adalimumab initiation. Adalimumab was well tolerated without remarkable clinical side effects.

**Conclusion:** Adalimumab showed safety of use and efficacy in a proportion of patients with RE, in term of seizure control and neurological deficit. The long-term effect of this treatment on larger series is needed to confirm these preliminary promising results.

0010

### SPASM CONTROL AT 3, 6 AND 12 MONTHS IN WEST SYNDROME: RANDOMISED, SINGLE BLIND CLINICAL TRIAL ON INTRAMUSCULAR LONG ACTING ACTH VERSUS ORAL PREDNISOLONE

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**Purpose:** Most literature on treatment for West syndrome, concentrate on the immediate spasm control. What is important is to identify the long term outcome in relation to spasm control and developmental outcome. Hormonal therapy is currently established as its first line therapy. However, which form of hormonal therapy i.e. intra-muscular long acting tetracosactrine (ACTH) or oral prednisolone is more efficacious for long term spasm control is not yet known.

**Method:** A prospective randomized, single blind clinical trial was conducted in Sri Lanka. Ninety seven newly diagnosed, previously untreated children with confirmed epileptic spasms, with hypsarrhythmia on EEG, were randomized to receive oral prednisolone or ACTH for 14 days according to the United Kingdom Infantile Spasm Study protocol. Spasm control was evaluated at different time points (3, 6, and 12 months). Spasm control was defined as absence of spasms for more than 1 week at these reviews.

**Results:** Forty eight infants on prednisolone and 49 on ACTH completed the treatment. Spasm cessation by 14th day occurred in 58.3% with prednisolone in comparison to only 36.7% with ACTH ( $p = 0.03$ ). The number of children completing follow up at 6 and 12 months were 29 and 29 for prednisolone and 23 and 25 for ACTH respectively. There were 3 deaths by 6 months and 6 deaths by 12 months. Absence of spasms at 3rd-month follow up was 66.7% with prednisolone and 38.2% with ACTH ( $p = 0.006$ ). Absence of spasms at 6 months with prednisolone was 60.4% compared to 46.9% with ACTH ( $p = 0.18$ ). Absence of spasms at 12 months was 60.4% for prednisolone and 51% for ACTH ( $p = 0.35$ ).

**Conclusion:** This trial shows that the spasm control for first 3 months was significantly better if treated with oral prednisolone. However, long-term spasm control at 6 and 12 months was similar for oral prednisolone and intramuscular ACTH.

## Platform Session: Epilepsy Surgery 1 Sunday, 6th September 2015

0011

### HIGH FREQUENCY OSCILLATIONS IN THE INTRA-OPERATIVE CORTICOGRAM BEFORE AND AFTER SURGERY: BETTER PREDICTION OF OUTCOME

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**Purpose:** The aim of intra-operative electrocorticography (ECoG) is delineation of epileptogenic tissue for complete resection. This tailoring currently relies on interpretation of interictal spikes. High frequency oscillations (HFOs, ripples 80–250 Hz, especially fast ripples (FRs, 250–500 Hz), are considered a better biomarker for epileptogenic tissue than

spikes. We studied the predictive value of HFOs versus spikes in combined pre- and post-resection ECoG for surgical outcome.

**Method:** We studied pre- and post-resection ECoG recorded at 2048 Hz in patients with refractory focal epilepsy. We marked FRs, ripples and spikes in 1 minute of each recording. We determined presence (+) or absence (-) of these events pre- and post- resection and defined four patient groups: pre+post- (+/-), pre+post+ (+/+), pre-post+ (-/+), and pre-post- (-/-). We compared residual post-resection events to outcome, given the presence or absence of pre-events (Fisher exact). Outcome was categorized into seizure freedom (Engel 1A) vs. seizure recurrence (Engel 1B-4).

**Results:** We included 54 patients (median age 15.5y, 33 TLE) with 25 months median follow-up. Twenty-four patients had recurrent seizures. The number of patients with FRs[+/-,+/-,-/-] were [28,10,2,14], with ripples [3,51,0,0] and with spikes [12,34,4,4]. Residual FRs, given the presence of pre-resection FRs(+/-,+/-) were significantly associated with outcome ( $p = 0.02$ ): eighteen out of twenty-eight patients with FRs before but not after resection were seizure-free and eight out of ten patients with FRs before and after resection had seizure recurrence. Presence or absence of residual FRs had no predictive value in the absence of pre-resection FRs(-/-,-/-) ( $p = 1.0$ ). There was no association with outcome for ripples ( $p_{(+/-,+/-)}=0.25$ ) and spikes ( $p_{(+/-,+/-)}=0.74$ ,  $p_{(-/-,-/-)}=1.0$ ).

**Conclusion:** The presence or absence of FRs in post-ECoG, given FRs in pre-ECoG is a prognostic marker for surgical outcome. The use of FRs for tailoring with repeated ECoG recordings might influence the success rate of epilepsy surgery in individual cases.

0012

### LONG TERM OUTCOME OF PATIENTS WITH OCCURRENCE OF SEIZURES IN FIRST YEAR AFTER EPILEPSY SURGERY

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**Purpose:** The aim of the study was to evaluate the long term outcome of patients with persisting seizures in first year after epilepsy surgery. The secondary objectives were to analyse the conditions with impact on this outcome.

**Method:** We retrospectively reviewed all patients who were surgically treated between January 1995 and January 2010 at the Epilepsy Center Brno. 96 patients (33.8% of all patients) with persisting seizures in first year after surgery and minimal 5 years outcome were included in this analysis. Outcome was assessed yearly by ILAE classification for first 5 years and variable last follow-up visit.

**Results:** At 5 year follow-up visit 27 out of 96 patients (28.1%) were classified as ILAE class I, 16 (16.7%) as class 2, 8 (8.3%) as class 3, 23 (24.0%) as class 4, 19 (19.8%) as class 5 and 3 (3.1%) as class 6. At the last follow-up visit (average of  $10.0 \pm 3.73$  years after surgery) were seizure free 35 (36.5%) patients. This finding is explicable by statistically significant difference between average time of onset add on AED therapy in patient class 2 (median 5.5) and other groups (medians 1.0–2.4 years). Outcome was dependent on localisation of epilepsy (at the last follow up visit: 50.0% seizure free patients with other temporal, 33.3% with mesial TLE associated with hippocampal sclerosis and 26.5% with extratemporo-

ral epilepsy) and initial outcome in first year (60.9% seizure free in initially class 3 patients and 25% in group initially class 5).

**Conclusion:** More than quarter of patients with seizures after surgery have a chance to be seizure free and AED strategy after resective surgery may be a potentially modifiable prognostic indicator influencing seizure outcome in patients with intractable epilepsy.

0013

### STEREOTACTIC ENCEPHALOGRAPHY (SEEG) IMPLANTATION OF THE INSULA; TECHNIQUE AND SAFETY IN PATIENTS WITH MEDICALLY INTRACTABLE EPILEPSY

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**Purpose:** We review our experience with SEEG recording in patients with medically intractable epilepsy and suspected insular involvement in the initiation and organization of the epileptic activity.

**Method:** 170 consecutive patients who underwent SEEG implantation between June 2009 and July 2012 were analyzed. We identified patients with suspected insular involvement based on seizure semiology, imaging (MRI, PET and SPECT) or scalp EEG recording. Patients with at least one insular electrode were included.

**Results:** A total of 1374 electrodes were implanted in 90 patients with suspected insular involvement (9–17 electrode per patient). 187 electrodes were implanted in the insula (1–4 electrodes per patient). 23 patients (25.6% of patients with insular implantation) were confirmed by SEEG to have insular onset or early involvement of insula in epileptogenesis. The most common trajectory of implantation was orthogonal to the insula. None of the patients experienced any medical or surgical complications related to the insular implantation.

**Conclusion:** Insular epilepsy is a rare entity. Stereotactic implantation of depth electrodes in the insula is a safe technique for investigating suspected insular involvement in cases of intractable epilepsy.

0014

### A COMPATIBILITY STUDY OF MRI AND FDG-PET FINDINGS WITH HISTOPATHOLOGICAL RESULTS IN PATIENTS WITH FOCAL CORTICAL DYSPLASIA

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**Purpose:** Focal cortical dysplasia (FCD) is an abnormality of cortical development that occurs during neuronal migration and often leads to medically refractory seizures. The aim of this study was to examine the compatibility of MRI, and PET findings in patients with epilepsy underwent surgery for refractory seizures and diagnosed to have FCD after pathological examination.

**Method:** Cranial MRI, FDG-PET and histopathological findings of patients who underwent surgery were included in the study. All data were reviewed retrospectively and analysed according to the different histopathological subgroups of FCD.

**Results:** There were 71 patients (38 females, 33 males); mean age at the seizure onset was 8.5 years (1 months- 30 years), at surgery was 21.6 years (4 months-46 years) and mean duration of disease was

21.8 years (3 months-38 years). According to the ILAE histopathological classification, 21.2% (n = 20) patients were classified as type 1a; 19.7% (n = 14) as type 1b; 33.8% (n = 24) as type 2a and 18.3% (n = 13) as type 2b. Localization of the lesions was as follows: temporal 35.2% (n = 25), frontal 46.4% (n = 33), parietal 16.9% (n = 12) and occipital 1.4% (n = 1). FCD was visible in MRI of 76.05% (n = 54) of patients, 29.6% (n = 16) of them had FCD type 1a; 14.8% (n = 8) type 1b; 33.3% (n = 18) type 2a and 22.2% type 2b. In 77.4% (n = 55) patients there was FDG-PET hypometabolism where 24.4% (n = 14) of them had temporal and FCD type 1a. In 59.1% (n = 42) patients both MRI and PET was positive and 30.9% of them had type 1a and type 2a. In 14.08% (n = 10) of them PET positive MR negative and 40% (n = 4) of them type 2a. The number of PET negative MRI positive was 11.2% (n = 8).

**Conclusion:** EEG, MRI and 18F-PET have different importance and should be evaluated in parallel before surgery.

0015

### TAILORED FRONTAL LOBECTOMY AFTER POSTERIOR QUADRANTECTOMY VERSUS FUNCTIONAL HEMISPHEROTOMY FOR HEMISPHERIC PEDIATRIC EPILEPSY PATIENTS

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**Purpose:** To study the outcome of Tailored Frontal lobectomy after posterior quadrantectomy for hemispheric pediatric epilepsy patients, compare to functional hemispherotomy.

**Methods:** A retrospective analysis of the Severance children's hospital's epilepsy surgery database was done in all children who underwent a Functional hemispherotomy (FH) and Tailored frontal lobectomy after posterior quadrantectomy (FLPQ) from February 2006 to December 2012. All patients underwent a delicate pre surgical evaluation. Seizure outcome was used by the Engel's classification. And complication related to surgery were compared with each group. FLPQ group was underwent second staged operations. 1<sup>st</sup> surgery was performed posterior quadrantectomy (behind motor cortex and temporo-occipital lobe) and subdural grid insertion on the frontal area. After surgery, patients underwent intracranial EEG monitoring using subdural grid for a week. Based on that result, We decided the Frontal resection margin. 2nd stage surgery was Frontal lobectomy along the determined resection margin.

**Results:** There was 39 patients (50 operation cases including revision of hemispherotomy) in FH group. Epilepsy etiology was due to Lennox-Gastaut syndrome, Rasmussen's encephalitis (RE), Infantile hemiplegia seizure syndrome (IHSS), Hemimegalencephaly (HM), Sturge-Weber syndrome (SWS) and due to post-encephalitis or post-traumatic sequelae (PES or PTS). Seizure control rate of functional hemispherotomy was 85.7% (42/49 cases, Engel classification I, II). 7 patients were inserted shunt after hemispherotomy and 7 patients were in need re-operation due to post-operative adhesion, incomplete disconnection. Another 5 patients were underwent 2nd staged Tailored Frontal lobectomy after Posterior quadrantectomy. 100% seizure control rate was seen in this group. (Engel classification I, II). Just 1 case had post-operative complication, hemiparesis. FLPQ group did not need to sacrifice the unilateral motor function.

**Conclusion:** Tailored Frontal lobectomy after posterior quadrantectomy was shown excellent seizure outcome. This new procedure could be treat the hemispheric epilepsy patient without sacrifice of motor function.

## Platform Session: Paediatric Epileptology 1 Sunday, 6th September 2015

0016

### LONG TERM OUTLOOK IN CHILDHOOD ABSCENSE EPILEPSY (CAE) AND IN JUVENILE ABSCENSE EPILEPSY (JAE)

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**Purpose:** To evaluate the clinical and EEG characteristics in CAE and JAE as predictors of outcome in a long term cohort.

**Method:** From our pool of approximately 7000 patients (from 1973 to 2013) we included, according to strict diagnostic criteria, the CAE and JAE patients, with at least 1 year of follow-up. We studied the clinical history, the neurophysiologic studies performed (EEG and VEEG), and neuroimaging (CT and/or MRI). The main variables analyzed were sex, age, family history of epilepsy, personal history of febrile seizures, seizure types, EEG parameters and seizure outcome. Statistical procedure was univariate analysis. Qualitative variables were studied by Chi-square, and the quantitative variables by ANOVA tests and t-Student analysis.

**Results:** We identified 168 CAE patients (43.5% male, 56.6% female) and 50 JAE patients (54% male, 46% female), with a mean years of follow-up of 29.4 and 25.4, respectively. Mean age of onset for CAE and JAE was 6.5 and 14, respectively. Positive family history of epilepsy (1st degree relative) in CAE group was 20.2%, and in JAE 20%. Previous history of febrile seizures was present in 3.6% of CAE group, and in 12% of JAE group. Seizure rate of more than one per day was 86.3% in CAE and 72% in JAE. Total seizure remission rate was 82.2% for CAE and 8% for JAE. Epileptogenic anomalies in EEG recordings were found in 88.1% of CAE, and in 80% of JAE. Delta posterior rhythm was only found in CAE patients.

**Conclusion:** Some authors consider CAE and JAE entities within the same continuum. From our patient population we saw the following differences which were statistically significant: seizure rate is higher in CAE, generalized tonic-clonic seizures are more frequent in JAE, seizure remission is higher in CAE. We thus conclude they are two different entities with a very different prognosis.

0017

### SEIZURES AND PAROXYSMAL NON-EPILEPTIC EVENTS IN CHILDREN WITH ANTI-NMDAR-ENCEPHALITIS: A VIDEO-EEG STUDY

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**Purpose:** Anti-N-Methyl-D-aspartate-receptor (NMDAR) encephalitis is a potentially treatable disease characterized by the abrupt onset of a constellation of symptoms resulting from diffuse brain dysfunction. In children, seizures and other paroxysmal events are frequently reported to be the presenting or prominent symptoms.

We report our experience with 13 pediatric patients, focusing on the electroclinical semiology of seizures, the co-occurrence of epilepsy and

movement disorders, and the differential diagnosis between seizures and paroxysmal non-epileptic events.

**Method:** The series includes 13 patients (7 females and 6 males) affected by anti-NMDAR-encephalitis, observed at our Department between 2007 and 2014. All patients underwent clinical, and laboratory assessment, including serial video-EEG-polygraphic recordings.

**Results:** The median age at disease onset was 10 years (3–17 years). The median time from disease onset and the first observation at our Department was 3 months (8 days–4 years). Median follow-up was 25 months (3–112 months). Seizures have been reported among the presenting symptoms in 10 patients. In most cases, seizures recurred at high frequency in the early stages, than frequency and severity decreased. Mixed seizure types have been recorded in 6 patients, particularly focal motor and dyscognitive. EEG is abnormal in almost all patients showing focal and/or generalized slowing, and misdiagnosed as non-convulsive status epilepticus in 3 cases. Paroxysmal non-epileptic events were observed in all patients but one. They included a wide variety of movement disorders (orofacial dyskinesia, choreoathetosis, catatonia, dystonia, opisthotonus, ballism, ataxia, and stereotyped and rhythmic movements) often in combination in the same patient. Seizures did not benefit from AEDs but disappeared after immunotherapy.

**Conclusion:** The differential diagnosis between epileptic and non-epileptic paroxysmal events was particularly challenging in patients in whom seizures and movement disorders were closely associated or intermingled. The video-EEG-polygraphy allowed the correct diagnosis of the different symptoms leading to the appropriate treatment.

0019

### BURDEN, CAUSES, RISK FACTORS AND BEHAVIOURAL CONSEQUENCES OF ACUTE SEIZURES IN PRESCHOOL CHILDREN IN RURAL KENYA: A POPULATION-BASED STUDY

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**Purpose:** Acute seizures are common in children admitted to hospitals in Africa, but there are no representative community based studies. Behavioural/emotional problems may occur in children with acute seizures, but the relationship between the two conditions is not understood. Community studies on the burden, risk factors and behavioural consequences of acute seizures are required in Africa for planning interventions.

**Method:** We screened for acute seizures in 7,013 children aged 1–6 years residing in a defined and regularly enumerated area in Kilifi, Kenya. Prevalence of acute seizures was accounted for attrition between first and second phases using multiple imputation. Disability-Adjusted Life Years (DALYs) were computed as Years Lived with Disability since mortality is relatively uncommon in acute seizures. Causes of acute seizures were identified using a WHO algorithm for Integrated Management of Childhood Illnesses. Risk factors for acute seizures were determined with a multivariable logistic regression model. Behaviour was assessed with preschool Child Behaviour Checklist.

**Results:** The adjusted prevalence of acute seizures was 4.0/100 population (95% confidence interval (95%CI), 3.5–4.5). The DALYs lost to acute seizures were 291/100,000 population (95%CI, 258–323). Commonest causes of acute seizures were malaria (51%), respiratory tract infections (35%) and gastroenteritis (7%). Factors associated with acute seizures were family history of seizures (odds ratio (OR)=4.53 (95% confidence interval (95%CI), 2.22–9.27)), family history of febrile seizures (OR=18.79 (95%CI, 9.73–36.31)), previous hospitalisation (OR=4.20 (95%CI, 2.05–8.60)), bed-net use (OR=1.90 (95%CI, 1.03–3.52)) and head injury (OR=0.08 (95% (0.00–0.80)). Behavioural problems were more common in those with acute seizures than those without (26% vs. 11%;  $p < 0.001$ ).

**Conclusion:** The burden of acute seizures in preschool children in Kenya is high. Infections are common causes of acute seizures while family history of seizures is an important risk factor. Acute seizures are associated with behavioural problems, but further studies are required.

0020

### NEURONAL NETWORKS IN EPILEPTIC ENCEPHALOPATHIES WITH CSWC

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**Aim:** Continuous spikes and waves during slow sleep (CSWS) is an age related epileptic encephalopathy characterized by occurrence of diffuse, continuous spike and wave discharges during NREM sleep, seizures and psychomotor impairment. The aim of our study was to investigate the neuronal networks underlying background oscillations of CSWC using the source analysis method Dynamic Imaging of Coherent Sources (DICS) and renormalized partial directed coherence (RPDC).

**Methods:** In order to investigate underlying network and effective connectivity within the detected network, a DICS analyses and renormalized partial directed coherence (RPDC) methods were applied. The baseline sleep EEG recordings and follow up sleep EEG recordings from 12 Patients with CSWS were used for the analyses.

**Results and Conclusions:** The results revealed that independent of aetiology and severity of the disease CSWS EEG pattern is associated with the complex network of coherent sources in medial prefrontal cortex, somatosensory association cortex/posterior cingulate cortex, medial prefrontal cortex, middle temporal gyrus/parahippocampal gyrus/insular cortex, Thalamus and cerebellum. The described network underlying CSWS was found on both group and individual levels and was no longer observed in follow up EEGs of the patients with normalized sleep EEGs, suggesting the specificity of the network for the CSWS pattern. Further on, for the first time, using RPDC analyses we investigated the hierarchy within the described network, which showed that Thalamus, together with mesial temporal and parietal regions may be seen as a central hub of the underlying network. The involvement of this thalamocortical network, which was no longer observed in normalized EEGs, and a further propagation towards the frontal region may interfere with restructuring of cognitive networks in the sensitive phase of development.

## Platform Session: Genetics 1 Sunday, 6th September 2015

0021

### EPILEPSY WITH AUDITORY FEATURES: A HETEROGENEOUS CLINICO-MOLECULAR DISEASE

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**Purpose:** Epilepsy with auditory features (EAF) is a rare focal epilepsy phenotype. In the rare familial epilepsy syndrome of autosomal dominant epilepsy with auditory features (AD-EAF), the majority of affected individuals usually have EAF and 50% of families have mutations in the leucine-rich, glioma-inactivated 1 gene (LGI1). EAF also occurs in isolated individuals, or in one or two members of families with marked phenotypic heterogeneity. Such families may not fulfill criteria for a specific familial epilepsy syndrome nor show a clear-cut inheritance pattern; little is known about their molecular basis. We sought to identify novel genes for EAF.

**Method:** We identified 15 probands with EAF in whom a LGI1 mutation had been excluded. We performed electroclinical phenotyping on all probands and available members affected with EAF or other epilepsy. We used Whole Exome Sequencing (WES) in 20 individuals with EAF (including 5 relatives) to identify single nucleotide, small insertions/deletions and copy number variants.

**Results:** In 4 families, WES revealed pathogenic variants in genes which had not been so far associated to EAF: a CNTNAP2 2-exon deletion, 2 truncating mutations of DEPDC5 and a missense SCN1A change. Additional candidate variants of unclear significance were observed in different genes (CACNA1H, RELN) already associated or not with epilepsy.

**Conclusion:** Occurrence of EAF in families with DEPDC5 and SCN1A mutations widens the phenotypic spectrum of the epilepsy phenotypes related to these genes. CNTNAP2 encodes CASPR2, a member of the VGKC-complex in which LGI1 plays a role. The finding of a CNTNAP2 deletion emphasizes the importance of this complex in EAF and shows biological convergence.

0022

### CLINICAL WHOLE-EXOME SEQUENCING IN FOCAL EPILEPSIES OF SUSPECTED GENETIC ETIOLOGY

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**Purpose:** Mutations in a growing number of genes have been implicated in the pathogenesis of different focal epilepsies, but how this information assists in routine clinical care has not been explored. We investigated the diagnostic yield of whole-exome sequencing (WES) in the management of patients with focal epilepsies in whom genetic factors were suspected to play a role.

**Method:** This was a prospective study of patients routinely assessed as either outpatients or inpatients who met predefined criteria: age >4 weeks; diagnosis of focal epilepsy; no MRI epileptogenic lesion; family history of epilepsy or febrile convulsions in first- or second-degree relatives. Previous genetic testing, severe intellectual disability and benign epilepsy with centro-temporal spikes were exclusion criteria. Patients underwent WES, and identified variants in 59 epilepsy genes were classified by pathogenicity. The "presumptive diagnostic rate" was the proportion of patients with pathogenic or likely/potentially pathogenic variants.

**Results:** Thirty-six patients were recruited (9 children, 27 adults). Twenty-seven patients had a single first- or second-degree relative with epilepsy or febrile convulsions, 6 had two affected relatives, and 3 had three. The presumptive diagnostic rate for the cohort was 22% (8/36 patients). Pathogenic and likely or potentially pathogenic variants were found in different genes, including *SCN1A*, *PCDH19*, *KCNT1*, *KCNQ2*, *GABRG2*, *POLG*, *SPTAN1*, and *PRRT2*. The presumptive diagnostic rate was 22% in both children and adults, 26% in patients with one-first- or second-degree affected relative and 11% in those with multiple affected relatives.

**Conclusion:** WES identifies pathogenic or likely/potentially pathogenic mutations in more than one in five patients with common focal epilepsies of suspected genetic etiology, supporting its use in the routine clinical care.

0024

#### QUANTITATIVE FEATURES OF *SCN1A* ASSOCIATED EPILEPSIES: RELATIONSHIPS AMONG GENOTYPE, FUNCTIONAL ALTERATION, AND PHENOTYPE

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**Purpose:** Mutations in *SCN1A* gene have been identified in epilepsies with widely variable severity, ranging from the extremely severe form of severe myoclonic epilepsy of infancy to the mild form of generalized epilepsy with FS plus, or pure FS. It is suspected whether there is a quantitative correlation between phenotype severity and mutation impairment.

**Method:** We systematically reviewed all *SCN1A* mutations and established a database (<http://www.gzneurosci.com/scn1adatabase/>). Further analysis was performed to explore the quantitative relationships among genotype, functional alteration, and phenotype.

**Results:** In total, 1,248 *SCN1A* mutations were identified in patients with epilepsy. There was a negative correlation between phenotype severity and frequency of missense mutation, which does not result in gross protein malformation. Missense mutations in the pore region were characterized by complete loss of function (LOF), similar to haploinsufficiency. Mutations with severe phenotypes were more frequently located in the pore region, with a quantitative correlation between the frequency of LOF mutants and the phenotype severity. To date, 30 mosaic *SCN1A* mutations have been reported. Mosaic mutation loads of <12.5% (a quarter of a heterozygous mutation) were not associated with any symptom; whereas mutation loads of >25% were associated with FS or mild epilepsy, and mutations with a load of 12.5–25.0% were potentially pathogenic with low penetrance.

**Conclusion:** The data from mosaic mutations showed that a 25% impairment of *SCN1A* function was pathogenic, suggesting that the normal excitability of the brain is highly dependent on the fully functioning of *SCN1A* gene. The phenotype severity of *SCN1A* mutation is quantitatively correlated with mutation impairment.

0025

#### GENE HUNTING IN DRAVET AND MYOCLONIC ATONIC EPILEPSY SYNDROME

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**Purpose:** Dravet syndrome (DS) and Myoclonic Atonic Epilepsy (MAE) are two infantile-childhood onset epilepsy syndromes showing some overlap in clinical features (e.g. myoclonic seizures), and genetic causes (e.g. mutations in *SCN1A*, *CHD2*). We aimed to find additional genes underlying these two related syndromes.

**Method:** Trio whole exome sequencing was performed on 31 DS patients and 40 MAE patients. Forty brain-expressed candidate genes with only a single de novo hit were selected for follow up screening of a larger cohort of 122 DS(-like) and 86 MAE patients, using a gene panel using Molecular Inversion Probe Sequencing (MIPS) technique. Eleven known genes linked to DS and MAE syndrome were added to the panel.

**Results:** A total of 95 novel variants were identified in the whole cohort. At the moment of abstract submission, segregation analysis of 60 novel variants was performed, and 16 variants occurred de novo, 44 variants were inherited. Eleven patients carried a de novo mutation in a known gene: Six DS patients in *SCN1A*, 1 DS patient in *HCN1*, and 2 DS-like patients in *SCN8A* and *PCDH19* respectively. Two MAE patients carried a de novo mutation in *SYNGAP1*. We further identified a second de novo mutation in 5 different candidate genes. Functional validation of these genes is ongoing.

**Conclusion:** Whole exome sequencing followed by targeted gene panel analysis is a powerful technique for novel gene identification, especially when performed in clinically well-defined patient cohorts. Collaborative networks are extremely valuable for the collection of large, well phenotyped cohorts. Ongoing functional studies will provide further evidence for the role of the five candidate genes in myoclonic epilepsies.

### Platform Session: Status Epilepticus Sunday, 6th September 2015

0026

#### CEREBROSPINAL FLUID TOTAL TAU PROTEIN AS A BIOMARKER IN STATUS EPILEPTICUS: A RETROSPECTIVE STUDY

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**Purpose and background:** Predicting status epilepticus (SE) outcomes is difficult and primarily based on clinical and EEG parameters. To date, no reliable biomarkers exist to predict SE outcome. Tau protein is a phosphorylated microtubule-associated protein, principally localized at neuronal and axonal level in central nervous system (CNS). High total tau (t-tau) levels in CSF are related to neuronal and axonal damage. No study has specifically evaluated the prognostic value of CSF t-tau level in SE.

**Methods:** We retrospectively identified 28 patients with SE in an 8-years-long period. Exclusion criteria were acute structural brain damage as causative event of SE. All patients underwent lumbar puncture at SE onset to exclude CNS infection. CSF t-tau level was measured in each

patient and correlations with SE electro-clinical variables, response to treatment, neurological and epilepsy outcomes were analyzed.

**Results:** t-tau level was extremely high (>50.000 pg/ml) in 6 patients, moderately high (between normal values and 50.000 pg/mL) in 7 and normal in 15 patients. A positive correlation between SE duration and t-tau levels was present. Out of 17 cases that resolved with anti-epileptic drugs, none had extremely high t-tau levels. Out of 11 cases that presented refractory or super-refractory SE, 7 had pathological t-tau levels (extremely high in 6 patients). Univariate logistic regressions performed with disability outcome as dependent variable showed that high CSF t-tau levels were significant predictors of disability development or worsening (OR=38.8,  $p = 0.004$ ). 30-day mortality was 3 in 13 cases with elevated t-tau levels.

**Conclusions:** CSF t-tau seems to be a good candidate biomarker for SE severity. In fact CSF t-tau reliably and independently predicted disability outcome after SE.

0027

### EEG STAGE PREDICTS IMPAIRMENT OF SPATIAL MEMORY AND LEARNING IN THE LITHIUM/PILOCARPINE AND THE KAINIC ACID MODELS OF EXPERIMENTAL STATUS EPILEPTICUS IN THE RAT

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**Purpose:** Status epilepticus (SE) is a dynamic state with progressive changes in behavior, response to treatment, extent of neuronal damage, and EEG patterns during prolonged episodes. SE also causes deficits in learning and memory, but no studies have correlated progressive impairment with increasing severity of SE. We tested the hypothesis that the EEG stage during SE, rather than the duration, predicts the extent of subsequent cognitive impairment.

**Method:** Sixty 250–280 gm male Sprague-Dawley rats were implanted with 4 stainless steel epidural electrodes for EEG recording. SE was induced by either LiCl, 3 mmol/kg IP, followed 24 hrs later by pilocarpine, 30 mg/kg, or kainic acid, 15 mg/kg IP. SE was stopped with IP diazepam, 10 mg/kg, plus phenobarbital, 25 mg/kg, at EEG stage I (discrete electrographic seizures), III (continuous ictal activity), or V (periodic epileptiform discharges). Spatial learning and memory were assessed 1 week before and 1 week after SE induction, using a modification of the Morris Water Maze (MWM). Effect of the SE EEG stage on the mean escape time to a submerged platform was compared.

**Results:** Initial MWM performance did not differ among all rats. However, for both models after SE the mean escape time for the first 6 trials on test day one (memory) and for all 24 trials (learning), was significantly worse ( $p < 0.001$ ) in Stage V rats, compared with Stage I and III rats. The mean time to Stage V for KA rats ( $354.1 \pm 10.7$  min) was significantly ( $p < 0.0001$ ) longer than for Li/pilocarpine rats ( $187.9 \pm 17.4$  min.) but the mean escape time at Stage V was not significantly different.

**Conclusion:** Prolonged SE results in a marked progressive impairment of visual-spatial memory and learning. These data provide further evidence that the EEG stage during prolonged SE is a better marker of its severity than is duration alone.

0029

### PREDICT FUNCTIONAL OUTCOME OF STATUS EPILEPTICUS

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**Purpose:** Status epilepticus (SE) is a frequent neurologic emergency with high mortality and morbidity. However, two available clinical scoring system for patients with SE, status epilepticus severity score (STESS) and epidemiology-based mortality score in SE (EMSE), are limited to predict individual in hospital mortality, not to functional outcomes. The aim of this study was to validate the prognostic utility of STESS and EMSE for prediction function for functional outcome in adult patients with SE.

**Method:** This study was performed in epilepsy center of ten academic tertiary medical centers in South Korea. The clinical and electroencephalographic (EEG) data for all adult patients with SE from January 2013 to December 2014 were derived from a prospective SE database, in order to calculate the STESS and EMSE. The primary outcome variable was defined as poor outcome that is score ranged 1–3 of Glasgow Outcome Scale (GOS) at discharge.

**Results:** Of total 73 with SE, excluding those who had anoxic etiology, 37 patients (50.1%) had poor outcome. The receiver operating curve (ROC) for prediction of poor outcome by the EMSE using a combination of etiology, age and EEG had an area under the curve of 0.712 ( $p = 0.0004$ ) with optimal cut-off point  $> 54$  (sensitivity=67.57%, specificity=67.12, NPV= 67.57%, PPV = 66.67%, corrected classified 67.12%) and by those using a combination of etiology, age, comorbidity and EEG had an AUROC of 0.727 ( $p = 0.0001$ ) with cut-off point  $>64$  (sensitivity= 67.57%, specificity=67.12, NPV= 67.57%, PPV = 66.67%, corrected classified 67.12). STESS could not predict poor outcome (AUROC 0.581,  $p = 0.2292$ ).

**Conclusion:** Although EMSE was the clinical scoring system focused on individual mortality, EMSE can explain the individual functional outcome using various combination.

0030

### STATUS EPILEPTICUS, AN EASY SCORE ASSESSMENT TO PREDICT MORTALITY OF SE

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**Purpose:** Status epilepticus (SE) has an important clinical impact, with a high short-term mortality. We aimed to find an easy score assessment to predict outcome in the initial evaluation of SE.

**Methods:** We reviewed consecutive patients with SE >16 years old at our Center between March 2011 and March 2014. We recorded demographic and clinical data. We estimated the modified Rankin scale (mRS) at admission. Patients with post-anoxic SE were excluded. We performed ROC curves to determine the best cut-off points of numeric variables to predict mortality. A logistic regression model was performed to assess the independent prognostic factors and estimate the scores of a new scale proposal.

**Results:** We included 136 patients. Mean age:  $62.01 \pm 17.62$  [19–95]. 54.4% male. Level of consciousness, (OR=7.989 IC [2.934–21.745],  $p < 0.001$ ), the modified-Rankin scale (OR=3.344 [1.037–10.790],  $p = 0.043$ ) and age  $>70$  years (OR=3.035 [1.116–8.313],  $p = 0.030$ ) were the only independent risk factors for mortality.

The coefficients of the logistic regression model and results of ROC curves allowed us to classify the variables as follows: Level of consciousness (0 = Alert/Confusion; 1 = Stuporous/Comatose), mRS (0 = mRS:0; 1 = mRS:1-3; 2 = mRS:>3) and Age (0 =  $\leq 70$ ; 1 =  $>70$ ). The results varied between 0 and 5 points for the score.

The capability of this score to predict mortality was 82.8% (IC: 74.7%–90.9%). By means of ROC curves, we divided the risk of short-term mortality as follows: Low (3.4%) scores 0–1, Medium (25%) scores 2–3 and High (66.7%) scores 4–5. Scores  $\geq 4$  established an overall accuracy of 83.3% to predict mortality.

**Conclusion:** We proposed a novel and easy score to assess the risk of mortality at admission in patients with SE, which includes a combined evaluation of the level of consciousness, age (70 years) and mRS.

## Platform Session: Clinical Trials 1 Monday, 7th September 2015

0031

### MULTICENTER, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED TRIAL OF SUSTAINED-RELEASE VINPOCETINE AS ADJUNCTIVE TREATMENT OF FOCAL-ONSET SEIZURES

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**Purpose:** Evaluating the efficacy and tolerability of vinpocetine as adjunctive therapy in children and adults with focal onset epilepsy.

**Method:** Patients between 6 and 65 years old with a diagnosis of focal epilepsy with at least 4 confirmed seizures per month, refractory to baseline antiepileptic therapy (1-3 AED) were invited. Patients were randomized assigned to receive vinpocetine or placebo in a clinical, double-blind and parallel-group trial (4-weeks baseline phase, 4-weeks titration phase and a 8 weeks follow-up maintenance phase).

**Results:** 87 patients (56 adults and 31 children) were recruited (41 patients were assigned to vinpocetine and 46 to placebo). The final dose of vinpocetine was 2 mg/kg/day. Vinpocetine was more effective than placebo in the reduction of frequency of seizures (50% with vinpocetine vs. 0% with placebo,  $p < 0.0001$ ). 69% of patients with vinpocetine experienced a reduction  $> 50\%$  compared to 13% in the placebo group. The adverse events associated with the use of vinpocetine were headache (7.9%) and diplopia (5.2%).

**Conclusion:** Vinpocetine as adjunctive therapy is more effective in reducing the frequency of seizures compare to placebo, besides being well tolerated. Vinpocetine shows a wide safety profile, all adverse events were known, of short duration and without sequelae.

0032

### MODIFIED ATKINS DIET IN ADULT PATIENTS WITH REFRACTORY EPILEPSY: A CONTROLLED RANDOMIZED CLINICAL TRIAL

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**Introduction:** The usefulness of the modified Atkins Diet (mAD) in refractory epilepsy in adults has been rarely investigated. We aimed to evaluate the efficacy of mAD in adult with refractory epilepsy.

**Method:** In a controlled randomized clinical trial, we enrolled 66 refractory adult epileptic cases from February 2010 to December 2012. The Patients were divided into two groups randomly, case groups (22 patients) used antiepileptic drugs and mAD and control group (32 patients) only use antiepileptic drugs. The primary outcome was at least 50% decrease in seizure frequency after 2 months of therapy.

**Results:** Our data showed no significant difference between groups regarding baseline characteristic. The differences of mean seizure attacks after 2 months ( $p \leq 0.001$ ) and fifty percent reduction in seizure frequency between the two groups showed significant differences [ $p \leq 0.001$ , Odd ratio= 2.19, 95% confidence interval (1.39, 3.47)]. There was a positive correlation between the mean urinary Ketone level and  $>50\%$  seizure reduction in case group ( $p = 0.04$ ). In repeated measures analysis and based on the per-protocol principle, there was a significant difference between Modified Atkins Diet and control groups regarding mean number of seizure attacks ( $F = 14.6$ ,  $p < 0.001$ ). Such differences were also significant in the intention- to- treat analysis ( $F = 6.14$ ,  $p = 0.01$ , Fig 2).

**Conclusion:** The mAD may be effective as a co-therapy treatment for adults with refractory epilepsy and can decrease 3.66 times seizure frequency in comparison with control groups. Trials with more tolerable dietary regime, with larger sample size and longer duration, should be performed in future.

0033

### HOW MUCH VARIABILITY IS THERE IN EPILEPSY DIAGNOSES? THE EPINET VALIDATION STUDY

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**Purpose:** 1) To determine variation in epilepsy diagnosis when neurologists are presented with identical case scenarios;  
2) To accredit investigators for the EpiNet-First trials.

**Method:** Epileptologists, neurologists and pediatricians with an interest in epilepsy were invited to assess 32 scenarios describing patients (6 children, 26 adults) with various events (21 epilepsy, 11 other paroxysmal events). Cases were presented on-line via the EpiNet database. For each patient, participants had to:

- determine how likely it was the patient had epilepsy;
- classify the patients' seizures (ILAE 2010 classification);
- determine the aetiology (structural/metabolic; genetic; or unknown), and epilepsy syndrome when appropriate.

In 24 cases, information was presented in 2 steps; clinical information was presented in Step 1. After completion of this step, neuroimaging and EEG studies were provided (Step 2).

18 cases were used to accredit investigators for EpiNet studies. Acceptable responses were determined by consensus amongst the EpiNet steering committee. 12 cases were initially assessed. If all responses were not satisfactory, a further 6 cases were checked.

**Results:** 201 participants from 35 countries completed the 32 cases. Full data was available for 189 participants, of whom 105 were accredited for the trials. Kappa values for step 1 for all 32 cases were: diagnosis of epilepsy; accredited,  $k = 0.70$  (entire group,  $k = 0.60$ ); seizure type(s),  $k = 0.47$  (0.39); etiology,  $k = 0.45$  (0.38).

Kappa values increased at Step 2 for all participants: diagnosis of epilepsy; accredited  $k = 0.77$  (entire group,  $k = 0.68$ ); seizure type,  $k = 0.59$  (0.48); and etiology,  $k = 0.51$  (0.44).

**Conclusion:** Agreement for the diagnosis of epilepsy between neurologists assessing identical scenarios was moderate when based on clinical findings alone. Agreement for seizure type and etiology was less good, but improved when investigations were included. Agreement was higher in all categories for investigators accredited for the EpiNet-First trials.

### 0034

#### FACTORS DETERMINING PLACEBO RESPONSE IN DRUG-RESISTANT FOCAL EPILEPSY

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**Purpose:** To determine factors associated with response in patients randomized to placebo in adjunctive-therapy randomized clinical trials of AEDs of patients with focal epilepsy.

**Methods:** Data on adult patients treated in the placebo arm in 16 partial-onset seizure randomized controlled trials conducted between 1990 and 2010 by 6 pharmaceutical companies were used in this analysis. All trials included a baseline period of at least 4 weeks, and titration and/or maintenance periods up to 20 weeks. Responder rate was calculated as the proportion of patients with 50% or greater reduction in seizure frequency during the treatment period compared to their baseline frequency. Patients' and protocol specific characteristics were collected for all trials. Multivariate logistic models were used to determine factors independently associated with the response to placebo with generalized estimating equations to account for clustering by study.

**Results:** The sample comprises 1719 adults aged 16–82 y.o. (mean age=37.7), of which 881 (51%) are women. Responder rates vary from 5.6% to 38.5% across the 16 trials. In univariate analysis Asia and East Europe showed higher responder rates (27.3% and 27.4%, respectively) than West Europe (13.4%) and the US (15.5%). In multivariate models controlling for age, gender and race, Asia was associated with increased

odds of response ( $OR=1.8$ ;  $p = 0.008$ ) while West-Europe was associated with decreased odds of response ( $OR=0.54$ ;  $p = 0.04$ ) compared to the US. The odds of response also decreased with increased number of concomitant AEDs ( $OR=1.11$ ;  $p = 0.02$ ) and the occurrence of AEs ( $OR=0.71$ ;  $p = 0.04$ ).

**Conclusions:** Preliminary analysis of a large dataset of individuals randomized to the placebo arm of adjunctive-therapy AED trials suggest that response to placebo are influenced by both patients' and protocol related factors. Further analyses are needed to confirm these results.

### 0035

#### SECONDARY SCREENING OF PATIENTS IN RANDOMIZED PERAMPANEL PGTC STUDY EXCLUDES 29.9% OF ELIGIBLE PATIENTS DUE TO INACCURATE CLASSIFICATION

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**Purpose:** Patients enrolled in clinical trials should be accurately classified to meet inclusion criteria. We assessed how many patients screened for enrollment in a randomized placebo-controlled study of drug-resistant primary generalized tonic-clonic (PGTC) seizures in idiopathic generalized epilepsy (IGE), using the noncompetitive AMPA receptor antagonist perampanel, were rejected due to inaccurate classification when reviewed independently by The Epilepsy Study Consortium (TESC).

**Method:** Patients were reviewed by TESC to ensure a clear IGE diagnosis. Sites submitted all information used to determine each diagnosis. Patients were excluded if submitted information could not confirm an IGE diagnosis (e.g. only GTC seizures and a normal EEG with no family history or supporting seizure types) or showed an incorrect IGE diagnosis (e.g. slow spike-wave, developmental delay, age of onset  $\leq 1$  year, or symptomatic cause). Patients considered ineligible were sent to a second, independent TESC reviewer. If both reviewers agreed, the patient was screen failed. If they disagreed, a third reviewer made the final decision.

**Results:** Of 307 patients screened, 143 patients failed (not meeting inclusion criteria;  $n = 117$ ). Of these, 70/117 patients failed only after TESC review (IGE misdiagnosis [ $n = 35$ ]; insufficient information to confirm diagnosis [ $n = 35$ ]). A third reviewer made the final decision twice. Ultimately 164 patients received perampanel or placebo (1:1) highlighting that TESC review eliminated 70/234 (29.9%) patients initially considered eligible. The trial demonstrated a median percent change in PGTC seizure frequency per 28 days during Titration/Maintenance Periods versus Baseline of -76.5% perampanel versus -38.4% placebo;  $p < 0.0001$ .

**Conclusion:** TESC review eliminated 29.9% inappropriate patients from inclusion. This was the first PGTC study that used external review to ensure appropriate classification of trial participants. Without such a review, the interpretability of results may be compromised.

## Platform Session: Epidemiology Monday, 7th September 2015

### 0036

#### SPECIFIC PATTERNS OF MONOAMINERGIC DYSFUNCTION AS BIOMARKERS OF EPILEPSY-ASSOCIATED DEPRESSION AND ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD)

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**Purpose:** Depression and ADHD are common comorbidities of epilepsy. Furthermore, high degree of comorbidity exists between depression and ADHD. Disentangling mechanisms of depression and ADHD is confounded by their overlapping monoamine transmitter substrates. We examined patterns of monoaminergic dysfunction and their correlation with depressive and ADHD behavioral impairments in animals with chronic epilepsy.

**Method:** Studies were done in male Wistar rats 4–8 weeks after the pilocarpine status epilepticus and the establishment of spontaneous recurrent seizures. Serotonergic tone in the raphe nucleus-prefrontal cortex pathway and noradrenergic tone in the locus coeruleus-prefrontal cortex pathway were measured by fast scan cyclic voltammetry. The function of 5-HT1A autoreceptors in raphe nuclei, and of  $\alpha$ 2A adreno-autoreceptors in locus coeruleus was examined by autoradiography. Profiles of serotonergic and noradrenergic transmission were correlated with behavioral perturbations reflecting depressive disorder in the forced swimming test, and those reflecting ADHD in the lateralized reaction time task.

**Results:** Around 2/3 of epileptic rats presented with depressive, and around 1/3- with ADHD behavioral impairments. Five-fifteen percent of animals exhibited both depressive and ADHD abnormalities. All depressed animals showed diminished serotonergic tone and the up-regulation of 5-HT1A autoreceptors. None of depressed-only animals had noradrenergic dysfunction. All ADHD rats showed diminished noradrenergic tone and the up-regulation of  $\alpha$ 2A-adrenoreceptors. None ADHD-only animals had perturbations in serotonergic transmission. Epileptic animals with depression and ADHD had both serotonergic and noradrenergic deficits. Within each comorbidity, the extent of respective monoaminergic perturbations strongly correlated with degrees of depressive and ADHD-like behaviors.

**Conclusion:** Epilepsy-associated depression and ADHD each has specific monoaminergic correlate evident as the respectively diminished transmitter tone and the up-regulation of a respective receptor. Such specific profiles of transmitter dysfunction should help with diagnosis and with devising effective therapies of these two comorbidities.

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### 0037

#### DIFFERENCE BETWEEN ELDERLY EPILEPTIC PATIENTS AND ELDERLY EPILEPSY

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**Purpose:** Epilepsy is more often in infants and old people. Nowadays, the population is getting older and the epilepsy prevalence is increasing. The type of epilepsy changes with the age.

**Method:** We present a prospective observational study to compare epileptic patients diagnosed before 65 and after 65, that now are  $\geq 65$  years old. We study the epilepsy features, comorbidity, dependency status and the antiepileptic drugs that they used (time, dosage and side effects).

**Results:** The sample was 123 patients, 62 who were diagnosed with  $\geq 65$  years old (group A), and 61 with  $< 65$  (group B). Both groups have similar percentage of gender, male 62.9% (N = 39) in A and 60.7% (N = 37) in B. The average age was  $77.29 \pm 6.73$  in group A and  $69.97 \pm 5.6$  in B. The most common type of seizure was partial complex, in both groups, in 53.2% (N = 33) in A and 41% (N = 25) in B. 16.1% (N = 10) had Status Epilepticus in group A and only 1.6% (N = 1) in B. The most frequent result in the EEG was normal in group A

(40.3%, N = 25) and focal in B(26.2%, N = 16). The etiology most common was vascular in group A(74.2%, N = 46) and cryptogenic in B (44.3%, N = 27). The Stroke incidence was 51.6% (N = 32) in A and 19.7% (N = 12) in B. The doses in almost all de the antiepileptic drugs that have been registred were lower in the group A. If we compare both groups, we saw stadistic significance in the hypertension (p = 0.00), diabetes mellitus (p = 0.00), stroke incidence (p = 0.00), ischaemic cardiopathy (p = 0.003), status epilepticus (p = 0.00), dependence grade (p = 0.00).

**Conclusion:** The epilepsy that starts after 65 years old, is related with cardiovascular risk factors that we should prevent. This epilepsy responds better with lower doses of treatment, however in some cases starts with a Status Epilepticus. Although both kinds are the same disease, the risk factors and the management are different.

### 0038

#### SUDEP IS NOT ALWAYS SUDEP! REPORT OF 70 DEATHS THROUGH A 20 YEARS PERIOD FROM A TERTIARY EPILEPSY CENTRE IN NORWAY

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**Purpose:** Patients with refractory epilepsy are referred to our national epilepsy centre from all over Norway. From the centre, SUDEP cases in the period 1967–1996 has previously been examined and published.

The aim of this study was to examine “new” SUDEP cases reported at our center in the period 1996–2015. Here we focus on the correctness of the SUDEP diagnosis and give some background characteristics from the cohort.

**Method:** We have examined the medical record from patients treated at the centre who were reported of having suffered SUDEP in the period 1996–2014. The study was approved by the local medical ethical committee.

**Results:** 70 SUDEP cases were reported. At closer examination, only 57 (81.4%) fulfilled the SUDEP criteria. Other causes of death were: suicides: 3, cancer related: 2, status epilepticus: 2, infection: 1, respiratory failure (Rett syndrome): 1, AVM (bleeding): 1, neurodegenerative disorder: 1, ceroid lipofucinose: 1, unknown cause, but not epilepsy related: 1. In 4 cases the death might have been seizure-related (accidents and drowning).

35 (63%) were male, mean age at death was 28.8 years. 9 (13%) had undergone epilepsy surgery. Additional 15 (26%) had gone through epilepsy surgery work-up. 12 (21%) had implanted Vagus Nerve Stimulation (VNS).

11 (16%) had seizure remission for more than 1 year prior to SUDEP. Two of these patients had reported seizure freedom in 10 and 15 years prior to SUDEP, respectively. Only 17 (24%) had co-morbid conditions.

In those not seizure free, the frequency of generalized tonic-clonic seizures (GTCS) showed large variations from daily seizures to 3-4/year.

**Conclusion:** Not all those reported to have suffered SUDEP turn out to have had SUDEP after a more thorough investigation. In order to identify predictors for SUDEP, we are preparing a case-control study.

### 0039

#### LARGE-SCALE, OBSERVATIONAL STUDY OF ALL-CAUSE MORTALITY AND SUDEP IN PATIENTS WITH DRUG RESISTANT EPILEPSY TREATED WITH VNS THERAPY

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**Purpose:** Annegers et al. (2000) reported that the rate of sudden unexpected death in epilepsy (SUDEP) in patients undergoing VNS Therapy<sup>®</sup> decreased from 5.5 per 1000 patient-years (PY) over the first 2 years to 1.7 per 1000 PY thereafter. Since that report, over 80,000 patients with drug-resistant epilepsy have been implanted worldwide, providing the opportunity to revisit the impact of VNS on SUDEP.

**Methods:** This retrospective study included all US patients with drug-resistant epilepsy who were implanted with VNS from 1988–2012 with known social security numbers. Exposure to VNS was calculated from date of implant until death, device explant, known date at which the device was disabled or the last follow-up date of December 31, 2012. Occurrence, date and cause of death were obtained from the Social Security Death Index Master File and the National Death Index, which provides ICD-9 or ICD-10 codes. A group of cause-of-death codes was selected as reflecting potential SUDEP and a sample categorized according to Annegers' SUDEP classification.

**Results:** A total of 40,443 patients (mean age at implant: 30.8 years) with a median follow-up of 7.6 years, representing 277,661 PY, were included. A total of 3,689 deaths were recorded, translating into a 13.3/1000 PY all-cause mortality rate (SMR=4.58). 953(26%) corresponded to cause-of-death codes that potentially include SUDEP, with a decreasing trend as duration of VNS increased. A preliminary review of a random sample of 200 of these cases adjudicated 109 (54.5%) as possible/probable/definite SUDEP (1.9/1000 PY).

**Conclusion:** This large mortality study of patients with VNS therapy offers an 80 fold increase in available PY of follow-up as compared to published data. Preliminary findings show crude all-cause mortality rates consistent with those observed in drug-resistant epilepsy. Ongoing analyses will provide specific information regarding SUDEP risk and the impact of VNS therapy.

0040

### PSYCHIATRIC CO MORBIDITY IN CHILDREN AND YOUTH TREATED AT THE NATIONAL CENTRE FOR EPILEPSY NORWAY

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**Purpose:** We have previously found a high frequency of psychiatric symptoms (31%) among children and youth with epilepsy (CYWE) in a population based questionnaire study without confirmed psychiatric diagnoses. The aims of this study were to assess the frequency of psychi-

atric symptoms and further classify psychiatric disorders among CYWE at a tertiary epilepsy centre.

**Method:** A prospective study of consecutive children and youth aged 10–19 years, referred to the National Centre for Epilepsy from January 2012 to June 2014. All participants and parents filled in the Strengths and Difficulties Questionnaire (SDQ). Those who scored in the borderline or pathological range were examined by a child psychiatrist using the Kiddie-SADS-PL.

**Results:** One hundred and nineteen children and youth with epilepsy were included. Mean age was 14. yrs (10–19) and there was a slight overweight of girls, 55%. Psychiatric symptoms were reported in sixty-five participants (55%). They underwent child psychiatric interview where a diagnosis was confirmed in 53 participants (82%). The most common diagnoses found were ADHD and anxiety. More boys than girls received a psychiatric diagnoses (58.5% vs. 41.5%,  $p = 0.03$ ). There was no difference in psychopathology between focal and generalized epilepsy.

**Conclusion:** We found psychiatric symptoms in 55% of children and youth referred to the National Centre for Epilepsy. Eighty two % of these had a clinically confirmed psychiatric diagnosis. Compared to the population based material the frequency of psychiatric symptoms is even higher in a tertiary care setting. The aetiology is complex, probably due to a combination of biological and psychosocial factors.

## Platform Session: Epilepsy Surgery 2 Monday, 7th September 2015

0041

### WHAT DETERMINES LONG-TERM EPILEPSY OUTCOME AFTER MULTILOBAR RESECTION?

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**Purpose:** There is no doubt that surgical treatment for medically intractable epilepsy can be a best option in seizure control and improvement of quality of life. However, scarce literatures demonstrated the long-term results following multilobar epileptic surgery. We aim to evaluate the surgical outcome of multilobar epilepsy and to explore prognostic factors of good outcome.

**Method:** We retrospectively reviewed the records of patients who had underwent multilobar surgery between 1995 and 2010 (more than 12 months of follow-up). Multilobar epilepsy syndrome was defined as having independent epileptic foci in more than two lobes. Engel class Ia and Ib were considered as seizure free.

**Results:** 73 patients were enrolled (mean follow-up 10.2 years, range 2.7–18.8). Mean age of seizure onset was 12.4 years and at surgery was 25.6 years. Fifteen (20.5%) had underwent surgery on more than three-lobes and the others had a surgery on two-lobes; 22 (30.1%) in fronto-temporal, 17 (23.3%) in temporo-occipital, 12 (16.4%) in parieto-temporal, and 7 (9.6%) in fronto-parietal resection. At postsurgical one-year, 55.4% of patients were seizure free (95% confidence interval, CI, 43–66), 43.2% at 5-years (CI 31–54), and 44.6% remained free at the last follow-up (CI 19–41). Reoperation was performed in one patient who was seizure free after second surgery. Significant risk factors in seizure recurrence were preoperative, contralateral interictal spikes ( $p = 0.03$ ) and the abnormal MRI findings contralateral to resection ( $p = 0.01$ ) in univariate analysis. The risk of abnormal MRI lesion was high as 3.0 (CI 1.10–8.17). Abnormal MRI findings significantly affected on the seizure outcome in multivariate analysis ( $p = 0.03$ ).

**Conclusion:** Long-term surgical outcome of multilobar resection was favorable. Nearly half of patients remained seizure free at the last follow-up. Preoperative MRI and PET and postoperative EEG findings are important for surgical prognosis.

0042

### MRI-BASED HIPPOCAMPAL SUBFIELD ANALYSIS ACCURATELY PREDICTS SURGICAL OUTCOME

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**Purpose:** Temporal lobe epilepsy (TLE) is the most common drug-resistant epilepsy in adults. Its hallmark lesion is hippocampal sclerosis, apparent on MRI as atrophy, T2 signal changes, and diffusion alterations. Surgery renders the most patients seizure-free; yet, individualized outcome predictors remain unknown. Subfield-level descriptors promise to provide novel markers of hippocampal pathology, with potential benefits for outcome prediction.

**Method:** We studied 39 drug-resistant TLE patients and 25 age- and sex-matched controls. MRI data were acquired on a 3T Siemens TimTrio, including submillimetric T1- and T2-weighted images, and diffusion-weighted MRI. One rater manually segmented the hippocampal subfields cornu Ammonis (CA) 1-3, CA4-dentate gyrus (DG), and subiculum. We automatically extracted medial sheets of a given subfield, on which we sampled surface-wise T2 intensity, mean diffusivity, and fractional anisotropy, and calculated local columnar volume. Surface-based comparisons assessed anomalies in patients relative to controls and the relationship to post-surgical outcome in operated patients (16 seizure-free out of 21 operated;  $48 \pm 18$  months follow-up). Findings were corrected for multiple comparisons at  $FWE < 0.05$ . A support vector machine with leave-one-out-cross-validation was employed to predict outcome in single patients.

**Results:** Compared to controls, patients showed T2-increases across all subfields bilaterally, with most marked effects in ipsilateral CA1-3 and CA4-DG; the latter subfields also showing increased mean diffusivity and decreased anisotropy. Columnar volume was decreased in ipsilateral CA1-3 and subiculum. Compared to those achieving seizure freedom, non-seizure free patients displayed bilateral mean diffusivity increases and contralateral columnar volume decreases. A classifier combining volume and mean diffusivity changes accurately predicted outcome in 20/21 (96%).

**Conclusion:** Surface-based analysis of morphology, signal and diffusion provides *in vivo* phenotyping of hippocampal subfield pathology in TLE, and accurately predicts post-surgical outcome.

0043

### EPILEPSY AND LOW-GRADE GLIOMAS: A UK SINGLE CENTRE RETROSPECTIVE ANALYSIS

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**Purpose:** Epilepsy is a common presentation of low-grade gliomas (LGG). Gross total resection (GTR) is the strongest predictor of seizure freedom, but with limited evidence regarding efficacy and tolerability of newer antiepileptic drugs (AEDs) in managing LGG epilepsy, we investigated factors affecting seizure control with AEDs and/or surgery to provide evidence-based guidelines for practice.

**Method:** Retrospective analysis of 238 suspected/confirmed LGG cases in a single neurosciences centre. Variables recorded: patient

demographics, tumour features (size/location/histology/molecular markers), seizure characteristics pre-/post- AED and post-surgery (type/duration/frequency), operative intervention (time from diagnosis/proportion resected), and use of adjuvant therapy. Long-term patient outcomes focused on seizure control.

**Results:** 33 patients excluded (found to be high grade within 12 months). 205 analysed: average age at diagnosis 36 (ranging 1–77), 2:3 female:male. 77% initially presented with seizure. LGG location predisposes to epilepsy, most common in frontal (45%) and temporal (33%) lobes, with seizure types most varied in the latter. No seizures occurred with non-cortical LGGs. All DNETs and 83% astrocytomas and oligodendrogliomas presented with seizures. Presence of IDH-1 mutation, 1p19q codeletion and MGMT methylation was increased in seizure patients. Overall post-AED seizure reduction at 12 months was 65% (69% in astrocytomas; 57% oligodendrogliomas; 50% oligoastrocytomas, and 71% in temporal; 65% frontal; 50% parietal lobe tumours). Monotherapeutic AED reduced seizures in 31%, with levetiracetam the most effective. 155/205 (76%) underwent surgery (resective in 53%), ranging from same day to 15 years post-diagnosis. Post-resective seizure reduction was 76%, with 59% seizure-free. This improved to 74% seizure-freedom with GTR.

**Conclusions:** Tumour location, histology, and cytogenetics affect seizure frequency and response to treatment. Significant seizure reduction with AEDs is achieved. Pharmacological conclusions are complicated by polytherapy and biased selection of AEDs. Ongoing analysis will evaluate AED properties and impact on seizure control and tumour progression. GTR remains the strongest predictor of seizure freedom.

0044

### PROLONGED POST-ICTAL CEREBRAL HYPOPERFUSION DETECTED BY ARTERIAL SPIN LABELLING (ASL) MRI - A POSSIBLE REPLACEMENT FOR ICTAL SPECT?

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**Purpose:** Seizures can be followed by transient neurological impairments (e.g., Todd's paresis). Several case reports of post-ictal hypoperfusion exist in literature. More recently, prolonged post-ictal hypoperfusion and hypoxemia (lasting up to 1 hour) has been demonstrated at the seizure focus in rats (Teskey GC, unpublished observations). Thus, our objective was to determine whether post-ictal vascular changes can be demonstrated in humans using Arterial Spin Labelling (ASL) MRI and whether they could assist in localizing the seizure onset zone.

**Method:** 3 Tesla ASL MR images were obtained in a group of 15 patients with refractory focal epilepsy undergoing scalp VEM within 90 minutes of seizure termination. Interictal baseline ASL scans were also obtained to generate cerebral blood flow (CBF) subtraction maps (baseline vs. postictal) to identify areas of postictal hypoperfusion. These results were compared to information obtained from routine investigations (video-EEG, PET, SPECT, MRI).

**Results:** Routine clinical investigations identified seizure foci in the patients as follows: 5 unilateral temporal lobe, 2 independent bitemporal, 3 frontal, 1 central, 2 broad left hemispheric with unclear localization, 2 non-lateralized. Five patients had unremarkable MR scans. ASL scans were obtained 45–83 minutes following seizure termination and focal post-ictal hypoperfusion was seen in 13/15 subjects as 2 patients could not be analyzed due to technical issues. The ASL was concordant to the 'presumed' seizure focus in 9 patients, providing localizing information in 3 and lateralizing information in 6 patients.

**Conclusion:** Prolonged focal post-ictal hypoperfusion can be seen using ASL MR imaging in the majority of patients, concordant with the seizure focus. Post-ictal vascular imaging may be a potentially useful tool to assist in localizing or lateralizing the seizure onset zone. It may therefore serve as a potential replacement for ictal SPECT, which is a labour and cost intensive investigation.

0045

### CONTINUING SEIZURES AFTER TEMPORAL LESIONECTOMY - IS IT IN THE HIPPOCAMPUS?

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**Purpose:** Non-mesiotemporal lobe epilepsy (TLE) may arise from various extrahippocampal (eHC) lesions (Dhiman et al. 2013). Although surgical resection usually leads to freedom from seizures, we have recently demonstrated that eHC lesionectomy bears a risk of longterm memory decline (Wagner et al. 2013) and may lead to ipsilateral hippocampal atrophy. We therefore sought to determine factors associated with continuing seizures after eHC lesionectomy.

**Methods:** All patients who underwent lesionectomy for unilateral, drug-refractory eHC TLE between January 2000 and December 2014 were screened for eligibility (singular pathology, availability of pre- and post-operative volumetric MRI). Fifty-two patients (29 left TLE; 28 male, mean age  $31.1 \pm 12.8$  years; mean duration of epilepsy 9.4 years) were enrolled. We employed voxel-based morphometry as integrated in SPM12 to extract hippocampal volumes by atlas-derived (SPM Anatomy Toolbox) masks. Volumes of the surgical lesion were semi-automatically calculated (Yushkevich u. a. 2006). To identify predictors, a binary logistic regression analysis including loss of hippocampal volume, mean duration of epilepsy and size of resection was performed.

**Results:** More than 2/3 of all patients were seizure-free (Engel I) at follow-up (72.9%, 3–6 months). A significant volume-loss in the ipsilateral hippocampus was observed at follow-up MRI (pre-op:  $2.65 \text{ ml} \pm 0.46 \text{ ml}$  vs. post-op:  $1.69 \pm 0.52 \text{ ml}$ ; mean loss  $-.96 \pm 0.55 \text{ ml}$ ,  $p < 0.001$ ). A longer duration of epilepsy ( $p < 0.05$ ) and smaller resection volumes ( $p < 0.05$ ) explained 85.4% of all unfavorable outcomes within the logistic regression model ( $p < 0.05$ ).

**Conclusion:** This study provides evidence that longer duration of epilepsy and smaller resection size, which is maybe incomplete, may lower the chance of seizure freedom. The role of hippocampal atrophy needs further investigation (Fernandes u. a. 2014). It is conceivable that atrophy leads to sclerosis and, potentially, secondary epileptogenesis within the hippocampus (Bonilha u. a. 2006). Prospective evaluation of patients with continuing seizures after lesionectomy will aid in clarifying this hypothesis.

## Platform Session: Paediatric Epileptology 2 Monday, 7th September 2015

0046

### PAROXYSMAL EVENTS IN CHILDREN AND YOUNG ADULTS WITH ACQUIRED NON-PROGRESSIVE BRAIN INJURY: REVISITING DIAGNOSIS FOLLOWING VIDEO-EEG

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**Objectives:** Acquired brain injury (ABI) is a well-known risk factor for epilepsy in children and young adults. However various paroxysmal phenomena can mimic epileptic seizures causing diagnostic confusion. This study was undertaken to estimate the occurrence of non-epileptic events identified by video-EEG in this specific population.

**Methods:** We carried out a retrospective review of EEG studies performed in children and young adults with ABI and paroxysmal events at a specialist epilepsy centre. Data was analyzed to identify and characterize these events, estimate their occurrence and establish the frequency of misdiagnosis.

**Results:** 70 children and young adults (M:F 46/24, mean age 11 years old, age range 1–26 years) with ABI underwent video-EEG at Young Epilepsy between January 2002 and January 2015. Events in question were captured in 50 cases (71.4%). Of these, 32% (16/50) of patients only had epileptic seizures, 32% (16/50) had only non-epileptic events and the remaining 36% (18/50) had both. At the time of referral non-epileptic events were suspected in only 44% of patients. In 34 patients a total of 48 non-epileptic events were recorded and the main types were: motor phenomena 16/48 (33%), staring events 11/48 (23%), behavioural episodes 8/48 (17%) and sleep related phenomena 5/48 (10%). In the remaining 8/48 (17%) a mixture of other events, i.e. abnormal eye movements, automatisms, autonomic changes were documented. Video-telemetry was successful in capturing and clarifying these events in 64% of the cases, whereas routine EEGs were useful in only 20%. Video-EEG findings resulted in revising the original diagnosis in 4/13 (30.8%) of patients who were taking AEDs unnecessarily.

**Conclusion:** The frequency of non-epileptic paroxysmal events is significant in children and young adults with ABI, often leading to misdiagnosis and inappropriate treatments. Video-EEG, and especially long term video-telemetry, is an invaluable tool in establishing the correct diagnosis and aiding management.

0047

### PREDICTORS FOR EPILEPSY AFTER NEONATAL SEIZURES

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**Purpose:** Neonatal seizures have a high risk of mortality and adverse neurological outcomes such as cerebral palsy, developmental delay and epilepsy. In previous studies a scoring system has been attempted for early prognostic information. Few clinical studies explored the early predictive factors for epilepsy. The aim of the study is to identify clinical risk factors for epilepsy after neonatal seizures, and to compare with previous studies.

**Method:** A retrospective study of 92 newborns (55.4% boys, 44.6% girls, 63% term, 37% preterm) (born January 2007–December 2012) who admitted to the Gazi University faculty of medicine, department of neonatology and experienced neonatal seizures were performed. Clinical variables such as the delivery of birth, gestational age at birth, 1-minute and 5-minute apgar scores, birth weight, the need for resuscitation at birth, seizure onset age, etiology, cerebral ultrasonography, response to anticonvulsant therapy, EEG findings, seizure duration were documented. Chi-square test and bivariate analysis were performed to determine the prediction of those parameters for epilepsy.

**Results:** Epilepsy rate 1 and 6 years follow up was 57.6%. Birth weight, gestational age at birth, the need for resuscitation at birth, cerebral ultrasonography, etiology were the most powerful risk factors for epilepsy. We found no association between delivery of birth, 1-minute and 5-minute apgar scores, seizure onset age, response to anticonvulsant therapy, EEG findings with epilepsy. Any patient had status epilepticus.

**Conclusion:** Term and preterm infants with neonatal seizures had poorer outcome for epilepsy development if low (<2500 g) birth weight,

<37 week gestational age at birth, need for resuscitation at birth, abnormal cerebral ultrasonography, hypoxic ischemic encephalopathy and intracerebral hemorrhage in etiology exist.

0048

### EPILEPTIC NEGATIVE MYOCLONUS: CLINICAL AND EEG-POLYGRAPHIC STUDY IN CHILDREN WITH FOCAL ONSET EPILEPSY

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**Purpose:** To describe clinical presentation, evolution, and polygraphic features of inhibitory seizures with Epileptic Negative Myoclonus (ENM) in children with focal-onset epilepsy of different etiology: symptomatic, idiopathic, cryptogenic.

**Method:** We retrospectively analyzed clinical charts and neurophysiological data of 91 children with partial onset epilepsy and anamnestic findings of presumed inhibitory phenomena. We included only patients with clear documentation of ENM and tailored polygraphic recording. Furthermore we analyzed clinical presentation of ENM as reported by patients or caregivers, EEG-polygraphic findings and outcome of ENM. We excluded cases with progressive diseases.

**Results:** 49 children were included (symptomatic = 47%, idiopathic = 29%; cryptogenic = 24%, M:F = 2:3) with the following features: mean age at epilepsy-onset = 2.9 year (0–8.0), at ENM-onset = 4.2 year (1.4–9.1), mean ENM latency from epilepsy-onset = 1.4 year (0–7.0), mean follow-up = 7.3 year (0–29.3). In the symptomatic group most frequent etiologies were anoxic-ischemic perinatal injury and malformation of cortical development; neurological examination was pathological in 61%. ENM was the first epileptic symptom in 31% overall, in 50% of idiopathic. In three cases ENM was CBZ-induced. The most common ENM-related clinical presentation was inability to maintain postural control with drops of head, trunk or limbs, fallings or gait instability, often accompanied with atypical absences; tremors/jerks (27%), underuse of one limb (16%) were also possible. EEG correlate of ENM was in most patients represented from peri-central spike/spike-wave, either focal unilateral (45%), bilateral asynchronous (8%) or diffuse (57%). Response to treatment is variable, however 93% of the 28 patients with ≥5 years follow-up underwent complete remission of ENM from at least 3 years.

**Conclusion:** ENM is often difficult to recognize only with clinical examination and its incidence in childhood epilepsy is probably underestimated due the great variability of clinical presentation, particularly in symptomatic forms with pre-existing neurological deficits. Accurate EEG-polygraphic recording is mandatory to prompt diagnosis and treatment.

0050

### ACCURACY OF BEDSIDE AEEG MONITORING VERSUS CEEG FOR SEIZURE DETECTION IN AT RISK FULL TERM NEONATES

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To compare the sensibility for seizure detection in full term neonates between 2-channel amplitude integrated electroencephalography (aEEG) and simultaneous continuous conventional electroencephalography (cEEG).

From August 2013 until November of 2014, full term neonates during their first week of life, were admitted to the neonatal intensive care unit (NICU) of Catholic University of Chile Hospital, with risk factors for seizures, were prospectively enrolled in this blinded observational cohort. Approval of the Ethics Committee and informed consent from parents were obtained. Both aEEG and cEEG were simultaneously installed and recorded for at least 24 hours. Biodemographical data were collected. The readings were blindly analyzed by skilled neurophysiologists (stEEG) and neonatologists (aEEG).

25 babies were monitored for a total of 615 hours. 12 patients were male. The most common diagnosis were hypoxic-ischemic encephalopathy (8 babies) and congenital diaphragmatic hernia (7 babies). The stEEG detected 327 seizures and 4 status epilepticus in 10 patients. The aEEG identified 96 seizures and 2 status epilepticus in 4 patients. Additionally, aEEG showed 81 seizures and 1 status epilepticus that corresponded to false positive events. As compared with stEEG, the aEEG seizure detection sensitivity (S) was 31%, specificity (Sp) 74%, positive predictive value (PPV) 54% and negative predictive value (NPV) 52%. S for alterations of the baseline activity with aEEG was 88%, Sp 96%, PPV 96% and NPV 89%.

Seizure recognition in neonates is a challenging clinical problem. EEG is essential for the diagnosis. aEEG has low sensitivity for seizure detection in full term babies. Even though its widespread use in NICU, our results support the use stEEG at least for 24 hours in babies at high risk for seizures, to contribute in decision making in order to improve accurate seizure detection, management and early treatment.

## Platform Session: Genetics 2 Monday, 7th September 2015

0051

### MUTATIONS IN THE GABA TRANSPORTER SLC6A1 CAUSE EPILEPSY WITH MYOCLONIC ATONIC SEIZURES

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**Purpose:** GAT-1, encoded by *SLC6A1*, is one of the major GABA transporters in the brain responsible for re-uptake of GABA from the synapse. Overlapping 3p25.3 microdeletions encompassing *SLC6A1* have been reported in individuals with a wide spectrum of neurodevelopmental disorders. Moreover, two single de novo mutations in *SLC6A1* were reported in two individuals with intellectual disability and autism who were part of large whole exome sequencing studies. These molecular genetics studies as well as the function of GAT-1 at the synapse, suggest *SLC6A1* is an excellent candidate gene for epileptogenesis.

**Method:** To investigate the role of *SLC6A1* in the etiology of the severe infantile and childhood epilepsies, we performed targeted resequencing in 644 individuals with a range of epileptic encephalopathies.

**Results:** We identified six mutations in *SLC6A1* in seven individuals. All presented with the syndrome of epilepsy with myoclonic-atic seizures (MAE). We describe two truncations and four missense alterations, all likely lead to loss-of-function of GAT-1 and thus reduced GABA reuptake from the synapse. These individuals share many of the electrophysiological properties of Gat1-deficient mice, including spontaneous spike-wave discharges.

**Conclusion:** Overall, pathogenic mutations occurred in 6/160 individuals with MAE, accounting for ~4% of unsolved MAE. Mutations in *SLC6A1* seem to occur specifically in individuals presenting with MAE. Collectively this suggests that *SLC6A1* mutations may cause a specific epilepsy syndrome, MAE that occurs in the context of abnormal early development, and this may be reflected in the specific function of GAT-1 and GABA transport in the human brain. While certain antiepileptic drugs are known to work on the GABA system, enhancement of GAT-1 provides a novel target for the development of precision medicines.

## 0052

### THE PHENOTYPIC SPECTRUM ASSOCIATED WITH *GABRB3* MUTATIONS: FROM FEBRILE SEIZURES TO SEVERE EPILEPTIC ENCEPHALOPATHIES

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**Purpose:** Mutations in *GABRB3* encoding the  $\beta 3$  subunit of the GABA<sub>A</sub> receptor have recently been reported in patients with epileptic encephalopathies. We aimed to delineate the clinical spectrum associated with *GABRB3* mutations.

**Method:** We used high-throughput sequence analysis of the *GABRB3* gene in 130 patients with a range of epileptic encephalopathies (EE) and childhood epilepsies. In addition, we ascertained cases with *GABRB3* mutations from other centers. A detailed clinical history was obtained together with a review of EEGs.

**Results:** Eleven patients/families with heterozygous mutations of *GABRB3* were studied. The phenotypic spectrum of the 11 probands varied from Febrile Seizures Plus (FS+) (2) and MAE (2) to Dravet syndrome (1), West syndrome (1) and unclassified EEs (5). Segregation analysis was performed in eight cases; six occurred de novo (2 MAE, 1

West syndrome, 3 EE), whereas one FS+ associated mutation and the Dravet associated mutation were found to segregate with a GEFS+ phenotype in the affected families. In total, we studied 17 individuals with febrile seizures or epilepsy due to a *GABRB3* mutation. Seizure onset ranged from day one to 3 years, however the majority of the probands had seizure onset around 6–9 months of age. Eleven of the individuals had febrile seizures, and two of them never developed afebrile seizures. The majority of the patients with epilepsy had multiple seizure types including GTCS, myoclonic seizures, absences, atonic seizures, focal seizures and epileptic spasms; seizures were refractory to antiepileptic therapy in approximately half of them. Ten had intellectual disability, ranging from mild to severe and 6 had neurodevelopmental disorders or behavioral problems including ASD, ADHD or aggressiveness.

**Conclusion:** The present study shows that *GABRB3* mutations are associated with a phenotypic spectrum ranging from febrile seizures, FS+ to severe epileptic encephalopathies, defining a novel genetic disease within the GEFS+ spectrum.

## 0053

### TESTING EPILEPTIC ENCEPHALOPATHY CANDIDATE GENES IN ADDITIONAL SAMPLES: PRIORITISING TOOLS

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**Purpose:** In recent studies of mutations underlying epileptic encephalopathies, numerous genes have been identified with insufficient statistical support. We seek to increase support for at least some of those genes.

**Methods:** samples from 362 patients with epileptic encephalopathy were tested on a panel of 370 known and candidate genes. The genes had been collected from literature and earlier experiments in our labs. Eighteen genes had OMIM-annotations for epileptic encephalopathy; 66 genes were expected to be recessive, 288 dominant, 13 X-linked, the remainder unknown. In the first screen, no parents were included. We looked for novel coding variants. We are using various databases such as RVIS, CADD and the Broad-Exac database, as well as the number of hits to prioritise genes for follow-up.

**Results:** Thirty-eight patients had probably pathogenic variants in OMIM-annotated genes. Over 600 other coding variants novel to EVS and dbSNP were found. OMIM genes and dominant candidate genes had significantly more hits per gene than X-linked or recessive genes. CADD scores were significantly higher for OMIM-genes than for dominant genes, with X-linked in-between.

**Conclusions:** Despite previous screening in part of the samples, possibly pathogenic variants in OMIM-genes were common. CADD-scores and number of hits per gene seem good filters to prioritise genes for further follow-up, i.e. testing parents to check de novo status. A shortlist of genes which combine high CADD-scores, low RVIS-scores and excess unique hits relative to Exac-database will be presented.

## 0055

### APPROXIMATELY 10% OF "DE NOVO" SCN1A MUTATIONS CAUSING DRAVET SYNDROME ARE INHERITED FROM UNDETECTED PARENTAL MOSAICISM

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**Purpose:** Mutations in the gene SCN1A were identified in approximately 70% of Dravet syndrome (DS) patients and most mutations are identified as de novo using Sanger sequencing. Parental mosaicism has been detected in few DS families by Sanger sequencing. Sanger sequencing cannot detect mutant alleles with low allelic fraction. It is reasonable to suspect that parental mosaicism may be under-detected, especially when the allelic fraction is low. We investigated how many of the “de novo” mutations as determined by Sanger sequencing might in fact be undetected parental mosaicism in a cohort of 363 DS families in China.

**Method:** For mutations determined by Sanger sequencing to be “de novo”, we subjected the parents’ DNA to a new protocol we developed to detect and quantify mosaicism using amplicon re-sequencing by Ion torrent Personal Genome Machine (PGM) followed by a Bayesian model.

**Results:** We discovered that a surprising 17 (9.8%) of the “de novo” mutations in DS were in fact inherited from parental mosaicism that was undetectable by Sanger sequencing. These mosaicisms were validated by pyrosequencing and RainDrop digital PCR. Eleven (64.7%) mutations originated from paternal mosaicism and only six (35.3%) from maternal mosaicism. Twelve (70.6%) of the mosaic parents did not have any epileptic symptoms, and their mutant allelic fractions were significantly lower than those in mosaic parents with epileptic symptoms ( $p = 0.01$ ). We identified mosaicism with varied allelic fractions in blood, saliva, urea, hair follicle, oral epithelium, and semen, demonstrating that postzygotic mutations could affect multiple somatic cells as well as germ cells. Together with five other cases of parental mosaicism detectable by Sanger sequencing, we identified a total of 22 (12.3%) cases of parental mosaicism.

**Conclusion:** Parental mosaicism in DS family is likely to be more common than previously thought by current Sanger-based technologies. Genetic counseling in DS family should be cautious.

## Platform Session: Neuropsychology Monday, 7th September 2015

0056

### ASSESSING ACCELERATED LONG-TERM FORGETTING IN NEWLY DIAGNOSED FOCAL EPILEPSY

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**Purpose:** Many people with epilepsy report an increased rate of forgetting for verbal or episodic memory (accelerated long-term forgetting; ALF). To date, there has been no research that assesses neuropsychological functioning, including ALF, of people with newly diagnosed focal epilepsy compared with healthy controls.

**Method:** Twenty-two people with newly diagnosed epilepsy (PWE) and 25 controls were included in the study. All participants completed neuropsychological assessments of executive functioning, memory and a novel episodic memory test.

**Results:** PWE generated significantly fewer words than control participants on a letter fluency task ( $t(45) = -2.775$ ,  $p = 0.008$ ), category fluency task ( $t(45) = -2.947$ ,  $p = 0.005$ ) and category switching task ( $t(45)$

$= -3.179$ ,  $p = .003$ ). PWE had significantly higher rates of ALF after a 4 week delay than controls for story recall ( $t(45) = 3.383$ ,  $p = 0.001$ ). Within the PWE group, a significant negative relationship was found between recall of verbal information after a 4 week delay and number of words generated in the letter fluency task ( $r = 0.544$ ,  $p = 0.009$ ). Assessment of caseness within the PWE group identified three participants with impaired letter fluency, three participants with impaired story recall at 4 weeks and no participants displayed impairment across both tasks. No control participant fell into the impaired range on either task. There was a trend towards higher rates of forgetting for PWE on the episodic memory task after a 4 week delay but this did not reach significance ( $t(45) = -1.883$ ,  $p = 0.069$ ). There was significant positive correlation between rates of forgetting in story recall at 4 weeks and episodic memory at 4 weeks ( $r = 0.394$ ,  $p = .006$ ).

**Conclusion:** These findings suggest the ALF phenomenon cannot solely be a product of chronicity as it is present in those with newly diagnosed epilepsy. Conventional verbal memory tests were found to be a practical way of assessing ALF and they were also a more sensitive measure than problematic episodic memory assessments.

0057

### TO EVALUATE QUALITY-OF-LIFE (QOL), BEFORE AND AFTER ADMINISTRATION OF COGNITIVE BEHAVIOURAL THERAPY (CBT) AS A TREATMENT IN PATIENTS DIAGNOSED WITH PSYCHOGENIC NON-EPILEPTIC SEIZURES (PNES) AND ASSESS THE SAME ON WHOQOL-BREF (FIELD TRIAL VERSION) AND M.I.N.I SCALE

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Despite the high prevalence and disabling nature of psychogenic non-epileptic seizures (PNES), treatment is unknown. We evaluated the effect of Cognitive Behavioral Therapy (CBT) on reduction of PNES. Psychogenic non-epileptic seizures, also known as Non epileptic attack disorder, are events superficially resembling an epileptic seizure, without the characteristic electrical discharges associated with epilepsy. Cognitive Behavioral Therapy has emerged as a “treatment of choice”, since it is used when patients are reluctant to make behavioural change. This abstract proposes many future directions to address these limitations in the efficacy and clinical effectiveness of CBT for patients with PNES.

**Methodology:** All PNES patient’s male/females and children above the age of 10 years were enrolled. To see the effect of minimum five CBT sessions of 30–60 minutes duration for patient and their family over the period of 1 year. The sample size was 50. Paired t test was applied to compute the differences between pre and post intervention.

**Result:** After administration of Cognitive Behavioral Therapy, we checked the significance of its effect on four domains of QOL scale. The average Social Relationship, Physical Health, Psychological and Environment score increased by 19.45%, 20.33%, 22.38% and 24.04% respectively. Pre and Post intervention statistical values were highly significant at  $p < 0.01$ . Likewise, the effect of CBT on Major Depressive Disorder, Anxiety, Dysthymia, Anorexia Nervosa and Panic disorder decreased the average score by 25%, 31.25%, 30%, 33.33% and 37.5% respectively.

**Conclusion:** This study supports the use of CBT for PNES patients in a population that is largely poor, illiterate and culturally biased. It is a successful cure for mental health and Quality of life of PNES patients. This study gives both therapist and patient an opportunity to understand not only the psychological distress but limit overprotection and misunderstood preconceived notions. Further therapeutic interventions are required to understand the dissociative psychological disorders in order to reduce disability and burden in PNES patients.

0058

### DECISION MAKING AND SKIN RESISTANCE AS A SOMATIC MARKER IN MESIAL TEMPORAL LOBE EPILEPSY

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**Purpose:** Iowa Gambling Test (IGT) showed that patients with frontal lobe lesions performed well on standard neuropsychological tests, however showed lower net scores on IGT. IGT is used to assess decision making (DM). Somatic marker hypothesis (SMH) proposes that emotional processes can be guided by a variety of somatic signals such as skin conductance, especially in decision making behavior. The purpose of this study is to test the SMH and to assess DM performances of patients with mesial temporal sclerosis (MTS) by using IGT with a control group.

**Method:** 22 patients ( $M \pm SS = 32.7 \pm 10.998$  for age) and 24 healthy participants with similar sociodemographic characteristic ( $M \pm SS = 31 \pm 9.8$  for age) were included. The computerized version of IGT had been used to assess DM as published elsewhere. Skin resistance was measured as an indicator of somatic marker during IGT. Skin resistance values are recorded just before -2 ms. the participant makes his choice and this measure is evaluated as an anticipatory response. These anticipatory responses then compared (AB and CD) to see if the groups generated somatic markers before making disadvantageous decks. The effect of deck on anticipatory responses had been analysed by using Univariate ANOVA statistics. Independent samples T-test had been used to compare IGT total net scores between control and epilepsy group.

**Results:** In control group, analysis of variance showed a main effect of deck (AB/CD) on anticipatory responses for AB decks ( $F(1,184) = 4.33$ ;  $p < 0.05$ ). No main effect had been found in epilepsy group. Results indicated that the scores were significantly higher for control group ( $M = 11.6$ ,  $SD = 14.5$ ) than for epileptic group ( $M = -2.55$ ,  $SD = 17.96$ ), ( $t(44) = 2.95$ ;  $p < 0.05$ ).

**Conclusion:** The control group makes more advantageous choices than the patient group in IGT. MTS patients showed different SM responses with controls. This result may be comparable with patients having ventromedial frontal lobe lesions.

0059

### CURRENT STANDARDS OF NEUROPSYCHOLOGICAL ASSESSMENT IN PATIENTS WITH EPILEPSY: RESULTS FROM A SURVEY IN 24 EUROPEAN EPILEPSY CENTERS

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**Purpose:** To assess the current practice of neuropsychological assessment in patients with refractory epilepsy in European epilepsy centers.

**Method:** In context of a European project on the harmonization of presurgical diagnostics in patients with refractory epilepsy (E-PILEPSY; a European pilot network of reference centers in refractory epilepsy and epilepsy surgery) funded by the European Agency for Health and Consumers, a survey was conducted on the status quo of neuropsychological testing.

**Results:** Responses of 24 participating centers revealed that neuropsychological assessment is considered to be an essential part of presurgical work-up. A mean number of 180 patients are tested per year. The most frequent indications comprise localization of dysfunc-

tions, pre- and postsurgical testing and monitoring of pharmacological effects. Most frequently assessed domains are verbal and nonverbal memory, attention and executive functions, language, visuo-spatial functions and IQ. There is a large variety of tests applied for each of these domains with little overlap between the centers. Even greater variability can be found in regard to the assessment of hemispheric language dominance, including different indications, methods and paradigms. The most frequent method is fMRI in addition to lateralizing neuropsychological tests and hand dominance. In general, the Wada test is very rarely performed (on average 7 patients per year) and cannot be regarded as a standard procedure.

**Conclusion:** While there is a huge variety in regard to specific tests in use, very high agreement can be found concerning the principles of neuropsychological testing. Differences in regard to the assessment of language dominance are more fundamental. Future efforts will aim for establishing a minimal consensus on standardized neuropsychological tests across the centers focusing on proven criterion and ecological validity of the measures in the field of epilepsy. This core test battery will then be sought to be normalized in context of the project.

0060

### INSOMNIA IN PEOPLE WITH EPILEPSY: PREVALENCE, PREDICTORS AND IMPLICATIONS

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**Purpose:** There is a well recognised, albeit poorly understood, complex, reciprocal relationship between sleep and epilepsy. Despite evidence showing insomnia is common in people with epilepsy (PWE) (Vendrame et al., 2013), there is a lack of research into its predictors and ramifications. This study aimed to determine the prevalence of self-reported insomnia symptoms in PWE referred to a hospital outpatient clinic. We examined the influence that epilepsy variables, mood, sleep hygiene, pre-sleep worry and dysfunctional beliefs about sleep had on insomnia severity. In addition we investigated relationships between insomnia and self-reported memory function and quality of life.

**Method:** A prospective sample of 90 English-speaking PWE, aged 18–65 completed the Pittsburgh Sleep Quality Inventory (PSQI), Sleep Hygiene Index (SHI), Generalised Anxiety Disorder-7 (GAD-7), Neurological Disorders Depression Inventory in Epilepsy (NDDI-E), Everyday Memory Questionnaire (EMQ) and Quality of Life Inventory in Epilepsy (QOLIE-31).

**Results:** 56% of the sample scored in the insomnia range on the self-report PSQI, a figure nearly three times higher than the reported base-rate for the general population of 19% (Bazil, 2003). Neither type of epilepsy, duration of disease, nor number of AEDs correlated with severity of insomnia symptoms. However, higher symptoms of depression and anxiety as well as poor sleep hygiene practices were related to insomnia severity. Insomnia severity was correlated with number of self-reported memory failures and lower quality of life.

**Conclusion:** A high proportion of PWE experience insomnia, but we found no specific disease-related factors to be associated with severity of self-reported insomnia symptoms. Instead insomnia severity was associated with poor sleep hygiene, anxiety and depression. Ramifications of insomnia included memory problems and lower quality of life. Given these findings, behavioural and psychological interventions tailored for PWE experiencing insomnia have the potential to be effective and have an important functional impact.

## Platform Session: Psycho-social Issues in Epilepsy Monday, 7th September 2015

0061

### PREHOSPITAL EPILEPSY EMERGENCY SCORE (PEES) FOR PRECLINICAL DIFFERENTIATION BETWEEN SYNKOPE AND EPILEPTIC SEIZURE IN EMERGENCY CASE

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**Purpose:** In preclinical emergency case of sudden loss of consciousness it is difficult to distinguish between syncope or an epileptic seizure. Without documentation essential information's are often lost. We aim to develop an easy to handle score for a preclinical setting, which may provide recognition of essential clinical signs for the differential diagnosis.

**Method:** 124 subjects were shown 4 videos with one syncope and three seizures, respectively according to ILAE IA, IB, IC. The Researcher asks the subject, after watching the video, to assess their clinical observations judged by what they have seen. SPSS 22.0 (Generalized estimating equation) was used for Data Analysis. The category "known epileptic" listed in the PEES (tabl.1) was not included in the statistical analysis, because this cannot be recognized by subject from the video information. The cut-off point is a score equal or greater to 5 as sign for an epileptic seizure.

**Results:** N = 124

Syncope: mean 2.6 (SD 1.0) Min: 0; Max: 6

Seizure IA: mean 6.8 (SD 1.7) Min: 3; Max: 10

Seizure IB: mean 5.3 (SD 0.9) Min: 3; Max: 8

Seizure IC: mean 8.5 (SD 1.3) Min: 4; Max: 10

The total-sum-score demonstrates sensitivity (0.97) and specificity (0.97).

**Conclusion:** The PEES records the basic clinical signs for syncope and epileptic seizures. The score system showed a high sensitivity across all averages. The cut-off point for seizure, which was defined as 5 or greater based on the results of the initial studies (1.2) should be now, with regard to the new results, >5 points. Based on these findings, the score should be tested in a field test project in prehospital emergency situations. The findings should be transmitted digitally to the receiving hospital and the results of PEES will be compared with the final diagnosis in a following study.

0062

### EXPLORING THE ROLE OF ANXIETY AND DEPRESSION IN THE LIVES OF AUSTRALIAN ADULTS WITH EPILEPSY; RESULTS FROM THE 2010 AUSTRALIAN EPILEPSY LONGITUDINAL SURVEY

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**Purpose:** Psychological distress is higher among people living with epilepsy than many other disease groups. Our purpose is to examine key determinants of anxiety and depression in a community sample of people with epilepsy.

**Method:** Data come from the 2010 Australian Epilepsy Longitudinal Survey, which explores the social impact of living with epilepsy in Australia. The HADS scale was analysed and Pearson correlations and block recursive regression were undertaken to identify key associations

between anxiety, depression and a range of variables to identify key determinants of anxiety and depression.

**Results:** Key factors to influence anxiety were social aspects of stigma, effectiveness of seizure control, employment status and the number of different epilepsy drugs a person was prescribed.

Determinants for depression were social effects of stigma, whether in employment and the effectiveness of seizure control. Stigma was also found to be an important mediating variable for employment, control and number of drugs.

**Conclusion:** These results indicate that psycho-social issues such as employment status and experience of stigma interact with epilepsy and its treatments to account for high rates of anxiety and depression in this community sample of epilepsy. The results reinforce the need for community-based measures to ameliorate the negative effects of unemployment and stigma in order to reduce anxiety and depression associated with epilepsy. Further research into the relationships between anxiety and depression and lived experience of epilepsy would assist in developing targeted strategies to alleviate the effects of anxiety and depression for people with epilepsy.

0063

### A COMPARATIVE STUDY INTO THE IMPACT OF THE EPILEPSY SPECIALIST NURSE ON PATIENTS' KNOWLEDGE, CARE PROCESS, SATISFACTION WITH CARE AND QUALITY OF LIFE

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**Purpose:** To determine if there is a difference in patients' knowledge of epilepsy, experience of care, satisfaction with care, and quality of life (QoL) for those receiving care from services with an Epilepsy Specialist Nurse, compared to those receiving care from services without an Epilepsy Specialist Nurse (ESN).

**Method:** Following ethical approval, outcomes for patients receiving care for more than a year within a service with an ESN (n = 255), were compared to outcomes from a cohort of patients receiving care within a service without an ESN (n = 271), using a validated survey. Both groups were comparable for all the demographic, psychosocial and epilepsy variables measured.

**Results:** Statistically significant differences were found in overall knowledge, with patients in the ESN sites having higher mean scores for knowledge (M = 4, SD=0.710) compared to the Non ESN sites (M = 3.67, SD=0.758) [t(493) = -4.914, p < 0.000]. There was a statistically significant difference in involvement in care with respondents from the ESN sites having higher mean scores (M = 4.23, SD=0.720) compared to the Non ESN sites (M = 3.94, SD=0.824) [t(491) = -4.254, p < 0.000]. Respondents from ESN sites also reported higher satisfaction with emotional support (M = 7.38, SD = 2.408) compared to respondents from Non ESN sites (M = 6.61, SD = 2.755) [t (475) = -3.185, p < 0.002] and higher satisfaction with practical support (M = 8.04; SD = 2.11) compared to respondents from Non ESN sites (M = 7.38; SD = 2.408) [t (480) = -3.231 p < 0.001]. The average QOLIE 10P score was similar for both Non ESN sites (M = 38.32, SD = 28.65) and ESN sites (M = 37.45, SD= 26.77) with no statistical difference observed [t (477) = .346, p = .729].

**Conclusion:** Although no differences were reported in QoL, patients receiving care within a service with an ESN report greater knowledge of

epilepsy, involvement in own care and satisfaction with support offered compared to those being cared for in a service without an ESN.

0064

### COMPARISON OF EPILEPSY AND ASTHMA PERCEPTION AMONG PRESCHOOL TEACHER IN TAIWAN - PAST AND PRESENT

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**Purpose:** Epilepsy and asthma are two common chronic illnesses of childhood. We had performed the study to investigate preschool teachers' perceptions to children with epilepsy and asthma in 2001; the results revealed that perceptions of these two chronic illnesses were different significantly. The purpose of this survey was to assess the changes in the attitudes and perceptions toward these diseases during a twelve years period by testing of preschool teachers in Taiwan.

**Methods:** Two hundred seventy-four preschool teachers were investigated with a questionnaire regarding their knowledge, attitude and practice. There were 22 paired questions (half for epilepsy and the others for asthma) in this questionnaire. Differences between teachers' perception of children with epilepsy and asthma were analyzed. We also compared the present results with past data performed on 2001.

**Results:** In recent survey, more teachers thought epilepsy was a hereditary disease and associated with insanity than asthma ( $p < 0.05$ ). Acceptance of a child with epilepsy was less than a child with asthma with significant difference. Teachers seem to have more understanding for asthma than epilepsy and this difference was also significant. Regarding to relations of illness with insanity, there are no significant differences between present and past 12 years results. More teachers are willing to accept a child with both epilepsy and asthma in the class than 12 years before. Teachers' worry of objection by other kids' parents to the child with epilepsy also declines significantly in two surveys. The participants felt that they have more resources for understanding knowledge of both for epilepsy and asthma with significant difference.

**Conclusions:** Perceptions of epilepsy and asthma among preschool teachers were different significantly in recent study. Even though they had more resources for understanding knowledge of epilepsy and more confidence to communicate with epilepsy children' parents compared with 12 years ago.

0065

### STIGMA AND ITS UNDERLYING CONTRIBUTORS IN CHINESE EPILEPSY PATIENTS

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**Purpose:** Epilepsy is a chronic disorder of the brain that affects people of all ages. Stigma and exclusion which affected quality of life are common features of epilepsy patients. Our study was aimed to study the stigma in epilepsy in Chinese patients and to investigate the underlying contributors.

**Method:** A total of 301 individuals with epilepsy were enrolled. A clinical questionnaire including clinical and demographic details was applied. Patient-perceived stigma was collected by using self-completed questionnaire (The Stigma Scale). The relationship between clinical variables and stigma scale was confirmed by Logistic regression analysis.

**Results:** The patients' scores of stigma ranged from 0 to 4. The percentage of patients with stigma score greater than or equal to 1 was 42.2%. Among them, 55 patients had stigma score 1(18.3%), 47 patients had stigma score 2(15.6%), 25 patients had score 3(8.3%). Patients with stigma score greater than or equal to 1 had lower age of onset and education year compared to patients with stigma score 0. There was no difference between two groups in age, sex, income, economic status, disease duration, seizure type, epilepsy etiology and taking antiepileptic drugs. Logistic regression analysis revealed that age of onset, education year and seizure frequency were independent risk factors of stigma in epilepsy patients.

**Conclusion:** Our study revealed high percentage of stigma in Chinese epilepsy patients. Age of onset, education year and seizure frequency are significant contributors on scores on the stigma scale. Further research should be done to seek for the way to reduce the percentage of stigma in patients with epilepsy.

## Platform Session: Clinical Trials 2 Tuesday, 8th September 2015

0066

### DIFFERENTIAL NEUROPSYCHOLOGICAL AND EEG EFFECTS OF LACOSAMIDE VERSUS CARBAMAZEPINE IMMEDIATE-RELEASE IN HEALTHY SUBJECTS: A FOCUS ON EEG EFFECTS

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**Purpose:** Antiepileptic drug (AED) tolerability is determined largely by adverse cerebral effects. This study evaluated the neuropsychological and EEG effects of lacosamide (LCM) versus carbamazepine immediate-release (CBZ-IR).

**Methods:** Neuropsychological and EEG effects of LCM (300 mg/day) and CBZ-IR (600 mg/day) were compared in healthy adults using a randomized, double-blind, double-dummy, two-period crossover design with assessments at screening, pre-drug baseline, end of each treatment period (3-week Titration; 3-week Maintenance Period), and end of each washout period (4 wks) after drug treatment. The primary outcome-variable was an overall neuropsychological composite Z-score derived from computerized and traditional neuropsychological measures, which assessed attention, processing speed, executive functions, and memory. EEG measures included relative delta power, relative theta power, alpha peak, and event-related potential latency.

**Results:** 60 adults (57% female, mean age 34y [SD 10.5]) were randomized; 44 completed both treatments. The primary analysis included 41 per-protocol subjects. The overall composite neuropsychological Z-scores differed in favor of LCM (0.33 [SD 1.36],  $p = 0.01$ ). Absolute Z-score differences compared with the average of non-drug conditions were -0.26 for CBZ-IR and +0.08 for LCM. In secondary analyses of individual neuropsychological variables, CBZ-IR was statistically worse than LCM on 25% (4/16); none favored CBZ-IR. The overall composite EEG Z-scores for the AEDs differed in favor of LCM (0.74 [SD 1.42],  $p = 0.0014$ ). Z-scores were significantly different ( $p < 0.05$ ) in favor of LCM for 75% (3/4) of the individual EEG measures. Drug-related adverse events (AEs) were reported in 22% of subjects on LCM and 49% on CBZ-IR. Discontinuations due to AEs occurred in 2 (4%) subjects during LCM and 8 (14%) during CBZ-IR treatment.

## Abstracts

**Conclusion:** LCM 300 mg/day monotherapy showed statistically significantly fewer untoward neuropsychological and EEG effects than CBZ-IR 600 mg/day in healthy subjects. Overall, fewer AEs and AEs leading to discontinuation were observed during LCM than during CBZ-IR treatment.

0067

### STRESS MANAGEMENT INTERVENTION FOR LIVING WITH EPILEPSY: RESULTS OF A RCT

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**Purpose:** Stress is the most common self-reported seizure precipitant in multiple surveys and many people with epilepsy believe stress reduction improves seizure control. We performed a prospective, randomized, controlled trial (RCT) of stress reduction with smartphone monitoring of stress and mood variables in people with medication resistant epilepsy.

**Method:** Three epilepsy centers recruited subjects with at least 2 focal onset seizures per month despite optimal medical treatment. Subjects identified stress or other factors as seizure precipitants. For 3 month treatment phase, subjects were randomized to active treatment with 2–3 times daily progressive muscle relaxation versus sham treatment with extremity movements and writing a journal of daily activities. Subjects recorded seizures and answered questions about stress and mood twice daily into a study smartphone. Each day subjects reported how likely they thought a seizure was in next 24 hours. In addition to diary counts of seizure frequency, subjects completed a treatment credibility scale that asked if the treatment reduced stress or seizures.

**Results:** 67 subjects were randomized; 64 completed the entire 5 month study. 94% of days all the diary entries were completed. Mean seizure frequency during baseline was 12 per month; range 2–99. Interim analysis (53 subjects) showed 81% of all participants reported stress was reduced during the study. In active treatment arm, 85% reported stress reduced; 77% reported seizures reduced. In the sham arm 78% reported stress reduced; 58% reported seizures reduced. Final results will be presented.

**Conclusion:** A RCT of stress reduction treatment for medication resistant seizures is feasible and subjects are highly compliant with treatment and daily diary entries. Subjects believed that both the active and sham arms reduced stress and seizures, but more seizure reduction was reported in the active treatment arm. Final results will be presented.

0068

### LONG TERM PATIENT OUTCOMES USING CARDIAC-BASED SEIZURE DETECTION

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**Purpose:** A novel vagus nerve stimulation (VNS) pulse generator, model 106, was developed with a cardiac-based seizure detection algorithm (CBSDA) to automatically trigger VNS (AutoStim Mode) in response to seizure activity associated with an increased heart rate. Patient follow-up

in the E-36 clinical trial is planned for a 2 year period to analyze the safety and clinical benefit of the new device.

**Method:** The E-36 study (NCT01325623) enrolled 31 patients with drug resistant epilepsy who were admitted to an Epilepsy Monitoring Unit (EMU) for up to 5 days of continuous video electroencephalography. Clinical benefit was assessed based on the proportion of seizures which ended during automatic stimulation, seizure severity scoring by patients (Seizure Severity Questionnaire, SSQ) and physicians (National Hospital Seizure Severity Scale, NHS3), and patient-rated quality of life. (QOLIE-31-P).

**Results:** Safety profiles were comparable to prior VNS Therapy trials. Within the EMU, 55% (6 of 11) of debilitating focal seizures ended during automatic stimulation. NHS3 scores for debilitating focal seizures showed significant improvement ( $p < 0.05$ ) at EMU discharge, and at 6 and 12 month follow-up compared to baseline. During 3, 6, and 12 month follow-up, patients reported significant improvement in key components of seizure severity compared to baseline, including: movements that could result in harm, overall recovery, and physical/cognitive aspects of post-ictal recovery. Nearly all categories within the patient-rated quality of life scale (QOLIE-31-P) showed significant improvement at the 12 month follow-up. Results from extended follow-up periods will be available at the meeting.

**Conclusion:** AutoStim delivered near seizure onset appears to have similar clinical benefit to magnet-activated (on-demand) stimulation. This convenience feature extends the benefits of acute stimulation to patients who cannot use the magnet to manually activate treatment. The NHS3, SSQ, and QOLIE showed sustained improvement over time using combined AutoStim and standard VNS modes.

0069

### A RANDOMIZED CONTROLLED CLINICAL TRIAL OF CATHODAL TRANSCRANIAL DIRECT CURRENT STIMULATION IN PATIENTS WITH TEMPORAL LOBE EPILEPSY WITH HIPPOCAMPAL SCLEROSIS REFRACTORY TO PHARMACOLOGICAL TREATMENT

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**Introduction:** Transcranial direct current stimulation (tDCS) is an emerging non-invasive neuromodulation therapy have demonstrated preliminary safety and efficacy in animals and patients with epilepsy. tDCS induce widespread changes of cortical excitability through a weak constant electric current depending of the polarity. Hyperpolarization using

cathodal tDCS suppress epileptiform interictal discharges (EIDs) and clinical seizures (Sz).

**Purpose:** Evaluate safety and efficacy of different cathodal tDCS protocols in the frequency of clinical Sz and EIDs in adult patients with temporal lobe epilepsy (TLE) with hippocampal sclerosis (HS).

**Method:** Clinical trial phase II, randomized, double blind, prospective with three arms (2 active [3 days and 5 days  $\times$  30 min, 2 mA] and placebo) that consisted of 3 phases:

- 1) pre-treatment,
- 2) intervention active (with tDCS stimulation device<sup>®</sup> (Hong Kong) or placebo and
- 3) post-treatment with follow-up at 30 and 60 days (Jan 2012–May 2014).

The frequency of Sz, EIDs and side effects were record in each phase. The EEGs recordings were performed at pre-treatment, immediately post-treatment, 30 and 60 days. We used descriptive statistics and ANOVA for analysis.

**Results:** We included 28 patients, 16/28 (57%) men, age 37.8  $\pm$  10.9 years-old (3 day  $n$  = 12, 5 day  $n$  = 8, placebo  $n$  = 8). We found a significant reduction of the number of Sz at 2 months between the two actives groups (–48%) versus placebo (–36%) ( $F$  = 6.824,  $df$  = 2,  $p$  < 0.008) and using Bonferroni test 3 days versus placebo (–43% vs. –36%,  $p$  < 0.015) and 5 days versus placebo (–55% vs. –36%,  $p$  < 0.027) were significance. We didn't found any reduction in EIDs at the follow-up or sz at 1 month. Cathodal tDCS was well tolerated in the active groups.

**Conclusion:** Cathodal tDCS sessions of 3 days and 5 days (2 mA, 30 min) decreased the frequency of Sz at 2 months in adult patients with TLE with HS compared with placebo.

## Platform Session: Epilepsy and Seizures: Causes and Precipitants Tuesday, 8th September 2015

0071

### GREAT SPHENOID WING DEFECTS IN REFRACTORY CRYPTOGENIC TEMPORAL LOBE EPILEPSY: A CONTROLLED STUDY

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**Introduction:** Bone defects of the skull may occur in middle cranial fossa and may lead to meningo-encephalocele, whose association with seizures is well established. Aims of this study are to investigate the prevalence of great sphenoid wing defects in refractory "cryptogenic" temporal lobe epilepsy (rcTLE) and in non-epileptic patients.

**Methods:** We included thirty consecutive patients (12 M; mean age 43 years; range 19–81) with rcTLE. Forty-four consecutive seizure-free subjects (24 M; mean age 72 years; range 33–91), admitted to our stroke unit for acute middle cerebral artery occlusion, were included. Both groups underwent a thin layer (0.6 mm thickness) cranial CT scan. CT images were off-line reconstructed on three orthogonal axes to detect the bone defects. Subjects with CT evidence of bone leaks of the middle

cranial fossa performed a supplementary ad hoc 1.5T brain MRI, using volumetric T1-weighted and FIESTA sequences.

**Results:** CT scan showed a significant ( $p$  = 0.0238) difference between patients (4/30; 13.3%) and controls (0/44) as regards the presence of great sphenoid wing defects. No bilateral bone defect was found. The side of the bone defect was always ipsilateral to the side of the rcTLE. Targeted brain MRI confirmed the presence of encephalocele in 2/4 patients, while meningocele was found in the two remaining subjects. One of the two patients with encephalocele underwent lesionectomy and he remained seizure-free during the 30-month follow-up.

**Discussion:** We firstly showed that great sphenoid wing defect was significantly associated with rcTLE as compared to controls, thus confirming its strict association with epilepsy. Middle cranial fossa bone defects should systematically be investigated in patients with rcTLE, since these anatomic lesions predispose to epilepsy probably by leading to temporal encephalocele. The latter is a treatable condition and lesionectomy may lead to seizure freedom. Relationship between temporal meningocele and refractory epilepsy remains unknown and should be investigated in future studies.

0072

### MORPHOLOGICAL CHANGES OF PEDUNCULOPONTINE NUCLEUS IN PATIENTS WITH SLEEP-RELATED SEIZURES IN CRYPTOGENIC EPILEPSY

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**Purpose:** Sleep, especially with Non-Rapid eye movement (NREM) increases the interictal epileptiform discharges and the frequency of seizure, whereas REM sleep suppresses them, in various epilepsy syndromes. Therefore, it could be speculated that brain structures regulating REM sleep have a control over epileptogenicity in relation to human wake-sleep cycle. Among REM-activating brain structures, the coordinate of pedunculopontine tegmental nucleus (PPN) is investigated in a MRI-based stereotactic localization study. We questioned if measured volume of PPN differs between sleep-related epilepsy patients and non sleep-related epilepsy, using a non-biased automated analysis of MRI.

**Method:** Subjects were diagnosed with epilepsy of unknown causes based on clinical and electroencephalography findings, and whose conventional MRI were negative for focal structural lesion.

Based on clinical data, two groups were compared for our hypothesis; (1) 33 subjects with more than 80% of seizures occurred during sleep, (2) 45 subjects who had no seizures during sleep. 3D T1 MR scans were acquired and analyzed with Voxel based morphometry-based, automated region of interest generation method.

**Results:** The two group did not differed in clinical localization, mean age at registration, proportion of male gender, age of disease onset, total count of seizures and total intracranial volume.

PPN volume was statistically smaller in sleep-related epilepsy patients than non-sleep related epilepsy (student's  $t$  test,  $p$  = 0.012).

Multivariate analysis revealed a significant of PPN volume difference between the two group after controlling for age, sex and intracranial volume (ANCOVA,  $F$  (1,74) = 6.63,  $p$  = 0.012).

**Conclusion:** This the first study which discovered structural change of PPN associated with predominant timing of seizure across the wake-sleep cycle.

Supported by investigation of PPN in animals, the structure is considered to be a modulator of both REM sleep and epilepsy. Our finding might help understand a intervenient pathomechanism that lies between sleep cycle and epilepsy.

0073

**THE ROLE OF AUTOIMMUNE ANTIBODIES IN CRYPTOGENIC EPILEPSY**

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**Purpose:** Autoimmunity is an emerging point of research in the etiology of different neurological disorders including epilepsy. We aimed to search for autoantibodies against VGKC, GAD, LGII, CASPR2, NMDA, AMPA and GABA receptors and investigate the clinical presentation as well as the risk factors which can be correlated with autoimmune etiology.

**Method:** Patients with cryptogenic epilepsy with focal seizures were included in this study. Patient demographics, age at seizure onset, seizure frequency, risk factors, seizure precipitants, type of seizures were noted. Plasma obtained from patients was frozen at -80 °C and analyzed for autoantibodies against VGKC, LGII, CASPR2, NMDA, AMPA, GABA receptors and GAD with immunocytochemistry techniques, ELISA method or radioimmunoassay technique as required. Positive samples were confirmed by immunohistochemistry and western blotting.

**Results:** There were 94 patients (55 male), with mean age 37.5, ±15 yrs (18–84). Thirteen patients had autoimmune antibodies, GAD (4 pt), VGKC (5 pt), NMDA (1 pt), AMPA (1 pt), both GAD and VGKC 2 pt). Higher incidence of autoimmune disease or serious infection in personal history was observed in seropositive group. Nine of 13 patients were seizure free during the last year on one or two antiepileptic drugs where the rest 3 had drug resistant seizures. Corticosteroids helped to control seizures in two patients. Statistical analyses did not reveal any significance for all parameters evaluated.

**Conclusion:** Autoimmune antibodies may be detected in a subgroup of cryptogenic epilepsy. Some of them may have drug resistant seizures with immune system related events in the patient's history where immunomodulator therapy may be considered in selected cases. These findings indicate the role of immunity in a subgroup of patients with epileptic seizures of unknown etiology and some specific features.

0074

**DO THE PROVOCATIVE FACTORS CHANGE WITH TIME IN JUVENILE MYOCLONIC EPILEPSY?**

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**Purpose:** In juvenile myoclonic epilepsy (JME), occurrence of seizures and epileptiform EEG discharges are influenced by some factors. Approximately two-thirds of the patients with JME, seizures are provoked by a variety of general factors like stress, fatigue, fever, and sleep and more specific precipitants like flashing sunlight, music, reading, thinking, and excess alcohol intake. The objective of this study was to assess the prevalence and long-term outcome of seizure provocative factors in JME.

**Method:** Data from 200 patients (85 men, 115 women) with JME who had presented our epilepsy outpatient clinic, were reviewed. All of them had a follow-up of at mean 7.6 ± 4.9 years, and their medical records were reevaluated. All patients completed a standardized questionnaire to assess for the presence of precipitant factors for their seizures in a face-to-face interview.

**Results:** The mean age of patients was 26.7 ± 8.46 (12–55). The mean duration of epilepsy was 10.7 ± 7.28 years (1–35). The most frequently used drugs were valproate (147), levetiracetam (12) and lamotrigine (19). Almost all of the participants could identify at least one provocative factor, including in order of frequency: stress (33.8%), sleep deprivation (36.3%), fatigue (27.9%), starvation (12.5%), specific thoughts/concentration (12.3%), flashing lights and playing games (15%), alcohol intake (0.5%), reading (3.4%), calculating (1%), writing (4.9%), listening to music (2%), menstrual cycle (9.4%) talking on the mobile phone (3.9%). The results show that some provocative factors were more frequent in certain age ranges and changed with time.

**Conclusion:** There are many things that can provoke the seizures in JME. Some provocative factors may change in time. Therefore, we shouldn't forget to ask about provocative factors, every visit.

0075

**CONVULSIVE AND NON CONVULSIVE SEIZURES AFTER CARDIAC SURGERY**

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**Purpose:** Neurological complication are the most frequent factors of mortality and morbidity after cardiac surgery under cardiopulmonary bypass (CPB). Convulsive and non-convulsive seizures are mostly predictor acute cerebral injury or persistent coma. Especially, non-convulsive status (NCSE) is not life threatening or brain damaging but should be recognized and treated.

**Method:** Under our observation there were 640 patients who needed cardiac surgery. 91 patients of them different type of neurological complications. The patients underwent through the following types of cardiac surgery: coronary artery bypass graft surgery (CABG) in 69 patients, valve surgery in 19 cases, surgery of ascending aorta and aorta arch 4 patients. All cases we used EEG study and CT scan. There been used cardiopulmonary bypass during cardiac surgery in all cases.

**Results:** In 19 cases we discovered different types of convulsive and non-convulsive seizures, there was shown focal and generalized epileptic activities on the EEG, in 12 cases of them we founded acute ischemic stroke on CT scan without clinical neurological changes. We divided all patient in two clinical groups:

**I group: patient with convulsive seizures and: II group: patient with NCSE.**

**Conclusion:** Cardiac surgery might cause some neurological complication among them are convulsive and non convulsive epileptic seizures, that are predictors of stroke. Early diagnosis and treatment is very important to outlet of neurological complications after cardiac surgery.

**Platform Session: Imaging  
Tuesday, 8th September 2015**

0077

**ASSESSING THE IMPACT OF INTERICTAL DISCHARGES ON RESTING STATE NETWORK CONNECTIVITY IN FOCAL EPILEPSY USING EEG FMRI AND A NATURAL STIMULUS TASK**

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**Purpose:** Patients with focal epilepsy have been widely studied using resting state fMRI where abnormalities have been frequently reported in the so-called 'default mode network' (DMN). However, the role of ongoing interictal epileptiform discharges (IEDs) and the relevance to these DMN abnormalities are unclear. We therefore decided to study alterations in network properties due to IEDs both during 'rest' and during a 'natural stimulus' video task requiring low level attention that was expected to produce more controlled changes in the DMN and salience networks.

**Method:** We collected simultaneous EEG-fMRI data at 1.5T using an MRI compatible EEG system. Subjects included 13 pre-surgical drug-resistant patients with mixed localisation and 11 age-matched controls, all between the ages of 9–18. The task consisted of a video condition watching a cartoon and an attending condition where a screen with the words 'please wait' was presented.

**Results:** We found a significant group level increase in activity in the 'please wait' condition that was greater in the controls relative to patients in the dorsal anterior cingulate, frontal poles, posterior cingulate, and precuneus regions, which are usually associated with the salience and default mode networks (DMN) respectively. We then explored the network integrity using functional connectivity within the salience and DMN networks based on the GLM derived seeds in precuneus and DACC. We found that there was stronger intra-network connectivity in controls compared to patients. These differences were significantly reduced when controlling for IEDs.

**Conclusion:** This result shows that brain networks that should be connected during a task block are perturbed by IEDs but their overall response to the task is not. Accounting for IEDs is important to interpret functional connectivity results in epilepsy.

0078

### ENHANCED DYSFUNCTIONAL WIRING BETWEEN THE HIPPOCAMPUS AND THE THALAMUS IN MEDIAL TEMPORAL LOBE EPILEPSY

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**Purpose:** Medial temporal lobe epilepsy with hippocampal sclerosis is often accompanied by widespread changes in ipsi and contralateral white matter connectivity. Recent studies proposed that patients may show pathologically enhanced wiring of the limbic circuits. To better address this issue, we specifically probed connection patterns between hippocampus and thalamus and examined their impact on cognitive function.

**Method:** A group of 44 epileptic patients (22 with right and 22 with left hippocampal sclerosis) and 24 healthy control participants were examined with high-resolution T1 imaging, memory fMRI and probabilistic diffusion tractography. Thirty six patients had further extensive neuropsychological testing. After whole brain segmentation with FreeSurfer, tractography streamline samples were drawn with hippocampus as the seed and thalamus as the target region. Two tractography strategies were applied: The first targeted the anatomical thalamic volume segmented in FreeSurfer and the second a functional region of interest in the medio-

dorsal thalamus derived from the activation during delayed recognition memory.

**Results:** We found a pronounced enhancement of connectivity between the sclerotic hippocampus and the ipsilateral thalamus both in right and left TLE as compared to healthy control participants. This finding held for both the anatomically and the functionally defined thalamic target. In terms of cognitive function, the number of hippocampal-thalamic connections was correlated with poorer performance in a variety of executive tasks, notably in the Trail Making Test, thus suggesting that the pathological wiring did not compensate cognitive curtailing.

**Conclusion:** We suggest that TLE is accompanied by an abnormal and dysfunctional enhancement of connectivity between the hippocampus and the thalamus, which is maximal on the side of the sclerosis. This pathological pattern of limbic wiring might reflect structural remodeling along common pathways of seizure propagation.

0079

### INCREASED RELAXATION TIME CORRELATES WITH ASTROGLIOSIS AND INCREASED CHONDROITIN SULFATE IN TLE PATIENTS

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**Purpose:** Patients with drug resistant temporal lobe epilepsy present increased hippocampal T2 relaxation time in pre-surgical examination. Although astrogliosis is believed to be responsible for this increase, it is possible that extracellular matrix molecules, which influence tissue water content, are also important factors. Our aim was to evaluate the correlations between relaxation time and tissue gliosis and extracellular matrix.

**Method:** Patients with TLE (n = 43) were scanned prior to surgical resection of the hippocampus in a 3 Tesla MRI scanner. For T2 relaxometry, spin echo images with multiples echoes (TE = 20, 40, 60, 80 and 100 ms; TR = 3 s) were acquired and post-processed. Age-matched controls were obtained from voluntaries (radiological control, RC, n = 20) for the MR measurements, and from autopsy tissues (histological control, HC, n = 14) for the pathological measurements. Immunohistochemistries for GFAP.

(a marker of reactive astrogliosis) and CS-56 (a marker for the extracellular matrix molecule chondroitin sulfate) were performed in formalin fixed, paraffin embedded tissues, and were evaluated as immunopositive area fraction. Results were considered significant at  $p < 0.05$ .

**Results:** TLE patients presented increased T2 values when compared to RC ( $p < 0.001$ ). Increased immunopositive GFAP area was observed in the hippocampus of TLE patients, when compared to HC,

in the molecular layers, granule cell layer, hilus, CA4, CA3, CA2, CA1 prosubiculum, and subiculum

( $p < 0.05$ ). Increased immunopositive CS-56 area was observed in the molecular layers, subgranule zone, hilus, CA4, CA3, CA2, CA1 prosubiculum, and subiculum ( $p \leq 0.002$ ) of TLE patients, compares to HC. Relaxation time correlated with GFAP area fraction in the subiculum ( $r = 0.541$ ;  $p = 0.0296$ ) and with the CS-56 area fraction in the hilus ( $r = 0.473$ ;  $p = 0.0303$ ) in TLE patients.

**Conclusion:** Our data indicate that astrogliosis and increased extracellular matrix molecules are associated with the increased hippocampal T2 relaxation observed in TLE patients.

0080

### THE IMPACT OF EEG-FMRI ON THE EPILEPSY PRESURGICAL CLINICAL DECISION MAKING PROCESS: A PROSPECTIVE STUDY

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**Purpose:** To establish the utility for a test conducted in clinical practice, its effect on the decision making process should be evaluated. We report results of an ongoing, long-term clinical study in epilepsy, where EEG-fMRI was evaluated through its impact on the presurgical clinical decision-making process.

**Method:** Adults with refractory extratemporal focal epilepsy, referred for presurgical evaluation, underwent EEG-fMRI. The EEG-fMRI based localization of epileptic focus was presented during a multi-disciplinary meeting after the team had defined the presumed epileptogenic zone, based on clinical, electrographic and imaging findings and were blinded to the EEG-fMRI findings. The impact of EEG-fMRI findings on the epilepsy surgery decision making process, in terms of changes in the placement of invasive electrodes or surgical candidacy was documented.

**Results:** Fourteen consecutive patients (six women) with a median age of 27 years were recruited. EEG-fMRI results were available in 11 patients, including 8 in whom IED were recorded; seizures were recorded in two patients; in one patient, no epileptic activity was captured during EEG-fMRI acquisition and IED topographic map correlation (between EEG recorded inside the scanner and long term video EEG monitoring) was used.

A change in the surgical decision, following presentation of the EEG-fMRI results, was recorded in eight (57%) patients; In two patients the EEG-fMRI results had an impact on the decision leading to additional non-invasive tests and in six patients the impact was on the placement of invasive electrodes.

**Conclusion:** Our study is specifically designed to assess the impact of EEG-fMRI on the clinical decision making process, indicating a significant role in epilepsy surgery planning. Decision in presurgical work up should synthesize the information and the impact of various diagnostic strategies, optimal for every surgery candidate, to help the decision making by clinicians.

## Platform Session: Paediatric Epileptology 3 Tuesday, 8th September 2015

0081

### PEDIATRIC PSYCHOGENIC NONEPILEPTIC EVENTS: NEWER PERSPECTIVE

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**Purpose:** To analyze clinical spectrum of Psychogenic nonepileptic events (PNEE) in children.

**Method:** This prospective study (AIIMS, New Delhi; September, 2012-April, 2014) included children (6–16 years) with clinically suspected PNEE, subsequently confirmed by short duration VEEG which was analyzed for semiological characteristics. Events were classified as per Seneviratne classification.

Stressors, associated co morbidities, Verbal IQ and behavioral abnormalities were assessed using questionnaires/tests - HTP test, DSM IV TR criteria, MISIC and CBCL.

**Results:** Children with clinically suspected PNEE (94), 5 had epilepsy so VEEG was done for 89. Events observed- spontaneously: 4, induced with simple methods: 76 (failed induction: 9). Eighty children {45 boys; mean age: 10.5 (±1.6) years} diagnosed as PNEE were enrolled. Median delay in diagnosis was 5 months (IQR- 0.5 to 48 months) and 45% patients were already on AEDs. Family history of seizures (6/80) and psychiatric disorders (6/80) was observed in 12/80 patients.

Semiological characteristics: Dialectic PNEE (42.5%), mixed PNEE (28.8%), Nonepileptic aura (13.8%) and Motor PNEE (15%). Most events were abrupt in onset, median duration: 180sec (IQR:11 to 1500sec). Ictal eye closure and unresponsiveness were observed in 67% patients. Pelvic thrusting and back arching were seen in 4/80 & 7/80 patients respectively.

Stressors in family and school were identified in 39/80 and 17/80 patients respectively. Psychiatric co morbidities were seen in 11/80 patients (commonest: adjustment disorder).

Mean Verbal IQ of PNEE patients was 100.7 (range 85.2–127.6) signifying no intellectual deficit. About 50% children had associated somatic complaints.

**Conclusion:** More than 90% of PNEE are inducible with simple methods. Unlike adults, Dialectic PNEE were frequent in children. Motor PNEE were observed more commonly in boys than girls. We suggest use of induction protocols and a high index of suspicion to pick these events early. We also suggest a comprehensive assessment protocol for pediatric PNEE.

0083

### DRAVET SYNDROME: A “NOCTURNAL” PATTERN OF SEIZURES

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**Purpose:** Dravet Syndrome (DS) is a rare epileptic encephalopathy with poor cognitive outcome. Seizures are refractory to AEDs, but they tend to decrease with age. A trend toward a switch from “awake” to “sleep/nocturnal” seizures is reported during the clinical course of DS but literature lacks details about the incidence of nocturnal seizures, the age onset and the proposed change in therapies.

**Method:** In a longitudinal cohort of 73 patients with DS followed at our centre, we report 20 patients who developed a pattern of almost exclusive nocturnal seizures. We have retrospectively analyzed the genotype (SCN1A mutation) and the epileptic phenotype at the onset and the last follow-up (seizure types, treatments, cognitive and behavioural outcome). As for the EEG, we detailed those realised during the phase of “sleep/nocturnal” seizures.

**Results:** This population presented a strong prevalence of males (14 M and 6 F). All had mutations in SCN1A and with a higher incidence of splicing mutations (35%). Median age of “nocturnal seizures” onset was of 6 y6 m(4y-11y). Last follow-up ranged between 5y11 m and 24y6 m (mean 14y4 m), and 19 over 20 patients still presented “nocturnal/sleep” seizures predominantly. All had the tritherapy (VPA, STP, CLB) before the nocturnal seizures onset. Seizures were difficult to control despite AEDs adjustment and many trials. On EEG, 8 showed paroxysmal anomalies, predominant in the frontal region. All had at last follow-up cognitive disability and behavioural disorders.

**Conclusion:** Despite the limits of our observation related to the retrospective data and the small sample, we could identify a sub-populations of patients with DS. A better and more systematic prospective collaborative data could help to better understand this group and to guide our treatments choices.

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0084

#### CLINICAL CHARACTERISTICS AND SEIZURE SPREAD PATTERNS OF OCCIPITAL LOBE EPILEPSY IN CHILDREN - AN SEEG STUDY

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**Purpose:** Occipital lobe epilepsy (OLE) is the least common among surgical series. We tried to determine the clinical characteristics and seizure spread patterns of OLE in a pediatric population.

**Method:** We included 20 children whose seizure onset zone (SOZ) was in the Occipital lobe, as defined by SEEG recordings. We divided the patients in two groups: an infra-calcarine (IC) group, whose SOZ was in the infracalcarine and basal part of the Occipital lobe, and supra-calcarine (SC) group.

**Results:** We observed four dominant seizure-patterns: Occipital (40%), presenting mainly with oculomotor symptoms and head turning, Temporal (30%), with the occurrence of hypomotor behavior and automatisms, Frontal (20%), with prominent tonic and/or clonic movements of the upper and/or lower limbs and asymmetrical spasms (10%). The patients from the SC group had seizures that spread predominantly to the internal part of the Parietal lobe, while the patients in the IC group showed a preferential seizure spread to the mesial and basal temporal structures, but also to the external part of the Temporal and Parietal lobe, insula and contralateral Occipital lobe.

From the patients in the SC group 5 exhibited an Occipital pattern, 2 a Frontal pattern and one patient had spasms.

From the IC group, 6 patients showed a Temporal pattern, 3 an Occipital pattern, 2 a Frontal pattern and one had spasms. Automatisms were only observed in the IC group ( $p = 0.001$ ) and there was a correlation between their occurrence and the involvement of the external part of the Temporal lobes ( $p = 0.007$ ).

The patients from the SC group had a better surgical outcome (87.5% Engel I) compared to the patients in the IC group (25% Engel I).

**Conclusion:** There are multiple seizure spread patterns in OLE, with different clinical expressions, but most of the patients showed an Occipital seizure pattern.

0085

#### LONG TERM EVOLUTION OF A GROUP OF PATIENTS WITH FEBRILE INFECTION-RELATED SYNDROME (FIRES): OUR EXPERIENCE

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**Purpose:** To analyse the long-term follow-up of patients with febrile infection-related epilepsy syndrome (FIRES).

Febrile infection-related epilepsy syndrome is a catastrophic epileptic encephalopathy in previously well children in a setting of a febrile illness. It usually rapidly evolves into refractory status epilepticus and in the long term, into a chronic refractory epilepsy with significant cognitive and behavioural impairment.

**Method:** Seven patients with FIRES were studied, four males and three females, with an age at presentation between 3 and 12 years. Clinical, electroencephalography (EEG), neuroimaging, and intellectual findings during the chronic phases were reviewed.

**Results:** During the chronic epilepsy phase, seizure characteristics were focal in all patients. The EEGs showed focal spikes predominantly in temporal and frontotemporal lobes.

Seizures were refractory to multiple antiepileptic medications in five patients.

Neuropsychologic testing revealed a borderline intellectual impairments in five patients and moderate to severe intellectual deficit in two. Behavioral difficulties, including aggression and impulsivity, were present in three male patients. These problems were severe and required involvement of personal carers, and antidepressant or antipsychotic medication.

**Conclusion:** Febrile infection-related epilepsy syndrome is a rare disease recently described. There are few works that communicate their long-term evolution. The outcome of our series of patients was generally severe, with seizures refractory to different therapeutic options and cognitive impairment in later evolution, with behavioral disorders in almost half of the cases.

#### Platform Session: Neurophysiology Tuesday, 8th September 2015

0086

#### HIGH-FREQUENCY OSCILLATIONS AND SEIZURE ACTIVITY AND IN THE HUMAN ANTERIOR NUCLEUS OF THE THALAMUS

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**Purpose:** Deep brain stimulation of the anterior nucleus of the thalamus (ANT-DBS) has recently been introduced into therapy for refractory epilepsy. The role played by the ANT in human epileptic seizures and the mechanisms leading to the anti-seizure effects of ANT-DBS have not yet been fully elucidated. This is the first report of recording interictal and ictal activity in the human ANT.

**Methods:** DBS electrodes were implanted in the ANT of six pharmacoresistent patients with temporal and extratemporal epilepsies who had not responded to vagus nerve stimulation. Interictal and ictal video-EEG was recorded via the DBS electrodes before the electrodes were internalized and a neurostimulation device was implanted.

**Results:** Interictal high frequency oscillations (HFO) of 80 to 240 Hz, in one case of 500 Hz, were recorded in four patients. Eight clinical seizures in four patients were recorded; a robust broad-band increase of power occurred in the early phases of all seizures. In two patients, the ictal changes preceded the clinical symptoms. No interictal epileptiform discharges were recorded; early epileptiform pattern preceding the clinical onset was recorded in one seizure.

**Conclusion:** Based on our recordings of HFO, of early ictal EEG modifications, and of occurrences of ictal epileptiform pattern, we suggest that the ANT may participate actively in the network elaborating seizures in human epilepsies.

0087

### CORTICAL CORTICAL EVOKED POTENTIAL RECORDINGS FROM STEREO EEG IN EVALUATING HUMAN PRECUNEUS CONNECTIVITY

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**Purpose:** Precuneus is a major association area that is implicated in high level of cognitive processing and aspects of consciousness. The purpose of this study is to evaluate functional and pathological cortical connectivity in human precuneus using the method of cortical cortical evoked potential (CCEP).

**Method:** We conducted a retrospective review and prospective recruitment of medically intractable epilepsy patients who underwent stereo EEG (SEEG) in Cleveland Clinic Foundation between the years of 2010 to now. We identified 19 patients, ten male and nine female. Age ranges from nine to sixty year old.

The SEEG implantation targets were determined by clinically generated hypothesis for the localization of epileptogenic zone.

Extra operative CEEP with stimulation to the precuneus, was performed through two adjacent contacts in a bipolar manner. Electrical stimulus consisted of a constant current square wave pulse of 0.3 msec duration and pulse frequency of 1 Hz with alternating polarity. Current intensity started at 2 mA, increasing by 2 mA in stepwise increments to 8 mA. Forty to sixty stimuli were delivered. Matlab 2014a was utilized to calculate root mean square (RMS) value of these averaged CCEP data.

**Results:** We identified four patients with anterior, five patients with posterior, three patients with ventral, four patients with central, two patients with anterior and posterior and one patient with posterior and central precuneus electrodes.

This study shows electrophysiological connectivity of the precuneus to the other part, including contralateral precuneus, angular gyrus, posterior cingulate, post central gyrus, superior and inferior parietal lobule. Lesser degree of connection was seen in insula, lateral temporal, precentral gyrus, amygdala and hippocampus.

**Conclusion:** This study shows functional electrophysiological connectivity between different region of precuneus and various components of the brain. This information is useful in aiding the invasive EEG implantation planning and in further understanding seizure propagation network.

0088

### MULTIMODAL RESPONSES INDUCED BY CORTICAL STIMULATION OF THE PARIETAL LOBE: A STEREO-ELECTROENCEPHALOGRAPHY STUDY

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**Purpose:** The main purpose of the current study was to explore the functional organisation of the dominant and non-dominant parietal cortices using electrical stimulations (ES), with a specific emphasis on hemispheric lateralisation.

**Method:** We retrospectively analysed all the clinical manifestations induced by intracerebral bipolar electrical stimulation in 172 patients suffering from drug resistant focal epilepsy (mean age 25.6, standard deviation 11.6; 44% females and 56% males) with at least one electrode stereotactically implanted in the parietal cortex.

**Results:** A total of 1186 electrical stimulations were included in the analysis. In the dominant parietal lobe, clinical responses were observed for 56 (25%) of the low-frequency stimulations and for 76 (50%) of the high-frequency stimulations. In the non-dominant parietal lobe, 111 (27%) low-frequency and 176 (55%) high-frequency stimulations were associated with a clinical response. Body scheme alteration was the only clinical effect showing a lateralisation, as they were evoked only in the non-dominant hemisphere. The occurrence of somatosensory sensations, motor symptoms, dysarthria and multimodal responses were significantly associated with stimulation of the post-central gyrus (OR 5.83,  $p < 0.001$ ; OR 8.77,  $p < 0.001$ ; OR 5.44,  $p = 0.011$ ; OR 8.33,  $p = 0.006$ ; respectively). Stimulation of the intraparietal sulcus was associated with the occurrence of sensory illusions or hallucinations (OR 8.68,  $p < 0.001$ ) and eyeball/eyelid movements or sensations (OR 4.35,  $p = 0.047$ ).

**Conclusion:** To our knowledge, this is the only currently available complete revision of electrical stimulation of the entire parietal cortex with the aim to evaluate the neurophysiology of this relevant brain region. Our analysis offers a general overview of the polyhedral function of the parietal cortex and supports its crucial role in different networks involved in complex integrative functions.

0089

### DYSREGULATION OF HYPERPOLARIZATION-ACTIVATED INWARD CATION CURRENT ( $I_h$ ) AFFECTS THE THALAMOCORTICAL OSCILLATIONS: THE ROLE OF AUXILIARY SUBUNIT TRIP8B ON HCN CHANNEL FUNCTION IN THALAMIC AND CORTICAL NEURONS

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**Purpose:** The hyperpolarization-activated cyclic nucleotide-gated cation (HCN) channels have a major role in controlling neuronal excitability and rhythmic oscillatory activity in individual neurons and neuronal networks and abnormal regulation of HCN channels has been implicated in different types of epilepsy including absence epilepsy. The aim of the present study was to determine how dysregulation of HCN channels due to the lack of expression of auxiliary subunit TRIP8b, alters the basic properties of hyperpolarization-activated current ( $I_h$ ) in thalamic and cortical neurons and consequently affects the thalamocortical oscillations.

**Method:**  $I_h$  was measured in whole-cell patch-clamp recordings from thalamocortical (TC) neurons of different thalamic nuclei, as well as pyramidal neurons in layer V and VI of the somatosensory cortex of TRIP8b-deficient (TRIP8b<sup>-/-</sup>) and control (C57Bl/6J) mice (p15 - p30).

Effects of  $I_h$  dysregulation on thalamocortical oscillations was monitored by local field potential (LFP) recordings from ventro-posterior thalamic nucleus (VPM), somatosensory cortex and motor cortex (p 90 - p120) in vivo.

**Results:** In all investigated brain regions,  $I_h$  amplitude was significantly lower in TRIP8b<sup>-/-</sup> as compared with control mice. Analysis of the half-maximal activation ( $V_{h,0.5}$ ) of  $I_h$  revealed that steady states activation curves were significantly shifted towards more hyperpolarized values in TRIP8b<sup>-/-</sup> mice. Analysis of cAMP dose-response curves showed a significant increase in the sensitivity of TC neurons for cAMP in TRIP8b<sup>-/-</sup> mice in comparison to control group. This higher sensitivity was shown by a stronger maximal shift of  $V_{h,0.5}$  induced by cAMP in TRIP8b<sup>-/-</sup>. Reduction of  $I_h$  also increased the probability of burst activity in TC neurons with lower depolarizing current injection and altered the cortical neuronal oscillations towards more slow activities.

**Conclusion:** The results of this study show that alterations in  $I_h$  properties due to the lack of TRIP8b auxiliary subunit may contribute to the generation of abnormal thalamocortical oscillations.

## Platform Session: Women's Issues Tuesday, 8th September 2015

0090

### FAMILY HISTORY OF CONGENITAL MALFORMATIONS DOES NOT INCREASE THE RISK OF FETAL MALFORMATIONS IN WOMEN WITH EPILEPSY

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**Purpose:** Ascertain the association between family history of congenital malformations (CM) and risk of fetal malformation for women with epilepsy (WWE).

**Method:** WWE are enrolled in the preconception period or first trimester of pregnancy. Three generation pedigree for CM was prepared for WWE and their spouses at registration. WWE with consanguineous partners were excluded. Family history is positive when one or more first or second relatives are reported to have CM. Malformation status is ascertained in pregnancy (ultrasonography) and after birth (clinical examination, echocardiography, abdomen ultrasonography at 3 months of age). All offspring with malformations formed the case group. Two offsprings without malformations (the enrolments just preceding and following each case) constituted the control group.

**Results:** 1351 WWE (Localization related epilepsy 49.2%, IGE 39.5%, unclassified epilepsy syndromes 11.3%) with pedigree chart had completed pregnancy (mean age  $25.9 \pm 3.7$ ). There were 122 (9.03%) offspring with CM. Pedigree analysis showed that there were 3614 family members (887 first degree, 2727 second degree) for the cases ( $n = 122$ ) and 7344 family members (1773 first degree, 5571 second degree) for the controls ( $n = 244$ ). Family history was positive for seven cases; positive among first degree relatives for 4 cases and positive among the second degree relatives for two cases and positive among first and second degree relatives for one case. For the controls, family history was positive for 38 of them, positive among first degree relatives for 22, among second degree relatives for 14 and among first and second degree relatives for 2). There was no significant difference ( $p = 0.64$ ; in the positive family history for cases (5.7%, 95% CI 0.03–0.11) when compared to controls (15.6%, 95% CI 0.12–0.21).

**Conclusion:** Family history of CM does not increase the risk of fetal malformation for WWE.

0091

### HYPERTENSIVE OBSTETRIC COMPLICATIONS IN WOMEN WITH EPILEPSY AND ANTIEPILEPTIC DRUG EXPOSURE IN PREGNANCY: A POPULATION-BASED COHORT STUDY

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**Purpose:** The aim of this study was to assess the risk of hypertensive obstetric complications in women with epilepsy (WWE) and to investigate the impact of treatment with the most common antiepileptic drugs (AED).

**Method:** Population based study including all deliveries recorded in Medical Birth Registry of Norway (MBRN) during 1999–2013. Only nullipara pregnancies were analysed. WWE and the three most common AED used as monotherapy were identified. Pregnancies of WWE were compared to women without epilepsy (WWOE) and pregnancies of WWE unexposed to AED also served as controls.

Main outcome variables were: gestational hypertension, mild and severe preeclampsia (PE), early preeclampsia, HELLP and eclampsia. Odds Ratios (OR) and corresponding confidence intervals (CI) were analyzed using logistic regression and adjusted for maternal age, maternal education and chronic diseases other than epilepsy.

**Results:** In all 893 330 deliveries, leaving 370 669 first pregnancies for analyses. 2886 (0.78%) pregnancies in WWE of whom 1071 were exposed to AED and 906 with monotherapy: Lamotrigine ( $N = 372$ ), Carbamazepine ( $N = 245$ ) and Valproate ( $N = 124$ ). WWE had an significant increased risk of mild PE (4.8% vs. 3.3%), OR 1.5 CI: (1.3–1.8), compared to WWOE. WWE not exposed to AED had similarly an increased risk for mild PE (4.5%) OR 1.5 CI: (1.1–1.7).

WWE exposed to Carbamazepine had an significant increased risk for mild PE (10.2%) OR 3.1 CI: (1.8–5.0) compared to WWOE and compared to WWE without AED, OR 2.2 CI: (1.3–3.8).

Lamotrigine was not associated with increased complications.

Valproat was nonsignificantly associated with an increase in mild PE (6.5%).

There were no significant differences in the risk for other hypertensive complications.

**Conclusion:** WWE have a significant increase in mild preeclampsia independent of AED exposure. Carbamazepine was associated with a significant risk for mild preeclampsia in pregnancy.

0092

### SEXUAL ABUSE IN WOMEN WITH EPILEPSY

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**Purpose:** To estimate the frequency of previous and recent sexual abuse in pregnant women with epilepsy compared to women without epilepsy and women with other chronic diseases.

**Method:** Pregnant women with epilepsy (WWE,  $n = 706$ ) were compared to all women without epilepsy (WwoE,  $n = 106 511$ ) and to women with other chronic diseases (WCD,  $n = 8372$ ) included in the population based Norwegian Mother and Child Cohort Study. Mothers reported on sexual abuse as a child and during the last year using items from the validated Abuse Assessment Screen. Additional information on maternal health and medication was obtained from the Medical Birth

Registry of Norway. Risk of sexual abuse was estimated as odds ratios (ORs) with confidence intervals (CI) using logistic regression with adjustment for age and adverse socioeconomic factors (low income, low education and being single).

**Results:** Sexual abuse during childhood was reported by 13.7% of WWE, 10.1% of WCD and 7.2% of WwoE ( $p < 0.001$  and  $0.006$  respectively). The last year, 5.5% of WWE, 3.5% of WCD and 2.3% of WwoE reported sexual abuse ( $p < 0.001$  and  $0.015$  respectively). Patients that needed more than one antiepileptic drug frequently reported abuse (15.4% during childhood and 13.7% during the last year,  $p = 0.02$  and  $< 0.001$  respectively). The odds of having experienced childhood and recent sexual abuse were also increased after adjustment (OR 1.9, CI 1.5–2.4 and 2.3 CI 1.6–3.4 respectively). Abuse history was not related to epilepsy aetiology or seizure characteristics.

**Conclusion:** Sexual abuse is frequent in the female epilepsy population. Possibly, sexual abuse is related to a less controllable epilepsy regardless of disease cause or type of seizures.

### 0093

#### PREGNANT WOMEN WITH EPILEPSY: OVERWEIGHT INCREASES COMPLICATIONS

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**Purpose:** To investigate whether overweight in epilepsy is associated with complications during pregnancy and delivery.

**Method:** This study is based on The Norwegian Mother and Child Cohort Study (MoBa) linked to the Medical Birth Registry of Norway. A pregnancy diagnosis of epilepsy was reported in 706 pregnancies. The remaining cohort ( $n = 106, 511$ ) served as the reference group. Overweight was defined as BMI > 25. The risks of pregnancy complications were calculated as odds ratios (ORs) with 95% confidence intervals (CIs) adjusted for maternal age, smoking, parity and socioeconomic factors.

**Results:** Women with epilepsy were more overweight than women without epilepsy (38.4% vs. 31.3%,  $p < 0.001$ ). Women with epilepsy and overweight had a significantly increased risk of caesarean section (OR 1.6, CI 1.1–2.3,  $p < 0.05$ ), gestational hypertension (OR 2.0, CI 1.1–3.5,  $p < 0.05$ ), preeclampsia (OR 2.3, CI 1.2–4.5,  $p < 0.05$ ), gestational diabetes (OR 10.5, CI 1.3–88.3,  $p < 0.05$ ) and neonatal transfers (OR 2.2, CI 1.3–3.6,  $p < 0.01$ ) compared to normal-weight women with epilepsy. Compared to overweight women without epilepsy there was an increased risk of caesarean section (OR 1.5, CI 1.04–2.3,  $p < 0.05$ ) and anxiety and/or depressive symptoms peripartum (OR 2.3, CI 1.4–3.7,  $p < 0.001$ ). Overweight women using lamotrigine had more caesarean sections (OR 3.2, CI 1.7–6.1,  $p < 0.001$ ), gestational diabetes (OR 4.0, CI 1.2–13.2,  $p < 0.05$ ), anxiety and depression symptoms peripartum (OR 2.6, CI 1.1–6.3,  $p < 0.05$ ), small for gestational age (SGA < 2.5 percentile) infants (OR 4.3, CI 1.03–6.3,  $p < 0.05$ ) and neonatal transfers (OR 2.7, CI 1.3–5.7,  $p < 0.01$ ) than overweight women without epilepsy.

**Conclusion:** Overweight in combination with epilepsy may produce a synergistic negative effect on risk of complications during pregnancy and delivery. Women with epilepsy at risk of overweight should be referred to a nutritionist when an antiepileptic drug is started, as well as when a pregnancy is planned.

### 0094

#### EPILEPTIC WOMEN IN REPRODUCTIVE AGE

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**Introduction:** Epilepsy is a frequently encountered neurological disease and affects 1% of general population. A significant part of epileptic patients are women in the reproductive age. These patients are a significant group in terms of pregnancy and contraceptive methods.

**Method:** 1140 patients who were followed in epilepsy department of neurology clinic in Antalya Training and Research Hospital between July 2011 and January 2015 were examined retrospectively. All patients with reproductive age were recruited into the study.

**Results:** Total 368 patients were examined; The age average was  $28.94 \pm 7.66$ ; the youngest one of patient was 15 years old and the eldest one was 45 years old. Average epilepsy terms were  $14.01 \pm 9.27$  years. There were 74 (20.1%) patients having catamenial epilepsy. While 210 (57.1%) of patients were not married, and 151 (41%) patients are married, information could not be obtained regarding marital status of 7 (1.9%) patients. While 229 patients (62.2%) have not a job, 71 (19.3%) patients were employed, information could not be obtained regarding employment status of 6 (1.6%) patients. While 330 (89.7%) patients did not become pregnant in our follow-up, 38 (10.3%) patients become pregnant. 206 (56%) patients were in partial onset epilepsy group, 100 (27.2%) patients in primary generalized epilepsy group, 56 (15.2%) patients were in the unclassified group. 6 (1.6%) patients were in the syndromic group. While 211 (57.3%) patients were receiving monotherapy, 153 (41.6%) patients were receiving polytherapy. 4 (1.1%) patients did not receive treatment. Among the patients who received monotherapy, there were 64 patients (17.4%) using valproic acid, 38 patients (10.3%) using lamotrigine, 53 patients (14.4%) using carbamazepine, 13 patients (3.5%) using oxcarbamazepine, 33 patients (9%) using levetiracetam, 3 (0.8%) patients using topiramate.

**Conclusion:** In reproductive age female patients, many factors such as pregnancy, contraception should be taken into account while planning epilepsy treatment.

## Adult Epileptology 1 Sunday, 6th September 2015

### p0095

#### PRE-ICTAL YAWNING AND TEMPORAL LOBE EPILEPSY

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**Purpose:** Yawning has been described in various medical conditions. The occurrence of yawning as a part of peri-ictal semiology in focal epilepsy has been described, mostly in case reports. In our case report we study pre-ictal yawning and temporal lobe epilepsy.

**Method:** Clinical case report.

**Results:** A 48-year old woman, left handed with no neurological antecedents. Began having epileptic attacks at age 20. The seizure semiology comprised psychic aura (anxiety) and generalized tonic-clonic seizures GTCS. Since the age of 20 years Phenobarbital PB at 100 mg/day was used in monotherapy. Brain CT and MR imaging were normal. Video-EEG recording showed yawning in the pre-ictal period followed by slow waves over left temporal regions. He had repetitive, irresistible and forceful yawning starting from one to 12 seconds. Yawning started with a deep inspiration through her wide-open mouth. She received carbamazepine CBZ 600 mg/day (start dose of 100 mg). We noted decrease in the frequency of yawning.

**Conclusion:** Video-EEG recording is useful in diagnosis of temporal epilepsy in patients with repetitive, irresistible and forceful yawning.

p0096

**PERIORAL MYOCLONIA WITH ABSENCES: TWO CASES**

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**Purpose:** The classification of idiopathic generalized epilepsies (IGEs) is still debatable. Perioral myoclonia with absences is one of the absence syndromes in this controversial group. Our aim is to demonstrate different presentations of absences with perioral myoclonia.

**Method and results:: First case:** 20 years-old female. Her seizures began at the age of 8 with absences. At the beginning seizures were well controlled with Na valproate. At the age of 12, generalized tonic clonic seizures (GTCS) commenced. Patient came our control 1 year ago with complain of absences with head drop, which were new onset. After 6 months she developed Status Epilepticus with perioral myoclonia with absences.

**Second case:** 31 years old male. His seizures began at the age of 4, in front of TV and in the form of GTCS. In the adolescent period he developed myoclonic jerks predominantly occurred just after he woke up early in the morning and followed with the diagnosis of juvenile myoclonic epilepsy. He was diagnosed as IGE. On the short-term video EEG; he had multiple generalized spike/multispike and slow waves and besides in one of these discharges predominantly left sided very brief perioral myoclonic jerks. We could not able to detect his consciousness level just because the event is too short.

**Conclusion:** We want to share two important points in the light of these patients. First, our observation showed that absences have distinct subgroups. POMA is one of them. We observed two patients nearly with the same ictal phenomenology and EEG findings with different response to AED treatment. Second, the Absence status epilepticus is frequently seen in POMA patients and resistant to routine regimens. Here we have a splendid response to oral lacosamide loading.

p0098

**LEVETIRACETAM IN THE TREATMENT OF EPILEPSY AS ADD ON OR MONO THERAPY**

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**Purpose:** To define the efficacy and safety of Levetiracetam (LEV) in the treatment of epilepsy as add on or monotherapy.

**Method:** A random sample of 52 patients with epilepsy, evaluated in a descriptive cross-sectional study for the efficacy and safety of LEV in epilepsy, they were collected among epileptic patients attending the Neurology consultation Clinic in Sulaimani city in the Iraqi Kurdistan Region from May 2012 to May 2013. All the patients were interviewed by using questionnaire forms with comprehensive history, clinical examination, radiological, EEG and laboratory studies done for all patients.

**Results:** The sample involved female patients 2 folds more than males. Mean patients age was 24.54 years. Mean duration of treatment; 2.7 years. Mean LEV dosage: 1475.9 mg/day. Seventeen patients received monotherapy and 35 patients received add on therapy. Mean Seizure frequency was 44 attacks/month before treatment and 4 after treatment. Mean percent of seizure reduction was 95.1% in mono therapy and 91.46% in add on therapy.

**Conclusion:** LEV is a safe, effective, broad spectrum antiepileptic drug that could be used as monotherapy or add on therapy in the treatment of generalized and focal epilepsy.

p0099

**THE HAZY TEMPORAL NEOCORTEX SIGN ON MAGNETIC RESONANCE IMAGING: CLINICAL SIGNIFICANCE IN TEMPORAL LOBE EPILEPSY**

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**Purpose:** To investigate the clinical and metabolic significance of the hazy temporal neocortex sign on Magnetic Resonance Imaging (MRI).

**Method:** A retrospective analysis was conducted for 124 consecutive patients who underwent temporal lobectomy for epilepsy. Grading of the hazy temporal neocortex (HTN) sign was done based on the density of temporal white matter on MRI. Correlation between MRI findings, surgical outcome, electroencephalographic (EEG) findings, Positron Emission Tomography (PET) scan, and histopathology was done. Comparison was done using chi-squared and Fisher's exact tests.

**Results:** Significant positive correlation was found between HTN high density on MRI and clinical-radiological variables such as duration of epilepsy, PET scan hypometabolism, EEG localization, and degree of heterotopia in neocortex histology. HTN was evident on MRI even in the absence of heterotopia in neocortex histology (6 cases) and histological hippocampal sclerosis (4 cases). High density HTN was found in all cases with radiological hippocampal sclerosis and neocortical atrophy.

**Conclusion:** Hazy temporal neocortex on MRI correlates well with the lateralization of temporal epilepsy and can be used as a radiological localizing and lateralizing sign even in the absence of hippocampal sclerosis features.

p0100

**CIRCADIAN DISTRIBUTION OF EPILEPTIC SEIZURES**

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**Purpose:** We investigate the temporal distribution of the seizures of epileptic patients during the day and the relationship with sleep.

**Method:** This study was conducted as a retrospective, non-interventional and descriptive research. 113 patients identified to have seizures and included in the study were investigated at Epilepsy and Sleep Center Laboratories from 2005 to 2011. Age and sex of the patients, types of the seizures they experienced, EEG pathologies, the times at which these seizures happened and the numbers of seizures were evaluated. EEG pathologies were classified according to ictal and interictal periods.

**Results:** There were 60 female (53%) and 53 male (47%) patients. Mean age of the patients was  $28.56 \pm 11.7$  years, total number of observed seizures was 497, mean duration of a seizure was calculated as 84.6 (2–560) seconds. Distribution of the types of seizures; 19.5% were primer generalized, 45.1% were partial, 32.7% were secondary generalized.

In 5 day video recordings were obtained, first seizure was experienced: 41.6% of the seizures were on day 1, 29.2% were on day 2, 22.1% were on day 3, 7.1% were on day 4. No seizure recordings were obtained on day 5. Partial and secondary generalized seizures happen more frequently during sleep ( $p < 0.05$ ).

Temporal distribution of the seizures based on ictal EEG pathology, the frontal and temporal seizures showed an increase from 00.00 to 05.59 am.

**Conclusion:** Our study demonstrates that follow-up of 3 days with video imaging could be sufficient for diagnosis purposes and some seizures types had a distribution in relation with sleep.

#### p0101

### ASSESSMENT OF NEURONAL AUTOANTIBODIES IN EPILEPSY PATIENTS WITH PERI-ICTAL AUTONOMIC FINDINGS

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**Purpose:** The aim of this study was to investigate frequency of neuronal autoantibodies that associate epilepsy patients with peri-ictal autonomic symptoms.

**Method:** Sera of consecutive patients with documented peri-ictal autonomic symptoms were investigated by RIA, ELISA and cell based assays for various neuronal auto-antibodies. The clinical and laboratory features of seropositive and seronegative patients were compared.

**Results:** A total of 62 consecutive patients (37 F, 25 M, mean age  $31.6 \pm 9.4$  years, mean duration of epilepsy  $16.2 \pm 9.2$  years) were included in the study. The investigated neuronal autoantibodies were present in the sera of 9 patients (14.5%) (3 F, 6 M, mean age  $31.8 \pm 11$  years). Antibodies were detected against N-methyl-D-aspartate receptor (NMDAR) in 3 (5%), voltage-gated potassium channel (VGKC)-complex in 3 (5%), glutamic acid decarboxylase (GAD) in 2 (3%) and glycine receptor (GLYR) in one

(2%) of the patients. In the seropositive group 6 patients (67%) had nausea and epigastric aura; 5 patients (55%) had tachycardia, 2 patients (22%) had abdominal pain and 2 patients (22%) had peri-ictal fever. Epilepsy etiology was hippocampal sclerosis in 4 (44%), cryptogenic in 4 (44%) and birth trauma in one (11%) patient. The number of male patients, history of psychosis, peri-ictal nausea, epigastric aura, and fever were significantly more frequent in the seropositive group ( $p < 0.05$ ). There was no correlation between duration of epilepsy, epilepsy etiology, antiepileptic drug resistance and seropositivity.

**Conclusion:** The relation between neuronal autoantibodies and epilepsy patients with peri-ictal autonomic findings are found at similar rates like other epilepsy patients and this group does not have higher risk for autoimmunity. Psychosis, epigastric aura, and peri-ictal fever were more frequent in seropositive group. Relevant autoantibodies should be screened for immunotherapy options in patients with antiepileptic drug resistance.

#### p0102

### FREQUENCY AND LATERALIZING VALUE OF PERI-ICTAL AUTONOMIC SYMPTOMS IN EPILEPSY

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**Purpose:** Autonomic changes during seizures are often overshadowed by other dramatic motor symptoms. The aim of this study was to investigate the frequency and lateralizing value of peri-ictal autonomic signs.

**Method:** Consecutive patients with documented peri-ictal autonomic symptoms who were followed up in our epilepsy center were included in the study. Localization and lateralization characteristics were supported by at least two diagnostic methods that were consistent with each other without any other evidence suggesting otherwise. In patients with non-specific/normal MRI and functional imaging findings lateralization of epileptogenic zone was decided only by the EEG and the seizure semiology.

**Results:** Peri-ictal autonomic symptoms were recorded in 35 out of 230 patients (15%) (21 F, 14 M, mean age  $30.2 \pm 8.8$  years) during video EEG monitoring. We observed the following peri-ictal autonomic findings: Epigastric aura, nausea and retching in 9 (26%), genital automatisms in 6 (17%), hypersalivation in 5 (14%), peri-ictal water drinking in 5 (14%), pilomotor aura in 4 (11%), cough in 4 (11%), spitting in 3 (8%), fever in 2 (6%) and urinary urge in one (3%) of the patients. Peri-ictal autonomic findings were most commonly observed in patients with temporal lobe epilepsy (TLE) (83%). Isolated autonomic seizures were observed in 4 patients (11%). Peri-ictal nausea and retching, hypersalivation, spitting and drinking were observed mostly in right; piloerection, cough, and genital automatisms were observed mostly in left hemisphere onset seizures. But the findings were not statistically significant. Fourteen patients were operated, 13 of them were classified as Engel 1.

**Conclusion:** The etiopathogenesis and lateralizing/localizing value of rare peri-ictal autonomic findings were investigated in a limited number of studies with contradictory results. Further investigation of these intriguing seizures may provide important clues for central nervous system networks and electrophysiological propagation patterns of temporal lobe structures.

#### p0103

### BENIGN TEMPORAL LOBE EPILEPSY IN MALAYSIA

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**Purpose:** Benign temporal lobe epilepsy (bTLE) remains as a common but poorly recognised clinical entity. We aimed to characterise bTLE in Malaysia.

**Method:** Patients were diagnosed as having temporal lobe epilepsy (TLE) if they fulfil at least one of the following criteria:

(i) semiology suggestive of TLE, or:

(ii) EEG showing temporal lobe discharges or slowing or: (iii) MRI brain showing temporal lobe abnormalities.

bTLE is defined as TLE with remission for  $\geq 1$  year; refractoriness is defined based on ILAE criteria.

**Results:** 586 (30.8%) out of 1903 epilepsy patients had TLE. 160 patients (27.3%) were classified as having bTLE, 32.4% refractory, and 40.2% unclassified. Of those with bTLE, mean age was 43.9 years old (SD 16.5), with mean age of onset of 26 years old (SD 17.7). Average disease duration was 17.7 years (SD 12.3). 21 patients (13.1%) fulfil all 3 criteria for TLE. 23 patients (14.4%) had viscerosensory and experiential auras, and 40% had secondarily generalisation. Only 7.5% had underlying cognitive impairment. Majority of our bTLE aetiologies were cryptogenic (63.1%), followed by structural (30%). Twelve (7.5%) had mesial temporal sclerosis (MTS). Majority of patients did not have family history of epilepsy, history of febrile seizures nor status epilepticus. Majority were on monotherapy (66.9%) and remission achieved with only one AED in 59.5%. 70.6% had been on remission for  $\geq 2$  years. As compared with those with refractory TLE, the age of onset was older (25.95 vs 18.07 years-old,  $p < 0.001$ ), duration of illness was shorter (17.69 vs 21.75 years,  $p < 0.001$ ), and less with MTS (21.1% vs 7.5%,  $p < 0.001$ ).

**Conclusion:** Our bTLE cohort had older age of onset, shorter duration of illness and less MTS as compared to those with refractory TLE.

p0104

### HEALTH-RELATED QUALITY OF LIFE (HRQOL) IN PATIENTS WITH EPILEPSY SWITCHING FROM LEVETIRACETAM (LEV) TO BRIVARACETAM (BRV): AN OPEN-LABEL PROSPECTIVE STUDY

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**Purpose:** Non-psychotic behavioural adverse events (BAEs) have been reported in patients receiving LEV. A study of patients experiencing BAEs who switched from LEV to BRV found that patients may benefit from a switch to BRV (Yates et al., AES 2014, abstract 3.300). HRQoL results from this study are reported here.

**Method:** Patients  $\geq 16$  years, on 2–3 AEDs including LEV 1–3 g/day and experiencing BAEs within 16 weeks of LEV treatment initiation, enrolled in a prospective, open-label, Phase IIIb study (NCT01653262) comprising  $\leq 1$ -week screening, switch of LEV to BRV 200 mg/day (without titration; other AEDs unchanged), and 12-week treatment period. HRQoL endpoints were change in Patient-Weighted Quality of Life in Epilepsy Inventory-Form 31 (QOLIE-31-P) from baseline to Week 12, Investigator Global Evaluation Scale (I-GES) and Patient Global Evaluation Scale (P-GES) at Week 12.

**Results:** Of 29 patients enrolled, 26 (89.7%) completed the study. Mean (SD) change from baseline to Week 12 in QOLIE-31-P Total Score was 12.1 (11.4), indicating improved HRQoL. There was a consistent mean (SD) increase in all QOLIE-31-P subscale scores: Cognitive Functioning 10.4 (19.0); Emotional Well-being 14.0 (17.4); Energy/Fatigue 10.6 (13.7); Medication Effects 27.6 (25.5); Overall Quality of Life 13.8 (13.3); Seizure Worry 12.1 (26.0); Social Functioning 10.3 (23.3); Health Status 6.5 (16.5). Improvements in P-GES and I-GES were recorded for most patients: P-GES: any improvement 20/26, 76.9%; no change 5/26, 19.2%; any worsening 1/26, 3.8%; I-GES: any improvement 24/26, 92.3%; no change 1/26, 3.8%; any worsening 1/26, 3.8%.

**Conclusion:** Switching from LEV to BRV due to BAEs was associated with improvements in HRQoL across all subscales in this study. The largest improvement was in QOLIE-31-P Medication Effects subscale, which may relate to a reduction in BAE incidence. However, these results should be interpreted with caution owing to small sample size and open-label nature of the study.

UCB supported

p0105

### ETIOLOGY IN PERIODIC LATERALIZED EPILEPTIFORM DISCHARGES

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**Purpose:** Periodic lateralized epileptiform discharge (PLEDs); consist of spike or sharp wave occur over variable extents of one hemisphere and occasionally appear over both hemispheres independently. PLEDs are found in patients with a variety of hemispheric lesions including acute infarction, hemorrhage, head injury, tumors, and infections especially when associated with metabolic abnormalities and chronic seizure disorder. In this study, we identified etiologic factors of patients with PLEDs.

**Method:** Ninety five with PLEDs between the years of 2004–2014 were examined and included in this study.

**Results:** The mean age of the patients (48 F, 47 M) were  $46.9 \pm 19.01$  (15–83) years old. The etiology of these patients were; 40% with epi-

lepsy, 23.2% with stroke, 11.6% with acute metabolic disorder, %2.1 with intracranial tumor, 6.3% with stroke and epilepsy, 6.3% with encephalitis (one of them with Jacobs-Creutzfeldt disease), 2.1% with head injury, 1.1% with vascular abnormalities, 3.2% with vasculitis of central nervous system and 4.2% with unknown etiology. Radiologic findings were related with their disease but only in 20% of the patients magnetic resonance imaging (MRI) were normal.

**Conclusion:** Classical knowledge is that acute destructive lesions can result in PLEDs. However these results show that PLEDs can result not only with acute disease but also with chronic disease.

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p0107

### CYSTICERCOSIS AS A CAUSE OF MEDICALLY-INTRACTABLE EPILEPSY: A SYSTEMATIC REVIEW

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**Purpose:** To determine the role of Neurocysticercosis (NCC) in medically-intractable epilepsy (MIE).

**Method:** MEDLINE, EMBASE, Scopus and LILACS were interrogated, since their inception until Jan of 2015, searching for clinical studies, including case reports and case series of patients with NCC and MIE. We investigated all cases where the ictal-onset zone was determined with standard pre-surgical evaluation in an epilepsy center. Only cases in which there was concordance between the anatomical location of NCC and the ictal-onset zone were included. 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 4427 references were identified using terms related to cysticercosis and epilepsy. After the first screening, 57 documents were read and critically reviewed. 5 final articles were selected. They included 13 patients. Nine (69.2%) of the patients had NCC in the temporal lobe. Mesial temporal sclerosis (MTS) was detected using MRI imaging in four (30.8%) patients (three had a NCC in the temporal lobe and one in the parietal lobe). One patient with frontal NCC 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 10 of them became seizure free at least 13 months. Details about histological description were available only in two patients, both demonstrated perilesional gliosis.

**Conclusion:** NCC rarely represents the ictal-onset zone in patients with DRE. There is a need of prospective studies to clarify the association between NCC and MTS and the role of NCC in DRE. Most importantly, the role of perilesional gliosis in NCC-related MIE.

p0108

### CONSCIOUSNESS IN EPILEPSY: OBJECTIVE AND SUBJECTIVE COMPONENTS

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## Abstracts

**Purpose:** The alteration of consciousness (AOC) during seizures is one of the most striking features in patients with epilepsy and their evaluation remains a challenge to the present. It is important to include in its assessment of both the appreciation of the observer and the subjective evaluation of the patient.

We investigated the AOC implementing an objective and subjective assessment during seizures.

**Method:** It was included 35 patients (104 seizures) with resistant epilepsy (19 temporal and 16 extratemporal), 50% temporal. Everyone had VideoEEG and IRM. The consciousness seizure scale (CSS) and Ictal Consciousness Inventory (ICI) were applied, and a scale designed by our group, Subjective Evaluation of Consciousness during Seizures (SECS). We asked patients self-reported duration and their memories during seizures before viewing video-EEG. Then we review the video with patients and ask them to check from when they stop to remember the beginning and when they recover the memory at the end of seizures.

**Results:** 62 seizures had profound, 38 moderate and 4 without AOC using CSS. Temporal groups had more seizures with profound AOC than extratemporal ( $p < 0.05$ ). We did not find differences in level and content of consciousness using ICI between temporal and extratemporal groups.

We found an adequately correlated ( $p = 0.006$ ,  $\rho = 0.274$ ) between the subjective perception of the duration of the seizure with the objective duration of it, being better in profound AOC ( $\rho = 0.381$ ,  $p = 0.002$ ).

The recovery of memory at the end of seizure took longer the higher the AOC ( $p = 0.019$ ) and when they had less content ( $p = 0.0001$ ). In addition, we found that memory recovery was delayed when seizures lasted longer ( $p = 0.002$ ).

**Conclusion:** The objective evaluation of AOC through the VideoEEG together with subjective evaluation by the patient, are a valuable tool for diagnostic accuracy. They are a contribution to the research of consciousness both behavioral and neurophysiological level.

### p0109

#### NOVEL AMBULATORY EMG-BASED GTC SEIZURE DETECTION DEVICE FOR HOME AND HOSPITAL USE

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**Purpose:** In the USA, there are no FDA-cleared devices outside of an epilepsy monitoring unit (EMU) that can reliably alert for generalized tonic-clonic (GTC) seizures and provide accurate semiological details to physicians. This study was a pivotal trial designed to validate the effectiveness of a novel EMG-based, real-time, GTC seizure detection system that can be discreetly worn in the biceps without interfering with activities of daily living.

**Methods:** This is a phase III double-blind controlled device trial at 11 EMUs of NAEC level IV Epilepsy Centers in the USA in over 150 subjects with history of GTC seizures. The sensitivity and specificity of the Brain Sentinel GTC seizure detection system was compared to video-EEG semiology to determine the effectiveness of the Brain Sentinel device to detect classic GTC seizures when it is placed accurately over the belly of the biceps muscle in children or adult patients with a history of GTC seizures.

**Results:** To date, 8217 hours of EMG and video-EEG data have been collected from 157 subjects with history of GTC seizures admitted to the participating EMU sites. Provisional analysis reveals a sensitivity for detection of GTC seizures comparable to current FDA-cleared automated EEG seizure detection algorithms while maintaining a high level of specificity and low number of false positive alerts. Recorded EMG data preserves clinically relevant semiology of events such as temporal components of motor recruitment during GTC seizures and EMG activity following convulsive events.

**Conclusions:** Brain Sentinel's system has promise to provide people with epilepsy greater independence and peace of mind in a home or clinical setting while providing physicians with useful data for seizure management.

### p0113

#### THE RELATIONSHIP BETWEEN THE TEMPORAL POLE SIGNAL ABNORMALITY AND ABNORMALITY OF EXTRA-TEMPORAL POLE ON MRI IN POSTOPERATIVE PATIENTS FOR INTRACTABLE EPILEPSY

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**Purpose:** To study the relationship between the characteristics of the temporal pole (TP) signals and the signals of the extra-TP on magnetic resonance imaging (MRI) in postoperative patients for intractable epilepsy.

**Method:** 339 postoperative patients (male: female = 224:115), aged  $23.16 \pm 8.00$  years, with intractable localization-related epilepsy were included. All patients were examined by long-term scalp and/or intracranial video EEG monitoring before operation. The signal characteristics of the TP and extra-TP on brain MRI were analyzed. The temporal pole MRI abnormalities are defined as a white matter increased T2 and/or T2 fluid-attenuated inversion-recovery (FLAIR) signal, resulting in a loss of gray-white matter demarcation, with or without associated atrophy. According to whether the temporal region was involved or not the patients were divided into the group with temporal involved or non-temporal involved. According to whether the mesial temporal structures were involved or not the patients were divided into the group with normal or abnormal mesial temporal structures. The data were statistically analyzed by chi-square test.

**Results:** Among the 339 postoperative patients for intractable localization-related epilepsy. The TP signal abnormality was correlated with the extra-TP abnormality on MRI ( $\chi^2=8.897$ ,  $p = 0.0029$ ). Almost all patients with the TP signal abnormality showed structural abnormality in extra-TP regions (97.33% (82/187)). The TP signal abnormality on MRI was more common in the temporal involved group than that in normal MRI and non-temporal involved group (72.17% vs. 23.81%, 27.36% respectively;  $\chi^2=66.270$ ,  $P < 0.0001$ ). The TP signal abnormality was also more common in the group with abnormal mesial temporal structures than that in the group with normal ones (77.24% vs. 38.66% respectively;  $\chi^2=49.940$ ,  $p < 0.0001$ ).

**Conclusion:** This study suggests the TP signal abnormality probably is useful for determination of the localization, especially the lateralization of the epileptic lesion.

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### p0117

#### A LONG TERM FOLLOW UP STUDY OF POST STROKE SEIZURES

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**Purpose:** Stroke is the most common cause of seizures in the elderly population. The epidemiological data for Post Stroke Seizures and their natural history is lacking in developing countries where there are no stroke registries. The present study was carried out to ascertain occur-

rence, associated risk factors and long term follow up of Post Stroke Seizures.

**Methods:** A consecutive 181 Stroke Patients were evaluated and followed up for 12 months. The occurrence of Seizures was studied during hospital stay and follow up visits in next 12 months. The patients were studied for predictive factors and type of seizures following Stroke.

**Results:** Mean age of the patients was 53.91 years. 127 patients had Ischemic Stroke, 49 patients had Intra Cerebral Haemorrhage and 19 patients had Sub Arachnoid Haemorrhage 19 (9.5%) patients had Seizures. 37% of these patients with seizures developed early onset seizures while 63% of these patients developed late onset seizures. The occurrence of the seizures was seen more in Ischemic Strokes and majority of these were cortical lesions. 26% of these patients developed generalized tonic clonic seizures (GTCS), 42% developed focal seizures and 32% of these patients had focal onset generalized seizures. 16% of these patients had puerperium related Strokes. Risk factors for recurrent seizures were large cortical Strokes, severe Strokes, Recurrent Strokes and puerperium related Strokes.

**Conclusion:** Post Stroke Seizures are not uncommon and are mostly focal or focal onset generalized seizures. Puerperium related Strokes, large cortical Strokes and recurrent Stroke patients are at a more risk to develop seizures.

#### p0118 SIMULTANEOUS OCCURRENCE OF NON-EPILEPTIC AND EPILEPTIC SEIZURES: AN UNDERREPORTED ENTITY WHICH MAY REQUIRE LONGER PERIODS OF CVEEG MONITORING

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**Purpose:** Psychogenic non-epileptic seizures (PNES) pose a diagnostic challenge to neurologists, particularly in patients with PNES and epileptic seizures (ES). There is limited data characterising this subgroup in the literature to-date. Accurate diagnosis of PNES requires continuous video electroencephalogram (cvEEG) monitoring, with a sensitivity of approximately 90%. Delay to diagnosis is common and estimated to be 7 years in those with PNES alone.

In the Epilepsy Monitoring Unit at our institution, we sought to explore the co-existence of both ES and PNES during a single cvEEG monitoring admission. We aimed to identify prevalence, establish any distinguishing patient characteristics and compare outcomes following diagnosis to those with PNES alone.

**Method:** This was a retrospective study of all patients diagnosed with PNES by cvEEG between June 2013 and February 2015 at the National Epilepsy Centre.

**Results:** Of 260 patients monitored, 58 were diagnosed with PNES. 17 patients had a diagnosis of epilepsy and PNES. This is higher than other published work. ES and PNES were recorded during the same admission in 13 patients. The majority of events recorded were non-epileptic. Non-epileptic events occurred earlier in admission, with epileptic events occurring later. We observed a female predominance, polypharmacy with anti-epileptic drugs and a greater delay to diagnosis in patients with ES and PNES. Longer periods of monitoring were required to record both ES and PNES to ensure accurate diagnosis.

A favourable prognosis was seen in patients with PNES following psychological intervention.

**Conclusion:** Patients with PNES and epilepsy are a unique cohort, with some distinguishing features compared to PNES alone. Longer periods of cvEEG monitoring are required to ensure maximal diagnostic accuracy

particularly where there are historical indicators of epilepsy. Shorter periods of monitoring may lead to misdiagnosis which may have devastating consequences.

#### p0119 CLINICAL AND ETIOLOGICAL PROFILES OF PATIENTS WITH SYMPTOMATIC EPILEPSY

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**Purpose:** The purpose of the study was to evaluate the etiological factors and clinical features of our patients with symptomatic epilepsy.

**Method:** A retrospective analysis was performed to 143 patients with symptomatic epilepsy attending our epilepsy department between 2011 and 2014.

**Results:** Mean age of 60F:83M patients was  $32.2 \pm 14.2$  (12–81) years. Age at seizure onset was between the first year of life and 80 years. Neurological examination was unremarkable in 82 (57%) patients, 17 (11.9%) patients had motor-mental retardation, 13 (9.1%) had mental retardation, 13 (9.1%) had hemiparesis and the rest (12.9%) had other neurological deficits. The most common identified etiological factors were trauma (41%), perinatal incidents (21.7%), mesial temporal sclerosis (30%), central nervous system infections (11.9%), brain operations (8.4%), congenital malformations (7%), stroke (5%), aneurysms/AVM (4.2%) and brain tumors (3.5%). Status epilepticus was detected in 9 patients (6.3%). The seizure types were mostly generalized tonic clonic seizures (52.4%), complex partial seizures (47.6%), secondarily generalized seizures (26.6%) and simple partial seizures (23.8%). EEG revealed pathological patterns in 88 (61.5%) patients. Polytherapy was applied to 73 (51%) patients, 67 (46.9%) patients were treated with monotherapy and the remainder discontinued medication.

**Conclusion:** The distinction between idiopathic, symptomatic and provoked seizures may sometimes be difficult due to multifactorial nature of epilepsy. At first glance, symptomatic epilepsies may be underestimated in terms of determining the underlying cause, classifying the seizures and in diagnosis but it could be more complex than it seems. We want to document our data and to draw attention to this nature of symptomatic epilepsies.

#### p0120 SEIZURE-PRECIPITATING FACTORS IN EPILEPTIC PATIENTS

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**Purpose:** The purpose of the study was to determine the most frequently reported seizure precipitants and to identify the frequencies of these precipitating factors. Moreover, we aimed to find out whether there exists any relationship between the seizure precipitants and the types of epilepsy.

**Method:** We analyzed patients who were followed up in our epilepsy department between 2011 and 2014, retrospectively. Information about precipitating factors was obtained during the interview or from the medical reports and telephone inquiries.

**Results:** Mean age of total 363 patients was  $30.9 \pm 13.9$  (10–83) years and 182 (50.1%) of them were female, 181 (49.9%) were male. Age at seizure onset was between the first year of life and 80 years. Patients

were divided into 3 groups regarding the classification of epilepsy syndromes; idiopathic (38.3%), symptomatic (39.4%) and cryptogenic (22.3%). The precipitating factors were emotional stress (31.4%), sleep deprivation (23.7%), fatigue (16.3%), television/computer (8%), missing meals (6.3%), missing medication (5.5%), menstruation (4.1%), fever (3%), flickering lights (2.2%) and alcohol (0.3%). Only one precipitating factor was reported by 19% of the patients whereas 8.4% reported two or more precipitating factors. The analysis of the relationship between the precipitating factors and the types of epilepsy syndromes showed significance only in stress factor ( $p < 0.05$ ). Patients with idiopathic epilepsy seemed to be less sensitive to stress than those with symptomatic and cryptogenic epilepsies ( $p = 0.01$  and  $p = 0.025$ ).

**Conclusion:** Seizures were triggered by one or more precipitating factors in our patients as emphasized in recent studies. Patient's awareness about triggering factors and modification of life styles may significantly reduce the seizure frequency.

#### p0123

### SYMPTOMATIC VERSUS IDIOPATHIC TEMPORAL LOBE EPILEPSIES: FINDINGS FROM A COHORT OF 75 PATIENTS

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**Purpose:** To determine clinical, electrical and radiological differences between mesial and neocortical variants of temporal lobe epilepsies in idiopathic versus symptomatic groups.

**Methods:** Retrospective study of clinical, electrical and radiological features in four groups: mesial symptomatic (MSTLE), neocortical symptomatic (NSTLE), mesial idiopathic (MITLE) and neocortical idiopathic (NITLE). This study was established in neurological department of Razi hospital between 2004 and 2012

**Results:** Total of 75 patients: 24 MSTLE, 33 NSTLE, 14 MITLE and 4 NITLE. The mean age of onset was respectively: 11.54, 22.63, 9.78 and 15.7 years. history of febrile seizures is found in 66% in MSTLE. The main types of seizures are automatisms and visceral sensory auras in MTLE symptomatic (75% and 58% respectively) and idiopathic (43% and 71% respectively). Psychic auras are the most frequent type in NSTLE (42%) and language alterations in NITLE (100%). spike-waves are common in mesial group. Pharmaco-resistance is more frequent in MSTLE (54%) and NITLE (50%). In the symptomatic group, brain MRI shows association of other temporal lobe abnormalities to mesial sclerosis in 46%.

**Conclusion:** Our study shows earlier age of onset with a higher frequency of febrile seizures and pharmcoresistance in MSTLE group. The Symptomatic group of TLE is characterized by older age and higher frequency of background EEG abnormalities. Some features are shared between the symptomatic or idiopathic variants and others depend on the mesial or neocortical localization.

#### p0124

### DEMOGRAPHIC AND CLINICAL PROFILE OF EPILEPSY IN TURKISH POPULATION

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**Purpose:** We aimed to address the commonest types of seizures, their etiologies, electro-encephalography and neuroimaging results and anti-epileptic drugs most commonly used in epileptic patients.

**Method:** Observational, descriptive, cross-sectional analysis of the recorded data from all patients diagnosed with epilepsy who attended to our Epilepsy Outpatient Unit in the last 20 years was performed.

**Results:** The sample included 1502 patients (749 men; 49.9%) with epilepsy. Mean age was  $36.7 \pm 14.5$ . Most frequent type of epilepsy was idiopathic generalized epilepsy ( $n = 853$ ; 56.8%). The main etiologic factors in symptomatic epilepsies were, intra perinatal pathology and cerebral vascular diseases. Most common focal epilepsy was temporal lobe epilepsy.

Only 7.2% of patients had no seizures over 1 year of pharmacological therapy and in 70.5% the frequency of seizures was 1–12 per year.

Valproate was most prescribed antiepileptic drug (in 52.5% of cases).

**Conclusion:** We found similar demographic, clinical and treatment response features with previous studies.

#### p0125

### EPILEPSY IN ADULT WITH SUPRATENTORIAL GLIOBLASTOMA: INCIDENCE AND INFLUENCE FACTORS

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**Purpose:** To discuss incidence of epilepsy in adult patients with supratentorial glioblastoma and its influence factors.

**Methods:** To retrospectively analyze clinical data of 184 adults who were not <18 years old and suffered supratentorial glioblastomas. All of the patients underwent comprehensive therapies in our hospital and died in 2003–2013. To count patients' incidence of epilepsy before and after first resective operation (FRO) every 2 month, and analyze the effect of epilepsy prophylaxes with anti-epilepsy drugs (AEDs) in patients who absented preoperative epilepsy.

**Results:** There were 43 (23.37%) patients with epilepsy before FRO, and 126 patients (68.48%) presented epilepsies in the whole history of glioblastoma. The active epilepsy reached over 80% in patients with survival time over 13 month of FRO. Patients with glioblastomas at frontal lobes and temporal lobes presented high incidence of epilepsy. Among the 33 adults with epilepsy before FRO, patients with total removal of glioblastoma presented significant less postoperative seizure than those without total removal. The patients with glioblastomas performed epilepsy prophylaxes with AEDs for not <6 month had significant less postoperative epilepsy and high Karnofsky score than those without AEDs or with AEDs for 1 month.

**Conclusion:** The incidence of epilepsy in adult patients with glioblastomas was high, and those epilepsy presented poor response to AEDs treatment in were poor. AEDs prophylaxes for epilepsy should be not <6 month.

#### p0126

### THE SUDEP SAFETY CHECKLIST LIST PROJECT: STEPS TOWARDS SELF-MANAGEMENT OF SUDEP RISK FOR PATIENTS WITH EPILEPSY (PWE)

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**Purpose:** To assess the usefulness and acceptability of the introduction of the SUDEP Safety Checklist to clinicians, PWE and their carers to routine clinical use across different settings.

**Method:** The Checklist is an easy reference, practical, evidence based tool that is quickly completed in clinic to support prioritisation of clinical activity, give a baseline to compare change of risk factors and have meaningful communication.

A comprehensive literature review developed the checklist (Shankar R et al. *Seizure* 12/2013). Further evidence was gained from a 9 year SUDEP population study (Shankar R *Seizure* 4/2014). Previously unrecognised findings included only 20% PWE had contact with specialist services in the previous year prior demise and in most deaths there was a noted clinical worsening of seizures in the previous 3–6 months. The Checklist was introduced in routine practice 2013 in local epilepsy clinics in Cornwall UK with feedback from 200 PWE/carers. A telehealth project used the Checklist on a quarterly basis to monitor 15 high risk but stable PWE of 90 PWE registered in a community-based general practice (catchment 16,000).

**Results:** 80% PWE accessing Cornwall epilepsy services had their SUDEP risk assessed and recorded compared to 4% nationally (Waddell B et al. *Seizure* 01/2013), following a NICE guideline (2004 & 2012). 98% PWE/carers responded positively to the use of the Checklist, whilst 2% were neutral. 17% PWE monitored using the telehealth Checklist received a step-up of care with interventions that would not have happened otherwise.

**Conclusion:** The SUDEP Safety Checklist is useful to both doctors and PWE leading to a step-up of care and better awareness of safety. Clinicians reported that the checklist raised awareness of management of patients at risk of SUDEP. The Checklist is now being developed as a digital Application to support PWE with self-monitoring of risk.

p0127

### HAND POSTURE AS LOCALIZING SIGN IN ADULT PARTIAL EPILEPTIC SEIZURES

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**Purpose:** One of the most challenging aspects for the medical treatment of adult epilepsies is their tendency to become resistant to antiepileptic drugs. It is estimated that 40% of chronic epilepsies fail to respond to medical treatment. While much interest is rising in the development of disease-modifying drugs, to this day the most effective intervention in controlling medically resistant epileptic seizures is the surgical removal of the epileptogenic zone. The clinical semiology of the epileptic seizures contains lateralizing and localizing information, but unlike lateralizing signs, distinct recognized localizing signs are few, rare and not easily detected on video. With this study we aim to identify specific localizing signs that could help the pre surgical evaluation, through the analysis of ictal hand postures.

**Method:** We evaluated ictal hand postures in videos of patients who underwent epilepsy monitoring and surgery between 1999 and 2005 at the Seizure Disorder Center of UCLA (62 patients) or at the Centro Specialistico Chirurgia dell'Epilessia "C. Munari" of the Ospedale Niguarda in Milan (53 patients). As we were aiming to investigate

the presence of distinct hand postures that correlated with specific localizations, inclusion criteria were 1 year of seizure freedom after surgery and a sustained hand posture in at least one of the recorded seizures.

**Results:** Sustained hand postures were present in 83% of frontal lobe patients (where they were mostly bilateral) and 59% of temporal lobe patients (where they were mostly contralateral). We divided hand postures into 7 classes depending on the reciprocal position of the fingers (extended hand, gun, thumb-up, fist, cup, pincer, thumb-on-top). We found a striking correlation between frontal localization and the "fist" and the "gun" posture, and between temporal localization and the "pincer" posture.

**Conclusion:** These results are meant to be used as a new complimentary tool, during phase 1 surgical evaluation.

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p0128

### EFFECTS OF PROBIOTIC CONSUMPTION ON ABSENCE SEIZURES

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**Purpose:** Probiotics are living microorganisms in intestinal microflora which are beneficial for human health. Childhood Absence Epilepsy is a common epileptic disorder of childhood. It is characterized by typical absence episodes with electroencephalography (EEG) pattern of bilateral, synchronous and symmetric 3 Hz spike-and-wave discharges. There are two validated similar rat models of absence epilepsy, Genetic Absence Epilepsy Rats from Strasbourg (GAERS) and Wistar Albino Glaxo from Rijswijk (WAG/Rij). To this date, there are no clinical neither experimental studies about effects of probiotics on absence epilepsy. In this study, we investigated the effects of probiotics on absence seizures in GAERS.

**Method:** GAERS were used to examine the effects of probiotics. Nine male rats were divided into two groups (Group 1, n = 5; Group 2, n = 4). The animal in both groups were fed with free access to food and water. Commercially available probiotic product was given in the water to one group of animals. This period was 1 month. Then surface electrodes were implanted for EEG recordings. Analysis of EEG recordings was considered in cumulative total duration and total number of absence seizures which are characterized by spike-and-wave discharges.

**Results:** Analysis of spike-and-wave discharges between probiotic group and standard group showed no significant difference in both aspects of cumulative total duration and total number (p > 0.05). On the other hand, probiotic group consumed more than the other group (p < 0.05).

**Conclusion:** The results of our study showed that probiotic consumption has no effect on total duration and number of spike-and-wave discharges of GAERS in 1 month feeding period. The consumption of water is increased in probiotic group because of the ingredients of the commercially available product. We hope that this study may shed light on interaction between absence epilepsy and probiotics. Further studies are needed.

p0130

### ACEA, A SELECTIVE CANNABINOID CB1 RECEPTOR AGONIST COMBINED WITH LEVETIRACETAM STIMULATES NEUROGENESIS IN ADOLESCENT MOUSE BRAIN

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**Purpose:** Hippocampal neurogenesis is very important for proper learning and memory functions. Seizure attacks, by alterations of neurogenesis, may contribute to progressive memory dysfunction. The aim of the study was in vivo evaluation of the impact of arachidonyl-2'-chloroethylamide (ACEA), a highly selective cannabinoid CB1 receptor agonist combined with levetiracetam (LEV) on proliferating neural precursor cells in mouse brain. Additionally, we established the relationship between treatment with ACEA in combination with LEV and hippocampal neurogenesis in mouse brain.

**Method:** All experiments were performed on adolescent male CB57/BL mice. The following drugs were used: levetiracetam (LEV), arachidonyl-2'-chloroethylamide (ACEA), phenylmethylsulfonyl fluoride (PMSF). PMSF was used to limit the degradation of ACEA by inhibiting the fatty acid amide hydrolase. Experiments were conducted in two time points: Time point 1- acute response of proliferating neural precursor cells to ACEA and LEV administration (Ki-67 staining) Time point 2 - long term response to ACEA and LEV administration (BrDU, Neun, GFAP staining). Confocal microscopy and cell counting was done using Zeiss microscope and ImageJ software.

**Results:** ACEA in combination with PMSF significantly increased the total number of Ki-67 positive cells comparing to the control group. Similarly, ACEA combined with LEV increased the number of Ki-67 positive cells, whereas PMSF, administered alone had no significant impact on proliferating cells. Moreover, ACEA with PMSF administered alone and in combination with LEV had a significant impact on neurogenesis increasing the total number of BrDU, particularly neurons comparing to the control group, whereas LEV administered alone significantly reduces the total number of NeUN/BrDU-positive cells compare to the control group.

**Conclusion:** ACEA combined with LEV stimulates the process of proliferation, migration and differentiation of newborn cells, while chronic administration of LEV itself decreases neurogenesis. Obtained results make possible in vivo determination of the neurogenesis after drugs administration.

p0132

### A DIRECT MECHANISM FOR THE MCT KETOGENIC DIET IN SEIZURE CONTROL

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**Purpose:** Ketogenic diets are low-carbohydrate, high-fat diets that are used to treat children and adolescents with refractory epilepsy. In the medium-chain triglyceride (MCT) ketogenic diet a large proportion of

fats is provided through the medium chain fatty acids decanoic acid and octanoic acid. Whilst ketogenic diets have been used successfully for decades in seizure control, their mechanism of action is not yet understood.

**Method:** We are using the *Xenopus laevis* oocyte expression system to investigate a potential role of medium chain fatty acids in reducing excitatory signal transduction mediated by AMPA receptors. AMPA receptors have been demonstrated to mediate neuronal hyperexcitability and seizure generation and are a target for epilepsy drug development. We employed the two-electrode voltage clamp (TEVC) method to study the effects of decanoic acid and octanoic acid on receptor activation in the presence of glutamate and the desensitization inhibitor cyclothiazide.

**Results:** Here we show that decanoic acid, but not octanoic acid, inhibits AMPA receptor mediated currents (IC50 0.52 mM at GluA2/3) in a non-competitive, subunit dependent and use-dependent manner. Using mutant constructs that are resistant to the well-characterized non-competitive AMPA receptor antagonist GYKI 53655, we also demonstrate that decanoic acid interacts with the receptor at a site distinct from the proposed GYKI binding site. To further investigate the mechanism by which decanoic acid reduced AMPA receptor activation we have assessed inhibition in the presence of cyclothiazide and show that the inhibitory effect of decanoic acid is influenced by AMPA receptor desensitization.

**Conclusion:** Our results suggest that the fatty acid decanoic acid contributes to seizure control by directly reducing AMPA receptor mediated currents through a novel mechanism that stabilizes the receptor conformation in the desensitized state.

p0133

### ANTI-EPILEPTOGENIC ACTIVITY OF SALVIANOLIC ACID B IN KAINATE-INDUCED MODEL OF TEMPORAL LOBE EPILEPSY IN THE RAT

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**Purpose:** Temporal lobe epilepsy (TLE) is a chronic neurological disorder that is characterized by spontaneous recurrent seizures. Among involved pathological mechanisms, the role of oxidative stress in the development of TLE has been documented. While salvianolic acid B (Sal B) is an efficient antioxidant with neuroprotective property, but its action has not been investigated in kainate-induced model of TLE. In the present study, the effect of Sal B was evaluated in this respect.

**Method:** Male Wistar rats (n = 40) were randomly allocated into four groups: sham-operated, Sal B-pretreated-sham-operated (intraperitoneal administration of Sal B at a dose of 10 mg/kg for 1 week), kainate (intrahippocampal injection of kainic acid at a dose of 0.8 µg), and Sal B-pretreated-kainate.

**Results:** In kainate group, seizure activity was high and recurrent, intense mossy fiber sprouting was observed, averaged iEEG amplitude was higher, a severe neuronal loss was observed in CA3 region of the hippocampus in Nissl staining and some markers of oxidative stress were greater in hippocampal homogenate versus sham group. In contrast, administration of Sal B significantly decreased these changes.

**Conclusion:** This study indicates that Sal B could attenuate some kainate-induced impairments in the rat through attenuation of oxidative stress and prevention of the development of epileptogenic circuits.

p0134

### ENDOGENOUS ACTIVITY OF NMDA RECEPTORS CONTRIBUTES TO THE ENHANCED GLUTAMATERGIC TONE AND HYPEREXCITABILITY IN RESECTED BRAIN SAMPLES OBTAINED FOR PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY

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**Purpose:** Altered synaptic transmission is one of the primary causes of seizure generation in patients with mesial temporal lobe epilepsy (MTLE). Enhanced excitatory drive-mediated by glutamate receptors is responsible for hyperexcitability in these patients. The present study is designed to delineate the contribution of NMDA receptors to the glutamatergic tone in patients with MTLE.

**Method:** Resected brain samples were obtained from patients with MTLE and for non-epileptic control experiments tumour margin obtained during tumour surgeries were used. Using whole cell patch clamp technique spontaneous excitatory postsynaptic currents (EPSCs), sensitive to NMDA receptor antagonist APV (50  $\mu$ M) and AMPA receptor antagonist CNQX (10  $\mu$ M) were recorded from pyramidal neurons at -70 mV in slice preparations obtained from patients with MTLE. We also examined the effects of selective receptor antagonists on spontaneous fast current transients (CTs), which represent action potentials, recorded from these pyramidal neurons under cell-attached configuration.

**Results:** We observed that frequency of EPSCs were higher in slices obtained from patients with MTLE compared to that in case of non-epileptic controls. Both APV and CNQX reduced the frequency of EPSCs but the magnitude of reduction of EPSC frequency by APV is higher compared to that by CNQX in case of MTLE. We found that the frequency of CTs in pyramidal neurons is higher in case of MTLE samples compared to non-epileptic controls. The frequency of CTs increased in the absence of extracellular  $Mg^{2+}$  in both MTLE and control samples. In  $Mg^{2+}$ -free condition APV completely blocked the CTs frequency in case of MTLE specimens.

**Conclusion:** This study suggests that there is increase in the basal synaptic glutamate activity in slice preparations obtained from patients with MTLE. Endogenous activity of NMDA receptors significantly contributes to the enhanced glutamatergic synaptic transmission and neuronal firing on to the pyramidal neurons in MTLE.

p0136

### EFFECTS OF CONTINUOUS LOW-DOSE MERCURY CHLORIDE (HGCL<sub>2</sub>) EXPOSURE IN GESTATIONAL AND LACTATION PERIODS ON SWD ACTIVITY AND SUBCONVULSIVE-DOSE PTZ-INDUCED SEIZURE IN GENETICALLY ABSENCE EPILEPTIC WAG/RIJ RATS

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**Purpose:** Mercury is a ubiquitous environmental toxin that causes a wide range of adverse health effects in humans, especially in the fetus' and infants' early neurodevelopmental period. Effects of chronic low-dose maternal exposure to mercury on features of absence epilepsy, epileptogenesis and subconvulsive dose of PTZ-induced seizure were investigated in 5-month-old offspring WAG/Rij rats.

**Method:** WAG/Rij pregnant rats were exposed low-dose HgCl<sub>2</sub> (im. injection) or saline chronically during gestational/lactation periods. Offspring rats were divided into four groups; HgCl<sub>2</sub>-exposed groups (which were subdivided; SWD activity and PTZ-induced seizure group) and control groups (which were subdivided; SWD activity and PTZ-induced seizure group) consisting of 32 rats. After 5 months, HgCl<sub>2</sub>-exposed and control rats were placed singly into plexiglas cage, connected to EEG leads, habituated to the experimental conditions. Then, the EEG was continuously recorded in freely moving rats for 1 h. Numbers and mean-durations of the SWDs were calculated off-line analysis. Next to the EEG, behavior changes during the subconvulsive-dose PTZ-induced seizure were observed and scored.

**Results:** All WAG/Rij rats exhibited spontaneously occurring SWDs (hallmarks of absence epilepsy) on EEG and behavioural symptoms of absence epilepsy. According to EEG findings, HgCl<sub>2</sub>-exposed group showed a significant decrease in number of SWDs compared to the control. Our results also suggest that a subconvulsive-dose of PTZ induced generalized tonic-clonic seizures and increased the seizure intensity in HgCl<sub>2</sub>-exposed group ( $p < 0.05$ ).

**Conclusion:** Mercury exposure was found to be associated with epileptogenesis at early period of brain development. While inorganic mercury-exposure in WAG/Rij rats lead to very rapid progression in PTZ-induced seizure steps, and increases seizure intensity, it suppressed absence epileptic SWD activity. We can explain these results with the degeneration of GABAergic inhibitor interneuron in cortical region after mercury exposure (O'Kusky et al., 1989, Inad et al., 2011).

p0137

### NO EVIDENCE FOR HUMAN PAPILLOMAVIRUS INFECTION IN FOCAL CORTICAL DYSPLASIA IIB

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**Purpose:** The aetiology of Focal Cortical Dysplasia Type IIB (FCDIIB) remains enigmatic in patients suffering from drug-resistant epilepsy, and an aberrant activation of the mammalian target of rapamycin complex 1 signalling pathway (mTORC1) was detected in this developmental brain malformation. Recently, the human papillomavirus (HPV) oncoprotein E6 has been identified as a potent activator of mTORC1, and HPV16 E6 described to persist in balloon cells obtained from surgical FCDIIB specimens. Although this observation was replicated by an independent second report, it contradicts current knowledge of HPV biology. HPV infects the squamous or mucocutaneous epithelium; haematogenic spread into other tissues has not been observed. In addition, brain carcinogenesis has never been reported in FCDIIB patients. Herein, we have tried to confirm two previous reports of HPV16 E6 infection using an independent series of 14 surgical specimens with histopathologically confirmed FCDIIB.

**Method:** Snap-frozen FCDIIB specimens were tested for HPV DNA using the primer set for amplification of the complete E6 reading frame of HPV16 and three other sets of primers (two consensus primer sets detecting multiple HPV genotypes, and another primer set specifically used for HPV16). Furthermore, formalin-fixed and paraffin-embedded (FFPE) histopathological preparations were immunohistochemically analysed using previously described antibodies directed against the HPV E6 oncoprotein.

**Results:** All 14 FCDIIB specimens were negative for HPV DNA with all four primer sets. Antibodies directed against the HPV E6 epitope showed weak labelling of cytoplasm in balloon cells, as previously described in FCDIIB, but also in other cell populations.

**Conclusion:** Our data did not confirm previously reported evidence for HPV16 detection in FCDIIB.

p0138

### CHARACTERIZATION OF THE CORTICAL INITIATION SITE IN MOUSE MODELS OF ABSENCE EPILEPSY

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**Purpose:** The EEG hallmark of absence seizures, spike-and-wave discharges (SWDs), are not generalized from their very start despite their classical characterization as generalized events. Experimental work has shown that in genetic rat models of absence epilepsy (WAG/Rij and GAERS), SWDs can be detected in a localized cortical area (i.e. the perial region of the somatosensory cortex) before they spread to other cortical areas and to thalamic territories. A similar observation has been made in children with absence epilepsy, where the existence of a putative cortical initiation site was found mostly in fronto-parietal areas. In particular, it will be interesting to know why human sufferers and rat models have different initiation sites, and whether all well-established animal models have a similar initiation site in somatosensory cortex. Thus, we investigated the presence of a putative initiation site by recording multisite local field potentials (LFPs) in different cortical areas of genetic mouse models (Stargazer and GAT-1 knock-out) and in the pharmacological  $\gamma$ -hydroxybutyrate (GHB) model of absence epilepsy.

**Method:** Animals were stereotaxically implanted with recording electrodes over the frontal, motor, anterior and posterior somatosensory, and visual cortices and allowed 3 days of recovery before the 2 h recording session start. The delays of propagation between each pair of recording sites were analysed.

**Results:** LFP recordings in freely moving Stargazer mice ( $n = 6$ ) revealed that typical SWDs at 4-7 Hz concomitant with behavioural arrest were observed in the primary motor cortex  $84.59 \pm 10.39$  msec before other cortical sites. In GAT-1 knock-out ( $n = 6$ ) and GHB ( $n = 5$ ) models, SWDs started in posterior somatosensory cortex  $120.6 \pm 10.72$  and  $67.54 \pm 17.3$  msec, respectively, before other cortical areas.

**Conclusion:** These results suggest that the cortical initiation site can vary across species and models of absence epilepsy. In stargazer mice the initiation site is in the motor cortex and different from the other mice models.

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p0139

### ELECTROENCEPHALOGRAPHIC CHARACTERIZATION OF A MURINE MODEL OF SEPTIC ENCEPHALOPATHY

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**Purpose:** Sepsis and septic shock is a major cause of admission and death in intensive care units. In 60% of cases, septic associated

encephalopathy complicates severe infections resulting in mortality or at least persistent cognitive dysfunction. The mechanisms underlying this septic encephalopathy are complex and involve ischemic and neuro-inflammatory processes. Electroencephalographic studies (EEG) in humans show early signs that can be predictive of this encephalopathy.

**Method:** To better understand the pathophysiological mechanisms underlying the EEG modifications present in this septic encephalopathy, we used a murine model. Sepsis is induced by caecal ligation and puncture (CLP) in adult WT c57bl6 mice previously implanted with a telemetric device for prolonged EEG recording.

**Results:** 31 mice were implanted with a telemetric device at least 1 week before inducing sepsis. Animals were monitored until full recovery and recording of a normal EEG. Sepsis was induced by CLP in 16 animals, and by intraperitoneal injection of LPS (lipopolysaccharid) in 10 animals. 5 animals were implanted and used as controls. 50% of the CLP induced sepsis mice died within 3 days. EEG recordings showed findings similar to humans, i.e slowing of the background activity, disappearance of circadian rhythms, slow waves, and a microvolted activity preceding death with a concomitant hypothermia.

**Conclusion:** The telemetric study of a murine model of septic encephalopathy successfully replicated the EEG findings of human septic encephalopathy. Therapeutic tests can therefore be performed in this model to improve the global and cognitive outcome of this severe condition.

p0141

### INCREASED SUPEROXIDE DISMUTASE 1 BY LAMOTRIGINE AMELIORATES SUPEROXIDE ANION-RELATED CELL DEATH AFTER PILOCARPINE-INDUCED STATUS EPILEPTICUS IN MICE

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**Purpose:** Various reactive oxygen species (ROS) afterpileptic seizure has been related to neuronal death and subsequent epileptogenesis. However, the role of superoxide anion, one of the powerful ROS, in the seizure-induced cell death has been remained unclear. We investigated the role of superoxide anion in seizure-induced cell death and the possible mechanism of neuronal protection underlying lamotrigine treatment in regard to superoxide dismutase (SOD)1, one of superoxide dismutases responsible for destroying free radicals.

**Method:** Adult male C57BL/6J mice were given injections of pilocarpine 30 min after scopolamine treatment. Seizures were terminated by diazepam injection after status epilepticus (SE) at various time points. Hippocampal cell death was assessed by cresyl-violet and TUNEL staining. The hippocampal superoxide anion was assessed using in situ detection of oxidized hydroethidine (HEt); administered intravenously after SE. SOD1 level was analyzed by both Western blot and semi-quantitative immunofluorescent staining in subfields of hippocampus. Various doses of lamotrigine (30, 60 mg/kg, i.p.) were administrated.

**Results:** Superoxide anion significantly increased after pilocarpine-induced SE, compared to normal control, which were in concordance with increased cell death by TUNEL and cresyl-violet staining. The production of superoxide anion in response to SE was least in dentate gyrus, which was reversely in agreement with maximal SOD1 increase in the same subfield. Treatment of lamotrigine significantly decreased the production of superoxide anion after SE, compared to vehicle treatment. In addition, hippocampal neuronal death was significantly attenuated by lamotrigine treatment in dose dependent manner. SOD1 also increased by lamotrigine treatment after SE, and the effect was the greatest in CA3

subfield, in which SOD1 was significantly decreased without lamotrigine treatment.

**Conclusion:** Increased production of superoxide anion after SE may contribute hippocampal neuronal death after seizure. The lamotrigine may inhibit superoxide anion-related neuronal cell death through increase of SOD1 in the hippocampus after SE.

p0142

#### ANTIPILEPTIC EFFECTS OF AXITINIB ON PENTYLENETETRAZOL-INDUCED KINDLING IN RATS

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Last time tyrosine kinase B receptor is supposed as a target for epilepsy development. Hence, the aim of the investigation was to identify peculiarities of pentylenetetrazol (PTZ) induced kindling development under conditions of axitinib administrations, which is able to inhibit intracellular tyrosine kinase signaling pathways. Experiments were performed on Wistar male rats, which have been kindled daily with PTZ (30.0 mg/kg, i.p.). Daily p.o. administrations of axitinib have been performed in 60 min before PTZ in a dosage of 5.0 mg/kg. The latency of kindled seizures was prolonged by axitinib and the difference with the control group (kindling + saline solution, p.o.) became significant started from 5th PTZ injection. The development of generalized seizures have been substantially postponed and the precipitation of generalized seizures was observed starting from 12th PTZ administration while in control group generalized fits have been observed after 7th injection of epileptogen. Significant differences when compared with the control group maintained up to the final 21-d PTZ injection. Electrographic manifestations were characterized by more than two-fold times decrease of amplitude and frequency of spike discharges along with shortening periods of generalized spike-wave activity in ventral hippocampus. Two weeks free from PTZ administration with the consequent injection of PTZ (30.0 mg/kg, i.p.) resulted in clonic type of seizures in rats treated with axitinib while in control kindled rats repeated generalized seizures have been registered. Axitinib (10.0 mg/kg, p.o.) did not modify acute generalized seizures induced with PTZ (60.0 mg/kg, i.p.), while in early period of kindling (24 h from the last administration of PTZ) prevented the development of generalized seizure fits. The pronouncement of antiepileptic action of axitinib was comparable with such one registered after diazepam administration in a dosage of 0.5 mg/kg, i.p. Hence, gained data showed antiseizure activity of axitinib on the model of PTZ-induced kindling.

p0143

#### ELECTRON MICROSCOPIC INVESTIGATION OF NEUROGENESIS AND GABA IMMUNOREACTIVITY IN GENETIC ABSENCE EPILEPTIC RATS

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**Purpose:** Hippocampal neurogenesis is an issue which has not been investigated in genetic absence epilepsy rats from Strasbourg (GAERS). In the present study, we investigated neurogenesis in adult and 3-week-old GAERS to determine if newly formed neurons form synapses with GABAergic terminals.

**Method:** Brain tissues were obtained by perfusion fixation and processed for electron microscopic assessments. Thin sections from hippocampal dentate gyrus were double-labeled for anti-GABA and anti-DCX (doublecortin) antibodies using a postembed immunogold method. Sections were photographed on the transmission electron microscope.

**Results:** DCX immunoreactivity was demonstrated in axons, dendrites and cell bodies in all groups. We observed that DCX(+) structures formed synapses and synapse-like contacts with GABAergic structures. There were more DCX(+) dendrites in all groups compared to DCX(+) axons. Also, the percentage of asymmetrical synapses formed by DCX(+) profiles was higher than that of symmetrical synapses in all groups. 21-day-old animals were qualitatively observed to have more GABA labeling in DCX(+) mossy terminals (MTs), compared to 3-month-old groups. DCX(+) profiles including GABA showed a tendency to increase in 21-day-old groups compared to 3-month-old groups; and there was a trend for an increase in GABA and DCX densities in GAERS, although the differences were not statistically significant.

**Conclusion:** Our data demonstrated that newly born DCX-ir neurons join the local hippocampal network. In 21-day-old animals, DCX(+) profiles had an increased tendency to be GABAergic; this may result from the trophic effects of GABA in immature animals. Our findings showing more GABA labeling in MTs of immature animals may suggest accumulation of GABA inside the terminal. Further studies are needed to measure extracellular levels of GABA. In our study, DCX and GABA densities had a tendency to increase in GAERS groups; suggesting that the alterations in the hippocampus may also have effect on the mechanisms of absence epilepsy.

p0144

#### PERAMPANEL EFFECTS IN THE WAG/RIJ RAT MODEL OF EPILEPTOGENESIS WITH COMORBID DEPRESSIVE-LIKE BEHAVIOR

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**Purpose:** Perampanel (PER), a selective non-competitive AMPA-receptor antagonist has demonstrated efficacy and tolerability in patients with partial seizures[1]. PER is approved for adjunctive treatment of partial seizures with or without secondarily generalized seizures in patients with epilepsy[1]. PER exhibited broad-spectrum efficacy in several animal models of acute seizures[2]. Prevention of epileptogenesis is a priority research field in epilepsy. Therefore, we determined whether an early long-term treatment with PER might alter both absence seizure development and onset of depressive-like behavior in the WAG/Rij rat model of absence epilepsy, epileptogenesis and comorbid depressive-like behavior.

**Method:** Rats were early long-term treated with PER (1 and 3 mg/Kg; o.s.), as previously described[3]. Briefly, drug treatment lasted 17 weeks and was started at P30. Age-matched control rats were kept under the same housing conditions over the same period of time with vehicle. At the age of ~6 and ~10 months, all WAG/Rij rats underwent three EEG recordings of 3 h each on 3 consecutive days and determination of immobility time in the forced swimming test (FST)[3]. Plasma PER levels were determined by HPLC-UV.

**Results:** PER (only at 3 mg/kg/day) significantly reduced (about 45%) the development of absence seizures in WAG/Rij rats both at 6 (1 month after treatment withdrawal) and 10 months of age (5 months after treatment withdrawal). In FST, PER at both doses tested reduced immobility time displaying antidepressant-like properties at 6 and 10 months of age. Mean plasma levels (ng/mL) throughout treatment were PER 1 mg/kg = 13.99 (SD 2.73) and PER 3 mg/kg = 33.13 (SD 9.83), which remained stable every month.

**Conclusion:** These findings suggest that PER might have antiepileptogenic properties and positive effects on animal behavior, displaying, therefore, possible disease-modifying properties.

- [1] Franco et al. *Expert Opin Pharmacother* 2014;15:637–44.  
 [2] Russo et al. *Expert Opin Investig Drugs* 2012;21:1371–89.  
 [3] Citraro et al. *Epilepsia* 2014;55:1284–91.

#### p0145

##### ZEBRAFISH-BASED IDENTIFICATION OF APICULAREN A AS AN ANTICONVULSANT COMPOUND FROM MYXOBACTERIA

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**Purpose:** Given the need for new and improved anti-epileptic drugs, this study focused on the identification of new anticonvulsant compounds from myxobacterial origin, using zebrafish larvae as the primary screening model.

**Method:** A library of 242 myxobacterial compounds from the Helmholtz Centre for Infection Research was screened for neuroactivity by the zebrafish photomotor response (PMR) assay. Next, neuroactive hits were screened for anticonvulsant activity by the zebrafish pentylenetetrazole (PTZ) seizure assay. Anticonvulsant activity was further investigated by local field potential (LFP) recordings of the zebrafish midbrain to evaluate the effect of a compound on PTZ-induced epileptiform discharges. Finally, anticonvulsant activity was investigated in the mouse timed i.v. PTZ assay to investigate activity in the mouse model.

**Results:** 56 myxobacterial compounds were identified as neuroactive by the PMR assay. 24 selected neuroactive hits were screened for anticonvulsant activity by the zebrafish PTZ assay. 8 compounds were identified as anticonvulsant hits and confirmed for their activity. Among them, apicularen A significantly reduced PTZ-induced seizure behavior with high efficacy in a concentration-dependent manner and significantly reduced PTZ-induced epileptiform discharges. Moreover, apicularen A significantly increased the PTZ dose needed to trigger forelimb clonus in the mouse timed i.v. PTZ assay.

**Conclusion:** Myxobacteria are increasingly recognized as producers of bioactive secondary metabolites and can be considered as a rich source for drug discovery. In this study, we identified for the first time anticonvulsant myxobacterial compounds using a zebrafish-based screening approach. The anticonvulsant activity of apicularen A was verified by LFP recordings of the zebrafish midbrain and confirmed in the mouse timed i.v. PTZ model. Our results not only support the potential of myxobacterial compounds, but expand their utility as an interesting source for anti-epileptic drug discovery.

#### p0146

##### EVALUATION OF BLOOD-BRAIN BARRIER DAMAGE USING GADOLINIUM-ENHANCED MAGNETIC RESONANCE IMAGING IN GENERALIZED SEIZURE MODEL MICE

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**Purpose:** Our aim was to non-invasively and sequentially evaluate blood-brain barrier (BBB) damage in generalized seizure model (GSM) mice, using gadolinium (Gd)-enhanced magnetic resonance imaging (MRI). In addition, we assessed whether valproate (VPA) could prevent BBB damage.

**Methods:** GSM mice were kindled with daily intraperitoneal administration of 40 mg/kg pentylenetetrazol (PTZ). After each PTZ injection, convulsive behaviors were observed, and seizures were classified and scored as follows: 0 = normal; 1 = immobilization, sniffing; 2 = short myoclonic jerk; 3 = continuous myoclonic jerk; 4 = generalized limbic seizures or violent convulsions; 5 = continuous generalized seizures. Five consecutive scores of 4 or 5 were required to ensure kindling. We evaluated changes in BBB permeability using the signal intensity (SI) ratio of Gd-enhanced MRI. Because the contrast material does not enter the brain parenchyma through the BBB in naive mice, an increase in SI was indicative of BBB damage. SI was sequentially measured at baseline, score 1, score 3, PTZ-kindled, and post-kindled 1 week after PTZ withdrawal. Moreover, SI was measured in the mice pretreated with VPA (400 mg/kg, p. o.) before PTZ injection.

**Results:** SI values (mean ± SE) at score 1, score 3, PTZ-kindled, and post-kindled increased to  $0.7 \pm 0.2$ ,  $7.2 \pm 1.9$ ,  $7.4 \pm 1.6$ ,  $6.8 \pm 1.3\%$ , respectively. All values (except at score 1) were significantly higher than those at baseline ( $p < 0.05$ ). We did not observe significant differences at score 3 or post-kindled, compared to PTZ-kindled. In VPA-pretreated mice, SI significantly increased to  $8.8 \pm 1.6\%$  compared to baseline, although convulsions were fully controlled.

**Conclusions:** Our data suggest that BBB damage started before PTZ-induced kindling was acquired. BBB damage was irreversible after PTZ-induced kindling. In addition, VPA prevented epileptic convulsive seizures, but could not suppress BBB damage in PTZ-kindled mice.

#### p0148

##### RNA-SEQ ANALYSIS OF HIPPOCAMPAL TISSUES REVEALS NOVEL CANDIDATE GENES FOR DRUG REFRACTORY EPILEPSY IN PATIENTS WITH MTLE-HS

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**Purpose:** Array-based profiling studies shows aberrant gene expression patterns during Epileptogenesis. We have performed transcriptomic analysis of the hippocampal tissue resected from the patients with MTLE-HS undergoing surgery by RNAseq to investigate the molecular basis of epileptogenicity, the anti-epileptogenic mechanisms and pharmacoresistance in MTLE.

**Method:** Resected brain samples were obtained from patients with MTLE and for non-epileptic control experiments tumour margin obtained during tumour surgeries were used. RNA sequencing was performed using standard protocols on Illumina HiSeq 2000 platform. Reannotation, mapping and bioinformatic data analysis was performed using the Bowtie/TopHat/Cufflinks/Cuffmerge/SAMtools and SIFT/PolyPhen/SpliceSeq algorithms. Differential gene expression data was validated through quantitative real-time polymerase chain reaction (qPCR).

**Results:** At a fold change of  $\geq 2$ , deregulation of more than 1000 genes was observed. Significantly at  $p < 0.005$ , 33 genes were up-regulated and 25 were down-regulated. SNP analysis revealed 7000 novel SNPs and 1517 novel Indels, 29 possible damaging mutations. Using SpliceSeq algorithm software we identified 58 novel differential splicing isoforms ( $\geq 10$ FPKM). Correlation analysis of gene expression, SNP and splicing data revealed 9 DEGs showing SNPs and 11 DEGs showing differential

splicing patterns. Only in one of the DEG SCN1 both SNPs as well as differential isoforms were observed.

**Conclusion:** Using RNAseq approach we could identify a set of differentially expressed genes, novel transcripts, pseudogenes, lncRNAs, gene fusions, SNPs and splicing isoforms of various genes associated with MTLE. The Gene Ontology and pathway analysis revealed important hubs of molecules involved in neuroinflammation, modulation of synaptic transmission, and the restructuring of neuronal networks supporting the intrinsic severity hypothesis of pharmacoresistance. This study identified few important molecules like SCN1, CSNK1B, CABP1, KIF5A and ASB4 which needs further evaluation for their potential as diagnostic/prognostic biomarkers in intractable MTLE.

p0149

#### COMPARISON OF SPIKE-WAVE DISCHARGES IN NORMAL ANIMALS TO SPONTANEOUS RECURRENT SEIZURES ACROSS SEVERAL ANIMAL MODELS OF ACQUIRED EPILEPSY

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**Purpose:** Several publications have reported spontaneous recurrent seizures in animal models of acquired epilepsy based on brain insults proposed to be more realistic than previous models. These studies have reported periods of oscillatory, spike-and-wave discharges (SWDs) with blank-stare behaviors, which have been considered to represent the non-convulsive seizures of acquired epilepsy. However, similar events are also seen in normal animals (i.e., non-injured controls). The present studies compare SWDs with non-convulsive and convulsive seizures recorded in diverse animal models of acquired epilepsy.

**Methods:** In addition to pilocarpine- and kainate-induced status epilepticus, animal models (rats) included unilateral carotid occlusion with hypoxia at postnatal day 7, controlled cortical impact in adults, and a model of penetrating brain injury in adults.

**Results:** SWD-like events in normal rats were much shorter in duration than the non-convulsive and convulsive seizures in the models of acquired epilepsy (see above). Normal SWD events were typically <5–10 second, but could be longer. The convulsive/non-convulsive seizures in the models of acquired epilepsy were routinely 20–40 second, but could also be longer (e.g., 2–3 min). The SWD-like events started abruptly; non-convulsive/convulsive seizures began with a progressive increase in amplitude and/or frequency. Inter-spike intervals were relatively homogeneous during normal SWD, while frequency of EEG spikes in non-convulsive and convulsive seizures was more variable with distinct shifts in pattern. The non-convulsive/convulsive seizures often had post-ictal depression, which was not seen with SWDs in normal rats.

**Conclusions:** Electrographic properties of SWD in normal rats (and after postnatal hypoxia or fluid percussion injury) could be readily distinguished from seizures characteristic of acquired epilepsy. Non-convulsive and convulsive seizures in these diverse models of brain injury were much more similar to each other than they were to the SWDs.

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## Clinical Neurophysiology 1 Sunday, 6th September 2015

p0150

#### CHANGES IN CARDIAC AUTONOMIC CONTROL DURING SEIZURES

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**Purpose:** The spread of ictal activity to autonomic centres in the central nervous system might lead to cardio-vascular changes observed in seizures. This might contribute to an increased risk of sudden unexpected death in epilepsy (SUDEP). Simultaneous monitoring of cardio-vascular variables during seizures could provide a better understanding of the mechanisms involved in SUDEP. Our aim is to identify autonomic patterns and correlate them with ictal electroencephalographic changes and different seizure types.

**Method:** We are undertaking a continuous and non-invasive study of autonomic parameters including heart rate (HR), blood pressure (BP), cardiac vagal tone (CVT) and cardio-sensitivity to baroreflex (CSB) during seizures in subjects undergoing pre-surgical evaluation in the telemetry unit at King's College Hospital.

**Results:** Of fifteen subjects recruited, only three had seizures during the study. We have analysed five simple partial seizures from subject one; one subclinical seizure and two complex partial seizures (CPS) from subject two and three CPS of which two became secondarily generalised from subject three. A consistent pattern in CSB is observed with a mean reduction in amplitude from baseline of 72% in CPS and 90% in secondary generalised. CVT showed no consistent pattern in the seizures. BP showed a tendency to increase during CPS and secondarily generalised seizures. Heart rate changes varied between patients in CPS but showed a trend in secondarily generalised: HR decreased during CPS phase ( $\bar{x}$ =26% from baseline) and subsequently increased after secondary generalisation ( $\bar{x}$ =41% from baseline).

**Conclusion:** Ictal events may affect neurological centres involved in the control of cardio-sensitivity to baroreflex, yet little has been published on this. A change in CSB might compromise haemodynamic stability and cardio-protection mechanisms making it a potential SUDEP risk factor. Inter-individual variability was seen in HR changes and CVT changes but not CSB. Further seizures will be recorded to confirm these findings.

p0152

#### A FAMILY WITH JUVENILE MYOCLONIC EPILEPSY COMPLAINING OF TREMOR: ANALYSIS WITH ACCELEROMETER AND SOMATOSENSORY EVOKED POTENTIALS

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**Purpose:** There are some juvenile myoclonic epilepsy (JME) patients complaining of tremor. The etiology and generators of this tremor are not clear and speculated as being a valproate (VPA) enhanced essential tremor (ET). On the other hand, some families from different countries with cortical myoclonic tremor and epilepsy have been reported. Unfamiliar-

ity with this syndrome often leads to an initial misdiagnosis of essential tremor or progressive myoclonus epilepsy. We aimed to report three siblings who had been initially evaluated as JME since their common complaints of tremor were under-recognized.

**Method:** We assessed three siblings (2 females) diagnosed with JME complaining of hand tremor by their median somatosensory evoked potentials (SEP) and accelerometric recordings, after their consent. In all of them, tremor had started before VPA treatment. We compared their results with JME patients without tremor (14 patients) and 14 patients with essential tremor (ET).

**Results:** These patients have characteristic clinical and EEG pictures of JME with photosensitivity. The N20-P25 and P25-N35 amplitudes of SEP were significantly higher in three siblings with tremor and epilepsy compared to both JME group without tremor and ET group. Typical “giant SEPs” were observed in all of the siblings. Tremor frequencies were similar with ET group whereas they had mild interrupting non-rhythmic myoclonus and lower amplitude of tremor, suggesting a different and cortical origin.

**Conclusion:** Our findings might be interpreted as tremor characteristics are different in JME patients in comparison to ET patients regarding to intervening myoclonus in distal part of the fingers and lower tremor amplitudes. JME patients complaining of tremor should be investigated with caution for other familial syndromes and possibility of cortical tremor.

#### p0153

##### DYNAMICS OF CONVULSIVE SEIZURE GENERATION, TERMINATION AND RECOVERY

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**Purpose:** To elucidate the nature of mechanisms underlying seizure onset, termination and postictal generalized EEG suppression (PGES) in convulsive seizures (CSs).

**Methods:** We validate predictions from a multi-unit neural mass computational model with EEG recordings from 48 CSs from 48 people with refractory, localisation-related epilepsy.

**Results:** We confirm a previous finding that both simulated and real ictal periods show a probability distribution suggestive of an underlying deterministic process and show that this is also the case for postictal periods. Plasticity towards the end of a seizure may be reflected by the exponential increase of interclonic intervals (ICIs). In the model, the plasticity feedback parameter determines the time needed for the system to recover to the normal state. In the human data, the ICI at the end of a seizure is associated with the occurrence and duration of PGES.

**Conclusion:** Our findings point towards an autonomous inhibitory neuronal process underlying seizure termination and PGES, relevant for understanding epileptic transitions and sudden unexpected death in epilepsy (SUDEP).

#### p0154

##### COMPUTER ASSISTED ANALYSIS OF RESPONSE TO HIGH FREQUENCY (50HZ) STIMULATION DURING INTRACRANIAL PRESURGICAL STEREOEEG MONITORING

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**Purpose:** Patients suffering from pharmacoresistant focal epilepsies candidate to epilepsy surgery are monitored using intracerebral stereo-EEG to identify the epileptogenic zone (EZ). In recent years an increasing number of computer assisted analysis of intracerebral human signals have been developed to define biomarkers of the EZ and to improve the definition of the boundaries of the area of resection during epilepsy surgery. We propose a method to automatically define a subset of EZ contacts, focusing on response to high frequency (HF, 50 Hz) stimulation performed for diagnostic purposes during invasive stereo-EEG studies with intracranial electrodes. Our study presents a new algorithm to evaluate signal parameters that

- 1) are characterized by a rapid response and
- 2) are masked by the HF stimulation artifacts,
- 3) cannot be visually identified by clinical neurophysiologist.

**Method:** We use time/frequency analysis, graph theory and clustering methods to extract parameters and to test their specificity to the EZ. The analysis was focused on 60–80 Hz activity that represents the largest frequency component evoked by HFS. The distribution of HFS-evoked fast activity across all recording contacts (up to 162) allowed to define different clusters of contacts. Retrospective correlation to the EZ identified by the clinicians on the basis of traditional visual stereo-EEG analysis allows to quantify and validate the algorithm performance.

**Results:** On a group of 13 retrospectively analyzed patients we found an average specificity = 84.8% and sensitivity = 81%, showing a good matching between the algorithm selection and the clinical identification.

**Conclusion:** HFS-evoked activities not only contributes to the definition of the epileptogenic network, but also represent a tool for biomarkers definition. Epileptogenic regions show different response patterns to HF stimulation, suggesting the opportunity to identify specific parameters automatically extracted by computer assisted analysis.

#### p0155

##### MODULATION OF CORTICO-CORTICAL FUNCTIONAL CONNECTIVITY WITH INTRACEREBRAL PAIRED-PULSES ELECTRICAL STIMULATIONS

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**Purpose:** Widely used with transcranial magnetic stimulation (TMS), paired pulses (PP) paradigm has scarcely been studied with intracranial stimulation, and never on distant cortico-cortical connections.

**Method:** We performed intracerebral PP electrical stimulation in three patients with refractory focal epilepsy investigated with depth electrodes located within the primary motor cortex:

(i) Functional connectivity between the primary motor cortex and the other brain regions was first explored using cortico-cortical evoked potentials (CCEPs). Electrical stimulation consisted in series of 10 pulses of 1 ms duration at 0.2 Hz frequency and 3 mA intensity.

(ii) We then studied the impact of PP stimulations, using 5, 15, 50, 100 and 200 ms interstimulus intervals (ISIs).

Given the variable morphology and duration of CCEP, theoretical PP curves were built to analyze ISI-induced modulation – inhibition, facilitation or unchanged –. To assess the paradigm validity, concomitant motor evoked potentials (MEPs) were recorded on the contralateral psoas. After electrodes withdrawal, these MEPs were compared to those obtained with MRI-guided TMS of the same area, with 120% resting motor threshold intensity and conditions identical to intracranial stimulations.

**Results:** Intracranial PP stimulation of the primary motor cortex could induce ISI-dependent modulation of both MEPs and CCEPs. The pattern of MEPs modulation observed with intracerebral stimulation was similar with that observed with TMS. Modulations of CCEPs after PP stimulations were more heterogeneous across cortico-cortical connections and could be different from those observed in concomitant MEPs.

**Conclusion:** Intracranial PP electrical stimulation can modulate MEPs as well as CCEPs, which provide interesting perspectives for future cortical excitability studies.

#### p0156

### DIRECT ELECTRICAL CORTICAL STIMULATION TO RECONSTRUCT EPILEPTIFORM AFTERDISCHARGE NETWORKS

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**Purpose:** Extra-operative direct electrical cortical stimulation (DCS) is widely employed to map eloquent cortex in patients with intracranial electrodes undergoing pre-surgical assessment for refractory epilepsy. Some DCS trials can evoke local paroxysms of epileptiform activity, known as afterdischarges (ADs). Currently, there is limited understanding of the neurophysiological underpinnings of ADs, and more generally of the effects of DCS on local neural dynamics. In this study, we compared intracranial electro-encephalogram (iEEG) traces containing post-stimulation ADs against baseline activity, using power-spectral and covariance analyses, to identify the AD-underlying networks.

**Method:** We collected iEEG data recorded from subdural grid electrodes of three patients with pharmacoresistant frontal lobe epilepsy secondary to focal cortical dysplasia. For each subject, we extracted a 32s interictal baseline trace, corresponding to a state of active wakefulness, and post-stimulation segments containing ADs. Power spectra for delta, theta, alpha, beta, low gamma and high gamma bands were obtained for all the extracted traces. Across each frequency band, we calculated the number of iEEG channels in the AD-containing epochs with power values significantly different from baseline levels (which we refer to as “nodes”), and quantified their discordance. Further, considering all frequency bands, we identified abnormal networks of nodes by comparing their covariance matrices with Fourier-adjusted surrogate data.

**Results:** Delta band power and, to a lesser extent, theta band power were increased in AD-containing post-stimulation traces compared to baseline. Conversely, alpha, beta, low gamma and high gamma band powers were in line with baseline levels. Covariance matrices for the AD-containing

traces showed striking reconfigurations of neural interactions compared to baseline.

**Conclusion:** After discharges evoked by DCS are associated with an increased proportion of slow components in the EEG power spectrum. Our analysis also allows us to define the network of nodes that participate in the after discharge.

#### p0159

### SEIZURES DUE TO FAMILIAL PAROXYSMAL KINESIGENIC DYSKINESIA LEADING TO MISDIAGNOSIS AS EPILEPSY

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Paroxysmal dyskinesias are movement disorders characterized by sudden episodes of involuntary movements, of which Paroxysmal kinesigenic dyskinesia (PKD) is the most common form, characterized by recurrent brief involuntary hyperkinesias triggered by sudden movements. Because of the similarity in clinical manifestation, and the fact that most patients respond well to antiepileptic drugs, PKD is easily misdiagnosed as epilepsy. We report a family with PKD in which the presenting patient, a 22 year old man, was misdiagnosed as Epilepsy for 12 years. He suffered intermittent paroxysmal episodic involuntary movements, including stiff rigidity in trunk and limbs only during physical exercise or when startled, which spontaneously ceased seconds later. In the family history, his father and younger brother also had similar symptoms. Second generation exon gene sequencing technology was used to determine *PRRT2* gene and 73 genes associated with epilepsy; results showed that the *PRRT2* gene exon 2 was found in abnormal sequence: c. 649 dupc, frameshift mutations, which was characterized finally as PKD. Subsequent treatment with Carbamazepine was successful. This case illustrates the difficulty in diagnosis, and differences in the pattern of intermittent paroxysmal episodic involuntary movements other than epilepsy.

## Comorbidities 1 Sunday, 6th September 2015

#### p0160

### EVALUATION OF SEX HORMONES IN EPILEPSY PATIENTS

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**Purpose:** The main focus of epilepsy treatment is seizure control with the minimum side effects of the antiepileptic drugs. These side effects are mostly on hematologic, dermatologic or liver and renal functions. However, in recent years, studies investigating the relation of antiepileptic drugs and sex hormones or sexual functions have increased.

**Method:** This study includes the epilepsy patients (18–45 years old) followed up in outpatient clinics of Haseki Research and Training Hospital, in the period of April to November 2014. Forty-five out of the 83 patients were treated with monotherapy (carbamazepine, valproic acid, lamotrigine or levetiracetam) and 38 with polytherapy. The patients and healthy controls (n = 40) were assessed by blood tests. These blood tests include sex hormones-dehydroepiandrosterone-sulphate (DHEA-S), sex hormone binding globuline (SHBG), follicular stimulating hormone (FSH), luteinizing hormone (LH), testosterone (TT), prolactin, estradiol (E2). In addition; valproic acid or carbamazepine serum levels were tested in the corresponding patients. Free androgen index (FAI) was calculated.

**Results:** We found that FAI was lower and SHBG was higher compared to control group ( $p = 0.002$ , for both). Serum carbamazepine levels of men were positively correlated with FSH and PRL, and negatively correlated with FAI ( $p = 0.046$   $p = 0.035$   $p = 0.032$ ; respectively). Women on carbamazepine treatment had a positive correlation between serum carbamazepine levels and PRL levels ( $p = 0.036$ ). Polytherapy did not show a statistical significant difference in sex hormone levels. The time length of lamotrigine use was positively correlated with E2 levels ( $p = 0.003$ ).

**Conclusion:** In conclusion, this study shows that levitracetam had no effect on sex hormones, and lamotrigine had nearly none. However, carbamazepine and valproic acid had affected sex hormones of epilepsy patients.

p0161

### QUALITY OF LIFE MEASURES EVALUTION OF THE PATIENT'S RELATIVES HAVING TEMPORAL AND EXTRATEMPORAL LOBE EPILEPSY AND WHOM EPILEPSY SURGERY APPLIED OR NOT APPLIED

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**Purpose:** In patients with epilepsy the life quality is depends mainly on the clinical properties of seizures, the type of seizures, the duration of epilepsy, the frequency and the seriousness of seizures as well as use of antiepileptic drugs, surgical processes, being in any psychiatric comorbid situations like depression or anxiety.

**Method:** In this practice we studied 203 patients followed in our neurological department, The University of Uludag, Medical Faculty. For each patient and the relatives Epilepsy Evaluating Form, socio-demographic informing form, The Scale of Life-Quality in Epilepsy, the short form life-quality scale, the short form life-quality scale of world health organization and the scale of social performance which evaluate the patients basic abilities and social attitudes in terms of their quantities were applied. Also to evaluate the depression and the anxiety in patients and the relatives, we applied other scales: Hamilton Anxiety Grading Scale and Hamilton Depression Grading Scale.

**Results:** Between the groups we found statistically remarkable differences in life-quality, social performances, depression and anxiety levels of both patients and the relatives. It was observed that the lowest scores was accompanied with the resistant TLE patients with regard to the sub scales of life quality and the social performance. The highest anxiety and depression scores were detected in those as well. It was thought that these results could be related to any damage in the limbic system components.

**Conclusion:** We found a negative correlation between the depression and anxiety levels and the life-quality in both the patients and the relatives. As a conclusion, in plans that aims to increase the life qualities of patients, it is needed to take precautions in order to enhance the social performance, to investigate the patients and the relatives in context with psychiatric comorbid situations such as anxiety and depression and to inform the patients to consult psychiatric specialists.

p0163

### HEADACHE IN PATIENTS WITH JUVENILE MYOCLONIC EPILEPSY

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**Purpose:** Headache and epilepsy are often comorbid disorders in the general population. The objective of this study was to assess the prevalence of headache in juvenile myoclonic epilepsy (JME).

**Method:** In this work, we studied in 200 patients with JME had presented our epilepsy outpatient clinic. Headache was classified in patients using a questionnaire, is validated according to ICHD-III beta. We investigated the correlations between the characteristics of the headache and the clinical manifestations of JME.

**Results:** One hundred-fifteen (57.5%) of patients conducted survey were women and 85 (42.5%) of them were men. The mean age of patients was  $26.7 \pm 8.46$  (12–55). The mean duration of epilepsy after seizures onset was  $10.7 \pm 7.28$  years (1–35). Headache was presented in 111 (55, 5%) patients. 47 had migraine [30 migraine without aura, 17 migraine with aura]. Four patients with migraine had tension-type headache in addition. Fifty-two patients had only tension-type headache. Headache of 81 (40, 5%) patients were not related with seizures. Headache was specified postictal in 18 patients (9%), preictal in 10 (5%), ictal in 2 (2%).

**Conclusion:** In this study, it is demonstrated that both migraine and tension-type headache in patients with JME is higher than expected from studies on the general population. Furthermore, migraine with aura, the subtype of migraine, was also found higher in patients with JME in comparison with general population. Because of their comorbidity and shared same risk factors, it gives strongly rise to thought that migraine and epilepsy have some common pathophysiological pathway.

p0166

### INFREQUENT A TRAUMATIC PAINFUL COMPLICATION OF SINGLE SEIZURE

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**Purpose:** Bilateral or unilateral fracture/dislocation of the shoulders is exceedingly rare. Typical position of the shoulder during a convulsion is adduction, internal rotation and flexion, with the spasm the humeral head is forced superiorly and posteriorly over the glenoid cavity, resulting in fracture/dislocation.

**Methods:** We describe three cases that presented to us with unprovoked seizures and were discovered to have fractures/dislocation.

**Results:** Case Series. **Case 1:** 51-years-old-male presented with a single unprovoked generalized tonic clonic seizure (GTCSz), developed post seizure, bilateral shoulder pain, history of seizure seven years ago, he was not on AEDs. X-ray Shoulder showed bilateral Comminuted humeral head fracture, which CT confirmed, started on AEDs. Neuroimaging & EEG were normal. Transferred to Orthopedics for further management. **Case 2:** 68-year-old-male presented with single GTCSz, right-sided shoulder pain post seizure, he had history of epilepsy and was seizure free and was taken off AEDs, prior history of head trauma. His X-ray Shoulder showed right sided fracture head of humerus and dislocation. He was restarted on AEDs, his neuroimaging and EEG were normal. Transferred to Orthopedics. **Case 3:** 65-year-old-male presented with first seizure of life time, GTCSz, developed post seizure bilateral shoulder pain. X-ray Shoulder showed bilateral humeral head fracture, confirmed by CT shoulders, his EEG and MRI brain-negative, started on AEDs, in view of severity of single seizure, transferred to Orthopedics.

**Conclusions:** We present three cases with fracture/dislocation, which were sequelae to a single unprovoked GTCSz and none of the patient were on any AEDs. Compliance and adherence to AEDs is the key for preventing these complications, in non-drug naïve patients.

p0167

### FROM DUSK, TILL DAWN; PATIENTS WITH BOTH EPILEPSY AND OBSTRUCTIVE SLEEP APNEA SYNDROME (OSAS)

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**Purpose:** With this study, we aimed to document the demographic data, polysomnographic (PSG) findings and analyze effects of PAP treatment on seizure control in OSAS patients with epilepsy.

**Method:** All 7092 PSGs performed between the years of 2006–2015 were reviewed retrospectively. All of the data is gathered from the patient files and via phone visits.

**Results:** In our sleep disorders unit, 456 PSGs were performed in patients diagnosed with epilepsy, 24 of them were diagnosed with OSAS and undergone PAP titration. The mean age was 43.83; male to female ratio was 19:5. Fourteen patients had comorbid diseases other than epilepsy. Four patients had NREM parasomnias, two had restless leg syndrome and two had REM sleep behavior disorder (RBD) clinically. Seventeen patients were diagnosed as severe OSA, ten patients had worsening of the OSA and/or desaturations in supine position and eleven patients during REM sleep. Ten patients had focal pathological activity during sleep EEG. Four patients had epileptic seizures during the PSG. Two patients had REM without atonia, one of them also had RBD. All patients were using at least one antiepileptic drug and 9 of them were using multiple antiepileptics. Three patients stopped using one or more antiepileptics and dosage was decreased in one patient during follow up. Two patients needed additional antiepileptic drugs, after PAP titration; both of them were not consistent with the PAP usage and follow up.

**Conclusion:** We aim to present the contribution of the PAP treatment on seizure control and antiepileptic drug necessity.

## Comorbidities 2 Sunday, 6th September 2015

p0168

### MIGRAINE AND EPILEPSY: METABOLIC ABNORMALITIES

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**Purpose:** Migraine and epilepsy are comorbid neurological diseases possessing a number of clinical and pathophysiological manifestations including a positive effect of taking anticonvulsants.

**Method:** 22 migraine and 28 epilepsy patients underwent <sup>1</sup>H-MRS (Proton magnetic resonance spectroscopy). Migraine and epilepsy were diagnosed according to International Recommendations. In brain, the peaks of N-acetylaspartate (NAA), choline (Cho), creatine (Cr) are the most evident ones. The statistical analysis was performed using the program STATISTICA 6.0.

**Results:** The results of 1H-MRS revealed the reduction in the most important correlation of NAA/(Cho+Cr) less 0.71 in hippocampus on the side of epileptic focus in the half of patients and in the other half - on both sides. Significant changes in the NAA/ (Cho+Cr) correlation in hippocampus were recorded in all patients, mainly on the side of a hemispheric localization, with being more marked in a comorbid aura seizure that ranged from 0.29 to 0.64 (normal - more 0.71). As for changes in the correlation of neurometabolites in thalamus, there was a downward tendency for all indices only in migraine with aura. Migraine without aura was characterized by Cho/Cr decreasing without changing other metabolite

concentration. The change in the correlations of neurometabolites in a frontal lobe in migraine without aura and significant Cho/Cr changes in migraine with aura attract our attention. Studying the investigated occipital lobe indices revealed their decrease in patients with aura on a hemispheric side which was similar to changes in the hippocampal complex ( $p < 0.05$ ).

**Conclusion:** Thus, hippocampus is one of the main structures in disintegrating neuronal combinatorics and forms peculiarities of clinical manifestations of paroxysmal states, involving these or those brain areas at these two diseases.

p0169

### THE PROGRAM FOR ACTIVE CONSUMER ENGAGEMENT IN SELF-MANAGEMENT (PACES) IN EPILEPSY

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**Purpose:** Self-management interventions provide patient education to improve medical, role, and emotional management. Previous interventions were developed primarily on expert opinion; reported issues with participant engagement/retention with limited follow-up evaluation. PACES used direct patient needs assessment to derive program content and design for a randomized controlled trial (RCT).

**Method:** Study 1: Sampled two populations: patients age 18 + with chronic epilepsy (n = 165) and epilepsy center health providers (n = 20). All completed surveys about patient psychosocial problems and self-management program design. Study 2: Participants age 18 + with chronic epilepsy, randomized to intervention (n = 41) or control condition (n = 42). The 8-week intervention involved weekly group sessions of 6–8 members co-lead by a psychologist and trained peer. Topics addressed psychosocial concerns from Study 1. Study 3: Telephone-based replication of Study 2 (n = 11); added booster component during follow-up. Study 4: Replication of Study 1 with diverse sample.

**Results:** Studies 1 and 4: Identified two patient subgroups: “epilepsy-only” and “epilepsy-plus,” marked by probable depression and/or cognitive problems. Subgroups differed by psychosocial problem severity. Providers rated patient problems more severe in all domains (Work, Independent Living, Socializing, Life with Epilepsy, Mood, Cognition, General Health and Well-Being, and Medical Care) relative to the “epilepsy-only” subgroup (all  $p < 0.001$ ). Study 2 and 3: At 8 weeks, PACES participants improved relative to controls on the ESMS ( $p < 0.0001$ ) and subscales (all  $p < 0.023$ ); ESES ( $p < 0.0001$ ); and QOLIE-31 ( $p = 0.002$ ). At 6 months, PACES participants remained improved on ESMS ( $p = 0.009$ ) and subscales [Information ( $p = 0.005$ ); Medication ( $p = 0.084$ )]; ESES ( $p = 0.040$ ) and QOLIE-31 Energy/Fatigue ( $p = 0.027$ ) and Medication Effects ( $p = 0.003$ ). Attrition was low (8%); program satisfaction exceeded 4.0 out of 5.0.

**Conclusion:** Findings demonstrate dissonance between patient and clinician perceptions of self-management problems. This has implications for engaging patients in therapeutic programs. A consumer generated epilepsy self-management program appears to be a promising intervention.

p0170

### LONG-TERM PSYCHOSOCIAL FOLLOW-UP OF EPILEPSY SURGERY IN TEMPORAL LOBE EPILEPSY WITH HIPPOCAMPAL SCLEROSIS IN A DEVELOPING COUNTRY: WHAT IS IMPORTANT TO EMPHASIZE?

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**Purpose:** To investigate patients' long-term follow-up of postoperative quality of life (QoL) with preoperative indicators of maladjustment status.

**Methods:** We analyzed a consecutive homogeneous series of 120 patients who underwent corticoamygdalohippocampectomy due to drug resistant mesial temporal lobe epilepsy with hippocampal sclerosis in Epilepsy Surgery Program at Universidade Federal de São Paulo between July 2002 and July 2014. Subjects had a follow-up period ranging from five to 10 years. Presurgical assessment of QoL included a semi-structured interview, Beck Depression Inventory (BDI), and Epilepsy Surgery Inventory (ESI-55). The following seven variables were selected to indicate adjustment degree, considered as possible predictors of unfavorable psychosocial outcomes:

- 1- unemployment in a period of 5 years;
- 2- no stable romantic partnership in a period of 5 years;
- 3- dropout from school and/or cognitive daily impairment;
- 4- lack of family support;
- 5- lack of significant friendly relationships in the community,
- 6- psychiatric diagnostic categories (DSM IV);
- 7- BDI scores more than 17 points.

We postulated that the presence of 50% of these variables might be indicative of poor psychosocial functioning. A multivariate analysis was done with a logistic regression model to identify possible clinical and socio-demographic predictors of post-surgical unfavorable adjustment outcome evaluated by clinical and psychosocial interviews.

**Results:** Thirty patients (25%) had four or more factors indicative of poor psychosocial functioning prior to surgery. Preoperative psychosocial maladjustment was related in a long-term follow-up to: dependence perception ( $p = 0.018$ ), worsening family relationship ( $p = 0.005$ ), worsening social status ( $p = 0.012$ ), unemployment ( $p = 0.035$ ), perception of cognitive impairment to remember names ( $p = 0.007$ ), antiepileptic drugs continuation ( $p = 0.003$ ), presence of psychiatric disorder ( $p < 0.001$ ), worsening in scores of Social Adjustment Scale ( $p = 0.008$ ) and QoL domains ( $p < 0.001$ ).

**Conclusion:** Psychosocial functioning before surgery is the most important predictor of psychosocial adjustment and QoL in a long-term follow-up surgical treatment.

Support: FAPESP, CAPES, CNPq. (Brazil)

p0173

### ICTAL ANALGESIA IN TEMPORAL LOBE EPILEPSY - THE MECHANISM OF SEIZURE-RELATED BURNS

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**Objective:** Seizure-related injuries have substantial role in the higher mortality risk of patients suffering from epilepsy. Besides cognitive alterations during seizures, ictal and postictal analgesia may have an impact on seizure-related injuries. We aimed to identify seizure-types increasing the risk of burns by the lack of nociception.

**Methods:** Our patients filled our self-designed burn and pain questionnaire and detailed epileptology data were collected.

**Results:** 51% of the patients reported of subjectively decreased nociception in the ictal or postictal phase and 18% of those answering sustained a burn-accident. Half of them suffered a seizure-related burn incidentally falling to a hot surface. Half of them grasped a hot object or boiling fluid while in complex partial seizure; without defending or removing the limb being burnt and without experiencing pain during or within some minutes after the seizures. All these patients had temporal lobe epilepsy.

**Significance:** The experimentally shown pain-modulator function of the dorsal hippocampus as well as the connections of the temporal lobe to the central pain modulator system could explain the analgesia related to temporal lobe seizures. We wanted to call attention to the existence of ictal analgesia as a risk factor for injuries and to the importance of advising increased burn-prevention for patients with temporal lobe epilepsy.

p0175

### EVALUATION OF ZEBRAFISH AS A POTENTIAL MODEL FOR COGNITIVE IMPAIRMENT ASSOCIATED WITH DRAVET SYNDROME

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**Purpose:** Dravet syndrome (DS) is one of the most frequent genetic epilepsies, with an incidence of 1/30,000. The large majority of DS patients are pharmacoresistant, and do not respond adequately to any of the more than 20 currently available anti-epileptic drugs (AED). Many DS patients suffer from cognitive impairment that can also be aggravated by the seizure medications prescribed. DS mouse models exhibit cognitive deficits similar to those of DS patients, but are only suitable for the evaluation of small number of compounds, thereby limiting their utility for drug discovery. An animal model with higher screening throughput would therefore be of value for drug discovery efforts focused on DS.

**Methods:** Recent studies on zebrafish have demonstrated its ability to be a promising in vivo model for DS. Two different zebrafish DS models - one based on a loss-of-function mutation in the zebrafish ortholog of SCN1A, the other based on an antisense knockdown of this gene - show seizure-like behavior (as determined by automated video tracking analysis of locomotor activity) and epileptiform discharges (as determined by local field potential recordings). Both phenotypes are exacerbated by hyperthermia, as is the case for human DS patients and mouse DS models.

**Results:** We are investigating the cognitive functions of these zebrafish DS models in order to determine possible similarities with cognitive impairment in human DS patients and mouse DS models. Initial data obtained in a light/dark transition assay indicates these DS zebrafish models to exhibit memory impairment. These findings provide an initial insight into the resemblance between human patients and zebrafish in terms of cognitive deficit.

**Conclusions:** Subsequent to an in-depth evaluation of the cognitive functions of these zebrafish DS models, we will use them to evaluate AEDs currently under investigation as potential DS therapeutics as to their possible procognitive activity.

p0176

### PRECEDING ANXIETY AND DEPRESSION IN FIRST SEIZURE PRESENTATIONS? - A SYSTEMATIC PROSPECTIVE APPROACH

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**Purpose:** There is increasing evidence that psychiatric comorbidities (PC) such as anxiety and depression may precede first seizure presentations. This suggests an abnormal biochemical brain environment in which the first seizure presents the “loudest noise” alerting the health care system. Systematic longitudinal data are entirely missing to explore this potential linkage.

**Method:** The Halifax First Seizure Clinic (HFSC) uses a strictly prospective cohort approach with multimodal data (clinical, social, genetics, structural [3T MRI], and functional [routine and sleep deprived EEG]) with follow-up visits at months 6, 12, 24 and 60. Screening for PC also occurred at the time of initial assessment. 63 patients screened for PC were identified with either a first unprovoked seizure (FS) only, n = 12; new-onset epilepsy (NOE= seizures occur within 12 months), n = 14; newly diagnosed epilepsy (NDE= seizures occur longer than 12 months), n = 14; first provoked seizure (FPS), n = 9; psychogenic non-epileptic seizure (PNES), n = 4; others (syncope, migraine etc), n = 10. All study patients completed 3 questionnaires: validated NDDI-E (depression), validated GAD7 (anxiety) and the newly developed Halifax Anxiety Screening Test (HAST). Scoring results were compared to 22 healthy controls. All assessments were performed prior to initial clinical assessment and diagnosis.

**Results:** There was no significant difference in scoring results for any of the identified subcategories compared to the control group except for the FPS that had significantly higher scores on the NDDI-E. A significant trend was observed with increasing scores for depression dependent on the stage/duration of diagnosis as identified by FS < NOE < NDE for the NDDI-E, but no significance for the anxiety tests.

**Conclusion:** Our pilot study confirms the feasibility of PC testing in first seizure assessments. Subcategory analysis suggests shared disturbed neuronal networks in some individuals with PCs manifesting prior to occurrence of an epileptic seizure and more significant PC the longer seizures existed.

## Drug Therapy 1 Sunday, 6th September 2015

p0180

### ANTICONSULSANT ACTIVITY AND MECHANISMS OF ACTION OF GINGER (*ZINGIBER OFFICINALE* ROSCOE) RHIZOMES

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**Purpose:** Ginger (*Zingiber officinale* Roscoe.) is used commonly in treatment of many ailments. Ginger contains many biologically active chemical compounds that are known to be important compounds for activation of vanilloid receptors (Vadim N et al. *Br J Pharmacol* 2002; 137: 793–798). These recently cloned vanilloid receptors and their agonists were reported to be involved in several pathological conditions (Awad E et al. *Sudan JMS* 2013; 8(4): 175–180; Calixto J et al. *Pharmacology and therapeutics* 2005;106:179–208). The present study aimed to investigate the potential anticonvulsant activity of ginger extract. Involvement of gamma aminobutyric acid (GABA) and vanilloid receptors in ginger mechanism of action as anticonvulsant were also investigated.

**Method:** Experimental animal models as maximum electroshock (MES) and pentylenetetrazole (PTZ) induced seizures were used to determine the anticonvulsant activity of ginger. Picrotoxin (noncompetitive GABA antagonist) and capsazepine (vanilloid receptor antagonist) were used to determine the possible mediation of GABA and vanilloid receptors respectively in the mechanism of action of ginger as anticonvulsant.

**Results:** Ginger extract (400 mg/kg) produced 100% seizure protection in MES and PTZ induced seizure animal models. The ED<sub>100</sub> of ginger in

the previous two models produced 20% seizure protection in picrotoxin induced seizure animal model indicating possible partial involvement of GABA receptors. Capsazepine produced 80% and 60% block to the anticonvulsant activity of ginger on the MES and PTZ seizure animal models respectively, indicating possible involvement of vanilloid receptors.

**Conclusion:** Ginger represents a potential source for anticonvulsant agents. GABA and vanilloid receptors have a role in the mechanism of action of ginger as anticonvulsant. Vanilloid receptors mediation seems to be a possible new mechanism of anti-epileptic drugs. Crude ginger could be used as potential anticonvulsant agent and/or as co-drug in combination with antiepileptic drugs, especially if further investigations are conducted clinically to explore its possible safety and efficacious use.

p0181

### USE OF LACOSAMIDE AS ADD-ON THERAPY IN CHILDREN AND YOUNG ADULTS WITH SYMPTOMATIC EPILEPSY CAUSED BY MALFORMATIONS OF CORTICAL DEVELOPMENT

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Use of lacosamide as add-on therapy in children and young adults with symptomatic epilepsy caused by malformations of cortical development. Malformations of cortical development (MCD) are recognized causes of neurodevelopmental disorders and drug resistant epilepsy; epilepsy type and outcome are variable. Lacosamide (LCM) is a new antiepileptic drugs mostly used in treatment of refractory epilepsy, approved for adults over 16 years but still off-label in children.

**Purpose:** The aim of the study is to evaluate efficacy of LCM as add-on therapy in children and young adults with refractory symptomatic epilepsy due to MCD.

**Method:** Prospective, uncontrolled, observational, open label therapeutic trial. Population: 22 patients (14 M). Age: range 4–27 y (median 14 y). Type of MCD: 10 patients with focal cortical dysplasia (FCD); 12 patients multilobar or hemispheric malformations. Type of epilepsy: 17 focal epilepsy; 5 epileptic encephalopathy. Follow-up 12 months. LCM was started at 1 mg/kg and increased weekly. Dose: 4–10 mg/kg/die in children and 200–400 mg/die in young adults.

**Results:** At the end of follow 54% of our patients were responders (13% seizure-free). Three patients of four younger than 6 years with FCD were responders without side effects. Better response was observed in patients with focal epilepsy (64%). Discontinuation rates: 18% for inefficacy. Side effects (dizziness, headache, somnolence, irritability) were observed in 4 patients during titration, disappeared with reduction of add-on therapy.

**Conclusion:** Despite limits of our study (small sample and uncontrolled trial) LCM seems efficacy and safety as add-on therapy in children and young adults with symptomatic refractory epilepsy due to MCD. We observed better results in younger patients with focal epilepsy.

p0182

### SEIZURE CONTROL WITH LACOSAMIDE (≤400 MG/DAY) FOLLOWING CROSS-TITRATION FROM A SODIUM CHANNEL BLOCKER IN PATIENTS WITH PARTIAL-ONSET SEIZURES RECEIVING STABLE DOSES OF LEVETIRACETAM

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**Purpose:** This subgroup analysis investigates the effect of in-label dosages ( $\leq 400$  mg/day) of adjunctive lacosamide (LCM) on seizure control following cross-titration from a sodium channel-blocking antiepileptic drug (SCB) in patients with partial-onset seizures not adequately controlled on levetiracetam and SCB dual therapy.

**Methods:** In this prospective, Phase 4, open-label study (SP0980; NCT01484977), LCM was titrated to 200–600 mg/day per investigator's judgment. SCB reduction started when LCM dosage reached 200 mg/day. A 12-week Baseline Period (8 weeks retrospective; 4 weeks prospective) was followed by a 21-week Treatment Period (9-week Cross-titration; 12-week LCM Maintenance).

**Results:** Of 120 patients who started on LCM titration, 118 had an efficacy assessment, 51 of whom received lacosamide  $\leq 400$  mg/day at any time during Treatment (mean age,  $41.4 \pm 12.1$  years; mean epilepsy duration,  $20.1 \pm 16.18$  years; median seizure frequency/28 days, 5.67; complex POS, 36/51 of patients; secondarily generalized seizures, 43/51). The most common concomitant SCBs were lamotrigine (21/51), carbamazepine (17/51) and oxcarbazepine (11/51). The median LCM dose was 398 mg/day (199–400 mg/day) during Maintenance ( $n = 39$ ) and 285 mg/day (67–375 mg/day) during Treatment ( $n = 51$ ). 33/51 (64.7%) patients completely withdrew their SCB. Of 37/51 patients who completed Maintenance, 7/37 (18.9%) were seizure-free. Seizure freedom was highest for patients who withdrew from carbamazepine (4/8, 50%). During the full Treatment Period, 16/51 patients (31.4%) experienced  $\geq 75\%$  reduction and 26/51 (51.0%) experienced  $\geq 50\%$  reduction in seizure frequency. The most frequently reported adverse events were dizziness (8/51 [15.7%]), headache (6/51 [11.8%]), fatigue (4/51 [7.8%]), and nausea, urinary tract infection, fall, and depression (3/51 [5.9%] each); 3/51 (5.9%) patients discontinued due to an adverse event.

**Conclusion:** In a relatively difficult-to-treat population, flexible titration of LCM to  $\leq 400$  mg/day with cross-titration of SCB, when added to a stable dose of levetiracetam, provided additional seizure control and was generally well tolerated.

**Disclosure:** UCB Pharma-funded.

#### p0183

### ANALYSIS OF ADJUNCTIVE BRIVARACETAM IN ADULTS WITH PARTIAL-ONSET (FOCAL) SEIZURES ACCORDING TO PATHOLOGICAL SUBSTRATE: METHODOLOGY FROM A PHASE III STUDY

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**Purpose:** Several studies in patients with newly-diagnosed and medically refractory epilepsy have shown that antiepileptic drug (AED) efficacy varies greatly according to patient pathological substrate (aetiology) identified by neuroimaging. However, clinical trials conducted to date to evaluate AED safety and efficacy have not stratified patients according to presence/type of epileptogenic lesion identified by neuroimaging. Here, we report on a post-hoc methodology to evaluate the feasibility of stratifying patients according to the pathological substrate.

**Method:** Subject Eligibility Criteria forms were routinely completed at screening. This analysis was conducted on data from a Phase III trial (N01358; NCT01261325) in adults with partial-onset (focal) seizures (POS) receiving add-on placebo, BRV 100 mg/day or 200 mg/day. To ensure that the correct aetiologies were identified, clinical semiology, neuroimaging and electroencephalogram data were independently

reviewed by three expert consultants blinded to efficacy and tolerability results. Lesions shown by neuroimaging were classified as epileptogenic/non-epileptogenic, and sorted into one of nine categories (vascular, mesial temporal sclerosis [MTS], tumoural, disorders of cortical malformations [DCM], neurocutaneous syndromes, traumatic, infectious, immunological, others). Kappa coefficient analysis was performed to measure agreement between the results of each reviewer. In cases of disagreement, the experts discussed the findings to reach agreement.

**Results:** Of 714 patients analysed, 39.4% lesions were considered epileptogenic; kappa ranged between 0.672–0.746, indicating substantial agreement between reviewers. Epileptogenic lesions were MTS (33.8%), DCM (21.0%), vascular (16.4%), traumatic (9.6%), infectious (6.4%), tumoural (5.0%), neurocutaneous syndromes (0.7%), immunological (0.0%) and other lesion types (7.1%). Kappa based on category ranged between 0.534–0.707, indicating substantial agreement.

**Conclusion:** In this subgroup analysis, epileptogenic lesions in adult patients with POS were most commonly classified as MTS, DCM and vascular lesions, with agreement between the three blinded reviewers. This analysis demonstrates the feasibility of stratifying POS patients participating in clinical trials according to pathological substrate.

UCB supported.

#### p0184

### PRELIMINARY DATA ON THE EFFICACY AND TOLERABILITY OF ESLICARBAZEPINE AS ADJUNCTIVE THERAPY IN PATIENTS WITH REFRACTORY PARTIAL EPILEPSY

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**Purpose:** To assess the efficacy and tolerability of eslicarbazepine, a new antiepileptic drug recently marketed in Italy, as add-on treatment in patients with refractory partial epilepsy.

**Method:** A prospective, open label, longitudinal study conducted in 24 patients with refractory partial epilepsy. The study included 3 periods: Baseline (3 months), drug titration (2 weeks), Observation, during which ESL could be increased until the maximum tolerated dose. Inclusion criteria comprised: age over 16 years, diagnosis of focal epilepsy, resistance to at least 2 previous antiepileptic drugs, stable concomitant antiepileptic therapy within 3 months. Exclusion criteria were: progressive neurological disease, poor compliance, history of pseudo-seizures, pregnancy. Efficacy has been evaluated by comparing the mean monthly seizures frequency of the last quarter observation period with baseline seizures frequency using T-test for dependent sample.

**Results:** The mean number of antiepileptic drugs tried before ESL was  $6.5 \pm 3.8$  (2–15). ESL was administered at a daily mean dose of 914 mg (400–1600). The mean duration of observation was 3.1 months: 8 patients didn't reach three months and were excluded from efficacy analysis which, therefore, included 16 patients. A statistically significant reduction of the mean monthly seizures rate was observed ( $25.22 \pm 26.47$  vs.  $18.04 \pm 19.7$ ,  $p = 0.03$ ). 1 patient withdrew ESL for seizure worsening, 2 patients (8%) complained side effects (somnolence) that did not lead to discontinuation.

**Conclusions:** Our data, even if preliminary, suggest good efficacy and excellent tolerability of ESL as add-on therapy in partial epileptic patients, especially considering the severe refractoriness of patients and the drug administration in polytherapy.

p0185

**ANTICONVULSANT EFFECTS OF BRIVARACETAM IN THE 6 HZ FULLY-KINDLED MICE**

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**Purpose:** Brivaracetam is a selective, high affinity ligand for the synaptic vesicle protein 2A (SV2A), which recently demonstrated positive phase III results as adjunctive treatment of focal-onset seizures in adults with epilepsy. Previous preclinical studies with brivaracetam revealed broad spectrum anticonvulsant properties in diverse models of seizures and epilepsy (Matagne et al., BJP 2008). We wanted to evaluate the potency and efficacy of brivaracetam in the newly developed 6 Hz corneal kindling model in mice, comparing its effects against both partial and generalised seizures.

**Method:** Chronic electrical stimulations at 6 Hz were carried out twice daily according to a previously described protocol (Leclercq et al., Epilepsy Res 2014). During the course of kindling stimulations, initial partial seizures evolved to secondarily generalised seizures. Fully-kindled mice displayed at least ten consecutive secondarily generalised seizures and were selected for testing after brivaracetam administration (ip, 30 min).

**Results:** Brivaracetam afforded protection against secondarily generalised seizures with an ED<sub>50</sub> value of 3.5 mg/kg. It was also able to reduce significantly the median seizure severity score from 5 to 2 from the dose of 3 mg/kg. Protection against partial seizures (scores 1-2) was also observed, with an ED<sub>50</sub> of 51.5 mg/kg.

**Conclusion:** These experiments confirm the high potency and efficacy of brivaracetam against both partial and generalised seizures in the newly developed 6 Hz kindling model.

p0186

**INTAKE OF ANTIEPILEPTIC DRUGS BY PATIENTS WITH EPILEPSY: A SURVEY IN PHARMACIES AND PATIENTS TREATED BY SPECIALIZED NEUROLOGISTS**

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**Purpose:** Poor adherence to antiepileptic drugs (AED) is considered as a main cause of breakthrough seizures. We assessed how patients handle drug intake, e.g. we asked the patients what they do if they recognize that they had missed a dose and for barriers to adherence.

**Method:** The study was performed in cooperation with the Regional Chamber of Pharmacists of Rhineland-Palatinate and 3 neurologists in private practice specialized in epileptology. In total, 108 patients surveyed in 43 pharmacies (Group-P) and 119 patients treated by neurologists (Group-N) completed anonymously a questionnaire on drug intake of AED.

**Results:** The efficacy of AED was rated higher by Group-P compared to Group-N ( $p < 0.01$ ) and more patients were seizure-free in Group-P (72.9% vs. 53.0%,  $p < 0.01$ ). The vast majority of patients rated the tolerability of AED as very good (42.5%) or good (36.2%). Most patients took their AEDs at a fixed time of the day (64.6%) or related to specific

activities, e.g. teeth brushing, (45.6%). Group-N more often used adherence aids, e.g. pill boxes, compared to Group-P (68.6% vs. 46.3%,  $p < 0.01$ ). If patients recognized that they had missed a dose, 45.3% skipped the missed dose (Group-P: 48.1%, Group-N: 43.0%, n.s.); this was especially the case (70.6%) in older patients ( $\geq 60$  years). Different types of tablets (20.9%), unpleasant intake (14.5%), division of tablets (12.3%), and fear of side-effects (10.9%) were the most frequently mentioned barriers to adherence.

**Conclusions:** Gaps in knowledge and shortcomings of AED regimes may affect adherence. Counseling of patients may improve reliability of drug intake and thus reduce the risk of breakthrough seizures. For example, patients should be informed about strategies to improve adherence, e.g. the use of pill boxes, and how to handle the situation when they miss a dose.

Sponsored by Desitin Arzneimittel GmbH.

**Drug Therapy 2  
Sunday, 6th September 2015**

p0188

**EXPOSURE TO LACOSAMIDE IN BLOOD PLASMA DURING ADJUNCTIVE THERAPY AND MONOTHERAPY: PHARMACOKINETIC ANALYSIS OF DATA FROM A CONVERSION TO LACOSAMIDE MONOTHERAPY STUDY**

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**Purpose:** To compare the exposure of lacosamide in blood plasma during adjunctive and monotherapy phases of a conversion to lacosamide monotherapy study in patients with partial-onset seizures.

**Methods:** The lacosamide conversion to monotherapy study (SP902, NCT00520741) comprised an 8-week Baseline, 3-week Titration, 6-week background AED Withdrawal and 10-week lacosamide Monotherapy Phase. Patients (16–70 years) on 1–2 AEDs were randomized to lacosamide 400:300 mg/day (3:1). Blood plasma samples for lacosamide concentration were taken during adjunctive lacosamide (Titration Phase; end of Weeks 1 and 2) and during monotherapy (Monotherapy Phase; end of Weeks 11 and 15, corresponding to 2 and 6 weeks after background AED Withdrawal). Patients providing plasma samples taken between 1.5 and 12 h after the actual dose during the Titration and Monotherapy Phase were included in the analysis. These single samples were used to approximate PK parameters peak and trough lacosamide concentration in plasma under steady state condition [ $C_{\text{peak,ss}}$ ,  $C_{\text{trough,ss}}$ ], area under the concentration-time curve at steady state [ $AUC_{\text{tau,ss}}$ ], and total body clearance [ $CL/F$ ] [Cawello et al. *Epilepsy Res.* 2014]. Log-transformed dose-normalized concentrations and PK parameters (except  $CL/F$  without dose-normalization) were used to conduct paired t-tests for all comparisons between monotherapy and adjunctive therapy. After back-transformation of the differences between means, geometric mean ratios (90%-confidence intervals [CI]) between monotherapy and adjunctive therapy were derived.

**Results:** Mean ratios (90%-CI;  $n = 138$ –173) for the dose-normalized PK parameters ranged from 1.039 (0.993, 1.086) to 1.071 (1.026, 1.118). Because of linear relationship, the results of ratios and CIs were identical for PK parameters  $C_{\text{peak,ss}}$ ,  $C_{\text{trough,ss}}$ , as well as  $AUC_{\text{tau,ss}}$ . The mean ratios for the concentrations were about the same ranging from 1.040 (0.993, 1.093) to 1.068 (1.021, 1.116). Ratios of  $CL/F$  resulted in ranges from 0.934 (0.895, 0.975) to 0.963 (0.921, 1.007).

**Conclusion:** Results of this post-hoc analysis suggest similar lacosamide exposure and  $CL/F$  during adjunctive and monotherapy.

UCB Pharma-Funded

p0189

**LONG-TERM OUTCOME OF 1,805 PEOPLE WITH NEWLY DIAGNOSED EPILEPSY**Z. Chen\*, M.J. Brodie†, D. Liew\*, ‡, P. Kwan\*, §

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**Purpose:** Our previously study demonstrated about two-thirds of the epilepsy patients could remain seizure-free during antiepileptic drug (AED) treatment and those who have an inadequate response to the first AED are likely to have refractory epilepsy. We expanded our study cohort and assessed the long-term response to AED therapy in patients with newly diagnosed epilepsy.

**Method:** We studied 1,805 newly diagnosed and treated epilepsy patients who were prospectively followed up for a minimum of two years (median 11, interquartile range [IQR] 7–16) between 1982 and October 2014. Epilepsy was classified as generalised or focal. Patients were considered to be seizure-free if they had not had any seizures for at least one year. Logistic regression was performed to assess the effect of number of AED used on the treatment outcome.

**Results:** Among the 1,805 patients (46% female, median age at diagnosis 33 years [IQR 21–50]), 1,143 (63%) were seizure-free at the end of study period. The seizure-free rate was not statistically different between patients with generalised and focal epilepsy (67% vs. 62%,  $P = 0.07$ ). 811 (45%) patients became seizure-free on the first AED schedule, 213 (12%) on the second schedule, 4.4% on the third schedule, 1.8% on the fourth to seventh schedules, but none beyond. Among the patients who became seizure-free, 97% did so within the first three schedules; 88% were taking monotherapy and 12% polytherapy. Patients who did not become seizure-free on the first AED had 1.77 times odds of uncontrolled epilepsy for each additional AED tried (95% confidence interval 1.60–1.96) after adjusting for epilepsy classification, age and gender.

**Conclusion:** The probability of achieving seizure-free diminishes for each unsuccessful AED schedule. Despite the available of new AEDs over the last decade, the long-term outcome of epilepsy has not improved substantially.

p0190

**STEVENS-JOHNSON SYNDROME (SJS) INDUCED BY OXCARBAZEPINE (OXC) TREATMENT IN CHINESE PATIENTS WITH EPILEPSY**Q. Dai

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**Purpose:** Investigate the incidence of SJS after treatment with OXC in Chinese epileptic patients.

**Method:** Observation of clinical individual cases .case 1, 17 year-old, male, had a 7 years epileptic history, attack form were SPC, CPC and SGTCS, with febrile convulsion history when he was 1 year old. The patient was treated with VPA 0.5g bid, poor control, on Nov 27, 2014 added OXC began from 150 mg bid for 1 week, then 300 mg bid for 1 week, and finally increased to 450 mg bid 3 days after the treatment with 450 mg bid, the rash occurred, and was diagnosed as SJS. HLA-B \* 1502 allele: positive, Cyp2c19 genetic testing: negative, the rash faded 10 days later after corresponding therapy, finally the AED was changed to LEV. Case 2.5 year-old, male, epileptic history for half a year, with 3 febrile convulsions history at 3–4 year-old, took VPA, seizure free, but EEG still showed epileptic form change of frontal lobe, so on Nov, 2014 VPA was decreased gradually, and OXC was added from 3 ml bid to 5 ml bid weekly, also the rash occurred 3 days later, confirmed SJS. HLA-B \* 1502 allele: negative, Cyp2c19 genetic testing: positive,

the rash also faded 10 days later after corresponding therapy, again the AED was changed to LEV.

**Results:** The SJS induced by OXC may be related with aromatic molecule structure and Asian population. Asian patients with positive HLA-B \* 1502, would have more serious rash if they take carbamazepine (CBZ), OXC has similar molecule structure with CBZ, positive HLA-B \* 1502 allele in our cases is 50%.

**Conclusion:** SJS induced by OXC has certain incidence in Asian population, needs pay more attention to.

p0191

**ESLICARBAZEPINE ACETATE AS ADD-ON TO ANTIEPILEPTIC MONOTHERAPY IN ADULTS WITH PARTIAL-ONSET SEIZURES (EPOS STUDY):****ANALYSIS BY BASELINE ANTIEPILEPTIC DRUG**P. Derambure\*, R. McMurray†, R. Sousa‡, M. Holtkamp§

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**Purpose:** Eslicarbazepine acetate (ESL) is approved as adjunctive therapy for adults with partial-onset seizures, with or without secondary generalisation. The Eslicarbazepine acetate in Partial-Onset Seizures (EPOS) study investigated the effectiveness and safety/tolerability of ESL as add-on to antiepileptic monotherapy in everyday clinical practice across eight European countries. It is important to obtain additional information on how effective an antiepileptic drug (AED) is in combination with different types of other AEDs. Here we present an analysis from the EPOS study of ESL's effectiveness by baseline AED.

**Method:** Adult patients with uncontrolled partial-onset seizures under antiepileptic monotherapy, whose clinician had previously and independently decided to initiate ESL add-on therapy, were included if they provided informed consent. Retention rate, responder rate ( $\geq 50\%$  seizure frequency reduction from baseline) and change from baseline in Quality of Life in Epilepsy Inventory-10 (QOLIE-10) scores were assessed after 6 months according to the most frequent baseline monotherapies ( $>5\%$  of patients).

**Results:** Of 219 patients included in the study, 85, 57, 31 and 14 received baseline monotherapy with levetiracetam (LEV), lamotrigine (LTG), valproate (VAL) and carbamazepine (CBZ), respectively. Retention rates (95% confidence intervals) at 6 months were 100% (76.8–100.0%) for CBZ, 85.5% (76.1–92.3%) for LEV, 80.0% (61.4–92.3%) for VAL and 75.9% (62.4–86.5%) for LTG. Responder rates at 6 months were 92.9% (CBZ), 88.5% (VAL), 81.9% (LEV) and 69.8% (LTG). Mean changes in QOLIE-10 scores at 6 months were -20.1% (LEV), -16.7% (LTG) and -13.1% (VAL); not calculated for CBZ due to low numbers.

**Conclusion:** The retention, efficacy and impact on quality of life of ESL as add-on to antiepileptic monotherapy were favourable regardless of the type of monotherapy to which ESL was added. These findings must be interpreted with caution due to low subgroup patient numbers.

Study supported by Eisai

p0192

**EFFECT OF TREATMENT WITH LEVETIRACETAM ON COGNITIVE EVOKED POTENTIALS AND COGNITIVE ABILITIES OF PATIENTS WITH EPILEPSY**W. Derkowski\*, †

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**Purpose:** To investigate the effect of levetiracetam on cognitive evoked potentials and cognitive functions in patients treated for epilepsy. Levetiracetam is a recognized and widely used antiepileptic drug especially in epilepsy with partial seizures and secondary generalized partial seizures, but also in idiopathic generalized epilepsies and juvenile myoclonic epilepsy (as additional therapy). Cognitive evoked potentials (e.g., P300 wave) are the evoked potentials recorded in response to cognitive processes occurring in the brain during decision making (Duncan C et al. *Clinical Neurophysiology* 2009; 120:1883–1908).

**Method:** Levetiracetam-treated patients with epilepsy diagnosis in addition to the standard electroneurophysiological examinations (EEG) and neuroimaging were performed several times in the course of therapy study of cognitive evoked potentials, especially with the assessment of P300 wave. They had also carried out a simple psychological tests for assessing cognitive function. We have examined 20 patients treated with levetiracetam and the results were compared with 20 patients treated for epilepsy, but with other drugs than levetiracetam. P300 wave was obtained as a result of visual stimulation using a proprietary protocol covering a variety of geometric patterns appearing in the field of view of the subject (Derkowski W, *Epilepsia* 53, 195, Suppl. 5).

**Results:** There are the differences in cognitive processes in patients receiving levetiracetam with epilepsy compared to the control group consisting of patients treated with other antiepileptic agents. There is a correlation between the efficiency of cognitive processing and cognitive parameters of evoked potentials, especially the P300 wave.

**Conclusion:** Cognitive evoked potentials, especially the P300 wave allow objectively monitor the efficiency of cognitive deficits in patients with epilepsy. In our study we have confirmed the beneficial properties of levetiracetam in terms of its impact on cognitive processes in patients. It was found usefulness of our own proprietary protocol of visual stimulation for obtaining cognitive evoked potentials- especially P300 wave.

#### p0193

### ASSESSMENT OF THE IMPACT OF LACOSAMIDE ON COGNITIVE ABILITIES OF PATIENTS TREATED FOR EPILEPSY

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**Purpose:** The aim of this study was to estimate the effect of lacosamid treatment on cognitive evoked potentials and cognitive functions in patients with epilepsy.

**Method:** Patients with epilepsy treated with lacosamid were performed during the therapy study of cognitive evoked potentials, especially with the assessment of P300 wave. They had also carried out psychological tests for assessing cognitive function- EpiTrack (Lutz MT, Helmstaedter C. *EpiTrack: Tracking cognitive side effects of medication on attention and executive functions in patients with epilepsy.* *Epilepsy Behav.* 2005 Dec;7(4):708-14). We have examined 20 patients treated with lacosamid and the results were compared with 20 patients treated for epilepsy, but treated without it. P300 wave was obtained as a result of visual stimulation using a proprietary protocol covering a variety of geometric patterns appearing in the field of view of the subject (Event-related potentials in patients with epilepsy treated with levetiracetam W Derkowski *Epilepsia* 53, 195, Suppl. 5).

**Results:** The results show the differences in cognitive processes in patients treated with lacosamid compared to the control group treated with other antiepileptic drugs.

**Conclusion:** We have found beneficial effects of lacosamid on cognitive processes. Examination of cognitive evoked potentials is the useful method of objectification of the results.

#### p0195

### PERAMPANEL IN THE TREATMENT OF EPILEPSY

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**Purpose:** Perampanel is a non-competitive  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPA) receptor antagonist recently licensed for add on therapy in partial epilepsy. In randomised double blind studies of short duration about one third of cases achieve improvements in seizures control. The purpose of this study is to assess the longer term efficacy and tolerability of the drug.

**Method:** A multicentre prospective audit has been initiated in adult patients. Data relating to monthly seizure counts, global assessments and adverse events have been recorded in all people who took the drug. The primary outcome measure is actuarial retention time on perampanel.

**Results:** Eighty-two cases, mean age of 41, 72 with partial epilepsy, have been identified. Thirty-six had learning difficulties. Mean duration of epilepsy was 23 years. An average of six previous and three current antiepileptic drugs were used. Mean follow-up was 9 months. Twenty-one were followed for 12 months or more. The actuarial percentage retention on perampanel was 83% at 6 months (.95 CI, 72–90) and 70% at 12 months (.95 CI, 58–79). Five percent were seizure free, and 25% reported a 50%+ reduction in seizures. The commonest side-effects were aggression (36%), sedation(15%) and weight gain(15%). Perampanel was withdrawn in 38%, two-fifths due to side-effects, one-fifth lack of efficacy and two-fifths both.

**Conclusion:** This study confirms the results of short term randomised trials. Around one third of cases have a significant and sustained period of improvement and retention time is high. The commonest side effects are irritability, drowsiness and weight gain.

#### p0196

### FYDATA STUDY: RETROSPECTIVE ANALYSIS OF PERAMPANEL IN A REAL-LIFE SETTING (6-MONTH INTERIM ANALYSIS)

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## Abstracts

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**Purpose:** Real-life experience with perampanel (PER) in a large series of patients with partial epilepsy.

**Method:** Multicenter, retrospective, 1-year, observational study. Inclusion criteria:

- 1) patients older than 12 years;
- 2) partial-onset seizures;
- 3) Add-on treatment with PER according to clinical practice;
- 4) At least 1 partial seizure in the year prior to starting PER.

The source of data was patient clinical records. Time-points for revision were considered at 3, 6 and 12 months.

**Results:** An interim analysis was performed at 6 months in 315 patients. The mean number of seizures per month at onset was 19.6 and the mean number of prior antiepileptic drugs (AED) was 8.5. A total of 89.8% and 79.4% of the patients remained on PER at 3 and 6 months respectively. The mean dose after 6 months was 6.4 mg (range: 2–12 mg). At 6 months, 8.6% of the patients were seizure-free and 32.9% were responder. Additional efficacy was observed in patients with secondary generalized seizures -the number of patients was reduced from 27.2% to 17.6%-, patients  $\geq 65$  years (responder rate (RR) 68.8%) - $p = 0.002$ -, and patients that had tried  $\leq 5$  AEDs (RR 42.3%) - $p = 0.029$ -. A tendency to a higher RR was observed if concomitant enzyme inducer were not used (38.3 vs. 23.2%). AE were reported by 55.9% of the patients, being most of them mild or moderate. The most frequent were dizziness (20.3%), somnolence (15.9%) and irritability (14.6%). 7.9% of patients discontinued because of AE. Psychiatric AE were statistically more frequent if patients had a prior psychiatric condition ( $p < 0.001$ ), but no differences were observed if they were on levetiracetam.

**Conclusion:** Preliminary results at 6 months in a refractory population with PER showed a promising response and retention rate. Main adverse events were psychiatric or central nervous system-related. Prior psychiatric condition should be considered to improve tolerability.

## p0197

### ANTIEPILEPTIC DRUG CHANGE PATTERNS AND QUALITY OF LIFE IN A COMMUNITY-BASED EPILEPSY COHORT

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**Purpose:** Antiepileptic drug (AED) changes are commonly regarded as an indicator of adverse treatment outcomes and reduced quality of life (QoL). This inference underlies epilepsy management and research, yet current studies often do not account for quality of life. Moreover, previous AED attempts (changes) are rarely included in the assessment of treatment results. We assessed AED change patterns and their association with QoL in a community-based setting.

**Method:** We performed a retrospective cohort study involving 248 people with epilepsy identified from public pharmacy records from whom we retrieved AED dispensing history. We assessed AED changes during the 2 years prior to the index date and current QoL using the validated Dutch QOLIE-31 questionnaire.

**Results:** Thirty-one percent had at least one AED treatment change during the study period. People who changed showed a significantly lower QoL (QOLIE score 68), than those without AED changes (score 74), with the lowest QoL for those who intensified their treatment (score 65). Each additional change was associated with a further reduction of -4.9 in QoL-score.

**Conclusion:** Changes in AED treatment are common practice and occur frequently even in people with longstanding epilepsy. Frequent changes are found associated with a lower QoL and thus seem to be an indicator of suboptimal treatment outcome. QoL should be acknowledged as the most important treatment outcome in epilepsy. However can be subjective and frequency of drug changes could be used as surrogate marker for QoL in daily clinical practice. This can be seen as a red flag requiring changes in epilepsy management such as earlier referral or more thorough evaluation in people with epilepsy, with the aim of optimizing epilepsy care. AED changes should also be acknowledged in treatment outcome research for a better translation and applicability of results to general practice.

## Drug Therapy 3 Sunday, 6th September 2015

## p0200

### PHARMACOEPIDEMIOLOGICAL ASSESSMENT OF THE MEDICINES FOR JUVENILE IDIOPATHIC GENERALIZED EPILEPSIES

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**Purpose:** To evaluate the long-term therapeutic outcomes of the juvenile idiopathic generalized epilepsies.

**Method:** We conducted a retrospective comparative analysis of the therapy of 93 patients (33 males and 60 females) with the juvenile idiopathic generalized epilepsies (JIGE): juvenile absence epilepsy (JAE) - 22 patients (24%), juvenile myoclonic epilepsy (JME) - 32 patients (34%) and epilepsy with generalized tonic-clonic seizures only (EGTCS) - 39 patients (42%). We calculated Risk Ratio (RR with Review Manager 5.2) of favorable therapeutic outcomes of different JIGE forms after 1 year from the start of treatment and after the 3-years follow-up. Favorable outcome: clinical remission (the number of patients without seizures).

**Results:** Monotherapy was used in 97% of all cases of JIGE: valproic acid 90.7%, topiramate 3.4%, lamotrigine 1.7%, levetiracetam 0.8%, succinamide 1.7%, carbamazepine 1.7% (solely for EGTCS). Polytherapy (valproates + succinamide) was used only for treatment of JAE. Mean prescribed daily doses of valproates used in monotherapy of JAE were 1276.9 mg; JME - 1128, 1 mg; EGTCS - 1096, 4 mg. RR calculations revealed comparable efficacy of valproate monotherapy of JAE versus JME (RR=1.04; 95% CI[0.80, 1.34]), JAE vs EGTCS (RR=0.95 95% CI [0.76, 1.20]), JME vs EGTCS (RR=0.92; 95% CI[0.75, 1.13]) after 1 year from the start of treatment. We found similar outcomes valproate monotherapy after 3 years of follow-up: JAE vs JME (RR = 1.10; 95% CI[0.80, 1.51]), JAE vs EGTCS (RR=0.99 95% CI[0.75, 1.13]), JME vs EGTCS (RR=0.99; 95% CI[0.75, 1.33]).

**Conclusion:** Valproates were the most commonly prescribed antiepileptics for all forms of the juvenile idiopathic generalized epilepsies. Juve-

nile absence epilepsy required the prescribing of higher doses of valproate monotherapy and, probably, polytherapy for achieving of clinical remission versus JME and EGTCS. We found no statistical differences in short-term and long-term outcomes valproate monotherapy between different forms of JIGE.

Conflicts of interest - None.

#### p0201

### ONE-YEAR CLINICAL EXPERIENCE WITH PERAMPANEL IN SPAIN: STUDY OF THE EFFICACY AND TOLERABILITY

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**Purpose:** To analyze the efficacy and tolerability of perampanel (PER) at 6 and 12 months in daily clinical practice conditions.

**Method:** Patients which started on PER in eight different Spanish hospitals were included. Data were collected at 6 and 12 months. The following data were collected: age, gender, age at onset of epilepsy, seizure and epilepsy types, aetiology, monthly seizure frequency, adverse events and number of previous anti-epileptic drugs (AEDs). Response was analysed in 6 and 12 month completers and defined as a > 50% reduction in monthly seizure frequency compared with the baseline.

**Results:** Two-hundred and eight patients were included in the study. After 6 months 175 patients (84%) continued on PER and 69/102 (67.6%) at 12 months. Mean number of AEDs used in the past was 6.99 and mean number of concomitant AEDs was 2.56. Mean PER dose was 7.09 mg and 7.74 mg at months 6 and 12, respectively. The responder rate was 45.4% and 44.9% at both follow up points. Seizure freedom at month 12 was achieved in 2/68 (3%). Adverse events were experienced in 64/208 (30.8%) and resulted in withdrawal in 36 (17.4%). The most common adverse events were somnolence, dizziness and irritability. Retention rate was 60.7% after 12 months. We found no significant differences between concomitant use of inducer and non-inducer AEDs, regarding dose and efficacy, but with more adverse effects with the latter.

**Conclusion:** In this long term study, PER showed efficacy in 45.4% of patients in daily clinical practice conditions. Tolerability was good in this drug-resistant population. The concomitant use of inducer AEDs did not modify the efficacy of PER.

#### p0202

### TRENDS IN CHOOSING CONVENTIONAL VERSUS NEW ANTI-EPILEPTIC DRUGS IN EPILEPSY TREATMENT

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**Purpose:** Recent studies reveal that conventional antiepileptic drugs (AEDs) used without alternative in the treatment of epilepsy for years, seem to leave their place to new AEDs during last two decades. We aimed to assess whether the results of those studies hold any truth in Turkish clinical practice. The study was carried out in two different hospitals from distinct places of Turkey.

**Method:** Medical records of patients that present to our clinic with the diagnosis of epilepsy 2007–2012 were investigated retrospectively.

**Results:** Data on 1126 patients were evaluated. Among them, 624 (55%) patients had monotherapy and 449 (40%) patients had polytherapy whereas 53 (5%) patients had no therapy. While 916 (81%) of the patients were on conventional AEDs, 447 (40%) of the patients were on AEDs. 887 (79%) of the patients were using either valproate or carbamazepine. 523 (84%) of 624 patients on monotherapy were on conventional AEDs whereas 101 (16%) patients were on new AEDs.

**Conclusion:** In our previous study, we found the percentage of choosing new AEDs as 1% before 1994, 10% in 1995–2000, 14% in 2000–2007, respectively. Although there was an increase (40%) in the use of new AEDs in 2007–2012 in our current study, it seems that conventional AEDs still keep their place as a first-line treatment choice, at least in the Turkish clinical practice. It is obvious that new AEDs are candidates for the throne as much more experience gained by both the epileptologists and the patients.

#### p0203

### IS ADJUNCTIVE PERAMPANEL AN OPTION FOR INTRACTABLE SEIZURES IN LAFORA DISEASE?

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**Purpose:** Perampanel (PER), non-competitive AMPA receptor antagonist, with specific action on glutamate-mediated neurotransmission, was approved for partial seizures in patients ≥12 years. Lafora disease (LD) is progressive myoclonus epilepsy with onset in late childhood/adolescence. It is characterized by intractable myoclonus and seizures, inexorable neurological deterioration, cognitive decline and poor prognosis. PER was reported as highly effective in LD case (Schorlemmer 2013).

**Method:** Eight LD patients, 5 females, 3 males, aged 16–31.5 (mean 21.6) were collected from Marseilles and Belgrade. All patients and/or their parents gave informed consent. Mutation of either EPM2A (3) or NHLRC1 gene (5) was identified. Three patients are bedbound. All had failed ≥3 antiepileptics in stable doses for mean 8.8 ± 4.3 years (range 3–14) and continued to suffer from daily myoclonus and frequent generalized tonic-clonic seizures (GTCS). Once-daily PER dosed 6–8 mg, was gradually used in co-medication with valproate (7), clonazepam (4) and levetiracetam (4). Patients experiencing adverse events (AEs) deferred up-titration or have their dose reduced.

**Results:** Compared with baseline, sustained remission of myoclonus and GTCS was achieved in 6 of 8 patients for a follow-up of 2–3 months. Reduction of myoclonus in 4 and its disappearance in two was noted. Five patients were GTCS-free and two had GTCS reduced for >50%. Two patients had discontinued PER, due to a lack of efficacy. In two patients co-medicated with valproate and levetiracetam, aggression

and irritability appeared with PER doses of 8 and 6 mg daily. Up-titration was deferred in one, while the dose was reduced to 6 mg in remaining patient. Frequently reported AEs (dizziness, somnolence, and headache) were rated mild-moderate.

**Conclusion:** Perampnel started in patients with advanced LD led to sustained remission in myoclonus and GTCS. Psychiatric side effects appeared at higher PER dose. In LD population, PER seems to be promising drug which requires further study.

#### p0204

### PERAMPANEL IN 28 ADULTS WITH LENNOX-GASTAUT SYNDROME AND RELATED ENCEPHALOPATHIES

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**Purpose:** The Lennox-Gastaut syndrome (LGS) is a severe epileptic encephalopathy, in which bilateral synchrony plays a major role. Perampnel (PER), an add-on in focal epilepsy, has a new mechanism of action and may be relevant. All LGS patients newly treated with PER have been prospectively added to a database in two tertiary epilepsy clinics.

**Method:** Patients were reviewed at 3 month intervals and frequent carer contacts were encouraged. We recorded all epilepsy parameters and actively looked for side-effects. There was no videoEEG quantification of discharges or seizures. We asked carers to quantify visible seizures.

**Results:** As of February 15, 2015, we have treated 17 patients with LGS and 11 with related epileptic encephalopathies (17 M, 11 F, mean age 40 years, range 18–68). All patients had a history of mixed seizures, mental handicap, and drug resistance. 12 were cryptogenic, 4 had had infantile spasms, 2 herpes encephalitis, 2 perinatal damage, 2 pachygyria, 6 other causes. They were receiving an average of 4.5 anticonvulsants (range: 3–7), 8 had VNS, all had daily seizures (including uncounted tonic seizures during sleep). All had tried recommended treatments, including valproate + lamotrigine cotherapy. Side effects included: behavioural disturbances, who stopped but retried PER later with slower titration, 1; seizure aggravation at 10 mg/d, with marked benefit at 6 mg/d, 1; improved alertness, mood and behaviour, 5. Among 14 patients with  $\geq 3$  months follow-up, 1 patient has seizure freedom, 6 a 50% to 90% seizure reduction, 4 are still uptitrating PER at 4 mg/d and above without clear improvement.

**Conclusion:** Although the follow-up is still short at this time, the use of PER in a cohort of LGS and LGS-like patients has allowed us to observe marked improvement in a majority of cases, without severe side-effects.

#### p0206

### PRELIMINARY EXPERIENCE FROM THE TURKEY EPILEPSY PREGNANCY REGISTRY

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**Purpose:** Use of antiepileptic drugs (AED) in pregnancy is associated with congenital malformations. The aim of our study is to examine the congenital malformations in children of mothers with epilepsy on AED

or mothers who discontinued AEDs during pregnancy to reveal any correlation between these anomalies and AEDs.

**Method:** The Turkey Epilepsy and Pregnancy Register is a prospective, observational registration and follow-up study set up to determine the effects of AED in pregnancy. Patients who were followed up by the 12 epilepsy outpatient clinics and got pregnant between the years of 2013–2015 were included in this study.

**Results:** In this study, 83 mothers with epilepsy were included. The mean age of the patients was  $29.4 \pm 4.9$  (20–39) years. Of all the mothers, 72 were on AEDs, whereas 11 discontinued AED during pregnancy. A patient had voluntarily curettage, one died, 7 had abortions. In the AED group, 59 (71.1%) of the pregnancies were completed under monotherapy, and the most frequently used drugs were carbamazepin (16), valproate (13), levetiracetam (12) and lamotrigine (12). Sixty-six (79.5%) patients used folic acid. In a patient who discontinued AED, had to have curettage because of her baby had a major cardiac anomaly. All of children with major malformation (7) were in the AED group (monotherapy=3 and polytherapy=4). There are no correlations between the congenital malformations and folic acid usage.

**Conclusion:** Using safe AEDs in pregnancy is important not only to render the mother seizure free but also to prevent teratogenic side effects in the baby. Our study may suggest that taking folic acid with AEDs does not eliminate teratogenic consequences.

## Drug Therapy 4 Sunday, 6th September 2015

#### p0208

### ADJUVANT LACOSAMIDE TREATMENT: EARLY EXPERIENCE IN PATIENTS WITH REFRACTORY PARTIAL ONSET SEIZURES

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**Purpose:** Lacosamide, is a new anti-epileptic drug (AED), which modulates slow inactivation of sodium dependent voltage channels. It is an effective treatment in patients over the age of 16 with refractory partial onset seizures with or without secondary generalizations. This study aims to report our short term experience with adjuvant lacosamide therapy in patients with uncontrolled seizures under other antiepileptic drugs.

**Methods:** Twelve female and 36 male patients with an average age of 31.7 (15–56) were included in the study. Demographic and clinical features of patients with refractory partial onset seizures with or without secondary generalizations were assessed.

**Results:** Etiologies of the patients included, mesial temporal sclerosis, focal cortical dysplasia, cerebral palsy, hydrocephaly, meningitis sequela, intracranial mass, WEST syndrome, poststroke and cryptogenic etiology. All patients were on polytherapy which consisted of different AED combinations. Lacosamide was included in the treatment regimen as the 2nd drug in 1 patient, 3rd in 24 patients, 4th in 21 patients and 5th in 2 patients. Preferred dose varied from 100 to 400 mg/day. Average treatment period was  $3.6 \pm 1.67$  months. There was no difference in seizure frequency in 6 patients. Nine were seizure free in their last month. Eight discontinued treatment due to side effects following an average period of  $1.91 \pm 1.69$  months. There was statistically significant improvement in seizure frequency in patients who were medicated at least 1 month ( $p = 0.0001$ ). Two reported increased seizure frequency after lacosamide. Encountered side effects were nausea in 2 patients, dizziness in 3 patients, anxiety/irritability in

2 patients, headache in 1 patient, diplopia in 1 patients and gastrointestinal discomfort in 1 patient.

**Conclusion:** Our early experience suggests that 100 to 400 mg/day lacosamide improve seizure frequency significantly. Lacosamide may be an effective adjuvant therapy in patients with refractory partial onset seizures, however side effects is a remarkable reason for non-compliance.

#### p0210

### POTENTIAL DRUG INTERACTIONS WITH ANTIPILEPTICS IN THE INTENSIVE CARE UNIT PATIENTS OF A UNIVERSITY HOSPITAL

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**Purpose:** Use of antiepileptic drugs which plays an important role in the occurrence of drug-drug interactions (DDIs) can be critical for intensive care unit (ICU) patients with many medications, co-morbid diseases and altered organ functions. Particularly phenytoin and levetiracetam are the well-known drugs used for seizure prophylaxis following traumatic brain injury in the ICU patients. This study aimed to determine the prevalence and clinical severity of potential DDIs with antiepileptics in surgical ICU patients of a university hospital.

**Method:** The Medical Pharmacology Department organized consultation reports for ICU patients in Marmara University Hospital for 6 months (from July-2014 to December-2014) to detect DDIs. DDIs were identified by databases; Micromedex, Rx Media 2014, Lexi-Interact™ Online “interactions checker” and Pubmed. Only clinically important ‘C, D or X’ risk rating category DDIs of Lexi-Interact™ Online database were analyzed.

**Results:** Of 177 ICU patients, 53 (30%) were on therapy with antiepileptics [levetiracetam (n = 28), phenytoin (n = 11), midazolam (n = 4), carbamazepine (n = 1) and polytherapy with antiepileptics (n = 9)]. Of 117 patients with DDIs, 27% were with antiepileptics. Potential C (n = 33.6%), D (n = 9.2%) or X (n = 1.2%) risk rating category DDIs with antiepileptics were detected. DDIs which can result with therapeutic failure or adverse and toxic reactions of antiepileptics were found between valproic acid and meropenem, phenytoin and nimodipine, cefazolin or cyprofloxacin, clonazepam and voriconazole and midazolam and dexamethasone or propofol. The most frequent DDI with antiepileptics was between levetiracetam and remifentanyl (9%) which both have depressive effects on central nervous system. The only contraindicated X risk rating category interaction was between phenytoin and nifedipine which can cause therapeutic failure of nifedipine.

**Conclusion:** In conclusion DDI mechanisms which can lead to changes in serum levels or degree of binding to plasma proteins of antiepileptics are noteworthy for effective seizure prophylaxis in the ICU patients.

#### p0211

### WHEN UNCONTROLLED EPILEPSY BECOMES CONTROLLED: A PROSPECTIVE STUDY IN RURAL WEST OF CHINA

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**Purpose:** In rural areas of China, about 41% of patients have never received appropriate treatment. To assess the clinical benefits of adequate AED therapy in rural west of China, prospectively follow up the outcomes of patients with uncontrolled epilepsy after further drug manipulation.

**Method:** Epilepsy patients were enrolled between 3 Dec 2010 and 18 Aug 2011. According to ILAE consensus definition, outcomes were categorized to: seizure-free; drug-resistant, undefended. At baseline, patients with “undefined” receiving at least one AED at <50% WHO defined daily dose (WHO DDD) will included and followed up for until 28<sup>th</sup> Jan 2014. Patients with current AEDs less than 50% DDD will principal increase dosage or substitute/ add other AEDs according to the doctors. Final outcomes, reasons for “undefined” and risk factors of drug resistant will analyzed at last follow-up.

**Results:** 197 patients included in this study. At the last follow up, 33 (16.75%) patients became to “seizure-free”, while 54 patients became “drug resistant” and 110 patients were still “undefined”. Most common reason for undetermined AEDs was inadequate dose both at baseline (93.29%) and last follow-up (51.56%). 17 of 93 patients became seizure-free after the dosage of their AED(s) was increased, while 16 of 104 did so after substitution or addition of AED(s). 3 patients with history of treatment failure became seizure-free, while 35 patients were drug-resistant (p < 0.001). There were similar probability of seizure freedom in patients received 1 compared with 2 to 4 regimen (p = 0.745). At last follow-up, there’re 31 AEDs stopped for AEs, compared 8 AEDs at baseline.

**Conclusion:** Patients with inadequate-dose AEDs can get seizure free with further drug manipulation. History of treatment failure is a risk factor to drug-resistant, while history of AEDs with inadequate dosage won’t affect further outcome. Inadequate dosage is the urgent problem in rural China which needs epilepsy education.

#### p0212

### REAL-WORLD DATA ON ESLICARBAZEPINE ACETATE AS ADD-ON TREATMENT TO ANTIPILEPTIC MONOTHERAPY IN ADULTS WITH PARTIAL-ONSET SEIZURES: THE EPOS STUDY

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**Purpose:** Eslicarbazepine acetate (ESL) is approved as adjunctive therapy for adults with partial-onset seizures, with or without secondary generalisation. Patients encountered in everyday clinical practice are more diverse in terms of clinical characteristics than those included in clinical trials and require individually tailored treatment to encourage long-term compliance and improve overall outcomes. ‘Real-world’ studies are therefore needed to complement evidence from clinical trials. The aim of the prospective, non-interventional Eslicarbazepine acetate in Partial-Onset Seizures (EPOS) study was to assess retention rate, seizure control and safety/tolerability of ESL as add-on to antiepileptic monotherapy in everyday clinical practice across eight European countries.

**Method:** Adult patients with uncontrolled partial-onset seizures under antiepileptic monotherapy, whose clinician had previously and independently decided to initiate ESL add-on therapy, were offered participation in the study if they provided informed consent. Primary endpoint was retention rate after 6 months. Other assessments included responder rate after 6 months (response defined as ≥50% seizure frequency reduction from baseline), seizure freedom rate after 6 months, and safety/tolerability.

**Results:** Overall, 219 patients were included (mean age 45.9 years; 57.5% male). Mean time since epilepsy diagnosis was 12.3 years. Mean ESL dose after titration was 944.8 mg/day (range 428.6–2800.0 mg/day). After 6 months, retention, responder and seizure freedom rates were 82.2% (95% confidence interval [CI] 76.5–87.0%), 81.8% (95% CI 75.5–87.1%) and 39.2% (95% CI 32.2–46.5%), respectively. Adverse events (AEs) were reported for 57 (26.0%) patients; eight (3.7%) patients experienced serious AEs. No AE was reported in >5% of patients. The most frequently reported AEs were dizziness (4.6%), headache (3.2%), convulsion (3.2%) and fatigue (2.7%).

**Conclusion:** ESL as add-on to antiepileptic monotherapy demonstrated a favourable rate of retention and seizure control, and was well tolerated by the majority of adult patients in a real-life setting.

Study supported by Eisai

### p0213

#### PREDICTORS FOR ADVERSE EVENTS OF PHARMACOTHERAPY IN EPILEPSY

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**Objective:** In patients taking antiepileptic drugs (AED) for epilepsy, adverse events (AE) are a common cause of impaired adherence or discontinuation of pharmacological treatment. This study aimed to identify independent predictors for abundant AE and to assess the role of specific AED in patients treated with monotherapy.

**Methods:** All outpatients 16 years and older with epilepsy lasting 12 months or more were routinely asked to complete the Liverpool Adverse Event Profile (LAEP; 19 items; score 19–76). Demographics, epilepsy and treatment variables were derived from our comprehensive outpatient database. Logistic regression analyses were used to identify independent predictors for high LAEP score ( $\geq 45$ ) and for distinct AE.

**Results:** A total of 841 patients (53.6% female; mean age  $45.9 \pm 16.7$  years) were analyzed. Independent predictors for a high LAEP score were female sex (OR 1.823), lack of 12-month terminal seizure remission (OR 2.097), pharmacoresistance (OR 1.464), and partial epilepsy (OR 1.791). In the subgroup of patients with AED monotherapy ( $n = 507$ ), the most common substances were levetiracetam ( $n = 151$ ), lamotrigine ( $n = 167$ ), valproic acid ( $n = 73$ ) and carbamazepine derivatives ( $n = 75$ ). None of these substances was associated with a high LAEP score. Distinct AE were mainly predicted by lack of 12-month seizure freedom (10/19 AE) and female sex (7/19 AE). Furthermore, AE were associated with intake of specific AED, namely shaky hands with valproic acid (OR 2.983), depression and sleep disturbance with levetiracetam (OR 3.001 and OR 2.355), memory problems with carbamazepine derivatives (OR 2.518), and concentration difficulties with lamotrigine (OR 2.594).

**Conclusions:** Predominant AE were predicted by female sex and clinical features of difficult-to-treat epilepsies, but interestingly not by AED polytherapy. The monotherapy setting allowed assessing the capability of individual substances to predict specific AE. Our findings may help to further identify patients with epilepsy at high risk for general and specific AE and to reduce non-adherence.

### p0215

#### EFFICACY AND TOLERABILITY OF STIRIPENTOL TO 3 PATIENTS WITH DIFFERENT SCN1A MUTATIONS

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**Purpose:** Stiripentol (STP) is a new drug limited to Dravet syndrome which has efficacy when combined with valproate (VPA) and clobazam (CLB). SCN1A mutation is found in more than 70% of patients with Dravet syndrome, while severity of the clinical feature is heterogeneous. Here we present three patients with different mutations of SCN1A, and compared efficacy and tolerability of STP.

**Subjects:** Patient 1 is a 14 year-old girl, who had myoclonic seizures and febrile induced seizures since 5 months of age. Seizures were not well controlled with antiepileptic medications (VPA, CLB). Patient 2 is a one year-old boy who had status epilepticus with fever at 5 months of age. Even after starting antiepileptic medications (VPA, CLB, PB), seizures were easily induced with fever. Patient 3 is a 3 year-old boy who had extremely severe hypotonia and multiple anomaly. He started to have myoclonic seizures and partial seizures since 12 months of age, and received antiepileptic medications (VPA, CLB, PB). Although frequency of the seizure was decreased, the seizures were easily clustered with fever and intensive cares were required.

**Results:** Genetic analysis was performed in three patients. De novo mutation of c.2819C>T (p.Ser940Phe) was found in patient 1, c.4554\_4555insA (p.Pro1519Thr fsX18) in patient 2, 11 Mb deletion including SCN1A in chromosome 2q24.2-31.1 was found in patient 3. STP treatment had started with three patients. Patient 1 discontinued STP because of insufficient efficacy. Patient 2 needed additional medication (TPM) to control seizures. Patient 3 became seizure free for 3 months after initiation of STP, dose up was difficult because of anorexia problem and needed additional therapy.

**Conclusion:** Although efficacy of STP to 3 patients was limited, conjunction therapy would be a key of the treatment.

## Epidemiology 1 Sunday, 6th September 2015

### p0218

#### UTILIZATION OF ANTIEPILEPTIC DRUGS IN EPILEPSY AND IN NON-EPILEPSY DISORDERS IN NORWAY

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**Purpose:** Antiepileptic drugs (AEDs), and especially the newer drugs are increasingly used in non-epilepsy disorders, as psychiatric disorders, neuropathic pain and migraine. Recently, several other new AEDs have become available as add-on in epilepsy as the orphan drugs (rufinamide, stiripentol). The aim of this study was to investigate changes in utilization of the newest and unlicensed AEDs in epilepsy and in non-epilepsy disorders in Norway to improve patient safety aspects by close drug surveillance.

**Methods:** Data consisted of all prescriptions of AEDs from the Norwegian Prescription Database (NorPD) from 2004 to 2013. Variables included anonymous data regarding age, gender, reimbursement codes

for specific diagnoses and utilization of AEDs until 2012 and data until 2013 regarding the newest AEDs.

**Results:** From 2004 to 2012, the utilization in non-epilepsy disorders accounted for 0.85 to 7.0 DDDs/1000 inhabitants/day (51% of the total use in 2012). Predominant AEDs in non-epilepsy disorders are lamotrigine in psychiatry, pregabalin and gabapentin in neuropathic pain and topiramate in migraine. The use of unlicensed (clobazam, ethosuximide, sultiame) and the newest AEDs (eslicarbazepine acetate, lacosamide, rufinamide, stiripentol, perampanel) has increased by 120% from 1003 patients in 2009 to 2230 patients in 2013 (0.14 DDDs/1000 to 0.31 DDDs/1000 inhabitants/day). A clear reduction in the use of retigabine was seen from 2012 to 2013 due to restrictions because of serious adverse effects reports. An increase in use of these drugs elucidates a need for establishing an extended analytical repertoire.

**Conclusions:** NorPD as a source to follow the utilization of these drugs is useful to offer an improved individualized treatment by establishing new analytical methods for drug monitoring, as a new orphan drug package. Awareness of the increased exposure of AEDs to new groups of patients followed by careful clinical considerations regarding safety aspects is of great importance and contributes to improved pharmacovigilance.

#### p0219

### LONG TERM PROGNOSIS OF EPILEPSY (PRO-LONG). MULTICENTRIC RETROSPECTIVE STUDY OF PROGNOSTIC PATTERNS IN NEWLY DIAGNOSED PATIENTS

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**Purpose:** The aim of the PRO-LONG study is to assess the long term prognosis of epilepsy according to pre-defined prognostic patterns in newly diagnosed patients.

**Methods:** This is a multicentric retrospective study recruiting 1000 unelected patients, newly diagnosed with epilepsy in secondary or tertiary epilepsy centers, with a minimum follow-up of 10 years. The interim analysis of the first 504 recruited patients, with a mean follow-up of 15 years from diagnosis, is presented. Clinical, EEG and neuroimaging data were collected, as well as remission periods (defined as seizure-free periods longer than 12 months). Patients were classified in four prognostic patterns: 1. Early remission: 1 + year remission from treatment onset to last observation; 2. Late remission: 1 + year remission to last observation after 1 + treatment changes; 3. Relapsing-remitting course: 1 + remission periods and not in remission; 4. No remission: no 1 + year remission period during follow-up.

**Results:** 29.2% of patients achieved remission (early or late), 61.9% displayed a relapsing-remitting pattern with at least 1 year of remission and 8.9% never achieved remission. Multivariate analysis showed that the probability of achieving remission (early or late) was inversely associated with age at disease onset (0–14 vs. >14;  $p = 0.0334$ ), duration of disease before diagnosis ( $p = 0.0277$ ) and number of antiepileptic drugs used ( $p < 0.0001$ ). Epileptic syndromes and etiology did not show a consistent effect on prognosis.

**Conclusions:** Long-term remission of epilepsy is achieved by about one third of newly diagnosed patients and could be anticipated based on demographic and clinical characteristics of the subject.

#### p0220

### EARLY SEIZURES IN ACUTE STROKE

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**Purpose:** The aim of this study was to assess the frequency and the predictive factors for early seizures as well the clinical outcome in patients with first-ever stroke.

**Method:** A total of 352 consecutive patients with first-ever stroke, admitted to our department, were included in this retrospective study. Early seizures were defined as seizures occurring within 7 days from acute stroke. Patients with history of epilepsy were excluded.

**Results:** About 47 patients (13%) had early seizure, and 8 had a status epilepticus. We had 28 women and 19 men. The mean age was  $71.6 \pm 14.6$ . They were significantly more common in patients with cortical involvement, severe and large stroke, and in patient with cortical associated hemorrhage. ES were associated with an increase in adverse outcome (mortality and disability).

**Conclusion:** Early seizures occurred in about 13% of patients with acute stroke. In these patients hemorrhagic transformation is a predictive factor for ES. ES seem to be associated with a worse outcome after acute stroke episode.

#### p0221

### PARENTAL INFLUENCE ON EPILEPSY RISK IN SIBLINGS

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**Purpose:** The recurrence risk of epilepsy in full siblings is increased. However, it is not known to what extent the recurrence is influenced by parental factors. We studied the recurrence risk of epilepsy in full and half siblings.

**Method:** This was a population-based cohort study in Denmark of all children born in Denmark between 1980 and 2006. Children were identified and followed up to December 31, 2012. Children having an older sibling with epilepsy were compared with children not having an older sibling with epilepsy. We identified a maternal sibling sub-cohort derived from mothers with at least two children and a paternal sibling sub-cohort derived from fathers with at least two children.

**Results:** We followed 1,663,302 children born in Denmark. The overall adjusted relative recurrence risk of epilepsy in siblings was 3.49 (95% CI: 3.15–3.87). In the maternal cohort the overall recurrence risk was 3.68 (95% CI: 3.25–4.16) - in full siblings it was 3.78 (95% CI: 3.30–4.33) whereas in half siblings it was 2.97 (95% CI: 2.20–4.02). In the paternal cohort the overall recurrence risk was 3.37 (95% CI: 2.96–3.85) - in full siblings it was 3.70 (95% CI: 3.23–4.25) whereas in half siblings it was only 1.57 (95% CI: 1.00–2.44).

**Conclusion:** The risk of epilepsy in children having an older sibling with epilepsy was 3–4 times increased compared with children not having an older sibling with epilepsy. In the maternal cohort the risk was similar in full and half siblings whereas in the paternal cohort the risk was lower in half siblings. The difference in the recurrence risk between full- and half-siblings in the paternal cohort supports the role of genetics in epilepsy,

while the significant recurrence risk in maternal half-siblings may support the role of factors associated with pregnancy and the maternal intrauterine environment in epilepsy.

**p0222**

#### HAEMORRHAGE RELATED TO RENAL ANGIOMYOLIPOMA IN PATIENTS WITH TUBEROUS SCLEROSIS COMPLEX. A FRENCH AND NORWEGIAN QUESTIONNAIRE STUDY

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**Introduction:** Tuberous Sclerosis complex is a rare genetic disorder which is characterized by benign tumours occurring in multiple organs. The brain, kidneys, lungs and skin are most frequently affected. Common symptoms are epilepsy, neurocognitive impairments, autism, and dysfunction in the renal and pulmonary organ systems. Angiomyolipomas (AML) occur in 60–80% of the patients, and they tend to increase in size with age. There is a risk of haemorrhage related to AMLs and the risk is associated with the size of the lesion. Screening and monitoring of renal lesions is indicated in all patients with TSC.

**Purpose:** To identify age of increased risk of renal bleeding in TSC patients.

**Method:** A cross-sectional study on renal manifestations in TSC patients was performed in France and Norway using a French questionnaire translated to local language. Three hundred and fifty seven patients were recruited, 257 in France and 100 in Norway.

**Results:** Fifty four percent ( $n = 189$ ) of those who answered ( $n = 350$ ) reported occurrence of AMLs (France, 143/254, 56%; Norway, 46/96, 48%).

Haemorrhage related to renal AML was reported in 11% of those who answered (26/248; France, 19/172/11%; Norway, 7/76/9%).

We found indications of an increased risk of first incidence of bleeding between 20–30 years, however the increase was small and may not be clinically significant.

**Conclusion:** Our results show that occurrence of first incidence of bleeding seems to be age-related.

**p0223**

#### DEVELOPMENT OF A PROGNOSTIC SCORE OF LATE-ONSET SEIZURES AFTER ISCHEMIC STROKE

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**Purpose:** Seizures after stroke have a negative impact on clinical outcome, however the prediction of the risk of post stroke seizures proved to

be difficult yet. We aimed to develop a prognostic score of late-onset (>7 days) seizures after ischemic stroke.

**Method:** Between 2002 and 2008 we included 1200 consecutive acute ischemic stroke patients in the prospective Stroke and Epilepsy Registry of Eastern Switzerland (SERES) who received telephonic or clinical follow up after  $36 \pm 19$  months. A prognostic score was developed using multivariate logistic regression modeling and internally validated with bootstrapping techniques.

**Results:** Late-onset seizures within 3 years of stroke onset occurred in 69 (6%) patients. Predictors were early onset seizures (5 points), cortical involvement (4 points), neglect at initial evaluation (2 points), involvement of the medial cerebral artery territory (2 points) and NIH Stroke Scale at admission (NIHSS 4–10: 1 point; NIHSS >10: 2 points). Internal validation corrected for overoptimism found the obtained 5 item score (range 0–15 points) to be a significant predictor of late-onset seizures ( $p = 0.001$ ). Model discrimination assessed with the area under the receiver operating characteristics curve was  $0.80 \pm 0.03$  ( $p < 0.001$ ) and the score was well calibrated ( $p = 0.18$ ). A score value of  $\geq 10$  points was 95% specific for late-onset seizures, whereas a score value of  $\leq 5$  points had a 99% negative predictive value for late-onset seizures.

**Conclusion:** This easily applicable prognostic score was a good predictor of the risk of late-onset seizures after stroke and might help guide diagnostic and therapeutic decisions in these patients.

**p0224**

#### DEVELOPMENT OF A POST-STROKE EPILEPSY RISK SCORE USING AN ADMINISTRATIVE CLAIMS DATABASE

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**Purpose:** To develop a scoring system to predict one-year risk of post-stroke epilepsy.

**Methods:** We included 59,975 stroke patients in the derivate cohort and 25,703 stroke patients in the validation cohort from the National Health Insurance Research Database of Taiwan. The risk score for post-stroke epilepsy was constructed with Cox regression analysis with the time from stroke to epilepsy as the response and age, sex, the stroke type, length of hospital stay and comorbidities as covariates. The one-year risk of post-stroke epilepsy was calculated by summing up the number of independent predictors weighted by their corresponding beta-coefficients.

**Results:** In the derivate cohort, 3.0% of patients had post-stroke epilepsy ( $N = 1776$ ) within a year of follow-up. A four-point score was derived based on multivariate Cox regression (subarachnoid hemorrhage or intracerebral hemorrhage = 1, length of hospital stay >10 days = 1, history of atrial fibrillation = 1, and pneumonia within 14 days after stroke = 1). The incidence of post-stroke epilepsy was 1.1 (95% CI: 1.0–1.23) at low risk (score = 0), 3.3 (95% CI: 3.0–3.6) at medium risk (score=1), 10.1(95% CI: 9.4–10.8) at high risk (score =2) and 17.5(95% CI: 14.8–20.7) at very high risk (score  $\geq 3$ ) per 100 person-year.

**Conclusion:** The risk of post-stroke epilepsy can be stratified based on the current scoring system. It might suggest that using the risk score instrument in creating individualized patient management algorithms and improving clinical practice aimed at preventing the occurrence of post-stroke epilepsy.

p0225

### SYSTEMATIC REVIEW AND META ANALYSIS OF EPIDEMIOLOGY OF EPILEPSY IN LATIN AMERICA

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**Purpose:** Epilepsy is a worldwide neurological disorder and has two broad aspects-lifetime and active epilepsy. We conducted a systematic review and meta-analysis of epilepsy in Latin America (LA), in order to better present the needs related to epilepsy in this region, with particular, but differentiating emphasis, on lifetime and active epilepsy.

**Method:** Literature search was performed on Pubmed, LILACS, BV Salud, and Google, using different keywords and their combinations (epilepsy, epilepsia, prevalence, prevalencia, incidence, incidencia), except on Google where free text search was conducted for each individual country. Results are presented in counts, proportions, and medians along with 95% confidence intervals (CI). Unpaired t-test with unequal variance was conducted and so were the regressions by taking four variables (study year, population size, age-group and population type), altogether and individually, and separately for lifetime and active prevalence as well as incidence.

**Results:** In total, 42 prevalence (56 after including children-exclusive studies,  $N = 751609$ ) and seven incidence estimates ( $N = 487997$ ) were identified from 14 out of 26 countries between 1970 and 2009. Most prevalence studies were from Columbia ( $n = 15$ ) and Brazil ( $n = 10$ ). Active prevalence was reported by 14 studies while lifetime prevalence was reported by 40 studies. Excluding children studies, median lifetime prevalence was 17.0 (95% CI 13.0–19.7, range 1.0–43.2) and active prevalence was 10.9 (95% CI 5.7–16.6, range 3.8–17.9). In LA, only, 64% of the total case-load requires active intervention for their epilepsy. Incidence (/100,000) varied from 7.0 in Brazil to 190 in Ecuador and median incidence was 92.7 (95% CI 16.0–181.2). Various methodological issues were identified.

**Conclusion:** Lifetime prevalence of epilepsy is high but methodological issues remain. Only, 64% of total case-load requires an active intervention for their epilepsy. Because of more focus on lifetime epilepsy, treatment gap is possibly over-estimated; yet >6.5 million need intervention for their active epilepsy in LA.

p0226

### EPIDEMIOLOGY OF THE ACCIDENTAL DEATH IN SEIZURE PATIENTS

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**Purpose:** To evaluate the demographical profile of the seizure patients who died by accident.

**Methods:** We retrospectively identified 115 patients who were treated because of seizure in Asan medical center in Korea and died on account of accident from January 1989 to December 2010. We excluded patients who killed themselves and died by accident instantly. Finally total 71 patients were included. We confirmed whether the patients die or not until December 2010 and cause of death through data of the National Statistical Office of Korea.

**Results:** Mean age when the patients visited our hospital for the first time is 32.25 year-old ( $\pm 20.37$  year) and mean age when the patients start to seizure is 24.05 year-old ( $\pm 20.99$  year). Among 71 patients, 55 patients were man and 16 patients were female. Frequency of seizure: 0–2 times per year is 28 cases (39.4%), 3–12 times per year is 20 cases (28.2%), 13–49 times per year is 15 cases (21.1%), over 50 times per year is 8 cases (11.3%). Etiology of death is traffic accident (29 cases), falling (17 cases), drowning (23 cases) and other (2 cases). Mean number of antiepileptic drug is  $1.71 (\pm 1.14 \text{ SD})$ . Almost all patients have no mental retardation (95.77%), familial history (91.55%) and psychiatric history (92.96%). We classified epilepsy in 4 categories as generalized seizure (1 case, 1.4%), partial symptomatic seizure (27 cases, 38%), partial cryptogenic seizure (9 cases, 12.7%) and undetermined (34 cases, 47.9%). Electroencephalography shows normal finding (45.1%) or abnormal findings including spike and sharp (43.7%) or slowing (9.9%). Over half of patients (56.3%) have brain lesion in magnetic resonance imaging which is congruent with seizure.

**Conclusions:** The results suggested that epileptic patients who died by accident had taken more than 1 AED and usually had symptomatic partial seizures with no mental retardation or psychiatric history.

p0227

### NOCTURNAL FRONTAL LOBE EPILEPSY (NFLE): LONG-TERM OUTCOME IN A LARGE COHORT

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**Purpose:** To evaluate the prognosis of NFLE in a large, representative cohort with long follow-up.

**Methods:** We included consecutive patients attending our Institute, diagnosed with NFLE on clinical and video-polisomnographic (VPSG) criteria and a follow-up period  $\geq 5$  years. Terminal remission (TR) was defined as seizure-free period of five or more consecutive years at the last follow-up. Potential prognostic factors examined included “any underlying brain disorder”, defined as at least one of the following: ID, pathological NE, brain abnormalities. To evaluate cumulative time-dependent probability of achieving TR from onset, survival curves were generated (Kaplan-Meier method). Univariate analysis (logrank test) and multivariate analysis (Cox's regression model) were performed to identify prognostic predictors.

**Results:** The final cohort included 139 patients (M/F:92/47) with a median follow-up of 27 years (range: 5–65). Mean age at onset was  $13.4 \pm 10.2$  years (range 1–56). About 86% of patients are sporadic cases, 14% had a positive history for epilepsy (5% ADSHE; 9.4% other focal epilepsy). Twenty-two (15.8%) were lesional cases.

Thirty-three patients (23.7%) achieved TR, with a cumulative probability of 9%, 17%, 24% and 32% by 10, 20, 30 and 40 years from disease onset, respectively.

At log-rank test, age at onset >11 years (median) and the absence of “any underlying brain disorder” condition were significantly associated with TR ( $p:0.048$  and  $p:0.003$ ). Cox model confirmed that the absence of “any underlying brain disorder” correlates independently with TR (HR:

3.47, CI 95% 1.04–11.58, p: 0.043). “Time to diagnosis” is inversely associated with TR (HR 0.93, CI 95% 0.89–0.97, p < 0.001).

**Conclusions:** Only about 25% of NFLE patients achieved TR after 30 years of disease. Absence of ID, structural brain abnormalities and pathological NE is associated with a three-fold higher probability of TR. The risk of not attaining TR increase by 7% per each year of delay in the diagnosis.

#### p0228

### CAUSE-SPECIFIC MORTALITY IN EPILEPSY. A SYSTEMATIC REVIEW

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**Purpose:** Epilepsy is associated with premature mortality, having a two to three folds increased risk of early death when compared to the general population. A systematic review was conducted to investigate the causes and determinants of premature mortality.

**Method:** A standardised search of online databases was made and selected suitable articles published between 1980 and 2014. The study extracted and reported the overall and cause-specific standardized mortality (SMR) and proportional mortality ratios (PMR).

**Results:** Twenty articles from eighteen cohorts met the inclusion criteria and were retrieved for qualitative synthesis. There were twelve population-based studies from nine cohorts and eight hospital-based studies from nine cohorts. The main findings revealed that people with epilepsy (PWE) have an overall increased risk of mortality, with an SMR range of 1.6–6.5 for population-based study and 1.4–3.6 for hospital-based study compared to the general population. They are at higher risk of dying from various medical conditions directly or indirectly related to occurrence of seizure. PWE were at increased risk of dying from cancer, stroke, cardiovascular disease, drowning, status epilepticus, SUDEP, suicide and road accidents. Deaths from low- and middle-income countries were higher for epilepsy-related deaths, whilst in high-income countries mortality was higher for causes indirectly-related to epilepsy. Mortality was elevated in the young compared to the elderly. There is an increase in the risk of death in all aetiological causes of epilepsy, especially in those with symptomatic epilepsy and congenital deficits.

**Conclusion:** Despite the heterogeneity and wide variation in the reported data, the finding in this study supports the evidence that PWE are associated with increased mortality. More research is needed to better understand the mechanisms, and to determine biomarkers for predicting mortality, with more efforts put in order to prevent this excess mortality.

## Epilepsy in the Elderly Sunday, 6th September 2015

#### p0229

### EPILEPSY AND ELDERLY

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**Purpose:** Epilepsy in the elderly is an important and increasingly common clinical problem. The prevalence and incidence of epilepsy are highest in later life with around 25% of new cases occurring in elderly people. The main reason for such a high incidence of epileptic seizures in elderly patients is the number of acute symptomatic (or situation-related) seizures. Major known causes include cerebrovascular disease, brain tumor, degenerative disorders such as Alzheimer disease, metabolic disturbances, traumatic brain injury, tumor, or drug therapy. The purpose of this study is to illuminate most common etiological factors and prognosis of epilepsy in elderly.

**Method:** In this study, 49 patients, with represented seizures over age 65 years, were analyzed retrospectively. We examined patients according to demographic and clinical properties, seizure etiology, the electroencephalogram, neuroimaging and other additional neurological and systemic disorders.

**Results:** 23 of the patients (46.9%) were men and 26 of them (53.1%) were women. The mean age of patients was  $75 \pm 8$ . In order of the most common causes were post-stroke seizure (36.7%), acute stroke presenting with seizure (14.3%), tumor (10.2%) and metabolic (10.2%). Infection, drug interruption and metabolic factors were found the most common causes of seizure in 23 of patients with previously known epilepsy. In EEG, epileptiform activity was showed only in 12 of patients. Four patients were died and their etiological factors were stroke presenting with seizure (1), dementia (1), brain tumor (2). Others patients were discharged with partial recovery.

**Conclusion:** The etiologic factors of epilepsy are different in elderly people than young people. Because of many comorbid diseases, management of the older patients with epilepsy is more difficult. So we must be aware of epilepsy in elderly.

#### p0230

### ACUTE SYMPTOMATIC SEIZURES AND EPILEPSY IN ELDERLY

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**Purpose:** Though epilepsy is thought to be a disease of early age, it is even most common among persons aged 65 and older. When an elderly patient presents with acute confusion, neuroimaging is normal and no metabolic disturbances, an epileptic seizure or nonconvulsive status epilepticus must be considered. We have got 60 hospital admission patients diagnosed as acute symptomatic seizures during last 6 months. Hyponatremia was the leading cause. After that acute stroke and nonketotic hyperglycemia were common causes. Epilepsy patients in old age admitted into hospital following a old stroke which was confirmed by neuroimaging was a leading cause of epilepsy. Neurodegenerative disorder with cognitive impairment was a frequent etiology of epilepsy. Sleep related seizures were also found. In intensive care units, during last six months 20 patients present with acute confusional state. Neuroimaging was normal and no metabolic abnormalities were found. EEG shows epileptiform activities and patients improved with antiepileptic drugs. So acute stroke and remote stroke both are causes of seizures in elderly patients. Neurodegenerative brain disorders are also causes of epilepsy in elderly patients. Any acute confusional state patients should be evaluated for nonconvulsive status epilepticus.

#### p0231

### CLINICAL FEATURE AND CAUSE ON EPILEPSY IN THE ELDERLY OF WESTERN CHINA

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**Purpose:** To investigate the common causes, clinical characteristics and prognosis of epilepsy in Chinese old populations in recent decade.

**Method:** 340 epilepsy elders over 65 years old in western China were continuously registered during 2003 to 2013, and their epileptic causes, clinical characteristics, outcomes were prospectively recorded.

**Results:** The onset age of 96.47% patients was after 65 years old. The most common causes of epilepsy were cerebral infarction (38.24%), brain surgery (9.71%), cerebral hemorrhage (7.65%). 54.73% patients had generalized tonic-clonic seizure and 37.57% had focal epilepsy, 7.10% have generalized tonic clonic seizure secondary to focal epilepsy. 80.59% patients were controlled by anti-epilepsy drugs (AEDs), and most of them take only one kind of AEDs. A total of 172 cases underwent EEG examinations, and 73.26% of them have abnormal discharge. All patients were followed up to date at least 12 months, and there were 139 patients (40.88%) alive, 81 patients (23.82%) dead, 120 patients (35.29%) loss. In those patients alive, 88 patients had no epilepsy recurrence. The prognosis in those patients with onset age after 65 years old was better than those ones whose onset before 65 years old ( $\chi^2=6.82$ ,  $p = 0.03$ ).

**Conclusion:** Most patients here had first epilepsy after 65 years old. The major cause of epilepsy is cerebral infarction, and generalized tonic-clonic seizure is the main epilepsy type. Epilepsy could be under control in most patients taking one kind of AEDs. There is correlation between the epilepsy prognosis and onset age, with statistical significance. However, the lost of follow up rate of our study is higher, which may be related to the common phenomenon "Empty nest elders" in China, and many patients could not attend to hospital for follow-up. As a result, the establishment of a complete health care guarantee system is urgent to assist the follow-up elder patients.

#### p0232

##### EPILEPSY IN ELDERLY PATIENTS AND AFFECTIVE DISORDERS

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**Introduction:** This makes the issues of epilepsy in elderly patients and of emotional and affective disorders more and more topical.

**Study objectives:** To study the structure of non-psychotic psychiatric disorders (NPD) in post-stroke elderly patients and in patients with symptomatic post-stroke epilepsy.

**Materials and methods:** Two groups of 105 patients were studied. In Group 1 (65 patients: 31 men and 34 women), the stroke was complicated by the development of symptomatic post-stroke localization-related epilepsy. In Group 2 (40 patients: 28 men and 12 women), no paroxysmal states of the epileptic nature were found. The average age of Group 1 patients was 63.00 years, of Group 2 patients, 62.5 years.

**Results:** In Group 1, affective depression-spectrum disorders were found more frequently than in Group 2 (Group 1 - 78.9%; Group 2 - 33.3%), whereas in Group 2, affective anxiety-spectrum disorders were found more frequently than in Group 1 (Group 1 - 21.1%; Group 2 - 66.7%). The average depression score in Group 1 and Group 2 was  $34.81 \pm 2.73$  and  $28.57 \pm 3.07$  on the BDI scale and  $21.84 \pm 1.50$  and  $13.79 \pm 1.36$  ( $p \leq 0.01$ ) on the HRDS scale, respectively.

In Group 1, a considerable correlation dependence between the index of the impact of depression and anxiety on the manifestation of other psychopathological factors (up to .819\*\*) and the General Severity Index (GSI) was found. In Group 2, a weak correlation dependence between anxiety and the GSI (up to .828\*).

**Conclusion:** The study results have shown a high severity of depression in elderly patients with symptomatic post-stroke epilepsy.

#### p0233

##### ANTIPILEPTIC DRUG USE AND EPILEPTIC SEIZURES IN ELDERLY NURSING HOME RESIDENTS IN THE PROVINCE OF PAVIA, NORTHERN ITALY: A REAPPRAISAL 12 YEARS AFTER A FIRST SURVEY

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**Purpose:** To assess the prevalence of antiepileptic drug (AED) use and epileptic seizures among nursing home residents and to compare findings with a previous survey conducted in 2000.

**Method:** We collected data on demographics, age at institutionalization, functional and cognitive status (Barthel's Index and MMSE), chronic drug use and diagnoses of all subjects aged  $\geq 60$  in 21 nursing homes. Data from residents with a diagnosis of epileptic seizures and AED users were compared with non-seizure, non-AED subjects. Results were compared with the previous study.

**Results:** Among the 2,163 subjects surveyed (79% females, age at observation  $84.9 \pm 7.8$  years, mean  $\pm$  SD), 278 (12.8%, vs. 4.3% in the previous survey) received chronic treatment with AEDs, in 174 cases without a diagnosis of seizures. The 116 residents with a diagnosis of seizures (5.4%, vs. 2.9% in the previous study) were mostly on AED treatment and had a significantly lower age (both at observation and institutionalization), lower cognitive abilities, and a significantly higher number of comorbidities and co-medications compared with non-AED-users and the whole sample. The most common AEDs in seizure subjects were phenobarbital (43.3%, vs. 70% in the previous survey) and levetiracetam

(27.9%, not available at the time of the previous survey). At multivariate analysis, a diagnosis of seizures was significantly associated with a younger age at observation, a history of neurological (cerebrovascular events, meningiomas) and non-neurological conditions (psoriasis and chronic bronchitis), and a lower MMSE score.

**Conclusion:** The prevalence of AED use and seizures was higher than in our previous study and more aligned with data from other countries. Seizures, AED use and co-morbidities were associated with earlier institutionalization. Utilization of newer and possibly more appropriate AEDs was  $> 12$  years ago, although treatments appeared to be suboptimal in many cases.

#### p0234

##### EPILEPSY IN ELDERLY PATIENTS

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**Purpose:** The incidence of new-onset epilepsy is higher among the elderly. In this study, we present the demographic characteristics, etiological factors, seizure types and response rates to treatment in the patients with delayed-onset epilepsy whose age was 65 or older.

**Method:** A total of 43 patients with delayed-onset epilepsy diagnosis aged 65 or older who were admitted to epilepsy clinics of Neurology Department of Medical Faculty of Bezmialem University were included in this study. Medical records of patients were evaluated retrospectively.

**Results:** Of the patients, 24 were male, 19 were female and the mean age was 74.9 (66–92). Underlying diseases were found to be cerebrovascular disease in 16 patients, brain tumor in 8, neurodegenerative diseases in 4, and trauma in 2 patients. In 2 patients, cerebrovascular disease and neurodegenerative disease were both present. In the rest 11 patients, any etio-

logical cause couldn't be found. Based on seizure types, 20 patients had secondarily generalized tonic clonic seizure, 13 had generalized tonic clonic seizure, 6 had simple partial seizure and 1 had generalized tonic seizure. EEG findings were neither lateralized nor localized in 16 patients, both lateralized and localized in 11 and only lateralized in 2 patients. In 14 patients, EEG examination was normal. Based on treatment protocols, 40 patients were taking monotherapy and 3 patients had combination of two antiepileptic drugs. When assessing the side effects of drugs, there was no complaint in 38 patients. In the last 3 months, 2 patients experienced 1 seizure and other patients were seizure free.

**Conclusion:** The most common etiological factor of new-onset epilepsy was found as cerebrovascular disease among elderly patients. Secondarily generalized tonic clonic seizure was the most common seizure type. In most of the patients, EEG findings were neither lateralized nor localized. All patients responds well to monotherapy and have a good prognosis.

#### p0238

### CLINICAL EXPERIENCE WITH ESLICARBAZEPINE ACETATE WITH FOCUS ON ELDERLY

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**Background:** Eslicarbazepine acetate (ESL) is with its favorable safety profile a widely used newer antiepileptic drug (AED) in adults with focal epilepsy. Age is a major factor influencing the pharmacokinetic profile of AEDs. Tolerability of ESL and whether there is need for dose-adjustments in elderly have not yet been reported.

The main aim of this study was to evaluate the effect and side effects of ESL in our patients at age 60 years or older.

**Method:** The retrospective analysis of 74 patients with focal epilepsy treated with ESL was carried out at the Epilepsy Clinic, Glostrup Hospital, Denmark. The subgroup of 13 patients aged 60 years or older was selected. Data were collected by reviewing the patients' clinical and laboratory files. The course of ESL treatment, doses, concomitant AEDs, seizure frequency and adverse effects to ESL has been analysed.

**Results:** The sex distribution was 54% men and 46% women with a mean age of 69.5 years (60–82). Epilepsy was caused by a structural brain lesion in 11 cases. In seven patients ESL was initiated due to lack of seizure control and in six due to adverse effects to previous AEDs. Five patients shifted to ESL from OXC and needed 12–65% lower dose to achieve seizure control, while two shifted from CBZ.

All the patients with uncontrolled epilepsy achieved better seizure control on ESL add-on. However, seizure reduction was not significant ( $p = 0.07$ ) after at least six months of treatment.

Good tolerability was seen in 10 patients. The most common adverse effect was somnolence. ESL was withdrawn because of side-effects (in three cases) and lack of seizure control (one case).

**Conclusion:** Although our study group is small, the results indicate that ESL has an advantageous profile according to seizure control and well-tolerated also in elderly. Further prospective studies are needed to confirm these data.

#### p0239

### POST-STROKE EPILEPSY IN ELDERLY PATIENTS

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**Purpose:** To estimate disease progression peculiarities, cognitive impairments, life quality in patients with post-stroke epilepsy.

**Method:** 21 patient with post-stroke epilepsy (1st group) and 12 patients with a stroke without epilepsy (2nd group) were examined according to the following parameters: clinic and anamnesis, MOCA test, HADS scale, SF-36 scale.

**Results:** A stroke with its focus located in the right hemisphere was exposed in 67% of patients in the 1st group and in 83% of patients in the 2nd group. Post-stroke seizures developed in  $196.72 \pm 36.45$  days. Secondary generalized seizures were observed in 35% of patients, while 65% of patients had simple motor seizures. MOCA test results in the 1st group were  $22 \pm 1, 11$  points, in the 2nd group  $-25.2 \pm 1.98$  points. Pursuant to life quality assessment SF-36, physical functioning index (PF) was equal to  $48.5 \pm 7.22$  points in the 1st group and  $34.3 \pm 6.5$  points in the 2nd; role-physical index evaluating physical problems impact to disability (RP) amounted to  $11.25 \pm 4.61$  points in the 1st group and 0 points in the 2nd; social functioning index (SF) was equal to  $57.1 \pm 6.95$  points in the 1st group and  $60.67 \pm 7.33$  points in the 2nd; role-emotional index evaluating emotional problems impact to disability (RE) was  $25.0 \pm 7.81$  points in the 1st group and  $5.5 \pm 3.7$  points in the 2nd; mental health index amounted to  $50.15 \pm 5.5$  points in the 1st group and  $46.67 \pm 5.5$  points in the 2nd; physical health index (PH) in the 1st group was  $35.4 \pm 2.12$  points, mental health index (MH) was  $34.0 \pm 2.91$  points in the 1st group,  $32.0 \pm 1.89$  and  $32.17 \pm 2.07$  points in the 2nd group correspondingly.

**Conclusion:** Terms of post-stroke epileptic seizures manifestation were  $196.72 \pm 36.45$  days, dextrocerebral stroke, simple motor seizures prevailed. Depression was more typical in patients who suffered a stroke without epilepsy, while cognitive impairments severity was higher among patients with post-stroke epilepsy.

#### p0240

### ELDERLY SUBJECTS WITH NEWLY-DIAGNOSED FOCAL EPILEPSY OF UNKNOWN CAUSE

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**Purpose:** To report clinical, EEG and neuroimaging characteristics of elderly subjects with new-onset unprovoked epileptic seizures of unknown cause.

**Method:** Medical records of subjects consecutively referred to our out-patient practice since 2005, with a diagnosis of unprovoked focal epileptic seizures of unknown cause with age at onset  $\geq 60$  performed by one of us (CG) and maintained after a one-to-20-year follow-up, were reviewed to collect demographics, clinical, EEG, neuroimaging data and treatment outcomes. CT/MRI signs of leukoaraiosis and/or non-focal cortical atrophy were not considered as aetiological factors. Subjects with psychogenic seizures and major psychiatric and cognitive disorders were excluded.

**Results:** Eighty patients (40 females) aged (mean  $\pm$  SD)  $70.5 \pm 6.6$  years at seizure onset and  $77.7 \pm 6.4$  years at the last observation, with a single (six subjects) or recurrent unprovoked seizures (74 subjects) were identified. Fifty-two (65%) patients had seizures with impairment of consciousness whose semiology suggested a temporal lobe origin, 24 (30%) convulsive attacks during wakefulness, 26 (32.5%) sleep-related convulsive seizures. At seizure onset: standard EEG (S-EEG) detected interictal epileptiform abnormalities (IEAs) in nine patients (11.2%); 24-hour home-recorded ambulatory EEG performed in 70 subjects, detected IEAs in 52 (mainly or exclusively during 3–4 NREM sleep in 27), involving temporal lobe derivations in all cases. All patients underwent brain neuroimaging (MRI in 57 cases), with normal findings in 38 patients, leukoaraiosis in 41 and/or non-focal cortical atrophy in three. Forty-one patients (51.2%) became seizure-free for at least one year taking the first AED (at the lowest target dose in 38 of them).

**Conclusion:** In our series, late-onset focal epilepsies of unknown cause seem to be mainly of temporal lobe origin, and show a favourable response to AED treatment. First S-EEG showed a poor sensitivity in these patients; however, spontaneous sleep EEG recordings revealed a remarkable propensity to express IEAs predominantly during 3–4 NREM sleep stages.

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p0241

### EPILEPSY SURGERY IN CHILDREN AND ADOLESCENTS: OUTCOME IN RELATION TO ETIOLOGY, LOCATION AND EPILEPSY DURATION

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**Purpose:** Epilepsy surgery reportedly produces remarkable results in terms of seizure outcome and quality of life for medically intractable focal epilepsy in children. We reviewed the epilepsy characteristics and duration, neuroradiologic findings, pathologic findings, surgical approaches, complications and clinical outcomes in pediatric patients following an epilepsy surgery.

**Method:** Prospective observational study that included 43 consecutive patients (20 males) with drug-resistant focal epilepsies between 2005 and 2014.

**Results:** The median age at epilepsy onset was 4.0 years (range, 0–14 years) and the median age at surgery was 10 years (range 1–21 years), with a median epilepsy duration of 6 years, longer in children with an epilepsy onset between 7–9 years ( $p > 0.05$ ). The epilepsy syndromes identified were: focal symptomatic epilepsy ( $n = 38$ ), West syndrome ( $n = 1$ ), and Rasmussen's syndrome ( $n = 4$ ). Histopathology revealed: malformation of cortical development ( $n = 19$ ), gliosis ( $n = 10$ ), tumor ( $n = 6$ ), Rasmussen's encephalitis ( $n = 4$ ), hippocampal sclerosis ( $n = 3$ ) and dysembryoplastic neuroepithelial tumor ( $n = 1$ ).

After a median follow up of 5.4 years, 27 patients (68.8%) had an Engel 1, (9/11 hemispherotomies, 2/3 posterior epilepsies, 9/13 temporal epilepsies, and 7/16 of the frontal epilepsies), with a median epilepsy duration of 6 years. (engel 2-3-4, median duration of 5 years,  $p = 0.7$ ).

Resective surgery was performed in all patients, with chronic invasive neurophysiology in 31 (72.1%) Functional hemispherotomy was performed in 11 patients, with a median epilepsy duration of 3 years. 9/11 were seizure free ( $p = 0.13$ ).

**Conclusion:** In our study population we observed that patients who underwent functional hemispherotomy had a shorter epilepsy duration and better outcome, however it was not statistically significant.

p0244

### PERCEPTUAL DISTURBANCES AFTER EPILEPSY SURGERY

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**Purpose:** To present and discuss data on unexpected perceptual changes found in patients after epilepsy surgery.

**Method:** As part of routine follow-up after epilepsy surgery, patients were asked to refer post-surgical modifications in mood, perception and behavior. All adult patients operated on since April 2010, able to provide reliable data, were included.

**Results:** 5 out of 15 patients reported changes in perception, experienced as enhanced perception of specific sensory modalities in all cases, and transient in time in 4: 2 olfactory, 2 visual, 1 auditory. They lasted from 3 to 9 months, and were usually associated to changes in mood and/or libido. All cases were resective surgeries: 3 mesial temporal sclerosis, 1 periventricular nodular heterotopia, 1 tumor.

**Conclusion:** Perceptual, as well as behavioral, sexual and mood changes, should be addressed in patients after epilepsy surgery. The identification of these phenomena could help to understand ictogenesis and compensatory mechanisms involving changes of excitability in functional networks somehow connected to epileptic foci.

p0246

### CASE REPORT - TEMPORAL OR FRONTAL EPILEPSY

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**Purpose:** Patient DL 18 year old right handed forwarded from Pediatric Clinic with frequent complex partial seizure. MRI read with normal range. Seizures duration was 30 sec., patient stare, left arm hanging with hand making discrete pendulous movements (flapping), tap with his left leg sometimes with urination but without generalized seizure. The seizure started from unexpected and noisy sound (ring bell, screaming).

**Method:** Controlled MRI was made (dual pathology- right frontal Taylor displasia and right temporal hippocampal sclerosis), EEG with fotostimulation. Video EEG (sharp and slow waves complexes localized over the right frontal- temporal region with contra lateral transmission).

**Results:** For the last 6 months the seizure has lasted longer from few minutes to several hours. It has been started like before with difficulty in breathing and gazing, with flapping on the left arm and leg which produce automatisms (opening and closing the watch, or replacing something in the room etc).

**Conclusion:** It is needed to think in different direction about aetiology of the seizures, possible temporal or frontal epilepsy.

p0247

### MORBIDITY AND MORTALITY ASSOCIATED TO DEEP ELECTRODES IMPLANTATION (SEEG) IN REFRACTORY EPILEPSY

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**Purpose:** To determine the complications rate related to deep electrodes implantation (stereoencephalography-SEEG) for pre-resective topographic diagnosis of the epileptogenic zone.

**Method:** Retrospective analysis involving patients implanted with deep electrodes carried out by the Department of Neurosurgery, Hospital Italiano de Buenos Aires, since November 2009 to December 2014. The implantations were performed under stereotactic guidance and were planned through merger of Angiography and Magnetic Resonance Imaging. Were excluded those patients who were simultaneously implanted with subdural grids. For complications analysis was used Wellmer's. Both relevant data patients and surgical management were collected.

**Results:** A total of 287 depth electrodes were placed in 22 implantation procedures. The average age was 32.5 (21–58) years. From the total 9

cases were men and 12 cases were women. On average, 13.0 (6–20) electrodes were placed per procedure, bilaterally in 12 (54.5%) of them. The average time of VEEG monitoring was 6.6 (2–19) days. There were 2 (9.1%) patients presenting postoperative complications due to development of intracerebral hematoma, requiring surgical evacuation. Tomographic anomalies were detected in control scans without clinical impact in three patients (*lineal subarachnoid hemorrhage, intracerebral hematoma, laminar subdural hematoma; respectively*).

The overall incidence of complications was 1.7% per electrode, while clinically relevant complications were 0.7% per electrode. There were no deaths.

**Conclusion:** The SEEG is useful for a correct identification of epileptogenic zone. This allows a good delineation of brain electrophysiology, and can study in a 3D fashion the epileptogenic networks. The use of electrodes is a safe process when associated with a proper execution of the preoperative preparation, planning implantation and surgical technique.

#### p0248

##### WEST SYNDROME ASSOCIATED TO UNILATERAL MESIAL TEMPORAL SCLEROSIS

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**Purpose:** Children with West syndrome often present with refractory and life-threatening seizures. Primary treatment is medical, but surgical options have been considered in very refractory patients. Resective procedures, mostly involving the posterior quadrant were performed in selected cases; neuromodulation has been sparsely employed. MRI is rarely positive. We describe a kid with West syndrome associated to a focal, usually epileptogenic lesion (mesial temporal sclerosis).

**Method:** This 1.5 year-old boy started having spasms by the age of 9 months. By that time, spasms were symmetric. Ictal and interictal EEG showed diffuse bilateral spike and wave discharges and an hypersarhythmic background. MRI showed left hippocampal edema by the time of seizure initiation. He was treated with high dose AEDs, ACTH, ketogenic diet and cannabidiol. At presentation, spasms were slightly asymmetric (right side predominance). EEG showed diffuse spike-and-wave-discharges and multifocal activity prevailing over the left posterior quadrant. MRI showed left mesial temporal sclerosis. PET showed marked temporal lobe hypometabolism. Development was retarded; at presentation he was sedated and was not able to sit.

**Results:** He was submitted to a temporo-parieto-occipital resection. There was a 90% reduction in spasms' frequency, which from then on concentrated on night-time. At one month postoperatively he was much more alert and able to sit with help. Pathological examination of the temporal lobe specimen showed mesial temporal sclerosis; the parietal-occipital cortex was normal.

**Conclusion:** This kid greatly benefited from surgery, suggesting that the removed cortex was indeed involved in his epileptogenesis. Mesial temporal sclerosis is rarely seen in kids with West syndrome. It is likely that mesial temporal sclerosis represented an epiphenomenon of a prevailing left hemisphere epileptogenesis and not the etiology of this kid's epileptic syndrome.

#### p0249

##### REFLEX SEIZURES INDUCED BY SENSORY STIMULI: A SEEG STUDY

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Seizure precipitation by sensory stimuli is a well-known condition in which a specific stimulus can induce a specific type of seizure. Photosensitive epilepsy is the best characterized syndrome. In the 2011–2015 period we studied 22 patients (M/F: 9/13) affected by focal epilepsy with SEEG. Among them two male patients presented focal seizures following somato-sensory stimuli. The first patient is a 28 year-old man with seizures characterized by a focal paresthesia in the left hand followed, after 30'', by an impairment of consciousness, some oral and bilateral gestural automatism. Secondary generalization were quite frequent (1–2 every month). The seizures were caused by sudden stimuli in the left arm or emotion. The interictal and ictal EEG showed a fronto temporal involvement. He was then studied with a right perisylvian SEEG exploration who evidenced a primary posterior insula involvement with diffusion in the SII region and opercular region. The second patient is a 5 year old boy with seizures characterized by left clonic buccal jerking. Jerks were mostly related to stimuli in the left inferior dental arch mainly induced by tooth brushing or by speaking. Like the previous patient sudden emotions can induce seizure. The SEEG, mainly centered in the central operculum, evidenced a quite extended ictal origin encompassing the central insulo-opercular region with a fast diffusion over the inferior part of the rolandic sulcus. Till nowadays some SEEG data come from seizures induced by eating and startle in which the insula and the SMA region, respectively, are the most involved regions. Here we report the first two patients with reflex seizures caused by somatosensory stimuli showing a clear cut epileptogenic zone in the central and post-central insulo opercular region highlighting the importance of the insula and SII region in the genesis of the reflex seizure.

#### p0250

##### ICTAL SEMIOLOGY CAN DISCRIMINATE TEMPORAL FROM EXTRATEMPORAL LOBE SEIZURES: THE ETESS MODEL

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**Purpose:** The aim of the present study is to develop and validate a computational model (ETESS: extratemporal and temporal epilepsy seizure semiology scale) to differentiate temporal from extratemporal lobe seizures, based on ictal semiology.

**Method:** We retrospectively analyzed 128 consecutive seizures recorded during pre-surgical monitoring at the three participating centers. Only patients with at least 1 year of follow-up after surgery and with a favorable outcome (Engel's class Ia) were admitted to this study. Video-EEG recordings of each seizure were independently and blindly analyzed by three experts. Fourteen symptoms and 15 signs, as well seizure duration, were analyzed for each seizure, and included in the computational model. In order to create and test the model all seizures were randomly divided in two groups: the "training group"

(103 seizures) and the "testing group" (25 seizures). ETESS was built on the training group calculating the odd ratio for each sign and symptom using multiple logistic regression analysis.

**Results:** In the testing group ETESS model recognized 19/25 seizures and the accuracy is 76%. The positive predictive value in recognizing a temporal lobe seizure is 73% whereas the negative predictive value is 80%. There is a significant association between the ETESS prediction and the lobe of seizure onset (Fisher exact test  $p = 0.015$ ).

**Conclusion:** ETESS can be a useful tool in distinguishing temporal from extratemporal lobe seizures, particularly when planning epilepsy surgery.

## Epilepsy Surgery 2 Sunday, 6th September 2015

p0251

### RETROSPECTIVE ANALYSIS OF EPILEPSY SURGERY PATIENTS: A SINGLE CENTER EXPERIENCE

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**Purpose:** Surgery is a widely approved approach to long-standing epilepsy patients for whom the pharmacological option is both an economical burden for the patients and a futile way to compensate the disease.

**Method:** Epilepsy surgery started in our department 20 years ago. We performed a retrospective study on total 449 surgery patients starting from 1995 to 2015. Patients' operation dates, the age at operation, socioeconomic status, localization of the lesion, the pathologies and the operation type were collected and analyzed.

**Results:** Of the patients analyzed 50% (225) were women and 50% (224) were men. 15% (69) of patients were under the age of 12, 13% (60) were between 13–18, 66% (297) were between 19–45 and 3% (13) were over 45. There were 7 patients younger than 2 years. According to years: 15% (67) were operated before 2000, 25% (111) between 2000–2004, 30% (135) between 2005–2009, 28% (126) between 2010–2014, unknown %2(10). 39.9% (179) of patients presented with mesial temporal sclerosis (MTS), 19.2% (86) with cortical dysplasia (CD), 18.7% (84) with tumoral lesions, 6.7% (30) with dual pathology, 1.1% (5) with developmental anomalies, 3.3% (15) with vascular lesions, 7.1% (32) others. %4(18) patients underwent corpus callosotomy, functional hemispherectomy and partial hemispherectomy. Ten patients were lost to follow-up. Throughout years the incidence of mesial temporal sclerosis and cortical dysplasia have changed reciprocally. MTS before 1999-%18(32), 2000–2004-%41(73), 2005–2009-%20(36), 2010–2014-%21(38). CD before 1999- %6(5), 2000–2004-%6(5), 2005–2009-%44(38), 2010–2014-%44(38). Surgery techniques differed according to the time and type of the operation such as: 14% (63) amigdalohippocampectomy, 34.3% (154) temporal lobectomy, 43% (193) non-specific excision, 0.7% (3) corpus callosotomy 4.2% (19) Hemispherectomy, 0.4% (2) lobectomy (frontal and occipital). It is noteworthy to state that the trend in amigdalohippocampectomy declined and replaced with anterior temporal lobectomy.

**Conclusion:** Epilepsy surgery is an effective treatment in well selected cases. The pathology and surgical procedures are changing during the years. Moreover number of children is increasing including the very young ages.

p0252

### SAFETY PROFILE OF STEREOTACTIC DEPTH ELECTRODE RECORDINGS IN DRUG RESISTANT EPILEPSY

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**Purpose:** Invasive stereo-electroencephalography (SEEG) with depth electrodes is a common approach to identify the epileptogenic focus in intractable partial epilepsy. The purpose of this study was to analyze the safety profile of depth electrode implantation in an experienced tertiary center and to identify possible risk factors for complications.

**Method:** We retrospectively examined the adverse events in the course of 163 procedures of depth electrode implantation performed in our institution between 1991 and 2014 in patients aged 15 to 60 years (mean 32.4 years). Implantation schemes comprised mostly oblique SEEG ( $n = 128$ ) but also occipito-hippocampal Spencer electrodes in combination with strip electrodes ( $n = 35$ ). A majority of patients (58.9%) had MRI negative non-lesional epilepsy. Complications were scaled in 5 grades of severity and classified as major (requiring treatment or leading to neurological impairment) or minor.

**Results:** The rate of overall complications was 4.9%, and complications classified as major occurred in 3.1% of procedures, but none were associated with permanent morbidity or mortality. Clinically relevant infection occurred in 1.2% and hemorrhage in 3.7% of patients, respectively. One case of epidural hematoma requiring emergency evacuation is reported. Collapsed over all patients, the risk of hemorrhage per electrode was 4.4‰. We identified only one significant risk factor for adverse events: MRI negative cryptogenic epilepsy, which was associated with a higher risk of overall ( $p = 0.04$ ) and hemorrhagic ( $p = 0.04$ ) complications. This might well be related to a higher number of implanted electrodes in non lesional versus lesional epilepsy. There was no correlation between the implantation technique and the overall complication rate.

**Conclusion:** Depth electrode implantations have a favorable safety profile. However, despite a well-standardized surgical technique, invasive workup can in rare cases lead to serious complications. Thus, the procedure requires a careful assessment of risks and benefits.

p0254

### THE EVOLVING ROLE OF MRI GUIDED LASER ABLATION IN RESECTIVE EPILEPSY SURGERY

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**Purpose:** Recognition of indications, outcome and management of patients undergoing MRI Laser Ablation as an alternative to open craniotomy resective epilepsy surgery.

**Method:** Review of last 5 cases treated with MRI Guided Laser Ablation.

**Results:** One patient with occipital periventricular heterotopia and four patients with hypothalamic hamartomas (HH) were treated with MRI Guided Laser Ablation. All patients with HH showed significant improvement in seizure control even if non gelastic seizures occurred.

One patient developed transient global amnesia and a second had significant cerebral edema. The patient with heterotopia showed significant reduction in seizures.

**Conclusion:** MRI Guided Laser Ablation provides a minimally invasive alternative to open resective epilepsy with good seizure outcome but awareness of potential complications should be noted.

#### p0255

### COGNITIVE OUTCOMES AND CORTICAL METABOLIC ACTIVATION CHANGES OF DIFFERENT SURGICAL APPROACHES IN MESIAL TEMPORAL LOBE EPILEPSY

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**Purpose:** Epilepsy surgery is a successful treatment option for drug resistant focal epilepsies. However, cognitive impairment is very common in epilepsy patients and could be negatively or positively affected by surgery. Long-standing debate of whether different surgical approach for mesial temporal lobe epilepsies may be superior with regards to seizure control as well as cognitive outcome. We aimed to investigate seizure control, cognitive outcome and cortical metabolic activation changes between two different selective amygdalohippocampotomy (SA) techniques in patients with unilateral mesiotemporal lobe epilepsy (MTLE).

**Method:** In this study, thirty-three patients with unilateral MTLE (17 females, mean age: 31.6 years, 12 right side) were enrolled. All of them were evaluated by routine pre-op test for MTLE (including neuropsychological tests, 18-fluorodeoxyglucose positron emission tomography (PET), magnetic resonance imaging (MRI), video-EEG). As for the surgical approach, five patient had standart AH+ anterior temporal lobectomy, 11 patient had transsylvian hippocampal transection and 17 patient had paramedian supracerebellar-transventorial PSTA. Post operative seizure outcome, neuropsychological test results and PET scan were evaluated.

**Results:** Thirty-two patients had complete follow-up. Twenty-seven patient were class I and three patient were class II seizure freedom was achieved. There were differences in memory outcome between the sides of operation, and between the operation types. On the left side, neuropsychological test results were significantly improved in PSTA group ( $p < 0.05$ ) Additionally, cortical metabolic activation changes before and after operation and between the surgery types were different. The PSTA group showed significant improvement on statistical parametric mapping of cortical metabolic activation values ( $p < 0.05$ ).

#### p0256

### HFO DETECTION IN INTRA-OPERATIVE ECOG RECORDINGS: VALIDATION OF A TIME-FREQUENCY BASED AUTOMATIC DETECTOR

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**Purpose:** High frequency oscillations (HFOs) in the electrocorticogram (ECOG) have recently been shown by several centers to be a specific bio-

marker for epileptogenic tissue. Time consuming and subjective visual inspection prevents to benefit from the HFO information in intraoperative sessions. While several automatic HFO detectors have been proposed, we validate here our time-frequency based HFO detection algorithm (Burnos et al., 2014).

**Methods:** Pre-resection intra-operative ECoG (N = 7 patients, 2xN recordings of 1 minute) was recorded at 2048 Hz in the UMC Utrecht and HFO events were marked visually. For each patient, we optimized the detector's parameters defining baseline and threshold on a first dataset (training), and validated it on a second dataset (test). The performance was quantified in terms of ROC (Receiving Operator Curve). Automatic detection of a visually marked event was considered as a True Positive (TP). A correctly undetected baseline interval was a True Negative (TN). False Positives (FP) were events detected but not marked visually, and False Negatives (FN) were undetected but visually marked events.

**Results:** In the ECoG with visually marked HFOs, we achieved high sensitivity and specificity (across patients TP rate >0.95, FP rate <0.01). The detector robustly identified baseline intervals (low FP rate). Optimal tuning of baseline and threshold parameters over 1 minute data emulated visual detection for each single patient (high TP rate). Interestingly, in the ECoG without visually marked HFOs, in test sessions the method provides very low FP rate (<0.01), corresponding to a very high specificity.

**Conclusion:** Our semi-supervised HFO detector rapidly and accurately emulates experienced visual HFO marking, which is currently considered the gold standard. It thereby holds promise for future clinical application.

#### p0257

### COMPARISON OF AUTOMATICALLY DETECTED PREOPERATIVE HIGH FREQUENCY OSCILLATIONS (HFOS) WITH CLINICAL OUTCOME

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**Purpose:** In recent years, invasively detected interictal HFOs - Ripples (R, 80–250 Hz) and Fast Ripples (FR, 250–500 Hz) - have been suggested as a reliable biomarker for epileptogenic tissue identification. Nevertheless, the functional significance of R and FR still remain to be clarified. A crucial aspect regarding the characterization of HFOs is their detection, which is mainly performed by visual marking, a highly time consuming process affected by subjective criteria. Here we present an innovative automatic detector, in order to describe the role of HFOs in comparison to the clinical outcome.

**Method:** Preoperative invasive data from five epileptic patients, three with good and two with poor clinical outcome, has been analyzed with a two stage automatic detector, based on instantaneous spectral estimation. This detector has been previously validated on a visually marked dataset. The analysis has been conducted separately for R (80–250 Hz) and FR (250–500 Hz) events. Areas with high HFO occurrence were compared with the clinically identified Seizure Onset Zone (SOZ) and the area of surgical resection.

**Results:** In patients with temporomesial electrodes, we observed both R and FR, while FR were more rarely detected in cortical signals. In patients with good outcome, we observed a high specificity of FR, while in 1/3 cases we observed the detection of possibly physiological R contralateral to the SOZ. In patients with poor clinical outcome, R and FR occurred in a subset of contacts showing epileptiform potentials and were present also outside resected areas.

**Conclusion:** The time-frequency based automatic HFO detection provides a rapid assessment of their potential contribution. The simultaneous

presence of R and FR shows a high specificity for the epileptogenic zone. The mismatch between the HFO area and the SOZ in patients with poor outcome needs further HFO investigation, now supported by an automated tool.

**p0258**

### ELECTROCORTICOGRAPHIC LANGUAGE MAPPING WITH A LISTENING TASK CONSISTING OF ALTERNATING SPEECH AND MUSIC PHRASES

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**Purpose:** Electrocortical stimulation mapping (ESM), the gold standard in pre-surgical language mapping of epilepsy patients, is time consuming, requires good patient cooperation and carries the risk of inducing afterdischarges and seizures. Electrocortical mapping of high gamma activity induced by language tasks has been proposed as an alternative, but it often reveals more areas involved in language processing than those considered critical with ESM. We investigated if critical language areas can be localized with a listening task consisting of speech and music phrases.

**Method:** Nine patients with implanted subdural grid electrodes listened to a short audio fragment in which music and speech alternated four times. We analysed ECoG power in the 65–95 Hz band and used principal component analysis to obtain task-related activity patterns in electrodes over language areas. We used *t*-tests to determine if discrimination between listening to speech and music was significant. The spatial distribution of discriminating sites was compared to ESM results using sensitivity and specificity calculations.

**Results:** Electrodes with significantly more high gamma activity during listening to speech compared to music or vice versa ('speech' and 'music' electrodes) were identified on the superior temporal gyrus and inferior frontal gyrus. Compared to ESM, our test of alternating speech and music phrases had a low sensitivity (0.32) but a high specificity (0.95).

**Conclusion:** Our test cannot replace ESM, but this short and simple task can give a reliable indication where to find critical language areas, better than ECoG language mapping using language tasks alone.

**p0259**

### COMPARISON OF NON-HARMONICITY AND HIGH-FREQUENCY OSCILLATIONS IN INTRA-OPERATIVE ELECTROCORTICOGRAPHY DATA

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**Purpose:** During epilepsy surgery, biomarkers in intra-operative electrocortical mapping (ECoG) can be of great value in guiding the neurosurgeon by effective delineation of the epileptogenic zone (EZ). We investigate the ability of a fast and automated algorithm, the AutoRegressive model Residual variation (ARR), to identify electrode positions delineating epileptogenic tissue. This was done by determining the correspondence between ARR and the amount of high-frequency oscillations (HFOs; 80–500 Hz).

**Method:** We analysed pre-resection intra-operative ECoG recordings of three patients with refractory focal epilepsy (2 temporal, 1 frontal). Per patient one-minute epochs in one or two grid orientations were selected, resulting in a total of five epochs. In each epoch we visually marked HFOs, resulting in a ripple (80–250 Hz) and fast ripple (FR; 250–500 Hz) rate per channel. ARR measures high residual variation after autoregressive model fit to quantify the presence of non-harmonicity in the signal. ARR values were calculated per channel for the same epochs and for five-second artefact-free sub-selections (ARR<sub>5</sub>). We analysed the association between ARR or ARR<sub>5</sub> results and the ripple and FR findings, using Pearson's correlation coefficient,  $\rho$ .

**Results:** 93 channels were analysed in total; 79 showed ripples and 20 showed FR. Combining results from the total dataset, correlation analysis between ripples and ARR showed  $\rho = 0.73$ , and  $\rho = 0.72$  for ARR<sub>5</sub>. Comparison with FR results showed even stronger correspondence:  $\rho = 0.89$  for ARR and  $\rho = 0.82$  for ARR<sub>5</sub>. All findings were significant with  $p < 0.0001$ .

**Conclusion:** These preliminary results suggest correspondence between brain areas producing HFOs and areas producing high ARR values, especially for more pathological FRs. Moreover, results indicate only a short five-second epoch is sufficient to obtain reliable ARR results. This method could be a valid tool for online intra-operative delineation of the EZ, as it is quick and easy to compute and requires only a very short measurement.

**p0260**

### FORAMEN OVALE ELECTRODES: "AN OLD NEW FRIEND". OBSERVATIONAL STUDY

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**Purpose:** Describe our experience with Foramen Ovale Electrodes and to determine the ability of foramen ovale electrodes to localize and lateralize epileptogenic foci in patients referred to the VideoEEG Monitoring department in a center in Colombia.

**Method:** We identified patients who had undergone to Foramen Ovale Investigation for to localize and lateralize epileptogenic foci in the Video Monitoring department of our center Neurocentro in Colombia by three years, between July of 2011 to July 2014 and analyzed retrospectively the surgical outcomes after the procedure, the indication for to underwent to videoEEG + FOE, average of time of register and take conclusions, the final result of VideoEEG + FOE study. all patients were followed up and were grouped on into three categories:

- (1) patients who underwent to surgery epilepsy. and freedom of seizures after the follow up.
- (2) patients who underwent to medical treatment,
- (3) patients who the study was no conclusive.

**Results:** Sixteen patients underwent VideoEEG + FOE investigation, all of them were conclusive. The first indication to indicate VideoEEG + FOE was lateralize epileptogenic foci 16 (100%), the average of time register was 72 hours (+/- 12 hours), Adverse Events was reported in 1(6%) a cerebral abscess 1 week after the FOE implantation. It was solved with antibiotic treatment, without sequelae. 7 (43%) were determined to be appropriate candidates for resective surgery. 9 (56%) were to medical treatment, for consider them at high risk for verbal memory deficit after surgery or poor candidates for surgical treatment.

**Conclusion:** We have evidence, that the Foramen ovale Electrodes implantation after 24 hours of initial register, is a safety procedure and a conclusive method when it is add to VideoEEG, that we can use for lateralize the initial ictal foci, in a Latinoamerican country where advance techniques of images are not broadly available.

## Genetics 1

### Sunday, 6th September 2015

p0261

#### IDENTIFYING PATIENTS WITH PHARMACORESISTANT EPILEPSY USING A PLASMA-BASED TEST

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**Purpose:** Refractory epilepsy occurs in ~30% of all patients and major causes are focal cortical dysplasia (FCD) and mesial temporal epilepsy (MTLE). Epilepsy surgery can be performed in order to achieve seizure control; nevertheless, this indication may be delayed due to a long clinical investigation. Therefore, the identification of biomarkers for pharmacoresistant epilepsy could improve diagnosis and decrease of this time. Circulating microRNAs (miRNAs) are potential candidates to be used as biomarkers. These small noncoding RNA have been associated with different disease states. In this context, the objectives of this study are

i) to determine if changes in expression of three candidate miRNAs, previously associated with mechanisms underlying MTLE and FCDs: **hsa-miR-23a**, **hsa-miR-31** and **hsa-miR-134** are present in plasma of patients with pharmacoresistant seizure and

ii) to verify if plasma levels of these miRNAs can distinguish between patients who respond to antiepileptic drug (AED) treatment and those who are resistant to drug treatment.

**Methods:** We determined plasma levels of these miRNAs by qPCR. This study is divided into two stages: an initial discovery phase and a validation study. In the first trial, miRNAs were quantified in 18 patients with FCD, 14 patients with MTLE, both with refractory epilepsy and 16 controls. To further verify the discriminating power of these miRNAs we accessed an additional cohort of patients with MTLE, divided into patients who are responsive to AED therapy (n = 38) and unresponsive (n = 40), as well as control subjects (n = 80). We used ROC curve and Wilcoxon test, corrected by Bonferroni.

**Results:** Our preliminary results indicate that **hsa-miR-31** is up-regulated in patients with FCD and MTLE when compared to controls; moreover, **hsa-miR-31** was able to distinguish patients with and without epilepsy, with AUC of 0.785.

**Conclusions:** Elevated **hsa-miR-31** is a potential non-invasive biomarker for pharmacoresistant epilepsy. Further validation studies are under way.

p0262

#### BROAD-SPECTRUM ANALYSIS OF POLYMORPHISMS INVOLVED IN PHARMACOGENOMICS OF DRUG-RESISTANT EPILEPSY. PRELIMINARY RESULTS OF AN ONGOING STUDY

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**Purpose:** To investigate the combined role of a broad spectrum of polymorphisms involved in pharmacogenomics of drug-resistant epilepsy patients accounting of almost 30% of total patients despite the recent advances in therapeutics.

**Method:** Two hundred consecutive patients were recruited in the study. All their electroclinical and imaging data were recorded and patients were classified according to their pharmacoresistance. Patients were genotyped for polymorphisms of proteins implicated in three steps of pharmacokinetics and pharmacodynamics: a) drug absorbance and transportation (ABCB1 and ABCC2), b) drug metabolism (UGT1A6, UGT2B7, CYP2C9, CYP2C19 and EPHX1) and c) target-proteins (SCN2A). In total, patients were genotyped for 17 polymorphisms, which, according to literature, are mostly implicated in drug-resistance.

This study has been co-financed by the European Union (European Regional Development Fund) and Greek national funds through the Operational Program "THESSALY- MAINLAND GREECE AND EPIRUS-2007-2013" of the National Strategic Reference Framework (NSRF 2007–2013).

**Results:** Genotyping has been completed in 69 patients (38 males). Subjects' median age was 37 years. Median age of epilepsy onset was 18 years. Twenty five patients (36%) have pharmacoresistant epilepsy. There was no statistically different distribution of genotypes and alleles tested with the exception of G2677A/T of ABCB1 protein (p = 0.049) and a trend for G1249A of ABCC2 protein (p = 0.090). This may suggest a possibly significant role of transport proteins in absorbance and distribution of antiepileptic drugs in drug-resistant patients.

**Conclusion:** The small number of genotyped patients does not allow any final conclusions. Of interest is the approach of investigation of possible interactions across different steps of pharmacokinetics and pharmacodynamics in drug-resistant epilepsy. Literature lacks such broad approaches which are necessary to understand the complexity of pharmacoresistance.

As soon as our study is complete, the aforementioned approach could be assayed and decided if it is worthy to be tested in larger populations.

p0263

#### TARGETED NEXT GENERATION SEQUENCING AS A DIAGNOSTIC TOOL IN 163 PATIENTS WITH EPILEPTIC ENCEPHALOPATHIES

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**Purpose:** Epilepsy is one of the most common neurological disorders, and is known to have a very heterogeneous background with a strong genetic contribution. In recent years several genes have been associated with epilepsy. However, making a genetic diagnosis in a patient can still be challenging as there is both genetic heterogeneity for a given epilepsy syndrome and phenotypic heterogeneity for a specific gene. The aim of

this study was to develop a diagnostic screening method to analyze the genetic basis of childhood epilepsies.

**Method:** A gene panel targeting 45 known epilepsy genes was developed for next generation sequencing. Potentially causative variants were evaluated by literature and database searches and submitted to bioinformatic prediction algorithms. Variants were verified by Sanger sequencing and parents were included for segregation analysis. We used this panel on an unselected cohort of 163 patients, sequentially referred for panel testing. The majority of the patients had a range of epileptic encephalopathies or childhood epilepsies.

**Results:** We identified a presumed disease-causing mutation in 40 of 163 patients. The aberrations encompassed known and unknown point mutations in several different genes e.g. *SCN1A*, *STXBPI*, *CDKL5*, *SCN2A*, *SCN8A*, *CHD2*, *GNAO1*, *GABRA1*, *GABRB3*, *KCNA2*, *STX1B*. All mutations were confirmed by conventional Sanger sequencing and, when possible, validated by parental testing and segregation analysis. A clinical follow-up showed that the genetic diagnosis had led to changes in medication in at least 10 of the patients.

**Conclusion:** We have developed a rapid and cost-efficient screening panel for the analysis of the genetic basis of childhood epilepsies. With this panel we were able to find a disease-causing genetic variation in 25% of the analyzed patients. Furthermore, this study demonstrates the potential for a genetic diagnosis to guide antiepileptic treatment.

#### p0264

### EPILEPSY PHENOTYPE IN PATIENTS WITH DOUBLE CORTEX: AN ARGENTINE SERIES

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**Purpose:** To analyze the clinical and neuroradiological features of patients with double cortex.

**Method:** A retrospective descriptive study was performed of 10 patients with diagnosis of HSB from January 2000 until June 2013.

**Results:** The mean age was 22 years, the average age of onset, 3.5 years, 60% were women. 40% had focal seizures, 20% generalized seizures and 40% both. Most patients had symptomatic focal epilepsy related to localization 50%, followed by 30% unclassifiable and 20% Lennox Gastaut syndrome. All had refractory epilepsy and developmental delay. Eight patients with moderate developmental delay and 2 severe. In the electroencephalogram, 50% had focal discharges, 40% both and 10% not present. The MRI showed diffuse involvement, 3 with anterior predominance and 2 with back predominance. The average number of drugs used was 6. Valproic acid was the most AED indicated (9p), followed by lamotrigine and carbamazepine (8p). The semiology was related to the focal dominance of the double cortex. (p 0.0039)

**Conclusion:** We found an association between the seizure semiology and focal predominance double cortex. No significant difference was found in other clinical variables and neuroradiological subclassification.

#### p0265

### NOVEL HCN ION CHANNELS MUTATIONS IN IDIOPATHIC GENERALIZED EPILEPSY

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**Purpose:** The Ih current, generated by the hyperpolarization-activated, cyclic nucleotide-gated (HCN) channels, controls intrinsic excitability in neurons. Because of their role, defective HCN channels are natural candidates in the search for the causes of epilepsy. We previously identified the first *HCN2* recessive mutation (E515K) in generalized epilepsy (IGE) (DiFrancesco et al., 2011). Recently, *HCN1 de novo* mutations have been identified in early infantile epileptic encephalopathy (EIEE) (Nava et al., 2014). So far, there are no reports of *HCN4* mutations linked to epilepsy, even if this channel is highly expressed in the CNS.

**Methods:** For this study, we recruited 226 IGE patients (children and adult subjects, both sporadic and familiar cases), characterized by clinical, pharmacological, neuroradiological and electrophysiological data. Patients were screened to search for mutations in *HCN* channels (isoform 1, 2, 4), using Next Generation Sequencing (NGS) TruSeq Custom Amplicon (Illumina).

**Results:** We report the identification of the first mutation on *HCN4* (R550C) in two male brothers, both affected by juvenile myoclonic epilepsy. Interestingly, this mutation affects the Arg550 residue of hHCN4 that is strategic for the correct channel's activity.

In one drug-resistant IGE case, we identified the L157V *de novo* mutation on *HCN1*, located on the S1 domain of the channel. Notably, the two sisters of the proband, both affected by absence epilepsy responsive to drug treatment, resulted negative for this mutation.

**Conclusion:** We report the first evidence in humans of a mutation on *HCN4*, presumably responsible for epilepsy. This result, together with the identification of a novel *HCN1* mutation, support an important role played by HCN channels in the pathogenesis of generalized epilepsies. Further studies are needed to better understand the pathogenetic mechanisms linking epilepsy to the dysfunction of HCN activity, potentially proposing these channels as possible therapeutic targets for the treatment of the disease.

#### p0267

### FAMILIAL TREMOR, EPILEPSY AND MENTAL RETARDATION

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**Purpose:** Familial cortical tremor, myoclonus, and epilepsy is a well described epilepsy syndrome that was first reported in Japanese families and later in European families. We describe an Egyptian family with tremor, epilepsy, and mental retardation with an autosomal dominant pattern of inheritance.

**Method:** Patients were recruited from outpatient clinics of Ain Shams University hospitals. Affected family members were invited for clinical examination. EEG and imaging studies were reviewed.

**Results:** The family included a father and two of his children. The father was 55 years old at the time of assessment. He had mild action tremors of the upper limbs that appeared in early adolescence and reached a peak in his early thirties then became less disruptive as he grew older. His son was 21 years old at the time of assessment. He had an IQ of 52. At the age of 10 he developed coarse action tremors involving both hands that increased in severity with time and interfered with daily activity such as dressing and feeding. At the age of 20 the patient started to experience generalized tonic clonic seizures. Neurological examination confirmed coarse postural and action tremors of both upper limbs and neck. EEG showed diffuse background slowing but no focal activity. MRI of the brain was unremarkable. The daughter was 23 at the time of presentation. She had an IQ of 54. She developed frequent GTC seizures from the age of 13, and CPS, likely of temporal origin from the age of 21. Seizures were well controlled on a combination of carbamazepine and valproate. Neurological examination revealed fine postural and action tremors of the upper limbs but is otherwise unremarkable. Inter-ictal EEG and MRI showed no abnormality.

**Conclusion:** The clinical features in this family make autosomal dominant cortical myoclonus with epilepsy the most likely diagnosis.

**p0268**

### FAMILIAL FOCAL EPILEPSY: DOES LOCALIZATION MATTER?

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**Purpose:** Studies in epilepsy genetics have often followed the traditional classification dividing epilepsies into generalized and focal, and then further classifying focal epilepsy based on seizure localization. This approach led to the identification of genetic focal epilepsy syndromes ADNFLE, ADLTE and ADFEVF. The classification of familial focal epilepsy based on localization of seizures may not be justified. To test this, we compared clinical features in a group of patients with familial temporal and frontal lobe seizures.

**Method:** Patients were recruited from the outpatient clinics of Ain Shams university hospital based on clinical features of partial epilepsy and positive family history of epilepsy or febrile convulsions. Patients with history or investigations evidence of an underlying lesion were excluded. Patient's evaluation included detailed clinical and family history, neurological examination, EEG and brain MRI. Patients were further classified according to presumed lobe of origin.

**Results:** The study involved 23 patients (10 males), with a mean age of 21.87 + /-10.6 years. Diagnosis was temporal lobe epilepsy in 15 patients and frontal lobe epilepsy in 8 patients. There were no significant differences in the frequency and type of epilepsy in families of patients with temporal or frontal lobe epilepsy. The two groups should no significant differences regarding age at onset, seizure types (simple partial, complex partial, secondary generalized) or seizure frequency.

**Conclusion:** In the absence of clinical features characteristic of well-defined familial focal epilepsy syndromes such as ADNFLE and ADLTE, localization of seizure onset has limited value in classification of familial epilepsy.

**p0269**

### FAMILIAL FOCAL EPILEPSY WITH VARIABLE FOCI IN AN ARGENTINIAN FAMILY: CLINICAL CHARACTERISTICS AND DEPDC5 MUTATION DIAGNOSED THROUGH EXOME SEQUENCING

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**Introduction:** Familial focal epilepsy with variable foci (FFEVF) is an autosomal dominant partial epilepsy syndrome. FFEVF is a relatively rare syndrome and the exact incidence remains unclear. Different family member share a unifocal epilepsy, with different cortical locations that include temporal, frontal, centroparietal, or occipital lobe regions.

**Purpose:** To describe a two generation argentinian family with a dominant focal epilepsy and a mutation in DEPDC5 gene.

**Methods:** Clinical characteristics, EEG and MRI findings were analyzed. Exome sequencing was performed followed by a pipeline analysis with bioinformatic tools. The findings were confirmed through Sanger sequencing.

**Results:** The mutation was found in three members of two generations without consanguinity history. Median age of onset was 9 years old. The

father had occipital lobe semiology and the two sibling frontal lobe epilepsy semiology. Physical, neurological examinations and MRI were normal. The three are seizure free, two with carbamazepine and one with valproate acid. The boy's VideoEEG showed a frontotemporal ictal onset. Exome sequencing revealed a new missense mutation in DEPDC5 gene, c.4657T>C p.Leu1553Pro.

**Conclusions:** The clinical characteristics of this family fulfilled criteria for FFEVF and exome sequencing proved useful as a diagnostic tool. As described in other reports, we observed an excellent response with carbamazepine.

**p0270**

### HICCUP-LIKE SEIZURES AND A NOVEL STOP CODON MUTATION IN A NEWBORN WITH NON-KETOTIC HYPERGLYCINEMIA

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**Purpose:** Non-ketotic hyperglycinemia (NKH) is an autosomal recessive inborn error of glycine metabolism, resulting in the accumulation of large amounts of glycine in body fluids and severe neurologic disturbances immediately after birth. This metabolic disorder is due to a defect in the liver enzyme complex, termed the glycine cleavage system. More than 80% of patients with NKH have a defect in P protein. Mutations in the GLDC gene are responsible for 70% of non-ketotic hyperglycinemia cases, whereas mutations in the AMT and GCSH genes account for 20% and <1% of non-ketotic hyperglycinemia cases, respectively. Here we report a novel stop codon mutation of AMT gene in NKH.

**Method:** Case Report.

**Results:** A four-month male infant was hospitalized in pediatric neurology department for hiccups, hypotonia and lethargy. Electroencephalography (EEG) indicated spike-wave activity in bilateral centro-temporal areas. Magnetic resonance imaging (MRI) demonstrates subdural hemorrhage in frontal area. The culturing and viral examination of cerebrospinal fluid produced negative results. Cerebrospinal fluid/plasma glycine ratio was 0.17 (normal <0.08). The child was homozygous for a sequence modification: the substitution of a cytosine by thymine at position 565 (c.565C>T, p.Q189\*) in the AMT gene. A diagnosis of NKH was made secondary to elevated plasma and cerebrospinal fluid glycine concentrations and sequence analysis of the AMT gene.

**Conclusion:** Non-ketotic hyperglycinemia should be included as a differential diagnosis in an unwell neonate presenting with hiccup, seizures and hypotonia. Metabolic studies of suspected patients with molecular analysis can confirm a diagnosis of NKH, support genetic counseling, and prenatal diagnosis. We would like to emphasize a novel stop codon mutation in NKH in this case report.

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**p0271**

### PHARMACOGENOMIC EXPLORATION OF LACOSAMIDE RESPONSE

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**Purpose:** Approximately 65 million people in the world have epilepsy. Seizures are effectively controlled by anti-epileptic drugs (AEDs) in up to 70% of patients. Lacosamide (LCM) is an AED that was first approved in 2008 for the treatment of focal-onset seizures. We aimed to determine the clinical relevance of genetic variation in predicting LCM response and predicting adverse drug reactions to LCM.

**Method:** Patients were recruited from four tertiary epilepsy referral centres: Dublin, Ireland; London, UK; Brussels, Belgium; North Carolina, USA. Response to LCM was determined into four categories; (a) seizure freedom, (b)  $\geq 75\%$  reduction in seizure frequency, (c) no response and (d) seizures worsening. Statistical analysis using Stata<sup>®</sup> was carried out to determine the clinical predictors of LCM response. Genome wide association studies (GWAS) and whole exome sequencing (WES) was used to investigate the potential importance of genetic variation in predicting LCM response.

**Results:** Overall, 13% of patients showed a positive response (seizure freedom or  $\geq 75\%$  reduction in seizure frequency) to LCM treatment, while 8% experienced an increase in seizures while on LCM. Response varied depending on epilepsy diagnosis, with idiopathic generalised epilepsy (also known as genetic generalised epilepsy) emerging as a potential target group for LCM treatment. Up to 40% of patients reported an adverse drug reaction (ADR), with variability across the four sites. Investigation into the contribution of common and rare variants in LCM response is ongoing.

**Conclusion:** 13% of patients showed a positive response to treatment with LCM. Response varied depending on epilepsy diagnosis - LCM could have potential benefits for patients with generalised epilepsy.

**Acknowledgement:** This project has been funded by an investigator-initiated grant from UCB Pharma.

#### p0272

### THE PHENOTYPIC SPECTRUM OF GABRA1 MUTATIONS: FROM GGE AND GEFS+ TO SEVERE EPILEPTIC ENCEPHALOPATHIES

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**Purpose:** Mutations in GABRA1, encoding the alpha subunit of the GABA<sub>A</sub> receptor, have been associated with mild genetic generalized

epilepsies and febrile seizures and recently been reported in severe epileptic encephalopathies such as Dravet syndrome. We aimed to delineate the clinical spectrum associated with GABRA1 mutations.

**Method:** Using high-throughput sequence analysis of the GABRA1 gene in 130 patients with a wide range of epileptic encephalopathies and childhood epilepsies. Cases with GABRA1 mutations were ascertained from other centers along with clinical data.

**Results:** Seven patients with heterozygous mutations of GABRA1 were found. The phenotypic spectrum varied from Genetic Generalised Epilepsy (1) to Generalised Epilepsy with Febrile Seizures Plus (1), Dravet Syndrome (1) and Epileptic Encephalopathies (4). Four de novo mutations (3 of the EE and the DS), while the remaining 3 probands had a epilepsy positive family history, not available for testing. Seizure onset between 5 and 17 months (mean 10 months) with a single outlier with seizure debut 13 years. Three had febrile seizures at onset, one experienced febrile seizures at a later point. Three never developed afebrile seizures. 6/7 patients had GTCS, and the majority had multiple seizure types including myoclonic seizures, atypical absence, atonic seizures and focal seizures with/without dyscognitive features. In 2 patients seizures were refractory to antiepileptic therapy; 3 patients became seizure free. Cognitive development normal in 3 patients, affected in 3 patients. Functional studies were made on two of the patients with de novo mutations and EE and one with familiar GGE - all showed reduced GABA-induced currents.

**Conclusion:** The present study shows that GABRA1 mutations are associated with a phenotypic epilepsy spectrum ranging from GE FS+ to severe epileptic encephalopathies, and a cognitive development ranging from normal to severe intellectual disability. This variety in outcome highlights the necessity for thorough knowledge when counseling families.

#### p0273

### SPECTRUM OF HLA-B ALLELES IN PERSONS WITH EPILEPSY WITH CUTANEOUS ADVERSE DRUG REACTIONS TO ANTI-EPILEPTICS IN NORTH INDIAN POPULATION

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**Purpose:** To assess HLA-B alleles present in persons with epilepsy (PWE) having cutaneous adverse drug reactions (cADRs) to antiepileptic drugs (AEDs) in north Indian population.

**Method:** This is a case-control study with 70 PWE having cADRs to any of AEDs CBZ, VPA, PHT, PB, CZP, OXC, LTG, GBP, TPM, LEV and 50 controls with no cADRs. Inclusion criterion was any PWE having cADRs after 2 or more months of AED consumption. DNA samples were genotyped for HLA-B alleles by PCR using sequence specific primers (PCR-SSP). Samples positive for HLA-B\*15 were further subjected to high resolution typing (SSO-One Lambda).

**Results:** In 68 PWE with cADRs, 56 had Maculopapular rash (MPE), Steven Johnsons Syndrome (SJS)-3, Toxic Epidermal Necrolysis (TEN)-2, Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)-3, Drug hypersensitivity Syndrome (DHS)-1, SJS/TEN overlap-2 and 1 had fixed drug eruption. 32 were males (47.05%) and 36 females (52.94%). Age ranged between 6 and 72 years. HLA-B\*15

was present in 8 cases (11.76%) (CBZ-2, PHT-3, LTG-1, multiple AEDs-2) and 10 controls (20%). Amongst cases HLA-B\*15:02 was present in 5 (4 heterozygous and 1 homozygous); and 1 was HLA-B\*15:08. Amongst the 50 controls 24 were males (48%) and 26 were females (52%). Age range was 8–70 years. HLA-B\*15:02 was found in only 1 control (2%).

Other HLA-B alleles present in patients with cADRs were B\*40 in 16 cases (23.52%) (PHT-5, CBZ-4, LTG-3, LEV-1, VPA-1, PB-1 multiple AEDs-1), B\*35 in 16 cases (23.52%) (PHT-6, CBZ-6, LTG-2, LEV-1, multiple AEDs-1) and 12 controls each (24%), B\*51 in 14 cases (20.58%) (PHT-4, CBZ-4, VPA-2, LTG-1, OXC-1, multiple AEDs-2) and 08 controls (16%), B\*07 in 08 cases (11.76%) (CBZ-4, PHT-3, multiple AEDs-1) and 04 controls (8%), B\*44 in 08 cases (11.76%) (CBZ-3, PHT-2, LTG-1, multiple AEDs-2) and 11 controls (22%), B\*13 in 4 cases (5.88%) (CBZ-2, LTG-1, multiple AEDs-1) and 1 control (2%), B\*27 in 2 cases (2.94%) (PHT-1, multiple AEDs-1) and 2 controls (4%).

**Conclusion:** Most rashes were due to CBZ (24) (35.29%) and least due to PB (1) and OXC (1) (1.47%). B\*40 and B\*35 mostly associated with LTG. There is no statistically significant difference in the prevalence of various HLA-B alleles studied, between PWE with and without cADRs. However, prevalence of B\*15:02, B\*40, B\*35, B\*51, B\*07, B\*13 was higher among cases. A larger sample size would be required to find any definite association of other HLA alleles with AED-induced cADRs in this population.

#### p0274

### GENOME WIDE ANALYSIS OF NOVEL COPY NUMBER VARIATIONS DUPLICATIONS/DELETIONS OF DIFFERENT EPILEPTIC PATIENTS IN SAUDI ARABIA

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**Purpose:** Epilepsy is genetically complex neurological disorder affecting millions of people of different age groups varying in its type and severity. Copy number variants (CNVs) are key players in the genetic etiology of numerous neurodevelopmental disorders and prior findings also revealed that chromosomal aberrations are more susceptible against the pathogenesis of epilepsy. Novel technologies, such as array comparative genomic hybridization (array-CGH), may help to uncover the pathogenic CNVs in patients with epilepsy.

**Methods:** This study was carried out by high density whole genome array-CGH analysis with blood DNA samples from a cohort of 22 epilepsy patients to search for CNVs associated with epilepsy.

**Results:** Pathogenic rearrangements which include 6p12.1 microduplications in 5 patients covering a total region of 99.9 kb and 7q32.3 microdeletions in three patients covering a total region of 63.9 kb were detected. Two genes *BMP5* and *PODXL* were located in the predicted duplicated and deleted regions respectively. Furthermore, these CNV findings were confirmed by qPCR.

**Conclusion:** We have described, for the first time, several novel CNVs/genes implicated in epilepsy in the Saudi population. These findings enable us to better describe the genetic variations in epilepsy, and could provide a foundation for understanding the critical regions of the genome which might be involved in the development of epilepsy.

#### p0276

### GENETIC TESTING IN ADULTS WITH INTELLECTUAL DISABILITY AND EPILEPSY

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**Purpose:** The genetic contribution to the development of epilepsies has in recent years been shown to be significant with new genes being linked to the disease frequently. However due to the heterogeneity of even a single epilepsy syndrome as well as the phenotypic spectrum of variations in a specific gene, it can be difficult to determine the causative genetic defect. Here we searched for point mutations and copy number variations (CNV) in adult patients with intellectual disabilities (ID) and epilepsy.

**Method:** A cohort of 67 well characterized adult patients with ID and epilepsy, with or without structural brain malformations, was analyzed using a Next Generation Sequencing (NGS) gene panel targeting 280 genes and by array CGH. Genetic variations were evaluated with database searches such as dbSNP, 1000Genomes, HGMD professional as well as an in-house database and prediction softwares MutationTaster and PolyPhen2. Segregation analysis was performed with Sanger sequencing to test inheritance when possible.

**Results:** Of the 67 patients we were able to identify damaging genetic variations in 16 cases – 11 from the gene panel (e.g. *SIX3*, *KCNQ2*, *GRIN1*, *GABRB3*, *KCNA2* etc.) and 5 using array CGH (e.g. 20p13, 5q33q35, dup17q12q21 etc.) In additional 9 patients we found potentially damaging variations but segregation analysis was not possible. An unsolved patient with progressive myoclonic epilepsy has since been tested positive for a mutation in *KCNC1*, a gene not on the panel.

**Conclusion:** We were able to detect point mutations and CNVs in 24% of adult patients with ID and various forms of epilepsy. In addition in 12% of the cohort we found potentially damaging variations. This study demonstrates the potential for clarifying genetic causes in adult patients with clear as well as unspecific epilepsy phenotypes and ID, using gene panels and array CGH.

#### p0277

### GENETIC VARIATION IN TNFA AND CLINICAL CHARACTERISTICS OF MESIAL TEMPORAL LOBE EPILEPSY WITH HIPPOCAMPAL SCLEROSIS

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**Background:** Epileptic seizures are associated with a profound change in gene expression. The immune response is among the most affected. Several studies have demonstrated high cytokines levels, such as IL-1 $\beta$  and TNF- $\alpha$ , in plasma and/or CNS in Mesial Temporal Lobe Epilepsy (MTLE) patients, that may contribute to the expression of the disease. Production of TNF- $\alpha$  may be influenced by the rs1800629 polymorphism (-308 G>A) in the promoter region of its gene. Our aim was to analyse the association of rs1800629 with MTLE-HS susceptibility and clinical characteristics in a Portuguese population.

**Methods:** A cohort of 162 MTLE patients all with Hippocampal Sclerosis (87F, 75M, mean age= 44 ± 11 years, age of onset= 13 ± 9 years, 82 with Febrile Seizures (FS) antecedents) was compared with a cohort of 206 healthy individuals (HI) in a case-control genetic association study. Genotyping used a PCR- Restriction Fragment Length Polymorphism (RFLP) assay.

**Results:** Genotypic and allelic frequencies were similar between patients and controls. Accordingly to FS antecedents, two subgroups of patients were considered. The frequency of the rs1800629 AA genotype was significantly lower in FS positive than in FS negative patients (0% vs. 5.4%,  $p = 0.047$  OR=0.945 [0.894 - 0.999]).

**Conclusion:** Our results do not support a role for rs1800629 in MTLE-HS susceptibility, at least in the studied population. The rs1800629 AA genotype has been associated with higher TNF- $\alpha$  expression which may interfere not only with immune response but also with neurotransmission. It has been argued that a different genetic background underlies MTLE-HS development in individuals with and without FS antecedents. Our results show that rs1800629 could be a factor contributing to that genetic difference.

#### p0280

### DE NOVO LOSS- OR GAIN-OF-FUNCTION MUTATIONS IN KCNA2 CAUSE EPILEPTIC ENCEPHALOPATHY

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Epileptic encephalopathies are a phenotypically and genetically heterogeneous group of severe epilepsies accompanied by intellectual disability and other neurodevelopmental features. Using next-generation sequencing, we identified four different de novo mutations in *KCNA2*, encoding the potassium channel KV1.2, in six isolated patients with epileptic encephalopathy (one mutation recurred three times independently). Four individuals presented with febrile and multiple afebrile, often focal

seizure types, multifocal epileptiform discharges strongly activated by sleep, mild to moderate intellectual disability, delayed speech development and sometimes ataxia. Functional studies of the two mutations associated with this phenotype showed almost complete loss of function with a dominant-negative effect. Two further individuals presented with a different and more severe epileptic encephalopathy phenotype. They carried mutations inducing a drastic gain-of-function effect leading to permanently open channels. These results establish *KCNA2* as a new gene involved in human neurodevelopmental disorders through two different mechanisms, predicting either hyperexcitability or electrical silencing of KV1.2-expressing neurons.

## Neuroimaging 1 Sunday, 6th September 2015

### p0284

### GENERALIZED EPILEPSY SYNDROMES AND CALLOSAL THICKNESS: DIFFERENTIAL EFFECTS BETWEEN PATIENTS WITH JUVENILE MYOCLONIC EPILEPSY AND THOSE WITH GENERALIZED TONIC-CLONIC SEIZURES ONLY

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**Purpose:** Although the definition of two well studied genetic generalized epilepsy syndromes (GGE), juvenile myoclonic epilepsy (JME) and epilepsy with generalized tonic-clonic seizures alone (GTCS), suggests the absence of structural cerebral abnormalities, such have been reported in both, particularly in JME. Their localization in the thalamus and mesial prefrontal regions raises the question whether JME is linked to midline structure abnormalities, possibly also involving the corpus callosum (CC), and suggesting a different pathophysiology from GTCS.

**Method:** We studied the CC in 22 JME patients, 15 GTCS patients, and 42 controls. The two epilepsy groups were matched for age, medication, and life time total GTCS. All three groups were statistically compared with respect to the local thickness of the CC.

**Results:** In both patient populations the CC was significantly thinner compared to controls. However, disease-related aberrations were more extensive in JME patients than in GTCS patients. Specifically, effects were evident within the callosal genu (JME < controls), isthmus (JME < controls, JME < GTCS), and posterior midbody (GTCS < controls).

**Conclusion:** Altogether, these data support the notion that callosal abnormalities exist in GGE, and are more pronounced in JME than in GTCS patients. The specific locations of the callosal aberrations suggest an impairment of interhemispheric communication between prefrontal, parietal and temporal cortices in JME, and between frontal and parietal cortices in GTCS alone. Together, this argues that the two types of GGE have their own anatomical signatures on which further research seems indicated.

### p0286

### LATERALITY AND MEDICATION EFFECTS IN THE FUNCTIONAL CONNECTIVITY OF MESIAL TEMPORAL LOBE EPILEPSY

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**Purpose:** Functional connectivity is abnormal in mesial temporal lobe epilepsy (MTLE). Left MTLE is probably associated with a more pronounced abnormality. The objective of this study was to investigate laterality and medication effect in the functional connectivity of MTLE.

**Method:** Thirty patients with MTLE (15 right and 15 left) and 37 controls were investigated. Images were acquired with a 3T scanner. 3D volumetric T1 sequences and functional BOLD data images were acquired. fMRI data was processed and analyzed by using Analysis of Functional NeuroImages (AFNI). Basically, EPI images were submitted to slice timing and motion correction, temporal filtering, registration, blurring and masking. Finally images were processed with regression analysis generating residual error time series. Regions of interest (ROIs) were bilaterally created for the hippocampus, amygdala and parahippocampal gyrus. Correlation maps were generated and submitted to a Z-score transformation. Whole brain voxel wise statistical analysis was performed using unpolled T test with a  $p < 0.05$ . Comparisons were performed between controls and patients with right or left MTLE. A subsequent comparison was conducted according to the dose of antiepileptic drug (AED).

**Results:** Total number of voxels with abnormal functional connectivity was 579 for right MTLE and 3400 for left. Major clusters were localized in the insula and superior frontal gyrus for patients with right MTLE ( $Z = 3.5, -4.1$  and  $-3.5$ ) and in the superior, middle and medial frontal gyrus for left MTLE ( $Z = 3.8, 3.9$  and  $4.3$ ). Analysis according to the AEDs showed 670 abnormal voxels for high dose (599 left, 71 right) and 1094 for low dose (868 left, 246 right). Major clusters were localized in the anterior cingulate, middle and superior frontal gyrus.

**Conclusion:** Areas of abnormal functional connectivity were disclosed in patients with MTLE. Left MTLE presented a more diffuse pattern. Doses of medications may influence these observations.

## Neuropsychology 1 Sunday, 6th September 2015

p0291

### INFLUENCE OF TOPIRAMATE ON COGNITIVE FUNCTIONING IN PATIENTS WITH MIGRAINE

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**Purpose:** To evaluate effect of incremental small doses of topiramate on language and cognitive function in patients with migraine.

**Method:** Participants were recruited from a headache clinic after topiramate was prescribed for migraine prophylaxis. Cognitive and language assessments were performed prior to administration of the first dose and 1 week after titration to 50 mg, 100 mg, 150 mg, and 200 mg. The final maintenance dose varied between patients. Final re-evaluation occurred 4 weeks after reaching the maintenance dose. Cognitive/language measures included Trail Making Test (A&B), Controlled Oral Word Association Test (COWAT), Revised Token Test (RTT), Story retell subtest from the Rivermead Behavioral Memory Test (RBMT), Boston Naming Test (BNT), and Aphasia Depression Rating Scale (ADRS).

**Results:** Fifteen participants were enrolled; nine participants completed the study. Premature termination was due to significant adverse effects on memory and mood requiring medication withdrawal (2 patients) and loss to follow up (4 patients). There were statistically significant changes in performance on the RTT from baseline to maximal dose ( $p < 0.03$ ) and from baseline to final assessment ( $p < 0.01$ ). Changes on story retell, COWAT (FAS), and Trail Making Test-A approached significance. There was no significant change on the BNT and ADRS.

**Conclusion:** The results indicate a negative effect of topiramate on frontal lobe functioning, as well as auditory comprehension and processing.

p0292

### UTILITY OF RBANS IN FOCAL INTRACTABLE EPILEPSY PATIENTS IN AN ARAB COHORT

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**Purpose:** The RBANS (Repeatable Battery for the Assessment of Neuropsychological Status) is a widely used screening battery in patients with neurological cerebral dysfunction. However, there is little published research in patients who have epilepsy. We present its utility in patients in an Arab cohort, who have focal intractable epilepsy.

**Method:** In this observational study, we selected patients with focal intractable epilepsy who were referred from an Epilepsy clinic for neuropsychological evaluation in a tertiary care hospital, in Al Ain, UAE. The RBANS was administered to patients and their standard scores were calculated for each of the five Indexes of the battery (Immediate Memory, Visuospatial/Constructional, Language, Attention and Delayed Memory) and compared to matched healthy controls. We collected demographics and underlying lesional etiology for epilepsy.

**Results:** Each group ( $n = 14$ ) was comprised of 1 male and 6 females, age in years  $\pm$  SD ( $26.71 \pm 4.6$ ) in the focal intractable epilepsy group and ( $28.29 \pm 3.7$ ) in the healthy matched controls. Four patients had temporal lobe epilepsy and three, extra-temporal lobe epilepsy. The Chi-Square test was performed to examine the relation between groups and Index scores that indicated potential impairment ( $<75$ ). The relation between these scores was significant,  $X^2 (2, N = 14) = 14 (p < 0.01)$ . Epilepsy patients showed impairments across RBANS Index and Total scores compared to healthy controls.

**Conclusion:** We conclude that RBANS is a quick and convenient tool for detecting cognitive impairment in a cohort of Arab patients with focal intractable epilepsy and can be used to identify impaired cognitive domains for further selective neuropsychological evaluation. The utility of the RBANS in a larger cohort of epileptic patients should be further investigated.

p0293

### FACIAL EMOTION RECOGNITION AFTER EPILEPSY SURGERY IN CHILDREN

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**Purpose:** To know whether epilepsy surgery in children has impact on their recognition of emotions expressed by faces and whether the latter is associated with demographic variables [age, sex and verbal intelligence (VIQ)] and illness variables (epilepsy duration, side of the surgery, surgery area, resection of the amygdala, etiology, anti-epileptic drug use and seizure freedom).

**Method:** Two years after epilepsy surgery, we administered the Facial Expression of Emotion: Stimuli and Tests (FEEST) to 41 patients (mean

age 13.5 years, mean VIQ = 84; 24 girls) and 82 age- and sex-matched controls (mean VIQ = 112). FEEST data obtained in a smaller group (11 patients and 22 matched controls) were explored longitudinally from shortly before surgery to 2 years thereafter. Scored and analyzed (MANOVA) were proportions of correct responses, controlling for VIQ.

**Results:** In the cross-sectional study, the mean proportion of correct responses differed significantly between patients and controls, to the disadvantage of the patients. Relationships between FEEST scores and illness-related variables were non-significant. Only age at assessment was associated with FEEST scores, in both patients and controls. The exploratory longitudinal data showed a 'dip' at the first postsurgical assessment; the six younger patients (age <13 years) were the only ones to dip. Over the 2 years after surgery, their scores recovered slightly but did not exceed the pre-surgical level. Five of the six younger children, all girls, had a left-hemisphere resection. The five older patients (two with a left sided resection) showed a continuous increase of scores, on a lower level than but similar to that in control children.

**Conclusion:** Two years after epilepsy surgery, recognition of emotions expressed by faces is deficient. The aberrant course of FEEST scores in the younger patients emphasizes the necessity of disentangling developmental, demographic and epilepsy influences.

#### p0294

##### WHAT'S THE IMPACT OF ANTERIOR TEMPORAL LOBE EPILEPSY IN FACES PERCEPTION?

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Estimates of the risk of decline in specific neuropsychological domains after epilepsy surgery assist surgical decision making in clinical practice. Face perception is a critical brain function, essential to social interactions. Neuropsychological and neuroimaging studies have recently pointed out the critical role of the anterior temporal lobe in face perception. Nevertheless, no studies have examined in details the impact of anterior temporal lobe epilepsy (ATLE) and its surgical therapy (anterior temporal lobectomy) on face perception. The aim of this study was to assess face perception performances in patients with left and right ATLE.

We included 26 patients with refractory ATLE (15 right, 11 left) as well as 26 matched controls. Patients and controls subjects performed tests on face detection, individual face discrimination and famous face recognition.

Overall, left ATLE patients showed normal performances on face perception. In the right ATLE group, one half showed normal performances and the other half was severely impaired. In this group, an effect of epilepsy duration is observed. At the moment, 10 ATLE (8 right, 2 left) were also tested after surgery and we did not find any significant decline.

Our results show that right ATLE impairs face perception performances and that this impairment increases with epilepsy duration. These results argue for an early surgical therapy in right ATLE and also for a systematic neuropsychological evaluation of face perception performances in these patients.

#### p0295

##### BETTER POST-OPERATIVE VERBAL LEARNING CAPACITY IN PATIENTS WITH EARLIER ONSET OF EPILEPSY

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**Purpose:** We investigated postsurgical verbal and nonverbal learning ability in a group of patients who underwent surgery for temporal lobe epilepsy. The aims were to examine whether there was:

- (i) a material-specific effect of the side of resection, and
- (ii) an effect of age of epilepsy onset and/or of age at surgery.

**Method:** We analysed postsurgical data from 75 participants (43 with surgery on the left and 32, on the right). The data covered a wide range of age of epilepsy onset (from age 4 months to 25 years) and of age at surgery (from age 6 to 46 years). The age at testing varied from 8 to 49 years. Verbal and nonverbal paired associate learning tasks were used, with recall tested over three learning trials. Analyses of covariance and multiple regression analyses were performed to assess the effect of side of resection, with age at onset of epilepsy and age at surgery as covariates.

**Results:** There was a significant interaction between side of resection and type of material ( $p < 0.001$ ), with poorer verbal learning after left than after right resections, and poorer visual learning after right than after left resections. In addition, there were effects on verbal learning of age at epilepsy onset ( $p = 0.033$ ) and of age at surgery ( $p = 0.034$ ), with linear declines in learning with increasing age. However, only age at epilepsy onset remained significant after controlling for age at test ( $p = 0.030$ ) and postoperative seizure outcome ( $p = 0.009$ ). Nonverbal learning remained constant along the age spectrum.

**Conclusion:** Patients with earlier onset of epilepsy have better postoperative verbal learning ability than patients with later onset, due perhaps to more effective cerebral reorganization after early onset.

#### p0296

##### COGNITIVE FUNCTIONS AND DRUG RESPONSIBILITY IN MESIAL TEMPORAL LOBE EPILEPSY

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**Purpose:** Mesial temporal lobe epilepsy (MTLE) is the most prevalent form of complex partial seizures with temporal lobe origin and affects several domains of cognitive functioning. In this study, we aimed to compare memory, verbal attention, executive function of drug responsive and pharmacoresistant MTLE patients.

**Method:** We included 79 patients of MTLE and 30 healthy controls. The patients were divided in to two groups according to seizure frequency indicating the response to antiepileptic drugs. Then we evaluated memory, verbal attention, executive functions.

**Results:** Of the 79 patients with MTLE, mean age was  $33.5 \pm 9.6$  years, 49 (62%) were female. The mean age of 30 participants from control group was  $35.9 \pm 7.9$  and 14 of them (46.7%) were female. The drug responsive and pharmacoresistant groups had poorer memory than the controls in all memory tests. However, the comparison of drug responsive group with pharmacoresistant group revealed that verbal attention test was significantly worse in pharmacoresistant group. The analysis of verbal memory functions revealed that the poor verbal function in left MTLE.

**Conclusion:** In our study, verbal attention were similar between the patients with drug responsive group and control group, pharmacoresistant patients were significantly worse and this result reveal that seizure frequency is the probable reason of verbal attention deficit. However, memory impairment in both of groups shows that memory dysfunction is the

result of underlying hippocampal pathology. Executive functions were worse in all patients compared to control group, this may be related to intense network between frontal and temporal lobe. Presence of nonverbal memory deficit in left MTLE and verbal memory deficit in right MTLE show that material specific memory dysfunction requires overview and more specific neuropsychological tests should be improved.

p0297

### MEMORY & LEARNING AFTER TEMPORAL LOBE SURGERY: EFFECTS OF HEMISPHERIC SIDE AND EXTENT OF SURGICAL REMOVAL

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**Purpose:** To examine

(a) long term learning and memory outcome in relation to hemispheric side and extent of temporal lobe excisions in patients with temporal lobe epilepsy.

(b) to determine whether or not there is a double dissociation in verbal and nonverbal learning of paired associates in relation to side of temporal lobe removal.

**Methods:** 48 adults with left (n = 28) or right (n = 20) temporal lobectomy (TL; n = 22) or amygdalohippocampectomy (AH; n = 26) and 11 normal controls (NC) participated in the study. Intelligence (Verbal, Nonverbal, Full Scale IQs), and Immediate and Delayed Verbal and Visual Memory and Learning were examined in all groups using the Wechsler Scales. In addition, an experimental nonverbal paired-associate recall task was administered together with, and as an analogue for, a verbal paired-associate task.

**Results:** There were no significant differences between the groups in IQ and MQ. Nevertheless, MQ was selectively lower than IQ in both left TL and left AH groups relative to the NC group. The same selective lowering of MQ relative to IQ was also seen in the left AH group compared to the RT group. Analyses of variance with repeated measures across the learning trials indicated that both the left AH and left TL groups were significantly poorer on the verbal than on the nonverbal paired associates, and that the reverse pattern was shown by the right AH and right TL groups on the learning and recall of nonverbal paired associates. Impairments in verbal or nonverbal paired associate learning were unrelated to extent of temporal lobe removals.

**Conclusion:** Both patient groups with left-sided excisions showed a selective lowering of memory in relation to intelligence. In addition, verbal paired-associate learning was more severely impaired after left-sided surgery than after right, whereas the reverse occurred after right-sided removals.

p0298

### PREVALENCE AND PROFILE OF AMUSIA IN PATIENTS WITH TEMPORAL LOBE EPILEPSY

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**Purpose:** To determine the prevalence and profile of amusia in patients with temporal lobe epilepsy of the National Medical Center "20 de Noviembre" at Mexico City.

**Method:** Adult patients with temporal lobe epilepsy (TLE) were included. We excluded patients with a history of neurosurgical procedures, structural epilepsy, psychiatric disorders and deafness. The Montreal Battery of Evaluation of Amusia (MBEA) was used (sensitivity 89%, specificity 78%). It contains tests that explore perception of melodic dimension (interval, scale and contour), of temporal dimension (rhythm and meter), and of musical memory. Amusia in general population has a prevalence of 4%, that was compared with the results obtained in our patients and between right and left focus.

**Results:** We studied 44 patients aged 19–61 years, 18 men, 26 women, 12 with right focus, 16 left and 16 bilateral or indeterminate. 16 (36%) met criteria for amusia. We found 9 patients (25%) with amusia of the melodic dimension, 2 (4.5%) with amusia of temporal dimension. 2 (4.5%) with alteration in both. 10 with alteration in the musical memory, (7 with simultaneous alteration of melodic perception, 2 with simultaneous alteration of temporal perception. only 1 with isolated amnesic amusia). amusia of the temporal dimension was greater in left epileptic focus (p < 0.0.1). There were no significant differences in the other results.

**Conclusion:** Prevalence of amusia in patients with TLE is 36%, 9 times higher than in the general population. It is primarily amusia of melodic dimension and musical memory. Amusia of the temporal dimension is preferably associated with left focus. Further studies are needed to determine whether the MBEA could be used as an aid in the location of the epileptic focus.

p0299

### VALIDATION OF THE DUTCH VERSION OF THE WECHSLER MEMORY SCALE - FOURTH EDITION IN PATIENTS WITH TEMPORAL LOBE EPILEPSY

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**Purpose:** The Wechsler Memory Scale (WMS) is one of the most widely used test batteries to assess different memory functions in impaired patients with brain dysfunctions of different etiologies. This study investigates the clinical validation of the Dutch version of the Wechsler Memory Scale - Fourth Edition (WMS-IV-NL) in patients with Temporal Lobe Epilepsy (TLE).

**Method:** A group of 139 patients with TLE (mostly surgical candidates) enrolled the study. Besides neuropsychological assessment including the WMS-IV-NL, patients underwent a thorough interview and extensive medical investigations. Patients with a clearly identified and localized epileptic focus based on video EEG monitoring and MRI were divided into two groups according to the lateralization of the abnormalities (84 left TLE and 53 right TLE). 230 matched healthy controls were also examined with the WMS-IV-NL.

**Results:** Results showed significantly poorer memory performance of patients compared to controls (p < 0.05). Moreover, patients with left or

right temporal focus performed equally on the auditory memory index and the visual memory index ( $p > 0.05$ ).

**Conclusion:** The WMS-IV-NL is capable of detecting memory problems in patients with TLE, indicating sufficient validity of this memory battery. Moreover, the findings support previous research, showing that the WMS-IV-NL has limited value in identifying material specific memory deficits for either left or right TLE patients.

### p0300

#### INTELLIGENCE QUOTIENT (IQ) OF CHILDREN WITH INTRAUTERINE ANTIEPILEPTIC DRUG EXPOSURE PRELIMINARY DATA

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**Purpose:** According to clinical studies fetal exposure to antiepileptic drugs increase the risk of neurodevelopmental impairment. Aim of the study was to assess long-term cognitive outcome of children prenatally exposed to AEDs.

**Method:** In this retrospective cohort study the children aged 3–6 years with fetal exposure of AED therapy were recruited. The control group was created by 3–6 years old children from mothers without epilepsy randomly selected from the database of primary health care unit. In all of them were performed neuropsychological assessment with Wechsler Preschool and Primary Scale of Intelligence (WPPSI - IV). Statistical analysis was performed using SPSS version 20 (SPSS Inc, Chicago, Illinois).

**Results:** In total 48 children (32– exposed and 16 controls) were assessed: 16 (50%) were exposed to intra-uterine VPA, 6(19%) to CBZ, 1(3%) to LTG, 2(6%) to PB, 7(22%) to polytherapy and 16 were unexposed.

Our primary outcome was intelligence quotient (IQ). From exposed group average IQ (91–110) was detected in 12 children (37%), low average IQ (81–90) in 9 (28%), borderline IQ (71–80) in 5(16%) and extremely low IQ (<70) in 6 (19%).

From unexposed group average IQ (91–110) was detected in 10 (63%), superior IQ (121–130) in 3(19%),very superior IQ (>131) in 1 (6%), borderline IQ (71–80) in 2 (12%).

**Conclusion:** Children with fetal AED exposure have reduction of cognitive abilities. The effects of VPA and polytherapy appear to carry more risks compared with AED-monotherapy.further research is needed.

**Acknowledgements:** The study was performed within the scientific grant from the Shota Rustaveli National Scientific Foundation (project FR/373/8-313/13).

## Neurostimulation 1 Sunday, 6th September 2015

### p0301

#### LONG-TERM PRODUCT RELIABILITY OF IMPLANTABLE GENERATORS FOR VAGUS NERVE STIMULATION THERAPY (VNS THERAPY®)

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**Purpose:** VNS Therapy® plays an expanding role in treating patients with drug-resistant epilepsy. In addition to device labeling and diagnostics, tracking device reliability informs physicians when to increase

patient follow-up for generator battery replacement. Reliability and battery longevity of the implantable pulse generator are important to patients, physicians and payers.

**Method:** Cyberonics has registered 80,000 generators for patients implanted with VNS Therapy having a known Social Security Number. All device-related complaints are investigated as potential failures, and all returned explanted products are analyzed for specific component failures. Survival curves for generator performance were calculated using the actuarial method from the date of implant to the date of the first occurrence of normal battery depletion, any device failure, or a censored event such as a patient's death or the cut-off date of the analysis. Battery longevity estimates incorporate the known under-reporting rate based on long-term follow-up as it is known that all batteries will eventually deplete.

**Results:** In the US, all VNS Therapy generators have accumulated over 450,000 patient years of experience. We report a median longevity of 7.9 years for Model 101 including normal battery depletion. Device failures are rare, as demonstrated by a reliability rating of 99.6% at 5 years post-implant for Pulse™ Model 102/102R generators. Data through July 2015 will be available at the time of presentation.

**Conclusion:** Improvements in technology in subsequent device models reflect design changes based on feedback from patients and physicians. These reliability data and battery longevity analyses summarize the expected performance of VNS Therapy to assist physicians in determining the optimal device for their patients and the frequency of patient follow up evaluations. We report the reliability of implantable generators for the VNS Therapy System with a 5-year defect free rate of 99.6%.

### p0302

#### LONG-TERM PRODUCT RELIABILITY OF IMPLANTABLE LEADS FOR VAGUS NERVE STIMULATION THERAPY (VNS THERAPY®)

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**Purpose:** The VNS Therapy® System has two implantable components: the pulse generator and the lead relaying the electrical signal from the generator to the vagus nerve. Tracking lead reliability helps interpret the expected failure rate at different time points following implant.

**Method:** Cyberonics has registered 50,000 unique patients implanted with VNS Therapy having a known Social Security Number. All device-related complaints were investigated as potential failures, and all returned explanted leads were analyzed for specific failures. Survival curves for lead performance were calculated using the actuarial method starting on the implant date and ending on the first occurrence of a device failure or a censored event such as a patient's death or the cut-off date of the analysis.

**Results:** In the US, all implanted leads accumulated over 450,000 patient-years of experience. Over sixteen years of follow-up data are available on the earliest lead Model 300, with a cumulative survival of 86.7% at 10 years. Design improvements in the currently distributed models have reduced the average annual failure rate by 61% (PerreniaFLEX® 304) and 67% (PerreniaDURA® 303) compared to Model 302. Data through July 2015 will be available at the time of presentation.

**Conclusion:** Improvements in lead models over time reflect design changes from internally identified improvements to fatigue resistance, validated through extensive testing. The newest PerreniaFLEX® 304 has a lower failure rate compared to the Model 302 yet maintains the handling characteristics during implantation of less fatigue-resistant models. High reliability of implantable leads minimizes loss of therapy delivery and need for additional surgical procedures. VNS Therapy System implantable leads have an average failure rate of approximately 1% per year across all lead models. Newer lead models reduced the lead failure rate by nearly two-thirds over previous models.

p0303

### 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:** Fourteen patients with temporal lobe epilepsy were studied. Four had normal MRI, 4 had bilateral MTS and 6 had unilateral MTS. Ten patients were implanted bilaterally in the hippocampus, and 4 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 intraoperatively. Continuous stimulation was carried out using 300usec, 130 Hz, 1-2,5V pulses.

**Results:** In 9 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 8 patients, high frequency intraoperative hippocampal stimulation reduced or abolished interictal spiking. Eleven patients received unilateral and 4 bilateral stimulation (3 with normal MRI and 1 with bilateral MTS) so far. Five patients with unilateral stimulation are seizure free and the other seven had at least 90% reduction in seizure frequency. Two patients with bilateral hippocampal stimulation were non-responders and the other two had 50% seizure frequency reduction. There was no memory decline in patients submitted to bilateral hippocampal stimulation. Mean follow-up time was 26 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.

p0304

### EFFICACY, SIDE EFFECTS AND OUTCOME OF VAGUS NERVE STIMULATION IN PATIENTS WITH DRUG RESISTANT EPILEPSY

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**Background:** Vagus nerve stimulation (VNS) is an adjunctive therapy for patients with drug-resistant epilepsy (DRE) who are excluded from ablative surgery or who have had such surgery with no optimal outcome. In this study, we provide an analysis of seizure outcomes after VNS implantation for patients with DRE.

**Method:** We retrospectively examined 14 adult cases (M/F: 9/5) of DRE that received VNS treatment in our center from 2004 to May 2014 and analyzed the parameters: age of patient with VNS, seizure frequency before and after VNS as well as treatment duration and etiological parameters of seizures. Patient outcomes were evaluated using the McHugh VNS-specific outcome scale.

**Results:** The overall response rate was 57.1% (8/14). The mean age of initial seizure was 13.7, the mean duration of VNS treatment was 4.5 years, seizure frequency before and after VNS were 32.5/19.4 per month. Epilepsy was caused by a structural or metabolic disorder of the

brain: neoplasm, infarct, trauma, mesial temporal sclerosis and encephalitis, in eight patients (57.1%). Positive response rate was 75% in this group. The well response rate was %33.3 in the genetic or unknown etiology group. The mean age of initial seizure ( $p = 0.26$ ) and VNS treatment duration ( $p = 0.24$ ) were not associated with better response to VNS. The most frequent side effect was hoarseness (35.7%) and 42.9% of the patients complained of no side effects.

**Conclusions:** VNS is a safe and effective treatment for DRE. Etiology of seizure may be a crucial factor on prognosis.

p0305

### RESISTANT SEIZURE CONTROL AFFECT QUALITY OF LIFE AFTER VAGAL NERVE STIMULATION: CLINICAL SERIES

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**Purpose:** Vagus Nerve Stimulation (VNS) has shown to be an efficacious and safe treatment for patients with refractory epilepsy.

**Method:** In last 2 years four patients were referred for having the VNS implantation in our clinic. All patients had medically refractory epilepsy after a period of medical treatment for  $21.83 \pm 8.22$  years, and were on average four medications at the time of referral.

**Results:** **Patient 1** (40.M) subcortical epileptic seizures plus frequent myoclonic and tonic-clonic attacks and twice suffered status epilepticus. He in general tolerated the calibration sessions quite well and by 18-months post VNS, his convulsions had decreased to maximum two seizures per month.

**Patient 2** (35.F). She experienced a general epileptic attack at the age of 20 and has experienced myoclonic seizures accompanied by sudden, high-pitched cries. 12 months post-VNS, the second patient showed a 70.56% reduction in the maximum number of spikes and 92.97% reduction in the number of seizures on EEG.

**Patient 3** (27.F) She, too, was diagnosed with secondary generalized, complex partial seizures and tonic-clonic attacks. In second 6 month of period, the effect of seizure showed obviously decrement response for life quality.

**Patient 4** (20.M). He suffered Complex Partial epileptic activity from the age of 6. For the last 1.5 year, daily seizure numbers reached up to 40–50. After VNS, the response was dramatically from the beginning such as seizure free days has been reached a week.

**Conclusion:** VNS is an effective therapy for medically refractory partial-onset seizures, with an approximate long-term decrease in mean seizure frequency of 40–50% and a short-term decrease in mean seizure frequency of 20–30%. In our presentation, the early findings of VNS achievement goes up seizure control up to 70% and also acceptable improvement in daily life quality is achieved in these patients.

p0306

### VNS THERAPY AUTOMATIC MAGNET MODE OUTCOMES STUDY IN EPILEPSY PATIENTS EXHIBITING ICTAL TACHYCARDIA

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**Purpose:** The Automatic Magnet Mode (AMM) feature of the Aspire SR® VNS Therapy® System stimulates upon detecting a heart rate increase associated with seizure onset. This study evaluates performance,

safety and clinical outcomes of the AMM feature during a 5-day Epilepsy Monitoring Unit (EMU) stay and follow-up visits for up to 2 years.

**Method:** The E-37 protocol (NCT01846741) is a prospective, unblinded, US multi-site study of the AspireSR<sup>®</sup> in subjects with refractory partial onset seizures and history of ictal tachycardia. AMM performance was evaluated in the EMU, and standard cycling VNS was added to AMM functionality at EMU discharge. Subjects were seen at 3, 6 and 12 months, while completing questionnaires (SSQ; Seizure Severity Questionnaire; QOLIE-31-P: Quality of Life In Epilepsy). Adverse events were monitored.

**Results:** Twenty subjects (ages 21–69) were implanted, and experienced 84 seizures in the EMU. 83.3% of simple partial and 38.5% of complex partial or secondarily generalized seizures stopped during 60 seconds of stimulation, on average 37.9 seconds after stimulation onset. QOLIE and SSQ scores exceeded twice the Minimal Important Changes (MIC) criteria at 3 and 6 months. QOLIE sub-domain of cognitive functioning and SSQ sub-domains of activity during seizures, postictal emotional and physical recovery exceeded three times the MIC. Twelve month data analysis will be updated.

**Conclusion:** This study shows that the AspireSR performed as intended in the study population. Seizure duration during EMU stay with only AMM stimulation was relatively short, but there was no controlled comparator. The SSQ and QOLIE questionnaires showed sustained improvement in seizure severity, post-ictal recovery and quality of life with combined AMM and standard VNS compared to baseline. These results suggest significant clinical benefit when the AMM feature is added to standard VNS therapy. Which factors are responsible for improvement remain to be determined.

### p0307

#### THE EFFECT OF VAGAL NERVE STIMULATION ON QUALITY OF LIFE IN PEDIATRIC CASES

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**Purpose:** To evaluate the value of vagal nerve stimulation (VNS) in improving quality of life, and mood in children with pharmacoresistant epilepsy.

**Method:** Eleven pharmacoresistant epileptic children implanted with the VNS Therapy device between 2010 and 2014 were included in this prospective longitudinal study. Clinical assessment for DSM-IV psychiatric disorders, schedule for affective disorders and schizophrenia for school children were applied. Childhood Depression Inventory (CDI), Beck Depression Inventory (BI) were filled. Child Behavior Checklist and The Pediatric Quality of Life Inventory (PedsQL) were filled by parents before the implantation. All of these tests were repeated at the first and the second year of implantation.

**Results:** Mean age at first VNS therapy device implantation was 11.5 (2.5 and 16). Mean duration of epilepsy prior to VNS implantation was 30.4 months (10–96). ILAE classification of predominant seizure type was partial in 7 and generalized in 4 patients. Decrease in number of seizures was 42% and 43% in the first and the second year respectively. While four of 11 patients had no psychopathology, different problems were determined in seven patients. There was no statistically significant difference between the scores of CDI/Beck DI at the beginning and the first year. Also the scores of CBCL and the Pediatric Quality of Life Inventory (PedsQL) prior to implantation and 1 year and 2 years after implantation didn't differ.

**Conclusion:** VNS is partially effective for controlling drug-resistant epilepsy. Although a positive effect on depression and quality of life

is reported in literature, the results of this study were not statistically significant. We think that the scores of depression inventory should gradually decrease in years as it is reported for seizure frequency.

### p0308

#### THE EFFICACY OF HIGH DUTY CYCLE VAGUS NERVE STIMULATION IN CHILDREN WITH CATASTROPHIC EPILEPSIES - OUTCOME ON SEIZURE FREQUENCY

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**Purpose:** Vagus Nerve Stimulation therapy (VNS Therapy<sup>®</sup>) is a well-established treatment for patients with drug resistant epilepsy (DRE). This study reports the outcome of using high duty cycle VNS Therapy (ON time divided by OFF time represented as a percentage) in children with catastrophic epilepsies; mainly Lennox Gastaut, Dravet, West and Ohtahara syndromes.

**Method:** Children with catastrophic epilepsy implanted with VNS were retrospectively evaluated. For those patients who did not respond to the standard 10–16% duty cycle, a duty cycle of 29% or higher was applied. Seizure frequency reduction was assessed at the last follow-up which was at least 3 months post programming of the high duty cycle.

**Results:** 26 children (9F/17M, median age 5 (6 months -18 years)) were included. Median VNS duty cycle was 44% (range 29% - 44%); with 73% (19/26) of patients on 44% duty cycle. The current was between 1.75 mA and 3 mA and was kept constant once the duty cycle was ramped up beyond 16%. Median follow up time was 2 years (range 1–5 years). 15 (57%) patients were responders ( $\geq 50\%$  seizure reduction), with 14 (54%) patients having a seizure reduction of  $\geq 75\%$ , 7 (27%) having a seizure reduction of  $\geq 90\%$  and 3 (11%) patients becoming seizure-free. 7 (27%) patients had some reduction in seizure frequency but did not reach response ( $\leq 50\%$ ) and 4 (15%) patients had no change in their seizures. 12 patients had amelioration in the severity of the remaining seizures, 6 patients had shorter seizure duration and 7 patients had shorter post-ictal state.

**Conclusion:** Using higher than standard duty cycles with VNS Therapy shows a reduction in seizure frequency in patients with catastrophic epilepsies. It is therefore crucial to assay all programming options including the higher duty cycles, even starting with high duty cycles, to increase the chance of response in difficult epilepsies.

### p0309

#### NEURONAL BEHAVIOUR DURING DELAYED RESPONSES TO SINGLE PULSE ELECTRICAL STIMULATION (SPES) IN SUBJECTS WITH EPILEPSY

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**Purpose:** To describe neuronal firing patterns associated with presence and absence of delayed responses to SPES in humans.

**Method:** Behnke-Fried microelectrodes were inserted in 35 consecutive patients assessed with depth electrodes for presurgical assessment of epilepsy. SPES (1 ms, 4–6 mA) was delivered at least 20 times at each implanted region. At each area with microelectrodes showing delayed responses to SPES, the proportion of neurones showing burst, suppression, burst-suppression or no change immediately after the stimulus was compared between those stimuli showing delayed responses and those not showing delayed responses.

**Results:** Among the 35 patients assessed with depth electrodes and microelectrodes, 4 showed delayed responses in areas with microelectrodes. Forty-one neurons were recorded in the regions showing delayed responses. After the stimuli that did not induce delayed responses, 24.3% of neurons showed burst, 19.5% suppression, 7.3% burst-suppression and 48.7% no change. After the stimuli that induced delayed responses, 39.0% of neurons showed burst, 21.9% suppression, 4.8% burst suppression and 34.1% no change. There was no significant difference in the proportions of each neuronal type between the stimuli showing and not showing delayed response ( $\chi^2 = 5.43$ ; 3 df;  $p = 0.14$ ).

**Conclusion:** There is no difference in the proportion of each neuronal type between the stimuli that induced delayed responses and those do not.

**Significance:** Mechanisms other than the proportion of each cell type may be responsible for delayed responses, such as the amount of inhibition or bursting.

### p0310

#### CHANGES IN SEIZURE FREQUENCY WITH VNS THERAPY IN JAPANESE PATIENTS WITH DRUG-RESISTANT EPILEPSY: 2 YEAR RESULTS FROM A 3-YEAR PROSPECTIVE REGISTRY

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**Purpose:** The efficacy and safety of vagus nerve stimulation (VNS) Therapy<sup>®</sup> has been established in the treatment of drug resistant epilepsy patients in the U.S and Europe. However, there are no published large scale prospective studies in Japan.

**Method:** VNS Therapy was approved for use in Japan in 2010. As a condition for approval a registry, to follow the natural course of patients treated with VNS was required. We conducted a multi-center, open-label, long-term, prospective registry of all patients with VNS Therapy in Japan to follow their clinical course and outcome. Patients who were expected to benefit from neurosurgical intervention were excluded. The final decision to include patients into the registry and to perform the implantation surgery was done by board-certified epilepsy surgeons. The primary objective was to assess responder-rate based on >50% reduction in baseline seizure frequency. Baseline data were collected prior to implantation and at 3, 6, 12, 24, and 36 months after the start of VNS Therapy. Two years of data has been collected.

**Results:** The registry included 385 patients aged 12 months to 72 years at time of device implantation (mean: 24.0 years), including 19% (72/385) who were <12 years of age at implant. Approximately half of patients had prior epilepsy surgery. Responder rates at 6, 12 and 24 months of VNS Therapy were 46.6%, 56.0% and 58.6% for all seizure types. Response for partial seizure was 49.8%, 55.6% and 59.3%. Response for generalized seizures, including secondarily generalized, was 55.0%, 63.7% and 68.2%, respectively. No new safety signal was identified.

**Conclusion:** Similar to the published literature from the US and Europe, the results from the preliminary analysis of the first, long-term, prospective registry in Japan support the safe and effective use of VNS Therapy in this population of Japanese patients with drug-resistant epilepsy.

## Others 1 Sunday, 6th September 2015

### p0317

#### OCT PARAMETERS IN PATIENTS WITH PHOTOSENSITIVE JUVENILE MYOCLONIC EPILEPSY

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**Purpose:** In this study, we aim to explore the relationship between the PPR and Optical Coherence Tomography (OCT) parameters in order to determine whether optic nerve layer or other structural differences have a causative role of photosensitivity in patients with JME.

**Method:** We studied 53 consecutive patients with Juvenile myoclonic epilepsy (JME) at our outpatient department. The interictal EEG findings for each patient were analyzed for the presence of any photoparoxysmal features. The peripapillary Retina Nerve Fibre Layer (RNFL) thickness, macula thickness and ganglion cell thickness were analyzed using OCT.

**Results:** We classified the 53 patients in our study into two groups as those with PPR (Group 1; 43.4%) and those without PPR (Group 2; 56.6%). There were statistically significant differences in the average RNFL thickness values of left eye between the two groups ( $p < 0.001$ ). Although the RNFL thickness of the right eye was higher in Group 1, no statistically significant differences were observed in this respect between the two groups. The RNFL thickness of the superior quadrants both in the right and the left eyes was significantly higher in Group 1 patients ( $p < 0.001$ ). Macular thickness of the right and left eyes were significantly thinner in Group 1 patients ( $p < 0.001$ ). Choroid thickness of the left eye was significantly higher in Group 1 than in Group 2 patients ( $p < 0.001$ ). Although choroid thickness of the right eye higher in Group 1 patients, no statistically significant differences was observed between the two groups.

**Conclusion:** We have found out that the RFNL thickness especially of the superior quadrants both in the right and left eyes, and choroid thickness were higher while macular thickness was significantly thinner in photosensitive patients with JME. In this study, we concluded that these structural features may be related to photosensitivity in patients with JME.

**p0318**

### THE SKIN OF FEAR EPILEPSY IN THE NOVEL OF JAVIER VÁSCONEZ

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**Purpose:** Javier Vásconez-an Ecuadorian writer- uses epilepsy as one guiding principle in his novel “The Skin of Fear”. Fear and epilepsy steep the development of the protagonist and of his environment. The objectives are to characterize the literary references concerning epilepsy in the novel, and to classify and analyze the literary description of epilepsy.

**Method:** Reading, identification, classification and analysis of the textual references pertaining epilepsy and its influence in the novel’s environment. Literary conceptualization of epilepsy.

**Results:** Fear appears as a clinical manifestation of seizures, but also as an emotional condition of the protagonist. Fear is also present in the protagonist’s relatives and friends, and even in the environment of the city, Quito. Other literary references regarding epilepsy describe postictal state, shame, self-compassion, secret, sorrow, excuse, stigma, supernatural power, insecurity, emptiness, alienation, identity or contrition.

**Conclusion:** Javier Vásconez presents epilepsy as a disease that goes beyond the biological and clinical aspects, having a great impact in the psychological and social fields, and even charging the urban environment with a perception of fear. It seems that these descriptions were derived from the epilepsy suffered by himself.

**p0319**

### POETRY OF CLEMENCIA TARIFFA: LIGHT IN A NEGLECTED EPILEPSY

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Poverty and epilepsy were lifelong mates of poetess Clemencia Tariffa. Beside these adverse situations she reached an autodidactic approach to literature and poetry. The splendor of her work was intense but passed frequently unrecognized. The macabre comfabulation of a neglected disease with social misery destroyed her mental and physical state leading finally to death. The case demonstrates how uncontrolled epilepsy associated to adverse social conditions harm human dignity and liberty.

#### Stranger

Another woman lives in me  
a stranger an intruder  
I cannot understand

#### Friendship

If our friendship  
wouldn’t be so pure  
like love  
we do in secrecy  
or so clear  
as your small chestnut colored eyes  
or so firm  
as the moon of ivory  
fluttering through my country  
seriously I wouldn’t write this night.  
I, only want your friendship.

## Others 2

Sunday, 6th September 2015

**p0321**

### TILT-INDUCED VASOVAGAL SYNCOPE AND PSYCHOGENIC PSEUDOSYNCOPE: OVERLAPPING CLINICAL ENTITIES

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**Purpose:** Vasovagal syncope (VVS) and psychogenic pseudosyncope (PPS) may both occur in the same person during a tilt table test: combined vasovagal syncope/psychogenic pseudosyncope (VVS/PPS). We described this combination to aid its clinical recognition.

**Method:** We identified tilt-induced VVS/PPS cases from two tertiary syncope referral centres. For each case three controls with tilt-induced VVS were selected at random from the same centre. Clinical characteristics were compared between both groups adjusting for multiple comparisons.

**Results:** Of 1164 tilt-table tests, 23 (2%) resulted in VVS/PPS; these 23 cases were compared with 69 VVS controls. VVS and PPS coincided more often than chance would predict: 2% vs 0.6%, ( $p < 0.001$ ). Typical VVS prodromes and triggers were reported in all VVS/PPS cases and VVS controls. Attack frequency was significantly higher in the VVS/PPS (2 per month, range 0.1–60) than in the VVS group (0.25 per month, range 0.02–4;  $p < 0.001$ ). Delayed recovery of consciousness was more frequently reported in the VVS/PPS group (83% vs. 10%,  $p < 0.001$ ), as were episodes without prodromes (57% vs. 10%,  $p < 0.001$ ), atypical triggers (43% vs. 9%,  $p < 0.001$ ), eye closure (43% vs. 12%,  $p = 0.002$ ), and duration of unconsciousness over 1 minute (91% vs. 32%,  $p < 0.001$ ).

**Conclusion:** VVS/PPS presents with a complex phenotype. High attack frequency, delayed recovery of consciousness, prolonged loss of consciousness, ictal eye closure, atypical triggers and the absence of prodromes may serve as indicators that PPS coincides with VVS.

**p0322**

### EFFECTS OF ANTIEPILEPTICS ON MITOTIC PROLIFERATION AT IN VITRO CELL CULTURES OF GLIOBLASTOMA AND NEUROBLASTOMA

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**Purpose:** The aim of the study was to identify the priority of antiepileptic agents on mitotic proliferation in glioblastoma and neuroblastoma cell cultures in vitro.

**Method:** The in vitro anti-tumoral activities of antiepileptic agents including gabapentin, pregabalin, valproic acid, levetiracetam, zonisamide, phenytoin and carbamazepine were assessed by a real-time cell analysis system by using E-plate 16. After inoculation of cancer cell lineages into wells, plate was placed into incubator and cell proliferation was monitored at every 1 hour. Tumor cells adhered to the bottom of wells and proliferated in appropriate nutrient and O<sub>2</sub>/CO<sub>2</sub> conditions. Following cells entered to rapid proliferation phase (log phase), agents to be evaluated for anti-tumoral activity was added to the wells predefined as experiment group in different concentration with a volume of 10 µL.

## Abstracts

The plates were again placed into incubator. Measurements were maintained at every hour after adding agents. Monitorization was maintained for 24–48 hours. The differences were evaluated by using analysis of variance (ANOVA) followed by post hoc Tukey test.

**Results:** The present study showed that xCELLigence is a convenient and rapid method to determine effects of antiepileptic agents on mitotic proliferation. Antiepileptic agents have diverse cytotoxic activities on tumor cells.

**Conclusion:** Within studied seven antiepileptic drugs while valproic acid and pregabalin had more cytotoxic effects on C6 glioma cells. Cytotoxic effects of gabapentin were not observed.

It was also found that, only valproic acid and zonisamide cause cytotoxic effects On NA/ANI neuroblastom cells. The other antiepileptic drugs showed no cytotoxic effects.

p0323

### TWO SIBLINGS WITH HOT WATER EPILEPSY: CASE REPORT

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Reflex epilepsies are seizures triggered by specific stimulants and account for 6% of all epilepsies. Hot water epilepsy is a rare form of reflex epilepsies which occurs while bathing. Pathophysiology of this clinical entity is complex and unknown. It is supposed that a defect in the thermoregulatory system leads to the seizures due to rapid rise of body temperature. Both partial and generalized seizures may occur. The diagnosis of the disorder is usually based on clinical history. Interictal EEG and neuroimaging studies are usually normal. Although the pathogenesis is not clear, familial clustering suggests that genetic factors may play a role in the development of the disease. In this report, two siblings, one of whom is 35 year old male and the other 39 year old female, who have complex partial seizures that are triggered by contact with hot water during bathing are presented. The aim was to review the relevant literature in view of these two cases diagnosed with hot water epilepsy.

p0324

### AN AUDIT OF ELECTRO-CLINICAL, EEG, ETIOLOGY AND PROGNOSTIC OUTCOME OF PATIENTS WITH SPINDLE COMA (SC)

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**Purpose:** To audit the electro-clinical, etiology and prognostic variables in patients with spindle coma.

**Method:** We analyzed 12 patients with spindle coma and audited their clinical, EEG, etiological and prognostic variables. Clinical out come at discharge were defined by modified rankin score (mRS). mRS >4 was considered to have poor outcome.

**Results:** The etiology of SC were hepatic encephalopathy (3, 25%), drug intoxication (3, 25%) infections (2, 16.7%), thrombotic thrombocytopenic purpura (1, 8.3%), trauma (1, 8.3%), cerebral bleed (1, 8.3%) and multifactorial encephalopathy in 1 (8.3%) case. Five (41.7%) patients had a Glasgow coma scale (GCS) of more than 9 and 7(59.1%) patients had a GCS <8. Two (16.7%) patients had poor outcome and 10(83.3%) had favorable outcome at discharge. EEG was reactive in all patients.

**Conclusion:** Majority (83.3%) of patients with SC had good outcome in our study. Contrast to some previous reports, EEG reactivity did not

influence the clinical out come nor the level of GCS. The underlying etiology of SC determined the clinical outcome. The two patients who had poor out come had multiorgan dysfunction syndrome and cortical venous sinus thrombosis with infarctions.

p0325

### ICTAL MUSICAL HALLUCINATIONS - A CASE REPORT

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**Introduction:** Auditory hallucinations are an unusual manifestation of seizures. In this work we report the case of a patient with musical aura.

**Clinical case:** A 76 years-old woman, with history of arterial hypertension and breast tumor submitted to surgery and chemotherapy with no signs of recurrence after 5-year of follow-up, followed in our hospital by a tonic-clonic seizure in the context of hyponatremia 2 years ago. During one appointment, she revealed experiencing several musical hallucinations in the past 6 months. Her hallucinations developed suddenly, without any identifiable case, and consist in different types of melodies, that the patient recognizes already heard them in youth or more recently. She denied any other symptom during the episodes and she didn't have any auditory complaints. Her neurological exam was unremarkable. Complete blood count, complete metabolic panel, sedimentation rate, homocysteine, iron, folic acid and vitamin B12 were normal. Anti-neuronal, anti-NMDA and anti-potassium channels antibodies were also normal. HIV, Hepatitis B and C, Herpes simplex and CMV serologies were negative. She has negative tumor markers and no signs of tumor recurrence in thoraco-abdominal tomography. Electroencephalography showed mild fronto-temporal bilateral paroxysmal activity. MRI revealed moderate cortical-subcortical atrophy and signs of ischemic leukoencephalopathy with periventricular predominance associated with multiple small hyperintense fronto-parietal bilateral subcortical foci related to gliotic ischemic foci. She started treatment with oxcarbamazepine with amazing improvement of her symptoms and a completely normal electroencephalography after 1 year of follow-up.

**Conclusion:** With this case report we intended to draw attention to this unusual form of epilepsy, not even fully yet understood, especially in what concerns the association between the auditory cortex, memories and how they are evoked.

p0328

### RAPID IDENTIFICATION OF ICTAL EVENTS IN LONG-TERM EEG RECORDINGS FROM EPILEPSY MONITORING

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**Purpose:** A quantitative EEG trending tool called NeuroTrend was used for rapid review of EEG recordings from an EMU in order to identify ictal events. NeuroTrend automatically identifies periodic discharges and rhythmic EEG activity and shows trends of their localization, frequency and amplitude. It furthermore shows trends of aEEG and background EEG frequency and allows viewing the corresponding EEG.

**Method:** Two reviewers used the NeuroTrend software to review long-term EEG recordings from 14 randomly selected patients from an EMU.

Only patients who had electrographic seizures during EEG monitoring were included. Patients with ictal EEGs characterized solely by paroxysmal fast activity were excluded. Mean recording duration per patient was 3 days and 20 hours. The reviewers were asked to compile lists of time instances with suspicious patterns that potentially correspond to seizures. They were not asked for a detailed assessment of the patterns. The lists of events were compared with the ictal events from the clinical reports from standard clinical review procedures. Sensitivity and specificity were assessed.

**Results:** The mean review time spent by the two reviewers was 3 minutes per 24 hours of EEG data. The two reviewers found 100% of the seizures in the EEGs of 8 out of 14 patients (57%) and more than 2/3 of the seizures in 11 out of 14 patients (79%). In 3 patients they found less than 2/3 but at least one of the seizures.

**Conclusion:** We could demonstrate the suitability of NeuroTrend for rapid review of long-term EEG recordings from EMUs. In our study it allowed identifying ictal events with a high mean sensitivity of 81% and a high mean specificity of 63%, while spending only 3 minutes for reviewing 24 hours of EEG recordings on average.

### p0329

#### THE CLASSICAL PHENOTYPE OF GLUCOSE TRANSPORTER-1 DEFICIENCY SYNDROME (GLUT-1 DS): DIFFERENT CLINICAL EXPRESSION AND KETOGENIC DIET RESULTS OF PEDIATRIC PATIENTS

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**Purpose:** The purpose of this study was to characterize patients who diagnosed with glucose transporter protein-1 deficiency syndrome (GLUT-1 DS), and also assess the efficacy of ketogenic diet (KD) therapy on seizure control, cognitive functions and other neurological disorders.

**Method:** We studied 6 unrelated Turkish patients with the classical phenotype of GLUT-1 DS, focusing on clinical and laboratory features, the KD therapy and outcome over the 25-month follow-up period.

**Results:** Five patients became seizure-free with the onset of ketosis, and anticonvulsants were discontinued. Other neurological features such as ataxia, spasticity, and dystonia improved less striking than the seizure control. There was no significant change in the IQ level and microcephaly after treatment of KD. In all patients, alertness, concentration, motivation, and activity resulted moderately improved with variable degree based on parents' reports and clinical presentations. On the KD epileptiform discharges had completely normalized in 5 patients. Slowing of background activity was still present in 1 patient. During follow-up, early-onset adverse effects of the KD as nausea, vomiting, constipation, and fatigue were observed in 5 patients but late-onset complications were not detected in any patients. The KD regimen was failed in 1 patient, therefore his diet was changed with alternative KD.

**Conclusion:** Treatment with a KD results in marked improvement of seizures and cognitive functions, and appeared less striking on other neurological disorders of patients. When the classic KD was not tolerate, another alternative ketogenic diet may be helpful.

### p0330

#### LATE-ONSET SSPE CASE SHOWING TEMPORARY AMELIORATION WITH CARBAMAZEPINE THERAPY

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**Introduction:** Subacute Sclerosing Panencephalitis (SSPE) is a rare progressive, fatal neurodegenerative disease caused by a persistent defective measles virus. Clinically, it is characterized by insidious onset of behavioral changes and deterioration in cognitive functions followed by myoclonus and result in vegetative state, coma and death. No curative treatment has been reported. We present a case diagnosed as SSPE and giving temporary response to carbamazepine therapy.

**Case:** 17 year old male patient presented with behavioral change, cognitive decline, urine incontinence, repulsive posture, followed by progressive myoclonus. Upon admission routine laboratory test results were normal. First Cranial Magnetic resonance imaging (MRI) revealed small size nonspecific hyperintense lesion in medial frontal region in T2 weighted image. Later Cranial MRI views showed bilateral diffuse cortical hyperintensity which is prominent in parieto-occipital region. EEG revealed generalized periodic spike and waves.

**Results:** Diagnosis of SSPE in stage 2 was suspected, CSF sample confirmed the diagnosis of SSPE with highly elevated titers. During follow-up his myoclonus frequency was increased and cognitive functions were deteriorated and he became mute and bounded to bed. There was no response to Vaproic acid therapy which was firstly started. After initiation of carbamazepine therapy his cognitive functions dramatically ameliorated, he was able to ambulate with support and had a speech with several basic words. The frequency of myoclonus was reduced. A month after treatment his progression was continued and progressed in to stage 3.

**Conclusion:** According to our classical knowledge, carbamazepine is an antiepileptic drug exacerbating myoclonic seizures and causing no improvements in cognitive functions. As it is shown in the literature as well as in our case temporary carbamazepine response in SSPE is one of controversy of classical carbamazepine treatment and underlying mechanism of this response is still unknown.

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### p0331

#### TEMPORAL LOBE EPILEPSY PRESENTED WITH ATYPICALLY PROLONGED POSTICTAL PSYCHOSIS: A PEDIATRIC CASE REPORT

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**Background:** Postictal psychosis (PIP) is a common complication, predominantly occurring in patients with temporal lobe epilepsy (TLE). PIP usually runs a benign and brief course although its psychopathology is often polymorphic, with abnormal mood, paranoid delusions, and impair-

ment of consciousness and orientation. We describe a girl with TLE who developed a prolonged episode of PIP lasting 3 months.

**Case:** A14 year-old girl was transferred due to uncontrolled recurrent seizures and psychotic symptoms. Her neurodevelopment was normal without a history of febrile seizures. About a month ago, she presented with dozens of dazzling and left side twinges and weakness, sometimes evolving left side clonic seizures with partly impaired consciousness. EEG and brain MRI revealed normal. After the first cluster of seizures, she had complained of severe continuous headache and she experienced another generalized tonic-clonic seizures (GTCS) followed by disorientation, anxiety and restless and aggressive behaviors 2 weeks after the first seizure. The psychotic symptoms did not respond to neuroleptic medications and GTCS recurred after introduction of antiepileptic drugs. Even after the discontinuation of all antipsychotic medications to exclude the deliriant side effects, her psychosis continued. Laboratory test to identify other medical causes was unremarkable. Repeated EEG recording revealed focal epileptiform discharges from right temporal area and definite postictal diffuse background slowings. Although recurrent GTCS were controlled by administration of phenytoin, her psychotic symptoms persisted despite multiple neuroleptic medications and multiple AEDs. However, her psychosis gradually disappeared from 2 months after the diagnosis. She completely recovered from the psychotic symptoms 3 months of treatment and now has been seizure-free without psychotic symptoms for 3 months.

**Conclusion:** We describe a rare case with TLE who developed the prolonged PIP following poorly controlled seizure. PIP can be another differential diagnosis of abnormal behavior or psychosis in children with epilepsy.

#### p0332

### NEURODEVELOPMENTAL OUTCOME OF CHILDREN WITH WEST SYNDROME IN A TERTIARY CARE CENTRE

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West syndrome represents a seizure disorder with unique clinical and electroencephalographic features. It is a catastrophic type of epilepsy where the outcome is guarded. The study was done to follow up the outcome of infants who were diagnosed as a case of West syndrome. It was a cross sectional study done in Child Neurology Unit, BSMMU. Forty seven diagnosed cases of West syndrome were followed up for a period of average 4.31 year (highest 10 year and lowest 2 years). Mean age of the patients were 14.6 months. In 12.8% patients age of onset of spasm was <3 months, 51% 3–6 months, 27.7% 6–9 months. Regarding developmental status, 57% of the patients were diagnosed as cerebral palsy while 23% had global developmental delay. Only 2 patients had normal development. Most of the patients had perinatal asphyxia 16 (34%) as risk factors. In EEG 29 patients had hypsarrythmia (17 classical and 12 modified) while other had multifocal spikes etc. Regarding neuroimaging, 81% had abnormal finding. Patients were treated with multiple antiepileptic drugs. ACTH was given in 8 patients, vigabatrin in 14, prednisolone 13 and valproate in 10 patients. In follow up we found, 36% patients had cerebral palsy, 27.6% patients has epilepsy, 12.7% patients died, 2 patients had autism while 5 patients had other complications. Only 11% patient had normal neurodevelopmental outcome. Regarding cognition, 37 patients had psychological assessment, out of them 81% had moderate to severe mental retardation. Causes of death of the patients were epilepsy (16%), discontinuation of antiepileptic drug (16%), pneumonia (16%) and unknown (50%). There are very limited studies involving the outcome of West syndrome, particularly in developing countries. This study highlights the clinical pattern and outcome of this disorder in a low resource country like Bangladesh.

#### p0337

### EFFICACY OF LEVETIRACETAM MONOTHERAPY IN CHILDHOOD EPILEPSY

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**Purpose:** Levetiracetam is a new antiepileptic drug especially approved for treatment of focal seizures in adults and children. The aim of this study was to investigate efficacy and tolerability of levetiracetam monotherapy in pediatric patients.

**Method:** In the study 225 children (aged 1 month-18 years) receiving levetiracetam and had being followed for at least 1 year were evaluated. The diagnosis of epilepsy was made by history of two or more unprovoked seizures. Dermographic characteristics, reason for antiepileptic treatment, the dose of levetiracetam, duration of the treatment, antiepileptic drugs used previously, seizure type, seizure duration, cranial MRI and EEG, seizure etiology and side effects of the drug were documented.

**Results:** A total of 225 patients, 95 girls and 130 boys, were enrolled in the study. 125 (55.6%) patients had generalized, 90 (40%) had focal seizures and 10 (4.4%) had epileptic syndromes of childhood. Overall, 186 (82.7%) patients remained seizure-free. According to the seizure type; 80.8% (101/225) of generalized and 87.8% (79/225) of focal seizures ended. When evaluated according to the EEG; 82.8% of generalized and 82.9% of focal seizures were terminated. There was no difference in the effectiveness of levetiracetam in partial and generalized epilepsy. Overall, 8 (18%) patients had adverse events. The most common side effects were evaluated as irritability and nervousness. There was no relationship between drug dose and side effects.

**Conclusion:** Levetiracetam monotherapy is effective in childhood epilepsies with focal and generalized seizures. It is well tolerated despite of mild and transient side effects which not require drug discontinuation.

#### p0339

### INSULIN-LIKE GROWTH FACTOR-1 IS ASSOCIATED WITH COGNITIVE OUTCOME IN INFANTILE SPASMS

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**Purpose:** The molecular mechanisms that lead to long-term consequences of infantile spasms (IS) are poorly understood. Insulin-like growth factor-1 (IGF-1) is regulated by insults that might be stressful to the brain, and is crucial for early brain development. The aim of the present study was to correlate cerebrospinal fluid (CSF) levels of IGF-1 with antecedent insults and cognitive outcome.

**Methods:** We studied CSF IGF-1 and the adrenocorticotrophic hormone (ACTH) concentrations in infants with idiopathic IS (IIS), symptomatic IS (SIS), and controls.

**Results and conclusions:** Infants with IIS had CSF IGF-1 concentrations similar to those of the control children, but children with SIS had markedly low CSF IGF-1 concentrations. In addition, CSF ACTH concentrations were significantly lower in the children with SIS than in those with IIS. High CSF IGF-1 concentrations were associated with an idiopathic etiology, absence of early (pre- or perinatal) insults or stress, normal brain imaging studies, good response to ACTH therapy, and favorable cognitive outcome. Low CSF IGF-1 concentrations were associated with low CSF ACTH concentrations, a history of early insults or stress, cerebral atrophy, poor response to therapy, and poor cognitive outcome. In children with IS, insults or stress in early life may affect the synthesis of IGF-1, which might play a role in the reduction of certain cognitive functions.

p0340

### SEIZURE DURATION WITH AND WITHOUT RESCUE MEDICATION IN A EUROPEAN SURVEY OF CHILDREN WHO EXPERIENCE PROLONGED ACUTE CONVULSIVE SEIZURES

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**Purpose:** To investigate the effect of rescue medication on seizure duration in children with epilepsy who have prolonged acute convulsive seizures (PACS).

**Method:** Practices in Emergency and Rescue medication For Epilepsy managed with Community-administered Therapy 3 (PERFECT-3) was a cross-sectional study in Germany, Italy, Spain and the UK. Eligible patients were non-institutionalized children aged 3–16 years who had been diagnosed with epilepsy  $\geq 12$  months previously, had experienced  $\geq 1$  PACS within the last 12 months and had currently prescribed rescue medication(s) for PACS. Investigators provided clinical assessments and parents/guardians completed web-based questionnaires. Assessments of average seizure length were based on parental recollections, not on measurements; seizure start- and end-points were not defined. Statistical tests were *post hoc*; *p* values are descriptive, non-inferential and uncorrected for multiple comparisons.

**Results:** At baseline, most of the 286 enrolled patients had prescriptions for diazepam (69.2%) or midazolam (55.9%), and some had two (26.6%) or three (2.4%) prescribed rescue medications. According to parents ( $n = 258$ ), the average length of children's prolonged seizures without rescue medication was 0 to  $<5$  minutes in 35.7% of patients, 5 to  $<10$  minutes in 42.6% and  $\geq 20$  minutes in 21.7%. When rescue medication was given, seizures reportedly lasted 0 to  $<5$  minutes in 69.4% of patients, 5 to  $<20$  minutes in 25.6% and  $\geq 20$  minutes in 5.0%. Rescue medication was statistically significantly associated with shorter seizures lasting  $<5$  minutes, compared with seizures lasting  $\geq 5$  minutes ( $X^2 = 58.8$ ;  $p < 0.0001$ ).

**Conclusion:** In this parent-reported survey of children with epilepsy who had  $\geq 1$  PACS in the previous year, significantly more children's seizures lasted  $<5$  minutes with rescue medication than without, and fewer children's lasted  $\geq 20$  minutes.

Study funded by ViroPharma (part of the Shire Group of Companies).

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p0341

### RISK FACTORS FOR EPILEPSY IN CHILDREN IN THE REPUBLIC OF MOLDOVA

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**Purpose:** The goal of this study was to identify the major risk factors for epilepsy in children with epilepsy in the Republic of Moldova.

**Method:** A total of 108 cases, in children aged 1–36 months were followed for epilepsy at the Pediatric Neurology Department during 2009–2012 and a control group of 108 children were included in the study. The most important examined risk factors examined were perinatal encephalopathy, febrile seizures, family history of epilepsy, arterial hypertension during pregnancy, head trauma, central nervous system infections. Data were obtained through a questionnaire, via personal interviews and the medical records and were assessed using univariate and multivariate analysis.

**Results:** We observed an increased risk for epilepsy in children with severe neonatal encephalopathy (OR 28.95, 95% CI 3.8319–218.7607), CNS infection (OR 22.84, 95% CI 2.9986–174.0101), severe head injury (OR 20.36, 95% CI 2.1254–163.0101), presence of maternal hypertension during pregnancy (OR 13.56, 95% CI 3.1011–9.2773), with a history of atypical febrile seizure (OR 11.31, 95% CI 2.5652–49.9060), history of epilepsy in first, second or third-degree relatives (OR 6.54, 95% CI 1.9930–265436).

**Conclusion:** The most important risk factors for epilepsy identified in this study were perinatal encephalopathy, history of atypical febrile seizures, severe head injury, CNS infection. Other identified important risk factors were a history of epilepsy in the family and maternal hypertension during pregnancy.

p0342

### BRAIN MR IMAGING AND MR SPECTROSCOPY FINDINGS IN CHILDREN WITH BREATH HOLDING SPELLS

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**Purpose:** Breath-holding spells are relatively common and generally benign paroxysmal attacks in infancy. However, it has been suggested that the neurological impairment secondary to cerebral hypoxemia occasionally accompanied in the children with breath-holding spells. Our aim in this study was to analyze the findings of brain magnetic resonance imaging and magnetic resonance spectroscopy of children with breath holding spells.

**Method:** This case-controlled cross-sectional study was performed at the Department of Pediatric Neurology, Harran University School of Medicine, Sanliurfa, in Turkey. Brain magnetic resonance imaging and magnetic resonance spectroscopy were performed in 18 (5 females, 13 males) children with breath-holding spells and in 13 (9 females, 4 males) controls.

**Results:** The radiological abnormalities such as delayed myelination in brain magnetic resonance imaging were not found in the all cases. Moreover, there was an insignificant difference in N-acetyl aspartate/creatinine, choline/creatinine, and myo-inositol/creatinine ratios between the patients and controls in the brain magnetic resonance spectroscopy (all  $p > 0.05$ ). Also, lactate peak was not found in any of the cases. On the other hand, a statistically significant difference was determined in respect of glutamate levels between the patients and the controls ( $p = 0.034$ ).

**Conclusion:** These new findings suggest that the permanent neuronal damage was not found in the patients with breath holding spells. Additionally, our results were demonstrated that increased glutamate levels certainly may play a role in the risk for developing neuronal hyperexcitability in these children.

p0343

### CLINICAL PARAMETERS IN CHILDREN WITH CEREBRAL PALSY AND EPILEPSY

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**Purpose:** Cerebral palsy (CP) is characterised by chronic nonprogressive neurological disorders of motor function, posture and movement. The purpose of this study was to determine the clinical parameters in children with CP and epilepsy.

**Method:** This retrospective study included 31 children with CP who were treated at the Clinic for Neurology and Psychiatry for Children and Youth. In all children were analysed the clinical form of CP, type of epileptic seizures, Apgar score, the presence of neonatal epileptic seizures, ultrasound (US) of the brain and electroencephalographic (EEG) results in the first year of life and positive family history for epilepsy.

**Results:** Epilepsy developed in 10 children with CP, and 7 children had partial seizures with or without secondary generalisation, and 3 had infantile spasms. In the group with epilepsy, 9 children had hemiparetic and quadriparetic form of the disease, and 1 child had diplegic form. Neonatal seizures and abnormal EEG showed statistically significant association with occurrence of epilepsy in children with CP ( $x = 5.9$ ,  $DF=1$ ,  $p < 0.05$ ;  $x = 5$ ,  $DF=1$ ,  $p < 0.05$ ), while US of the brain ( $x = 2.8$ ,  $DF=1$ ,  $p > 0.05$ ), low Apgar score ( $t = 0.183$ ,  $p > 0.05$ ) and positive family history for epilepsy ( $x = 3.1$ ,  $DF=1$ ,  $p > 0.05$ ) did not showed such significant association.

**Conclusion:** Neonatal seizures and early EEG are good predictors for later occurrence of epilepsy in children with CP, while US of the brain, Apgar score and positive family history for epilepsy are not such a good predictor. The most common type of CP associated with epilepsy were hemiparetic and quadriparetic type.

p0344

### PAEDIATRIC OFF-LABEL USE OF ANTIEPILEPTIC TREATMENT IN INTRACTABLE CHILDHOOD EPILEPSY: A SURVEY IN A LARGE COHORT OF PATIENTS WITH DRAVET SYNDROME

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**Purpose:** The aim of this study is to explore the extent of off-label use of antiepileptic drugs (AEDs) in a cohort of patients with Dravet Syndrome (DS), a pharmacoresistant epilepsy.

**Method:** We proposed auto-administered semi-close on-line survey to families of pediatric patients with DS in December 2013 on the website of DS alliance, France. Questions addressed different aspects of patients' medications in particular the off-label including all aspects of drug prescription not included in the SPC: therapeutic indication, posology, pharmaceutical form and route of administration.

**Results:** 89 families answered the questionnaire. Patients were aged from 0.84 years to 17.60 years (mean 8.06).

The most used AEDs were the following:

- clobazam (92%, CLB)
- valproate (90%, VPA)
- stiripentol (81%, STP)
- topiramate (46%, TPM)

We reported the major category of off-label use for these four drugs:

- 28% of patients use CLB out of the age-subsets,
- All patients with TPM are not in therapeutic indication for DS,
- 35% takes STP in a mixture non indicated with this treatment,
- The usual posology is not appropriate for TPM, VPA, CLB and STP respectively in 93%, 66%, 52% and 21% of patients,
- The dosage for age is not appropriate for CLB, STP, VPA and TPM respectively in 57%, 26%, 11% and 10% of patients,
- Care givers should manipulate CLB, STP, VPA and TPM in respectively 63%, 31%, 13% and 12% of patients.

**Conclusion:** This study raises the difficulties in families with children with DS using often off-label AEDs polytherapy. These results emphasize the need for further development and studies of paediatric formula of drugs currently used in Dravet Syndrome.

**Acknowledgement:** Funds were provided by Ansm, France.

p0346

### NATIONAL REGISTRY OF DRAVET'S SYNDROME AND OTHER SYNDROMES CORRELATED WITH GENES SCN1A AND PCDH19

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**Purpose:** Patient registers have been recognized by the European Community as one of the priorities of strategic intervention in the Rare Illnesses sector and as an essential instrument for improving understanding of the illness through the systematic and continual registration of data for basic, clinical and epidemiological researches. The objective of Dravet Italy registry is to collect the cases of Dravet S. and other syndromes related with SCN1A and PCDH19 mutations.

**Method:** The working group, after having identified the main aims of the registry, elaborated its structure, establishing 9 headings: Anagraphic Data; Genetic Investigations; Familial and Personal History; Semeiology, Frequency and Evolution of different Seizures; EEG and Neuroradiological features; Neuropsychological Outcome, Treatments and Adverse Events. The data are longitudinally collected.

**Results:** Preliminary dates: They have been thin to now inserted 102 patients of which 86 with mutation of the gene SCN1A (46 F and 40 M) and 16 PCDH19 (F); of these 10 between 1 and 3 years old, 13 among 3 and 5, 20 among 5 and 10, 24 between 10 and 15 and 35 older than 15 years. The analysis of genetic mutations, seizures semeiology at onset and during evolution neuropsychological picture at the used AED will be presented and discussed.

**Conclusion:** The collected data confirm that the Registry could represent an important instrument for the systematization of data regarding DS and other syndromes related with SCN1A and PCDH19 mutations.

p0347

### EFFICACY OF RUFINAMIDE THERAPY IN CHILDREN WITH REFRACTORY EPILEPSY

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**Purpose:** Rufinamide is a new antiepileptic drug (AED) approved for adjunctive treatment of partial-onset seizures with and without secondary generalization in patients  $\geq 12$  years, and adjunctive treatment of seizures associated with Lennox-Gastaut syndrome in children  $\geq 4$  years. We studied the efficacy of Rufinamide in children with refractory epilepsy.

**Method:** We studied patients treated with Rufinamide for refractory epilepsy at Hacettepe University Children's Hospital Department of Pediatric Neurology between January 2012–2015. We reviewed the medical charts and documented demographic and clinical data, seizure outcome and side effects. Missing information was completed by telephone interviews with parents.

**Results:** Thirty patients (14 boys and 16 girls) were studied. The mean age when rufinamide was started ranged between 2 years and 19 years, the mean age at seizure onset was 2.7 years (1 month–10 years). The most common underlying etiologies were cortical dysplasia (9/30), followed by the perinatal hypoxia and infections of the central nervous systems. The patients were on 1–5 AEDs, 2 patients underwent epilepsy surgery, 3 had vagus nerve stimulation, and 3 previously tried ketogenic diet. Nineteen patients (63%) had tonic-clonic seizures, 7 had (23%) focal seizures, 6 (20%) had epileptic spasms, 10 had (33%) drop attacks, 5 (17%) myoclonic seizures. Average follow up duration on rufinamide treatment was 13 months (1–27 months). Thirteen patients (43%) achieved 50% or more seizure reduction, 6 patients (20%) had 25–50% reduction, and remaining 10 patients (33%) had no change, one patient experienced increased frequency and severity of the seizures. Patients with drop attacks responded best to treatment. There was no difference in seizure frequency with respect to underlying etiology.

**Conclusion:** Rufinamide was well tolerated and showed efficacy in children with refractory epilepsy as add on therapy, particularly in the management of drop attacks.

#### p0348

### EVALUATING THE ASSOCIATION BETWEEN DRONABINOL USE AND OCCURRENCE OF SEIZURES

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**Purpose:** Cannabis has received much attention for its potential antiepileptic properties and novel mechanism of action. The main components of cannabis are tetrahydrocannabinol (THC) and cannabidiol (CBD). THC has been shown to be anticonvulsant but also induce epileptiform activity. Dronabinol (Marinol) is synthetic delta-9-tetrahydrocannabinol, not extracted from the cannabis plant. It was first FDA approved in 1985 for nausea and vomiting in patients undergoing cancer chemotherapy. The objective of this study was to evaluate whether dronabinol use was associated with subsequent seizures and/or epilepsy.

**Method:** A retrospective cohort study was performed in patients who received dronabinol at Texas Children's Hospital from October 1, 2010 until January 15, 2015 using the electronic medical record. Patients were excluded if administration and/or dose of dronabinol was undetermined. The following data was collected for each patient: baseline demographics, date of administration and dose of dronabinol, diagnosis of seizure and/or epilepsy based on ICD-9 diagnostic code(s), and antiepileptic drug utilization.

**Results:** Two hundred and thirty patients received dronabinol over the 4 year study period, 34 patients were excluded, for a total of 196 patients meeting study criteria. The majority of patients were male (61%) with a median age of 15 years (range 3–31 years). Median dose of dronabinol was 10 mg/day (range 2.5–60 mg/day). Thirteen patients were identified with a diagnosis of seizure and/or epilepsy. Only 4 (2% of included patients) had received dronabinol prior to the diagnosis. Of the 4 patients with clinical seizures following dronabinol use, one had EEG confirmed epileptiform activity and was treated with clonazepam.

**Conclusion:** Of the 196 patients included in this study, 1 patient (0.5%) had subsequent EEG correlated epileptiform abnormalities, and 4 patients (2%) had a diagnosis of epilepsy following dronabinol administration. Therefore, it appears that using dronabinol is not associated with a significant risk of subsequent seizures.

#### p0349

### TUBEROUS SCLEROSIS COMPLEX (TSC): A NORWEGIAN INTERDISCIPLINARY GUIDE

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**Purpose:** Making an interdisciplinary TSC guide to reach a broad range of people.

**Method:** The guide was authored by a multidisciplinary team consisting of a pediatrician, a specialist in genetics, a neuropsychologist, a special education teacher, two nurses and an information consultant. Methods for diagnostics, treatment and long term follow-up was adjusted to the Norwegian health care system, using the international guidelines for TSC. Because TSC is a multiorgan disease with several medical, psychiatric and neurocognitive difficulties, we established a reference group consisting of

- Medical specialists in neurosurgery, genetics, psychiatry, neurology, pediatrics, skin and internal medicine.
- The Norwegian TSC Alliance
- Special nurse working with rehabilitation
- Specialist in clinical neuropsychology
- Dentist with specific knowledge about TSC School nurse with special education in the field of sexology

The reference group contributed with second opinions and securing the quality of the contents.

**Results:** All questions about the disease are registered at the National Centre for Rare Epilepsy-Related disorders.

- Medical specialists
  - GPs
  - The Norwegian Tuberos Sclerosis Alliance
  - Rehabilitation
  - Language- and speech therapists
  - School
  - Nurses in the school system
  - Kindergarten
  - Institutions and private caretaking homes
  - Parents
  - People with TSC
- have contacted us, asking questions about treatment.

#### **Conclusion:**

- Patients and caregivers report that they bring the guide to their local doctor, and the doctor further uses the internet based TSC guide in referring to specialists.
- The cooperation between an interdisciplinary team and the Norwegian Tuberos Sclerosis Alliance has been a success. There is now a network of people with good knowledge about TSC throughout the counties, as well as in the TSC Alliance.

#### p0350

### A COMPARISON BETWEEN CLINICAL FEATURES OF CHILDREN WITH FEBRILE SEIZURES FOLLOWED BY BENIGN EPILEPSIES AND OF CHILDREN WITH FEBRILE SEIZURES PLUS

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**Purpose:** Febrile seizures (FS) are the most common cause of seizure activity in early childhood. The relationship between FS and childhood epilepsies has been a topic of major clinical interest. The aim of this retrospective study is to delineate clinical features in patients with FS followed by idiopathic epilepsy and to compare that with patients with FS extending beyond 6 years (FS<sup>+</sup>).

**Methods:** The study group consisted of 74 patients (37 females) with FS evolving to idiopathic epilepsy (group 1) and 22 patients (8 females) with FS<sup>+</sup> (group 2). Because group 1 consisted of patients with FS naturally evolving to epilepsy, the patients with hippocampal sclerosis or any other MR abnormality which may be causally related to a prolonged FS episode were excluded.

**Results:** The age onset of seizures was 23.5 months in group 1 and 22.6 months in group 2. Total number of FS were significantly increased in group 2 (5.0) compared to group 1 (3.1) ( $p < 0.05$ ). The family history for FS or epilepsy did not demonstrate any significant difference between 2 groups. The occurrence of febrile status did not show any significant difference between 2 groups (15% of patients in group 1 and 22% in group 2). There was no significant difference between 2 groups regarding the recurrence rate of FS in the first 24 hours or in the first week. Epileptic syndromes were classified as focal in 36 (49%), generalized in 32 (43%) and unclassified in 6 children.

**Conclusions:** This study showed that two subphenotypes of FS syndrome (the evolution of febrile seizures to a benign epilepsy or extending beyond early childhood without associated with afebrile seizures) share the similar clinical features and seem to be participated in the same spectrum.

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### p0351

#### EFFICACY OF BIOFEEDBACK IN TEENEGERS WITH PNES AND EPILEPSY

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Psychogenic nonepileptic seizures (PNES) can be defined as paroxysmal events that resemble or can be mistaken for epilepsy without being associated with abnormal electrical activity in the brain (Brown RJ et al 2011). Psychogenic nonepileptic seizures represent a puzzling clinical condition for which etiology, evidence-based treatments and outcomes are not yet defined. Epilepsy is considered a risk factors for PNES with prevalence up of 58% (Reuber M et al 2003). We report data from three adolescent patients (mean age 17 years) with PNES and Epilepsy for which we have used biofeedback for psychological assessment and treatment of PNES. All patients achieved a good control of epilepsy (1–3 seizures /year) but developed PNES (1–3 PNES/month). The semiology of the PNES resembled for two patients the semiology of epileptic seizures and was different for one patient. We have differentiate between PNES and epileptic seizures with video-long-term monitoring EEG. Assessment of psychological profiles was made with CBCL 6–18 and MMPI and neuropsychological profiles with WISC-IV/WAIS IV. All patients showed a normal cognitive functioning but low IQ (between 75 and 85); psychological findings didn't show criteria for depression, conversion disorders or personality disorders. In all patients electrodermal biofeedback pointed out an increase in skin conductance (measured in microsiemens) related to an increase of arousal level in emotional task (as waiting physical discomfort). We have proposed a biofeedback training (for a total of 8 sessions); during session trained the patient actively covert physiological activity and learn self-directed strategies to obtain and control a physiological response. The training also explicitly emphasized the

goal of transfer of the skills learned during the session into everyday life and the patient was encouraged to practice at home self-regulation skills in PNES-prone situations. All the patients showed a marked reduction in PNES frequency (60–70%) during months of biofeedback treatment.

### p0352

#### CLINICAL, EEG AND CYTOGENETIC FEATURES OF 4 CASES WITH RING CHROMOSOME 20 SYNDROME

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**Purpose:** Ring chromosome 20 syndrome (R20) has an almost constant association with refractory epilepsy and intellectual and behavioral disabilities. Early diagnosis is usually difficult, yet particular electroclinical patterns have been found to be very helpful. Here, we present the clinical, EEG and cytogenetic correlations in four R20 patients.

**Method:** Four patients, aged 17, 13, 4 and 7 years, respectively, were studied by video-EEG monitoring (VEEG) for drug-resistant seizures. Brain MRI was normal; standard EEGs showed anterior epileptiform activity with one-sided predominance, correlating to some ictal clinical features; intellectual and behavioral problems increased with age and disease course. VEEG was considered as a part of presurgical evaluation for refractory epilepsy.

**Results:** All three patients presented an electroclinical pattern consistent with frontal lobe epilepsy. They also had subclinical or subtle clinical episodes, both awake and in sleep, corresponding to non-convulsive status epilepticus (NCSE). The epilepsy started at age 1 ½ year in the 7-year old patient with the most severe epilepsy resembling Dravet syndrome, and at 3 years in the youngest patient presenting with focal status epilepticus. The seizures started later (age 7 and 9 years, respectively) and were rarer in the first two patients, who showed mild cognitive and behavioral disability. Due to the particular electroclinical picture R20 was suspected and cytogenetic analysis was performed. It revealed R20 mosaic karyotype, at 10%, 25%, 45% and 40%, respectively.

**Conclusion:** The presented cases show again that the R20 syndrome diagnosis is usually delayed and is based on the very characteristic for the syndrome electroclinical NCSE pattern and the "frontal lobe" seizure appearance. Our cases add further evidence for the genotype-phenotype correlation in the syndrome, since the degree of mosaicism reflects the age of epilepsy onset, the severity and refractoriness of the seizures, and the severity of the associated intellectual and behavioral disabilities.

### p0355

#### EPILEPSY12 - UK COLLABORATIVE CLINICAL AUDIT OF HEALTH CARE FOR CHILDREN AND YOUNG PEOPLE WITH SUSPECTED EPILEPTIC SEIZURES

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**Purpose:** To assess changes in the quality of care for UK children and young people with seizures and epilepsies.

**Method:** Epilepsy12, a UK wide audit, commenced in 2009 with the aim of evaluating epilepsy care against national guidelines. All hospital and community paediatric services managing children with epilepsy were invited to participate. A second round was undertaken between 2013 and 2014 to assess changes since Round 1 and results are reported here. Children referred for first EEG were used ascertain a second cohort of eligible children aged 1 month to 16 years receiving a first paediatric assessment between January and April 2013 for afebrile paroxysmal episodes. Retrospective case-note analysis was undertaken using a web-based platform and audit pack. Service descriptor data were collected on census day, 1 January 2014. Patient reported experience measures (PREM) were collected from sequential attendees at clinics, February-March 2014.

**Results:** 192/196 paediatric services enrolled. 186 units provided service descriptor data, 174 clinical audit data and 145 PREM data. The clinical cohort consisted of 3449 patients; median age 5.2 years; male:female 55:45%. PREM data were received from 2335 parents, carers, children and young people. 45% of first assessments occurred within an acute presentation. 35% of children had epilepsy diagnosed by 12 months. 22.6% of children had a documented neurodisability. 68% of paediatric services now have an Epilepsy Specialist Nurse (ESN). There has been a significant increase in percentage of children having ESN input; access to a paediatrician with expertise in epilepsies; appropriate assessment, classification and investigations in 2014 compared to 2012. PREM data showed 88% (1897/2148) overall satisfaction with services.

**Conclusion:** There is evidence of significant improvements in the provision of medical and nursing epilepsy care. Systematic audit, alongside other quality improvement initiatives, can demonstrate improvements in care.

p0356

#### SUCCESSFUL VNS TREATMENT OF EPILEPSY WITH MYOCLONIC ABSENCES: THE REPORT OF 2 CASES

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**Purpose:** To evaluate VNS therapy efficacy in epilepsy with myoclonic absences

**Methods:** Two boys (aged 11 and 5 years) with epilepsy with myoclonic absences were followed prospectively for the period 1–3 years since VNS-therapy initiation. Both patients have been treated with 5 AEDs in different combinations prior to VNS-therapy. One child had also tried ketogenic diet without sufficient effect. The clinical efficacy and tolerability of VNS treatment have been assessed during the entire treatment period and at the end of follow-up.

**Results:** Both patients achieved the complete seizure control after 13–16 months since VNS therapy initiation. One child has been seizure-free 2 years 4 months on VPA monotherapy and VNS. In the other patient the number of concomitant AEDs was reduced from 3 to 2 after reaching the complete seizure control on VNS therapy. Of interest, the complete seizure control in both children has been observed on the same VNS settings. No adverse events have occurred during the entire study period.

**Conclusion:** VNS therapy might be considered the first choice therapeutic option for treating this drug-resistant epileptic syndrome. More studies are needed to provide further evidence in favor of that conclusion.

p0357

#### IDIOPATHIC EPILEPSIES CHILD: STUDY OF A RETROSPECTIVE COHORT OF 186 CHILDREN FOLLOWED DURING 3 YEARS AT FANN TEACHING HOSPITAL (DAKAR - SENEGAL)

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**Purpose:** Epilepsy is a public health problem in Senegal with a prevalence of 8–14%. It was to study the therapeutic and evolutionary epidemiology, clinics, idiopathic epilepsies and assess the impact on them education.

**Method:** Retrospective, descriptive and analytical study from July 2003 to July 2011, of 186 children with idiopathic epilepsy aged from 1 month to 19 years followed for at least 3 years.

**Results:** Male predominated with a sex ratio of 1.3. A family history of epilepsy and parental consanguinity, respectively, were found in 34% and 24% of cases. Eighty-nine patients had an idiopathic generalized epilepsy and 90 others idiopathic partial epilepsy. Seven children had repeated febrile seizures. The median time to treatment was 7.1 years and the extreme 1 month and 14 years. In idiopathic partial epilepsy, epilepsy with rolandic paroxysms were more frequent with 46% followed by 5% occipital idiopathic epilepsies. In idiopathic generalized epilepsy, epilepsy with generalized tonic-clonic seizures (81%) were at the forefront, followed by epilepsy absences (18%). Of the 184 patients, 89% were on monotherapy and 11% in the combination therapy. Two patients had no treatment. The most commonly used molecules were valproic acid (48%), Phenobarbital (43%) and carbamazepine (8%). PHB-CBZ was the most frequent combination. Monotherapy remission was noted in 93% of cases. Adverse effects (17%) were noted primarily with VPA and PHB to type hyperactivity, weight gain, memory impairment, drowsiness, learning difficulties, lethargy, hypotonia, allergy and trophic disorders. One hundred twenty five patients were of school age. Among them, 107 children (86%) were enrolled, 11 others (9%) were dropouts and 7 (5%) were unschooled.

**Conclusion:** Idiopathic epilepsy is a good prognosis but still there are many problems supported in underdeveloped countries.

p0359

#### LEFT INTERMITTENT VAGAL NERVE STIMULATION IN CHILDREN WITH REFRACTORY EPILEPSY

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**Purpose:** To observe the tolerance and efficacy of periodic left vagal nerve stimulation (VNS) in a group of children with medically intractable epilepsies.

**Method:** A vagal nerve stimulator (Cyberonics Inc.) was implanted in 32 children with medically and surgically refractory epilepsies. Two of them were after neurosurgical operations conducted to cure epilepsy. These children were followed up for 2 months to 4 years. Mean (SD) age of the patients was 10.8 years (range 2 to 18). They underwent complete presurgical evaluation including detailed clinical history, magnetic resonance imaging, and long term video-EEG with ictal and interictal recordings.

**Results:** 18 (56%) of the 32 patients had a > 70% reduction in the number of monthly seizures. Five patients (15%) became seizure-free after the VNS implantation. Global evaluation scores indicated that there were no deteriorations from baseline and that there was a considerable number with improved status. Four patients were able to reduce the number of antiepileptic drugs used. No significant adversities were noted.

**Conclusion:** Stimulation of the left vagal nerve appears to be a safe, adjunctive therapy for the treatment of children with epilepsy intractable to available antiepileptic drugs. The reduction in seizure frequency in children was similar to that reported in adults. The specific epilepsies or seizures were not detected that were sensitive to this intervention.

p0360

### ICTAL AND PERIICTAL HEADACHE IN CHILDREN WITH EPILEPSY - CORRELATION WITH TYPE OF SEIZURES AND EEG-CHANGES

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**Purpose:** Data from the literature show that 34–47% patients with epilepsy suffer from periictal, mainly postictal headache. There are poor information about correlations between type of headache with children's age and sex, type of seizures, type of eeg changes, localization of headaches and differentiation if the headache is preictal, ictal or postictal in children. The aim of the study was to evaluate the frequency of the preictal, ictal and postictal headaches in children with epilepsy and correlation between these symptoms with types of seizures and changes in eeg.

**Methods:** The prospective study conducted in the Department of Developmental Neurology in Medical University of Gdańsk, include 30 patients, 6–17 years old, with diagnose of epilepsy and periictal headaches. The study group was divided into three subgroups according to the headache: preictal, ictal or postictal.

**Results:** In 76% children focal seizures, in 40% secondary generalized and in 16% primary generalized seizures were observed. 73% patients suffered from postictal headache, ictal headache occurred very rarely (7%). The mean intensity of the pain measured with the VAS scale was 6.5. We found the correlation between lateralization of headache and interictal changes in eeg in patients with focal seizures.

**Conclusion:** The frequency of periictal headaches correlates with type of seizures and type of changes in eeg.

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p0362

### PREVENTABLE CAUSES OF EPILEPSY IN MEXICAN CHILDREN. COMPARATIVE STUDY OF TWO POPULATIONS

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**Purpose:** The objective of this investigation is to identify and measure the preventable causes in mexican children and compare the frequency of said causes amongst two different populations with different socio-economic status.

**Method:** We analyzed the medical records from a 10 year period (2004–2014) of patients that had been diagnosed with epilepsy (ILA-IBE, 2005) from a public (Hospital Infantil de Mexico) and private institution (Hospital Español) to find attributed causes of epilepsy and then classified into preventable and non-preventable causes.

**Results:** We identified 334 patients, (139 public institution and 188 private institution). 149 (45.5%) were classified to have a preventable cause, 109 (32.6%) from the public institution and 40 (12%) from the private institution. Preventable causes that occurred during the prenatal period were 4 times as common in the people attending the public institution (68.8% vs 17.5%). The most common preventable cause was inadequate prenatal care (21.5% p < 0.005). Other important preventable causes were: perinatal hypoxia (16.1%), prenatal asphyxia (14.1%), and maternal infections during pregnancy (9.4%). Patients with preventable causes tended to have drug resistant epilepsy (24.16% vs 19.66%).

**Conclusion:** Epilepsy in mexican children had a preventable cause in almost half of the instances, suggesting that improving seems to be the most effective way of having a positive impact in the prevention of epilepsy. We proposed that future efforts in developing countries should be focused in more cost effective strategies like improving prenatal care, instead in spending resources in newer and expensive antiepileptic drugs.

p0363

### WEST SYNDROME: ABOUT 26 CASES IN DAKAR (SENEGAL)

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**Purpose:** Determine epidemiology, etiology, treatment and outcome of West syndrome.

**Method:** This was a retrospective study in which we reviewed the charts of patients treated in the pediatric neurology consultation Fann and Albert Royer Hospital from July 2003 to December 2011, with a follow-up of at least 2 years.

**Results:** Twenty-six cases of patients have been recorded. The average age was 12 months. The youngest are aged 3 months and the oldest 6 years. The sex ratio (M/F) was 3.3. The average of the disease onset was 4 and a half months; 42.3% had the onset of disease between 1 and 6 months. In about 69.5% of cases, the initial psychomotor development was abnormal. Perinatal asphyxia was found in 46.3% children. All patients had spasms in flexion and 34.6% had more than three crisis. The most frequent types of crisis in 30% of patients were myoclonic seizures and partial motor seizures. In 3.85% of children, these 2 types of seizures were associated. The main clinical findings at examination were axial hypotonia (49.9%) and language delay (19.2%). Fifty percent of children had a poor social contact. A cerebral scan was normal in 15.4% of cases. 34.62% of scanners showed cortical and / or subcortical atrophy and 11.4% had porencephaly. 57.7% of patients were followed for 3 to 4 years. 38.5% of them required antiepileptic treatment. The most frequent drugs used were sodium valproate (61.54%), clonazepam (30.77%) and carbamazepine (23%). In 53.8% of cases, the progression of the disease was favorable with stopping of the seizures however the cognitive dysfunctions persisted. 19.2% of patients were not in school.

**Conclusion:** West syndrome is a pharmaco-resistant epilepsy, characterized by multiple risk factors. It combines various neurological deficit which affect the quality of life and makes it harder to treat.

p0364

### LOW FREQUENCY PREICTAL EEG WAVES PRECEDING EPILEPTIC SEIZURES ORIGINATING FROM RIGHT FRONTAL LOBE

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**Purpose:** Seizure prediction despite the fact that there is not yet a consistent and general methodology, could provide an alternative solution for persistent and sudden epileptic seizures. Patient oriented predictive features can probably derive from scalp EEG signals. This work describes one case of probable predictive evidence.

**Method:** The study till this time consists of 15 drug resistant pediatric epileptic patients recorded with long term video EEG using the 10–20 system, at the University General Hospital of Iraklio, Crete. Only 6 of them (3 males/3 females, aged 8–16 years old) presented seizures during monitoring. The dataset contains a total of 27 seizures.

**Results:** An 8 year old female patient suffering from focal epilepsy originating from the right frontal lobe presented a specific EEG pattern with increased activity of rhythmic delta EEG waves (0.5–4 Hz) a short period (6–17 second) before seizure onset. Although this phenomenon appears only on this patient, it still occurs repetitively in her vast majority of seizures (7 out of 8 seizures observed) in at least 6 bipolar pairs of right frontal and central electrodes. All seizures occurred during sleep. Spectral power of delta band were significantly greater ( $p < 0.01$ ) between preictal period (15 sec before seizure onset) and normal EEG periods. In this preictal period and the selected bipolar pairs, delta band power presented high concentration of  $93.01\% \pm 1.74\%$  of total power.

**Conclusion:** A case of distinctive repetitive EEG pattern with increased rhythmic preictal delta waves of right frontal focal epilepsy is presented. Since this is the case for only one specific subject, it enforces the fact that a computational predictor could yield findings if it is personalized to each patient. This evidence could be a valuable feature towards prediction of the same seizure type.

p0365

#### EFFICACY OF NEW ANTIEPILEPTIC DRUGS (AEDS) IN CHILDREN WITH PARTIAL ONSET SEIZURES

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**Purpose:** To evaluate influence, clinical usefulness and safety of three new AEDs (levetiracetam, lacosamide and oxcarbazepine) in monotherapy and add-on therapy in children.

**Methods:** We compared efficacy and tolerability of three AEDs in a group of 101 children of age between 6 and 18 years which were on monotherapy or add-on therapy with either of three drugs (LEV, LCM, OXC). There were 47 children treated with only one AED and 54 children on 2 or more AEDs.

**Results:** During our period of observation we noted a slightly higher efficacy of treatment with either LCM or LEV than with OXC while all the patients were on full therapeutic doses of the drugs.

**Conclusions:** There was no statistical significance in the efficiency of treatment of partial onset seizures with either of three studied AEDs.

p0366

#### EPILEPTIC SPASMS IN CONGENITAL DISORDERS OF GLYCOSYLATION - ELECTRO-CLINICAL CHARACTERIZATION OF FIVE PATIENTS

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**Purpose:** Congenital Disorders of Glycosylation (CDG) are a group of rare metabolic diseases, characterized by impaired glycosylation of proteins and lipids. Multisystemic involvement is common and neurological impairment is severe and disabling, concerning central and peripheral nervous system. Epilepsy is frequent, but detailed electro-clinical description is rare. West syndrome has been described in only two patients with CDG syndrome with -Im subtype. However, epileptic spasms without hypsarhythmia have not yet been reported in CDG patients.

**Method:** We describe retrospectively the electro-clinical features in five children with CDG syndrome, Ik, Ic and Ip subtypes, and epileptic spasms.

**Results:** Spasms occurred at an early age, before 6 months in all cases, except one who started at 18 months. In this patient, spasms had an unusual aspect, they did not occur in clusters and were immediately preceded by a myoclonus. All but one children presented also rare myoclonias. On EEG, background activity was poorly organized with abundant posterior spike and fast rhythm activity but without hypsarhythmia. At last evaluation (age ranged between 6 and 12 years), two patients still presented epileptic spasms and subcortical myoclonias, one showed rare generalized tonic-clonic seizures and two were seizure free.

**Conclusion:** In CDG disorders associated with epileptic spasms, particular features were noted, such as posterior EEG anomalies, absent hypsarhythmic pattern and unusual combination of epileptic spasms with myoclonus. These features, associated to preexisting developmental delay and subcortical myoclonias, may contribute to the diagnosis of CDG syndrome.

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p0370

#### PROFILE NON-EPILEPTIC EVENTS IN CHILDREN

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**Purpose:** Paroxysmal manifestations occupy an important place between the children diseases. Differential diagnosis of non-epileptic paroxysmal events with epilepsy is a major problem in Neuropediatrics.

**Method:** Appreciation of clinical peculiarities in children with critical manifestations toward the differentiation of the non-epileptic paroxysmal clinical events from the epileptic ones. The study included 387 patients with clinically suspected diagnosis of "epilepsy", aged between 0–18 years who were investigated by complex neurological examination and laboratory tests: electroencephalography (EEG), echocardiography (ECG), computed tomography brain (CT) and magnetic resonance brain imaging (MRI) (if necessary).

**Results:** Abnormal paroxysmal motor events that might be not discovered as epileptic because of their unusual characteristics were diagnosed in 130 children (33.6%) exposed to the research, that constituted: anoxic/hypoxic convulsions - 67.7%, toxic agents-determined paroxysmal

strokes - 1.54%, pseudoepileptic convulsions and other psychiatric manifestations - 3.08%, hyperventilation syndrome - 6.15%, movement's paroxysmal disturbances - 0.77%, other disturbances of movement - 1.54%, episodes characterized by the damaging of response to stimuli - 2.31%, migraines and periodical syndromes - 10.76%, paroxysmal disorders during the sleep - 6.15%.

**Conclusion:** Approximately 33.6% of patients with suspected diagnosis of "Epilepsy" actually suffered from paroxysmal non-epileptic states. The most of diagnostic errors of paroxysmal manifestations may be avoided by a meticulous anamnesis, which remains the major step in diagnostic establishment. The second step of the diagnostic is the objective examination, to which we add laboratory examinations, adjusted to each case, which constitutes the third step of diagnostic and leads to the differentiation of the epilepsy from other non-epileptic paroxysms. The misinterpretation of EEG or its interpretation without taking into consideration the case history represents a source of error to epilepsy diagnostic. The differential diagnosis between the paroxysmal states and the epilepsy is possible only by creating offices and special centers equipped with video-EEG monitoring.

### p0373

#### LYSINE-RESTRICTED DIET IN PYRIDOXINE-DEPENDENT EPILEPSY

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**Purpose:** Pyridoxine-dependent epilepsy (PDE) is an autosomal recessive epileptic encephalopathy caused by deficiency of antiquitin (ATQ), an enzyme that facilitates cerebral lysine catabolism (MIM# 266100). While seizures usually are controlled by pyridoxine treatment, 75–80% of patients develop mental retardation regardless of therapy. Add-on treatment with lysine-restricted diet has been shown to improve biomarkers of lysine degradation (1). We aimed to assess whether add-on treatment with lysine-restricted diet will result in improvement of development.

**Method:** In 6 patients (5f, 1 m) with genetically confirmed ATQ deficiency, lysine-restricted diet was initiated at a median age of 4.41 y (0.39–11.75). All patients received a lysine-free amino acid supplement fortified with micronutrients (Lys-2 prima, Nutricia metabolics, Germany). One patient discontinued the diet after 6 m, the others continue for a median duration of 2.7 y (2.13–6.39).

**Results:** The diet was well tolerated. Physical examination and biochemical safety panels showed no evidence of malnutrition. Break-through seizures during infections occurred in 2/6. Interictal EEG showed epileptiform discharge in 5/6. Developmental test yielded normal results in 2/6 and abnormal results in 4/6. Follow-up tests available in 3/6 showed improvement in 2 and no change in 1. Additionally, parents initially reported features suggestive of autistic spectrum disorders in 3/6 which improved following initiation of the diet. In 3 of 4 patients with a squint, deficits of visual perception were identified.

**Conclusion:** In PDE, add-on treatment with lysine-restricted diet is safe. Whilst in our cohort, a positive effect on the developmental prognosis of the children could not be established by standard neurocognitive tests, parents frequently describe improved behaviour. In order to assess the natural course of the disease and treatment effects, an international Red-Cap database is being suggested (1). (1) van Karnebeek et al (2014). Lysine-Restricted Diet as Adjunct Therapy for Pyridoxine-Dependent Epilepsy: The PDE Consortium Consensus Recommendations (2014). JIMD Rep.

### p0374

#### EFFICACY OF ADD ON CORTICOSTEROIDS IN THE MANAGEMENT OF PHARMACO RESISTANT EPILEPSY IN LENNOX GASTAUT SYNDROME (LGS), MULTI CENTER PILOT STUDY

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**Purpose:** Lennox-Gastaut syndrome (LGS) is a childhood epileptic encephalopathy, which is notoriously difficult to treat. Children often end up on poly-pharmacy with numerous anticonvulsants, causing hazardous adversities. The aim was to investigate efficacy of corticosteroids in the management of pharmaco-resistant epilepsy in LGS.

**Method:** Single armed, open-labeled, efficacy trial with add on corticosteroids was performed over 24-weeks. Primary outcome parameter was seizure freedom, secondary outcome parameters were safety, improvement in behaviour and quality of life. Intravenous Methyl-Prednisolone was given 30 mg/kg over 5 days, followed by oral Prednisolone 2 mg/kg for 9 days. Steroid was weaned gradually over 6 weeks. Twice weekly pulses of Prednisolone (2 mg/kg) were commenced thereafter, 30 mg/kg intravenous Methyl-Prednisolone once in 6-weeks. Patients were monitored closely at regular intervals.

**Results:** Twenty one children, mean age 5.7 years (2.3–16.3 years), males-11, fulfilled the inclusion criteria. All had daily seizures; axial/axio-rhizomeic tonic seizures (21), myoclonic (16), drop attacks (11), atypical-absences (05). Average numbers of seizures were 6/day (2–12/day). Four dropped out on days 05,08,12 and 13 due to hospital-acquired-infection, maternal concerns, uncontrollable hypertension and severe urinary tract infection respectively. All who completed up to day-14 had >50% seizure reduction (Seizure freedom in 12). Two relapsed between 18–24 weeks. Three had positive urine sugar, all had significant rise in BMI. Height-velocity and electrolytes remained unchanged. The quality of life and childhood behavior scores improved significantly ( $p < 0.05$ ) by 24 weeks.

**Conclusion:** Majority achieved significant seizure control through steroids, with minimum adverse effects. The quality of life and behavior scores improved significantly. Suggest randomized-blinded-placebo-controlled study to confirm the findings.

### p0376

#### EEG SENSITIVITY IN SUBTLE CORTICAL DYSPLASIA ON MRI

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**Purpose:** Malformations of cortical development (MCD) is a wide range of lesions varying from congenital lesions and represent a major cause of developmental disabilities and severe epilepsy. MRI is important to detection such lesions. Sometimes it is difficult to detect on MRI due to type of subgroups or small for detection. We presented two cases that were followed previously as intractable seizures and non lesional epilepsy, and then detected cortical dysplasia on MRI depends on EEG findings for suspicious MCD.

**Method:** Two patients aged 13 and 17 year old and diagnosed with intractable epilepsy were submitted to Video EEG Monitoring Unit at Gazi University School of Medicine. Their EEG findings and final diagnosis were discussed.

**Results:** When evaluated of EEG records, interictal EEG shows repetitive fast spikes and intermittent slow on left parasagittal region in patient one while paroxysmal fast activity and persistent spikes on posterior head regions in patient two. Depends on these EEG findings, MRI's are repeated and obtained as 3T thin sliced epilepsy protocol, especially targeted the regions of suspected areas on EEG. Their final diagnosis was focal cortical dysplasia in left anterior cingulate gyrus in patient one and double cortex-pachygyria in posterior head region in second patient.

**Conclusion:** There are highly epileptogenic electrographic patterns due to extreme hyperexcitability in MCDs. Scalp EEG or invasive records can show continuous, rhythmic or semirhythmic spikes; paroxysmal bursts of high frequency spikes; recurrent electrographic seizures. In particular, the continuous rhythmic spiking suggests that an intradysplastic, self-sustained, hyperexcitable areas in the brain. As supported by our findings, if the patients have such EEG findings, they need to careful and appropriate examination on MRI even if normal MRI findings previously.

p0377

#### EEG UTILITY IN NEWBORNS

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**Purpose:** Electroencephalogram (EEG) is most important tool for differentiate epileptic or non epileptic events. Newborns are unique age group for clinical presentation of many disorders and needs to appropriate diagnosis to prevent subsequent neurologic co-morbidities. Neonatal seizures are one of an acute manifestation of central nervous system disorder. We aimed to evaluate EEG utility and benefits in neonatal age group in terms of differential diagnosis of epileptic-non epileptic events and correlation of neurological status.

**Method:** This study was conducted from January 2014 to January 2015 at Gazi University School of Medicine Department of Pediatric Neurology & Routine EEG Unit. Neonatal EEG's was re-evaluated in terms of contribution of the differential diagnosis. For this purpose, postconceptional age (Limited to neonatal age, sex, age, EEG trace, and cranial magnetic resonance imaging (MRI) was analyzed and compared to reason of EEG request and final diagnosis.

**Results:** We analyzed 1246 EEG trace and 268 of them were recorded from term or preterm newborns. Seventy-one patients were re-evaluated for EEG, MRI and neurological conditions and final diagnosis. The most common indication was the suspected seizures. Thirty nine patient were term newborn and 39.9 of those patients had abnormal EEG .

**Conclusion:** The recent technological advances in neonatal care have changed aetiological profile of neonatal seizures. Eighty percent of neonatal seizures occur in the first week of life, constituting the most common and distinctive sign of neurological dysfunction. We found EEG features of term and preterm newborns is valuable for predict subsequent neurologic status and diagnosis.

p0378

#### BRAIN MRI ABNORMALITIES DIFFER BETWEEN TSC1 AND TSC2 PATIENTS - A PILOT STUDY

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**Purpose:** TSC1 or TSC2 mutations are found in 80% of patients with Tuberous Sclerosis Complex (TSC). The expression of neurological features varies between patients and the exact relation between genotype and brain MRI abnormalities has to be further explored. This pilot is the first study to compare TSC1 to TSC2 mutations on a large range of TSC-related MRI characteristics.

**Method:** In this retrospective explorative study we included patients with a DNA confirmed diagnosis of TSC, refractory epilepsy, and MRI of sufficient quality, who were referred to our center for presurgical evaluation. We evaluated the most recent MRI (either 1.5T or 3T), with at least T1, T2, and FLAIR sequences. We compared the following MRI characteristics between patients with TSC1 and TSC2 mutations: tubers according to the tuber classification of Gallagher et al. (i.e. type A, B, C tubers), subependymal nodules (SEN), subependymal giant cell astrocytoma, focal cortical dysplasia (FCD)-like features, white matter lesions, radial migration lines, cysts, calcifications and hydrocephalus.

**Results:** 30 patients, 8 with TSC1 and 22 with TSC2 mutations, were included. Epilepsy characteristics and level of development were comparable between groups. Type C tubers were more frequent amongst patients with TSC2 mutations (0% of patients with TSC1, versus 45.5% of those with TSC2 mutations) and FCD-like features were more common amongst patients with TSC2 mutations (90.9% vs. 50% in TSC1). The other MRI characteristics did not differ between TSC1 and TSC2.

**Conclusion:** The findings of this pilot-study add to previous research that found evidence for a more severe phenotype in patients with TSC2 mutations, as FCD-like features and type C tubers were more common amongst patients with TSC2. We are currently extending the MRI analysis to the entire population with genetically determined TSC in our center.

p0379

#### A NEW CASE OF ALPERS SYNDROME WITH RAPID ONSET OF PARTIAL STATUS EPILEPTICUS: NEURORADIOLOGICAL AND ELECTROPHYSIOLOGICAL EVOLUTION

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**Background:** Alpers-Huttenlocher syndrome (AHS) is at the severe end of a broad clinical spectrum of disorders due to mutations of POLG1 gene. EEG and MRI features can be pathognomonic in some cases. It is unclear whether different MRI and EEG patterns reflect the timing of electroencephalograms in relation to the stage of cerebral degeneration or if they identify different patients' populations.

**Case presentation:** We report on a 6 years old girl who rapidly developed myoclonic status epilepticus. Initially EEG and polygraphic recordings documented rhythmic high-amplitude delta with superimposed (poly)spikes associated with myoclonic jerks, followed after 1 month by epilepsy partialis continua, characterised by continuous multifocal asynchronous myoclonus without any clear correlation between muscle activation on EMG and EEG discharges. Epilepsy, which was initially drug resistant, eventually ceased spontaneously

after 11 months. Brain MRI at the onset showed symmetric hyperintensities of the hippocampi mimicking limbic encephalitis; after 3 months she presented abnormal cortical and thalamic signal at Diffusion Weighted Imaging and a marked increase in lactate associated with N-acetylaspartate reduction at Spectroscopy. POLG1 gene sequencing in exon 21 documented a *de novo* heterozygous mutation, consisting in a T to G substitution of the nucleotide 3294 of the cDNA of the gene (NM\_002693: c.T3294G). This substitution has never been described before, but we reasonably consider it to be pathogenic because it is predicted to be damaging with high score and based on its evolutionary conservation. Three years later our patient is still alive with a need of close medical support.

**Conclusion:** Our case provides detailed information on neuroradiological and electrophysiological temporal evolution of AHS. Peculiar MRI and EEG findings became evident at different stages of the disease course, preventing early diagnosis of AHS.

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p0380

### SHORT FORMS OF THE WECHSLER INTELLIGENCE SCALES FOR CHILDREN (WISC-III) IN PAEDIATRIC EPILEPSY: ARE RESULTS RELIABLE?

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**Purpose:** Time constraints may press psychologists to use short forms of the WISC. In satisfactory short forms, 81% of the IQs fall within the 90% CI of the full-length form. Two short forms of the Dutch WISC-III - short-form4 (Information, Vocabulary, Picture Arrangement, Block Design) and short-form6 (Information, Similarities, Comprehension, Picture Completion, Block Design, Puzzles) - were tested on children most liable to show elevated subtest scatter: children with lateralized epilepsy with/out MRI lesions.

We studied

(1) the utility of each short form, and

(2) the contribution of laterality and MRI-status to measurement errors.

All children had originally taken the full-length form.

**Methods:** Participants were 83 children (54% boys) with partial epilepsy (48 LH/35 RH), 29 with MRI+ (17LH /12RH) having short-form4 FS-IQs between 65 and 125. Mean age at epilepsy onset: 5.7 years ( $\pm$  3.4). At testing, age in years= 10.1 ( $\pm$  3.1), median number of AEDs= 1 (range 0–3). FS-IQ on the full-length WISC-III: 87.47 ( $\pm$  11.7).

**Analyses:** (1) Overall rates of children falling within the 90% CI of full-length form.

(2) MANCOVA for contribution of seizure lateralization and MRI status (with duration of epilepsy as covariate) on absolute differences between short and full-length IQs (=short-form deviations).

**Results:** (1) Rates within 90% CI, short-form4/short-form6: VIQ 80.7%/85.5%, PIQ 84.3%/79.5% and FS-IQ 85.5%/86.7%.

(2) Short-form4/short-form6: No significant contribution of seizure onset side or MRI status was seen on the short-form deviations on any scale. Short-form4: A side\*MRI-status interaction on the verbal scale indicated that RH MRI+ increased the short-form deviations.

**Conclusion:** Both short forms proved satisfactory for paediatric epilepsy. However, increased measurement errors appeared in MRI+ (short-form4). Short forms should be tested for utility.

p0383

### ICTAL POUTING “CHAPEAU DE GENDARMA”

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**Purpose:** Clinical semiology and EEG findings of frontal lobe seizures are complex and difficult to understand because of its anatomic position and richness of neuronal network. Recently, a new type of facial expression is called ictal pouting which is also named “chapeau de gendarme”, turned-down mouth looks like the hats of gendarme’s at the time of Napoleon. A patient had frontal lobe seizures and sign of ictal pouting was presented.

**Method:** A Nine-year-old male patient was referred to Gazi University School of Medicine, Pediatric Video EEG Monitoring Unit center due to his intractable seizures.

**Results:** The seizures of the patient were characterized by forced expiration, eye blinking, tonic contraction of the face, turned-down mouth (ictal pouting) “chapeau de gendarme” and followed by hypermotor seizure lasted for 15–20 seconds. Both ictal and interictal activity was pointed to bilateral frontal and parasagittal region. 3T MRI showed that suspicious of left inferior frontal gyrus focal cortical dysplasia (FCD). Positron emission tomography (PET) confirmed hypometabolism in left inferior frontal gyrus. The lesion was found overlapped with Broca’s region at functional MRI. Therefore, he was planned to continue medical treatment and VNS (vagal nerve stimulation) therapy if necessary in the future.

**Conclusion:** Ictal pouting, ‘Chapeau de Gendarme’ was defined by symmetrical turned-down mouth (>5 s), and contraction of the chin. An SEEG study showed anterior cingulate cortex (ACC), less orbitofrontal cortex, inferior frontal gyrus and insula are responsible for ictal pouting. The lesion of our patient was in left inferior frontal gyrus resulted from cortical dysplasia as supported of the limited literature. Ictal pouting is a rare semiology, for the patients who cannot be localized or lateralized by radiological or electrophysiological, must be keep in mind for the epileptogenic zone of frontal lobe and insula.

p0385

### CLINICAL PREDICTORS OF INTRACTABLE EPILEPSY IN CHILDHOOD

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**Purpose:** Despite the use of antiepileptic drugs either individually or in combination, up to 20% of epileptic patients will continue to have seizures. These individuals are regarded as having intractable epilepsy. Intractable epilepsy often has deleterious effects such as intellectual disability, psychiatric comorbidity, physical injury, sudden unexpected death, and poor quality of life. Early identification of these patients is important in considering the use of alternative treatments. In this retrospective study, we aimed to determine the clinical, electroencephalographic, and radiological factors associated with medically intractable seizures in children.

**Method:** Records of the patients with intractable epilepsy and well controlled epilepsy were reviewed to identify the variables that may be associated with seizure intractability. Intractable epilepsy is defined as at least 1 seizure in a month in the past 6 months despite treatment with at least 2 antiepileptic drugs and at least 1 year-long seizure-free time is defined as seizures under control.

**Results:** There were 458 epileptic children (210 female and 248 male) with a mean age of  $7.73 \pm 4.72$  years. 177 of them had intractable epilepsy and 281 had well controlled epilepsy. Univariate analysis showed that age at seizure onset, having mixed seizure types, history of status epilepticus, history of neonatal seizures, having daily seizures at onset, abnormality on first electroencephalogram, abnormal neurodevelopmental status, abnormal neuroimaging, having a symptomatic etiology were significant risk factors for the development of intractable epilepsy ( $p < 0.05$ ). Side effects of antiepileptic drugs were significantly higher in intractable epilepsy group.

**Conclusion:** There are a number of clinical features that can be identified in the course of childhood epilepsy that may predict the outcome. Early identification of patients at high risk of developing intractable epilepsy will guide appropriate therapy. These findings have to be verified by further prospective studies.

#### p0387

##### SEIZURE PRECIPITANTS IN DRAVET SYNDROME

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**Purpose:** To determine seizure precipitants in Dravet syndrome (DS) compared to other people with epilepsy.

**Method:** Seizure precipitants as reported in a Dutch cohort of DS children with pathogenic SCN1A-mutations ( $n = 71$ ), were compared with those of a childhood epilepsy cohort ( $n = 149$ ) and a community-based epilepsy cohort ( $n = 248$ ); all three Dutch cohorts used the same type of questionnaire. Seizure precipitants were categorized as 'fever', 'visual stimuli', 'sleep deprivation', 'stress, including physical exercise', 'auditory stimuli' and 'other'.

**Results:** For 70 of 71 (99%) DS children at least one seizure precipitant was recalled by parents. Seizure precipitants that were reported in more than half of the DS cohort were: fever (97%), a cold (68%), a bath (61%), acute stress (58%) and physical exercise (56%). Seizure precipitants freely recalled by parents were often related to ambient warmth or cold-warmth shifts (41%) and to various visual stimuli (18%). DS children had more positive seizure precipitant categories (median 4) compared to the childhood (median 2) and community-based epilepsy cohort (median 0) ( $p < 0.001$ ) and showed the highest percentage in each category (all  $p < 0.001$ ). Within the category 'stress, including physical exercise', physical exercise was more often reported to provoke a seizure in stress-sensitive children within the DS than in the childhood epilepsy cohort (78% vs. 35%,  $p < 0.001$ ). Within the childhood epilepsy cohort physical exercise was more often reported in fever-sensitive than in other children (25% vs. 12%,  $p = 0.042$ ).

**Conclusion:** Our study shows a high prevalence of a range of seizure precipitants in DS, compared to patients with other epilepsies. Our results underscore elevated body temperature as an important seizure precipitant, whether caused by fever, warm bath, ambient warmth or physical exercise. Knowledge of these seizure precipitants may improve preventive strategies in the otherwise difficult treatment of DS.

#### p0388

##### STRETCH SYNCOPE: A RARE CASE MIMICKING SEIZURE

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**Introduction:** Syncope is characterized by a temporary loss of consciousness and postural tone secondary to a lack of adequate cerebral blood perfusion. The peak incidence is around the age of 15 years, more frequent in girls than boys. The most common cause of syncope in young subjects is a reflex syncopal event and in particular a vasovagal faint. Prolonged standing especially in combination with warm temperature, crowded or confined environments, standing quickly, pain, emotional circumstances, early after intense exercise, lack of sleep, menstruation, fatigue, illness with fever, micturition, hyperventilation, stretching, coughing and rapid weight loss may be trigger a reflex syncope. We report this rarely seen 7 years old stretch syncope who was admitted with complaint with seizure.

**Case:** A 7 years girl admitted to emergency department with complaint fainting while her mother browsing her hair. There was no history with syncope or seizure. Her physical and neurological examination was normal. After a detailed history was learned that fainting was occurred after hyperextension of the neck while browsing. Routine laboratory tests, electroencephalogram and cardiac evaluation were normal and she was diagnosed as stretch syncope.

**Conclusion:** Stretch syncope is a rare condition associated with decreased systemic blood pressure and decreased cerebral blood flow due to mechanical compression of the vertebral arteries. Mechanical compression may occur during stretching the neck hyperextended while standing or browsing hair. Seizure, syncope and psychogenic fainting may be considered when a patient presented with loss of consciousness.

#### p0389

##### EPILEPSY IN ANGELMAN AND PRADER-WILLY SYNDROMES

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**Purpose:** To examine the age of epilepsy onset, seizures characteristics and the effectiveness of antiepileptic therapy of epilepsy in children with Angelman (AS) and Prader-Willy syndromes (PWS).

**Method:** At the period of 2005–2014 were studied 7 children with genetically identified AS and 14 children with PWS. For all the children were provided dynamic video-EEG monitoring.

**Results:** AS manifested with epilepsy in all cases. Only one girl has a 1 type of seizures, in 1 case - 2, in 3 cases - 3 and one - 4 types. The most frequent seizure types were: atypical absences - 4 (57.1%), myoclonic - 3 (42.9%), GTCS - 3 (42.9%), tonic versive - 3 (42.9%), rarely - serial infantile spasms, axorhizomelic tonic, myoclonic-astatic, atonic-astatic, pharyngo-oral and hemiconvulsive types - in one case each (14.3%). Clinical remission was achieved in 3 children (42.9%) and 4 children (57.1%) showed significant decrease of seizures with persistence of high index epileptiform discharges. The most effective drugs were valproates with ethosuximide. In PWS the most frequent seizure types were: tonic spasms - 3 (50%), myoclonic - 2 (33.3%), autonomic (33.3%), rarely - atypical absences, GTCS, focal versive and atypical febrile - in one case each (16.7%). Electro-clinical remission was achieved in 3 children (50%) and 3 children (50%) showed a significant decrease of seizures

and index of epileptiform discharges on the EEG. The most effective drugs were valproates in monotherapy and in combinations with topiramate, carbamazepine and ethosuximide.

**Conclusion:** Epilepsy is an obligate symptom of AS and characterized by early onset and polymorphic seizure types. In PWS 42.9% patients suffered from epilepsy. In AS positive prognosis for epileptic seizures is combined with a poor prognosis for the persistence of epileptiform discharges on EEG, severe cognitive deficits and manifestations of atypical autism. Children with PWS had better prognosis for clinical and EEG signs of epilepsy.

## Psychiatry 1 Sunday, 6th September 2015

p0390

### FORCED NORMALIZATION FOLLOWING USE OF LACOSAMIDE

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**Purpose:** In this report we present a case of forced normalization and review its clinical characteristics and the potential pathogenic mechanisms. Forced normalization is a phenomenon that has been reported secondary to several anti-epileptic drugs use. In this report we describe its occurrence after use of lacosamide in a 21 years old man with refractory complex partial seizures and known bitemporal epileptogenic zones. The patient had failed numerous anti-epileptic drug trials, had some improvement following VNS implantation but kept on having disabling seizures and multiple hospital admissions per year for status epilepticus. Following introduction of lacosamide, seizures resolved but he had psychotic symptoms associated with this remission and disappearance of the epileptiform activity or subclinical seizures on video-EEG monitoring.

p0391

### PSYCHIATRIC FEATURES OF EPILEPSY IN ACCRA, GHANA

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**Purpose:** Epilepsy has for many years been considered a psychiatric disorder. In recent times, the physical basis of epilepsy has been emphasised and the psychiatric feature regarded more as comorbidity. To what extent this is true is arguable but this may underlie the reason for considering epilepsy as a psychiatric disorder in most low and middle income countries. In Ghana, epilepsy remains a strong preserve of psychiatry and the prevalence of typical psychiatry presentations in epilepsy has not been studied. The management of the psychiatric symptoms in epilepsy forms a very significant part for the control of seizures in epilepsy. In this study we evaluated the prevalence and patterns of affective and anxiety disorders in patients with epilepsy in Accra Ghana.

**Method:** Over 500 patients with chronic epilepsy were identified from the only dedicated epilepsy clinic at the Korle Bu Teaching hospital, Accra Ghana. All patients who consented and agreed to be a part of the study were evaluated using the 53 item Brief Symptom Inventory.

**Preliminary results:** Suggests a high incidence of depression and other affective disorders with a high incidence in the older age group and the patients with lower socioeconomic background.

p0392

### PSYCHIATRIC EVALUATION OF EPILEPSY PATIENTS WITH PERI-ICTAL WATER DRINKING

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**Purpose:** Peri-ictal water drinking (PIWD) is a rare vegetative symptom which has been reported in temporal lobe epilepsy (TLE). Underlying reasons and related psychological factors of this behavior are not appropriately known. Our aim was to investigate the psychiatric comorbidities of the patients who report PIWD in their seizures.

**Method:** Patients reporting "water drinking" behavior, without asking, more than two times in their visits, as a consistent peri-ictal phenomenon were included and systematically questioned for the characteristics of PIWD. The demographic and clinical information consisting of age, sex, age at onset of epilepsy, seizure types and semiological findings of their seizures, syndromic diagnoses, EEG findings, MRI findings, and neuropsychological evaluations were recorded from patients' medical files. Epileptic patients having same epileptic syndromes without PIWD (Group II) and age and sex matched normal subjects (Group III) were included the study as two control groups for psychiatric evaluations.

**Results:** Yale Brown Obsessive Symptoms, Dissociative Experiences Scale, Hamilton Anxiety Rating Scale and Depression Rating Scale scores were significantly high in the main study group (Group I) compared to normal controls (Group III) but these scores were not different compared to Group II. Although there was not any difference between the Group I and Group II according to comorbid psychiatric diagnoses, compulsive symptom category of "washing" was detected significantly more frequent in the group with PIWD (p:0.007).

**Conclusion:** Although the presence of PIWD does not seem to have a specific association with substantial psychiatric comorbidity in patients with TLE, our study is providing preliminary evidence for the first time, the presence of PIWD might be associated with only a specific type of compulsions, namely washing compulsions.

p0393

### FREQUENCY OF SEIZURE DISORDER IN PATIENTS UNDERGOING ALCOHOL DETOXIFICATION WITH FRONT-LOADING DIAZEPAM - FINDINGS OF AN AUDIT

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**Purpose:** The abrupt cessation of heavy alcohol consumption results in alcohol withdrawal symptoms and seizures are a recognized complication. A fixed dose treatment with long acting Benzodiazepines is

routinely offered to individuals presenting in a state of alcohol withdrawal. An alternate is to offer front-loading dose of Diazepam. The purpose of this audit is to establish seizure related safety of the alternate treatment regime.

**Method:** Patients who attended Emergency Department with alcohol withdrawal symptoms were assessed for suitability of front-loading regime. Any serious underlying physical illness like head trauma, sepsis were ruled out. A front-loading regime with diazepam 20 mg was initiated in eligible patients and their symptoms were recorded periodically. The patients then received additional 20 mg of Diazepam two hourly if indicated until a light sedation was achieved. A three days treatment plan was carried out followed by transfer to community based services.

**Results:** Out of the 79 patients, majority (75.9%) were men. Average reported weekly consumption of alcohol was 37.5 units. Physical comorbidities were common (74.6%). A witnessed seizure was recorded in 30.3% while 11.3% were found collapsed with a suspected seizure. Only 1 patient undergoing front loading regime sustained a seizure and required transfer to medical unit. 9 patients discharged themselves against medical advice while the remaining completed treatment and were successfully discharged.

**Conclusion:** Some previous studies have highlighted the benefit of front-loading regime against conventional fixed dose titration but report a higher incidence of seizures during front loading regime. This audit establishes the benefit of front-loading regime and highlights its safety. No serious or life threatening complications were reported. The length of stay in hospital was significantly reduced. The overall dose of Benzodiazepine used was significantly lower than that used in fixed dose regime.

p0394

#### MONITORING INTERACTION BETWEEN ANTI-EPILEPTIC AND PSYCHOTROPIC DRUGS IN PEOPLE WITH INTELLECTUAL DISABILITIES

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**Purpose:** The prevalence of epilepsy in people with Intellectual Disabilities (ID) is significantly higher than that in general population and varies in direct proportion to severity of ID. According to an estimate, the prevalence of epilepsy in people with moderate ID ranges between 1 in 4 and 1 in 5 such patients. The cumulative risk for developing epilepsy is estimated as high as 38% at the age of 22 years. People with ID and epilepsy very commonly present to psychiatric clinics with challenging behaviour or co-morbid psychopathology. It is common practice for them to receive treatment through psychotropic drugs. Most psychotropic drugs interact with Anti Epileptic Drugs (AEDs) and some even potentiate the effect. The purpose of current audit is to monitor how these interactions are recorded in psychiatric clinics and whether introduction of a simplified drug interaction algorithm improves the overall quality of care.

**Method:** We propose to review medical records of all people with ID and Epilepsy attending community psychiatric clinic who receive treatment with AEDs and psychotropic drugs. We aim to monitor if interactions are recorded, explained and communicated before and then after introduction of drug interaction algorithm. We also aim to assess if and what impact the intervention has on overall delivery of care.

**Results:** The project is at data collection stage and we aim to complete it by June 2015.

**Conclusion:** The provision of a simplified algorithm will improve the overall quality of care and influence the outcomes positively like fewer attendances to emergency department or improved compliance with medication.

p0395

#### PSYCHIATRIC ASPECTS IN FAMILIES WITH AUTOSOMAL DOMINANT CORTICAL TREMOR, MYOCLONUS AND EPILEPSY

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**Purpose:** To assess the psychiatric comorbidity in Autosomal Dominant Cortical Myoclonus and Epilepsy (ADCME) patients by using reliable and valid psychodiagnostic scales.

**Method:** Patients with a clinical and electrophysiologic diagnosis of ADCME from two Italian centers. Two control groups: healthy subjects and patients with Juvenile Myoclonic Epilepsy (JME). A myoclonus score was assigned to each ADCME patient by using the Unified Myoclonus Rating Scale. Psychiatric evaluation battery included: BDI (Beck Depression Inventory), STAI-Y (State-Trait Anxiety Inventory Y: 1 and 2) MMPI-2 (Minnesota Multiphasic Personality Inventory-2) and QoLIE-31 (Quality-of-Life in Epilepsy Inventory). Kruskal-Wallis rank test, Wilcoxon rank-sum test or one-way analysis of variance (ANOVA), according to the normality of the distribution, and Pearson  $\chi^2$  test, were used. Spearman correlation analysis was used to identify relationships between the neuropsychological scores and the myoclonus score, after Bonferroni correction for age.

**Results:** The STAI-S score was higher in ADCME than JME patients and controls ( $p = 0.035$ ,  $p = 0.019$ ) The STAI-T score in ADCME group was not different from JME ( $p = 0.087$ ), but higher than healthy controls ( $p = 0.017$ ). The BDI score was increased in ADCME patients compared with JME patients and controls ( $p = 0.040$  and  $p = 0.017$ ). The overall QoLIE-31 score was lower in ADCME than JME ( $p = 0.006$ ), but there was no difference in the single subscales score. A higher prevalence of elevated score in at least one MMPI-2 subscale was found in the ADCME group ( $p = 0.012$ ). ADCME patients showed a higher prevalence of elevated scores in hypochondriasis, depression and schizophrenia subscales, than JME and healthy controls.

**Conclusion:** This study firstly reports a high prevalence of mood disorders, particularly depression and anxiety, in ADCME patients, often associated to pathological traits of personality. A statistically significant correlation is present between anxiety and myoclonus severity. Moreover these patients show a worse quality of life compared to other patients presenting only with seizures.

p0397

#### SYMPTOMS OF ANXIETY IN PERSONS WITH EPILEPSY

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**Purpose:** Though anxiety is common in persons with epilepsy, it often understudied relative to other psychiatric comorbidities. The current study aims to estimate the prevalence of anxiety, examine associations and correlates, and characterize common symptoms of anxiety in persons with epilepsy.

**Method:** Consecutive persons with epilepsy (n = 225) from the epilepsy program clinic in a city of 1.2 million people completed questionnaires, including the Hospital Anxiety and Depression Scale (HADS) to assess anxiety symptoms, and the Short Form 12 (SF-12) to measure physical and mental quality of life.

**Results:** According to the HADS, the prevalence of anxiety was 26.7% (95% Confidence Interval (CI): 20.8–32.5), and depression was 15.5% (95% CI: 10.7–20.2). The most common symptoms of anxiety were worrying thoughts (33.8%; 95% CI: 27.9–40.2), the feeling that something awful will happen (27.9%; 95% CI: 22.5–34.2), and feeling tense or wound up (27.4%; 95% CI: 22.0–33.6). Anxiety was significantly correlated with physical ( $r = -0.18$ ;  $p = 0.02$ ) and mental quality of life ( $r = -0.54$ ;  $p < 0.0001$ ). Persons were more likely to have anxiety if they: were smokers (Odds Ratio (OR): 2.37; 95% CI: 1.20–4.69), reported antiseizure medication side-effects (OR: 2.01; 95% CI: 1.10–3.69), reported more severe epilepsy (OR: 3.17; 95% CI: 1.61–6.24), and very disabling seizures (OR: 2.07; 95% CI: 1.08–3.98).

**Conclusion:** In our sample of persons with epilepsy, anxiety was more common than depression. Some symptoms of anxiety are more often reported than others in epilepsy. By identifying factors associated with anxiety in epilepsy, interventions to improve disease management and quality of life can be appropriately targeted.

p0398

#### PATIENTS WITH EPILEPSY AND PSYCHOGENIC NON-EPILEPTIC SEIZURES

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**Purpose:** Psychogenic non-epileptic seizures (PNES) can be defined as paroxysmal involuntary behavioural patterns that mimic epileptic events without organic cause. The incidence of PNES is between 2–33/100.000 in general population. The purpose of our study is to evaluate patients with PNES and epilepsy associated with PNES.

**Method:** We evaluated data of 2086 patients retrospectively. PNES was diagnosed with video - EEG monitorization and/or observation of PNES.

**Results:** Fifty patients had PNES and 37 patients had epilepsy associated with PNES. 66 patients are women (75.9%) 21 are men (24.1%). The diagnoses had been made with video - EEG monitorization in 24 patients (27.6%) and with observation in 63 patients (72.4%). Half of the patients (50%) who had PNES had been on AEDs and 48 (96%) of them were on psychiatric treatment but 34 patients came to follow up visit and just 5 of them had benefits from psychiatric support. Five patients had an epileptic family member. The mean diagnose duration was  $5.9 \pm 6.5$  years. Thirty two epileptic patients associated with PNES and 86.5% of them took psychiatric treatment and 29 patients came to follow up visits and 4 of them had benefits from psychiatric support.

**Conclusion:** The prognosis of PNES in adults is not favorable. The rate of false diagnosis in PNES is very high and the diagnose duration calculates with years. Also PNES and epileptic seizures can be together in a same patient. Multi discipliner treatment strategy needs to treat PNES and epilepsy associated with PNES. In our study the response to psychiatric treatment is low this result consistent with literature.

## Social Issues 1 Sunday, 6th September 2015

p0399

#### INFORMATION SEEKING BEHAVIOR FOR EPILEPSY: AN INFODEMOLOGICAL STUDY OF WIKIPEDIA ARTICLE SEARCHES

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**Purpose:** Millions of people worldwide use the Internet daily as a source of health information. Wikipedia is a popular free online encyclopedia used by patients and physicians to search for health-related information. Our aim was to evaluate information seeking behavior of English-speaking Internet users searching Wikipedia for articles related to epilepsy and epileptic seizures.

**Method:** Using Wiki Trends, which provides quantitative information on daily article views; data on global search queries for Wikipedia articles related to epilepsy and seizure were analyzed. The daily Wikipedia article views on syncope, psychogenic non-epileptic seizures, migraine, and multiple sclerosis served as comparative data. The period of analysis covered from January 2008 to December 2014.

**Results:** Overall, the Wikipedia article “epilepsy and driving” was found to be more frequently searched than that on “epilepsy and employment” and “epilepsy in children”. Since January 2008, Wikipedia article “multiple sclerosis” was more often searched than that on “epilepsy”, “syncope”, “psychogenic non-epileptic seizures” and “migraine”. The article “epilepsy” ranked 3,779 and was less searched than that on “multiple sclerosis” (rank 571) in traffic on Wikipedia. The highest peak in search volume for the article “epilepsy” corresponded to news of a celebrity having seizures.

**Conclusion:** Fears and worries about epileptic seizures, their impact on driving and employment, and news about celebrities with epilepsy might be major determinants in searching Wikipedia for information.

p0400

#### SOCIAL AND FAMILIAL PROBLEMS BETWEEN PATIENTS AND THEIR FAMILIES REFER TO EPILEPSY ASSOCIATION, TEHRAN, IRAN

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**Purpose:** High rate of epilepsy in the society and negligence of social-familial problems is one of factors in reduction of life quality of the epilepsy patients, which deprives the patients from a normal life. This study is an attempt to determine social and familial problems of the patients from the patients and their families' viewpoint.

**Method:** The present study was conducted as a descriptive study on 120 patients and 120 of their family members. Sampling method was convenience sampling and two researcher designed questionnaires were used for data gathering. The patients' questionnaire included

three sections of demographic information, disease information, and social/familial information. The families' questionnaire was comprised of two sections of demographic information and social/familial problems from the families' viewpoint. Based on literature review results and using Peirce and Harris questionnaires, the measure of family solidarity and compatibility was built. Validity of data gathering tools was ascertained using face and content validity and for reliability, internal consistency method with correlation coefficient of 83% was used.

**Results:** The results showed that social problems from the patients' viewpoint were severe and moderate in 65.52% and 34.48% of the cases respectively and from the families' viewpoint were 88.24% moderate, 9.5% no problem, and 1.96% severe. Familial problems from the patients' viewpoint were moderate and severe in 56.32% and 37.93% of the cases respectively. From the families' viewpoint, familial problems were 74.76% moderate and 25.24% no problem.

**Conclusion:** The differences between viewpoints of families and the patients regarding social and familial problems showed lack of enough information among the family members regarding the patients. The results herald the necessity to implement training courses to increase mutual understanding between the family members and the patients; while there is a need to pay more attention to the problems of social and familial nature.

#### p0401

##### TYPE OF SEIZURE INFLUENCE DEPRESSION AMONG AN EPILEPSY PATIENT

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**Purpose:** Depression is a common mental disorder in epilepsy patient but often undertreated or even underdiagnosed. This study is an attempt to estimate the prevalence of depression among patients with epilepsy.

**Methods:** A cross sectional study was conducted to 30 epilepsy outpatients in neurology clinic Sarjito Hospital. Epilepsy patients with intracranial lesion and comorbid of psychotic and schizophrenia were excluded. Neurological Depression Disorder in Epilepsy (NDDIE) was performed to all patients to assess depression, NDDIE score above 16 is confirmed diagnosis of depression.

**Result:** The subject of study were 30 patients with epilepsy, 14 are female (46.67%) and 16 are male (53.33%). Subject  $\leq 21$  years were 5 patients (16.6%) and  $\geq 21$  years are 25 patients (83.33%). Of 30 patients with epilepsy, 56.67% patients were having depression according to their NDDIE score. general tonic clonic seizure occurred in 11 patients (36.6%) and 6 of them (54.4%) experience symptoms of depression. While subject with partial simple seizure are 8 patients (26.6%) and only 1 of them (12.5%). Four patients (57.1%) of 7 who experienced absence seizure, and 1 of 4 (25%) patients with partial complex seizure were having depression at the time of the interview. Chi square test showed that general tonic clonic seizure has greatest prevalence ratio (8.45) but it's not statistically significant ( $p = 0.061$ ). We also evaluate the use of single and multiantiepileptic drugs among the patients, but no significant correlation between antiepileptic drugs and depression.

**Conclusion:** Depression was found to be highly prevalent psychiatric co-morbidity among the patients with epilepsy. The study demonstrated a relationship between partial simple seizure and depression among epilepsy patient. The study emphasized need for proper psychiatric evaluation for overall management of patients with epilepsy.

#### p0402

##### EPILEPSY KNOWLEDGE IS THE KEY TOWARDS SOCIAL ACCEPTANCE AMONG UNIVERSITY STUDENTS IN JAPAN

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**Purpose:** Stigma and discrimination associated with epilepsy have been persistent worldwide. In Japan, many children with epilepsy experience interpersonal issues (i.e., bullying, isolation), while adults with epilepsy often face reduced employment and social opportunities. Much of these is caused by the society's long-standing myths and misunderstanding about epilepsy. This study investigated the knowledge and attitudes towards people with epilepsy among university students in Japan.

**Method:** A modified version of a pre-tested questionnaire was used to make inferences regarding the participants' experience and knowledge about epilepsy. A semantic differential (SD) rating scale was used to derive attitudes towards epilepsy. Two hundred seventy-one university students were recruited from 9 academic departments at a Tohoku regional university. Data were analyzed statistically.

**Results:** Among 271 participants, 8% personally knew someone with epilepsy, and 16% had witnessed an epileptic seizure. 51% perceived themselves as having some knowledge about epilepsy. While only 10% objected to females with epilepsy getting married in general, 36% objected to their own children marrying to one ( $\chi^2 = 116.32$ ,  $df = 3$ ,  $p < 0.001$ ). Exploratory factor analysis and cluster analysis yielded 3 attitude groups towards epilepsy:

- empathy group,
- negative feeling group, and
- indifferent group. Furthermore, analysis of variance (ANOVA) revealed the empathy group showed significantly higher knowledge about epilepsy than the other two groups ( $F(2,268) = 9.66$ ,  $p < 0.001$ ).

On the contrary, no significant group difference was observed based on personal interaction with individuals with epilepsy.

**Conclusion:** The present findings demonstrated that epilepsy knowledge may be associated with empathetic attitudes towards people with epilepsy. This provides a strong future implication for public education and outreach activities towards gaining social acceptance of epilepsy in Japan.

#### p0403

##### KNOWLEDGE, ATTITUDES AND PRACTICES REGARDING EPILEPSY AMONG CHRISTIANS CLERICS COMPARED TO THEIR CONGREGATION IN SOUTH WESTERN NIGERIA

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**Purpose:** Epilepsy is a common chronic brain disorder, in Sub-Saharan Africa. The traditional and religious beliefs concerning epilepsy contribute to the stigma, exclusion of Persons with Epilepsy (PWE) and late presentation to hospital.

**Method:** The study is a cross-sectional study carried out from June to August 2012 among urban and rural churches. A structured questionnaire was used to obtain information on the socio-demographic profile, knowledge and attitudes of the participants regarding epilepsy.

**Results:** One hundred and fifty congregation members (male: female ratio 2:1) and 12 clerics (all male) responded to the questionnaires (re-

sponse rate of 83.3%), mean age was  $37 \pm 1$ . Majority of the clerics (58%) believed that epilepsy was due to possession by a spirit compared to 22% of the congregation. A quarter of both groups believed that epilepsy was contagious. The knowledge of the features of generalized seizures was similar for both groups, while none of the clerics were aware of staring as a feature of epilepsy. Although two thirds of both clerics and congregation recommend medical consultation, half of the clerics and 95% of the congregation would recommend a healing or deliverance session. Members of the congregation were more tolerant toward epilepsy compared to the clerics.

**Conclusion:** Clerics do not have adequate knowledge of epilepsy and were less tolerant towards PWE compared to their congregation. Both clerics and congregation recommend church/spiritual/divine healing and/or deliverance session in addition to medical consultation. Epilepsy awareness educational programmes are needed in churches in South Western Nigeria to improve the knowledge of epilepsy among clerics which would improve the quality of advice they give their congregation.

#### p0404

##### FIGHTING STIGMA OF EPILEPSY THROUGH MUSIC

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**Purpose:** Epilepsy is a common neurological condition frequently associated with psychosocial difficulties. Prejudice and discrimination (stigma) are often worse than the seizures themselves in terms of impact on daily life of people with epilepsy (PWE). We produced a song and a movie clip regarding epilepsy and evaluated the impact of this song in general population.

**Method:** A song and a related brief movie clip with 4 minutes duration were developed addressing the most common stigma issues on epilepsy and attitudes and perceptions towards someone having a seizure. Before and after listening to the song and watching to the movie healthy individuals were evaluated using the Stigma Scale of Epilepsy (SSE), which is a previously validated instrument in Brazil that allows quantification of stigma in epilepsy expressed as a scale. Also, individuals answered to a semi-structured interview addressing their knowledge about epilepsy.

**Results:** There were 128 interviewed individuals, who scored (mean  $\pm$  standard deviation)  $38.15 \pm 14.08$  (minimum and maximum = 13–76) before and after  $24.20 \pm 14.74$  (1–71) listening to the music ( $p < 0.0001$ ). Their age was an average of  $25.98 \pm 10.04$  (11–62), 71% were female and 83% have completed high-school. Among diverse questions addressing their knowledge about correct attitudes and perceptions towards someone having a seizure, we highlight that 43 individuals answered they would hold the tongue of a person having a seizure before listening to the music, while 13 answered the same after listening to the song ( $p < 0.0001$ ).

**Conclusion:** There is an urgent need to improve the level of education in relation to epilepsy and knowledge, attitudes and perception about epilepsy can be easily improved through simple actions such as listening to a brief song.

#### p0405

##### PARENTING STRESS IN PEDIATRIC EPILEPSY: A CASE-BASED TIME-SERIES STUDY OF THE EFFECTS OF THE RELAXED PARENTING PROGRAM

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**Purpose:** To evaluate a newly developed parenting stress reduction program for parents of children with epilepsy (Relaxed Parenting Program; RPP) on parenting stress, parenting behavior, and child behavior by means of a Single Case Experimental Design (SCED). Aim of the study is to examine whether the treatment generates daily improvement in maternal and child outcome and how this improvement unfolds over time: the process of change.

**Methods and results:** This study is part of a greater study into the effects of RPP. For the purpose of this study online daily diaries and pre- and posttreatment questionnaires of  $N = 9$  mothers will be examined. Daily improvement: effect sizes for treatment effects will be calculated with simulation modeling analysis (SMA). The daily process of change: this will be examined with SMA via cross-correlational analysis. Pre- and posttreatment questionnaires will be evaluated with the Reliable Change Index (RCI).

**Conclusion and discussion:** RPP will be discussed as a possibly efficacious treatment with regard to parenting stress, parenting, and the reduction of child behavioral problems. If former inadequate parenting strategies will successfully be changed, with positive consequences child behavior, RPP may be a promising treatment for parents of children with epilepsy.

#### p0406

##### RESTRICTIONS IMPOSED ON CHILDREN WITH EPILEPSY AND ITS ASSOCIATION WITH CHARACTERISTICS OF EPILEPSY IN THE AGE GROUP OF 6 TO 12 YEARS

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**Purpose:** Epilepsy is the most common neurological disease in children and adolescents. The fear of injury and impact on social stigma results in parental restrictions on many of the activities children love to do.

This descriptive cross sectional study was performed to evaluate the restrictions imposed on children with epilepsy, and the association of these restrictions with epilepsy characteristics such as seizure type, frequency, seizures with loss of consciousness, age at first seizure, history of status epilepticus and family history of epilepsy.

**Method:** Children aged 6–12 years with epilepsy for at least 6 months, were identified from a tertiary care neurology clinic at the premier children's hospital in the country, with bed strength of 900. Children with problems in ambulation, permanent disability, impairment/loss of vision and hearing were excluded. Interviewer administered questionnaire modified from **Hague Restrictions in Childhood Epilepsy Scale (HARCES)** was used to collect data on activity restrictions. Seven important determinants of daily childhood activities were tested.

**Results:** Primary care givers of 150 children (mean age of 8.54 years) were interviewed. Participation in indoor (94.6%) and outdoor sports (85.9%) was allowed by parents adequately. General daily play outside the house (97.3%) and pursuing hobbies (100%) were also allowed frequently. A large majority of children (77.9%) were not allowed to swim. This was significantly association with occurrence of seizures with loss of consciousness ( $p = 0.01$ ) and poor seizure control ( $p = 0.04$ ). More than one third (37.6%), were not allowed to go on trips, but no significantly associated cause was identified.

**Conclusion:** Significant restriction was imposed on swimming and going on trips among Sri Lankan children with epilepsy. Awareness on appropriateness of these activity restrictions needs to be improved among primary care-givers.

p0407

**PERCEIVED STIGMA AND ITS ASSOCIATES IN ADULT EPILEPSY PATIENTS FROM ISTANBUL***K. Yeni\**, *Z. Tulek\**, *N. Bebek†**\*Istanbul University, Florence Nightingale School of Nursing, Istanbul, Turkey, †Istanbul University Istanbul Faculty of Medicine, Department of Neurology, Istanbul, Turkey***Purpose:** Epilepsy is one of the most stigmatizing medical conditions. The purpose of this study was to examine the perception of stigma and factors associated with stigma.**Method:** This descriptive cross-sectional study has been carried out among patients attending to an epilepsy outpatient clinic of a university hospital between February-October 2014. One hundred-ninety-four patients with age above 18, able to communicate and having diagnosis of definite epilepsy constituted the study sample. Patients seizure-free for 2 years were excluded from the group. Three-item Jacoby's Stigma Scale was used to determine level of stigma and also Social Support Scale, Generalized Self-efficacy Scale, Epilepsy Knowledge and Attitude Scales were used to examine factors associated with stigma.**Results:** In total, 66 out of 194 subjects (34%) reported feeling stigmatized, with almost half of them (n = 31) feeling highly stigmatized. Education, income, age of onset, seizure frequency in previous year, social support and knowledge and attitudes toward epilepsy were significant factors determining scores on stigma scale. It was also determined that stigma was associated with injuries, seeking help from mystics, disclosure of the diagnosis, impact of epilepsy on private life and self-efficacy.**Conclusion:** This study confirms the findings of previous studies that have identified the importance of both clinical and nonclinical factors in understanding the stigma of epilepsy. Findings support the need for social support, knowledge and awareness to decrease the stigma associated with epilepsy.**Status Epilepticus 1  
Sunday, 6th September 2015**

p0408

**EFFICACY OF CARBAMAZEPINE IN TEMPORAL COMPLEX PARTIAL STATUS EPILEPTICUS***W. Abdellaoui, S. Bahbouh, R. Benalia, M.R. Belabed, E. Attal, M. Ait-Kaci-Ahmed**Ait Idir Hospital, EEG Laboratory, Department of Neurology, Algiers, Algeria***Purpose:** Temporal complex partial status epilepticus TCPSE is a condition usually manifest as variable periods of confusion with a prolonged epileptic episode in which fluctuating or frequently recurring focal electrographic epileptic discharges, arising in temporal regions. In our case report on two patients with TCPSE we study the response to carbamazepine after failure of first and second line therapy.**Method:** Clinical case report.**Results:** A 39-year old women had a history of cryptogenic epilepsy, was treated since the age of 20 years with phenobarbital PB 100 mg/day. She was admitted for prolonged disturbed consciousness over 3 days, after abrupt withdrawal of PB. She had complex partial seizures characterized by motor automatisms, and appeared to be experiencing visual and auditory hallucinations. EEG showed continuous left temporal spike/wave and slow waves discharges. Normal brain MRI. A diagnosis of TCPSE was made. No response to intravenous Diazepam 0.15 mg/kg and PB 15 mg/kg after 4 days. Phenytoin PHT was not available in our hospital. Clinical improvement and ictal EEG pattern resolved after oral Car-

bamazepine CBZ treatment 600 mg/day (initial dose of 100 mg/day). Case 2: A 61-year old women with symptomatic complex partial seizure disorder, secondary to CNS lymphoma resected 18 years earlier. Was treated with Phenobarbital PB 100 mg/day and Carbamazepine CBZ 600 mg/day. Her established complex partial seizures were manifest by confusion with agitation and experiencing visual hallucinations, after abrupt withdrawal of CBZ. EEG revealed continuous temporal slow waves. CT scanning was unchanged from imaging studies 6 months earlier. No response to intravenous Diazepam 0.1 mg/kg and PB 15 mg/day after 3 days. Improvement in her clinical delirium and EEG pattern after oral CBZ treatment 600 mg/day (start dose of 100 mg/day).

**Conclusion:** Carbamazepine CBZ was effective and safe in controlling TCPSE in our patients. Oral administration of CBZ is an effective alternative.

p0409

**RISK FACTORS FOR STATUS EPILEPTICUS IN PAEDIATRIC PATIENTS***M.A. Ahmed, J.R. Pitts, Z. Aldahash, A. Haque**Queen's Hospital, Romford, Paediatrics, London, UK***Purpose:** The study aimed to identify risk factors for patients presenting with a single episode of status epilepticus (SE) in paediatric patients with an aim to identify methods that could reduce its occurrence.**Method:** Notes for children presenting with seizures between August 2009 and August 2014 were collected by audit department. Patients were excluded if they went on to have further SE episodes.

Case notes were manually reviewed and included in the study if there was evidence of prolonged seizure (&gt;20 minutes) or multiple seizures without a documented complete recovery back to baseline behaviour.

**Results:** Of the notes retrieved 36 (53% male, 47% female) met inclusion criteria. The mean age of cases was 4.8 years with the majority preschool children (53% under 3 years old). 11% had metabolic or neurodevelopmental syndromes 44% had no previous history of epilepsy (or had suffered from simple febrile convulsions only). 56% had a history of previous seizures (excluding febrile convulsions); 25% of these had poor control requiring increase in anti-epileptic treatment prior to the SE event. In 17% the SE event was associated with multiple seizures without documented full recovery in between seizures. These cases tended to be longer than SE with a single convulsive period and associated with significant delay in administration of rescue medication. Only 25% of cases was treatment beyond benzodiazepines required to terminate the SE event. Causes of SE event are febrile illness (44%) or non-febrile infection in child with epilepsy (8%), poor adherence (8%), suboptimal prophylactic treatment and delayed benzodiazepine treatment were also common.**Conclusion:** Excellent parental education is vital in particular in the following areas: need to always take rescue medication with them, ensuring understanding on indications for use; prompt treatment of fever with antipyretics in at risk children and seeking medical attention when suffering febrile illnesses.

p0410

**NONCONVULSIVE STATUS EPILEPTICUS: A 7 YEARS REVIEW***R. Almendra, V. Espírito Santo, A. Veiga, A. Matas, A.G. Velon, R. Chorão, P. Guimarães**Centro Hospitalar de Trás-os-Montes e Alto Douro, Vila Real, Portugal***Purpose:** Nonconvulsive status epilepticus (NCSE) is an under diagnosed condition. A high index of clinical suspicion is required to its

recognition and to perform an electroencephalographic study to establish a correct diagnosis.

**Method:** Retrospective study, from 2008 to 2014, of a group of patients categorized as a nonconvulsive status epilepticus electroclinical diagnosis. Medical records were reviewed to analyse age, history of epilepsy, aetiology, clinical presentation, neurophysiological findings, treatment and outcome.

**Results:** 33 patients were identified in a total of 34 episodes of NCSE, with a mean age of 72.7 years [45–94] and a slight predominance of females (53%,  $n = 18$ ). There was a previous history of epilepsy in 30% ( $n = 10$ ). The most frequent type of NCSE was the complex partial type (56%,  $n = 19$ ) and disturbance of language was the most common neurological sign. The electroencephalogram showed a predominant hemispheric epileptiform activity in 82% ( $n = 28$ ) of patients. The most frequent aetiology was structural vascular lesions (48%,  $n = 16$ ) followed by post-traumatic structural lesions (15%,  $n = 5$ ). Regarding the antiepileptic treatment, polytherapy was used in 76% ( $n = 26$ ) of patients and at least three antiepileptic drugs was the regimen of 44% ( $n = 15$ ). The hospital mortality rate was 35% ( $n = 12$ ).

**Conclusion:** This analysis highlights the advanced age of the population studied and concordant vascular aetiology. It is also important to emphasize the use of polytherapy in a high proportion of patients, and the high mortality. Despite the limitations of this retrospective study, the present data are in agreement with published literature.

#### p0411

### NEUROPROTECTIVE ROLE OF ARGAN OIL AGAINST THE DEVELOPMENT OF STATUS EPILEPTICUS IN LITHIUM-PILOCARPINE MODEL OF TEMPORAL LOBE EPILEPSY IN THE WISTAR RAT

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**Purpose:** Temporal lobe epilepsy (TLE) is the most common form of human epilepsy. Patients with TLE often have a clinical history including an initial precipitating injury, such as status epilepticus (SE). In this regard, neuroprotective treatments are considered a promising therapy for preventing and treating TLE. Thus, being well known for its physical and chemical composition, particularly vitamin E, and unsaturated essential fatty acids, we are interested in Argan oil pretreatment in order to examine the neuroprotective effects on the development and severity of SE in lithium-Pilocarpine (Li-PC) model of TLE.

**Method:** Wistar rats (21 days of age) were gavaged daily with Argan oil or with NaCl (1 ml/100 g) during 3 months. SE was induced in adult rats by lithium (3 mEq/kg) followed 18 h later by Pilocarpine (30 mg/kg), yet it is interrupted by diazepam in all rats. SE severity and Racine stages are assessed by video-recording.

**Results:** Pilocarpine injection induces a high mortality rate (40%) and high frequency of tonic-clonic seizures (stage 5 of Racine) in the control rats, while pretreatment rats with Argan oil significantly decreased the index. Indeed, 50% of rats pretreated with Argan oil have shown resistance to develop SE; whereas, all control rats have developed the affection.

**Conclusion:** The current study suggests that Argan oil pretreatment is capable of attenuating seizure severity of Li-PC induced SE. This indicates that Argan oil provides a neuroprotection against the TLE.

#### p0414

### A SERIES OF 30 PATIENTS WITH EPILEPSIA PARTIALIS CONTINUA

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**Purpose:** Epilepsia partialis continua (EPC) is a rare type of localization-related motor epilepsy. It is characterised by simple partial motor seizures, restricted to one part of the body with repetitive regular or irregular clonic jerks without loss of consciousness. In this study, we want to discuss etiology, clinical and electroencephalographic characteristics of EPC with our patients findings.

**Method:** Patients diagnosed as EPC were ascertained from medical records of the hospital for the period 2008–2015. Demographic datas, affected body parts from seizure, electroencephalographic (EEG) findings during seizure, pathology on cranial imaging were analyzed.

**Results:** We identified 30 patients (16 female, 14 male) with EPC. Their ages ranged between 16 to 82 years. Majority of them had the diagnosis of malignancy and epilepsy before. Facial and distal limb muscles were preferentially involved and with other parts, motor seizure on tongue ( $n = 5$ ), abdominal muscles ( $n = 3$ ) and scrotum ( $n = 1$ ) were also seen. Focal EEG abnormalities commonly consisted of discrete spikes, sharp waves or slow-wave activity but there was no ictal activity on EEG in 12 patients. Primary brain tumours and metastasis were main pathologic findings in our patients but ischemia, gliosis and encephalitis were also seen on neuroimaging.

**Conclusion:** Although rare, EPC can be seen with a varied causes, and structural brain abnormality most commonly seen. Generally, localization of ictal and interictal activity correlate with body parts where seizure seen. Sometimes there was no any activity on scalp EEG so clinician should be alert.

#### p0417

### RISK FACTORS FOR RECURRENT STATUS EPILEPTICUS

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**Purpose:** The aim of this study was to identify risk factors for multiple episodes of status epilepticus (SE) among children with either epilepsy, either pre or post-diagnosed.

**Method:** Patients attended the emergency department because of SE were identified by combining 'seizure', with 'Resus' between the dates of August 2010– August 2014. Case notes of all eligible patients were manually analysed. Data included patient's details, seizure semiology, epilepsy diagnosis, medications, and causes of SE, fever/infection, and characteristics of each episode of SE.

**Results:** 16 patients (9 males; average age = 6.1 years) had recurrent SE with an overall total of 69 episodes. 7 patients were of ethnic origin and 6 were known to social services. Of the 16 patients, 12 had febrile convulsion, 10 had positive FH of epilepsy, 15 had global developmental delay, 5 had cerebral palsy, 8 had visual difficulties, 2 had hearing impairment and 1 was within the autistic spectrum. Seizures were generalised ( $n = 4$ ), focal ( $n = 12$ ). Epilepsy diagnoses included symptomatic ( $n = 11$ ) and idiopathic ( $n = 5$ ). 15 patients were on prophylactic AEDs and 14 on rescue AED. Poor compliance was reported among 3 patients. Average age of 1<sup>st</sup> SE was 2.6 years and duration ranged from 30 minutes to 9 hrs. Causes of SE were identified in 65/69 episodes, including CNS infection (1.5%), metabolic disorders (5%), recent AED change/ withdrawal (29%) and febrile illnesses (46%).

**Conclusion:** The main risk factors that we have highlighted span from socioeconomic to therapeutic with specific eminence placed upon ethnicity, febrile illness, neurological abnormality, epilepsy diagnosis, early age of onset of both seizure and SE and poor seizure control and late initiation of AED treatment being related to higher rates of recurrent SE.

**p0418**

### STATNET EEG, A FAST AND RELIABLE OPTION TO DIAGNOSE NCSE IN EMERGENCY SETTING

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**Purpose:** The conventional method of EEG lead application could be time consuming and can only be performed by specially trained personnel that are not always available. The StatNet electrode set is a system that can be applied by non-EEG technologist after minimal training. The primary objectives of this study are to assess the quality of the recordings and the ability to detect abnormal findings. Secondary objectives are to compare the setup duration and time delay from EEG request to start of acquisition between the StatNet and conventional EEG (cEEG) test.

**Method:** Over 10 months, 19 patients with suspected NCSE were included from Saskatoon Royal University Hospital ED, ICU, and hospital wards. Each patient received a StatNet EEG by minimally trained epilepsy fellow and a cEEG by trained technologists. We compared the two studies, in a blinded fashion, for the time from EEG order to acquisition, the setup time, duration of artifact, and detection of abnormal findings. The nonparametric Mann-Whitney two-sample T-test was used for comparisons. The kappa score was used to assess congruence between readers.

**Results:** Mean age of patients was  $61 \pm 16(25-93)$  years (63% females). The inter-observer agreement for detection of abnormal findings was 0.83 for StatNet EEG and 0.75 for cEEG. NCSE was detected in 10% (2/19) in both studies. The delay from the time of EEG requisition to acquisition was significantly shorter in the StatNet ( $22.4 \pm 2.5$  minutes) than the cEEG ( $217.7 \pm 44.6$  minutes)  $p < 0.0001$ . The setup time was also significantly shorter in the StatNet ( $9.9 \pm 0.8$  minutes) compared to the cEEG ( $17.8 \pm 0.8$  minutes)  $p = 0.0001$ . Finally, there was no difference in the percentage of artifact duration between StatNet and cEEG (42% vs. 39%,  $p = 0.89$ ).

**Conclusion:** This study demonstrates that StatNet EEG is a practical and reliable tool, which reduces the delay of testing compared to cEEG, without significant compromise of study quality.

## Women's Issues 1 Sunday, 6th September 2015

**p0419**

### WOMEN WITH EPILEPSY IN MOHAMMED VI UNIVERSITY HOSPITAL OF MARRAKESH, MOROCCO

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**Purpose:** The incidence of epilepsy is the same in men and women, but social and medical issues seem to be different according to gender especially in developing countries. Few studies were conducted in Arab world to objective the impact of epilepsy on women. We aimed to describe social and medical aspects of a series of women with epilepsy (WWE).

**Method:** Descriptive study among WWE who consulted neurology outpatient of Marrakesh university hospital in Morocco among 1 year.

**Results:** Among 161 epileptic patients, 77 were female. Mean age of WWE was 36.29 years (ranging between 14 and 78 years). 36/77 patients were single whereas 28 were married with mean number of children of 4.22 (ranging between 1 and 10). 61.03% of patients were unemployed and 39.2% of them were illiterate. 10% of patients were born from consanguineous marriage, 15.7% had familial history of epilepsy and 11.4% febrile seizures. 54.5% had partial epilepsy with predominance of frontal and temporal lobe epilepsy. Majority of patients had monotherapy with problems of AED's compliance due to financial problems. 4 patients were pregnant under prohibited AEDs. Majority of patients had depression.

**Conclusion:** Although there was a great focus on women's issues in epilepsy in recent time, studies on WWE in Arab and African countries are still lacking. In this study, we objective social burden of epilepsy on women with Low household income, high unemployment rate, and low educational attainment. Serious Health problems in pregnancy and depressive comorbidity were seen in our patients.

**p0420**

### HORMONAL PATHOLOGY IN WOMEN OF CHILDBEARING AGE WITH JUVENILE MYOCLONIC EPILEPSY

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**Purpose:** To identify the nature of hormonal abnormalities in women of reproductive age with juvenile myoclonic epilepsy taking anti-epileptic drugs as mono and polytherapy for over a year and to assess the role of epilepsy and anti-epileptic drugs in the genesis of hormonal abnormalities.

**Method:** The study involved 48 women with juvenile myoclonic epilepsy aged 17–35 years and 15 women in the control group, identical in age and lack of gynecological pathology. Levels of gonadotropins and sex steroids were defined in the blood serum in the first phase of the cycle. Progesterone levels were determined in the second phase with a cycle of 28 days ( $n = 6$ ). During the study the patients received drugs of valproic acid 63%, levetiracetam -10.9%, Topamax-8.7%, lamotrigine-2.2%, and valproate combination with levetiracetam-8.7%, and lamotrigine -6, 5%.

**Results:** while evaluation of hormonal status in patients a significant increase in LH levels by 53.2% and testosterone by 61.25% was established compared with the control group. In general, patients had an increase tendency in LH levels with increasing duration of the disease, in absence of clinical remission by 29%, with irregular cycle by 29%. There was a tendency of increase in estradiol levels with increasing age of onset of the disease – by 18.2% and 38.8%, increase in testosterone levels by 54.3%, with irregular cycle, decrease in progesterone level by 4 times with irregular cycle, and by 67% at polytherapy. In general, the ovaries dysfunctions were found in 58.7% ( $n = 27$ ), most often when taking valproate -69%.

( $n = 20$ ).

**Conclusion:** endocrine profile in patients with juvenile myoclonic epilepsy statistically is significantly different from healthy women. It depends on the disease duration, onset of the disease. Influence of anti-epileptic drugs on the nature and abnormalities frequency was doubtful, but more often occurred while taking valproate.

p0421

### EPILEPSY OF PREGNANT WOMEN AS AN INDICATION FOR DELIVERY BY OBSTETRICAL SURGERY

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Despite the great progress in diagnosis and treatment of epilepsy, the questions about the way of delivery in pregnant women with epilepsy are still discountable.

**Purpose:** To determine the frequency and the main indications for Sectio Caesarea (SC) in pregnant women with epilepsy (PWWE).

**Method:** The survey is prospective and covers a period of 16 years (1997–2012), 283 PWWE are tracked over time during this period. 195 of them got delivery in Risk Pregnancy Clinic of the University Hospital-Pleven, 77 in other hospitals and for the rest 11 PWWE the pregnancy finished with abortion. In all the PWWE the etiology and the prescription of epilepsy, the type and frequency of the seizures were clinically determined. EEG records, ultrasound of fetus and cardiocograph monitoring were made.

**Results:** The frequency of SC for the whole group is 33.83%. Partus Normalis (PN) is assessed in 65.07% and vacuumextractio and forceps (VE/F) - in 1.10%. In PWWE who got delivery in Plevan the frequency of SC is 38.46%, PN - 60.00% and VE/F - 1.54%. In 76 cases with delivery by SC for 56 the indications were obstetrical and in 19 (25.33%) the major indication was epilepsy. It was the main indication for SC for pregnant women with frequent and pharmacoresistant epileptic seizures. The higher frequency of SC in PWWE who got delivery in the University Clinic is explained by the fact that the most complicated cases are concentrated there.

**Conclusion:** The good collaboration between the neurologist - epileptologist and the obstetrician, planning and supervising the delivery of PWWE, may contribute to the selection of the most appropriate way of delivery, leading to a favorable outcome for the mother and the newborn.

**Keywords:** Epilepsy, pregnancy, delivery, Sectio Caesarea, Partus Normalis

p0422

### HYPERTENSIVE DISORDERS IN PREGNANT WOMAN WITH EPILEPSY

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**Purpose:** To determine the frequency and the course of hypertensive disorders in pregnant women with epilepsy (PWWE).

**Method:** The survey is prospective and covers 206 PWWE during the period 1997–2012 year, monitored and treated in Risk Pregnancy Clinic of University Hospital - Plevan. All the patients (PWWE) are with clinically established etiology and prescription of epilepsy, type of seizures and their frequency. EEG records, ultrasound of fetus and cardiocograph monitoring were conducted. Eleven of PWWE were with Praeclampsia - Eclampsia (PE-Ecl).

**Results:** The frequency of PE-Ecl is 5.33%. Praeclampsia and Eclampsia were found (monitored) during two consecutive pregnancies in one of the PWWE. Six patients were with severe Praeclampsia and one of them was with data of HELLP syndrome. There were three cases with Eclampsia. Delivery by surgery was made in 8 cases, (7 patients, but for one of them twice). The other 4 pregnant women with moderate Praeclampsia got delivery per vias naturales. Epileptic seizures during pregnancy were

recorded for 5 of PWWE. One patient was with generalized clonic-tonic seizures and 4 other were with partial seizures. During the period 24 hours after delivery seizures were noted for 4 patients. Six PWWE were without therapy with antiepileptic drugs (AED). Three of them started monotherapy with AED during pregnancy. One other patient with pharmacoresistant symptomatic epilepsy (meningiomas of the brain with two neurosurgical operations) was on polytherapy with 3 AED during the whole pregnancy. The EEG study showed focal activity predominantly occipital, occipito-temporal and parieto-occipital.

**Conclusion:** The detection of arterial hypertension and proteinuria in PWWE should focus attention on PE-Ecl. The united active clinical monitoring and treatment by a neurologist-epileptologist and obstetrician is the most accurate clinical behavior.

**Keywords:** Epilepsy, pregnancy, preeclampsia-eclampsia, AED

p0423

### EPILEPSY AND REPRODUCTIVE HEALTH: AFRICAN COHORT

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**Purpose:** Epilepsy is a public health problem in Senegal and Africa because of its severity and its social importance. It occurs at any age sparing no sex. It can influence the sexual life and vice versa. The objective of this work is to study the effects of antiepileptic drugs on the sex lives of women with epilepsy, the influence of these drugs on pregnancy and when breastfeeding.

**Method:** This prospective study was conducted in the month of March in the month of August 2011 in the neurological clinic teaching hospital Fann Dakar Senegal and is directed only at women with epilepsy.

**Results:** We collected, 120 patients aged 16–64 years with a mean age of 30.58 years, 45% married, 44.16% were uneducated preponderant. All patients were taking antiepileptic drugs, 89.16% was alone. 55% of our patients had epilepsy for at least 6 years. 45.83% had generalized epilepsy, 44.17% of partial seizures. In our cohort, 64.16% were under phenobarbital, 69.16% had good adherence. As side effects of drugs 90% had sexual problems. 75% enjoyed an active sex life, was noted a decrease in the number of sex per week for the disease [31/55 = 56.66%]. In addition, 51.17% were using contraception, including 38.7% of oral kind. 64.86% had noticed an increase in seizure frequency during their pregnancies. Of the 74 women who had contracted a pregnancy, 41.89% had premature infants, 16.21% have made abortions. 61.17% had psychosocial life affected.

**Conclusion:** People with epilepsy often experience sexual problems that may be caused by epilepsy, antiepileptic and / or reactions of the partner and the other facing the diagnosis of epilepsy.

p0424

### EVALUATING HYPOTALAMO-HYPOPHYSEAL FUNCTION UNDER TREATMENT VALPROAT AND CARBAMAZEPINE THERAPY IN WOMEN EPILEPTIC PATIENTS

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**Purpose:** To determine the association of long-term valproate and carbamazepin therapy with reproductive endocrine disorders in women with generalized or partial epilepsy.

**Method:** Clinical parameters, ovarian morphology, and serum reproductive hormone concentrations were evaluated in 25 clinically normal and 52 reproductive age women with epilepsy who were newly initiated on valproate or carbamazepine therapy. Longitudinal evaluations were done in these women after 1 year of therapy.

**Results:** Of the 43 women who completed 1 year follow-up, we observed clinically relevant weight gain in 40%, hirsutism in 20%, menstrual abnormalities in 30%, polycystic ovaries (PCO) in 20%, polycystic ovarian syndrome (PCOS) in 20%, and a significant increase in mean serum testosterone ( $p = 0.046$ ). A significant positive correlation existed between weight gain and the development of menstrual abnormalities ( $r = 0.66$ ,  $p < 0.0001$ ), hirsutism ( $r = 0.53$ ,  $p = 0.006$ ) and PCO ( $r = 0.51$ ,  $p = 0.012$ ). Yearly follow-up for next 1 year in some of these women revealed persistence of menstrual abnormalities, hirsutism and PCO, a significant linear increase in mean body weight, body mass index, and serum testosterone concentrations, and an increase in serum LH levels. This study will complete after 5 patients utilized test of menstrual hormones and this results will be able to change at the end of study.

**Conclusion:** Long-term valproate and carbamazepine therapy in women with epilepsy is associated with development of hirsutism, significant weight gain, stable or progressive alterations in reproductive hormonal function, and ultimately a higher occurrence of PCOS. Researchers should collaborate to develop interventions treatments that incorporate reproductive considerations.

#### p0425

##### CATAMENIAL EPILEPSY

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**Purpose:** Catamenial epilepsy is characterized by an increase in seizures during particular phases of the menstrual cycle. Reproduction hormones decrease the seizure threshold in women with epilepsy. It was reported that seizures get worse with puberty and menarche in about 1/3 of women with epilepsy.

**Method:** In this study; 1140 patients who were followed in Epilepsy Department of Antalya Training and Research Hospital were examined retrospectively. Increases which epileptic female patients aged between 15–45 in fertility period experienced in menstrual period, in seizure frequency were examined.

**Results:** Total 368 female patients were in reproductive age. Information of 1 patient was not obtained. 74 (20.1%) of these patients were catamenial epilepsy patients. Age average of patients was  $29.04 \pm 0.8$ , average epilepsy duration was  $17.38 \pm 1.008$ . Of the patients, 49 (66.2%) patients were partial-onset epilepsy patients, 14 (18.9%) patients were generalized epilepsy, 9 (12.2%) patients were unclassified and 2 (2.7%) patients were syndromic patients. While 31 of patients (41.9%) were taking monotherapy, 43 patients (58.1%) were taking polytherapy. 43 patients (58.1%) were married, 31 of which (41.9%) were not married. There was no statistically significant difference between catamenial epilepsy patients and other female patients in reproductive age in terms of the age and marital status distribution.

**Conclusion:** It is reported that catamenial seizures are seen in about 12% of female with epilepsy. It was shown that there is a relation between ovary hormones and neuronal hyperexcitability. It was reported that estrogens decrease epilepsy threshold, progesterone shows protective impact on seizures.

#### p0426

##### TWO RARE CASES OF MAJOR CONGENITAL MALFORMATIONS WITH LEVETIRACETAM USE IN PREGNANCY

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**Purpose:** Levetiracetam is considered to be one of the safest antiepileptics in pregnancy. Based on the available pregnancy registry data, the risk of a major congenital malformation (mcm) with Levetiracetam monotherapy is 0.7%. (Confidence Interval 0.19%-2.51%). We attempted to look at the mcm rate with Levetiracetam monotherapy at our centre.

**Method:** This was a retrospective study and included women with monotherapy of Levetiracetam during pregnancy. Patients on Levetiracetam polytherapy were not included. Patients with other co-morbid illnesses or addictions which could lead to malformations were also excluded.

**Results:** Out of 60 pregnancies with Levetiracetam, there were two cases of mcm. One baby was born with anencephaly. The diagnosis in this case was made antenatally in the 3rd trimester by ultrasound examination. The parents decided to continue with the pregnancy and the baby died shortly after birth. The second baby was born with duodenal atresia. The diagnosis in this case was made with both clinical and ultrasound examination after birth. The baby underwent surgery in the neonatal period and survived. There were ten cases of low birth weight. No major cardiac malformation or skeletal malformation were reported.

**Conclusion:** Major congenital malformations with Levetiracetam are exceedingly rare. Animal experiments suggested that they may be skeletal, while pregnancy registry reported it to be mainly cardiac. These were one of the first cases to show neural and gastrointestinal tract malformations with Levetiracetam. Based on these findings, we suggest that more studies are needed before recommending Levetiracetam as a safe anti epileptic in pregnancy.

#### p0427

##### DELIVERY OUTCOMES IN WOMEN WITH EPILEPSY IN BRITISH COLUMBIA

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**Purpose:** The objective of this study is to compare rates of cesarean section delivery and induction of labour among women with and without epilepsy in British Columbia.

**Design/methods:** 545 women identified in the British Columbia Perinatal Data Registry as having epilepsy or convulsions at labour admission were compared to 545 women identified as not having epilepsy at labour admission who gave birth between 1/1/2000 - 31/12/2010.

**Results:** Women with epilepsy were significantly more likely to require a cesarean delivery compared to women without epilepsy (30.8% vs. 19.3%; OR, 1.87; 95% CI, 1.41–2.47). In women with epilepsy who had cesarean deliveries, the most prevalent indication for delivery was “Other” (31.6% vs. 7.6%). Induction of labour was more likely to occur in women with epilepsy compared to women without epilepsy (31.3% vs. 21.8%; OR, 1.63; 95% CI, 1.19–2.24) with the most common indication listed as “Maternal condition” (36% vs. 19.8%). Compared to women without epilepsy, women with epilepsy were more likely to receive epidural anesthesia when delivering vaginally (36.9% vs. 23.6%; OR, 1.89; 95% CI, 1.41–2.47), more likely to have assisted vaginal delivery (21.5% vs. 11.1%; OR, 1.83; 95% CI, 1.23–2.74) and more likely to receive general anesthesia during cesarean delivery (12.5% vs. 3.8%; OR, 3.61; 95% CI, 1.20–10.82).

**Conclusion:** The most frequently given indication for delivery was "Other" in women with epilepsy who had cesarean deliveries. The most frequently listed indication in women with epilepsy for induction of labour was "Maternal condition". Epilepsy is not an indication for induction or for cesarean delivery, however, seizures are. Still, a review of the literature suggests that <2% of women with epilepsy experience a seizure during labour. Health care providers and patients need to be counselled surrounding this issue and encouraged to pursue normal birth.

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p0430

### CLINICAL AND EEG FINDINGS OF ROTATORY EPILEPSY

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**Purpose:** In this report two patients with rotatory epilepsy were evaluated retrospectively in terms of their clinical, EEG findings, aetiological features and response to treatment.

**Case:** The first patient is 26 years old female suffering from rotatory seizures for 10 years. When she was admitted to our epilepsy-outpatient department she had totally eight seizures characterized by deviation of the head and eyes to the right side followed by one complete clockwise turn without loss conscious but evolved to be generalized tonic-clonic seizure every time. Her video-EEG monitoring showed generalized spike and wave discharges lasting one-two seconds and none of them was associated with absences. She was followed for 10 years under lamotrigine treatment and remained seizure free. The second patient is thirty 2 years old male with rotatory seizures for 2 years. His seizures started with forced deviation of head and eyes to the right side followed by complete turns without disturbing of conscious and ended with generalized tonic-clonic seizure. He had only three seizures before treatment. His video-EEG monitoring revealed generalized spike and wave discharges. After 1 year levetiracetam treatment, his seizures ended like the first patient. The cranial MRIs of both patients are normal.

**Result:** Both patients were seizure free when treated with adequate anti-convulsive medications.

**Conclusion:** Although rotatory seizures are uncommon and occur mainly secondary to a focal intracranial pathologies, this type of seizure is also described in patients with primary generalized epilepsies like our patients.

p0433

### ANTI-GAD MEDIATED DRUG RESISTANT EPILEPSY: A CASE REPORT

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**Purpose:** We present the case of a patient with immune-mediated drug resistant epilepsy and very high titers of antibodies against glutamate decarboxylase (GAD-Abs) and we discuss the therapeutic management and outcome. Antibodies against glutamate decarboxylase are associated with neurological disorders such as stiff-person syndrome, refractory epilepsy, cerebellar ataxia and most recently with limbic encephalitis characterized by temporal lobe epilepsy, neuropsychological deficits and neuroimaging findings in the medial temporal lobes.

**Method:** We describe the case of a 44 year old female patient who developed refractory temporal lobe epilepsy, impairment of recent memory, Hashimoto's thyroiditis and vitiligo. Brain MRI showed abnormal T2 signal in the mesial temporal lobes bilaterally. The EEG showed bitemporal focal slowing and epileptiform discharges. Thorough radiological investigations, tumor blood markers and paraneoplastic antibodies (anti-Hu, Yo, Ri, Ma2/Ta, CV2, amphiphysin) were all negative. The immunological screening (NMDAR, LGI1, CASPR2, GABAb1R, AMPA1R, AMPA2R, GAD) revealed extremely high GAD-Abs titers in serum and CSF (4.161.678 U/ml and 591.108 U/ml respectively) with the presence of oligoclonal bands in CSF.

**Results:** Due to the high titer of GAD-Abs, the patient underwent 10 sessions of plasma exchange followed by an oral treatment with prednisone that led to neuropsychological and EEG improvement, reduction of seizures and a significant decline in GAD-Abs titers.

**Conclusion:** The patient belongs to the subgroup of patients with anti-GAD limbic encephalitis and associated epilepsy with a good response to plasma exchange. The administration of steroids, IVIg and plasma exchange have shown varied efficacy while monoclonal antibodies may be a future therapeutic approach. However there are no established therapeutic guidelines. In our case, the reduction of seizures and the improved neuropsychological deficits were related to the decrease of the GAD-Abs titer.

p0434

### PREGNANCY OUTCOME IN GENETIC GENERALIZED EPILEPSIES ON VALPROATE TREATMENT

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**Purpose:** The aim is to evaluate the pregnancy outcome in genetic generalized epilepsies (GGE) treated with VPA during pregnancy.

**Methods:** 41 pregnant women with GGE on age 17–35 years gave birth to 57 newborns.

**Results:** Out of these 57 newborns there was one female newborn with meningomyelocela in lumbal spinal region. This was the second pregnancy of the mother who gave birth to 3 single newborns while taking VPA 900 mg per day during her first pregnancy with 5 mg folan supplementation, and 600 mg per day during her second and third pregnancy with 0.4 mg folan supplementation. There were 3 spontaneous abortions, one in second pregnancy of a woman who gave birth to healthy newborn, at her age of 17, but after her divorce became noncompliant to VPA with uncontrolled seizures. Her second pregnancy ended with spontaneous abortion in the second month of pregnancy. The other 2 abortions happened subsequently in the same woman while she was on combination of VPA and TPM, but with VPA monotherapy she gave birth to two single healthy newborns in the following years. Her EEG helped for correct diagnosis of GGE instead of focal epilepsy of unknown cause. As to the development of children in the following years after birth there is one child with ADHD of a mother taking VPA and TPM during pregnancy who gave birth to 2 healthy newborns. There is a finding of major malformation in newborn while his pregnant mother was on phenobarbiton, and a healthy newborn and child from her second pregnancy while on VPA and 5 mg folan supplementation.

**Conclusion:** Despite a small number of findings that suggest that other factors except pharmacotherapy are involved in pregnancy outcome, there is a need for more detailed and individual approach in evaluating women with epilepsy and pregnancy outcome.

p0435

### PREDICTORS OF RESPONSE IN PATIENTS WITH EPILEPSY IN A DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF BRIVARACETAM

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**Purpose:** A study of patients with inadequately controlled partial-onset (focal) seizures found that 100 and 200 mg/day brivaracetam was well tolerated and led to statistically significant reductions in seizure frequency (Klein et al. AES 2014, abstract 2.417). This post-hoc analysis was intended to identify factors that may predict response to brivaracetam. Predictors identified for response to brivaracetam were also evaluated for placebo to determine if there were common predictors.

**Method:** Patients taking 1–2 antiepileptic drugs (AEDs) enrolled in a prospective, double-blind, placebo-controlled Phase III study (NCT01261325) comprising 8-week screening and 12-week treatment period, were categorised by response (100%, 90%, 80%, 75%, 60%, 50% reduction in seizure frequency from baseline). Relationship between response and various predictor variables (brivaracetam dose, epilepsy duration, age, gender, classification of epileptic syndrome, aetiology, seizure profile, historical seizure frequency, baseline seizure frequency, prior AED count, inducer status, prior levetiracetam use at entry, concomitant AEDs and region) was examined using a logistic regression model.

**Results:** Among brivaracetam responders, statistically significant predictors were: lower historical seizure frequency for 100%, 90% and 80% responders; lower prior AED count for 90%, 80%, 75%, 60% and 50% responders; and lower baseline seizure frequency for 75%, 60% and 50% responders. Among placebo-treated patients, due to low sample size or the potential of extreme splits on frequency distribution of either dependent or independent variables, the model fit was questionable for 100%, 90% and 80% responder rates. Both lower prior AED count and negative inducer status were found to be statistically significant predictors for the 75% and 60% responder rates.

**Conclusion:** Historical seizure frequency and prior AED count were significant positive predictors of response in patients receiving brivaracetam, which is not unique among AEDs. Prior AED count was also predictive of placebo response, the only predictor common to both brivaracetam and placebo responders.

UCB supported.

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p0440

### STRESS-SENSITIVITY OF SEIZURES INFLUENCES THE RELATIONSHIP BETWEEN CORTISOL FLUCTUATIONS AND INTERICTAL EPILEPTIFORM DISCHARGES IN PEOPLE WITH EPILEPSY

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**Purpose:** People with epilepsy often report seizures precipitated by stress, which possibly results from effects of stress hormones on neuronal excitability and seizure threshold. Stress hormones are released in a circadian rhythm with additional hourly pulses. The effect of these ultradian hormone level peaks on epileptic activity is unknown. We expected that (1) stress hormone levels correlate with the incidence of epileptiform abnormalities in the electroencephalogram (EEG), and (2) this relationship is stronger in people with stress-precipitated seizures.

**Method:** We included people with pharmaco-resistant localization-related epilepsy who were admitted for long-term video-EEG monitoring. Cortisol levels were measured in saliva samples obtained every 15 minutes for five hours, starting directly after awakening, on one or 2 days. The incidence of interictal epileptiform discharges (IEDs) was determined for the same periods. We compared cortisol levels to the incidence of IEDs per patient and on group-level. We analyzed the effect of individual, epilepsy and recording characteristics, including self-reported stress sensitivity of seizures, on the strength and direction of this relation.

**Results:** Twenty-nine recordings were performed in twenty-one people. Overall, cortisol levels showed a significant positive relationship with the incidence of IEDs ( $\beta = 0.11$ ,  $p = 0.046$ ). On an individual basis both positive and negative correlations occurred. In multivariable analysis, the relationship between cortisol and IEDs was positively associated with the self-reported stress sensitivity of seizures ( $\beta = 0.32$ ,  $p = 0.005$ ), and not with other individual, epilepsy or recording characteristics.

**Conclusion:** The relationship between cortisol levels and the incidence of IEDs suggests that stress hormones may influence the occurrence of IEDs as biomarkers of epilepsy, also under basal conditions. Self-reported stress sensitivity of seizures partly explains individual differences in this relationship, which provides indirect proof for the existence of a pathophysiological basis for this subjective phenomenon.

p0444

### THE EFFICACY OF ADD-ON THERAPY AND THE COGNITIVE FUNCTION OF PATIENTS WITH DRUG-RESISTANT PARTIAL EPILEPSY TREATED WITH TIAGABINE - OBSERVATIONAL STUDY

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**Purpose:** The purpose of the study was to assess the efficacy of tiagabine as add-on therapy in patients with drug-resistant, partial epilepsy, and to assess the patient's cognitive functions, when used in everyday clinical practice.

**Method:** Multicenter, open-label, single arm, observational study performed in Q1 2013-Q2 2014 in Poland (3 visits: V0 - upon enrolment of the tiagabine-treated patients into the study, V1 -4 weeks after reaching the initial dose of tiagabine, V2 -4 weeks after reaching the target dose of tiagabine). Patients ( $n = 437$ ) with drug-resistant partial epilepsy, treated with tiagabine as add-on therapy at a dose of 15–50 mg per day were observed. The type and number of seizures, antiepileptic therapy used, auxiliary therapy and adverse effects were analysed. The McNemar's, Wilcoxon's and Fisher's tests were used. The patients' cognitive functions were assessed using the MMSE scale.

**Results:** The mean observation time was 90 days. About 80% of the patients took valproic acid and carbamazepine before adding tiagabine. The percentage of patients experiencing epileptic seizures was reduced

from 72.2%: between V0-V1 to 58.7% between V1-V2, ( $p < 0.001$ ). A reduction was observed in the average number of seizures (V1-V2: by an average of 2.9 in the 18-39 years age group, by 1.6 in the 40-59 age group and by 2.1 for patients above 60 years for age,  $p < 0.001$ ). The proportion of patients without seizures increased from 9.6% (V0) to 41.5% (V2),  $p < 0.001$ . Adverse events occurred in 4 (0.9%) patients. The Mini Mental State Examination (MMSE) was performed in 25% of patients. Cognitive functions did not deteriorate (an average 22.6 points (V0) and 23.6 (V2),  $p = 0.19$ ). The average MMSE score corresponded to a mild level of cognitive impairment.

**Conclusion:** Tiagabine is a well-tolerated drug, effective in controlling partial seizures, showing no unfavourable effect on cognitive functions.

**p0446**

### MALFORMATIONS OF CORTICAL DEVELOPMENT AND EPILEPSY: A COHORT OF 150 PATIENTS IN WESTERN CHINA

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**Purpose:** Malformations of cortical development (MCDs) are increasingly identified as important etiology for refractory epilepsy. Little is known about the spectrum, distribution and clinical features of MCDs, especially in a resource-limited region. This study investigates the distribution of MCDs and compares the clinical features and long-term prognosis among three subtypes and between simple and multiple forms in a cohort of Chinese patients.

**Method:** Consecutive 150 epilepsy patients with radiologically confirmed MCD were included from a tertiary epilepsy center in western China. Patients were divided into three subtypes according to the scheme of Barkovich. Distribution of MCDs was presented and comparison of the clinical features and long-term prognosis were made among three subtypes and between simple and multiple forms in Chinese patients.

**Results:** The mean age was 23, female 47%. The most common type of MCD is focal cortical dysplasia, followed by heterotopias, polymicrogyria, schizencephaly and pachygyria. Comparing the three groups, we found pre-perinatal insults more common in Group3 patients. Furthermore, we identified multiple malformations in 36/150 patients. Patients in the multiple group had higher rates of delayed milestones, cognitive impairment and neurological deficits. Extra-temporal epilepsy was more commonly seen. They were younger at the seizure onset and at assessment, also had worse outcomes comparing to the simple group. Patients with heterotopias were more commonly associated with other abnormalities.

**Conclusion:** Malformations of cortical development are important causes for drug-resistant epilepsy, also a big challenge for resource-limited countries. Imaging techniques are crucial in diagnosing and classifying cortical deformities. Multiple malformations (combined with other cortical or cerebral malformations) lead to more severe clinical features and poorer prognosis.

**p0447**

### BURDENS IN WORKING FOR EPILEPSY PATIENTS IN JAPAN

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**Purpose:** For epilepsy patients of the adulthood, working is one of the important elements in point of getting worth doing and means to become independent socially. We examined problems bearing upon working epilepsy people.

**Method:** Subjects were patients who visited to our department from April 2013 to March 2014. We investigated the epilepsy patients who were working, about clinical information and working situation.

**Results:** 170 people (male: 97, female: 73) corresponded to working-age population (15-64 year) among 260 epilepsy patients who visited our department during this period (male: 146, female: 114). 105 patients were employees (61.4%), 43 patients were non-employee (25.0%), and 23 (13.0%) patients were unclear. In terms of the occupational category, 11 patients (10.5%) were working in service or production process, 13 (12.4%) in businesslike occupations, and 17 (16.2%) in specialized technical occupations, respectively. In aspects of seizure control, 74 (43.5%) patients obtained seizure free more than 2 years. 48 (28.2%) patients had yearly seizure, and 25 (14.7%), 9 (5.3%), 8 (4.7%) patients had monthly, weekly, and daily seizure, respectively. However, the employment rate (66.7-84.0%) did not relate with the seizure frequency. In the patients who developed their epilepsy after starting the work, five patients (4.7%) were drivers, four patients (3.8%) were engaged in the shift work including the night duty, and three patients (2.9%) were on the dangerous duties in high places. After the onset of epilepsy, five patients could continue to work by changing the position, but five patients resigned because of epilepsy.

**Conclusion:** Epilepsy patients could find work regardless of their seizure control; however sometimes need to work under appropriate consideration. The transfer in the workplace might be difficult and result in quitting a job. We should be conscious of the necessity for living guidance and planning prescription along the working situation of each patient.

**p0448**

### PERINCAT: EXPERIENCE WITH PERAMPANEL IN CATALONIA

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**Purpose:** To describe clinical experience with perampanel (PER) as regards efficacy and tolerability in a series of patients with refractory partial-onset epilepsy.

**Method:** Multicenter, retrospective, observational study developed in several centres in Catalonia. Patients received PER because of partial onset pharmacoresistant epilepsy or side effects in previous antiepileptic treatment according to clinical practice. Results at 6 months are presented.

**Results:** PER was administered to 128 patients. Only 78 of the were suitable to 6 month analysis. The main reason to add PER was lack of control of seizures in 97.4%. The mean seizure count in the previous year was 12.1 (1-40) per month and the previous number of antiepileptic drugs used was 6.3 (2-15). The mean dose of PER used was 6.3 mg (2-12). Retention rate was 82.1 and 70.5% at 3 and 6 months. The seizure-free patients were 6.5% and 29.9% were responders.

Seizure reduction was significant at 3 months in complex partial seizures ( $p < 0.001$ ) but not between 3 and 6 months, and secondary

generalized seizures ( $p = 0.006$ ). Concomitant use of non inducers disclosed an improvement in efficacy. Adverse events (AE) were reported in 69.2% of patients, leading to PER withdrawal in 19.2%. The main AE were dizziness (35.9%), somnolence (24.4%) fatigue (12.8%) and irritability (10.3%).

**Conclusion:** PER in clinical practice, at 6 months and in a highly resistant population shows an efficacy similar to that disclosed in clinical trials and a high retention rate. Efficacy seems to be shown already at 3 months.

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p0451

### FOCAL EPILEPSIES WITH VISUAL SYMPTOMS

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**Purpose:** Visual symptoms as ictal manifestation are often neglected by patients, or misdiagnosed by physicians. Aim of this study was to analyze etiology, semiology and diagnostic pitfalls in patients with focal epilepsy with visual signs.

**Method:** Retrospective review of patients referred to our centre in years 2013–2014 was carried out. Inclusion criteria: verified diagnosis of focal epilepsy with visual signs. Clinical, EEG and MRI data, along with time span from first clinical manifestation to correct diagnosis were taken into consideration.

**Results:** 22 patients, 10 males and 12 females were included into the study. Age range: 11 - 74 years. Seizures were presented with elementary visual hallucinations (EVH) in 14 patients and with complex visual hallucinations (CVH) in 8 patients. Distribution of interictal spikes and/or slowing on standard EEG was: 8- occipital, 9-mixed occipital and temporal, 4 -mixed occipital and parietal, 1 -mixed occipital and frontal. Complex visual hallucinations correlated with mixed focal distribution of interictal spikes and slowing on EEG, as well as with false psychiatric diagnosis. Structural changes on MRI were established in 8 cases, in 14 patients MRI remained normal. Diagnosis by the time of reference was: 12 cases - secondarily or primary generalized tonic-clonic seizures, psychiatric disorder - 4 patients, migraine - 2 cases and 4 patients remained without diagnosis. Time span to correct diagnosis varied between 3 months and >30 years (mean 6.75 years). Only 2 patients received antiepileptic treatment, 12 received other medication but anticonvulsants and 8 stayed without any treatment.

**Conclusion:** Neglecting importance of visual symptoms for diagnosis of focal epilepsy may lead to long lasting diagnostic and treatment failure with serious medical and social consequences.

p0452

### EVALUATION OF BALANCE AND GAIT ABNORMALITIES IN REFRACTORY EPILEPSY: COMPARISON WITH REMISSION EPILEPSY

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**Purpose:** Falls due to seizures and related complications are well known. Problems of balance and gait unrelated to seizures constitute a distinct

area of interest. The aim of this study is to evaluate abnormalities of balance and gait and to estimate the risk of falling in epileptics.

**Method:** One hundred and four patients are classified in two groups: Treatment-resistant epilepsy (TRE) and remission epilepsy (RE). All patients were applied Tinetti Balance and Gait Scale (TBGS) and Falls Efficacy Scale (FES). Afterwards, they completed Modified Clinical Test of Sensory Interaction on Balance, Walk Across, Tandem Walk, Step/Quick Turn, Limits of Stability tests in Balance Master systems.

**Results:** There were 54 patients in TRE, 50 in RE group. Groups were compatible for age, sex, body mass indexes. The scores of standing eyes open and on a foam surface eyes open, speed of tandem walk, degree of swing to the right, reaction time, movement velocity, endpoint and maximum excursion, directional control tests were markedly abnormal in TRE group by comparison to RE group ( $p < 0.05$ ). Negative correlations were found between TBGS and seizure types, duration and number of antiepileptic medications. Correlations between diversity of seizure types and FES score; age at onset of disease and eyes open balance were positive. Accordingly, the correlation between Short Test of Mental Status (STMS) and reaction time towards a target was negative.

**Conclusion:** Our results point that the abnormalities of balance and gait are related not only to the frequency and total number of the seizures, but also to diversity of the seizure types, duration of the treatment, number of antiepileptic drugs, age at onset of the disease and existence of some cognitive dysfunction. As we found remarkable abnormal findings in RE group, we conclude that factors other than frequency and total number of seizures must be operative in balance and gait abnormalities.

p0453

### DURATION AND AMPLITUDE OF INTRACEREBRALLY RECORDED HIGH FREQUENCY OSCILLATIONS AND EPILEPTOGENIC NETWORKS

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**Purpose:** Interictal high-frequency oscillations (HFO) in frequencies over 80 Hz (ripples and fast ripples) have been repeatedly identified in recordings from invasive EEG monitoring in epileptic patients. These phenomena may serve as biomarkers for epileptic brain. Conversely, the studies describing the presence of interictal HFO of nonepileptic nature are on the increase. The purpose of present study is to identify if there are frequency-independent HFO parameters (amplitude and duration) which potentially differ in epileptic and non-epileptic region.

**Method:** We studied 31 consecutive patients with medically intractable focal (temporal and extratemporal) epilepsies. Automated detection was used to detect HFO. All of the contacts of electrodes in each patient were categorized by independent visual identification in standard SEEG into three groups - the seizure onset zone (SOZ), the irritative zone (IZ) and areas outside the irritative zone/seizure onset zone (nonSOZ/nonIZ). The characteristics (amplitude and duration) of HFO within these three groups were statistically compared.

**Results:** The rate of fast ripples (FR) in SOZ was significantly higher than in nonSOZ/nonIZ region, for IZ the result was not significant. In ripple range (R) the differences among groups of contacts were not significant. The relative amplitude of HFO (both ripples and fast ripples) was higher in SOZ in comparison with IZ and nonIZ/nonSOZ region. Statistical analysis showed significantly shorter duration of ripples in SOZ in comparison with duration of HFO in either nonSOZ/nonIZ or

## Abstracts

IZ (in FR range the result was significant only between SOZ and non-SOZ/nonIZ).

**Conclusion:** In SOZ fast ripples are significantly more frequent and shorter with higher relative amplitude than in nonSOZ/nonIZ region. SOZ can be differentiated from IZ through the duration of R.

p0454

#### EPILEPSY; IMPROVING THE PATIENT JOURNEY. SEVEN SHORT FILMS AND ACCOMPANYING BOOKLETS

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**Purpose:** Epilepsy is a common co-morbidity in people with a learning disability. It has a negative impact on quality of life and life expectancy. Access to healthcare and up take in clinical investigations is more difficult in this population. Our aim was to produce accessible resources to help adults with epilepsy and a learning disability understand more about their condition and how to live well with epilepsy.

**Method:** People with a learning disability who had previously undergone hospital tests shared their experiences of anxiety not knowing what to expect. This helped in the planning and development of a series of short films and booklets. People with a learning disability and epilepsy took the lead parts in the films. A patient focus group reviewed draft versions of the films and booklets and provided constructive criticism to help produce the final products in an accessible format.

The films portray patient journeys. In the Transition film, the patient and parent were filmed before, during, and after transition to the adult epilepsy service to obtain their views and perspectives about the process.

**Results:** Seven short films and accompanying booklets have been produced and are available in hard copies and on the internet via our service webpage at Nottinghamshire Healthcare NHS Trust and Nottingham University NHS Trust websites [www.nottinghamshirehealthcare.nhs.uk/epilepsy](http://www.nottinghamshirehealthcare.nhs.uk/epilepsy), [www.nuh.nhs.uk/our-services/services/neurology/epilepsy-and-seizure-disorders/](http://www.nuh.nhs.uk/our-services/services/neurology/epilepsy-and-seizure-disorders/)

**Conclusion:** The resources will promote better access to specialist investigations and treatment of epilepsy, raise awareness of the services available for people with epilepsy and a learning disability, encourage and enable patients to be more involved in the management of their condition, enhance the experience of young people and their families in the transition from paediatric to adult epilepsy care, and encourage people with epilepsy and a learning disability to live a full and active life.

p0457

#### UNDERSTANDING CLINICAL EPILEPTOGENESIS - NEW HYPOTHESES DRIVEN BY A FIRST SEIZURE CLINIC APPROACH (THE HALIFAX EXPERIENCE)

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**Purpose:** To arrive at a deeper understanding and new perspective on the evolution and mechanisms of epileptogenesis by collecting multimodal longitudinal data on any patient diagnosed with a first seizure (FS).

**Method:** As of 2/2015, the Halifax First Seizure Clinic has assessed 630 patients with either strictly FS, n = 196, new-onset epilepsy (NOE = > 1 seizure < 12 months), n = 152, or 3) newly-diagnosed epilepsy (NDE = seizures > 12 months), n = 53. 229 patients were excluded (no seizure, n = 193 or not confirmed seizure, n = 36). All patients were assessed in detail with regards to clinical information (including psychiatric comorbidities), epilepsy protocol MRI, routine and sleep-deprived EEG, social parameters, and life style. Follow-up visits occurred at 6, 12 and 24 months.

**Results:** Interim analysis of the current data suggests the following hypotheses

- A) Preceding anxiety and depression are common suggesting subtle changes in brain biochemistry before seizure occurrence,
- B) Marijuana use is over presented, compared to the general population; it either reflects coping strategy for A or is icetogen itself,
- C) Prognostication of pharmacoresistance (PR) in the early course of epilepsy is almost impossible as of a highly diverse temporal pattern with long phases of seizure freedom,
- D) MRI findings usually associated with poor treatment prognosis may actually have a good prognosis in early stages (example: focal cortical dysplasia),
- E) Combining volumetric findings of the amygdala and preexisting psychiatric symptoms may serve as early predictors for seizure recurrence,
- F) The frequent MRI findings in late-onset epilepsy are not well understood with regards of epileptogenesis and need further sophistication and exploration.

**Conclusion:** Our preliminary data provide exciting new hypotheses for clinical epileptogenesis which challenges knowledge originating from retrospective studies in advanced stages of epilepsy. A well organized longitudinal prospective cohort approach needs to be a critical component in an academic comprehensive epilepsy program.

p0458

#### DELAYED ICTAL ATONIA IN TEMPORAL LOBE SEIZURES AS A SIGN OF SEVERE ICTAL CARDIAC BRADYARRHYTHMIA

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**Introduction:** Ictal bradycardia and asystole (IB and IA) are rare autonomic manifestations in focal seizures, with a prevalence of 0.4%, associated with injuries from falls and/or sudden unexplained death (SUDEP).

**Objectives:** Generate alert between the association of seizures with falls because of delayed ictal atonia (DIA) and IB/IA in patients without pre-existing cardiac disorders, highlighting the usefulness of videoelectroencephalogram with simultaneous electrocardiogram (VEEG-EKG) to recognize symptoms and perform appropriate and precocious treatment.

**Material and methods:** Description of two cases with DIA

**Results:** Case 1: 45 year-old woman with refractory epilepsy since age 18, presenting focal dyscognitive seizures. Recently she refers sudden falls, having had head trauma in an opportunity. She is on Oxcarbazepine 1200 mg/day. Brain MRI is normal; EEG showed left temporal sharp waves. The VEEG-EKG captured 5 seizures with left temporal electroclinical semiology; in one of the events, 30 second-long asystole was observed after 49 seconds of ictal onset with DIA and myoclonus. The patient was treated with cardiac pacemaker with no additional falls. Case 2: 32 year-old young man with epilepsy since age 15, presenting focal

dyscognitive seizures with aura of Deja-vu and/or throat paresthesia, occasionally followed by falls with atonia. He is on Oxcarbazepine 1800 mg/day and Clobazam 15 mg/day. Brain MRI shows right hippocampal sclerosis. VEEG-EKG registered three electroclinical seizures with right temporal semiology. In two events DIA was observed in association with 10-second long asystole occurring 44 seconds after seizure onset. The patient underwent right anterior lobectomy 6 months ago, seizure free since then.

**Conclusions:** Atypical clinical presentation of focal seizures with temporal lobe semiology and delayed ictal atonia with or without myoclonus should generate suspicion of severe ictal cardiac bradyarrhythmia. Diagnosis by VEEG-EKG is critical for an earlier and more aggressive treatment, including surgery and / or pacemaker, in order to reduce morbidity.

**p0459**

### EARLY ICTAL SIGNS IN MESIAL TEMPORAL LOBE EPILEPSY WITH ISOLATED HIPPOCAMPAL PATHOLOGY AND EXCELLENT EPILEPSY SURGERY OUTCOME

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**Purpose:** Identification patients with mesial temporal epilepsy (MTLE) is crucial, because such intractable epilepsy is associated with encouraging surgical outcome.

The aim of the study was assessment of early ictal signs in cases with isolated medial temporal pathology.

**Method:** We studied video-EEG recorded seizures in 14 (9 F, 5 M) patients who underwent anterior tailored temporal resections with refractory MTLE, and had isolated hippocampal pathology: 9 pure hippocampal sclerosis, 3 gliomas (ganglioglioma, 1 astrocytoma), 1 cavernoma and 1 focal cortical dysplasia type IIIB. All patients were with excellent outcome (seizures free of disabling seizures; Engel class 1A or 1 B) for at least five years. The ictal signs for the period of first 30 seconds were assessed.

**Results:** Early ipsilateral upper-limb elementary automatisms occurred in all seizures. Head and eyes deviations (13/14 subjects), oroalimentary automatisms (12/14 subjects) contralateral upper-limb dystonic posturing (11/14 subjects), contralateral lower limb tonic posturing (10/14 subjects), and vocalizations (8/14 subjects) were frequent early ictal signs. Verbal automatisms was observed during 2 seizures beginning in nondominant temporal lobe. Initial loss of contact was never observed.

**Conclusion:** Our findings may be useful in differentiation of MTLE semiology with pure hippocampal pathology from other forms of temporal lobe epilepsy.

**p0460**

### TEMPORAL ENCEPHALOCEL: A RARE CAUSE OF INTRACTABLE SEIZURES

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Encephalocèles are defects of the skull and meninges, which are usually congenital. Temporal lobe encephalocèles are rarely recognized and may cause epileptic seizures. Here we present a case of drug resistant temporal lobe epilepsy due to temporal lobe encephalocel which is a rare cause of seizures. Twenty years old man has suffered from intractable partial seizures since he was sixteen years old. Seizures usually started with bad odour and then followed by oral automatism with loss of consciousness. Secondly generalized seizures were rare and postictal aphasia was also reported. Seizures were not controlled despite the combined therapy carbamazepin and levetiracetam. There was head trauma history when he was fourteen years old. In the family, his nephew suffered from epileptic seizures since childhood due to hippocampal sclerosis. His physical and neurologic examination were normal. During long term video EEG Monitoring, ictal and interictal EEG showed epileptiform activity in the left temporal lobe. Brain MRI initially was reported as normal but then reviewed again, and left temporal lobe encephalocel and probable cortical dysplasia in adjacent cortex could be identified. He underwent epilepsy surgery including left temporal lobectomy without hippocampotomy but with lesionectomy. Although pathology showed non specific changes such as Chasline degeneration, he is seizure free over 1 year since surgery. Middle fossa encephalocèles should be recognized as a potential epileptogenic lesion in patients with partial seizures. Temporal lobe encephalocèles can easily be missed when brain MRI is reported and patients can be defined as having nonlesional temporal lobe epilepsy. As reported few patients' data with intractable seizures and temporal lobe encephalocel who underwent surgery, our patient's data and follow up also suggest that hippocampus may not be included the resection and sparing of mesial temporal lobe structures allows individuals to continue to have normal verbal memory postoperatively.

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**p0461**

### CEREBELLAR NUCLEI STIMULATION STOPS EPILEPTIC ABSENCE SEIZURES IN CACNA1A/TOTTERING MOUSE MUTANTS BY OVERRULING OSCILLATORY ACTIVITY IN THALAMIC NUCLEI

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Absence seizures appear as generalized spike-wave discharges (GSWDs) in electrocorticographical recordings (ECoG) and most studies on generalized forms of epilepsy have focused on disturbances of activity in thalamocortical networks. Given the dense input of cerebellar nuclei (CN) afferents on the thalamus, we recently explored the impact of CN stimulation on GSWDs in two unrelated mouse models of absence seizures. Increasing the frequency and regularity of CN activity by pharmacological or optogenetic manipulations decimated seizure occurrence, whereas blocking their activity dramatically increased the occurrence of seizures (Kros et al., 2015, Ann Neurol, in press). Here, we explored the underlying mechanisms of these effects by extracellular recordings in thalamic nuclei and ECoG in awake, head-restrained homozygous *tottering* (*tg*) mice during pharmacological or optogenetic manipulation of CN neurons. During absence seizures, we found that in a subset of recordings the action potential firing pattern of neurons in thalamic nuclei were significantly modulated at 6–9 Hz, i.e., the representative frequency for SWDs in *tg* mutants. We found that the firing patterns of the thalamic neurons that were phase-locked to GSWDs changed drastically upon successful optogenetic manipulation of CN neurons. More specifically, the rhythmic, phase-locked and low-frequency activity of these neurons switched into an irregular but tonic, high-frequency activity when the seizures were

stopped using optogenetic stimulation of CN. These data indicate that increased CN output can stop absence seizures by potently driving thalamic action potential firing and altering the regularity, which together overrule thalamocortical oscillations.

p0462

#### PLASMA MICRORNA PROFILING IDENTIFIES POTENTIAL BIOMARKERS OF HUMAN TEMPORAL LOBE EPILEPSY

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**Purpose:** There is an important and unmet need for biomarkers of epilepsy to identify patients at risk of epilepsy development, progression or remission. Epilepsy biomarkers could also support decisions on when and how to treat and differential diagnosis. Imaging and EEG biomarkers are either time-consuming or expensive. A molecular biomarker in biofluids such as blood would help solve this problem. Although several studies have attempted to identify blood biomarkers of epilepsy, focusing on protein-coding transcripts and protein markers, no sensitive and specific biomarker has yet been proven. MicroRNAs are a class of small non-coding RNA that regulate gene expression at a post-transcriptional level. MicroRNAs are important contributors to brain function and emerging animal and human data suggest microRNAs control multiple pathways in epilepsy. MicroRNAs are also detectable in various body fluids and their stability as well as link to disease mechanism makes them potentially ideal molecular biomarkers of epilepsy.

**Method:** To determine whether there are microRNA biomarkers of human epilepsy we collected blood samples from 20 temporal lobe epilepsy patients during in-patient video-EEG monitoring, along with blood from 20 age and gender-matched healthy volunteers. We profiled levels of over 800 microRNAs in each sample using the OpenArray miRNA analysis platform run on a 12K Flex QuantStudio PCR.

**Results:** Over 200 microRNAs were consistently called present in control plasma, confirming high specificity of the profiling platform. There were expected high levels of known plasma microRNAs including miR-16, miR-24, miR-150 and miR-484 and low or undetectable levels of brain-expressed microRNAs.

**Conclusion:** A number of significantly differentially expressed microRNAs were identified between control and epilepsy samples including known brain-expressed microRNAs implicated in epilepsy. These results support the existence of a set of microRNAs implicated in disease pathogenesis that may be biomarkers of human epilepsy.

p0463

#### BYPRODUCTS OF PROTEIN OXIDATIVE DAMAGE AND ANTIOXIDANT ENZYME ACTIVITIES IN PROGRESSIVE MYOCLONUS EPILEPSY

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**Purpose:** It has been shown that oxidative stress may contribute to neuronal hyperexcitability, while antioxidants may alleviate the progression of progressive myoclonus epilepsy (PME). However, the molecular mechanisms underlying oxidative stress and its role in PME remain elusive. Since oxidative damage to proteins is one of the major mechanisms underlying neuronal cell damage, we evaluated byproducts of oxidative damage to proteins (protein thiol groups and nitrotyrosine), as well as, activities of major antioxidant enzymes, superoxide dismutase (SOD) and glutathione peroxidase (GPX) in patients with PME.

**Method:** 26 patients with PME (5 had Unverricht-Lundborg disease, 14 Lafora body disease, 5 myoclonic epilepsy with ragged red fibers and 2 had late infantile neuronal ceroid lipofuscinosis) and 66 healthy, non-epileptic subjects, without any drug treatment, matched for sex, age, ethnicity and geographic origin were included in the study. The amount of protein thiol groups (P-SH) in plasma, as well as, SOD and GPX activities were determined spectrophotometrically, while nitrotyrosine content was measured by enzyme immunoassay.

**Results:** Although the content of P-SH, important chain breaking antioxidant in plasma, was lower and nitrotyrosine, a reliable marker of nitrosative damage to proteins, was found to be higher in patients with PME in comparison to healthy controls, this change in byproducts of protein damage did not reach statistical significance ( $p > 0.05$ ). However, the activities of antioxidant enzymes, SOD and GPX, were found to be statistically significantly higher in PME patients when compared to controls ( $p = 0.003$  and  $0.005$ , respectively).

**Conclusion:** Due to increased antioxidant enzyme activities, it may be concluded that oxidative stress is associated with pathogenesis of progressive myoclonus epilepsy.

p0464

#### THE ASSESSMENT OF LEARNING, MEMORY, BEHAVIOR AND NEURONAL DAMAGE, AMOUNT OF GABA-A ALPHA 1 RECEPTOR AFTER PENTYLENETETRAZOLE-INDUCED STATUS EPILEPTICUS IN IMATURE AND MATURE RATS

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**Purpose:** We aimed to evaluate age-dependent cognitive and behavioral changes, neuronal damage, the amount of GABA-A Alpha 1 receptor in mature and immature rats after status epilepticus (SE).

**Method:** Following PTZ-induced SE, open field and Morris water maze test were applied in pups (17 days), adolescent (45 days) and adult (150 days) rats. All rats were underwent histological investigation to assess neuronal cell damage (caspase and calpain activity) and amount of GABA A alpha 1 receptor, and compared with control groups.

**Results:** No statistically significant differences were seen between control and experimental groups according to behavioral tests in early stage after SE. The calpain mediated neuronal damage with necrotic

morphology was seen in adult rats, but in adolescent and pups rats were not observed. The caspase mediated neuronal damage with apoptotic morphology was seen in pups, after SE. The amount of GABA A Alpha 1 receptor decreased in the three experimental groups compared with control groups. The amount of GABA A alpha 1 receptor is seen the least in adult experimental group. The decrease of amount of GABA A alpha 1 receptor is more prominent in hippocampus than it is in cortex.

**Conclusion:** Our data show that PTZ-induced SE did not effect learning and behavior in early stage after SE, histological data proved that it lead to calpain and caspase mediated neuronal damage with necrosis. Calpain-mediated cell necrosis was seen particularly in the adult group and caspase-dependent apoptotic morphology was observed in immature rats. The decreased of GABA A alpha 1 receptor is the highest in the adults. Our study has supported that SE induced cell damage getting higher with increasing age and the calpain-mediated cell damage was observed in the adult group, too. We need to long-term follow-up studies to understanding the long term effect of SE-depending neuronal damage on cognition and behavior.

#### p0465

### EFFECTS OF LOW DOSE MERCURY CHLORIDE (HGCL<sub>2</sub>) EXPOSURE IN GESTATIONAL AND LACTATIONAL PERIODS TO ON BEHAVIOR, LEARNING AND HEARING LOSS IN WAG/RIJ RATS

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**Purpose:** Our aim was to investigate the effects of inorganic mercury exposure in gestational/lactational periods on litters' behavior, learning and hearing function in 5-week-old and 5-month-old WAG/Rij rats.

**Method:** Chronic exposure was begun with IM injections of low-dose HgCl<sub>2</sub> or saline to pregnant rats. Injections were applied to mothers during gestation/lactation periods. 5-week-old and 5-months-old rats were divided in four different groups and tested to locomotor activity, morris water-maze, passive avoidance for learning and memory performance and distortion product otoacoustic emission responses (DPOAE) tests for observing age-dependency.

**Results:** There was no significant difference between 5-week-old rat groups in locomotor activity. Significant difference was detected in mercury-treated group in passive avoidance and morris water-maze and DPOAE tests compared to the control group. There was no significant difference between the groups of 5-month-old rats in locomotor activity, morris water-maze and passive avoidance tests except DPOAE tests which became worse in mid and high frequency hearing. Mercury-treated 5-week-old group exhibited worse emotional memory performance in passive avoidance test, worse spatial learning and memory performances in morris water-maze tests. Mercury-treated 5-month-old group were not differed from control group in same tests. Hearing loss seen in 5-week-old rats became worse in 5-month-old rats that caused poor hearing.

**Conclusion:** According to our results, mercury exposure during gestation/lactation periods may deteriorate learning and memory performances, hearing at high frequencies in young rats. There was no difference in behavior-learning tests in adult rats, but DPOAE test was found to be deteriorated. These results clearly indicate that DPOAE test is very sensitive in determining age-dependent mercury ototoxicity. Early detection of effects of mercury exposure provides the medical team an opportunity to determination treatment regimens and to mitigate hearing changes. For this purpose, DPOAE tests can be used in clinical and experimental research investigating heavy metal ototoxicity and hearing loss.

#### p0466

### THE CORRELATION OF GABA AND ADENOSINE CONCENTRATIONS WITH CHANGES IN HIPPOCAMPAL EXCITABILITY AFTER STATUS EPILEPTICUS IN IMMATURE RATS

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**Purpose:** Status epilepticus (SE) induced in immature rats may result in development of spontaneous seizures. Majority of spontaneous seizures is generated in hippocampus therefore we started to study hippocampal excitability after SE. The functional changes were correlated with concentration of neurotransmitters (GABA, adenosine) in this structure.

**Method:** LiCl-pilocarpine SE was elicited in P12 rats and hippocampal epileptic afterdischarges (ADs) were studied in P15, P18, P25, P32 rats with electrodes implanted into dorsal hippocampus. Control animals received saline instead of pilocarpine. All age groups consisted of 10–14 animals. Rats were stimulated with suprathreshold intensities (2-s series of 60 Hz pulses of 1-ms duration) at 20-min intervals six times. Thresholds and duration of ADs were evaluated. The hippocampal homogenate of P15 and P32 rats (both controls and SE) was analyzed for concentration of GABA and adenosine by HPL chromatography.

**Results:** Threshold for hippocampal ADs was significantly higher in P15 SE rats in comparison with controls. The P18 and P25 groups did not exhibit a difference between SE and controls but 32-day-old group revealed significantly lower threshold for SE rats than for controls. Corresponding changes were found in AD duration - shorter ADs were recorded in P15 SE rats whereas ADs in P32 SE rats were significantly longer in comparison with appropriate controls. These findings correlated with concentration of inhibitory neurotransmitters - increased GABA in P15 SE rats and decreased adenosine in P32 SE rats in contrast with their age-matched controls.

**Conclusion:** Our data demonstrated that during 20 days after SE complex changes of hippocampal excitability took place. P32 rats revealed higher excitability of dorsal hippocampus than age-matched controls. The changes in hippocampal excitability after SE correlated with changes in GABA and adenosine in this structure.

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#### p0468

### AUTONOMOUS ICTAL ACTIVITY IN THE DENTATE GYRUS IN THE STATUS EPILEPTICUS RAT MODEL OF EPILEPSY

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The dentate gyrus (DG) plays an important role in the pathophysiology of epilepsy. The DG is believed to serve as a gatekeeper against uncontrolled propagation of neuronal activity into downstream structures by means of massive intrinsic inhibitory activity. During epileptogenesis, the DG loses its gate function and therefore enables propagation of ictal activity into the hippocampal loop. The epileptic DG in principle should be able to generate ictal activity in an autonomous and input-independent manner. However, apart from a single report of ictal activity in the isolated DG in hippocampal slice cultures (Gutiérrez et al. 1999), there is currently little evidence for this hypothesis as in various rodent models of epilepsy, ictal activity originated in other regions such as the CA3 and CA1, but not in the DG. In the current study, we used intrinsic optical imaging in combination with electrophysiological recordings in the low-Mg<sup>++</sup> in vitro model inducing ictal epileptiform activity. In brain slice preparations from epileptic animals exposed to low Mg<sup>2+</sup>, we observed

spontaneous and autonomous epileptiform activity in the DG. Importantly, this activity was completely independent from epileptiform activity generated in adjacent neocortical structures. Thus, in an *in vivo* model of TLE, the DG can serve as an independent generator of epileptic activity contributing to general hyperexcitability and increasing the seizure load in the temporal lobe.

p0469

#### RESVERATROL ATTENUATES OXIDATIVE STRESS ASSOCIATED WITH STATUS EPILEPTICUS IN IMMATURE RATS

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**Purpose:** We have demonstrated recently that status epilepticus (SE) induced in immature rats leads to oxidative stress and mitochondrial dysfunction. The aim of the present study was to investigate potential protective effect of a natural polyphenol Resveratrol.

**Methods:** Seizures (having a character of SE) were induced in immature 12-day-old male Wistar rats by substances with a different mechanism of action, namely by DL-homocysteic acid (bilateral *i.c.v.*, 600 nmol/side), 4-aminopyridine (bilateral *i.c.v.*, 100 nmol/side), Li-pilocarpine (*i.p.*, LiCl 127 mg/kg and the next day pilocarpine 35 mg/kg) and kainic acid (*i.p.*, 6 mg/kg). Dihydroethidium (Het) method was employed for detection of superoxide production in brain *in situ*. The determination of the oxidized products of Het (reflecting superoxide production) was assessed microscopically by fluorescence (>600 nm). Mitochondrial function was evaluated by measuring respiratory chain complex I activity in isolated mitochondria. Resveratrol was given *i.p.* in two or three doses (25 mg/kg each), 30 min before, 30 min or 30 min and 90 min after induction of SE.

**Results:** The treatment with resveratrol provided a clear protective effect in all the studied models of SE. It prevented or significantly reduced the increase of superoxide formation and it substantially attenuated the inhibition of complex I activity associated with SE.

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

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p0470

#### A CRITICAL PERIOD TO SUPPRESS EPILEPTOGENESIS

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**Purpose:** Using the fruit fly *Drosophila melanogaster* as an experimental model, we investigated whether epileptogenesis can be prevented by early intervention during embryogenesis.

**Method:** Seizure behaviour, in defined genetic seizure mutants, was tested in the larval stage using an electroshock assay. Electroshocked larvae exhibit a temporary paralysis, corresponding to a period of seizure-like activity, until resumption of normal motile behaviour. Manipulation of neural activity during embryogenesis, using both optogenetic and pharmacological tools, prevents epileptogenesis from proceeding in these mutants. Optogenetic manipulation defines a critical period for this effect. Targeted optogenetic expression, in a cell-specific manner, allowed the contribution of different neuron types to be evaluated. Finally, electrophysiological recordings quantify the levels of synaptic excitation of larval motoneurons following optogenetic manipulation.

**Results:** We report that preventing hyper-excitability in *bang-sensitive* mutants, a genetic seizure model, is sufficient to dramatically reduce postembryonic seizure-behaviour. Moreover, we have identified a critical period during embryogenesis, corresponding to onset of action potential firing in developing locomotor networks, in which disturbance of neuronal activity results in altered seizure susceptibility at postembryonic stages. This effect can be blocked by prior treatment of gravid females with the same antiepileptic drugs currently used to treat human epilepsy. Whole-cell recordings revealed an increased synaptic excitation of larval motoneurons consequent to embryonic manipulation. Again, these changes can be reverted by early drug intervention.

**Conclusion:** Preventing abnormal neuronal activity during a critical period of embryogenesis is sufficient to prevent epileptogenesis in defined *Drosophila* genetic seizure models. These results provide persuasive evidence that early drug intervention during development can suppress seizure occurrence in later life, offering a new perspective for the treatment of human idiopathic epilepsy.

p0471

#### ANTICONVULSIVE EFFECTS OF SELECTED NEW GENERATION ANTIEPILEPTIC DRUGS IN THE 4-AMINOPYRIDINE IN VITRO RAT MODEL OF EPILEPSY

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During the last years, several new generation antiepileptic drugs (AEDs) have been introduced on the market and their clinical use keeps to increase due to good efficacy and tolerability. However, little is known on the efficacy of these compounds in acute epilepsy models. Due to its good reproducibility, the 4-aminopyridine (4-AP) acute *in vitro* rat model of epilepsy is a widely used approach to study ictal activity in brain slices. Here, we used extracellular recordings in combination with intrinsic optical imaging to test the anticonvulsive efficacy of three new antiepileptic drugs with putatively distinct mechanisms of action: levetiracetam, lacosamide and zonisamide. Horizontal entorhinal-hippocampal slices were prepared from male, adult Wistar-Han rats. After 60 min of exposure to 4-AP (100  $\mu$ M) and full appearance of seizure like events (SLEs), tested drugs were applied in varying concentrations for the duration of 60 min and followed by a wash phase of another 60 min. Levetiracetam (33  $\mu$ M-100  $\mu$ M-300  $\mu$ M) reduced the incidence of SLEs in a concentration-dependent manner but had no effect on the duration or the amplitude of SLEs. Similarly, application of lacosamide (10  $\mu$ M-33  $\mu$ M-100  $\mu$ M) or zonisamide (33  $\mu$ M-100  $\mu$ M-300  $\mu$ M) resulted in a concentration-dependent reduction of SLE incidence whereas no change of SLE duration or amplitude were observed. In addition, a reduction of the tonic component of SLEs was observed upon application of lacosamide. In contrast to levetiracetam and zonisamide which reduced but did not abolish SLEs, lacosamide completely blocked SLE incidence when used at higher concentrations (100  $\mu$ M). Moreover, at higher concentrations all three compounds reduced the extent of seizure propagation as observed by intrinsic optical imaging. All reported effects were reversible during the wash-out phase. We conclude that the clinical efficacy of the new generation antiepileptic drugs levetiracetam, lacosamide and zonisamide is adequately reflected in the 4-AP acute *in vitro* model of epilepsy.

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p0475

#### ESSENTIAL ROLE THALAMIC NEURONS IN GENERALIZED ABSENCE EPILEPSY

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**Purpose:** Disruption in thalamocortical circuits is responsible for generalized absence epilepsy. However, the role of thalamic relay neuron activity in absence epilepsy is controversial. Human studies report blood flow increases in thalamus during electroencephalographic (EEG) spike wave discharge (SWD) of absence seizures. Yet animal studies report that at the single neuron level, thalamic relay neurons only participate in a sparse manner, suggesting that large-scale synchrony of thalamic neurons is not required to support the seizures. This raises the question of whether or not active participation of thalamic relay neurons is required at all, and has implications regarding seizure therapies that might target thalamus versus cortex. We tested for necessity of thalamic neuron firing using optogenetic inactivation of relay neurons in two rodent genetic absence models, stargazer mice and WAG/rj rats.

**Method:** An enhanced version of the inhibitory opsin (eNpHR 3.0) was expressed in thalamic ventrobasal neurons through viral transduction driven by CamKII promoter, which targets excitatory relay neurons. Animals were instrumented with optrodes which allowed targeted delivery of light to thalamus, as well as depth electrode thalamic recordings and surface corticography (to provide an analog of EEG).

**Results:** Yellow, but not blue light was able to interrupt absence seizures and the associated SWD in both stg and WAG/Rij animals. This was associated with a blockade of neural firing, as obtained with depth electrodes.

**Conclusion:** These data show that continuous activity is indeed required in thalamic neurons to sustain the large scale synchrony during generalized absence epilepsy.

#### p0476

##### ANTIPILEPTOGENIC EFFECT OF INTERMITTENT FEEDING DIET IN MOUSE PTZ-INDUCED KINDLING MODEL

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**Purpose:** Epilepsy is one of the common neurological disorders with over 50 million patients worldwide. Over 30% of patients have pharmacoresistant seizures. Additionally, current anticonvulsant drug therapy only suppresses seizure and doesn't cure underlying epileptogenic lesion. Intermittent feeding (IF) has been shown to be neuroprotective and reduce seizures in animal models. In this study we investigated the effect of IF regimen on pentylenetetrazole (PTZ)-kindling model of epileptogenesis in mice.

**Method:** Animals (all male mice, 20 g) were divided into 2 groups. Group I (AL, ad libitum, n = 5) received food every day while group II (IF) received food on alternate days for five 5 weeks. The IF group was divided into 2 sub-groups (IF-1, PTZ given on IF feeding days, and IF-2, PTZ given on AL feeding days, n = 7 each group). Epileptogenesis was induced by PTZ (35 mg/kg, s.c.) on alternate days and animals were observed for 30 minutes for seizure severity by the Becker's five point scale. Seizure severity and kindling process were compared between the groups.

**Results:** Seizure stages according to Becker's five point scale were significantly delayed in IF-1 group compared to the AL and IF-2 groups. AL group achieved stage 5 after 23 sessions (p < 0.05); however, IF-1 group

didn't achieve full stage after 23 sessions. There was no significant difference between AL and IF-2 group (p > 0.05).

**Conclusion:** Results show that IF regimen significantly delays PTZ-kindling induced epileptogenesis attributable to its acute on chronic effect. In order to elaborate mechanism of anti-epileptogenic effect of IF diet, further studies are suggested.

**Keywords:** PTZ-kindling, intermittent feeding, anti-epileptogenesis, mice

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#### p0477

##### MICRORNA PROFILE OF THE TUBEROUS SCLEROSIS COMPLEX CORTICAL TUBERS USING NEXT GENERATION SEQUENCING

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**Purpose:** Tuberous sclerosis complex (TSC) is a rare genetic disease, frequently associated with severe epilepsy which is often unresponsive to anti-epileptic drugs. Recent studies have implicated microRNAs (miRNAs) as crucial regulators of various processes involved in epilepsy pathogenesis. MicroRNAs interact with protein-encoding mRNAs usually leading to translational repression. Deregulation of miRNA expression has been reported previously in human epileptic brain samples. The aim of the present study was to characterize the miRNA profile in TSC cortical tubers and corresponding perituberal tissue using Next Generation Sequencing and identify candidate miRNAs associated with these cortical malformations that may contribute to their epileptogenicity.

**Method:** Total RNA, including miRNA, was isolated from cortical tubers (n = 16) and matched perituberal cortex (n = 4) from TSC cases and age matched control cortex (n = 13). The samples were processed using the Illumina TruSeq Small RNA-Seq Sample Prep Kit and sequenced on the Illumina HiSeq 2500 Sequencer. The sequences were aligned to the *Homo sapiens* GRCh37 reference build and further aligned over known miRNAs, quantified by read count quantification and normalized by matched distribution using the Seqmonk platform.

**Results:** A total of 12 miRNAs were differentially expressed between TSC tubers and age-matched control samples. Eight of the 12 miRNAs, including miR34b, recently shown to be expressed at increased levels in TSC tubers associated with epilepsy, showed increased reads whereas 4 showed decreased reads in tubers compared to control tissue. Unsupervised cluster analysis showed 3 main groups, with a majority of tubers

## Abstracts

(14/16) clustering together. A large proportion (7/14) of TSC tubers in the major cluster showed a mutation in *TSC2*. Validation of the differentially expressed miRNAs by qPCR is in progress.

**Conclusion:** The study demonstrated differential expression of miRNAs in cortical tubers, which might help identify important pathways involved in the epileptogenicity of these lesions and new candidates for targeted interventions.

p0478

### THE LINK BETWEEN CHOLESTEROL AND HEDGEHOG SIGNALLING IN EPILEPSY AND AUTISM SPECTRUM DISORDER: A CELLULAR MODEL OF SMITH-LEMLI-OPITZ SYNDROME

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**Purpose:** Disorders of cholesterol metabolism cause epilepsy, autism spectrum disorder, and uniquely amongst the inborn errors of metabolism, congenital malformations. The commonest disorder, Smith-Lemli-Opitz syndrome (SLOS) results from mutations in the enzyme, DHCR7 leading to a cholesterol deficit and an accumulation of its precursor, 7DHC in fetal tissues. Congenital malformations in SLOS bear a striking resemblance to those seen in sonic hedgehog (SHH) deficient states, and SLOS pathogenesis is thought to be mediated by aberrant SHH signalling. SHH signalling critically depends on signal transduction through the transmembrane protein, Smoothed (SMO), which is susceptible to potent positive and negative regulation by sterols. SMO dysregulation is thought to occur in SLOS as a result of an altered sterol environment, but whether the accumulation of 7DHC or a deficit of a cholesterol-derived sterol is responsible is unclear.

**Aims:** 1. To establish a cellular model of SLOS.  
2. To determine how cholesterol metabolism affects SHH signalling.  
3. To propose a mechanistic model for how deficient SHH signalling in SLOS could result in epilepsy and ASD.

**Method:** 1. Development of a cell culture model system to test the effect of cholesterol deficiency on SHH signalling.

2. We assess the effect of DHCR7 disruption on the SHH signalling pathway in two ways. First, SHH signalling output is assayed by qPCR for targets of SHH signalling, and using a luciferase reporter assay. Second, we use quantitative cell biological techniques that probe critical molecular-subcellular systems that mediate SHH signalling.

**Results:** 1. A cholesterol deficit, independently of known sterol regulators of SMO, impairs SMO activation in SLOS.

2. 7DHC does not block SHH pathway activity.

3. Cholesterol deficit impairs SHH signaling by reducing SMO translocation to the appropriate sub-cellular compartment.

**Conclusion:** Epilepsy and ASD in SLOS could arise through a SHH-dependent mechanism rather than through 7DHC toxicity.

p0479

### DETECTION OF HHV-6B IN ADULT MESIAL TEMPORAL LOBE EPILEPSY: ASSOCIATION OF VIRAL INFECTIOUS STATE WITH INFLAMMATORY CYKELETON IN BRAIN TISSUE AND CSF

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**Purpose:** HHV-6B has been confirmed as an important etiologic factor of mesial temporal lobe epilepsy. Here, we aimed to analyze the different course of HHV-6B infection and the association with inflammatory factors in MTLE brain tissue and cerebral spinal fluid (CSF).

**Method:** Nested polymerase chain reaction (nPCR) was performed to detect HHV-6B DNA, and immunohistochemistry (ICH) HHV-6B protein. Real-time PCR, immunofluorescence and suspension bead array were performed for cytokines in brain tissues and CSF.

**Results:** HHV-6B DNA was detected in 18 of 49 MTLE patients (36.73%) and 1 of 19 controls (5.26%) in brain tissue, but not in CSF. ICH showed different course of HHV-6B protein of latency stage(U94) in 8 patients (16.32%), early state (P41) in 3 patients (6.12%), late state (gp116/54/64 or P98) in 5 patients (10.20%), and multiple stages (two or more different stage specific proteins) in 9 patients (18.36%). None of these HHV-6 related proteins were found positive in control brain tissue. PCR revealed up-regulation of IL-1 $\beta$  and IL-7 in tissue with complex virus state, but not in lesion with simple virus state. Suspension bead array in csf confirmed up-regulation of IL-1 and IL-7. The logistic analysis revealed the association with seizure frequency and complex virus state.

**Conclusion:** The data showed HHV-6B may be in different infection courses. The virus replicates and reactivates periodically. In MTLE patients with HHV-6B protein positivity, different course of HHV-6 infection may be associated with seizure frequency. It may also play an important role in up-regulation of inflammatory factors.

p0480

### MORPHOLOGICAL ALTERATIONS IN THE MODEL OF NON-LESIONAL TEMPORAL LOBE EPILEPSY

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**Purpose:** Temporal lobe epilepsy (TLE) is the most common form of epilepsy and hippocampal sclerosis represents the main underlying structural abnormality. Approximately 20% of TLE cases are non-lesional due to absence of any obvious epileptogenic lesion and tetanus toxin model is traditionally considered as a model of non-lesional TLE. In this study we utilized direct markers of cell degeneration to evaluate the cell damage in this model.

**Method:** Epilepsy was induced in nine Wistar rats by injection of 10 ng of tetanus toxin to the right dorsal hippocampus. Control animals were injected with 50 mM PBA 2% BSA solution. After the injection, animals were placed on video monitoring to verify the development of spontaneous seizures. On day 16 animals were perfused and brains extracted. Postfixed brains were sectioned to 50  $\mu$ m slices and labeled using Nissl and FluoroJade B staining (FJB).

**Results:** All animals developed spontaneous seizures. In 3/9 animals areas of decreased Nissl staining were observed in contralateral hippocampus. FJB revealed presence of degenerating neurons in the areas corresponding to decreased Nissl labeling. In rostro-caudal direction, the areas containing degenerating neurons extended over  $3.0 \pm 1.2$  mm. In 1/9 animals hippocampal sclerosis was present. No structural abnormalities and presence of FJB positive neurons were observed outside the hippocampus.

**Conclusion:** This study demonstrates that from the perspective of classical neuropathology the tetanus toxin model can be still classified as a non-lesional. However, microscopic cell loss is present and must be always considered when this model is used for experimental purposes.

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p0481

### ASSESSMENT OF THE ANTI-CONVULSANT EFFECTS OF CANNABIDIOL WHEN CO-ADMINISTERED WITH ANTI-EPILEPTIC DRUGS IN ACUTE MODELS OF SEIZURE AND THEIR INDIVIDUAL TOLERABILITY PROFILES

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**Purpose:** Plant-derived cannabidiol (CBD) has previously demonstrated anti-convulsant properties in chemically-induced, in vivo models of seizure. Here, the effects of CBD in combination with commonly used antiepileptic drugs (AEDs) on generalised and temporal lobe seizures were investigated to:

- (1) ascertain whether CBD retains its anti-convulsant effects when co-administered with AEDs,
- (2) whether CBD is well-tolerated when co-administered with AEDs and
- (3) reveal any beneficial drug-drug interactions. Moreover, the tolerability profiles of CBD and these AEDs is described.

**Method:** CBD effects were investigated in the pentylenetetrazole and pilocarpine models of seizure by using a known, effective anti-convulsant dose of CBD (100 mg/kg) co-administered with effective anti-convulsant doses (ED<sub>25</sub>, ED<sub>50</sub> and ED<sub>75</sub>) of AEDs, sodium valproate, phenobarbital and ethosuximide. The tolerability profile of CBD and the AEDs (ED<sub>25</sub>, ED<sub>50</sub> and ED<sub>75</sub> anti-convulsant doses in the pentylenetetrazole model of generalized seizure) in rats was investigated using the static beam test.

**Results:** CBD retained its anti-convulsant effects when co-administered with the AEDs in the pentylenetetrazole- and pilocarpine-induced models of seizure, and was well-tolerated and devoid of any negative drug-drug interactions. Moreover, a beneficial drug-drug interaction in the pentylenetetrazole model was revealed when CBD was co-administered with sodium valproate. In comparison to these AEDs, CBD did not produce any motor deficits or neurotoxicity in the tolerability assay.

**Conclusion:** These results demonstrate promising anti-convulsant effects of CBD in combination with AEDs in two chemically-induced acute in vivo models of seizure and tolerability test. This suggests that CBD may be a novel therapeutic candidate for a range of human epilepsies, with a potentially favourable tolerability profile, supporting further clinical investigation.

p0482

### ENHANCING KCC2 BY ACUTE TRKB INHIBITION RESCUES PHENOBARBITAL-RESISTANT SEIZURES IN A MODEL OF NEONATAL ISCHEMIA

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**Purpose:** Hypoxic-ischemic encephalopathy (HIE) accounts for 50–60% of the reported cases for neonatal seizures, and results in adverse neurodevelopmental morbidity and lethality depending on the severity of the underlying brain injury. HIE-associated neonatal seizures are difficult to treat because of their well-known resistance to 1st-line anti-seizure drugs such as phenobarbital (PB) and benzodiazepines. In this study, using a previously established ischemic mouse model, we investigated a novel therapeutic strategy of enhancing KCC2 to rescue the occurrence of PB-resistant neonatal seizures.

**Method:** The ischemic seizure model in CD1 mice develops acute PB-resistant seizures at postnatal day 7 (P7) that are PB-responsive at P10. Using this model, this study addressed the question of whether the PB-resistance can be reversed by the presence of a KCC2 modulator, ANA-12. The therapeutic potential of an acute dosing with ANA-12 (IP; 2.5 mg/kg), a small molecule selective TrkB receptor antagonist was investigated at P7 and was compared to P10. The main evaluation criteria for ANA-12's therapeutic benefit included: 1) quantitative electroencephalographic (EEG) seizure burden and 2) KCC2 and NKCC1 protein expression levels with and without its treatment after an acute ischemic insult.

**Results:** ANA-12 treatment significantly rescued PB-resistant seizures at P7. Additionally, ANA-12 enhanced the PB efficacy at P10. Western blot results showed that ANA-12 + PB treatment significantly prevented the acute post-ischemic KCC2 downregulation documented in the model. NKCC1 expression was not affected either by ischemia or ANA-12 treatment. At both ages investigated, bumetanide a NKCC1 antagonist, not only failed to act as an efficacious adjunct therapy, but resulted in a significant aggravation of the effectively subdued post-PB seizures.

**Conclusion:** This study shows that KCC2 modulation helps reverse the occurrence of PB-resistant seizures recorded in P7 mice that may be a potent strategy in treating this fragile patient population.

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p0483

### MULTIMODAL METHOD AND ANALYSIS OF THE IN VITRO HUMAN CORTICAL SPONTANEOUS SYNCHRONOUS POPULATION ACTIVITY

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**Purpose:** From the cortical slices of epileptic and non-epileptic tumor patients maintained in physiological medium in vitro spontaneous synchronous population activity (SPA) emerges. SPA was recorded until now by our group using sharp intracellular and laminar extracellular methods to analyze the neural mechanisms giving rise to population synaptic/trans-membrane and spiking activity. We introduced the two-photon line scan Ca-imaging technique on human in vitro slice preparations to gain additional information about the network mechanisms involved in the SPA generation. The excellent spatial coverage and resolution of this technique supplements the laminar extracellular, sharp intracellular and whole cell patch techniques.

**Method:** Human slices were maintained in a dual superfusion chamber of high flow rate physiological incubation medium and otherwise conventional submerged technique to elicit SPA in a two-photon microscope. The population activity was recorded by laminar extracellular and extracellular patch electrodes. Bulk loading of OGB-1-AM and SR101 was applied on the tissue. This way we were able to image the SPA related Ca-transients in pyramidal or interneuron cells with two-photon technique, simultaneously with extracellular and whole cell patch measurements. The patched cells were loaded with biocytin as well for later anatomical analysis. The filled cells were 3D reconstructed, and observed with light microscope, and transmission electron microscope.

**Conclusion:** Combining high spatial resolution two-photon Ca-imaging technique and high temporal resolution extra- and intracellular electrophysiology techniques may permit a deeper understanding about the network properties of SPA in the human cortex.

p0485

#### SPATIO-TEMPORAL PROFILE OF SEIZURE INITIATION IN TEMPORAL LOBE EPILEPSY OF HIPPOCAMPAL ORIGIN

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**Purpose:** Despite decades of study of the pathophysiology of TLE, the role of the individual limbic structures in seizure genesis is still not well understood. Traditional models of TLE (kainate, pilocarpine) do not allow for determination of the causal role of each limbic structure in ictogenesis due to widespread damage across the limbic system induced by the initial status epilepticus. The goal of this study was to elucidate the spatio-temporal profile of seizure initiation in TLE induced in the dorsal hippocampus.

**Method:** TLE was induced in seven adult rats by injection of 10 ng of tetanus toxin into the right dorsal hippocampus. Following the injection, animals were implanted with bipolar recording electrodes in the following structures of both hemispheres: amygdala, dorsal hippocampus, ventral hippocampus and piriform, perirhinal and entorhinal cortices. The animals were video-EEG monitored for 4 weeks.

**Results:** In total 140 seizures (20 seizures per animal) were analyzed. The average duration of each seizure was  $53.2 \pm 3.9$  s. Seizure onsets were classified as hypersynchronous with high-amplitude spikes initiated simultaneously across several sampled structures. Analysis of seizure onset revealed that the majority initiated in the ipsilateral (41%) and contralateral (21%) ventral hippocampi. These structures had a significantly higher probability of seizure initiation than other studied structures. The involvement of other limbic structures varied between individual animals. Only 7% of seizures initiated in the injected dorsal hippocampus.

**Conclusion:** This study demonstrates the involvement of multiple limbic structures in seizure initiation in TLE induced in the dorsal hippocampus. Furthermore, it confirms the significance of the epileptogenic network concept to understand TLE ictogenesis, in which the ventral hippocampi play the dominant role.

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p0490

#### ASSESSMENT OF ANXIETY AND COGNITIVE PERFORMANCE IN POST-STATUS EPILEPTICUS RATS TREATED WITH CURCUMIN AND LEVETIRACETAM

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**Purpose:** Patients with epilepsy have been associated with anxiety and cognitive dysfunction. This study investigated the effects of levetiracetam and curcumin on anxiety and cognitive performance of post-status epilepticus (SE) rats.

**Method:** Kainate induced SE in Wistar rats were used in the experiments. Pre and post performance tests were conducted prior to kainic acid administration and after 7 days treated with either levetiracetam or curcumin, respectively. The anxiety assessment was conducted by using the Open Field Test and Light/Dark Box Test, and the cognitive performance assessment was conducted by using the Novel Object Recognition Task and Object Location Recognition Task. Overall anxiety evaluation was based on locomotor activity, exploratory activity and anxiety-like behaviour.

**Results:** Kainate-induced status epilepticus not only caused an increase in anxiety-like behaviours, but also impaired both spatial and non-spatial recognition memory in rats (all  $p < 0.05$ ). Levetiracetam-treated epileptic rats exhibited anxiolytic behaviours ( $p < 0.05$ ), however, levetiracetam treatment showed no effect in ameliorating cognitive impairments caused by kainic acid, either in spatial or non-spatial recognition memory. Curcumin showed the ability to ameliorate anxiety and non-spatial recognition impairment due to kainic acid ( $p < 0.05$ ), but yet no effect on spatial recognition impairment.

**Conclusion:** Both levetiracetam and curcumin may be useful in improving anxiety condition, however, only curcumin has the potential to improve cognitive function in post-kainate induced SE rats.

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p0494

#### ROLE OF ROUTINE BENZODIAZEPIN IN ELICITING CLASSICAL EEG RESPONSE IN SUSPECTED SUB-ACUTE SCLEROSING PANENCEPHALITIS (SSPE) CASES

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**Purpose:** This ongoing study was undertaken with a view to improving classical EEG sensitivity after routine IV Benzodiazepine during EEG recording in a resource poor country like Bangladesh. The purpose of the study is therefore to find out necessity of administration of Benzodiazepine during EEG recording of SSPE cases and to compare the efficacy of Diazepam and Midazolam in eliciting EEG pattern.

**Method:** It is a clinical trial done on consecutive suspected cases of SSPE based on clinical and positive measles antibody in serum/CSF. Diazepam and Midazolam were given IV during EEG recording on alternate cases.

**Results:** In Diazepam group, 3 (50 suggestive %) had typical periodic slow wave complexes (PSWC) from beginning of EEG recording which increased in amplitude and more regular after Diazepam. 2 (33.3%) of them had normal EEG even after Diazepam. Interestingly

1 (16.7%) had normal EEG initially which showed typical PSWC after Diazepam. In Midazolam group, 3 (60%) had typical PSWC from the beginning of EEG and the changes after Midazolam was similar to Diazepam in positive PSWC patients. 1 (20%) developed PSWC after Diazepam which had normal EEG initially. There was also 1 (20%) with normal EEG which did not change even after Midazolam.

**Conclusion:** At this stage of evaluation of study it is apparent that Benzodiazepin has a positive impact in eliciting classical EEG finding.

p0495

#### CLINICAL VALUE OF SOURCE LOCALIZATIONS WITH GAMMA BAND OSCILLATION DURING ICTAL STATE: AN MEG STUDY

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**Purpose:** We evaluated the diagnostic value of MEG source localization for power spectral activity during preictal period in relation with surgical outcome, and compared the results with manually selected time and frequency analysis at ictal onset.

**Method:** Data for 13 epilepsy patients who showed an ictal event during MEG were analyzed. Several seconds of preictal data were localized in the theta, alpha, beta, and gamma bands by using wavelet transformation and the sLORETA algorithm. The same analysis was performed with narrow time and frequency band. Localization concordances to the surgically resected area were compared.

**Results:** Source localization in the gamma band for a 10 s window before ictal onset showed best concordance to the resection cavity. Eight of 13 patients showed sub-lobar concordance in the 10 s gamma band localization, whereas 3 showed concordance in the narrow time and frequency analysis. In terms of surgical outcome and pathology, 4 of 7 patients with focal cortical dysplasia pathology achieved seizure free outcome and all of 4 patients showed sub-lobar concordance, whereas none of remaining 3 showed the concordance. Moreover, 2 of 4 showed no abnormal findings on MRI.

**Conclusion:** A 10 s time window gamma source localization method can be used to delineate the epileptogenic zone. The use of a long period during preictal gamma source localization has the potential to become a localizing biomarker of the epileptogenic zone in candidates for surgical intervention, especially in MRI-suspected FCD or even non-leisonal cases.

p0496

#### INITIAL EEG PATTERNS AS AN ADJUNCTIVE PROGNOSTIC INDICATOR IN CARDIAC ARREST PATIENTS UNDERGOING THERAPEUTIC HYPOTHERMIA

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**Purpose:** Continuous EEG (cEEG) is used frequently to provide real-time neurological information in post cardiac arrest (CA) patients undergoing therapeutic hypothermia (TH) and medically induced coma. We set to investigate if specific EEG pattern correlates with outcome.

**Method:** We retrospectively identified 83 consecutive post CA patients who have undergone TH and cEEG. cEEG was started within 6 hours of initiating TH and continued past 24 hours after the patient had achieved normal body temperature. The findings were categorized into the following groups: *diffuse slowing, epileptiform abnormality/seizure, burst suppression, background attenuation, and isoelectric background*. Neurologic outcomes were measured at discharge according to Glasgow-Pittsburg Cerebral Performance Category (CPC) 5-point scale.

**Results:** Of the 83 post CA patients included in this study, 29 had initial cEEG pattern of diffuse slowing, 24 burst suppression, 23 background attenuation, 3 epileptiform abnormality/seizures, and 4 isoelectric background. Seven of 29 (24.1%) patients with initial cEEG showing diffuse slowing did not survive. In comparison, the mortality rate of patients with initial cEEG patterns of isoelectric background, epileptiform abnormality/seizure, burst suppression, and background attenuation were 100% (4/4), 66.7% (2/3), 66.7% (16/24), and 87% (20/23), respectively. Among those who survived, 12 of 22 (54.5%) patients with initial cEEG pattern of diffuse slowing had good neurological outcome (CPC scores 1-2) whereas the ratios for those with isoelectric background, burst suppression, and background attenuation were 0%, 25%, 33.3%, respectively.

**Conclusion:** Similar to previous studies, the survival in our patients was poor. However, 54.5% of those who had initial cEEG patterns of diffuse slowing had good neurological outcome. Thus, the finding of diffuse slowing as an initial cEEG pattern may be an adjunctive indicator for prognosis at the onset of TH for post CA patients in whom the neurological examination findings are of limited reliability.

p0497

#### CORRELATION BETWEEN HIPPOCAMPAL CONNECTIVITY AND MEMORY PERFORMANCE IN MESIAL TEMPORAL LOBE EPILEPSY

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**Purpose:** Left mesial temporal lobe epilepsy (mTLE) patients generally show greater impairment in memory than right mTLE patients. Since memory function is associated with the function of the hippocampus in the brain, we hypothesized that hippocampal connectivity would be different between right and left mTLE patients and might be correlated with memory performance.

**Method:** We investigated the resting state functional connectivity with mutual information at the source level with magnetoencephalography in 41 mTLE (left mTLE: 22, right mTLE: 19) patients who had hippocampal sclerosis that was surgically removed and who were postoperatively seizure free (>2 years of follow-up) in the theta, alpha, beta, and gamma frequency bands. Network-based statistics (Zalesky et al., 2010) was performed to identify which functional connectivity would be statistically different between groups (*t*-value threshold = 3.8, and 10,000 permutations with a *p*-value <0.01 as significant).

**Results:** Left mTLE patients showed more impaired verbal delayed memory function than right mTLE patients. We found that functional connectivity between the right hippocampus (HIP\_R) and the left middle frontal gyrus (F2\_L) in the theta frequency band was stronger in

right mTLE patients than left mTLE patients. More interestingly, functional connectivity between HIP\_R and F2\_L in the theta frequency band was positively correlated with verbal delayed memory performance.

**Conclusion:** Our results suggest that more impaired verbal delayed memory function in left mTLE patients than right mTLE patients might be attributed to the decreased hippocampal connectivity in the theta frequency band.

**p0498**

### FRONTAL INTERMITTANT RHYTHMIC DELTA ACTIVITY (FIRDA): CLINICAL AND LABORATORY CORRELATES IN 20 PATIENTS

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**Purpose:** Frontal intermittent rhythmic delta activity (FIRDA) is a frequent transient electroencephalographic finding in adults. Its pathophysiologic significance is unknown. So far clinical, laboratory and neuroimage findings related to FIRDA have been reported in the literature. In the light of these findings, we want to evaluate our patients and share the results.

**Method:** All electroencephalograms (EEGs) with FIRDA between January 2009 - December 2014 at our institution were identified. Demographic data, clinical history, laboratory results and neuroimaging studies were recorded.

**Results:** We identified 20 patients with this electrographic pattern. FIRDA was detected on EEGs recorded at the time of hospital admission or during clinical follow up. Age of patients ranged from 23 to 74 years. 11 of them were female and 9 were male. Chronic illness was present in 8 patients. 3 patients were epileptic before and 2 were pregnant. EEGs were performed because of history of seizures in 7 patients, altered state of consciousness in 10 patients, forgetfulness in 1 patient, speech disturbance in 1 patient. In 1 patient there was no any complaint. Normal background activity was observed in 3 cases. Epileptic discharges accompanying FIRDA were seen in 3 patients. Amongst the 20 patients with FIRDA, 5 had asymmetric pattern on EEG. Renal function impairment was present in 1 patient and 1 patient had elevated serum ammonia level. Cranial magnetic resonance imaging was abnormal in 9 of 19. Intrahemispheric lesions, hemorrhage, encephalomalacia, tumor, were present in 5, and basal ganglia hemorrhage in 1. In 1 patient, hydrocephalus was detected.

**Conclusion:** FIRDA can be seen with a variety of conditions and is not a specific marker of brain tumor, hydrocephalus or encephalopathy.

**p0499**

### THE EPILEPTIC BRAIN: A STRESSFUL NETWORK

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**Purpose:** People with epilepsy show EEG functional network alterations, most prominently in the theta frequency band. Stress is one of the main seizure-precipitating factors in epilepsy. Cortisol, one of the main stress hormones, has not yet been investigated in relation to functional network changes. We attempted to study the effect of the natural circadian rhythm of cortisol on global network characteristics in patients with epilepsy.

**Method:** Long term EEG recordings and cortisol samples were available of 17 subjects diagnosed with focal epilepsy. Saliva samples were acquired to measure cortisol concentration every 15 minutes over a period of 5 hours following awakening. For every saliva sample taken, we selected up to four EEG epochs of 4 seconds each. The phase lag index (PLI) was used to compute an undirected weighted network and a minimum spanning tree (MST). Then we calculated the normalized shortest path ( $\lambda$ ) and the MST diameter, both measurements of global integration, lower in a more random network as opposed to an ordered network. We compared  $\lambda$  and MST diameter (theta band) to cortisol levels using a linear mixed model.

**Results:** We found  $\lambda$  to decrease slightly when cortisol increased (estimate:  $-0.00042$ , p-value: 0.02). We found no time lag between cortisol and  $\lambda$ . MST diameter did not decrease (estimate: 0.00088, p-value: 0.65). We did not yet study the influence of potential confounders.

**Conclusion:** These preliminary findings suggest a tendency towards a more random global network as cortisol increases. Further analyses are needed to interpret the data correctly to understand how this might influence seizure susceptibility. This study invites to evaluate the effect of stress and cortisol in epilepsy from a graph analytical perspective.

**p0500**

### COMPARISON OF AUTOMATIC AND VISUAL HIGH FREQUENCY OSCILLATIONS DETECTION

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**Purpose:** To compare automatic and visual high frequency oscillation (HFO) detection.

**Methods:** We compared automatic and visual high frequency oscillations (HFO) detections in 5 patients. HFO were automatically detected by a custom made matlab detection algorithm. First, the signal in the statistical window (10 s) was filtered in a series of overlapping frequency bands. Power envelopes and the frequency stability between narrow band signal and broad band signal were computed. HFO detections were obtained by thresholding the normalized dot product of the power envelopes and frequency stability. To increase algorithm specificity amplitude, frequency stability and duration thresholds, previously obtained from HFOs marked by expert reviewer, were applied on putative HFO. This automatic detection was compared with visual HFO analysis.

**Results:** We reached excellent congruence between manual and automatic HFO detection measured by Cohen's kappa ( $K = 0.8$ ).

**Conclusion:** We managed to prove excellent concordance between automatic and visual HFO detection.

**p0501**

### A FUNCTIONAL CONNECTOME OF THE HUMAN BRAIN, BASED ON INTRACRANIAL ELECTRICAL STIMULATION

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**Purpose:** Several MRI and DTI methods already delivered a whole brain connectome, however none of them are able to probe the brain connectivity using native signaling: electrical pulses. The study of cortico-cortical evoked potentials using high-density stereoelectroencephalographic (SEEG) recordings represents perhaps the most direct way of exploring brain connectivity. However, SEEG investigations are limited to the patients with drug-resistant epilepsy, which may present disrupted connectivity patterns. In order to dissociate pathological from physiological connectivity, we propose a method that combines individual patient's connectivity with saliency maps and epileptogenicity of the cortical areas calculated retrospectively on a larger patient dataset.

**Method:** 16 patients with refractory epilepsy were implanted with depth electrodes for presurgical evaluation. Single pulse electrical stimulation, using biphasic pulses with 3 ms pulse duration and current intensity in the 0.25–5 mA range was applied to each pair of adjacent contacts and responses evoked by stimulation were recorded from other contacts located in remote brain areas. We calculated the RMS value over the 10–110 ms interval after each stimulation pulse. We considered that a contact is activated by stimulation if the responses are correlated with the stimulation current (Spearman's  $r > 0.5$ ,  $p < 0.05$ ) and the mean RMS value across all stimulation pulses in a trial is higher than the 3<sup>rd</sup> quartile value (Q3) of all the responses recorded within a patient. Responses from the activated contacts were weighted by the epileptogenicity of each area and averaged for each patient. Further weighting was performed by calculating the saliency of each non-pathological connection in the patient database. The directionality of the connections was assessed by pairwise analysis of stimulated structures.

**Results:** We obtained the physiological functional connectivity between 68 brain structures from both hemispheres.

**Conclusion:** Through direct electrical stimulation, we deliver a physiological functional connectome covering a large number of brain structures, including the directionality of connections.

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p0504

### ENLARGING THE SPECTRUM OF SCN8A-RELATED EPILEPTIC SYNDROMES

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**Purpose:** Mutations in *SCN8A*-gene, encoding a voltage-gated sodium channel, have been recently associated with more or less severe mental retardation, epilepsy and neurological deficits (Larsen et al, 2014). We aim to further describe the heterogeneous phenotypic pictures of *SCN8A*-related epilepsy.

**Method:** We compared the clinico-neurophysiologic data of patients with *SCN8A*-mutation.

**Results:** We identified three different clinico-neurophysiologic subtypes: 1) Sporadic patients with de novo heterozygous mutations of *SCN8A*, presenting with early onset severe drug resistant epilepsy, cognitive deterioration, pyramidal/extra-pyramidal signs and SUDEP (ca.12% of this cases). Patients had both generalized and focal prolonged seizures,

with prominent hypomotor and vegetative symptoms, evolving to secondary generalization. EEG showed progressive background deterioration with epileptic abnormalities predominant in the posterior regions.

2) Sporadic patients with de novo heterozygous mutations of *SCN8A*, presenting with mild to moderate intellectual disability, mild or none neurological signs and drug resistant epilepsy with extended seizure-free periods. EEG showed multifocal epileptiform abnormalities.

3) Interestingly, three unrelated families with the same *SCN8A* missense mutation presented with a very mild form of epilepsy, remitting before puberty, and not associated with any cognitive or neurological deficit. Interictal EEG was either normal or showed non specific diffuse abnormalities in all adult affected members.

**Conclusions:** We provide new data that further enlarge the phenotypic spectrum of *SCN8A*-related epilepsy including familial and sporadic cases, ranging from severe early onset encephalopathy with epilepsy, milder form of drug resistant epilepsy to familial cases with a very mild form of epilepsy.

p0505

### UTILITY OF ELECTROENCEPHALOGRAPHY AT A US TERTIARY CARE MEDICAL CENTER

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**Purpose:** Electroencephalography (EEG) is a common but resource-intensive diagnostic test for real-time assessment of brain function. We aimed to assess the utility of EEG at a top tertiary care center in the US to determine its diagnostic yield and accessibility.

**Method:** Our retrospective chart review sampled continuous EEGs (cEEGs) from ICU (n = 100) or inpatient wards (n = 100) and spot EEGs (sEEGs) in the ED (n = 100). Diagnostic yield was assessed as the percentage of EEGs found to be abnormal. Accessibility (*time to EEG*, in hours) was calculated as the time from study request to the study's start. Access predictors (ward, priority, time, and day of week) were coded as dichotomous independent variables. EEG result was coded according to Crepeau et al.'s (2013) guidelines. Differences in *time to EEG* associated with categorical predictors were evaluated with Kruskal-Wallis one-way ANOVA.

**Results:** While the indication for EEG was to rule out seizures (90% ICU, 100% inpatient/ED), only 8.5% of cEEGs (ICU 9%, inpatient 8%) and 1% of sEEGs revealed seizure activity. Epileptic discharges were reported in 24% ICU, 21% non-ICU and 8% ED cases. The median (and maximum) *time to EEG* was 2.4 (20) for ICU, 2.8 (26) for inpatient, and 1.5 (23) for ED, and by result was 1.9 (26) for normal, 1.9 (17) for mildly abnormal, 2.6 (21) for moderately abnormal, and 2.2 (24) hours for severely abnormal ( $p = 0.183$ ). Median *time to EEG* was lower by 0.1 for stat requests ( $p = 0.32$ ), 0.8 for studies during work-hours ( $p = 0.01$ ) and 0.9 for studies on weekdays ( $p = 0.05$ ).

**Conclusion:** Our study demonstrates reduced yield and imperfect accessibility of EEG, which together underscore the importance of not only optimizing current hospital routines to greatly improve the utility of the EEG in guiding appropriate therapy, but also devising novel EEG devices that provide faster, point-of-care information about brain function.

p0506

### RELATIONSHIP BETWEEN ICTAL EEG AND NEUROIMAGING FINDINGS IN PATIENTS WITH TEMPORAL LOBE EPILEPSY

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**Purpose:** Classifications of ictal EEG findings in patients with temporal lobe epilepsy (TLE) have been proposed. Recently, neuroimaging studies including 3-tesla MRI and FDG-PET have been widely used for presurgical evaluation. However, the relationship between ictal EEG and neuroimaging findings has not been clarified. This study compared the ictal EEG findings with the suspected etiology/neuropathology based on neuroimaging findings in patients with TLE.

**Method:** This study included 21 patients who had complex partial seizures with electro-clinical diagnosis of TLE (8 men, 12–54 years). All patients underwent long-term video EEG monitoring, 3-tesla MRI, and FDG-PET for presurgical evaluation. The patients were classified into the following 3 groups based on MRI and FDG-PET findings: Group A, hippocampal atrophy (HA) on MRI and temporal hypometabolism (TH) on FDG-PET; Group B, no HA but TH; and Group C, neither HA nor TH. A total of 62 seizures from these patients were retrospectively reviewed and ictal EEG findings assessed during the initial 10 seconds and 10 to 30 seconds after onset.

**Results:** Five of 7 patients in Group A showed temporal rhythmic delta activity during the initial 10 seconds followed by temporal rhythmic theta activity during the 10 to 30 seconds after onset. Five of 7 patients in Group B showed temporal rhythmic alpha-theta activity during the initial 10 seconds evolving to theta-delta activity. Seven patients in Group C presented with various ictal EEG patterns including initial attenuation of background activities.

**Conclusion:** The present study identified characteristic ictal EEG findings corresponding to HA and TH. Rhythmic delta followed by theta activity indicated seizures arising from the hippocampus, especially hippocampal sclerosis. Rhythmic alpha-theta followed by delta activity indicated seizures arising from the neocortex of the temporal lobe, especially focal cortical dysplasia.

#### p0507

### RELATIONSHIP BETWEEN CARDIAC AUTONOMIC DYSREGULATION AND SEIZURE LATERALIZATION IN PATIENTS WITH FOCAL EPILEPSY

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**Purpose:** Heart rate variability (HRV) is an established parameter for the assessment of cardiac autonomic regulation, a balanced parasympathetic-sympathetic autonomic activity. Patients with epilepsy show abnormal HRV during interictal periods, which may correlate with sudden unexpected death in epilepsy (SUDEP). However, the clinical factors associated with abnormal HRV remain unclear, and the relationship between abnormal HRV and seizure lateralization is controversial. This study investigated the effect of seizure lateralization on HRV in patients with focal epilepsy.

**Method:** The present study included 15 patients with focal epilepsy (4 men, aged 16–51 years; 8 left and 7 right) and 11 with non-epileptic seizures (4 men, aged 15–39 years). EKG for HRV analysis, polysomno-

graphic data for sleep stage, and video EEG monitoring for epilepsy diagnosis were retrospectively reviewed. HRV spectra consist of high frequency (HF; 0.15–0.4 Hz) and low frequency (LF; 0.04–0.15 Hz) regions. Analyses were performed for 3 hours of each wakefulness and non-rapid eye movement (NREM) sleep recording.

**Results:** Patients with right hemispheric focal epilepsy showed significantly lower HF power during NREM sleep than non-epileptic patients and patients with left hemispheric focal epilepsy. Patients with left hemispheric focal epilepsy showed significantly higher LF power during NREM sleep than non-epileptic patients.

**Conclusion:** Right hemispheric cerebral infarction showed higher correlation with lower abnormal LF and HF than left hemispheric cerebral infarction. Lower abnormal HF in right hemispheric epilepsy is similar to stroke, but higher abnormal LF in left hemispheric epilepsy is different from stroke. The findings were more complex for focal epilepsy compared to stroke, possible because of the irritative effect of the epileptogenic focus. Notably, these abnormalities only occurred during NREM sleep, which may indicate a relationship with SUDEP, which usually occurs during sleep.

#### p0508

### CLINICAL PRESENTATION ON EPILEPSY VISA VISE BEHAVIOR CHANGE, BY JOAN KAGEMA REGISTERED NURSE KENYATTA NATIONAL HOSPITAL, NAIROBI, KENYA

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**Introduction:** Epilepsy is one of the commonest neurological problems in the world, and one of the oldest conditions known to mankind. The belief held in many countries is that a person with Epilepsy is being possessed by supernatural forces of powers. This has been largely responsible for stigma against persons living with epilepsy. This has widely held belief is incorrect as there is now evidence that seizures are as a result of ABNORMAL ELECTRICAL DISCHARGES in a group of BRAIN CELLS. This is a clinical presentation and scenario whereby EPILEPSY can manifest in an ABNORMAL BEHAVIOR resulting to patients being incarcerated in a psychiatric unit. Most of this abnormal behavior is a symptom or sign of either a seizure will occur. This can be Pre-ictal or Post-ictal phase. Many patients 'will present differently before actual seizures occur.

**Objectives:** · To distinguish behavior change that occurs on, before, and after a seizure or a convulsion in epilepsy.

- To distinguish the pre-ictal and post-ictal behavior, in patients with mental disorder due to epilepsy.
- To analyze the trends and issues of behavior change in epilepsy.

**Conclusion:** What is this syndrome?

New Psychiatric problem?

Is it a new type of seizures?

Could it be side effects of drugs?

#### p0509

### EFFECTS OF HIGH PLASMA ESTRADIOL LEVELS ON EEG

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**Purpose:** Reproductive hormones in women may increase the risk of seizures by lowering the seizure threshold which is especially noteworthy in

the case of catamenial epilepsy. Although it is widely accepted that estrogens have proconvulsant effect, in some studies anticonvulsant activities were also showed. In this study, we aimed to show the effects of estradiol (E2) on electroencephalography (EEG) of the women who receiving IVF (in vitro fertilization) treatment.

**Method:** Two EEG analyses were performed before and at the peak-E2 levels state in a patient group who will receive IVF treatment. Routine EEG recordings according to international 10–20 system were obtained from each patient for about 30 minutes duration. Low and high frequency filters were kept as 0.5 and 70, respectively. Intermittent photic stimulation was carried out at 1-2-8-10-15-18-20-25-40-50-60 flash frequencies. EEG findings were analyzed by a neurologist. First and second EEG results were compared statistically by using Kruskal-Wallis test.

**Results:** Thirteen women between the ages from 25 to 37 (mean 30.7) were enrolled in this study. Basal and peak serum levels of E2 were measured  $53.3 \pm 26.7$  pg/mL and  $2243.2 \pm 1255.9$  pg/mL, respectively. Abnormal EEG findings were reported % 46.2 of the women when the first EEG recorded but this percentage was raised to % 61.6 at the time of the peak-E2 measurement. Slow baseline EEG rhythm and generalized slow wave discharges were the main abnormalities which were observed.

First and second EEG results were compared statistically by using Kruskal-Wallis test.

**Conclusion:** High dose E2 treatment causes slow baseline EEG activities and increases generalized slow wave discharges. These findings might support the hypothesis about estrogens proconvulsant effects.

#### p0511

### SEEG PROPAGATION PATTERNS IN DRUG-RESISTANT TEMPORAL LOBE/TEMPORAL PLUS EPILEPSY AND ITS CORRELATION WITH THE OCCURRENCE OF ORAL AUTOMATISMS

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**Purpose:** The oral automatisms are a common finding in clinical symptomatology of patients with TLE. In the current literature the anatomical correlate resulting in the appearance of the oral automatisms during temporal lobe seizures is not described with invasive studies. We describe the pattern of ictal propagation and the electrodes involved in the appearance of oral automatisms in a survey of patients with temporal lobe/temporal plus epilepsy studied by SEEG in our center.

**Method:** A retrospective study of 19 patients implanted between 2011 and 2014. We removed from the analysis extratemporal patients or those who were implanted with the sole purpose of lateralization of epilepsy because of the insufficient number of electrodes. The pattern of spread was studied with coherence analysis, and a novel set of nonlinear analysis tools including techniques that measure permutation entropy. We analysed whole seizures and seizures up to the event of interest (oral automatisms). We provide network maps of these analyses.

**Results:** Records of 10 patients were analyzed. 9 had oral automatisms. In 8/9 patients these were produced simultaneously to the involvement of the entorhinal cortex in the low region of the frequency domain. The most interesting results come from the analysis of patients who presented seizures with or without oral automatisms. The maps of activation significantly differed between the two types of seizures.

**Conclusion:** Oral automatisms have no lateralization value in temporal lobe epilepsy but imply participation of the mesial region. The involvement of the entorhinal cortex seems to be a relay access point to the subcortical and cortical structures related with the control of alimentary primitive reflexes.

#### p0512

### MEG BEAMFORMER FOR ICTAL FAST ACTIVITY MAPPING: AMPLITUDE VERSUS KURTOSIS

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**Purpose:** Fast ictal oscillations in EEG and MEG are an important marker of ictal onset zone (IOZ). The MEG source localization of this activity, however, is challenging. Synthetic aperture magnetometry (SAM) beamformer has been demonstrated as a promising tool for ictal and interictal MEG source localization.

**Method:** We retrospectively compared the source solutions of two SAM beamformer approaches: absolute amplitude based SAM (SAM (amplitude)) and excess kurtosis based SAM (SAM (g2)), using the fast (filtered by 40 and 130 Hz) ictal MEG signal of two patients with epilepsy. Patient 1 relapsed after previous surgery, but resection specimen contained partially removed focal cortical dysplasia. Therefore, surgical cavity margins were used as an epileptogenic zone marker. In Patient 2 the MEG sources were compared to ictal subdural grid recordings.

**Results:** In patient 1 SAM (g2) demonstrated both preictal and ictal activations at resection cavity margin with incremental time-course (mostly preictal). SAM (amplitude) demonstrated ictal (but not preictal) activation on the same area. The absolute amplitude rose mostly during the ictal stage, simultaneously with excess kurtosis drop. In patient 2 SAM (amplitude) localized preictal and ictal activation maxima contralaterally to the invasively proven IOZ. SAM (g2) localized the preictal maximum anterior to proven IOZ and ictal maximum - to invasively proven IOZ.

**Conclusion:** SAM (amplitude) and SAM (g2) beamformers provide non-redundant information complementing each other in ictal MEG source localization.

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#### p0514

### FRONTAL LOBE EPILEPSY AND ANXIETY: BIDIRECTIONAL RELATIONS / AN ADOLESCENT CASE REPORT

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**Introduction:** Frontal Lobe Epilepsy is the second most frequent type of partial epilepsy and is the disorder that begins in childhood. The relationship between epilepsy and psychiatric disorders, as well as their reciprocal interaction, has been confirmed in many studies. Patients with focal epilepsies have higher incidence of depression, anxiety or psychosis. Here, we report a case of asymmetric motor seizures after anxiety attacks in terms of difficulties to diagnose during follow up.

**Case:** 12 year old boy was admitted with the complaints of 6 years history of episodes that include locking, contraction with anxiety and fear, and there was no response to verbal stimuli during attacks. In the video taken by family, the upward extension of the arms, then flexion of the right arm, lastly, occurring clonic jerks on head and arms was observed

during sleep. Neurological examination and cranial MRI were normal. Synchronous epileptic activity in the midline and right frontocentral regions, and asymmetric generalized discharges were identified on EEG. Carbamazepine treatment, been started at another center, was continued. His mother described that his seizures have decreased but still have tended to occur after intense fear and anxiety. The diagnosis of Generalized Anxiety Disorder, Obsessive Compulsive Disorder, Social Phobia was made following consultation with child psychiatry, and he was referred for cognitive behavioral psychotherapy. Later, his treatment was added antidepressant drug. Fear of contraction started to decline, severity and number of attacks reduced during follow up.

**Conclusion:** The greater prevalence of mood disorders in persons with epilepsy is most probable a reflection of a bidirectional relation between the two issues. The educational and social development of a child with epilepsy depends not only on seizure control but also on cognitive and behavioral factors. Cooperation between disciplines offers the best hope for early diagnosis and treatment of these conditions.

#### p0516

### BRAIN TUBERCULOMAS REVEALED BY EPILEPTIC GENERALIZED SEIZURES AFTER TUBERCULOSTATIC TREATMENT: A CASE REPORT

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**Purpose:** Central nervous system is a rare localization for tuberculosis (TB) compared to other systems, affecting predominantly children and immunosuppressed adults. A paradoxical reaction occurring after completion of appropriate antituberculous therapy, consisting in development of intracranial tuberculomas, is rare and may represent a clinical and radiological challenge.

**Method:** We present the case of a 25 year old man, immunocompetent, previously diagnosed with pulmonary tuberculosis and tuberculous meningitis that successfully underwent antituberculous treatment for 1 year.

**Results:** The brain imagery performed at the time of the diagnosis revealed no intraparenchymal TB lesions. Six months after the tuberculostatic treatment was stopped, the patient presents generalized tonic-clonic seizures. The neurologic examination shows no focal abnormality. The initial cerebral CT scanning without contrast was normal and only after contrast enhancement reveals multiple tuberculomas located both infra and supra-tentorially. The tuberculostatic therapy is reinitiated, conjointly with antiepileptic treatment (levetiracetam), with favorable clinical and radiological outcome at 6 months follow-up interval. We present the EEG record and CT images.

**Conclusion:** Seizures are commonly associated with CNS tuberculomas and most often resolve after successful medical treatment of the underlying CNS tuberculosis. However, these patients should be kept under observation even after completion of anti-tuberculous treatment.

**Keywords:** CNS tuberculomas, epilepsy, tuberculostatic therapy

#### p0517

### EFFECT OF VALPROATE ON THE SLEEP MICROSTRUCTURE OF PATIENTS WITH JUVENILE MYOCLONIC EPILEPSY

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**Introduction:** Studies looking at the effect of epilepsy and/or anti-epileptic medications on the sleep microstructure are sparse. The aim of this study was to compare the sleep microstructural characteristics of drug naïve patients with juvenile myoclonic epilepsy (JME) and those on valproate monotherapy.

**Methods:** This prospective study included subjects who underwent overnight polysomnography (3 subgroups- 20 each): group 1- drug naïve JME (mean age: 21.2 ± 4.06 years; women = 9), group 2 - JME on valproate (mean age: 21.85 ± 4.28 years. women = 11); group 3-controls (mean age: 21.85 ± 4.28 years; women = 9). Scoring and analysis of arousals [ASDA (2002)] and cyclic alternating pattern (CAP) [Terzano et al (2002)] parameters was performed. Kruskal-Wallis test followed by pairwise comparisons [Tukey and Kramer (Nemenyi) test] between 3 groups ( $p \leq 0.05$ ) was done.

**Results:** The arousal indices were comparable among the 3 groups, both during NREM ( $p = 0.607$ ) and REM ( $p = 0.123$ ) sleep. The overall CAP rate was higher in group 1 ( $p < 0.001$ ) and 2 ( $p < 0.001$ ) compared to controls. The CAP cycle and sequence indices were higher in group 2 compared to controls ( $p = 0.012$ ) and group 1 ( $p < 0.001$ ). The duration of CAP cycles/sequences, phase A1 ( $p = 0.042$ ) and A2 ( $p = 0.01$ ) indices were lower in group 1 compared to controls, and similarly, they were also lower in group 1 compared to group 2 ( $p < 0.001$ ). Finally, the phase A1 percentage ( $p = 0.003$ ) was lower and A3 percentage ( $p = 0.045$ ) was higher in group 1 compared to controls.

**Conclusions:** We found significant alterations in several CAP parameters in patients of JME (with and without valproate) compared to controls. Valproate significantly increased the CAP cycling and reduced the duration of CAP cycles and some of the phase A indices suggesting differential influence of valproate on arousal mechanisms of patients with JME, thereby altering the sleep integrity and microstructure.

#### p0518

### ADHD-LIKE BEHAVIOURAL PROFILE IN DOGS WITH IDIOPATHIC EPILEPSY

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**Purpose:** Psychiatric disorders are common comorbidities in human patients with epilepsy, with attention-deficit/hyperactivity disorder (ADHD) one of the most common co-occurring disorders alongside depression and anxiety. ADHD-like behaviours have also been observed in laboratory rat models of epilepsy. Naturally occurring epilepsy in the domestic dog could mirror human epilepsy; however, the behavioural profiles of these dogs have been little studied thus far. The purpose of the study was to examine the behavioural profile of dogs with epilepsy to see if they exhibit ADHD-like symptoms similar to rodent models and humans with epilepsy.

**Method:** Twenty-one dogs diagnosed with epilepsy were fed the same diet consistently for 3 months (as previous studies have shown dietary effects upon ADHD symptoms). Owners completed a validated behavioural questionnaire to measure 11 defined behavioural domains at the end of the study to report their dogs' behaviours in this time period. All dogs were suspected to have idiopathic epilepsy based on an unremarkable MRI scan and CSF analysis; no clinically significant findings on

haematology and biochemistry or dynamic bile acid results; and unremarkable interictal neurological examination. All dogs were receiving anti-epileptic drugs.

**Results:** The three most prominent behavioural factors of the 11 measured were excitability (mean±SD: 1.92 ± 0.57), chasability (1.84 ± 0.97) and attachment/attention seeking (1.30 ± 0.62), mirroring behavioural traits of humans with epilepsy and ADHD. In contrast, the ‘trainability’ behavioural domain was relatively low (0.41 ± 0.57), with two thirds of owners reporting that their dog is ‘always’ easily distracted by interesting sights, sounds and smells.

**Conclusion:** Our data suggests that dogs with actively treated idiopathic epilepsy may exhibit behaviours that mirror ADHD found in children with epilepsy, and rat models of epilepsy, adding further evidence to the notion that there may be common neurobiological mechanisms present in epilepsy and ADHD.

p0519

#### KNOWLEDGE OF EPILEPSY BY CAREGIVERS WORKING IN AN INSTITUTION FOR PEOPLE WITH AN INTELLECTUAL DISABILITY

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**Purpose:** To acquire information regarding the required knowledge with respect to epilepsy according to the guidelines of The Dutch Association of Doctors for Intellectual Disabled (NVAVG) for caregivers, working in an organization for patients with intellectual disability (ID).

**Method:** The guideline of the NVAVG specifically indicates the required information with respect to epilepsy for caregivers working in an organization for patients with ID. To assess whether the knowledge of the caregivers is in line with this guideline, an epilepsy questionnaire was taken among 135 caregivers, working within a care facility in the south-west of the Netherlands. The questionnaire contained 30 “true”, “false” or “don’t know” questions about epilepsy.

**Results:** According to the test the knowledge was adequate in 44 (34%) caregivers. In 53 (40%) caregivers the knowledge was just reasonable and in 34 (26%) caregivers the knowledge was insufficient. Scores were divided in items as described by the NVAVG guidelines. The scores on general items like: “forms of epilepsy”, “anti-epileptic drugs” and were relatively adequate. In contrast, knowledge for example with respect to “seizure types”, “risk factors of epilepsy and precepts” was relatively poor. Caregivers with a nursing background, those working fulltime as well as those who had followed an learning module on epilepsy performed significantly better.

**Conclusion:** We conclude that the knowledge of epilepsy is, according to the guidelines of the NVAVG not sufficient in caregivers working with patients with both ID and epilepsy. Our results suggests that investment in the nursing staff and training of staff might improve the quality of care.

p0520

#### THE ANTI-DEPRESSION EFFECT OF XYLARIA NIGRIPES IN PATIENTS WITH EPILEPSY: A MULTICENTER RANDOMIZED DOUBLE-BLIND STUDY

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**Purpose:** The comorbidity of depression in patients with epilepsy is common and treatment is still controversial. This pilot study was aimed at evaluating the efficacy and safety of *Xylaria nigripes* for treating depressive symptoms in patients with epilepsy during 12 weeks of treatment.

**Method:** A multicenter, double-blind, placebo-controlled, randomized superiority study was performed. A total of 104 patients with epilepsy who fulfilled the study criteria were randomized 1:1 to receive *Xylaria nigripes* (the Wu Ling group) or placebo (the placebo group) treatment in the 12-week period of study. The participants were visited on weeks 0, 2, 4, 8, and 12 of the treatment course.

**Results:** Eighty-one patients finished all of the visits. The primary efficacy endpoint in this study was the total effective rate for depression, which was significantly greater in the Wu Ling group (51.3%, n = 39) than in the placebo group (35.7%, n = 42, 0.51 and 0.36 = 0.15, 95%CI - 0.06-0.37, U = 2.83, P = 0.002) after 12 weeks of treatment. No differences in seizure frequency or changes in severity were found between the Wu Ling and the placebo groups. In addition, the quality of life and seizure worry subscale scores in patients with epilepsy were also improved more notably in the Wu Ling group than in the placebo group (p < 0.05). Most of the adverse effects (AEs) in this study were mild and there were no differences between the Wu Ling and the placebo groups. The reasons for dropout were mostly due to withdrawal of consent or AEs.

**Conclusion:** *Xylaria Nigripes* can alleviate depressive symptoms with 12 weeks treatment and is well tolerated in patients with epilepsy.

p0521

#### UPREGULATED EXPRESSION OF N-METHYL-D-ASPARTATE RECEPTOR NR2B SUBUNIT AND EPILEPSY-ASSOCIATED DEPRESSIVE BEHAVIOURS IN LITHIUM CHLORIDE-PILOCARPINE RAT EPILEPSY MODEL

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**Purpose:** Depression is a common comorbidity in patients with epilepsy with unclear mechanisms. This study is to explore the role of glutamate N-methyl-D-aspartate (NMDA) receptor NR1, NR2A and NR2B subunits in the comorbidity of epilepsy and depression.

**Method:** Lithium chloride (LiCl)-pilocarpine chronic rat epilepsy model was established, and rats were divided into epilepsy with depression (EWD) and epilepsy without depression (EWND) subgroups based on forced swim test. Control Rats were also administered LiCl but used saline instead of pilocarpine. Expression of NMDA receptor NR1, NR2A and NR2B subunits was studied by western blot and immunofluorescence methods.

**Results:** No differences of spontaneous recurrent seizure (SRS) counts and latency were found between EWD and EWND groups. Immobility time (IMT) was significantly greater in EWD group than in EWND group. The number of NeuN positive cells was significantly less in LiCl-Pilocarpine model group than Control group, but had no difference

## Abstracts

between EWD and EWND groups. The ratios of p-NR1/NR1 and p-NR2B/NR2B were significantly greater in the hippocampus in EWD group than in EWND group. Selective blockage of NR2B subunit with ifenprodil could alleviate depressive behaviour of LiCl-pilocarpine rat epilepsy model.

**Conclusion:** In conclusion, NR2B subunit of glutamate NMDA receptor was involved in the pathogenesis of comorbidity of epilepsy and depression, and might be a target for treating epilepsy-associated depression.

p0522

### PROFILING SOCIAL COGNITION IN PEOPLE WITH EPILEPSY: EVIDENCE FOR SHARED MECHANISMS BETWEEN EPILEPSY AND AUTISM SPECTRUM DISORDER

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**Purpose:** We conducted meta-analyses to determine if features of autism spectrum disorder (ASD) are found in people with epilepsy (PWE) without intellectual disability. We also investigated how demographic (age, IQ, sex) and epilepsy-related factors (seizure onset age, frequency, duration, laterality and focus) relate to the expression of ASD features. We hypothesized that phenotypic traits of ASD, such as poor facial emotion recognition (FER) and theory of mind (ToM), would be more common in PWE than healthy controls. We also compared our findings in PWE with findings of relatives of individuals with ASD (ASD-relatives) compared to controls.

**Method:** A systematic search of studies examining FER and ToM in PWE versus controls, and in ASD-relatives versus controls, was conducted across three databases: PubMed, PsycINFO, and Current Contents Connect. Four meta-analyses were conducted to examine objective measures of FER and ToM in PWE and ASD-relatives. Further meta-analyses, ANOVA, and meta-regressions examined the relationship of demographic and epilepsy-related factors to social cognition.

**Results:** Thirty studies of PWE (N = 1434: 77% TLE, 10% extra-TLE, 5% GGE) and 21 of ASD-relatives (N = 1284) were ascertained. FER and ToM were reduced in PWE compared to controls (p < 0.001) whereas only ToM was reduced in ASD-relatives compared to controls (p < 0.001). Effect sizes indicated that ToM was poorer in PWE than ASD-relatives. There were no significant associations between FER and ToM and the demographic or epilepsy-related factors.

**Conclusion:** Overall, social cognition was poorer in PWE and ASD-relatives compared to controls with a more pronounced ToM deficit in PWE than in ASD-relatives. These findings suggest shared mechanisms between epilepsy and ASD, independent of intellectual disability, that provide intriguing insights into the neurobiology of these disorders.

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p0523

### DUPUYTREN'S CONTRACTURE AND PROLONGED TREATMENT WITH PHENOBARBITAL

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**Purpose:** Dupuytren's contracture is a progressive fibrotic condition affecting the palmar and digital fascia, leading to a progressive and irreversible flexion of the fingers. Antiepilepsy drug like Phenobarbital PB have been implicated in the development of Dupuytren's contracture. In our case report on two patients we study the association between prolonged treatment with PB and Dupuytren's contracture.

**Method:** Clinical case report.

**Results:** Case 1: A 45-year old male had a history of cryptogenic epilepsy with generalized seizure. Since the age of 20 years PB at 100 mg/day was used in monotherapy. No others significant risk factors for Dupuytren's contracture. The patient presented palmar fibromatosis of the right hand IV and the left one III, severe extension deficit without pain. PB was substituted by Lamotrigine LTG 50 mg/day. Subsequently a partial aponeurotomy of the hand was performed. Case 2: A 29-year old male had a history of symptomatic epilepsy with focal seizures due to meningitis, was treated since the age of 5 years with PB monotherapy. The palmar fibromatosis occurred after 24 years of drug therapy at dosage 200 mg/day. No history of the risk factors for palmar fibromatosis. Flexion contracture without pain of the right little finger. PB was substituted by Levetiracetam LEV 1500 mg/day. Surgical treatment was performed by partial aponeurotomy.

**Conclusion:** Phenobarbital PB is implicated in palmar fibrosis. Development of Dupuytren's contractures may take longer after initiation of Phenobarbital.

p0524

### LACOSAMIDE TREATMENT FOR PATIENTS WITH DRUG-RESISTANCE EPILEPSY

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**Purpose:** Lacosamide (LCM) is a novel anti-epileptic drug (AED) that enhances the slow inactivation of voltage-gated sodium channels. The aim of this study was to report the first experiences of using LCM in patients with drug-resistance epilepsy in Eskisehir, Turkey. To evaluate the efficacy and safety of lacosamide in 50 patients with uncontrolled seizures.

**Methods:** Thirty of the patients were male and twenty were female. Fifty epileptic patients with different etiologies (patients with Lenox-Gastaut Syndrome, Myoclonic Epilepsy with Ragged Red Fibers, Dandy-Walker Syndrome, Rett Syndrome, sequelae of cerebral palsy, idiopathic generalized epilepsy, operated medullablastoma, encephalomalacic area in the left temporal region, cerebral infarction in the left occipital region, liver embryonal sarcoma operation, gliosis in the left temporal lobe, an autism spectrum disorder, frontal cortical-subcortical hyperintense lesions, frontal cortical dysplasia, a right frontal cortical-subcortical hyperintense lesion, post-traumatic epilepsy, post stroke epilepsy) were included in this report. The seizure types of the patients were generalized tonic-clonic, complex partial, secondary generalised partial seizures and complex partial seizures in accordance with myoclonias in one. Twelve of the patients received 4 AEDs, 18 received 3 AEDs, 12 received 2 AEDs, 8 received 1 AEDs.

**Results:** The mean age of the patients were 29.46 (19–47). The mean duration time for taking LCM was 8.2 months. LCM therapy was started between January 2013–March 2015 in these patients. The seizure frequency and severity were reduced < 50% in 8, >50% in 11 and

50% in 5 patient. Sixteen patients reported complete seizure freedom. No changes were reported in 5 of the patients yet. In four patients, instability, difficulty walking, and blurred vision or dizziness were reported.

**Conclusions:** The results of this study provide preliminary evidence for the efficacy of lacosamide in patients with refractory epilepsy.

#### p0525

### THE EFFECT OF TOPIRAMATE ON CEREBRAL GLUCOSE METABOLISM IN PATIENTS WITH IDIOPATHIC GENERALIZED EPILEPSY

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**Purpose:** The effect of anti-epileptic drugs (AEDs) on global cerebral-glucose metabolism or cerebral blood flow may be associated with their mechanism of action and impact on cognitive performance. Topiramate is well-known AED to deteriorate cognitive and language function in epilepsy patients, but its detail mechanism and related brain metabolism are not clear. To investigate the effects of topiramate on cerebral metabolism, we performed  $^{18}\text{F}$ -fluorodeoxy glucose positron emission tomography (FDG-PET) in patients with drug-naïve idiopathic generalized epilepsy.

**Method:** FDG-PET was performed twice in 23 patients before and after topiramate treatment (M/F = 13/10,  $23.2 \pm 3.5$  years) who had been seizure free for at least 16 weeks. For SPM analysis, paired pre- and linearly transformed post-topiramate FDG-PETs were spatially normalized into a standard PET template, provided in SPM-99, using a 12-parameter affine and a non-linear transformation. Spatially normalized images were then smoothed by convolution by using an isotropic Gaussian kernel with a 14 mm full width at half maximum. The paired *t*-test was used to compare the pre- and post-topiramate PET images.

**Results:** Mean dose of topiramate at the time of post-topiramate FDG-PET scanning was  $244.7 \pm 44.7$  mg/day. SPM analysis showed the significant hypometabolism in the bilateral caudate nuclei, bilateral anterior cingulate gyri, bilateral anterior thalami, corpus callosum, and white matters of both fronto-parietal lobes at a level of false discovery rate  $p < 0.05$  after topiramate administration. No brain region showed post-topiramate hypermetabolism.

**Conclusion:** This study is the first to reveal that topiramate treatment reduces glucose metabolism more in subcortical gray and white matters such as corpus callosum, which may be related to unavoidable side effects such as cognitive decline and naming difficulty observed in patients who have taken topiramate for a long time.

#### p0526

### CLINICAL EXPERIENCE WITH ADJUNCTIVE PERAMPANEL IN ADULT PATIENTS WITH UNCONTROLLED EPILEPSY: A UK AND IRELAND MULTICENTRE STUDY

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**Purpose:** To derive clinically useful information about the efficacy and tolerability of adjunctive treatment with perampanel for refractory epilepsy in an outpatient setting.

**Method:** We pooled retrospective data from the case notes of adult patients with refractory epilepsy that had been prescribed perampanel from 15 hospitals throughout the UK and Ireland.

**Results:** Three hundred and ten patients were included (mean age 40.9, 50% women, 27.7% with learning disability). The mean duration of epilepsy for these patients was 26.7 years (range 2–67 years) and 91.9% were taking two or more anti-epileptic drugs at the time of perampanel initiation. Mean retention time was 6.9 months (range 1 day–22.3 months). The retention rates were 86% at 3 months, 71% at 6 months, 47.6% at 12 months and 27% at 18 months. At the final follow-up a > 50% reduction in seizure frequency was reached in 39.7% of those with tonic-clonic seizures, 52.2% of those with complex partial seizures and 45.8% of those with simple partial seizures. 11 patients (3.5%) became seizure free. Two hundred and nine patients (67.4%) experiences adverse effects and of these 59.3% withdrew treatment due to their effects. The most common were sedation, behaviour/mood disturbance, dizziness, and unsteadiness.

**Conclusion:** Although few patients in this highly refractory population described achieved complete seizure control, perampanel was found to be a safe and effective treatment when used as adjunctive therapy in patients with uncontrolled partial epilepsy.

#### p0528

### EVALUATION OF RETINAL NERVE FIBER LAYER WITH OPTIC COHERENCE TOPOGRAPHY IN PATIENTS USING VIGABATRIN

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**Purpose:** To evaluate the thickness of retinal nerve fiber layer (RNFL) in patients using vigabatrin and to compare the results with healthy control group.

**Method:** The patients who have received vigabatrin for the treatment of epilepsy were included. Inclusion criteria was the absence of eye pathology and the diseases affecting retina. Healthy control group with similar age and sex was constituted. The thickness of RNFL was measured with spectralis optic coherence tomography in all the participants.

**Results:** Mean age was  $32.96 \pm 12.95$  years ranging between 6 and 60. Mean age was  $32.64 \pm 13.69$  in patient group and  $33.33 \pm 12.62$  in control group. There were 13 (50%) males and 13 (50%) females. No significant difference was found in the thickness of temporal and inferior quadrants between two groups ( $p > 0.05$ ). However, significant retinal thinning were observed in nasal and superior quadrants of patient group compared to control group ( $p < 0.01$ ).

**Conclusion:** Optic coherence tomography is a practical noninvasive method without need of patient compatibility and it is useful in the assessment of retina morphologically for the patients using vigabatrin.

p0529

**RELATIONSHIP BETWEEN PERAMPANEL EXPOSURE, SEIZURE OUTCOMES AND TREATMENT-EMERGENT ADVERSE EVENTS (TEAEs) IN PATIENTS WITH PRIMARY GENERALIZED TONIC-CLONIC (PGTC) SEIZURES IN IDIOPATHIC GENERALIZED EPILEPSY (IGE): A RANDOMIZED, DOUBLE-BLIND PHASE III STUDY**

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**Purpose:** Characterize relationships between perampanel exposure, PGTC seizure outcomes, and TEAEs in patients with IGE.

**Method:** Patients aged  $\geq 12$  years with IGE and uncontrolled PGTC seizures received placebo or adjunctive perampanel (Study 332; NCT01393743). Following a 4–8-week Baseline Period, perampanel was up-titrated over 4 weeks (2-mg/week; target dose 8 mg/day, Maintenance 13 weeks). Primary endpoints were percent change in PGTC seizure frequency per 28 days and 50% responder rate. Pharmacokinetic/pharmacodynamic models were used to describe relationships between perampanel exposure and seizure outcomes, and neuropsychiatric TEAEs of special interest (e.g. hostility/aggression-related TEAEs using Standardized MedDRA Queries), in an actual dataset of patients with seizures and pharmacokinetic data.

**Results:** Perampanel reduced PGTC seizure frequency in a log-linear exposure relationship with no time effect (perampanel,  $n = 72$ ; placebo,  $n = 77$ ) versus placebo. During Maintenance, the model predicted PGTC seizure frequency reductions of perampanel 62.3% versus placebo 31.7% for a typical male without concomitant enzyme-inducing AEDs (EIAEDs). Concomitant EIAED treatment reduced probability of responding due to lower perampanel exposure (perampanel 8 mg/day: no EIAEDs 0.85, concomitant carbamazepine 0.80; placebo: 0.39). In the dataset of exposure-safety assessments (perampanel,  $n = 73$ ; placebo,  $n = 78$ ), median perampanel exposure was higher in patients experiencing hostility/aggression-related TEAEs ( $n = 12$ ) than in those without, although concentrations overlapped substantially. High variability in event probability and low patient numbers prevented formal modeling of the exposure-AE incidence relationship.

**Conclusion:** Higher perampanel exposure was associated with greater reduction in average PGTC seizure frequency and probability of responding. Median perampanel exposure was higher in patients experiencing hostility/aggression-related TEAEs versus those without, although concentrations overlapped substantially.

p0530

**CURCUMIN RESIST THE EFFECT OF POST TRAUMATIC EPILEPSY ON MIR-3120 EXPRESSION**

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**Purpose:** Epilepsy is a chronic disorder which is characterized by generation of seizure which occur due to abnormal excessive or synchronous activity of neurons. In post traumatic epilepsy (PTE) seizures are developed because of traumatic head injury. MicroRNAs (miRNA) are evolutionary conserved class of small non-coding RNA which function as post-transcriptional regulators of gene expression by targeting protein-coding mRNAs. So miRNAs can coordinate the expression genes in response to neuronal activity. miR-3120 is a novel brain specific mirror-miRNA of class miR-214 already shown much relation

in cell apoptosis. In this study attempts have been made to find relation of miRNA-3120 with Post traumatic epilepsy. Curcumin is an antioxidant and it have already shown anti-epileptic effects so in this study we will try to observe the effect of dietary curcumin on miR-3120 expression.

**Method:** Intracortical injection of FeCl<sub>3</sub> dissolved in normal saline (5ul, 100 mM/5 min) was injected to the somatosensory region of rat brain. Electrophysiological recordings were done to verify the PTE model. Rats were sacrificed, brain was isolated, microdissected then RNA was isolated from cortex and hippocampus. miRNA expression was quantified by RT-pcr. Bioinformatical Target identification and Comparison of miR-3120 were done. To see the effect of curcumin on this micro-RNA, rats were fed with normal feed mixed with curcumin at a concentration of 1000 ppm.

**Results:** Our EEG recording data confirms our PTE model as the increased burst and Multi unit activity spike count in EEG recording pattern indicates the generation of seizures. Gel pictures shows increase in expression of miR-3120 with progression of epilepsy.

**Conclusion:** RT-pcr data shows that there is a relationship of the micro-RNA with epilepsy as expression of miR-3120 is increasing with progression of epilepsy. Decrease in miR-3120 along with simultaneous decline in epileptic bursts is an indicative of beneficial effect of Curcumin on post-traumatic epileptic seizure.

p0531

**GENERALIZED ELECTROENCEPHALOGRAPHIC FEATURES AND DRUG RESISTANCE IN JUVENILE MYOCLONIC EPILEPSY**

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**Purpose:** Juvenile myoclonic epilepsy (JME) is an idiopathic generalised epilepsy syndrome characterised by myoclonia, absence and generalised tonic-clonic seizures. Ictal and interictal electro-encephalography (EEG) demonstrates fast, generalised, usually irregular wave and spike and polyspike and wave discharge activities. Under appropriate antiepileptic drugs up to 85% of patients become seizure-free. We aimed to search the correlations between EEG asymmetry and treatment response.

**Method:** Thirty patients with JME who had EEG with asymmetrical generalised discharge and 15 patients with JME who had EEG with symmetrical generalised discharge and 15 healthy controls were included. Patients were under the valproate treatment. The demographic and clinical features of patients were noted. The patients were divided into two groups according to their response to antiepileptic drugs.

**Results:** Of the 45 patients with JME, mean age was  $22.89 \pm 6.77$  years, 34 (75.6%) were female. The mean age of 15 participants from control group was  $23.20 \pm 4.72$  and 11 of them (73.3%) were female. Mean VPA dose was  $783.33 \pm 379.14$  mg/day with a range of 250–1500 mg/day. 30 respondents had asymmetric EEG, while 15 respondents had symmetric EEG. Thirteen patients were in pharmacoresistant group. The patients who had asymmetric EEG were more drug resistant and it was statistically significant.

**Conclusion:** There is a subgroup of patients with JME who are drug resistant and the asymmetric EEG features may be associated with drug resistance.

p0532

**PHENOTYPE OPTIMISATION IN EPILEPSY USING AN ELECTRONIC PATIENT RECORD***M. White\**, *M. Fitzsimons†*, *L.M. Slattery‡*, *G.L. Cavalleri‡*, *N. Delanty\*,‡**\*Beaumont Hospital, Division of Neurology, Dublin, Ireland,**†Beaumont Hospital, Department of Medical Physics and Clinical Engineering, Dublin, Ireland, ‡RCSI, MCT, Dublin, Ireland*

**Purpose:** Anti-epileptic drug (AED) side-effects are an important phenotype in gene discovery research. The fidelity of this phenotype is highly dependent on the standards used by individual clinicians when describing a side-effect during clinical documentation at the point of patient care. Electronic patient records (EPR) can play a key role in optimising phenotypes.

**Aim:** To illustrate the role of an epilepsy EPR in optimizing the AED side-effect phenotype.

**Method:** A centrally hosted, secure web-based epilepsy EPR used in epilepsy centres across Ireland was interrogated to anonymously analyse data for 4846 individual patients and 9190 AEDs (i.e. average of 1.8 AEDs per patient). When recording the occurrence of side-effects in association with particular AEDs, EPR users can select from a drop-down list of 15 items, select "other" and enter a free text comment, select "none", or leave the field blank.

**Results:** Taken as a whole, the side-effect field was left blank for 49% of AEDs; "none" was selected for 17%; "other" 9%; Cognitive/behavior 7%; fatigue 6%; 2% each for rash, weight gain; 1% each for weight loss, hyponatraemia, headache, visual symptoms, ataxia, tremor; 0.5% each for insomnia, visual field constriction, hepatotoxicity; Thrombocytopenia and bone marrow suppression were each selected in <0.5%. Examination of the "other" free-text comments showed side-effects such as hair loss, sleep disturbance etc. It was also possible to demonstrate the profile of side effects for each of 34 different AEDs.

**Conclusion:** EPRs facilitate both improved clinical care and the efficient collection and standardization of phenotypes. Opportunities for enhancing the side-effect drop-down categories (e.g. commonly used "other" comments) and for clinician training (e.g. leaving the field blank when "none" intended) were identified. Using the EPR, interrogation of the data was conducted in 30 minutes. The traditional paper-based medical chart could not enable an examination of such a volume of data.

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### Monday, 7th September 2015

p0534

**IMPACT ON QUALITY OF LIFE AND CLINICIAN-RATED GLOBAL IMPROVEMENT WITH ESLICARBAZEPINE ACETATE AS ADD-ON TREATMENT TO ANTIEPILEPTIC MONOTHERAPY IN ADULTS WITH PARTIAL-ONSET SEIZURES**
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**Purpose:** It is important to assess how an antiepileptic drug affects quality of life (QOL), particularly since this may influence treatment compliance. Here we present an analysis from the EPOS (Eslicarbazepine acetate in Partial-Onset Seizures) study of the impact of eslicarbazepine

acetate (ESL) on patient-rated QOL and clinician-rated global improvement. ESL is approved as adjunctive therapy for adults with partial-onset seizures, with or without secondary generalisation. The prospective, non-interventional EPOS study investigated the effectiveness and safety/tolerability of ESL as add-on to antiepileptic monotherapy in clinical practice across eight European countries.

**Method:** EPOS included adults with uncontrolled partial-onset seizures receiving antiepileptic monotherapy, whose clinician had previously and independently decided to initiate ESL add-on therapy. QOL was assessed (at baseline and after 3 and 6 months) using the QOL in Epilepsy Inventory-10 (QOLIE-10) at sites where the QOLIE-10 was used in routine clinical practice and in countries where it was available and validated in the local language. Global improvement was assessed (after 3 and 6 months) using the Clinical Global Impression-Global Improvement scale (CGI-GI).

**Results:** Overall, 219 patients were included in the study (mean age 45.9 years; 57.5% male). Median number of seizures during 3 months prior to baseline was 9.0. Complete QOLIE-10 data were available for 109 patients. Mean QOLIE-10 score decreased from 2.9 (n = 128) at baseline to 2.4 (-14.6%; n = 114) after 3 months and 2.1 (-20.8%; n = 109) after 6 months. The majority of patients were shown to have 'much improved' or 'very much improved' on the CGI-GI after 3 months ('much improved', 49.8%; 'very much improved', 14.9%; n = 211) and 6 months ('much improved', 41.7%; 'very much improved', 33.9%; n = 192).

**Conclusion:** In this open-label, prospective study, ESL as add-on to antiepileptic monotherapy provided beneficial effects on patient-rated QOL and clinician-rated global improvement.

Supported by Eisai

p0535

**USE OF LACOSAMIDE LOADING-DOSE IN THE TREATMENT OF SEIZURE CLUSTERING**
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**Purpose:** In an epileptic patient, seizure clustering is defined by the occurrence of three or more seizures in a day as a changing of the typical seizure pattern; it is a condition where it would be useful an intravenous antiepileptic drug which, moreover, should be continued by oral administration. The aim of this study is to evaluate efficacy and tolerability of lacosamide (LCM) administered with an intravenous loading dose followed by oral intake, in refractory focal epileptic patients with seizure clustering.

**Method:** Prospective open-label study. Inclusion criteria: age 16–65 years; refractory focal epilepsy; seizure clustering. Exclusion criteria: generalized epilepsy; status epilepticus, pregnancy, pseudoseizures. LCM was administered with a first intravenous dose of 200 mg over 15 minutes followed after 12 hours by intravenous dose of 100 mg over 15 minutes. After 24 hours from the first intravenous dose, oral LCM treatment was began at the dose of 100 mg twice daily. Concomitant antiepileptic drugs were maintained unchanged. ECG and EEG recordings were performed before and 24 hours after intravenous LCM dose. Efficacy was evaluated comparing daily seizure frequency 7 days after and before LCM. Tolerability was evaluated reporting adverse effects and changing in P-R interval in ECG recordings.

**Results:** Five patients were included in the study. They were affected by refractory focal epilepsy, two cryptogenic and three symptomatic (one by oligoastrocytoma, two by focal cortical dysplasia). Seizure daily frequencies before and after intravenous lacosamide were respectively: patient1: 7–8 and 7–8; patient2: 4 and 0; patient3: 4–6 and 4–6; patient4: 3 and 1;

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patient5: 3-4 and 0-1. No patients complained adverse effects. No variations in P-R interval were observed comparing ECG recordings. All patients continued LCM oral intake.

**Conclusion:** Our preliminary results suggest LCM loading dose as useful and safe option in the treatment of refractory focal epilepsy with clustering seizures.

p0536

### ESLICARBAZEPINE ACETATE IN REFRACTORY EPILEPSY: EXTENSIVE USE OF VARIOUS POLYTHERAPIES AND CLINICAL EVALUATION OF THE SUGGESTED REFERENCE RANGE

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**Purpose:** Eslicarbazepine acetate (ESL) is used as add-on treatment in patients with focal seizures. Patients with refractory epilepsy often use antiepileptic drugs (AEDs) in polytherapy. Therapeutic drug monitoring (TDM) is useful to optimize clinical efficacy and tolerability, and forms the basis to evaluate the suggested reference range (50–140 mmol/L).

**Methods:** Retrospective data from main laboratories providing TDM of ESL in Norway during 2012–2013 were included. Drug fasting samples at steady state were used. A clinical evaluation of efficacy and tolerability was performed by the treating clinicians and handled anonymously. The study was approved by the Regional Ethics Committee.

**Results:** TDM-data and clinical evaluation were available for 108 patients with refractory epilepsy. The pharmacokinetic variability as measured by concentration/dose-ratios was 10-fold. 44% of the patients had concentrations below the suggested reference range. There were no significant differences between the patients having no effect, some effect, good effect or CNS-related adverse effects with mean concentrations of  $46-59 \pm 21$   $\mu\text{mol/L}$ . This could be due to small subgroups or that clinical efficacy was evaluated at an early, suboptimal stage. 30 patients had tapered ESL; 15 of them due to adverse effects. In 10 of these patients, serum concentrations were available with a mean of  $80 \pm 45$   $\mu\text{mol/L}$ . Seven patients used ESL in monotherapy. 101 patients who used ESL in polytherapy (2–4 AEDs) used 31 different combinations. The most commonly used co-medications were valproate (n = 21), lamotrigine (n = 18), levetiracetam (n = 15) and lacosamide (n = 12).

**Conclusions:** The extensive use of various polytherapies in patients with refractory epilepsy makes it difficult to evaluate the efficacy and tolerability of ESL. Our data indicate however, that many patients respond well to ESL. The suggested reference range for ESL appears to be too high in clinical practice. TDM may be useful to optimize ESL treatment in the individual patient.

p0537

### DRUG-TARGETING OF VOLTAGE-GATED SODIUM CHANNEL SPLICING PROVIDES EFFECTIVE SEIZURE CONTROL

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**Purpose:** Seizure often results from increased neuronal voltage-gated persistent sodium current ( $I_{\text{NaP}}$ ) expression. Whilst many clinically-approved antiepileptic drugs (AEDs) target  $I_{\text{NaP}}$ , none exclusively repress this current without also adversely affecting the transient voltage-gated sodium current ( $I_{\text{NaT}}$ ). The fruitfly, *Drosophila*, has one voltage-gated sodium channel gene (*DmNa<sub>v</sub>*) that is highly homologous to its mammalian counterparts. In *DmNa<sub>v</sub>*, the magnitude of  $I_{\text{NaP}}$  is regulated by alternative splicing of a pair of mutually-exclusive spliced exons, termed K and L. Inclusion of exon L results in a channel with a large  $I_{\text{NaP}}$ , but no change in  $I_{\text{NaT}}$ , compared to when exon K is present. Moreover, expression of exon L is increased in genetic seizure mutants. Conversely, conditions that favour inclusion of exon K effectively ameliorate seizure severity. Manipulation of splicing of mammalian voltage-gated sodium channels may, therefore, represent an attractive route for achieving seizure control.

**Method:** Two luciferase-based mini-genes to report splicing at exon K/L of *DmNa<sub>v</sub>*, were used to screen a *Drosophila* genome-wide dsRNA library in S2R+ cells. Splicing regulators identified from the screen were behaviourally tested by expressing RNAi constructs in two different genetic seizure mutants, *bang-sensitive*<sup>1</sup> and *bang-senseless*<sup>1</sup>.

**Results:** We identify 291 splicing regulators that, on knockdown, favour exon K inclusion. A behavioural screen shows knockdown of 95 of these genes significantly reduce seizure duration. Importantly, inhibition of the protein products of many of these genes is anti-convulsive in *Drosophila*. Many suppress seizure-activity in both genetic seizure mutants, indicative that they are part of well-conserved pathways and may, therefore, be optimal candidates to take forward to mammalian seizure studies.

**Conclusion:** We have developed a new screen to identify compounds with anti-convulsive properties. Based on the similarity between flies and mammals, there is every reason to predict that these compounds will have anti-epileptic properties and may catalyse the development of novel AEDs.

p0539

### MONO AND POLYTHERAPY IN EVERYDAY PRACTICE - OUR EXPERIENCE

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**Purpose:** To evaluate factors which could have an influence on the number of antiepileptic drugs (AEDs) in epilepsy treatment and to correlate the number of AEDs in therapy with disease control.

**Method:** 248 patients with epilepsy were included in the analysis. Inclusion criteria were the diagnosis of epilepsy, good compliance and available brain MRI finding.

**Results:** There is statistically significant difference in the number of AEDs in therapy between patients with good seizure control and non-responders to the AED therapy ( $p < 0.001$ ). Twenty-nine different combinations were used in patients on two AEDs, twenty-seven in patients with three AEDs and fourteen in patients on four AEDs. Patients on four and more AEDs in therapy are all non-responders. In the group of patients with good seizure control the number of AEDs in therapy has no influence on the length of the seizure free period ( $p = 0.11$ ). There is no statistically significant difference between patients with generalised and those with partial seizures as first presentation of the disease and the number of AEDs in the further therapy ( $p = 0.08$ ). Patients experiencing more than one seizure type in their history take more AEDs than those with only one seizure type ( $p < 0.001$ ); they also have shorter seizure free period than those with only one seizure type ( $p = 0.007$ ). Epilepsy etiology has no influence on the number of AEDs in therapy ( $p = 0.94$ ).

**Conclusion:** Initial presentation of the disease and the etiology have no influence on the number of AEDs in therapy while more different seizure

types in patient's history increases the possibility of higher number of AEDs in the further therapy. and lower seizure control.

**p0540**

### MONOTHERAPY EXPERIENCE WITH ESLICARBAZEPINE ACETATE

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**Purpose:** Our purpose was to assess the monotherapy experience with Eslicarbazepine acetate (ESL) in our centre, in terms of safety and efficacy profile.

**Method:** This is a retrospective single-centre 4-year series of cases. All the patients who initiated single treatment with ESL within this period were consecutively included. Follow-up was considered until November '14. Data was collected on demographics, clinical features, adverse events and treatment response, using a standardized data form.

**Results:** We included 77 patients between 11–85 years old, 51% female. Minimum follow-up was 3 months and for a mean period of 17 months. 90% suffered some kind of comorbidity and all of them coursed with partial seizures: at some point of their disease 40% had presented simple partial seizures, 66% complex partial seizures, 46% secondary generalized seizures and 9% partial status. 43% had an active epilepsy being 10% considered drug-resistant. 84% of all patients had tried other AEDs previous to single treatment with ESL. Six-month retention rate was 91%, 87% for 1 year. Around 13% of the whole discontinued monotherapy with ESL: 2% presented some adverse effect, 7% required to add up or change to other AED and 4% did not need AEDs any longer. All the rest (87%) were good responders and keep on being well controlled on ESL monotherapy to present, 84% of which are seizure free.

**Conclusion:** According to our experience, monotherapy with ESL seems to be a good alternative for the treatment of partial epilepsy. However, further studies must be carried out to confirm it.

**p0542**

### PRELIMINARY DATA ON PERAMPANEL ESTABLISHING THE UTILITY OF THE CORNWALL UK INTELLECTUAL DISABILITY (ID) ANTI- EPILEPTIC DRUG (AED) REGISTER USED FOR COLLECTING AND MEASURING OUTCOMES OF LICENSED AEDS IN PATIENTS WITH EPILEPSY (PWE) AND ID

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**Purpose:** To ascertain utility of Cornwall UK ID AED Register focusing on safety of Perampanel in PWE and ID.

**Method:** The Register was set up in 2015 to ascertain safety of licensed AEDs post 2000 in PWE and ID. Ethical approval was received from the National Research Ethics Service UK to collect data for 10 years. Participants are assessed for nature of ID based on GP register and categorised as non-ID, mild, medium or severe. Assessments occur every 3 months on dropout rates, safety profile and AED efficacy outcomes. Data of 21 PWE (ID =15, general = 6) collected in the last 3 months in Cornwall were compared.

**Results:** Non-parametric data testing was conducted using a three way log linear analysis and one-way ANOVA. No significant relationship ( $p < 0.05$ ) emerged between severity of ID/non-ID, side effect profile and discontinuation of Perampanel. However there was a notable lack of numbers for conclusive opinion.

**Conclusion:** 25% of PWE have ID and are at higher risk of various comorbidities. They can respond differently to medications compared with the general population. This has been poorly studied scientifically till date. In the current sample there is no statistical evidence to suggest that Perampanel is more likely to influence side effect severity in PWE with ID than non-ID. Our preliminary data do not raise any concerns of tolerability and efficacy of Perampanel in the population studied. These are early trends and possibly non-conclusive due to lack of numbers but highlight the potential usefulness of the Register long term when larger samples are looked to identify relevant clinical associations in a poorly studied population esp. given the swiftness of recruitment, longitudinal, practical nature of study and availability of national ethics to recruit UK wide. The collection is on-going and the updated results on Perampanel would be presented.

## Drug Therapy 7 Monday, 7th September 2015

**p0544**

### PROMETEO: INTERIM PRELIMINARY ANALYSIS OF A PROSPECTIVE OBSERVATIONAL STUDY TO ASSESS THE TREATMENT EFFECT AFTER INTRODUCTION OF A DIFFERENT AED IN PATIENTS WITH PARTIAL EPILEPSY FULFILLING THE 2010 ILAE CRITERIA OF DRUG-RESISTANT EPILEPSY

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**Purpose:** The recent publication of the ILAE consensus definition of drug-resistant epilepsy (*Epilepsia* 2010;51:1069–77) emphasized the need for prospective, long-term studies to obtain further evidence on the probability of achieving sustained seizure control after failure of successive informative trials of AEDs. This prospective, observational study was designed to assess treatment outcomes in adults with focal epilepsy meeting ILAE criteria of drug-resistance.

**Methods:** Consecutive patients with focal seizures considered drug resistant by the enrolling physician were followed for 18 months to assess treatment outcome after introduction of one or more additional AEDs. Seizure-free patients, who at the 18-month visit required further follow-up to determine outcome, remain in the study for up to an additional 16 months. Appropriate application of ILAE drug-resistance/outcome criteria is being determined by an external Expert Panel. This interim preliminary analysis using the Full Analysis Set (FAS; treatment outcome with the first additional drug introduced) is based on the initial, non-validated classification of pharmacoresistance/outcomes made by the enrolling physician.

**Results:** 1063 patients received an additional AED and were enrolled at 45 sites in Italy from 2011 to 2012. Mean age was 44.4 (SD 14.25) years, mean epilepsy duration was 23.1 (SD 15.2) years, median baseline monthly seizure frequency was 5.0 (range 0–220.0) and median number of previously tried AEDs was 5 (range 0–33). 874 (82.2%) patients completed 18-month follow-up. Of the 1043 patients included in the FAS and evaluated using ILAE outcome criteria, 91 (8.7%) were

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seizure-free, 639 (61.3%) had treatment failure, and 313 (30.0%) were undetermined.

**Conclusion:** This preliminary analysis confirms that most patients considered to be pharmacoresistant by the enrolling physician remain resistant after introducing another AED. However, almost one out of ten patients achieved seizure freedom. Further follow-up after validation of the classified outcomes is needed to better characterize the prognostic features of this population.

UCB Pharma-funded.

## p0545

## ANTIPILEPTIC DRUGS AND WEIGHT CHANGES

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**Purpose:** Weight gain or loss can be a serious side effect of antiepileptic drugs in epileptic patients. In this study, we investigated the weight changes of the body associated with drug treatment.

**Method:** We included patients aged 18 years and over with a diagnosis of epilepsy. We measured their body weights before drug using and 12 months after starting antiepileptic drugs. We calculated the weight difference.

**Results:** Hundred and fifty-three patients were identified in total. Weight gain was seen in 60% of patients on valproat, 32% on carbamazepine, 24% on levetiracetam, 18% on pregabalin. Weight loss was encountered on topiramate and zonisamide treatment, 58% and 41%, respectively.

**Conclusion:** Valproat, carbamazepine, levetiracetam and pregabalin were associated with weight gain, and topiramate and zonisamide with weight loss. Lamotrigine and oxcarbazepine were not associated with any weight change.

## p0547

## PERAMPANEL ADMINISTRATION EXPERIENCE IN TREATMENT OF PATIENTS WITH REFRACTORY FOCAL EPILEPSY

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**Purpose:** To evaluate efficacy and safety of perampanel as adjunctive therapy in combination with other antiepileptic drugs in patients with uncontrolled focal seizures.

**Method:** 11 patients were observed: 4 men and 7 women. Their average age was  $33.45 \pm 6.6$  years. The average duration of the disease -  $19.55 \pm 8.5$  years.

**Results:** Changes in morphological structure of the brain were detected by MRI in 6 (54.55%) patients in the form of mesial sclerosis, and in 1 (9.09%) patient as a cerebrospinal fluid cyst of parietal region, no pathology was identified in 4 (36.36%) patients. Simple partial seizures in combination with complex ones were observed in 2 (18.18%) patients, complex partial seizures in combination with secondary generalized tonicoclonic seizures - in 4 (36.36%) patients, secondary generalized tonicoclonic seizures in combination with simple partial seizures and complex partial seizures - in 5 (45.45%) patients. All patients had a high incidence of seizures: daily - in 3 (27.27%) patients, 1-6 times a week - in 6 (54.54%) patients, 2-4 times a month - in 2 (18.18%) patients. Alongside with perampanel 1 (9.09%) patient received 1 antiepileptic drug; 10 (90.90%) - 2. The combination of perampanel with two antiepileptic

drugs was as follows: oxcarbazepin + levetiracetam - 4 (36.36%), carbamazepine + levetiracetam - 6 (54.55%). The daily dose of perampanel was 4-8 mg/day. Reduction of seizure frequency by more than 50% was achieved in 3 (27.27%) and by <50% in 4 patients (36.36%) and therapy was ineffective in 4 (36.36%) patients. Side effects such as dizziness, drowsiness occurred in 7 (63.64%) patients, but were transient and disappeared after the dose stabilization.

**Conclusion:** As a result of this study high efficacy and safety of perampanel in treatment of drug-resistant epilepsy was established. It is planned to include more patients in the further study.

## p0548

## A DESCRIPTIVE STUDY OF THE EXPERIENCES OF RELATIVES/CARERS WITH THE USE OF BUCCAL MIDAZOLAM IN THE COMMUNITY SETTING

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**Purpose:** Prolonged seizures can increase the risk of status epilepticus which is potentially harmful and life threatening. Buccal midazolam (BM) is recognized as an effective, safe and acceptable form of first-line treatment for prolonged seizures in the pre-hospital setting. The person most commonly responsible for administration of BM is the relative or carer of the person with epilepsy. However there are a limited number of studies in the literature examining the use of BM from the relative/carers perspectives. The purpose of this study is to explore and describe the experiences of relatives/carers with the use of buccal midazolam in the community setting.

**Method:** A qualitative descriptive design was employed. Semi-structured telephone interviews were used for data collection and a total of 16 interviews were undertaken. Data analysis was performed using Colazzi's Data Analysis Framework (1978).

**Results:** Participants reported anxiety and distress when faced with seizures in the community. Many of participants found BM easy to use and effective in stopping seizures. Many reported that BM made them feel safe and reassured and reduced emergency department attendances. However there was a significant lack of awareness of time in relation to the duration of seizures and at what stage BM should be administered. Despite having been informed about BM by clinicians there was a knowledge deficit amongst participants in regards to BM administration, its actions, potential side effects, dosing and seizure response.

**Conclusion:** Dealing with seizures can be a stressful experience with associated negative emotions for the relative/carer. They require comprehensive education on recognition of seizures, appropriate response to seizures and BM administration so that they can manage these situations more effectively. A variety of training methods should be considered to cater for the varying educational needs of relatives/carers as well as supportive documentation such as individualized seizure care plans.

## p0550

## DERMATOLOGIC ADVERSE EFFECTS OF ANTIPILEPTIC DRUGS

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**Purpose:** In patients under antiepileptic medication it is very essential to receive the drug regularly. Common adverse effects may impair patient compliance and require alternative therapies. We investigated the derma-

toxic issues and their frequency in most preferred drugs in our department.

**Method:** We detected 361 epileptic patients' records for skin rash and hair loss complaints in this retrospective analysis. The patients were examined by dermatologists to differ the drug side effects from other etiologies. The most prescribed 4 antiepileptic drugs were incorporated in the study. Patients receiving combined therapy also are taken into account by the state.

**Results:** In our 361 patients including series; usage of valproic acid was present in 221 patients, carbamazepine in 152, levetiracetam in 125 and lamotrigine in 47. Hair loss was determined in 19 (8.59%) patients while skin rash in 1 of 221 patients receiving valproic acid. In carbamazepine group skin rash was present in 6 (3.94%) of 152 patients and no hair loss was observed. 2 (1.6%) of 125 patients using levetiracetam had skin rash and one of them had hair loss. In 4 (8.5%) of 47 patients using lamotrigine skin rash was recorded while only one of them complained about hair loss.

**Conclusion:** Antiepileptic drugs may create skin health or cosmetic problems. Possible dermatological problems in the follow-up of epileptic patients should be kept in mind.

p0551

#### FIRST GENERATION ANTIPILEPTIC DRUGS: EFFECT ON CARDIOVASCULAR RISK MARKERS

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**Purpose:** We aimed to determine whether antiepileptic drugs (AEDs) induce modifications on cardiovascular risk markers.

**Method:** 138 patients receiving first generation AEDs monotherapy (carbamazepine, valproate, phenobarbital) or polytherapy (n = 36) for at least 1 year and 63 matched controls had serum lipid profile, erythrocyte sedimentation rate (ERS), uric acid and carotid intima media thickness (C-IMT) measured.

**Results:** Compared to controls, patients on phenobarbital (n = 25) had total cholesterol significantly higher (p = 0.007, t test), VPA group (n = 22) had significantly lower HDL-c (p = 0.004, t test) and increased uric acid (p = 0.004, t test) and ESR (p = 0.026, t test), polytherapy group had higher ESR (p = 0.01, t-test). No significant difference in lipid profile was observed in carbamazepine (CBZ) and polytherapy group. FB group also had total cholesterol (p = 0.006, chi-square), LDL-cholesterol (p = 0.004, chi-square) and triglycerides (p = 0.055, chi-square) rates above the reference ranges, compared to controls. None of the groups had increased carotid intima-media thickness (C-IMT) compared to controls. Age and duration of therapy had positive correlations to lipid profile and C-IMT.

**Conclusion:** First generation AEDs had different effects on cardiovascular risk markers, even among inducers of P450 system. Our results suggest a need for monitoring serum TC, HDL-cholesterol, LDL-cholesterol and triglycerides specially in aged and in individuals high cardiovascular risk.

p0552

#### OLIGOHYDRISIS: ADVERSE EFFECT OF ZONISAMIDE

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**Purpose:** Zonisamide is classified as a sulfonamide and is characterized having multiple antiepileptic action-mechanisms including inhibiting

carbonic anhydrase, which may lead to the oligohydrosis. The purpose of this study is including the followings:

**(1) to determine the incidence and:** (2) to reveal the risk factor of oligohydrosis-related symptoms in epileptic patients treated with zonisamide.

**Methods:** I prospectively studied 153 patients under 20 ages who was newly diagnosed with epilepsy or referred from other hospitals for controlling a seizure. The patients were treated with zonisamide as a monotherapy or adjuvant therapy. The data was collected by direct interview at least 3 months after taking zonisamide. Facial flushing, lethargy, itching sensation, irritability with hyperthermia, heat sensation and heat intolerance were considered as a oligohydrosis-related symptom.

**Results:** 24.8% of patients were treated by zonisamide as a monotherapy, and the other patients were treated by zonisamide as an adjuvant therapy. The oligohydrosis-related symptoms were observed in 11.1% of patients, and 2% of the patients have stopped taking zonisamide due to the symptoms. The oligohydrosis-related symptoms were observed more frequently in the patients between 15 and 20 years old than younger ages, and more frequently in the patients who had taken topiramate.

**Conclusion:** The frequency was significantly higher than the results from previous studies. Clinicians should monitor the patients who are taking zonisamide regarding the oligohydrosis-related symptoms. Especially, the patients between 15 and 20 years old ages and the patients who have a drug history of topiramate should be observed carefully.

## Epidemiology 2 Monday, 7th September 2015

p0553

#### MORTALITY IN PEOPLE WITH CONVULSIVE EPILEPSY: 12 YEARS OF FOLLOW UP IN A RURAL COMMUNITY IN EAST CHINA

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**Purpose:** Data of long-term mortality risk of epilepsy are rare from resource-poor settings. We conducted a 12 years follow up study to explore the causes of death, mortality risk and related impact factors among people with convulsive epilepsy in a rural community in east China.

**Method:** In 2014, we traced 60 people who had previously diagnosed with convulsive epilepsy in a community-based epidemiological survey in 2002. Putative causes of death for those who died were obtained by verbal autopsy, and recorded according to the International Classification of Diseases. We calculated the proportional mortality ratios (PMRs) and standardized mortality ratios (SMRs) for each age-group and cause. Survival analysis was used to determine risk factors associated with increased mortality.

**Results:** We successfully followed 55 (92%) people with convulsive epilepsy, and obtained 11 death cases, indicating 20% of the case fatality rate. The highest PMRs were for cancer (27%), cerebrovascular disease (18%), diabetes (18%) and chronic obstructive pulmonary disease (18%). The risk of premature death was 2.8 times greater in people with epilepsy than in the general population. Older (50–65 years) people with epilepsy had a high relative mortality risk with SMR 1.7–3.8. A much higher risk (SMR=18) was found in middle aged (40–45 years) people with epilepsy. Age and partial seizure were risk factors for premature death.

**Conclusion:** Our results indicated that among people with chronic epilepsy, the most common causes of death were cancer and geriatric diseases. High mortality risk found in middle aged and older people suggested efficient interventions to protect those people with very long duration of epilepsy.

p0554

### ETIOLOGIC FEATURES AND UTILIZATION OF ANTI-EPILEPTIC DRUGS IN PEOPLE WITH CHRONIC EPILEPSY IN CHINA: REPORT FROM THE EPILEPSY COHORT OF HUASHAN HOSPITAL (ECHO)

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**Purpose:** Chronic epilepsy is estimated to affect more than 2 million people in China. However, data of its clinical characteristics is still lacking in China. In the present study, we summarized the etiologic features and utilization patterns of antiepileptic drugs (AEDs) in people with chronic epilepsy in a tertiary medical center in China.

**Method:** We recruited people with chronic epilepsy treated at the Epilepsy Outpatient Clinic of Huashan Hospital during October 2009 to August 2013. Demographic data, clinical characteristics, AED treatment, epilepsy-associated risk factors and medical history, and results of supplementary examinations of each participant were collected via an interviewer-administered questionnaire and confirmed by the medical records.

**Results:** Among 554 people with chronic epilepsy, 58.0% of them were male, 66.8% had focal seizure, and 29.2% had symptomatic cause. Developmental anomalies of cerebral structure (16.7%) and cerebral trauma (16.7%) shared the leading cause of symptomatic epilepsy among children with epilepsy. While cerebral trauma (29.1%) and cerebrovascular disorder (36.4%) were the most common causes in groups of adults and elderly. Fifty percent of participants were taking AED monotherapy. Proportions of people with idiopathic, cryptogenic and symptomatic epilepsy treated by multitherapy were 35%, 46% and 45.6%, respectively. Valproic acid (VPA) was the most frequently utilized AED as monotherapy (32.7%) and within multitherapy (62.5%).

**Conclusion:** This hospital-based study reported that etiologic features were diverse in different age groups of people with chronic epilepsy. VPA was widely utilized to treat chronic epilepsy in mainland China.

p0556

### MARIJUANA USE BY PATIENTS ADMITTED TO A CANADIAN EPILEPSY MONITORING UNIT

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**Purpose:** In Canada, medical marijuana is legal for epilepsy. We aim to determine the prevalence of marijuana use and assess the perceived effects in intractable epilepsy patients compared to those found not to have epilepsy.

**Method:** Information was collected over 14 months from consecutive adult patients admitted to our Epilepsy Monitoring Unit using a 27 item self-administered questionnaire. Only patients able to give consent for participation were recruited. Readmissions were excluded. Subjects were divided into 2 groups, those with proven epilepsy and those without.

**Results:** 310 patients median age 36 (range 28–49) years, 57% female were studied. Median duration of spells was 9 (range 3–21) years occurring daily or weekly in 49%. Epilepsy was documented in 215, non-epileptic attacks in 76 and unknown in 19. Overall, 56% had tried marijuana. Use over the past year was 38% in epilepsy and 36% in non-epilepsy. Only 6% was government approved. Utilization was daily in 56% of epilepsy users and 32% in non-epilepsy. Estimated mean dose was 1 gm/day. Overall cigarette use was 31%, alcohol 43% and street drugs 3%. In current users, perceived improvement in seizures/spells was 84% in epilepsy and 79% in non-epilepsy. In the 2 groups stress was decreased in 85% and 89%, sleep improved in 79% and 89%, memory/concentration better in 37% and 32% and drug side effects less in 75% and 67%. Perceived effect on seizures/spells correlated with the effect on

stress ( $r = 0.4$ ,  $p < 0.001$ ) Adverse effects of marijuana included impaired memory/concentration 17% and worsening of seizures 3%.

**Conclusion:** Patients investigated for intractable epilepsy use marijuana more than the general population and perceive improved seizure control, lower stress, better sleep and reduced drug side effects. Those with non-epileptic events describe the same effects. Stress reduction contributes to the impact of marijuana on seizures and non-epileptic events in adults.

p0557

### THE PREVALENCE OF SYMPTOMATIC EPILEPSIES AMONG CHILDREN IN TWO LARGE PEDIATRIC NEUROLOGY CENTERS IN POLAND - 2 YEAR PROSPECTIVE STUDY

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**Purpose:** To evaluate the prevalence of symptomatic epilepsies among children and adolescents with epilepsy.

**Method:** All epilepsy patients who entered the Developmental Neurology Departments (In and Outpatients Clinics) in 2 years period between were included in the study and followed prospectively. 1553 children and adolescents with diagnosed and treated epilepsy entered the study. The symptomatic epilepsy group consisted of 703 patients - they presented clear documented etiology. The comparison of type of seizures and treatment effects was performed.

**Results:** The most common type of seizures among symptomatic patients were complex partial seizures and generalized seizures (mainly tonic, myoclonic and atypical absences). There were 64% of patients from symptomatic group who were drug resistant according to proposed definition (Kwan et al. 2010). The comparisons between symptomatic and non-symptomatic group was done. There were significant differences in types of seizures, seizure freedom and number of drugs in therapy.

**Conclusion:** This large population based study shows the differences between the treatment strategies among symptomatic and non-symptomatic groups, in our opinion not always justified and presents the surprisingly high incidence of drug-resistant epilepsies among children and adolescents with symptomatic epilepsies.

p0562

### DETERMINING CHARACTERISTICS OF ACUTE STROKE RELATED WITH EARLY AND LATE ONSET SEIZURES

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**Purpose:** According to International League against Epilepsy, seizures occurring in 2 weeks after stroke are defined as early-onset-post-stroke-seizures (EOPSS). Late-onset-post-stroke-seizures (LOPSS) are the seizures occurring 2 weeks after acute stroke. The aim of the study is to determine characteristics of Acute Stroke related with EOPSS and LOPSS.

**Method:** 150 patient (67 female and 83 male) experiencing post stroke seizures and admitted our clinic between 2006 and 2014 were included in this retrospective study. Patients having intracranial malignancy, subarachnoid hemorrhage, cerebral sinus thrombosis and former epilepsy

were excluded. Patients were grouped in two according to having EOPSS and LOPSS. Characteristics of Acute Stroke according to stroke type, ischemic stroke (136 patient) or hemorrhagic stroke (14 patient), localization of infarction and etiology of acute stroke were determined. EEG findings and other demographic findings were also compared between two groups. Chi-square test and Mann-Whitney-u test were used statistically.

**Results:** Early onset seizures were highly seen with hemorrhagic strokes while late onset seizures highly seen with ischemic stroke ( $p = 0.005$ ). Seizures related to cardio embolic stroke or large artery atherosclerosis related stroke showed significant association with late onset post epileptic seizures ( $p = 0.006$ ). There were no statistically significant differences among gender, EEG findings, hemispheric localization and cortical involvement.

**Conclusion:** Since different pathophysiological mechanism work in EOPSS and LOPSS, both type requires different clinical approach. While EOPSS are related with high risk of mortality, LOPSS are related with high recurrence of the seizures. Determining Characteristics of EOPSS and LOPSS could be helpful to improve right approach to post stroke seizures.

p0563

#### RISK OF MORTALITY AMONG PEOPLE WITH EPILEPSY IN TAIWAN

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**Purpose:** The aim of this study is to estimate the risk of mortality among patients with epilepsy (PWE) in Taiwan and clarify the causes of death in different age groups of PWE, using a nationwide population-base data set.

**Method:** All patients who were newly diagnosed as epilepsy (ICD-9-CM code 345.x) between January 1, 2002 and December 31, 2006 ( $n = 6,005$ ) were selected. Another 6,005 control subjects were randomly selected with adjustment of age, gender and enrolled year. The endpoint of observation is either death of subject or 3 years after the enrolled date. Information on date and cause of death were retrieved from the Taiwan Death Registry. We divide the PWE group into 2 parts by the age of 30 to differentiate the five leading causes of death.

**Results:** There are 1,156 (19.3%) deaths noted in the PWE group and 388 (6.5%) in the controlled group (hazard ratio 3.48, 95% confidence interval 3.10–3.90). In the observation period of 3 years, the median age of death is 73 in PWE group and 77 in control group. The leading causes of death in PWE with age > 30 years are trauma, cerebrovascular disease, diabetes mellitus, pneumonia and liver cirrhosis. The leading causes of death are trauma, malignant brain tumors, epilepsy, sepsis and liver cirrhosis in PWE with age < 30 years.

**Conclusion:** In our study, we concluded that patients with newly diagnosed epilepsy had 3.48 times risk of death than patients without epilepsy. The average age of decease in PWE is 4 years younger. As trauma is the leading cause of death in PWE, the importance of prevention of trauma is indisputable. As for younger PWE, aggressive treatment of epilepsy to reduce seizure attack may improve the survival.

p0564

#### PREVALENCE OF CHILDHOOD EPILEPSY IN SRI LANKA

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**Purpose:** The prevalence of epilepsy in children from the developed countries range between 3.4– 4.0 per 1000. The estimated prevalence of epilepsy in developing countries is much higher. The prevalence of childhood epilepsy in Sri Lankan children is still not known.

**Method:** A two phase survey was performed in a district which has a population of 650,000 and has the most balanced representation of all ethnic groups in the country. A house to house survey was performed for 0–5 year age group and a school-based cross sectional survey was performed for 6–16 age group. Screening was performed using direct interview for household survey and pretested questionnaire for the school survey. Those screened were subsequently evaluated in detail by a paediatric neurologist for classification of broad epilepsy syndromes according to 1989 ILAE classification. Detailed history, review of clinic records, EEGs and neuro-imaging were used to classify the epilepsies.

**Results:** Total of 5090 children (1090 from the community and 4000 from school survey) were screened. Response rates were 100% in the house to house survey, while was only 81% for the school survey. Total number of children screened as having epilepsy was 39 out of which epilepsy was confirmed only in 25 children. Three of the 25 epileptics did not present for detailed evaluation of epilepsy syndrome. Prevalence of epilepsy in the 0–5 year age group was 6.4:1000 while prevalence in 6–16 age group was 5.5:1000. Commonest broad epilepsy syndrome was symptomatic focal epilepsy. Idiopathic generalized epilepsy occurred in 4%, idiopathic focal epilepsy in 8% and symptomatic generalized epilepsy in 8%, transition from one to another in 4%.

**Conclusion:** Overall epilepsy prevalence among Sri Lankan children is 5.8:1000 and was higher in the 0–5 group. Prevalence of epilepsy in Sri Lankan children is higher than that described for children in developed countries.

#### Epilepsy in Severely Resource-restricted Settings Monday, 7th September 2015

p0565

#### HIPPOCAMPAL SUBFIELD VOLUMES IN PHYSIOLOGICAL DÉJÀ VERSUS MESIAL TEMPORAL LOBE EPILEPSY AND SCHIZOPHRENIA

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Using Source-Based Morphometry a significantly less gray matter was recently revealed within a set of cortical (predominantly both-sided hippocampi) and subcortical regions in healthy subjects experiencing déjà vu (DV) when compared to déjà vu non-declarers (Brázdil et al, 2012). Importantly in these regions gray matter (GM) volume was inversely correlated with the frequency of déjà vu. Despite observed GM volume differences mirrored the distribution of GM volume reduction in subjects suffering from mesial temporal lobe epilepsy (MTLE), the pattern of GM differences within hippocampi were distinctive between MTLE and DV (Brázdil et al, 2013). Schizophrenia (SCH) represents another condition in which hippocampal GM volume was found to be significantly decreased (Haukvik et al, 2014). In this study we compared differences in GM volume within distinctive hippocampal subfields (CA1; CA2 + 3; CA4 + DG; Subiculum; Presubiculum) among healthy DV non-declarers ( $N = 26$ ) and healthy DV declarers ( $N = 85$ ), MTLE ( $N = 47$ ) and schizophrenia ( $N = 46$ ) patients alternatively. The images were automatically segmented and registered using SPM8 and its toolbox DARTEL. Local GM volume was corrected with respect to age, gender and total intracranial volume. The decrease of local GM volume across voxels (relatively to the nonDV group) was correlated between DV and

MTLE and between DV and SCH. The results revealed significant correlations between GM volume reduction in DV and SCH as well as DV versus MTLE in the majority of analyzed hippocampal subfields. Importantly GM volume correlations were significantly higher for SCH (than MTLE) within left CA4 + DG, left and right CA2 + 3, and left pre-subiculum. The only significantly higher correlation for MTLE was observed within right subiculum. Our findings reveal common structural features of hippocampal involvement in physiological déjà and both investigated SCH and MTLE.

**p0568**

### INJURIES IN UNTREATED EPILEPSY IN RURAL INDIA: A CROSS-SECTIONAL PARALLEL GROUP STUDY

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**Purpose:** With a treatment gap of up to 90% in some parts of rural India, many patients have frequent generalized seizures. Untreated or inadequately treated epilepsy (UE) patients are at a greater risk of physical injury compared to adequately treated epilepsy (TE) patients. Our study compared injuries in UE and AE patients.

**Method:** In this cross-sectional parallel group observational study UE patients were recruited from the epilepsy clinic on the Lifeline Express, a mobile train hospital serving rural communities while TE patients were recruited from the Neurology Outpatient Department of All India Institute of Medical Sciences, New Delhi. A questionnaire was used to collect information on each patient's seizure frequency, medication and history of injury.

**Results:** We had 106 UE and 149 TE patients. There was no significant difference between the two groups with respect to age at onset, gender and family history of epilepsy. Daily, weekly and monthly seizures were present in 13%, 20% and 35% of the UE patients compared to 6%, 5% and 13% in the TE. Only 6% of UE patients had <1 seizure per year compared to 44% in the TE group. Of the TE patients, 97% were on AEDs where as only 54% of the UE patients reported ongoing AEDs. Injuries were reported by 41 (39%) of the UE and 12 (8%) of the TE patients. Most injuries in both groups were facial injuries and also soft tissue injuries. There was one burn injury in the TE and six in the UE group.

**Conclusions:** UE has multiple implications including the potential to cause serious injuries. The scars and mutilation associated with injuries including burns adds further to the stigma associated with epilepsy.

Acknowledgement: Impact India Foundation and Lifeline Express are acknowledged for the opportunity to work for rural Indian epilepsy patients.

**p0570**

### TRADITIONAL MEANINGS OF EPILEPSY TREATMENT AND THEIR SOCIO-CULTURAL INTERPLAYS IN AYETE, SOUTHWEST NIGERIA: AN INTERPRETIVIST-APPROACH

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**Purpose:** Cultures throughout the world give different meanings to illness. These meanings which determine the culturally-driven healing processes are embedded in symbols and require interpretations. This work uses an interpretivist-approach to explain the traditional meanings of

epilepsy treatment and their sociocultural interplays in Ayete, southwest Nigeria.

**Method:** The study was a mini-ethnographic research in Ayete community, southwest Nigeria. An interpretivist-approach that looked at the way cultures use symbolic meanings to describe and understand health and disease was used. The research design was based on multiple ethnographic case studies explaining each stage of the healing processes within its context. Multiple data collection methods like life history, interview, observation and content analysis provided information on social meanings, symbols, and experiences of participants. The relationship of cultural beliefs and practices in connection with the health and healing processes of people living with epilepsy was described.

**Results:** The study is significant in different respects. First, it narrated the life histories of epileptic patients from childhood to adulthood and the events that changed their life-courses. Secondly, it uses ethnographic techniques to discuss the cultural-dimension of traditional healing from the healers and patients' perspectives, explaining the healing processes which fall outside the current biomedical understanding. Finally, it provides new culturally-driven healing processes on epilepsy for similar sociocultural-settings.

**Conclusion:** Since traditional cultural beliefs regarding causes of illness—spirit aggression, witchcraft, and god's punishments—have effects on psycho physiological processes, including inducing both healing and stress responses cultural explanation of the healing processes that fall outside the current biomedical understanding is needed.

**p0571**

### KNOWLEDGE, ATTITUDE AND REACTIONS TOWARDS EPILEPSY AMONG STUDENTS OF ECONOMICS IN HERAT, AFGHANISTAN

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**Purpose:** We conducted this explorative study on knowledge, attitude and reactions towards epilepsy in Afghanistan, where Islam has to come to terms with shamanistic elements derived from earlier beliefs and practices and the concepts of modern medicine.

**Method:** In order to determine the knowledge of, attitude and reactions towards epilepsy by students at the Faculty of Economics, University of Herat, Afghanistan, we designed a self-administered 23-item questionnaire mainly based on questions used in previous similar studies. We obtained the official permission from the Dean of the Faculty of Economics for our study. Questionnaires in which gender and number of semesters studied so far were not revealed were excluded from the analysis. Also questionnaires in which the item "not familiar with epilepsy" was marked were not included in the analysis. Finally all questionnaires in which the observation of seizure symptoms was stated without having witnessed a seizure were excluded from the analysis.

**Results:** 515 of 520 questionnaires were returned. After excluding questionnaires according to the criteria given above 276 questionnaires (filled out by 208 male and 68 female students) were available for analysis. 9 students (= 3.26%) revealed to have epilepsy themselves. About 50% of the students stated that they had witnessed a seizure. 33.33% thought that a seizure is caused by an abnormal psychic reaction. 15.42% supposed a seizure to be result of jinn possession and another 5.43% considered witchcraft as a possible cause for a seizure. For a relative with epilepsy only 48.9% would recommend to see a doctor. 28.3% would recommend to see an Imam and 9.42% would recommend to see a magician.

**Conclusion:** There are tremendous deficits concerning knowledge, attitude and reactions towards epilepsy in resource poor countries like Afghanistan even in the higher educated population.

p0572

**STARTLE EPILEPSY**

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**Purpose:** Startle epilepsy is characterized with seizures precipitated with sudden, unexpected noise or somatosensory stimulus. This study aimed to describe patients suffering from startle epilepsy.

**Method:** Medical records of 38 patients suffering from startle epilepsy were investigated retrospectively. Clinical and laboratory features of the patients were evaluated.

**Results:** Onset of seizures of 19 males and 19 females patients varied from birth to 28 years. Touching or striking to any part of the body in patients (specially to head in) was the main triggering stimulus. Sudden noise in 6, touching and noise in 13, and drop in 1 patient were the other stimulus. One patient described self induction property. The seizure pattern was different: Secondly Generalized tonic clonic in 16 patients, simple or complex partial in 9, myoclonus in 3. 76.3% of the patients had also spontaneous seizures. Head trauma in 6 patients, birth injury in 8 patients and febrile or nonfebrile convulsion in 8, and a patient had a subdural hematoma surgery at the first month of his life were present in their medical history. Epilepsy history in family was reported in 6 of patients. Neurologic examination revealed mental retardation in 11 and hemiparesis in 7 patients. Neuroimaging (CT and/or MRI) showed generally parietal lesions in 14 patients and was normal in 6. EEG showed pathologic activity in 21 patients, and normal in 9. The response of antiepileptic treatment was followed in 16 patients. In 7 patients seizure frequency was decreased.

**Conclusion:** Startle epilepsy is frequent, symptomatic type of epilepsy. Sensorimotor stimulus is most prominent triggering factor. Seizure patterns shows a wide variety. Neuroimaging and neurological examination reveal pathological finding in majority of patients. Insufficient control of frequent and unexpected seizures is the main reason of poor quality of life.

p0573

**REASONS FOR REFERRAL DELAY AMONGST EPILEPSY SURGERY CANDIDATES IN INDIA - A QUESTIONNAIRE BASED STUDY**

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**Purpose:** India has 500,000 potential epilepsy surgery candidates but < 200 surgeries happen annually. Referral delay contributes to surgical treatment gap and our aim was to identify factors contributing to this.

**Method:** Doctors attending a Neurology conference answered a questionnaire. Questions included respondents' perception of drug resistant epilepsy (DRE) and factors that led to surgical referral of DRE.

**Results:** Responses of neurologists 100/114 were analyzed; 57% were young (practicing for < 10 years) and 78% treated >20 epilepsy patients/month. Epilepsy surgery was available >100 kilometers from the practice of 47% respondents. 'Failed monotherapy' meant patients failing two AED monotherapy trials for 43% respondents and three trials for 57%. For diagnosing DRE, patients should have failed AED combination trials, 87% respondents needing at least 2 and 36% needing 3 failed trials. Knowledge of epileptogenic foci (93%), seizure frequency (89%), patient's willingness for surgery (81%), seizure type (82%), epilepsy duration (80%) and patient's age (67%) were factors

considered before referral. In TLE, 82% respondents referred for surgery only if MRI showed HS and 17% even if MRI was normal. In ETLE, 52% referred if MRI was abnormal and 14% if MRI was normal. Seizure frequency of at least 1 per month had to be present for 88% respondents to consider referral. 85% thought epilepsy surgery was under recommended; 25% had never referred any patient. Factors considered important by neurologists who had referred patients for surgery included serious surgical complications (81%, 30 of 37), seizure freedom (80%, 44 of 56), getting feedback from referral centre (80%, 29 of 37), and opportunity to follow-up patients after surgery (70%, 29 of 41).

**Conclusion:** Educating neurologists about benefits of epilepsy surgery may reduce referral delays. Indications for surgery, criteria for diagnosing DRE and prognostic indicators of good surgical outcomes have to be reiterated.

p0574

**HEALTH CARE UTILIZATION AND OUT-OF-POCKET COSTS OF PEOPLE WITH EPILEPSY IN RURAL SOUTH AFRICA: A CROSS-SECTIONAL SURVEY**

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**Purpose:** Epilepsy is a common neurologic disorder, with 80% of cases found in low- and middle- income countries (LMICs). Studies from high-income countries have found significant economic burden associated with epilepsy, yet few studies from LMICs, where out-of-pocket costs for healthcare are substantial, have explored these costs for outpatient epilepsy care.

**Methods:** Two hundred-fifty people, previously diagnosed with active convulsive epilepsy within an established health and demographic surveillance system in rural South Africa, were administered a questionnaire to assess self-reported health care utilization. We determined patient's out-of-pocket, medical and non-medical costs resulting from epilepsy outpatient consultation and treatment.

**Results:** In the 12-months prior to the study, 132 people with epilepsy (53%) reported consulting for epilepsy at a clinic, 162 (65%) at a hospital and 34 (14%) with traditional healers. Of those with epilepsy, 168 (67%) have consulted both biomedical and traditional caregivers at some time. Direct outpatient, median costs per visit varied significantly ( $p < 0.001$ ) between hospital consultations (2010 International dollar (I\$) 32.82; IQR: I\$22.93-I\$39.56) and clinic consultations (I\$ 12.17; IQR: I\$7.38-I\$20.40). Traditional healer consultations were found to cost I\$52.36 (I\$34.90-87.26) per visit. Annual outpatient, clinic and hospital out-of-pocket costs totaled I\$158.31 (IQR: I\$77.46-\$276.86) or nearly 2% GDP per capita, with 73% of this cost due to time spent traveling to and waiting to be seen by the healthcare worker.

**Conclusions:** South Africans with epilepsy in this rural area practice dual health-seeking behavior, consulting both biomedical and traditional caregivers. Local primary care clinics, which should form the foundation of the South African health care system, are used less often than hospitals for epilepsy consultation. Given efforts to revitalize primary health care in South Africa, interventions aimed at strengthening epilepsy care at primary care clinics by reducing transportation costs and waiting time could substantially reduce the out-of-pocket cost of outpatient epilepsy care.

p0575

**CREUTZFELDT-JAKOB DISEASE: A CASE REPORT WITH TYPICAL EEG AND MRI FINDINGS***M.F. Yetkin, F.F. Erdoğan, S. Ismailoğullari, M. Mirza**Erciyes University Faculty of Medicine, Neurology Department, Kayseri, Turkey*

**Purpose:** Sporadic Creutzfeldt-Jakob (sCJD) disease is a rare neurodegenerative disorder of unknown etiology that causes rapidly progressive dementia with myoclonus, visual disturbances, and cerebellar, pyramidal and extrapyramidal signs. The aim of this study is to report a case of Creutzfeldt - Jakob disease to express clinical presentation and typical EEG and MRI findings.

**Method:** Case report and review of the literature.

**Results:** The patient was a 66-year-old woman who was referred for further investigation for rapidly progressive dementia and ataxia. Three months before admission forgetfulness was started, after a month patient was unable to walk because of lower extremity weakness and cerebellar ataxia. Subsequently generalized asynchronous multifocal myoclonic jerks occurred and finally patient was unable to talk and was unable to recognize her close relatives. Her past medical history was non-contributory. She had not had any previous surgeries, and her family history was not significant. Neurological examination revealed; akinetic mutism, seriously impaired cerebellar tests and weakness in both lower extremities. Her first EEG exhibited just slowing background activity. Diffusion-weighted brain magnetic resonance imaging showed diffuse hyperintensity in bilateral cerebral cortices. With these findings EEG examination was repeated 1 week later on suspicion of sCJD. EEG demonstrated periodic synchronous discharges (PSD). Later on, the protein 14-3-3 in the cerebrospinal fluid came back positive, which supported the diagnosis of CJD. On the basis of history, clinical and laboratory findings, typical brain MRI and EEG changes, diagnosis of sporadic CJD was made.

**Conclusion:** Clinical signs combined with MRI, EEG, and 14-3-3 and/or tau protein determination might be sufficient to diagnose or exclude sCJD but our findings suggest that EEG findings may be subtle or equivocal to diagnose CJD, EEG examination should be repeated on the suspicion of CJD.

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p0576

**PEDIATRIC EPILEPSY SURGERY: A STUDY OF 201 PATIENTS ACROSS 20 YEARS***C. Gunbey\*, B. Bilginer†, K.K. Oğuz‡, E.L. Ergun§, F. Soyomezoglu¶, N. Akalan†, M. Topcu\*, G. Turanlı\*, D. Yalnizoglu\***\*Hacettepe University, Pediatric Neurology, Ankara, Turkey,**†Hacettepe University, Neurosurgery, Ankara, Turkey,**‡Hacettepe University, Radiology, Ankara, Turkey, §Hacettepe**University, Nuclear Medicine, Ankara, Turkey, ¶Hacettepe**University, Pathology, Ankara, Turkey*

**Purpose:** Epilepsy surgery has proved efficacy both for children and adults with medically intractable epilepsy. We analysed pediatric patients who underwent epilepsy surgery in order to analyse the changing patient profile over time.

**Method:** A total of 236 children underwent epilepsy surgery at Hacettepe University Children's Hospital between June 1994-January 2015. We excluded 35 patients who had corpus callosotomy and retrospectively studied the remaining 201 patients.

**Results:** The median age at seizure onset was 36 months (first day of life-14 years), the age at surgery ranged between 2 months-19.8 years, time to surgery after seizure onset ranged between 1 month-15 years. Among 201 patients, 110 (54.7%) patients had temporal lobe resection, 62 (30.8%) had extra-temporal resection and 29 (14.4%) had hemispherectomy/hemispherotomy. Temporal resections showed better seizure outcome than the other surgical techniques. The majority of underlying etiologies were central nervous system (CNS) tumor (23.3%), and developmental abnormalities of the CNS (%22.6). Seventy three patients underwent surgery between 1994 and 2004, and 128 patients between 2005-2015. The patient profile of two decades revealed that age at the time of surgery was significantly younger in the second group, yet age at seizure onset showed no difference. Etiological profile showed that CNS tumors were the leading cause in both groups, however in the second group patients with malformations of cortical development increased significantly.

**Conclusion:** Children with intractable epilepsy who underwent epilepsy surgery at our center increased over time with younger age at the time of surgery. Etiological profile of patients showed that patients with malformations of cortical development increased which might be due to improvement in presurgical evaluation protocols and surgical technique.

p0577

**EPILEPSY SURGERY IN CHILDREN WITH EPILEPSY: A TERTIARY CENTER EXPERIENCE***T. Hirfanoglu\*, A. Seradroglu\*, I. Capraz†, E. Bilir‡, G. Kurt‡, A. Erdem§, M. Ucar¶, A.Y. Oner¶, O. Akdemir\*\*, O. Kapucu\*\*, K. Aydin\*, E. Arhan\***\*Gazi University School of Medicine, Department of Pediatric**Neurology, Ankara, Turkey, †Gazi University School of**Medicine, Department of Neurology, Ankara, Turkey, ‡Gazi**University School of Medicine, Department of Neurosurgery,**Ankara, Turkey, §Ankara University Faculty of Medicine,**Department of Neurosurgery, Ankara, Turkey, ¶Gazi University**School of Medicine, Department of Radiology, Ankara, Turkey,**\*\*Gazi University School of Medicine, Department of Nuclear**Medicine, Ankara, Turkey*

**Purpose:** Epilepsy is one of the most common chronic neurological disorders. Despite many effective AEDs therapies, about 20-30% of patients are not successfully treated and still having harmful seizures especially in terms of quality of life and cognitive functions. As advanced surgical techniques were developed with time, successful and satisfying results are obtained from the epilepsy surgery. The purpose of this study was to evaluate the efficacy of resective surgery in children with focal epilepsy.

**Method:** This study was designed as retrospectively among 48 children aged between 2-18 year old who were evaluated for presurgical work up in Gazi University Department of Pediatric Neurology Pediatric Video EEG Monitorization Unit and then underwent epilepsy surgery. Detailed history, Video EEG, neuroimaging, and postoperative seizure freedom was evaluated.

**Results:** Twenty six (54.1%) patients were girl, 22 (45.8%) patients were boys. While 37 (77%) patient were diagnosed as TLE, 11 (23%) of those were extra TLE depends on electrographic records Twenty patient had hypometabolism in different lobe but predominantly in temporal lobe at PET CT. fMRI was performed to 9 (18.75%) patient. As to pathology, 22 (45.8%) patient had hippocampal sclerosis and second frequent was gliosis (33.3%). 85.4% of patient was seizure free after resective surgery.

**Conclusion:** Resective surgery is one of the effective treatment methods in children with pharmacoresistant epilepsy. Seizure reduction depends of the localization and nature of the lesions. Temporal lobe localization

and hippocampal sclerosis is the best results in terms of seizure freedom. In early life period, resective surgery for appropriate patients reduces the morbidity and increase quality of life. As develop supportive and advanced techniques, deciding the margin of the surgery is easier and confident for physician.

p0578

### INTERICTAL EPILEPTIFORM ACTIVITY ALTERS PERFORMANCE IN MEMORY TASKS

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**Purpose:** We have previously reported that interictal epileptiform activity (IEA) during a memory task causes deficits in performance. The deficits that we have shown were dependent on the location of the IEA in the brain, i.e. whether it occurred bilaterally or ipsilateral/contralateral to the seizure focuses. In addition, the IEA only produced a performance deficit when it occurred during the recognition phase of the experiment. In order to determine whether IEA alters performance in other types memory tasks we have analyzed data collection from free recall and virtual navigation experiments.

**Method:** 78 patients were monitored with intracranial EEG and had depth electrodes implanted either bilaterally or unilaterally in the hippocampus. We analyzed hippocampal EEG that was collected from subjects while they performed free recall or spatial navigation tasks. The EEG was analyzed, and IEA was marked using a custom spike detection algorithm. Each trial for either task was separated into an encoding and retrieval condition to determine the timing specificity of the task.

**Results:** In the free recall task we determined that there was an effect of IEA during word encoding but not during recall. We tested whether the occurrence of IEA during word presentation reduced the likelihood that the word would later be recalled, and compared that probability against a bootleg dataset of shuffled spike times and found a significant effect ( $n = 78$ ,  $p < 0.05$ ). In the virtual navigation task we did not see an effect in performance as measured by percent distance error from the target with IEA in either encoding or retrieval ( $n = 6$ ).

**Conclusion:** We found alterations to task performance in the free recall task when the activity occurred during the encoding phase of the task. Spatial navigation may be less affected by IED, but a greater sample size is needed.

p0579

### SYSTEMATIC REVIEW AND META-ANALYSIS OF MEDICAL VERSUS INVASIVE EPILEPSY THERAPY FOR PATIENTS WITH ARTERIOVENOUS MALFORMATIONS OF THE BRAIN

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**Purpose:** Routine intervention to prevent future hemorrhage for patients with unruptured arteriovenous malformations (AVMs) has been associated with increased short-term risk of stroke and death. We performed a systematic review and meta-analysis to determine if invasive AVM therapy targeted specifically for epilepsy is superior to conservative anti-seizure drug (ASD) only management.

**Method:** We searched Medline, Embase, and Cochrane Central using Medical Subject headings and keywords related to epilepsy and AVMs. We included original research involving observational cohort studies (OCS) or randomized controlled trials (RCTs) comparing

seizure outcomes in those undergoing invasive AVM therapy to those managed only with ASDs. We also compared case series of invasive AVM therapy containing  $\geq 20$  patients (all lacking a conservatively managed ASD only arm) to those derived from controlled OCS and RCTs. Study quality was evaluated and a random-effects model was used to derive a pooled risk ratio (RR) for Engel class I seizure freedom for OCS and RCTs.

**Results:** Of 1865 identified abstracts, 155 were reviewed in full-text. Two OCS ( $n = 106$  patients) met all eligibility criteria. Both were similar with respect to demographics and AVM-related variables, but varied by study quality. The pooled RR of 0.99 (95% CI 0.69–1.43) did not indicate superiority to either approach. Twenty-five case series met eligibility criteria but a meta analysis was not performed due to statistical heterogeneity ( $I^2 = 93.6\%$ ;  $p < 0.001$ ). Seizure freedom in case series ranged from 19% (95% CI 11–30%; stereotactic radiosurgery) to 93% (95% CI 87 to 96%; microsurgery) at last follow-up. These outcomes are comparable to the ASD arms of the two OCS (57% [95% CI 35 to 79%] and 46% [95% CI 26 to 65%]).

**Conclusion:** There is insufficient evidence available to recommend universal invasive AVM management for seizure control. A randomised-controlled trial of interventional *versus* medical management using standardized epilepsy-specific pre-surgical protocols is warranted.

p0580

### LONG-TERM TREATMENT OUTCOME OF CORPUS CALLOSOTOMY IN LENNOX-GASTAUT SYNDROME

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**Purpose:** Lennox-Gastaut syndrome (LGS) is a severe childhood-onset epileptic encephalopathy that causes significant cognitive decline and behavioral problems. The aim of this study is to evaluate the long-term treatment outcome of corpus callosotomy in LGS patients in a single center.

**Method:** We reviewed 78 cases of corpus callosotomy of LGS patients treated at Severance Children's Hospital between 2003 and 2012, with a minimum follow-up of 3 years. All patients failed multiple trials of antiepileptic medication, and had no data clearly indicating the hemisphere of seizure onset.

**Results:** The age of patients at the time of surgery was between 2.9 and 20.7 years ( $8.9 \pm 4.4$  years). Time from seizure onset to surgery ranged from 0.9 to 17.5 years ( $6.3 \pm 3.8$  years). At an average postoperative follow-up of  $6.2 \pm 2.5$  years, 14 patients (17.9%) had no seizures. More than 50% seizure reduction including seizure free were noted in 61 patients (78.2%), who were 23 of 31 (74.2%) patients with atonic seizure, 21 of 25 (84.0%) with tonic seizures and 7 of 9 (77.6%) patients with epileptic spasms. On high-resolution MRI, 49 patients (62.8%) showed normal or mild cerebral atrophy, and others had structural or destructive lesions. Thirteen patients (16.5%) experienced mild postoperative complications that were all transient, and there was no mortality. Seventeen patients showed lateralized epileptiform discharges on long-term moni-

toring electroencephalogram after corpus callosotomy. Among them, 10 patients were performed resective surgery, and 5 patients achieved seizure free via resective surgery.

**Conclusion:** Corpus callosotomy is a safe treatment option for LGS with high expectation of seizure reduction.

**p0581**

**CHANGES IN CENTRAL AUDITORY PROCESSING IN PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY AFTER ANTERIOR TEMPORAL LOBECTOMY WITH AMYGDALOHIPPOCAMPECTOMY**

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**Purpose:** The aim of this study was to investigate the effect of anterior temporal lobectomy with amygdalohippocampectomy (ATL-AH) on central auditory processing (CAP) in patients with mesial temporal lobe epilepsy with hippocampal sclerosis (mTLE-HS), and identify the factors that may contribute to postoperative worsening of CAP.

**Method:** We performed frequency pattern, duration pattern, and dichotic tests before and after epilepsy surgery in 22 patients with normal hearing on pure tone audiometry.

**Results:** While there was no significant difference in CAP scores between preoperative and postoperative tests, there was a strong association between postoperative worsening in right-side dichotic test results and surgery of the language-dominant hemisphere ( $p < 0.05$ ). The probability of decreased performance on the right-side dichotic test after surgery was 7.5 times higher in patients who underwent surgery on the dominant hemisphere than in those who underwent surgery on the non-dominant hemisphere. The association of postoperative worsening in CAP with verbal I.Q., non-verbal I.Q., or side of lobectomy was not significant.

**Conclusion:** Our results suggest that dominant temporal lobectomy in patients with mTLE-HS may worsen postoperative right-side dichotic function on CAP test.

**p0582**

**A MULTIMODAL APPROACH TO ACHIEVE SUPERIOR OUTCOMES IN THE SURGICAL MANAGEMENT OF EXTRATEMPORAL LOBE EPILEPSY (ETLE)**

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**Purpose and objective:** To analyse seizure outcomes in ETLE surgery following a multimodal presurgical and surgical approach beyond the traditional semiology, scalp EEG and MRI.

**Methods:** A prospective study of all patients undergoing surgery for ETLE at Amrita Advanced Epilepsy Centre over a 4 year period (2010–2014) was performed. Patients with medically refractory epilepsy (ILAE criteria of 2 drug failure) were included.

**Results:** Among 90 patients undergoing epilepsy surgery, 21 lesional and 11 nonlesional (20 adults and 12 paediatric) ETLE cases were included. The mean duration of epilepsy was 14.5 years  $\pm$  4.5. Addi-

tional modalities used presurgically were interictal FDG-PET (20), Ictal SPECT (6), 3T MRI (21) and WADA (1). Intracranial EEG (ICEEG) monitoring was performed using subdural and conventional depth electrodes in 14 and Stereo-EEG in 4. Extraoperative electrocortical stimulation mapping of language, sensorimotor, visual and supplementary motor cortex was performed in nine patients. Intraoperative transcranial-MEP and ECOG were used in 11 patients. Surgical procedures were image-guided (3T MRI/PET) resection (15), ICEEG-guided resection (13), hemispherotomy (3), posterior quadrantic disconnections (3), and multiple subpial transection (1). The mean follow up period was 18.5 months  $\pm$  1.5. One year seizure-free outcome (Engel 1a) was achieved for 87% (13/15) of phase 1 discordant and 94% (15/16) of phase 1 concordant patients. Postoperative complications included grade 4 limb paresis in 2 non-hemispherotomy patients (6.7%) and no mortality.

**Conclusion:** Excellent seizure freedom rates with good functional outcome is possible for patients with both lesional and nonlesional focal ETLE when using a multi-modal approach.

**p0583**

**TWO CASES OF EPILEPSY SURGERY VIA SUPRACEREBELLAR TRANSTENTORIAL APPROACH**

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**Purpose:** Lesions in the posterior medial temporal area (PMTA) could be causes of complex partial seizures, due to its proximity to the mesial temporal lobe. It seems difficult to resect epileptogenic area completely since the posterior limit of an operative field secured by anterior approach is around the lateral geniculate ganglion. On the other hand, supracerebellar transtentorial approach (SCTA) is reported to be useful for lesions in more posterior parts. We experienced two cases of epilepsy surgery using SCTA approach, which seems to be unfamiliar to most neurosurgeons. We will present our operative videos and discuss tips, usefulness, and limitations of SCTA. Case 1: 53 y.o. female. The onset was a generalized tonic clonic seizure at age 21. MRI showed a gadolinium-enhanced brain tumor in the right PMTA, which increased in size during a short period. The tumor was resected via SCTA with the operator positioned at the patient's right side. Bridging veins existed in the medial and lateral side, which narrowed the operative field, resulting in a residual lesion. Pathological diagnosis was ganglioglioma. Case 2: 66 y.o. female. Her seizure was characterized as visual hallucination followed by deterioration of consciousness. Weekly seizures continued more than 20 years. MRI showed a cavernous malformation in the right PMTA. Whereas ictal EEG pattern was typical of mesial temporal lobe epilepsy, a limited cortical area including the lesion was considered the epileptic focus based on the seizure semiology. The lesion was completely removed via SCTA with the operator positioned at the patient's left side, which allowed us an enough operative field.

**Conclusion:** Slight modifications in the surgical setup produced a significant difference of the operative field. With careful consideration and appropriate management of the venous sinus, bridging veins and the tentorium, SCTA will provide an optimal operative field for surgery in PMTA.

**p0584**

**RESECTIVE OPERATION COMBINED CORPUS CALLOSOTOMY IN PATIENTS WITH LENNOX-GASTAUT SYNDROME**

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**Purpose:** Lennox-Gastaut syndrome (LGS) in typical medicine intact-able epilepsy. Resective operation can render seizure free in half patients with lesional LGS, but cognitive stagnation and behavioral problem are still seen in most patients. We designed this prospective randomized controlled trial to study the safety and validity for resective operation combined corpus callosotomy for patients with LGS.

**Method:** 198 patients with LGS were enrolled, and 87 of them finished preoperative evaluation. thirty four cases underwent resective operation, including 11 operations in 18 months after evaluations (late resection group), 9 in 2 months after evaluations (early resection group), and 12 early operations combined with aCCT (combined group). Also, 21 patients without FEZ underwent aCCT as exclusive operation (CCT group). The patients' clinical characteristics and surgical outcomes were compared among groups.

**Results:** The patients with FEZ presented higher score of QOL and full-IQ, and age at first seizure than those without FEZ. The scores of QOL and full-IQ in later operation group decreased 5.02 and 4.51 from preoperative evaluation to operation period respectively, and improved 6.38 and 4.04 from operative period to 2 years follow-up after surgery. Percentages of postoperative seizures free were 50% in resection group, 58.3% in combined group, and 14.3% in CCT group at 2 years follow-up. No significant differences were found in seizure control or complication between resective group and combined group, and between early and later resective group. However, patients in combined group showed more improvement of QOL and full-IQ than those in resective groups.

**Conclusion:** Resective operation combined corpus callosotomy is safe and can render improvement of QOL and full-IQ in patients with Lennox-Gastaut syndrome epilepsy and FEZ.

p0585

#### EPILEPSY SURGERY IN SLOVENIA: FOLLOW UP RESULTS AFTER A 10 YEAR EXPERIENCE FROM A CROSS-BORDER COLLABORATION

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**Purpose:** In small countries cross-border collaboration might be an effective way of performing epilepsy surgery. An ongoing collaboration exists between the Department of Neurology at the University Medical Centre in Ljubljana, Slovenia, and the Epilepsy Centre and the Neurosurgical Department at University Hospital in Erlangen, Germany. In order to evaluate the effectiveness of this collaboration we retrospectively reviewed the results.

**Method:** Data were obtained from medical records and from additional follow-up assessment in all patients. We evaluated seizure and medication outcome, psychiatric comorbidity, psychosocial outcome and patient satisfaction. We also conducted postoperative neuropsychological assessment.

**Results:** Between 2001 and 2012 a total of 53 Slovenian adult patients, age 18 to 58 years (mean 34.3 years), with medically intractable epilepsy underwent surgical treatment in Erlangen. Nearly 90% suffered from temporal lobe epilepsy (47% left and 43% right), in 10% extra-temporal lobe epilepsy was diagnosed. We found that 42 (89.4%) patients were free of disabling seizures (Engel Class 1). Complete seizure freedom

(1A) was achieved in 29 (61.2%) patients. Four of the remaining patients still experience occasional auras (1B). An additional two patients were classified as having an Engel 1C outcome. Clinically important level of Cognitive decline after surgery was recorded in 2 (4%) patients, and de novo mood disturbances were mostly of a transient nature in 9 (17%) patients. Surgical treatment did not impact employment status. The majority of patients (89%) felt that the surgical treatment largely fulfilled their expectations.

**Conclusion:** This study demonstrates that despite additional challenges of cross-border collaboration, distant epilepsy surgery can be a very effective way to start epilepsy surgery program. The promising results may be attributed to the careful selection of patient and the high level of professional collaboration between the two centers.

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p0586

#### EPILEPSY SURGERY TRENDS IN SWEDEN 1990 - 2013

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**Purpose:** To improve the understanding of the reasons for the underutilization of epilepsy surgery in patients with drug-resistant focal epilepsy, studies of temporal trends and referral patterns are needed. The aim of this study was to analyse temporal trends in Sweden for all kinds of epilepsy surgery procedures both at national and regional level during the time period 1990–2013.

**Method:** In this study, we analysed data from the prospective and population based Swedish National Epilepsy Surgery Register (SNESUR) focusing on temporal trends for all epilepsy surgery procedures (resective and non-resective) in adults and children annually and in 4-year periods. Among the variables studied are: time from epilepsy diagnosis to presurgical investigation; referring region; MRI pathology; scalp or invasive seizure monitoring; surgical procedure; main histopathological findings.

**Results:** 1495 epilepsy surgery procedures were performed during the time period, 1317 resective and 178 non-resective. The number of surgeries has decreased from up to 90/year the first 4-year period to 50-60/year the last 4-year period. There was a non-significant trend over the years towards slightly shorter epilepsy duration at surgery. During the first three 4-year periods temporal lobe resection (TLR) was by far the most common resection type and hippocampal sclerosis (HS) the most common histopathology. During the last three 4-year periods extratemporal resections have increased in frequency and malformations of cortical development (MCD) have become as common as HS. There are clear-cut differences in the number of operated patients from different regions in Sweden, and these differences remain fairly constant over the years.

**Conclusion:** In Sweden as in other countries fewer patients undergo TLR for HS while extratemporal resections and histopathological diagnoses of MCD have increased. Fewer patients are operated today compared to 20 years ago. There is an important variation in the number of operated patients from different regions in Sweden.

p0588

**CHANGING SPECTRUM OF PAEDIATRIC EPILEPSY SURGERY IN MALAYSIA**

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**Purpose:** To describe the spectrum of surgery performed in children with refractory epilepsy following expansion of the paediatric epilepsy surgery programme in Malaysia in 2012.

**Method:** Review of presurgical and outcome data of 45 children (age range 1.8–18.2, median 11.1 years) who underwent epilepsy surgery following evaluation at the Paediatric Institute, Hospital Kuala Lumpur, Malaysia between June 2012 until February 2015.

**Results:** Presurgical evaluation included brain MRI and video EEG monitoring in all and FDG-PET in 12. EEG was well lateralised in 35 children and showed bilateral abnormalities in 10. MRI showed clear lesions in all except four children. When performed, FDG-PET added localising/ lateralising information in children with no clear lesions (n = 4), bilateral EEG changes (n = 5) or multiple lesions (n = 2). The most common procedure was temporal lobectomy (n = 21), followed by functional disconnection (hemispherotomy in 12 and temporo-parieto-occipital disconnection in 1) and focal resection (n = 11). Intra-operative electrocorticography was performed in six children. Cortical malformations were the most prevalent epileptogenic substrate (n = 22), followed by tumours (n = 11), atrophy/gliosis (n = 7), hippocampal sclerosis (n = 4) and Rasmussen encephalitis (n = 1). One child developed mild post-operative hemiparesis following resection of an adherent uncus tumour. Of those with at least 6 months follow up, 85% are seizure free.

**Conclusion:** Earlier paediatric epilepsy surgery series in Malaysia concentrated on children with clear lesions and concordant EEG findings. Expansion of the epilepsy surgery programme through training and collaboration with established epilepsy surgery centres have allowed more complicated cases to be evaluated and operated.

p0589

**POSTOPERATIVE OUTCOME AFTER EPILEPSY SURGERY IN RESPECT OF KEEPING OR STOPPING OF ANTIPILEPTIC MEDICATION**

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**Purpose:** The postoperative antiepileptic drug (AED) withdrawal remains problematic. The aim of the study is to assess the relation between the keeping or stopping of AEDs after epilepsy surgery and long-term seizure outcome.

**Methods:** A total of 582 adult patients, who underwent presurgical evaluation and epilepsy surgery at the Epilepsy Center, Medical University of Vienna, from 1994 until 2013 were analyzed. We collected data on clinical, imaging and electrophysiological patient characteristics. Only patients with at least 1 year of postoperative follow-up, were included in final analyses.

**Results:** 215 patients did not fulfill inclusion criteria, thus the data of 367 patients were analyzed. 308 patients (83.9%) underwent resection on temporal lobe: 137 patients (37.3%) had selective amygdalohippocampectomy, 119 patients (32.3%) had anteromesial resection and 52 patients (14.1%) underwent resection of epileptogenic tumors localized in temporal lobe. 59 patients (16.1%) had epilepsy surgery due to extratemporal lesional and nonlesional causes. Mean postoperative follow-up time was 110 month (range 12–210 month). Overall 290 patients (79%) achieved an excellent postoperative outcome with Class 1a, 1 and 2 according to ILAE Classification (Wieser et al.). 45 patients had outcome Class 3, 21 patients Class 4 and 11 patients class 5. 68 patients (45%) out of 154 patients who were absolutely seizure free after operation (Class 1a) were off medication, whereas only 28 patients (24%) of 117 with Class 1 and none of 19 patients with Class 2 (only auras). 39 patients (14.3%) out of 271 patients who were on AEDs at the last follow-up visit, had at least once tried to stop the medication, however had to start the treatment after seizure recurrence.

**Conclusion:** AED withdrawal increases the risk of breakthrough seizures after epilepsy surgery, but the seizures are usually well controlled after readministration of medication. Large randomized studies are necessary for validation of the data.

p0591

**POSTERIOR QUADRANTIC SCAR EPILEPSY: EXCELLENT SEIZURE AND COGNITIVE OUTCOMES WITH REGIONAL DISCONNECTIVE SURGERY - A CASE SERIES**

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**Purpose:** Posterior quadrant gliotic scars commonly result from neonatal cerebral injury and can be associated with a progressively refractory focal epilepsy. The electroclinical and imaging features are reviewed and correlated with surgical outcomes.

**Method:** Patients with medically refractory posterior quadrant epilepsy and MRI evidence of unilateral or bilateral peri-calcarine gliosis undergoing posterior quadrant disconnective surgery were retrospectively analysed over a 3 year period.

**Results:** Six patients (age 10–31) finally underwent posterior quadrant disconnective surgery after completion of a phase 1 noninvasive (2) or followed by phase 2 invasive evaluation (4). Two were left-handed, one ambidextrous. The average age of onset of seizures was 2 years (range 3 months to 6 years). A visual aura was present in two (33%), four (67%) had lateralizing features in the motor component of the seizures, and four patients (67%) had preoperative homonymous hemianopia which lateralized concordantly with the electroclinical and imaging features. Interictal epileptiform discharges correctly lateralized in five (83%) and scalp EEG ictal rhythms lateralized in 5 (83%). MRI revealed peri-calcarine cortical volume reduction and gliosis - bilateral in 3 (50%) and unilateral in the remaining. Following posterior quadrant disconnective disconnection, all patients had Engel 1a seizure freedom on follow-up ranging from 3 to 19 months. Complete neuropsychological evaluation showed preoperative performance IQ 50–72, and postoperative assessment at 6–12 months showed improved scores in all patients. Transient neurological deficits were noted in language function (1 - ambidextrous) and motor weakness (1), but no long term deficits. One patient with bilateral imaging findings and visual field defects preoperatively, suffered from visual agnosia.

**Conclusion:** Parieto-occipital gliotic scar epilepsy represents an important clinical syndrome frequently refractory to medications. Posterior quadrantic disconnective surgery results in excellent seizure and cognitive outcomes. Further standardization of the electroclinical and imaging-based selection of patients for surgical intervention is warranted.

p0594

### MESIAL TEMPORAL LOBE EPILEPSY SYNDROME: CAN AND SHOULD WE DISTINGUISH IT BECAUSE OF SURGICAL OUTCOME?

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**Purpose:** Mesial temporal lobe epilepsy syndrome (MTLE) with specific electroclinical characteristics and hippocampal sclerosis (HS) on MRI is considered the prototype of syndromes with good surgical prognosis. Recent studies, however, question its status as a sharply delineated syndrome suited for surgery. Ictal onset zones have been found outside the hippocampus. Temporal lobe (“plus”) epilepsies (TLEs), due to a lesion or dual pathology, may imitate MTLE electroclinically and may also be associated with a similar surgical prognosis. We compared MTLE with HS with these lesional TLEs and assessed if the MTLE characteristics influenced surgical outcome.

**Method:** We performed a retrospective cohort study including 389 persons with temporal MRI abnormalities who underwent temporal lobe resection, and divided them into “HS only” or “lesional” TLE. We assessed surgical outcome and fulfillment of the MTLE criteria in both groups. We defined MTLE according to 9 electroclinical criteria, adapted from Engel.

**Results:** 57% patients had ‘HS only’. Five electroclinical signs (age at onset, febrile seizures, memory dysfunction, auras and contralateral dystonic posturing) distinguished ‘HS only’ from ‘lesional’ TLE. Freedom of disabling seizures (Engel class I) rates after surgery were similar; 66% in ‘HS only’ and 67% in ‘lesional’ TLE. Neither presence of HS, nor electroclinical criteria were associated with surgical outcome.

**Conclusion:** Our findings support the idea that MTLE is not a sharply delineated syndrome but more likely to be part of a larger spectrum of temporal lobe or temporal ‘plus’ epilepsies with similar characteristics and outcomes. MTLE with ‘HS only’ does not stand out from ‘lesional’ TLEs with respect to surgical outcome, questioning the prognostic relevance of discerning this syndrome.

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p0595

### A PROPOSED NEW PROTOCOL OF COMPLICATIONS IN EPILEPSY SURGERY AND INVASIVE DIAGNOSTIC PROCEDURES

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**Purpose:** Much work is presently being done to increase safety and promote good outcome of epilepsy surgery worldwide. Both epilepsy surgery and invasive diagnostic procedures (including Wada test) carry a risk for serious complications, including permanent neurological morbidity or even death. A number of studies and reviews deal with this subject. However, definitions and classifications of complications vary markedly between studies. Furthermore, since many complications are rare, multi-center studies are needed to collect the number of patients necessary for analyzing risk factors. The aim of this study is to propose a uniform and evidence-based protocol for prospective reporting of complications in epilepsy surgery and in invasive diagnostic procedures.

**Method:** Based on the literature, a first version of the protocol was developed by the present authors. The feasibility of web-based systems to increase the speed and ease of entering data has been of fundamental importance in the design of the protocol. The protocol was then discussed within the E-epilepsy consortium (an EU-funded project with the title: A European pilot network of reference centres in refractory epilepsy and epilepsy surgery) and within the ILAE Commission on Surgical Therapies, and thereafter revised and endorsed.

**Results:** Separate protocols are proposed for invasive diagnostic procedures and for epilepsy surgery. For both invasive diagnostic procedures and epilepsy surgery, technical details of the procedure are specified. All complications are registered in a multiple-choice fashion. Furthermore, it is specified whether a complication has any patient-related impact (e.g. unplanned surgery, or prolongation of hospital stay), if it results in permanent morbidity, and, if so, whether activities of daily life are affected.

**Conclusion:** A protocol for multi-axial reporting of complications has been developed and has been endorsed by the E-epilepsy consortium and by the ILAE Commission on Surgical Therapies. The structure of the final protocol will be presented.

p0596

### EFFICACY OF INTRA-OPERATIVE ELECTROCORTICOGRAPHY IN TERMS OF SEIZURE OUTCOMES IN FOCAL EPILEPSY

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**Introduction:** Intra-operative electrocorticography (ECoG) is a useful tool to guide surgical resection of both the lesion and epileptogenic zone (EZ). The outcome of epilepsy surgery becomes clear only after serial follow up, incomplete removal of EZ as a main cause for early relapses. In this study, we evaluated the efficacy of ECoG on post-operative seizure outcome in patients with focal epilepsy.

**Methods:** The present study reviewed 68 patient (33 females, mean age: 26.01 years) ECoG recordings data from April 2009 till January 2015 performed at our center. The study included 63 focal epilepsy patients, who had been surgically treated. Inclusion criteria for this series included only those cases with concordance seen on video-EEG, MRI, PET and neuropsychological test results. The ECoG recordings were performed 32-channel machine. Recording from neocortical surfaces were usually performed by using a different size grids and/or strips electrodes. Recording from deep structures like hippocampus were usually performed by using a depth and/or strip electrodes.

**Results:** Intraoperative ECoG recording before resection demonstrated frequent epileptiform discharges in all patients. If significant abnormal

activity was still recorded from the margins, further resection was performed. In terms of functional cortical areas some resections were not completed even if the existence of residual spiking. 11 patient have Class II or III seizure freedom and the remaining all patients have Class I seizure freedom.

**Discussion:** In this observational study, we found the main determinant of seizure freedom is underlying etiology. Although the numbers are small in respect to meaningful comparison between the groups, the seizure recurrence mainly occurred in grade-II or higher-grade glial tumor patients. Especially in the mesial temporal sclerosis, cavernoma and cortical dysplasia group we had very high seizure free rates. Our results show that sequential ECoG recordings guided surgical resections has an additional beneficial effect on good seizure outcomes.

**p0599**

#### THE SPATIAL RELATION BETWEEN EARLY AND DELAYED RESPONSES EVOKED BY SINGLE PULSE ELECTRICAL STIMULATION IN PRE-SURGICAL EVALUATION OF EPILEPSY PATIENTS

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**Purpose:** Single pulse electrical stimulation (SPES) assists delineating epileptogenic tissue during long-term intracranial monitoring for pre-surgical evaluation. The SPES protocol consists of systematic stimulation of neighboring electrode pairs and analysis of responses in all other electrodes. SPES evokes early (ER) and delayed (DR) responses. DRs occur in epileptogenic tissue, but are stochastic: 10 stimuli are needed to reliably establish a response. ERs occur in healthy and diseased tissue and require only a single stimulus. We studied the spatial relation between ERs and DRs. If it is possible to predict DRs from ERs, this might improve the efficiency of SPES.

**Method:** Data of one patient with TLE recorded in 84 grid electrodes were used. We counted per electrode the number of stimulus pairs that evoked ERs (eER) and per stimulus pair the number of ERs that were evoked (sER). Similarly, for DRs, eDR and sDR were determined. Also, per electrode we counted the number of stimulus pairs that evoked both ERs and DRs, eERDR and vice versa for sERDR. We selected electrodes with eER or sER > median as eER50 or sER50. We tested whether values for eDR and sDR were significantly more in the eER50 and sER50 groups. Finally we tested whether the ratios eERDR/eDR and sERDR/sDR differed significantly from 0.5.

**Results:** eER values ranged from 0 to 41, median=8; sER:3-27, median=17; eDR:0-28, median=17 and sDR:0-26, median=9. eDR and sDR values were higher in eER50 ( $p < 0.001$ ) and sER50 ( $p = 0.1$ ) electrodes. The ratios of eERDR/eDR and sERDR/sDR ranged from 0 to 1, median=0.24 and 0–0.64, median=0.25 respectively, with the average significantly lower than 0.5 ( $p < 0.001$ ).

**Conclusion:** The correlation between eER50 electrodes and high values of eDR indicates that ERs and DRs seem to occur within the same network. The low ratio eERDR/eDR suggests that ERs and DRs are not directly related. We will analyze more patients to confirm these findings.

**p0600**

#### LONG-TERM OUTCOME AFTER HEMISPHERECTOMY IN CHILDHOOD

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**Purpose:** To assess cognitive, behavioural and psychosocial outcome as well as health-related quality of life (HrQoL) at least 5 years after hemispherectomy in childhood.

**Method:** We performed a countrywide cohort study of 31 patients who underwent hemispherectomy between 1994 and 2009, in whom we had a semi-structured interview with parents, assessed cognitive outcome (using intelligence or developmental scales), screened for behavioural and psychosocial problems [parents rated the Strength and Difficulties Questionnaire (SDQ)], and addressed HrQoL [Euro-qol-5D, a questionnaire that inventories overall and specific HrQoL (mobility, self-care, usual activities, pain/discomfort and anxiety/depression)].

**Results:** Exploration of the data compelled the formation of three groups: a) 9 children [median age 9.7 years (0.25 at epilepsy onset, 1.4 at hemispherectomy)] who could not be assessed with age-appropriate instruments, b) 14 school-age children [all younger than 18 years (median age 0.3 at epilepsy onset and 2.6 at hemispherectomy); median IQ 62], and c) 8 young adults [18 years or older (median age at epilepsy onset 1.2 and at hemispherectomy 9.9); median IQ 63]. All children in group a) were severely mentally retarded and almost totally dependent on others in activities of daily living. This group had the highest proportions of preoperative contralateral MRI-abnormalities, postoperative seizure recurrence and behavioural and psychosocial problems, compared to both other groups. Most parents rated overall HrQoL positively. In group a), overall HrQoL was better in seizure-free participants than in those with seizure recurrence. As for specific HrQoL, parents perceived most problems with respect to self-care, daily activities and mobility. Most important perceived changes after the hemispherectomy were according to parents' seizure freedom and/or restart of development.

**Conclusion:** Functional long-term outcome of childhood hemispherectomy is best described in terms of a broad spectrum, varying from almost total dependence to more or less unproblematic cognitive, behavioural and psychosocial functioning.

**p0602**

#### COULD HISTOPATHOLOGICAL FINDINGS IN SURGICALLY TREATED MESIAL TEMPORAL LOBE EPILEPSY INFLUENCE THE SEIZURE OUTCOME?

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**Purpose:** Surgery represents the treatment of choice for mesio-temporal lobe (MTLE) drug resistant epilepsy. Patients undergo extensive pre-surgical evaluation for surgical planning and outcome prediction. Evidence of mesial temporal sclerosis (MTS) is considered a prognostic indicator of good surgical outcome. Several studies identified other pre-surgical favorable prognostic factors that will be discussed. Despite of electroclinical, neuroradiological and neuropsychological concordance and positive prognostic factors, post-surgical seizures recurrences may occur. We suggest that recent neuropathological classification according to Blumke et Al of MTS (type 1 and type 2) and granule cell pathology (GCP, 3 different patterns) could represent another predict-

ing factor explaining unexpected seizure recurrences and neuropsychological outcome.

**Method:** We describe 34 consecutive patients (19 females and 15 males) presenting with MTLE and magnetic resonance concordant MTS finding. After non invasive extensive pre-surgical evaluation, they underwent tailored antero-mesial temporal lobe resection between 2001 and 2012. MTS was always pathologically confirmed. Mean follow-up after surgery is 7.9 years. Seizure outcome was separately correlated either with pathological findings according to Blumke classification or with the predicting pre-surgical factors.

**Results:** 29 patients (82.85%) are on Engel class I (15 pts=Ia; 2 pts=Ib; 5 pts=Ic; 7 pts=Id); 5 pts on class II. 27 pts are still on simplified anti epileptic drugs treatment. Best results were achieved in patients with MTS type 1 associated with GDC type 1 or 2. Lack of GDC seems related to seizures recurrence after drugs withdrawal. Recurrence of seizures mainly occurred in patients with MTS 2 and lack of GDC, despite of a number of positive pre-surgical prognostic factors and concordance in pre-surgical data.

**Conclusion:** Pathological substrate seems to be taken in account as an important element for seizures recurrence and consequent decision about drug withdrawal following surgery for intractable TLE. Neuropsychological outcome according to neuropathological findings is still on evaluation.

#### p0603

### SURGICAL OUTCOME IN TEMPORAL LOBE EPILEPSY: COMPARISON OF SELECTIVE AMYGDALA-HIPPOCAMPECTOMY VS. ANTERIOR TEMPORAL LOBE RESECTION

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**Purpose:** Epilepsy surgery is a favorable option for patients with medically refractory temporal lobe epilepsy (TLE). There is still controversy about advantages of selective amygdala-hippocampectomy (SAHE) over standard 2/3 resection of the temporal lobe. Therefore we evaluated the postoperative outcome in TLE patients at the Medical University Innsbruck.

**Method:** We retrospectively analyzed data of patients operated in our epilepsy center between 1999 and 2014. Outcome and morbidity after SAHE and standard resection respectively was compared.

**Results:** 210 patients (101 male; 100 right) had surgery in the temporal lobe, 89 (42%) SAHE (group I), 62 (30%) standard 2/3 resection (group II), 59 (28%) other. Outcome Engel IA in group I was 52% after 5 years (n = 65), 47% after 10 years (n = 43); in group II 44% after 5 years (n = 43), 30% after 10 years (n = 10). Four patients not seizure free after SAHE had then standard resection. Histology showed mesial temporal sclerosis in 67/89 pt. in group I and 32/63 pt. in group II. For those pts. outcome (5 ys FU) was Engel IA in 53% of group I and 61% of group II. Complications were rare in both groups.

**Conclusion:** Both, SAHE and standard temporal lobe resection lead to a comparable favorable postoperative outcome. Patients should be selected for one procedure according to all findings of an extensive preoperative workup.

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#### p0604

### FOCAL EPILEPSY WITH AUDITORY FEATURES: A NOVEL GEFS+ PHENOTYPE

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**Purpose:** To identify the mutation underlying ADEAF in a family negative for *LGII* mutations.

**Method:** All ten affected family members underwent clinical investigation, including comprehensive neurophysiological assessment in three. Whole exome sequencing (WES) analysis was performed on the proband and her affected daughter.

**Results:** Of the ten patients (M/F:3/7; mean age at onset: 4.5 years), seven had epilepsy whilst three had isolated febrile seizures (FS). The proband and her daughter had focal epilepsy with auditory features (EAF). Among the other patients, one had another type of focal epilepsy, three generalized seizures in childhood and one infantile epileptic encephalopathy. Intellectual disability (ID) and/or psychiatric disorders were reported in five family members. Three of the family members with epilepsy had a history of prolonged FS. Interictal EEG in four subjects showed generalized spike-wave discharges, which coexisted with clear-cut focal epileptiform abnormalities in the proband. Neuroradiological findings were unremarkable. WES disclosed a p. M956T mutation in *SCN1A*, encoding the voltage-gated sodium channel 1 (Nav1.1). Screening of 15 familial and sporadic EAF patients revealed a different p. Tyr790Phe mutation in a sporadic case with typical phenotype and no antecedent FS. Supporting the causality of both mutations, the wild-type residues are evolutionarily conserved, the changes are predicted as pathogenic and the mutations have previously been implicated in different epilepsy phenotypes.

**Conclusion:** We describe missense pathogenic mutations in *SCN1A* in association with EAF. These findings show that *SCN1A* should be considered in the screening of *LGII*-negative EAF patients and that mutations in major genes other than *LGII* can be associated with familial and sporadic EAF characterized by both atypical and typical phenotypes.

#### p0605

### CLINICAL AND GENETICAL FEATURES OF DYSSYNERGIA CEREBELLARIS MYOCLONICA

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**Purpose:** To investigate the clinical and genetical features of two Chinese families with Dyssynergia Cerebellaris Myoclonica.

**Method:** All the clinical information was collected based on the members of the families, patients' onset age, symptoms, signs and

auxiliary examinations. Pedigree charts of the two families were finished.

**Results:** The proband of family category I was female aged 9. When she was 4 years old, she was unable to walk steadily as ordinary people. She signaled unusual actions like swing of her upper limbs. Gradually, kinetic tremulous movements of her hands happened and the burst-like speech emerged. Intelligence was normal. Cerebellar language, cerebellar ataxia and horizontal nystagmus of both eye balls were positive. Muscle strength and muscle tension were normal. There was no sensory impairment. Limb tendons exhibited hyperreflexia and pathological signs were negative. Brain MR scan showed nothing abnormal except slightly widened cerebral sulcus. Evoked potentials and bilateral TSEP were normal. EEG demonstrated atypical multiple spike and slow wave bursts. Dyssynergia Cerebellaris Myoclonica was diagnosed. The results of treatment was poor. The proband of family category II was male aged 54. Since his age at 20, he complained of hand tremor when reaching the goal subjects with the jerk of the limbs. He developed the burst-like speech at the age of 45. The examinations and the diagnosis were alike as the proband of family category I. The pedigree of family category I and category II included 16 patients (M/F: 9/7) and 5 patients (M/F: 2/3) respectively. All members are non-consanguineous marriage. All the patients are ataxia and myoclonus onset without tonic clonic seizure or cognitive impairment.

**Conclusions:** DCM is transmitted as an autosomal dominant trait. The main clinical features of DCM are ataxia and myoclonus without tonic clonic seizure or cognitive impairment. The pathogenic gene identification will be tested by the Second Generation Sequencing approaches.

#### p0606

### ADVANTAGES OF WHOLE EXOME SEQUENCING FOR PATIENTS WITH EPILEPSY

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**Purpose:** Approximately one third of patients with epilepsy do not have a known etiology, despite extensive evaluations. Some patients have syndromes unique to the patient or the family. Whole exome sequencing (WES) analyzes the exons or coding regions of thousands of genes simultaneously using next-generation sequencing techniques. There are approximately 180,000 exons in the human genome, which represents about 3% of the genome. These 180,000 exons are arranged in about 22,000 genes. WES includes a mitochondrial genome sequencing. It has been commercially available since 2011 and provides a diagnosis in about 30% of previously undiagnosed cases. It identifies those variants found in the coding region of genes which affect protein function. It allows identification of novel gene mutations that could be causative for the patient's epilepsy.

**Method:** Patients with unique or rare syndromes diagnosed via whole exome sequencing were identified through a single center comprehensive epilepsy program.

**Results:** Five patients were identified with rare or novel genetic causes for epilepsy including: a novel homozygous mutation in MTFMT, a female with a KIAA 2022 mutation, a patient with an SLC35A2 mutation, a PCDH19 mosaicism mutation in a male, and two half-brothers with a UPF3B mutation. An epilepsy panel (Athena) sequences 141 genes. Whole exome sequencing covers approximately 22,000 genes.

**Conclusion:** Whole exome sequencing is a useful tool in identifying rare and novel mutations that would otherwise not be identified through single gene or gene panel testing. It is a potentially cost effective measure that should be considered early when there is a question of a genetic etiology for patients with epilepsy or when the etiology of the epilepsy is unknown.

#### p0609

### PROTEOMIC ANALYSIS OF DORSAL AND VENTRAL DENTATE GYRUS FROM EPILEPTIC RATS INDUCED BY PERFORANT PATHWAY STIMULATION

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**Purpose:** Proteomic analysis is a promising tool for the identification of key biological processes leading to epilepsy. However, the power of such "omic" approach is dependent on the preparation of homogeneous cell populations. In this context, laser-capture microdissection presents the ability to select specific cell populations that would give the most informative data in proteomic studies. The aim of this study is to identify differentially expressed proteins in the dorsal and ventral Dentate Gyrus (dDG and vDG) from epileptic rats. Epilepsy was induced by a perforant pathway stimulation protocol which leads to classical hippocampal sclerosis.

**Methods:** Rats were induced as described by Norwood et al., 2010. Frozen sections were prepared and the dDG and vDG were laser microdissected (Zeiss PALM). Total proteins were obtained from using 8M urea and analyzed by LC-MS/MS using an LQT-Orbitrap (Waters).

**Results:** We identified a total of 1271 proteins in samples of dDG and vDG combined. Of these, 42 proteins were found to be differently expressed in dDG and 50 in vDG. Although there was some overlap between proteins that were differently expressed in dDG and vDG, we found that 76% of proteins differentially expressed in dDG and 80% in vDG were unique to these sub-fields. Most of the differentially expressed proteins are involved in neuronal pathways such as GABA-receptor recycling and cytoskeleton remodeling, as indicated by gene ontology analysis employing the Metacore® software (Thomson Reuters).

**Conclusion:** The identified proteins can indicate new pathways involved in epileptogenesis. Furthermore, we found that additional information molecular complexities could be observed as hippocampal subfields were analyzed separately. We believe that the further integration of the proteomic data with other "omics" approaches could generate even more informative data about those neuronal processes.

#### p0610

### GENE DISCOVERY AND HIGH-THROUGHPUT RESEQUENCING OF CANDIDATE GENES IN EPILEPTIC ENCEPHALOPATHIES

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**Purpose:** Whole exome studies in patients with epileptic encephalopathies (EE) have demonstrated the breadth of genetic heterogeneity in these severe childhood epilepsy syndromes. Our previous study identified 329 *de novo* mutations in 305 genes when 264 trios (affected child and unaffected parents) were sequenced. We aimed to identify additional patients with *de novo* mutations in 27 of these candidate genes to confirm the role of each gene and the phenotypic spectrum in the genetic etiology of EE.

**Method:** We performed targeted capture and high-throughput resequencing of 27 genes in which a *de novo* mutation was identified in one or more proband with Infantile Spasms (IS) or Lennox-Gastaut syndrome (LGS) in our prior study. More than 600 patients with diverse EE phenotypes were screened.

**Results:** We have identified at least 16 patients with *de novo* mutations in 7 genes. Among these are recurrent mutations in *CACNA1A*, *GABRB3*, *GNAO1*, and *ALG13* highlighting the importance of these genes in EE. Segregation studies are pending for additional probands but it is likely that genes involved in glutamate transport, endocytic trafficking, and transcriptional regulation are important for healthy neural circuitry, and mutations in these pathways cause EE. We will report the frequency of *de novo* mutations for each gene screened in our cohort as well as investigate genotype-phenotype correlations for genes in which multiple patients harbor mutations.

**Conclusion:** We have confirmed the role of at least 7 additional genes in the genetic etiology of EE and expanded the phenotypic spectrum associated with these genes beyond IS and LGS in which they were first discovered.

#### p0611

##### EXPANDING CLINICAL SPECTRUM OF *GRIN2A* MUTATIONS TO ATYPICAL RETT SYNDROME

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**Purpose:** *GRIN2A* encodes a subunit of N-methyl-D-aspartate (NMDA) receptor. *GRIN2A* mutations have been reported to be mainly responsible for focal epilepsy, such as epilepsy-aphasia spectrum disorders (benign epilepsy with centrotemporal spikes [BECTS], Landau-Kleffner syndrome, and epileptic encephalopathy with continuous spike and wave during sleep), idiopathic focal epilepsy, and intellectual disability. We examined possible involvement of *GRIN2A* mutations in patients with infantile epilepsy.

**Method:** Blood samples and clinical information were collected from the patients and their parents. Written informed consent was obtained from their guardians. Patients were analyzed by *GRIN2A*-focused WES analysis, and candidate *GRIN2A* mutations were validated by Sanger sequencing.

**Results:** We detected one novel missense mutations in *GRIN2A* and one splicing mutation in two families. Individual 1 with a *de novo* c.1643C>G mutation in *GRIN2A* showed febrile seizures, stereotypical hand movements, respiratory abnormality, severe intellectual disability, and epilepsy. She was diagnosed as atypical Rett syndrome. Individual 2 with unclassified epileptic encephalopathy and autism carrying a splicing mutation (c.1007 + 1G>A) developed febrile seizures at 1 year of age, followed by focal clonic seizures and developmental deterioration. Electroencephalography showed multifocal sharp waves on left hemisphere. The mutation was found in her mother and grandmother, who also showed epilepsy during childhood without autistic features. All the mutations were not found in our 575 control exomes, and were predicted to be damaging by Web-based prediction tools.

**Conclusion:** Our study suggests that *GRIN2A* mutations can be associated with atypical Rett syndrome. A variety of severity is to be noted in patients with *GRIN2A* mutations.

#### p0612

##### VARIANTS IN MICRORNA GENES: CAN THEY CAUSE EPILEPTIC ENCEPHALOPATHIES?

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**Purpose:** The role of miRNAs in the pathomechanism of epilepsy is increasingly researched. Variants in miRNA genes can have a drastic effect on their processing and functioning. However, a mutation analysis of these genes has never been performed for the epileptic encephalopathies (EE). We anticipate that variants in brain-expressed miRNAs can alter the expression of their target genes, leading to the severe phenotype of EE.

**Method:** We screened miRNA genes in EE patients and their healthy parents using 'Multiplex Amplification of Specific Targets for Resequencing' (MASTR) assays (Multiplicom NV). The first assay amplifies 289 human brain-expressed miRNAs and was used to screen 119 trios, 13 duos, 2 quartets and 54 probands with EE. Furthermore, we created and optimized a second MASTR assay containing 183 additional miRNA genes and the coding region of six genes involved in miRNA biogenesis (*AGO2*, *DICER1*, *DGCR8*, *DROSHA*, *TARBP2*, *XPO5*). The second assay was used to screen 45 trios, 4 duos, 2 quartets and 38 probands with EE. Further screening is currently ongoing. Prioritization of variants was done using different inheritance models, the position and predicted impact on the structure of the miRNA and their frequency in controls.

**Results:** So far, we identified one *de novo* variant, which is present in the mature miRNA and predicted to severely disrupt the secondary structure of the miRNA. Functional follow up is now started to evaluate the impact of the variant on the miRNA biogenesis and function.

**Conclusion:** Identification of miRNAs linked to EE will lead to novel insight into the underlying pathomechanisms of epilepsy.

#### p0613

##### TWO CASES WITH EPILEPSY AND DYSMORPHIC FEATURES ASSOCIATED WITH 17Q21.31 MICRODELETION SYNDROME

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**Purpose:** The 17q21.31 microdeletion syndrome is characterized by intellectual disability, epilepsy, distinctive facial dysmorphism, hypotonia and friendly behavior. Here we report on two Turkish patients with the 17q21.31 microdeletion syndrome.

**Method:** Both of the cases have clinical features which mostly overlap with reported 17q21.31 microdeletion syndrome cases. Additionally, we determined syringomyelia in our first case which expanding the phenotypic spectrum. Array CGH analyses identified a 740 kb deletion on chromosome 17q21.31.

**Results:** Array CGH analyses identified a 740 kb deletion on chromosome 17q21.31 (chr17: 43513428-44254354 bp) in case 1. The deleted region in case 1 contains the following genes: MAPT, CRHR1, KANSL1, SPPL2C, PLEKHM1 and STH. In second case, array-CGH analyses identified a 1.3 Mb deletion on chromosome 17q21.31 (chr17: 42579621-43846470 bp) in case 2. The deleted region in case 2 contains the following genes: CRHR1, EFTUD2, PLEKHM1, GFAP, DBF 4B, FMNL1, DCAKD, PLCD3, GJC3, ADAM11, C17 ORF 104, ACBD4, HEXIM2, MAP3K14, and ARHGAP24. But the microdeletion region in case 2 does not include KANSL1 gene which also confirmed by Real-time PCR.

**Conclusion:** To the best of our knowledge this is the first report of a patient with the 17q21.31 microdeletion which does not encompass KANSL1 gene. As this patient presents the classical phenotype of 17q21.31 syndrome, these data make it possible to find another gene or genes causing similar phenotype in this region. Further investigations and new cases will help to clarify this challenging question.

## Neuroimaging 2 Monday, 7th September 2015

p0614

### DIFFERENTIAL DISTRIBUTION OF CORTICAL THINNING AND SUBCORTICAL WHITE MATTER DIFFUSION ANOMALIES IN TEMPORAL LOBE EPILEPSY

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**Purpose:** Quantitative MRI studies have consistently demonstrated that drug-resistant temporal lobe epilepsy (TLE) is associated with multilobar cortical thinning. Diffusion MRI studies have also reported widespread white matter (WM) changes, but mainly along deep fibre tracts, thus, with an unclear spatial relationship to cortical pathology. Here, we analysed conjointly diffusion properties of the immediate subcortical WM with cortical thickness measures in a unified surface-based framework.

**Method:** We studied 61 drug-resistant TLE patients (31/30 left/right) and 42 healthy controls. Based on T1-weighted 3T MRI, we generated cortical surface models and measured cortical thickness across thousands of surface-spanning vertices. We computed a Laplacian potential field between cortex and ventricles, which guided the placement of subcortical surfaces at 1, 2, and 3 mm depth below the GM-WM boundary, with vertex-correspondence to the cortex. Based on co-registered diffusion MRI, we sampled mean diffusivity (MD) and fractional anisotropy (FA) on subcortical WM surfaces. Hemisphere-specific measurements of left and right TLE patients were normalized with respect to controls, and sorted into ipsilateral/contralateral. We performed vertex-wise t-tests to detect thickness and WM diffusion differences between patients and controls across all surfaces. Findings were corrected for multiple comparisons at  $FWE < 0.05$ .

**Results:** Patients showed bilateral cortical thinning in anterior temporal, frontal, and centro-parietal regions; conversely, subcortical WM diffusion changes (MD increase and FA decrease) were largely limited to ipsilateral parahippocampus, anterior cingulate, lateral temporal, and orbitofrontal regions. Diffusion anomalies overlapped with cortical thinning only in temporo-limbic regions including parahippocampal, lateral temporal and prefrontal regions.

**Conclusion:** Our study compared for the first time point-wise patterns of cortical morphology and diffusion-derived parameters of subcortical microstructure and architecture in TLE, revealing a differential distribu-

tion of anomalies. Ipsilateral limbic diffusion alterations may reflect gliosis and demyelination due to mesiotemporal deafferentation; bilateral mainly fronto-central GM atrophy is likely secondary to excitotoxic seizure spread.

p0615

### CONTRIBUTION OF EEG-FMRI IN THE PRE-SURGICAL EVALUATION OF PEDIATRIC PATIENTS WITH EPILEPSY

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**Purpose:** EEG-fMRI can contribute to more accurate localization of the epileptic focus in focal epilepsy. Furthermore, EEG-fMRI activations have good correlation with intracranial EEG. Studies targeting large sample of patients and focusing in challenging groups of patients such as MRI negative and large lesions aiming for partial resections are needed to evaluate its contribution in the clinical setting. In this study we use EEG-fMRI to localize the epileptic focus in a large population of children with drug resistant epilepsy and analyse the contribution of this technique in the presurgical evaluation.

**Method:** 48 children with drug resistant epilepsy recruited from the pre-surgical epilepsy program underwent simultaneous EEG-fMRI scan. Patient's fMRI time series were analysed using a general linear model to determine the presence of regional interictal epileptiform discharges (IED)-related BOLD changes in SPM8. EEG-fMRI maps were classified as concordant or discordant with the presumed epileptogenic region.

**Results:** 81% of patients had IED during EEG-fMRI sessions, from these, 84% had significant BOLD signal changes related to IED. Sensitivity of EEG-fMRI was 81% for the detection of focal activations in the presumed epileptogenic region. 15 out of 22 patients with normal MRI had IED during EEG-fMRI. Focal activations on the presumed epileptogenic region were observed on 66% of them. In 9 out of 26 patients with structural lesions, the clinical evaluation aimed of the detection of 9 of them had large lesions and the aim was to attempt a partial resection. In 66% of these, a focal region within the lesion was shown by EEG-fMRI. Validation for 30% of these patients has been obtained so far.

**Conclusion:** EEG-fMRI can contribute to localize more accurately the epileptogenic region in 45% of patients with normal MRI and 66% of patients with large lesions. This information may be relevant in planning the implantation in these patients.

p0616

### CEREBRAL HYPERPERFUSION MR FINDINGS FOLLOWING SEIZURE PRESENTING WITH TODD'S PARALYSIS

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**Purpose:** Patient who have focal or transient neurological deficit, it is not easy to distinguish post ictal neurological deficits after seizure from those because of cerebral ischemia. In that situation, cerebral perfusion study can help to identify postictal state with helping to exclude large vessel territory stroke. Cerebral perfusion can be rapidly decreased or

increased following seizure termination. We called it as postictal switch. We reported the MR findings following seizure presenting with Todd's paralysis. Case report: A 67-years-old female was awakened from sleep and founded with left side hemiparesis by her son. No one knew the exact time of onset and circumstance when her symptoms occurred. On admission, she had moderate degree of dysarthria, both eye ball deviation to right side and Left hemiparesis (MRC grade 5/1, 5/3). It suggested that right MCA territory infarction. We performed brain MR with perfusion study. In brain MR with perfusion study, mild diffuse cortical edematous swelling at right entire cerebral hemisphere and increased regional CBF & CBV and rapid TTP in right cerebral hemisphere with normal diffusion weighted image were observed. Also, in brain MRA, more increasing vascularity of right cerebral hemisphere compared to contralateral side was observed. These MR findings are indicated the hyperperfusion status of right cerebral hemisphere. And electroencephalography revealed diffuse slow wave in right hemisphere without ictal findings. The next day after almost 24 hours of onset of symptoms, the symptoms of patients was fully recovered and we performed brain MR with perfusion study again. Compared to previous study, brain MR with perfusion study showed normal findings and electroencephalography had no abnormal waves.

**Conclusion:** Todd's paralysis can be misdiagnosed as acute cerebral infarction. In this situation, cerebral perfusion study such as brain MR with perfusion study can be helpful diagnostic method for distinguishing between seizure and cerebral infarction.

#### p0617

### EEG RESTING-STATE DIRECTED CONNECTIVITY IN TEMPORAL LOBE EPILEPSY VS HEALTHY CONTROLS

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**Purpose:** The characterisation of pathological networks in the absence of interictal epileptiform discharges (IED) could have an important diagnostic/prognostic value. Using high-density EEG, we investigated resting-state directed brain connectivity independent from IED in left and right temporal lobe epilepsy (LTLE and RTLE) compared to healthy controls.

**Method:** Twenty LTLE, 20 RTLE patients and 20 healthy controls underwent a resting-state high-density EEG. Source activity free of IED was obtained for 82 regions of interest (ROI) using an individual head model and a distributed linear inverse solution. Granger-causal modeling was applied to the source signal of all ROIs in theta, alpha and beta frequency bands to estimate the summed outflow (SO) from each ROI (to all others) and pair-wise connectivity between ROIs with high SO. Correlations with the duration of the disease were computed.

**Results:** In all regions and groups, SO peaked in the alpha band. Consistent across frequency bands and groups, the highest SO occurred in the hippocampus, amygdala, parahippocampus, posterior cingulate cortex (PCC) and anterior cingulate cortex (ACC), concordant with the Default Mode Network (DMN). In LTLE, SO of the ipsilateral amygdala, PCC, olfactory and contralateral ACC was significantly lower than in controls. SO of the contralateral hippocampus, amygdala and ACC and ipsilateral ACC was significantly decreased in RTLE. In the alpha-band, the strongest connections in controls were from the PCC, while in both patient groups these were from the ipsilateral hippocampus. In RTLE, disease duration was negatively correlated to SO in bilateral amygdala and

contralateral hippocampus, olfactory and rectus. No correlation was found in LTLE.

**Conclusion:** In TLE, we identified connectivity impairments in regions of the DMN and known to play a major role in TLE. RTLE was more contralaterally affected than LTLE. These network abnormalities could help identify patients when interictal abnormalities cannot be detected.

#### p0618

### PLASTICITY OF LANGUAGE FUNCTION AFTER SURGERY FOR FOCAL EPILEPSY IN CHILDREN

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**Purpose:** Surgery for medication-resistant epilepsy often involves resection of tissue in close proximity to eloquent cortex. The long-term effects of surgical resections on language ability are poorly understood, especially in children.

**Method:** We present preliminary findings from a follow-up study of 38 children who underwent assessments for epilepsy surgery and 13 healthy sibling controls. Twenty-nine children went on to have surgery (5 hemispheric, 14 temporal lobe, 4 parietal lobe, 3 frontal lobe and 3 multi-lobe surgeries). The remaining 9 children were deemed not suitable candidates for surgery. Mean elapsed time from baseline to follow-up was 6 years for the surgical group and 5 years for the non-surgical group. All patients with epilepsy underwent neuropsychological assessments and language fMRI at baseline and follow-up. Language fMRI using verb generation was used to determine language lateralisation in Broca's and Wernicke's areas.

**Results:** At follow-up, 69% of the surgical group was seizure-free compared to 0% in the non-surgical group. In the surgical group, 90% showed stable or increased verbal IQ (VIQ) compared to 44% in the non-surgical group (of whom none improved and 66% deteriorated). Pre- to post-operative change in VIQ was not related to age at surgery, pre-operative VIQ, resection lobe or resected hemisphere. Seizure-freedom and being free from medication was associated with significant gains in verbal and performance IQ, and in processing speed. Lateralisation of language function to the left temporal lobes evidenced by fMRI at follow-up, as well as a leftward change in lateralisation from pre-op to follow-up, was associated with gains in VIQ.

**Conclusion:** Our findings suggest better verbal intellectual outcome in those who had surgery and became seizure-free, regardless of the extent or location of the resection. Additionally, our findings suggest that a more typical temporal lobe language lateralisation is associated with better long-term verbal outcome.

#### p0620

### EPILEPTOGENIC MRI LESION DETECTION USING TIME-EFFICIENT EPILEPSY-DEDICATED FIRST FIT MRI PROTOCOL

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**Purpose:** To ascertain the diagnostic yield and frequency of detecting epileptogenic lesions in MRI scans using a time-efficient epilepsy-dedicated first fit MRI protocol.

**Method:** All consecutive patients attending the first fit clinic at St George's Hospital over the course of 1 year were included. Patients were referred from the emergency department or via primary care following a suspected first seizure. All patients were assessed by an Epileptologist and referred for MRI if an epileptic seizure diagnosis was suspected. A 'first fit MRI protocol' was used, comprising axial FLAIR and DWI (5 mm slice thickness), coronal T2-weighted turbo spin echo angled perpendicular to the temporal lobes (3 mm slices) and sagittal T1-weighted scans (5 mm slices) through the whole brain in 15-minute scan time. All scans were acquired on a 1.5T machine and interpreted by Consultant Neuroradiologists during routine reporting sessions. MRI reports were then reviewed retrospectively with findings classified as epileptogenic lesions, non-epileptic abnormalities or normal.

**Results:** 121 patients were screened and first fit MRI protocol scans were acquired in 67 patients. Potentially epileptogenic lesions were detected in 15 patients (22.3%), consisting of vascular anomalies [n = 3], malformations of cortical development [n = 3], other epileptogenic (scarring) [n = 4], tumour [n = 1] and probable lesions warranting further imaging [n = 4]. Non-epileptogenic abnormalities were detected in 12 patients (17.9%). Normal scans were reported in 39 patients (58.2%). One patient did not tolerate the MRI and the scan was abandoned.

**Conclusion:** Our reported pick-up rate of epileptogenic lesions following a 15-minute shortened first fit MRI protocol is equivalent to detection rates reported using a longer MRI protocol, for example the 23% lesion detection rate reported by Hakami *et al.* (2013). We conclude that a shortened MRI protocol is sufficient for detecting epileptogenic lesions in patients presenting with a new-onset seizure disorder whilst enabling more efficient use of MRI scanner time.

#### p0621

### TYPE II FOCAL CORTICAL DYSPLASIA: EX VIVO HIGH RESOLUTION 7T MR IMAGING WITH HISTOPATHOLOGICAL COMPARISON

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**Purpose:** Focal cortical dysplasias (FCD) type II are highly epileptogenic lesions frequently reported in surgical series of patients operated on drug-resistant focal epilepsy. The success of epilepsy surgery largely depend on the precise localization and complete excision of the epileptogenic zone that often coincide with the site of the lesion. MRI allows many cases of FCDII to be visualized, however, in some pathology-proven cases, MRI changes are subtle or overlooked. Aim of the present work is to investigate the histopathological correlates of the MRI abnormalities in order to determine the efficacy of high-resolution imaging in lesion detection.

**Method:** Cortical specimens obtained either from patients with a clinical MRI diagnosis of FCD or MRI-negative were used: These specimens,

after fixation, were admitted to imaging protocol on a 7T scanner. Subsequent histological and ultrastructural analysis were performed to define the neuropathology (FCDIIb=10 and FCDIIa=4) and confirm MRI findings.

**Results:** In 7T T2wi we observe:

1) inhomogeneous signal intensity in the grey matter that clearly defined the boundary between the lesion and adjacent perilesional area. This altered signal match with the presence of abnormal cells (DNs and BCs, when present) and fibers disorganization.

2) A different extent of white matter hyperintensity in FCDIIb only, that corresponds to axonal degeneration, dramatic reduction in the number of myelinated fibres, vacuolization and presence of numerous abnormal cells.

3) No evident T2 signal alteration in MRI-negative patients that corresponds to white matter integrity and poor cortical alterations.

**Conclusion:** The present imaging-histopathological study suggest that high resolution 7T MRI is able to identify the boundaries between the lesion and adjacent perilesional area but highlight the need of a quantitative approach in MRI-negative cases.

#### p0623

### MULTICONTRAST MRI PROFILING OF FOCAL CORTICAL DYSPLASIA TYPE-II

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**Purpose:** Focal cortical dysplasia (FCD) Type-II is a common cause of drug-resistant extra-temporal epilepsy. This lesion is histologically characterized by cortical dyslamination and dysmorphic neurons, either in isolation (Type-IIA) or with balloon cells (Type-IIB). FCD computational models of cortical thickening, blurring of the grey and white matter transition and intensity on T1-weighted MRI have increased detection rates relative to standard evaluation. Here, we propose a new approach to describe the lesional spectrum through multicontrast MRI data.

**Method:** Multicontrast lesion profiling was performed in patients with histologically-verified FCD (9 Type-IIA, 24 IIB) using T1-weighted, FLAIR, and diffusion-weighted MRI acquired on 3T MRI. Two experts manually segmented lesions. Using multiple surfaces running through cortex and underlying white matter, we quantitatively assessed multiparametric features (morphology, intra/sub-cortical tissue intensity, fractional anisotropy and mean diffusivity) vertically across cortical depths. We also analyzed adjacent cortex in the horizontal direction along the cortical mantle as a function of geodesic distance from the lesion. Supervised machine-learning validated our approach to automatically predict FCD subtypes.

**Results:** Compared to 41 controls, Type-IIB was characterized by marked alterations in morphology, tissue intensity and diffusion properties, while abnormalities in IIA were subtle and restricted to FLAIR intensity ( $q_{FDR} < 0.05$ ). Anomalies in IIB were seen across all intra- and sub-cortical levels whereas those in IIA clustered around the cortical interface ( $q_{FDR} < 0.05$ ). Peri-lesional analysis demonstrated atypical features in up to 6 mm in both subtypes, but again more severely in IIB. Our machine-learning classifier predicted the histological grading with 93% accuracy, supporting a subtype divergence at individual level.

**Conclusion:** In agreement with histopathology, FCD Type-II present with distinct MRI patterns. Given that imaging features extend beyond the visible FCD into the adjacent normal-looking cortex, quantitative modeling may assist accurate definition of the surgical target.

## Neuroimaging 3 Monday, 7th September 2015

p0624

### MEMORY ENCODING IN PATIENTS WITH JUVENILE MYOCLONIC EPILEPSY AND THEIR UNAFFECTED SIBLINGS: AN FMRI STUDY

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**Purpose:** Impaired frontal lobe functions are reported for patients with Juvenile Myoclonic Epilepsy (JME) and their unaffected siblings. In both groups, previous functional magnetic resonance imaging (fMRI) studies revealed co-activation of the motor cortex and supplementary motor area during a working memory task. The extent to which temporal lobe functions are also affected in this syndrome remains controversial. We aimed to characterize memory encoding networks and recognition performance in JME and their unaffected siblings.

**Method:** We studied 31 JME patients, 12 siblings and 20 healthy controls using an fMRI memory encoding paradigm: 210 items were presented inside a 3T MRI scanner, grouped in 30s blocks of 10 pictures (black and white nameable line-drawn objects), 10 words (single concrete nouns) and 10 faces (photographs unfamiliar to the subjects), separated by 15 s cross-hair fixation. Participants were instructed to actively memorize the items for subsequent out-of-scanner recall, in which the 210 presented items were randomly intermixed with an additional 105 novel items.

**Results:** Recognition performances did not differ across the three groups. Compared with controls, JME patients exhibited greater activations in the left sensory-motor cortex, bilateral supplementary motor areas, superior temporal gyri and rolandic opercula across different stimulus types. Siblings showed greater activations than controls in the left motor cortex, right temporal gyrus and rolandic operculum.

**Conclusion:** Both JME patients and their siblings showed a hyperactivation of the motor system during a memory encoding task, which further emphasizes the hyperexcitability of the motor cortex during cognitive tasks as an imaging endophenotype of JME. In the absence of between-group performance discrepancies, we interpret increased activations in the superior temporal gyri and rolandic opercula as a compensatory mechanism for known frontal lobe disturbances in JME and their siblings.

p0625

### SPECIFICITY OF EPILEPTIC NETWORKS ESTIMATED IN THE ABSENCE OF SCALP EPILEPTIC SPIKES

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**Purpose:** Epileptic activity arises from dysfunction of pathological neuronal networks (epileptic networks) exhibiting coherent fluctuations independently from the occurrence of IEDs on scalp EEG. This suggests that epileptic network could represent a new/modified resting state physiological network in drug-resistant epilepsy. The aim of this study was to assess the specificity of such epileptic networks.

**Method:** From EEG-fMRI database we select the resting state recordings of 10 drug-resistant patients with focal epilepsy, having multifocal BOLD response and maximal t-value in the spike field. For each patient we performed a seed-based Functional Connectivity (FC), considering as seed a 10 mm-diameter sphere drawn around the BOLD map maximum. For the same seed we obtained the FC maps in a cohort of 20 healthy subjects, matched for age to the individual patients. We calculated the Z-scored FC map of each patient. In order to quantify the specificity of the FC network in individual patients we considered thresholds of  $Z > 2$  and  $Z < -2$ .

**Results:** In each patients, FC maps were significantly different from the group FC maps. Particularly, patients FC maps had increased FC in regions ipsilateral to the epileptic focus, ( $Z > 2$ ), whereas the FC of contralateral hemisphere diminished ( $Z < -2$ ).

**Conclusion:** Epilepsy involves a reorganisation of brain FC patterns that is specific for each patient and can be detected in the absence of scalp spikes. The interaction between the epileptic and physiological resting networks remains to be elucidated.

p0627

### STUDY THE BRAIN METABOLITES BY 1H MRS METHOD IN PATIENTS WITH EPILEPSY AND DEPRESSION

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Functional neuroimaging is used for localizing the brain dysfunction, primarily through the breach in the metabolism of the brain.

**Purpose:** Study the brain metabolites by 1H MRS method in patients with epilepsy and depression.

**Method:** MRI of brain and proton magnetic resonance spectroscopy (1H MRS) was performed 32 patients with epilepsy (PE), 28 patients with epilepsy and depression (PED), 20 patients with depression only (D) and 40 healthy volunteers (HV). Method 1H MRS was used to analyze the metabolism of N-acetyl aspartate (NAA), choline (Cho) and creatine (Cr) by calculating its concentration peaks, and to determine the ratio of these metabolites.

**Results:** In the group of PE all investigated parameters were significantly reduced relative to the norm, and the ratio of these metabolites were as follows:  $NAA / Cho = 1.58 \pm 0.22$  and  $1.78 \pm 0.22$ ;  $Cho / Cr = 1.00 \pm 0.14$  and  $1.00 \pm 0.14$ ;  $NAA / Cho = 1.50 \pm 0.22$  and  $1.50 \pm 0.22$  ppm, respectively. In D group, the ratio of  $NAA / Cho$  was equal to  $1.58 \pm 0.22$ ,  $Cho / Cr = 0.96 \pm 0.14$ ;  $NAA / Cho = 1.50 \pm 0.22$  ppm, and in PED noted marked reduction all investigated parameters:  $NAA / Cho = 1.38 \pm 0.22$ ,  $Cho / Cr = 0.90 \pm 0.14$ ;  $NAA / Cho = 1.40 \pm 0.22$  ppm.

**Conclusion:** We obtained data decrease of three main brain metabolites in PED: Cho, marker of neuron's membranes, component of phospholipid metabolism; Cr, marker of aerobic brain processes and NAA- marker of neurodegeneration, using method 1H MPC that allows non-invasive biochemical study of brain metabolism, indicating a common pathogenetic mechanisms of epilepsy and depression and increased metabolic abnormalities in combination. These finding are particularly impor-

tant in diagnosis, choice of treatment strategy and prognosis of the disease.

**p0628**

### THE CLINICAL SIGNIFICANCE OF MRI SIGNAL CHANGES IN PATIENTS WITH FIRST SEIZURES

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**Purpose:** There has been few information about the clinical significance of MRI signal changes, especially in patients with first seizures. The aims of this study were to determine the clinical significance of MRI signal changes in patients with first seizures visiting to emergency room.

**Method:** We conducted a retrospective study subjecting patients with their first seizures visiting to emergency room from March, 2010 to August, 2014. The inclusion criteria for this study were patients with

- 1) first seizures regardless of acute symptomatic seizures or not, and
- 2) MRI performed within 24 hours of the first seizures.

The definition of MRI signal changes was any signal changes on MRI including possibly periictal signal changes. The clinical variables were analyzed with multivariate logistic regression with or without MRI signal changes as a dependent variable.

**Results:** Of 427 patients with seizures visited to emergency room from March, 2010 to August, 2014, 74 patients met inclusion criteria. Twenty one patients (28.3%) had MRI signal changes; 11 with acute symptomatic seizures, 4 with first unprovoked seizures, 6 with remote symptomatic seizures. Of 21 patients with MRI signal changes, 6 patients showed possibly periictal signal changes as a consequence of their seizures. Multivariable analysis revealed that acute symptomatic seizures (odds ratio 7.3, 95% confidence interval 1.9–28.4,  $p = 0.0039$ ) and age (odds ratio 0.96, 95% confidence interval 0.94–0.98,  $p = 0.0004$ ) were independently significant variables predicting the presence of MRI signal changes in patients with their first seizures.

**Conclusion:** The MRI signal changes in patients with first seizures were associated with acute symptomatic seizures. In addition, the younger age may more frequently develop the MR signal changes.

**p0630**

### MRI PROSPECTIVE EVALUATION OF PATIENTS WITH DRUG-RESISTANT FOCAL EPILEPSY: 3T VS. 1.5T

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**Purpose:** Magnetic resonance imaging (MRI) is an essential tool in the presurgical evaluation of patients with epilepsy. Our aim was to evaluate the value of re-imaging patients with drug-resistant focal epilepsy who were initially scanned with 1.5T, using 3T 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. The findings identified from radiologists of non-specialized

centers were compared with reports from neuro-radiologists of our center.

**Results:** Mean age of patients was  $30 \pm 11$ , 87% had onset seizures in the frontal or the temporal region. The intra-observer agreement for the first radiologist was 0.74 for 1.5T and 0.71 for 3T. In the second radiologist was 0.82 and 0.66 respectively. The inter-observer agreement was 0.76 for 1.5T and 0.77 for 3T. Three non-consistent lesions (10%) were identified by general radiologists in non-specialized centers using a 1.5T standard protocol. In our center a consensus between two neuro-radiologists using epilepsy protocol identified seven lesions (23%) using 1.5T and ten lesions (33%) using 3T-MRI ( $p < 0.02$ ). In two of seven patients (28%) this additional information resulted in a change in clinical management.

**Conclusion:** Use of 3T-MRI, epilepsy protocols and interpretation by experienced neuroradiologists can improve the diagnostic yield in focal epilepsy. This is extremely relevant for patients who are assessed for surgical work-up, especially in developing countries where MRI and other imaging tools are not always available.

**p0631**

### LANGUAGE FMRI TASK IS FUNCTIONALLY CONNECTED WITH EXECUTIVE FUNCTION AREAS IN MESIAL TEMPORAL LOBE EPILEPSY

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**Purpose:** Functional magnetic resonance imaging (fMRI) based on task is a noninvasively method useful to determine language dominance in mesial temporal lobe epilepsy (MTLE). We studied a well-established fMRI language method, tone decision-semantic decision-Brazilian-version (TD-SD-bv) (Binder, 1995) in MTLE and correlated with 12 known functional networks. Our aim was to investigate the differences in the functional connectivity (FC) between MTLE's groups and the correlation between networks and TD-SD-bv.

**Method:** We scanned 96 subjects on a 3T-MR to obtain functional imaging during a language task, including 27 healthy volunteers and 69 patients with frequent (FS) and infrequent seizure (nFS); with right (R), left (L) or non hippocampal atrophy (nl): 11 nFS-L; 11 nFS-nl; 14 FS-R; 18 FS-L and 15 FS-nl. We performed the functional connectivity (FC) preprocessing using UF2C toolbox ([www.lni.hc.unicamp.br/app/uf2c](http://www.lni.hc.unicamp.br/app/uf2c)) and added 84 ROIs in 12 functional networks to extract BOLD time series and performed a full cross-correlation analysis (between all ROIs time series). We used the SPSS®21 to carry out the GLM analysis with Tukey's-post-hoc test to compare the average inter-connectivity between groups and to test the correlation between the TD-SD-bv and the networks.

**Results:** There were no differences between groups related to age ( $F = 0.664$ ;  $p = 0.652$ ) and educational level ( $F = 0.795$ ;  $p = 0.556$ ). We found no difference related to FC between groups in the 12 networks ( $p > 0.05$ ). The higher correlation occurred between TD-SD-bv and executive control network ( $r = 0.6$ ) and the lower correlation with the salience and basal ganglia networks ( $r = 0.3$ ).

**Conclusion:** We concluded that all groups connected equally within the networks to perform language task, suggesting that the FC between networks is not associated with side of hippocampal atrophy or seizure frequency in the MTLE. In addition, language task strongly activates network areas related with goal-directed behavior and cognitive control, whereas network areas related with behavioral changes and action selection are less activated.

p0633

### NEURAL CORRELATES OF RHYTHMIC THETA/Delta ACTIVITY PRECEDING SPIKE AND WAVE GENERATION IN HUMAN ABSENCE EPILEPSY

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**Purpose:** Studies on animal models of absence epilepsy (AE) enhanced the presence of oscillatory slow (“theta”) activity preceding the onset of generalized spike and wave discharge (GSWD) recorded from both cortical and thalamic neurons. In human absence epilepsies these rhythmical EEG oscillations preceding GSWD have not been clearly identified. The aim of this study is to assess GSWD in human AE by means of multimodal EEG and fMRI techniques to reveal and characterize in terms of neural generators rhythmical theta activities preceding the onset of spike and wave complexes.

**Method:** 35 patients with AE underwent video-EEG-fMRI at 3 Tesla. For each patient a two-step analysis was conducted:

(1) presence and topography of theta/delta rhythms preceding GSWD was evaluated by means of EEG Independent Component Analysis (ICA), FFT and CSD maps;

(2) EEG periods with theta activity and GSWD were used to inform fMRI signal analysis to reveal related BOLD changes.

Finally, second level group fMRI analysis was obtained for “theta” and GSWD ( $P < 0.001$  uncorrected).

**Results:** absence seizures ( $n = 182$ ) were recorded in 18 patients. In all patients a rhythmic theta/delta activity (mean FFT peak 3 Hz) preceded the appearance of GSWD on EEG by a mean of 9.8 sec. fMRI analysis related to GSWD and theta/delta activity showed BOLD signal changes in the same cortical subcortical network involving default mode network (DMN) areas and thalamus. Contrasting theta-related versus GSWD-related BOLD changes showed areas of increased BOLD signal in DMN.

**Conclusion:** A rhythmic theta/delta activity anticipating GSWD by a few seconds was reliably observed in each AE patients. This activity may contribute to the initiation of 3 Hz GSWD, as observed in animal models of absence epilepsy. The theta/delta activity correlated to a BOLD increment in DMN areas that may be crucial for the generation of absence seizure.

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p0634

### A COMPARISON OF ALTERNATIVE NON-INVASIVE TESTS OF LANGUAGE LATERALIZATION TO THE WADA-TEST: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Purpose:** Functional magnetic resonance imaging (fMRI) is increasingly used as a non-invasive alternative to the intracarotid amobarbital test (IAT or Wada-test) to evaluate language dominance prior to epilepsy surgery. However, fMRI is restricted by patient cooperation, age and availability. We aim to provide a systematic review of the most common other non-invasive alternatives to the IAT according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.

**Method:** A structured electronic literature search was conducted in March 2015 for studies comparing the eight most common alternative non-invasive methods to the gold-standard, the IAT. The literature search yielded 476 results, of which 53 studies were included in the final analysis. Sensitivity and specificity were analyzed and studies were assessed with the Quality Assessment of Diagnostic Accuracy tool (QUADAS-2).

**Results:** The following techniques were included in the analysis: dichotic listening ( $n = 7$  studies), diffusion tensor imaging ( $n = 4$ ), functional transcranial Doppler sonography ( $n = 3$ ), magnetoencephalography (MEG;  $n = 20$ ), near-infrared spectroscopy ( $n = 5$ ), positron emission tomography ( $n = 5$ ), structural magnetic resonance imaging ( $n = 4$ ) and transcranial magnetic stimulation ( $n = 5$ ). Sensitivity and specificity showed a wide range and might be misleading as the base rate of atypical language dominance is often low. Many studies had pilot character introducing new measurements, paradigms and analyses. On a descriptive level, the classification of bilateral language dominance was often more difficult than determining unilateral language dominance.

**Conclusion:** While MEG is best studied, more validation studies using consistent paradigms including multi-method comparisons are still needed. Variability in paradigms may confound comparisons between studies. There continues to be a need for exploring new methods or paradigms in search of a valid assessment tool that will determine both unilateral and bilateral language dominance.

p0636

### TALKING ABOUT THE RIGHT HEMISPHERE: STUDY ON COMMUNICATION ABILITIES IN TEMPORAL LOBE EPILEPSY PATIENTS

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**Purpose:** Language research in epilepsy has previously been focused on dominant hemisphere processing and mainly at single word level. Communication skills like discourse abilities, that enable social functioning and in which the right hemisphere has a central role, have remained unexplored. The purpose of this study was to investigate narrative and conversational discourse abilities in patients with right lateralized medial temporal lobe epilepsy (TLE).

**Method:** Sixty patients with TLE and hippocampal sclerosis that were candidates for surgical treatment were evaluated: 28 with a right epileptic zone (EZ) (RTLE) and 32 with a left EZ (LTLE). Subjects underwent a battery of tests that measure abilities on: sentence to text comprehension; conversational and narrative discourse; prosody; social inference, indirect speech and idiom expressions’ comprehension; verbal fluency; naming and logic-temporal sequencing. Disease related variables and general neuropsychological data were evaluated.

**Results:** RTLE compared to LTLE patients, showed interictal conversational and narrative discourse impairments, a tendency to tangential and disintegrated speech, lack of hierarchical and categorized codification, and misinterpretation of social intention. RTLE showed lower performance in conversational discourse, narrative comprehension retelling and production, idiom expressions' and indirect speech's comprehension, social meaning inference, emotional prosody, strategies for lexical and categorization. Otherwise, LTLE group showed lower performance in logical temporal sequencing.

**Conclusion:** RTLE patients showed deficits which are similar to what has been described in right hemisphere damaged patients. It is therefore important to evaluate these skills in RTLE patients to detect potential impairments. Medial and anterior temporal lobe structures seem to have a key role in discourse processing as a link between semantic, world knowledge, and social cognition associated areas to construct a contextually related coherent meaning.

#### p0637

### DURATION OF EPILEPTIFORM DISCHARGES NEGATIVELY PREDICTS MEMORY AND GENERAL COGNITIVE ABILITY IN GENETIC GENERALISED EPILEPSY (GGE)

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**Purpose:** The current study investigates the relationship between the total duration of epileptiform discharges and cognition in GGE, controlling for variables known to compromise cognitive function in epilepsy.

**Method:** As part of a larger prospective cohort study, 63 patients with EEG-confirmed GGE aged 11-58 (mean age: 28 years) underwent detailed neuropsychological assessment using the Woodcock Johnson III Tests of Cognitive Abilities during a period of 24-hour ambulatory EEG monitoring.

**Results:** Standard multiple linear regression analyses revealed that the total duration of epileptiform discharges during the 24-hour EEG monitoring period explained 39% of the variance of general cognitive ability (standardised beta coefficient =  $-0.39$ ,  $p < 0.001$ ). None of the included covariates were significant predictors: AED treatment; epilepsy duration; history of absence seizures (standardised beta coefficients =  $0.25$ ;  $0.06$ ;  $0.02$ , all ns). The overall adjusted model fit was  $R^2 = 0.10$ ,  $F(4, 58) = 2.80$ ,  $p < 0.05$ . Total duration of epileptiform discharges explained 46% of the variance of memory function (standardised beta coefficient =  $-0.46$ ,  $p < 0.001$ ). None of the included covariates were significant predictors: AED treatment; epilepsy duration; history of absence seizures (standardised beta coefficients =  $0.10$ ;  $0.13$ ;  $-0.09$ , all ns). The overall adjusted model fit was  $R^2 = 0.19$ ,  $F(4, 58) = 4.67$ ,  $p < 0.01$ . All assumptions of linear regression were met.

**Conclusion:** These results suggest that the total duration of epileptiform discharges negatively predicts general cognitive ability and memory function specifically, when controlling for AED use, epilepsy duration and history of absence seizures. To our knowledge this is the first time such a relationship has been demonstrated in GGE, measuring general and specific cognitive functioning (i.e. beyond reaction time and attention) or with 24-hour EEG recording. Further research is required to elucidate the extent of epileptiform discharges impacts on specific GGE syndromes and causal mechanisms.

#### p0638

### IN-DEPTH NEUROPSYCHOLOGICAL ASSESSMENT IN PATIENTS WITH NOCTURNAL FRONTAL LOBE EPILEPSY (NFLE)

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**Purpose:** To study systematically the neuropsychological profile of a cohort of patients with Nocturnal Frontal Lobe Epilepsy (NFLE), focusing particularly on frontal lobe functions.

**Method:** All NFLE patients referred to our Institute from July 2013 to December 2014 were invited to participate. All consenting patients underwent a neuropsychological assessment including evaluation of general intelligence (Wechsler Intelligence Scale for Adults and Raven's Progressive Matrices). A subgroup of selected patients (normal intelligence, aged  $>16$  years) underwent an extensive standard neuropsychological battery focused on executive functions: language, verbal and non-verbal memory, working memory, visuospatial abilities, attention, mental flexibility. All results were calculated after adjustment for age and education level and collected in an ad hoc database.

**Results:** We recruited 33 cases (M:F = 14:19; mean age 40.3 years, range 17-69; handedness: right 100%) for the neuropsychological study. Three patients showed cognitive impairment and did not undergo the further specific battery. In 27 patients (M:F = 11:16; mean age 40.1 years) the evaluation of general intelligence showed a worse score in verbal IQ (mean total IQ 97.7; verbal IQ 92.7, performance IQ 104.3). Patients with at least one impaired neuropsychological test of the extensive battery were 63%. Phonemic fluency and selective visual attention tests were impaired in 34.5% and 31% of patients respectively. Working memory was impaired in 10.4% of patients, whereas 34.4% showed deficits in verbal and non verbal memory. Performance on the mental flexibility and shifting tests were normal in all tested patients. Among five patients with multiple impaired tests, two had drug-resistant epilepsy with weekly/daily seizures.

**Conclusion:** These preliminary data suggest that performance IQ is better than verbal IQ in NFLE patients. Verbal fluency, memory tasks and selective visual attention are the cognitive patterns most often impaired, whereas performance on the mental flexibility is preserved.

#### p0639

### ARE PATIENTS WITH NONDOMINANT MESIAL TEMPORAL SCLEROSIS MORE PRONE TO NONCONVULSIVE STATUS EPILEPTICUS DURING VIDEO EEG MONITORING?

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**Purpose:** Epilepsy is a disturbance of neuronal networks with altered connectivity. Seizures of each temporal lobe (TL) may have different aspects as a result of so-called connectivity differences. We speculate that epileptic seizures of unilateral hippocampal sclerosis may vary between each TL in terms of seizure duration during video EEG monitoring and nonconvulsive status epilepticus may be more prevalent in non-dominant TL epilepsy.

**Method:** All right handed patients with intractable TL epilepsy who had unilateral hippocampal sclerosis on cranial MR, unilateral concordant neuropsychological test were included. During video EEG monitoring, the dose of each drug was decreased approximately by 25% every con-

secutive day. All complex partial seizures (CPS) were evaluated in terms of seizure duration. If there was secondary generalisation, it was noted. A nonconvulsive status epilepticus (NCSE) is defined when CPS lasts more than 5 minutes.

**Results:** We evaluated 78 epileptic seizures of 40 patients (25 female). Twenty one patients had right MTLE-HS. The mean age was  $26.9 \pm 9.0$  in right,  $32.7 \pm 9.7$  in left sided patients ( $p = 0.060$ ). Patients with left and right MTLE-HS were compared in terms of age at seizure onset, duration of epilepsy, history of febrile seizures, history of secondarily generalized seizures, number of antiepileptic drugs without any significant difference. Duration of seizures between left and right sided MTLE-HS were not different statistically (R:  $160.8 \pm 158.5$  sec vs. L:  $133.6 \pm 157.7$  sec,  $p = 0.358$ ). Number of seizures which evolved into NCSE were 9 (20.9%) on right and 2 (5.7%) on left sided MTLE-HS. This ratio reached statistical significance ( $p = 0.053$ ).

#### p0640

### JUVENILE MYOCLONIC EPILEPSY AND DEPRESSION

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**Purpose:** Depression is common but underdiagnosed in people with epilepsy. The purpose of this study is to determine the rate and severity of depression in patients diagnosed juvenile myoclonic epilepsy (JME).

**Method:** Nineteen patients (17 women, 2 men) suffering from JME and regularly followed by our Epilepsy Outpatient Department were screened for depression using Beck Depression Inventory (BDI). None of the patients had generalised tonic-clonic seizure in the last 1 year and all patients were under monotherapy with valproic acid, lamotrigine or levetiracetam.

**Results:** According to the scores of BDI 8 patients did not any sign of depression. Six patients had mild, two moderate and three severe depression. JME accounts for 25–30 percent of idiopathic generalised epilepsies and upto 10 percent of all cases of epilepsy.

**Conclusion:** There is growing evidence that patients with JME are at increased risk for comorbid psychiatric illness and personality disorder. our preliminary data support these findings.

#### p0641

### LIFE AFTER BEING DIAGNOSED WITH PSYCHOGENIC NON-EPILEPTIC SEIZURES (PNES): A SOUTH AFRICAN PERSPECTIVE

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**Purpose:** The purpose of the study was to explore the life experiences of South Africans who have been diagnosed as having psychogenic non-epileptic seizures (PNES), with a focus on the aspects of the challenges which these individuals face, as well as the resources and coping strategies which are either made available to them or used by them in order to cope with PNES.

**Method:** Ten qualitative, semi-structured interviews were analysed by means of thematic analysis in order to explore themes around challenges and resources for those diagnosed with PNES.

**Results:** Although many challenges were encountered by those who are diagnosed with PNES, substantial resources on which these individuals lean on in order to live fulfilling and satisfactory lives were identified. Some of the challenges included unexpected seizures, medical professionals, belief systems as well as family. However, resources to counteract these challenges were social support, medical professional as well as religion and spirituality.

**Conclusion:** Exploring the lives of those diagnosed with PNES in South Africa is a new chapter in helping to discover methods to make the lives of people with PNES easier, and ensuring that knowledge is spread in order that those who have the symptomology can be readily and accurately diagnosed, and given adequate information about the condition. By uncovering life experiences, those who are diagnosed with PNES can know that they are not alone. As more information and research is assembled, more resources may become available to benefit these individuals and allow them to recover from PNES.

#### p0642

### EXPLORING THE EXPERIENCES OF INDIVIDUALS DURING THE DIAGNOSTIC PROCESS OF PSYCHOGENIC NON-EPILEPTIC SEIZURES (PNES)

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**Purpose:** Psychogenic non-epileptic seizures (PNES) are often misdiagnosed as epilepsy. It may take many years for someone to receive the correct diagnosis of PNES. The purpose of this study was therefore to explore the experiences of individuals during the diagnostic process of PNES. The focus was on the challenges that individuals face during the diagnostic process, as well as the resources that help these individuals to cope during the process of getting to a diagnosis of PNES.

**Method:** Thematic analysis was used to explore the qualitative, semi-structured interviews that were conducted with ten individuals with PNES.

**Results:** Data analysis revealed several themes relating to challenges and resources. The first major challenge that emerged was healthcare providers; especially with regards to misdiagnosis, medication and the negative side effects, and uninformed healthcare providers. The second major challenge to emerge was medical aid. The third was loss of independence with regards to driving, socialisation and employment. The last challenge was comorbid disorders; with the main comorbid disorder being depression. The major resources were social support, medical aid, healthcare providers and religion.

**Conclusion:** This study suggests that patients with PNES face many challenges during the diagnostic process of PNES, but are also able to make use of several resources. The role of healthcare providers during the diagnostic process was highlighted as tremendously important. This study will hopefully contribute to the improvement of the services provided by healthcare providers in particular to facilitate the experiences of these individuals in a positive way.

#### p0643

### LONG-TERM EVOLUTION OF DRAVET SYNDROME: COGNITIVE IMPAIRMENT, BEHAVIORAL PHENOTYPE AND ADAPTIVE FUNCTIONING

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**Purpose:** To report on clinical picture of adult patients with Dravet syndrome, with particular attention to the cognitive and behavioral phenotypes, and to the adaptive functioning.

**Method:** Thirteen adult patients (mean age: 28.3 years, range 19–48 years) and their caregivers underwent a comprehensive standardized evaluation of:

## Abstracts

- 1) cognitive functioning: Mini Mental State Examination (MMSE), Severe Impairment Battery (SIB), Raven test;
- 2) neuropsychiatric symptoms: UCLA Neuropsychiatric Inventory;
- 3) adaptive functioning: modified Barthel Index, Vineland Adaptive Behavior Scale;
- 4) family problems: Multidimensional Scale of Perceived Social Support (MSPSS), structured interview.

**Results:** All patients but one still experience seizures. The clinical neurological picture is dominated by extrapyramidal symptoms (bradykinesia, hypomimia, rigidity, dystonia) and by orthopedic problems (scoliosis, kyphosis, valgism, pes planus). Mental deficits are present in all cases. The severity of clinical picture precluded a standardized evaluation in 5/13 patients. Language, attention and memory are the most impaired areas (SIB battery administered to 8 patients). Only 4 patients were able to sustain Raven test, and performed below 25th centile. Behavior disorders, reported in all cases but two, are mostly characterized by aggressiveness, agitation, and irritability. Eleven patients still live with their own families, two patients in supervised community. The mental age, according to the Vineland Scale is lower than 3 years in 7 patients, and between 5 and 12 years in 6. Accordingly, all the patients but one are dependent from caregivers, albeit a certain degree of self care is preserved in 5 patients (Barthel index). MSPSS and interviews highlight difficulties in finding respite care outside family, and the heavy impact of the disease on the caregivers' lives.

**Conclusion:** Our data confirm that the disability of DS patients and the quality of life of their families is mainly related to the severity of mental deficits and the level of dependency from caregivers.

## Neurostimulation 2

### Monday, 7th September 2015

p0645

#### LONG-TERM OUTCOME OF VAGUS NERVE STIMULATION IN CHILDHOOD ONSET REFRACTORY EPILEPSY

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**Purpose:** Vagus nerve stimulation (VNS) has been used as an adjunctive therapy for children and adults with medically intractable epilepsy for the last three decades. We report our experience and long-term follow-up in patients with medically intractable who underwent VNS implantation.

**Method:** We reviewed clinical data and long-term outcome of 53 children (39 boys, 14 girls) with VNS followed between 1998 and 2014 at Hacettepe University Children's Hospital.

**Results:** Age at seizure onset ranged between 1 month and 14 years, median duration of epilepsy was 9.6 years. The mean age at VNS implantation was 12.5 years (4.6–18 years), the minimum follow-up duration was 3 months. The most common underlying etiologies were perinatal insult (32.5%), malformations of cortical development (22.4%), meningoencephalitis (8.2%), Rett syndrome (6%), and 16% had negative MRI. Seven patients had undergone epilepsy surgery before implantation (3 patients with corpus callosotomy, 4 with resective surgery). The majority of patients had cognitive and/or behavioral problems. Overall 40 patients had adequate follow-up data. Three patients (7.5%) were seizure free including one with resolution of electrographical status epilepticus in sleep; underlying etiologies were cortical dysplasia, meningoencephalitis, and perinatal insult, each in one patient. 12.5% of the patients had ≥90% decrease in seizure frequency, 22.5% had 50–90% seizure reduction, 20% had <50% seizure reduction, whereas 37.5% had

no significant change in seizure frequency. Two patients underwent corpus callosotomy, one resective surgery after VNS. Vocal disturbances and paresthesias were the most common side effects, in two patients VNS was removed due to local reaction.

**Conclusion:** Our long-term follow-up results showed that VNS is an effective and well-tolerated therapy for intractable childhood epilepsy. Almost half of our patients had more than 50% seizure reduction following VNS implantation. Our patients had a diverse etiological profile, and seizure outcome was not related to the underlying etiology.

p0646

#### VAGUS NERVE STIMULATION IN CHILDREN WITH DRUG-RESISTANT EPILEPSY: A LONG TERM FOLLOW-UP DATA IN A SINGLE CENTER

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**Purpose:** To evaluate long-term efficacy and safety of vagus nerve stimulation (VNS) in children and adolescent with drug-resistant epilepsy.

**Method:** The medical records of pediatric patients who underwent VNS implantation in a single Korean tertiary center were reviewed. At 6 months, 1 year, 3 years, and 5 years after VNS implantation, the major seizure frequency reduction from the baseline was assessed. The responders were defined as the ≥50% reduction in baseline seizure frequency at 1 year follow-up and the patient characteristics were compared between responder and non-responder group.

**Results:** Thirty-five patients were identified. The mean age at implantation is 10.9 years (range, 4.2–19.9 years) and mean follow-up period after VNS implantation is 6.9 years (range, 0.4–13.2 years). At 6 months, 1 year, 3 years, and 5 years after implantation, 33.3%, 45.1%, 51.8%, and 58.3% of patients showed ≥50% seizure frequency reduction. Patients with generalized seizures were more likely to be responders than those with focal seizures at 1 year after VNS implantation ( $p = 0.020$ ). The discontinuation rate was 11.4% (4/35), which is attributed to wound infection in two of them and lack of efficacy in others. Other adverse events were not reported.

**Conclusion:** This study suggests that VNS is well tolerated and effective adjuvant therapy in pediatric patients with drug-resistant epilepsy. To optimize the management of VNS, further studies are needed.

p0647

#### HIPPOCAMPAL DBS: FOLLOW-UP OF 3 PATIENTS WITH MESIAL TEMPORAL EPILEPSY IN NEUROCENTRO

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**Purpose:** Mesial temporal lobe epilepsy (MTLE) is often refractory, increasing the risk of cognitive and psychosocial dysfunction. Hippocampal deep brain stimulation (Hip-DBS) is proposed in patients with refractory MTLE in whom a resective surgery is not an option.

**Method:** Case reports.

**Results:** We present the results of 3 patients who underwent to Hip-DBS for refractory MTLE. The mean follow-up time was 6 months. No cognitive impairment after surgery was observed. **Case 1:** Female, 20 years old. Complex partial seizures (CPS) since age 7 months. Median seizure frequency 1-2/week, catamenial exacerbation. Therapeutic failure of seven AEDs. Video-EEG: one left mesial temporal seizure onset. Brain-MRI: left mesial temporal sclerosis (MTS). Neuropsychological testing: without significant differences between visual and verbal memory. Left Hip-DBS was implanted, became seizure free with low-voltage stimulation (0.4–0.6 V). Seizure frequency was increased until electrophalographic status when the stimulation intensity was higher. **Case 2:** Female, 50 years old. CPS since age 3 years. Median seizure frequency: 9/month. Uncontrolled after 6 AEDs trials. Video-EEG: four temporal seizures onset (1 left/3 right). Brain-MRI: right MTS. Neuropsychological testing: visual and verbal memory impairment, worse verbal. Bilateral Hip-DBS was implanted. The mean monthly seizure frequency decreased by 67% to 2V. **Case 3:** Male, 43 years old. CPS since age 24 years, daily frequency. Uncontrolled after 10 AEDs trials. Video-EEG: 10 temporal seizures (7 left/3 right). Brain-MRI: bilateral MTS. Neuropsychological testing: visual and verbal memory impairment, worse visual. Bilateral Hip-DBS was implanted, the mean seizure frequency reduction was 80% to 0.4V, with left hippocampal stimulation alone.

**Conclusion:** Hip-DBS is a safe and effective therapeutic option for patients with MTLE not candidates to resective surgery. Our patients, had a mean seizure frequency reduction by 60%. Without observed additional cognitive deficit. The response has high variability. The stimulation parameters should be evaluated periodically and individually.

p0648

#### HIGH FREQUENCY CORTICAL FOCAL STIMULATION IN ABSENCE EPILEPTIC RATS: TIMING OF STIMULATION MATTERS FOR ACUTE AND LONG TERM EFFECTS

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**Purpose:** Seizure control is one of the ultimate aims of epileptology: here acute and prolonged effects of 24 h high-frequency stimulation of the epileptic onset zone of spontaneous, occurring spike and wave discharges (SWD) were investigated in an animal model of absence epilepsy. Closed and open-loop stimulation were compared according to a yoked control design allowing to investigate the effect of timing, while controlling for amount and intensity of stimulation.

**Method:** WAG/Rij rats were implanted with stimulation electrodes in the deep somatosensory cortex, and recording electrodes in cortex and thalamus. Closed and open loop stimulation (1sec trains, biphasic 0.4 msec pulses, 130 Hz) were presented for 24 h according to a yoked control design in a counterbalanced order. The stimulation days were preceded and followed by 24 h recordings.

**Results:** Closed-loop stimulation interrupted SWD and duration of SWD was shortened. Both groups showed a reduction in SWD number during stimulation days. Closed-loop stimulation also resulted in less SWD during the last 8 hours of the post-stimulation day. Open-loop stimulation sometimes induced low-frequency afterdischarges.

**Conclusion:** SWD can be aborted by closed-loop stimulation at seizure onset zone while their number was reduced. It can be regarded as relatively safe neuroplastic technique without habituation or a rebound of SWD. The reduction of SWD during open-loop stimulation session might be caused by the afterdischarges. The reduction of SWD on the post-stimulation day demonstrates the critical relevance of timing for the induction of plasticity: it suggests that absence seizures themselves might be involved in their reoccurrence.

p0650

#### SEIZURE ONSET ZONE FUNCTIONAL CONNECTOME AS REVEALED BY SINGLE PULSE ELECTRICAL STIMULATION IN STEREOENCEPHALOGRAPHIC STUDIES

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**Purpose:** Focal epilepsy is regarded increasingly as a network disease. In this conceptual frame, standardized tools that define the functional connectivity of the seizure onset zone (SOZ) are needed.

**Methods:** We selected 16 consecutive patients with pharmaco-resistant epilepsy that were explored in the SEEG method during their presurgical evaluation. Single pulse electrical stimulations (SPES) (biphasic, 3 ms, 0.25–5 mA) were applied to adjacent contacts while recording responses from the rest. We calculated the early responses in the 10–110 ms interval and considered only connections between contacts having a RMS value within the 3rd quartile of all the responses in an individual patient, correlated with the stimulation current (Spearman's rho >0.5, p < 0.05). Sublobar anatomical structures projecting to SOZ (inbound connections), as well as SOZ's projections to other structures (outbound connections) were systematically assessed. These were classified as either pathologic (containing at least one contact with interictal epileptiform activity) or physiologic. We thus defined SOZ's connectome in each patient, naming it generically "epileptome", and listed its nodes before and after tailored resections. Postsurgical outcome was evaluated after >6 months interval (mean 9) firstly in respect to seizure freedom (10 yes vs. 6 no) and then as Engel class.

**Results:** A large range of structures 8–100% (mean 55%, SD = 25%), sampled for the SEEG exploration, were part of each patient's epileptome. Postsurgical outcome was highly correlated with the proportion of pathologic structures in the inbound connections, both pre and post-surgery (62% in seizure free lot vs. 88% in not seizure free lot, Mann-Whitney-U p = 0.02, Spearman for Engel score rho=0.654, p = 0.006), on the same order of magnitude as it was to the ratio of unresected to total SOZ contacts (p = 0.03).

**Conclusions:** The balance between pathologic and physiologic structures projecting to SOZ is associated with post-surgery outcome in our lot and can be assessed preoperatively.

p0651

#### VAGUS NERVE STIMULATION ACTIVATES INHIBITORY NEURONAL NETWORK IN HUMAN CEREBRAL CORTEX

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**Purpose:** Vagus nerve stimulation is a surgical treatment for intractable epilepsy as a palliative therapy for of its less invasiveness and good seizure outcome. More than half patients can get 50% seizure reduction compared to preoperative seizure frequency. Although vagus nerve stimulation is widely performed for drug resistant epilepsy, little is known about how the left cervical vagus nerve stimulation affect on the cerebral cortex. To address this issue, we investigated the cortical activity during vagus nerve stimulation using electrocorticography.

**Method:** Electroencephalography, direct recording of cortical activities, during vagus nerve stimulation were performed with 6 hemispheres of 4 patients. Eleven electrode sheets containing 20, 40 or 60 grid arranged contacts were placed on the lateral surface of frontal or temporal lobe on left and/or right hemisphere. Neuronal activities were recorded through macro electrodes with a sampling rate of 2 kHz, and recorded signals were analyzed offline. To evaluate the inhibitory neuronal network, gamma coherence ranging 60 to 120 Hz between electrodes were calculated and analyzed. The value of gamma coherence was normalized with Z-score in each electrode sheet before statistics.

**Results:** Eleven electrode sheets of 420 contacts were implanted. Among them, 4 electrode sheets, 160 contacts, were placed on the left side while 7 sheets, 260 contacts, were on the right side. We found elevated gamma coherence in stimulating period compared to inter stimulating period. Normalized gamma coherence of stimulating period was significantly higher than inter stimulating period (paired *t*-test,  $p < 10^{-4}$ ). This phenomena was most observed in right hemisphere ( $p < 10^{-5}$ ).

**Conclusion:** Our results suggest that increased activity of inhibitory neuronal network elicited by vagus nerve stimulation especially observed in right hemisphere consequently suppresses seizure occurrence.

#### p0653

### PAINFUL HYPERSTIMULATION PHENOMENA ASSOCIATED WITH VAGUS NERVE STIMULATOR MAGNET FIRING: 2 CASE REPORTS IN CHILDREN WITH REFRACTORY EPILEPSY AND REVIEW OF LITERATURE

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**Purpose:** Vagal Nerve Stimulation (VNS) is a well-established treatment modality for refractory epilepsy in children and adults. Pain is a rare complication associated with VNS therapy. When reported, the pain tends to be localized and persistent. We report two patients with recurrent episodes of severe pain that occurred during VNS stimulation but independent of volitional VNS magnet mode stimulation. These episodes abated after the VNS magnet function was disabled.

**Method:** We report two patients with transient, intolerable painful phenomena associated with spontaneous VNS stimulation. We discuss characteristics of pain phenomena reported in other epilepsy patients with VNS implants based on a review of the literature.

**Results:** Our cases were unrelated adolescent males with seizures since early childhood. Their vagal nerve stimulators had been implanted 14 and 22 months prior to the onset of their pain episodes. Neither had experienced significant side effects with their VNS previously. Neither patient had seen significant decreases in seizure frequency or severity following VNS placement. No recent VNS adjustments had been made prior to symptom onset. Both patients reported acute onset of repeated episodes of sudden, brief, paralyzing pain centered around the VNS device and radiating to the chest and neck. There was no consistent correlation with electronics usage or patient activity at the time of the attacks. The episodes recurred until the magnet currents were set to zero microvolts. Reactivation of the magnet setting in one patient caused recurrence of pain episodes. As of 5 months following VNS magnet mode deactivation, neither patient had experienced a return of the pain episodes. In our literature review, we found no reports of VNS patients with repeated painful episodes that eased with deactivation of the magnet settings.

**Conclusion:** Unintended magnet-mode activations should be investigated as an etiology of transient painful phenomena in epilepsy patients with VNS.

#### p0654

### THE ROLE OF ANTERIOR NUCLEI OF THE THALAMUS IN COGNITION. AN INTRACEREBRAL RECORDING STUDY

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**Purpose:** To study the involvement of the anterior nuclei of the thalamus (ANT) as compared to the involvement of the hippocampus in cognitive processes of encoding and recognition.

**Method:** We studied intracerebral recordings in patients with pharmaco-resistant epilepsy who underwent deep brain stimulation (DBS) of the ANT with depth electrodes implanted bilaterally in the ANT and compared the results with epilepsy surgery candidates with depth electrodes implanted bilaterally in the hippocampus. We recorded the event-related potentials (ERPs) elicited by the visual and auditory memory encoding and recognition tasks.

**Results:** We observed ERPs elicited by visual and auditory memory encoding and recognition tasks in the hippocampus. ERPs in the ANT were recorded by the visual encoding and visual and auditory recognition tasks. No significant ERPs were recorded during the auditory encoding task. In the recognition tasks, the ERPs in the ANT preceded the ERPs in the hippocampus.

**Conclusions:** Memory disturbance should be considered in patients with ANT-DBS and in patients with ANT lesions according to the observed role of the ANT in the memory processes, especially in the memory recognition.

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#### p0655

### POST-TRAUMATIC EPILEPSY: A CASE SERIES STUDY

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**Purpose:** Seizures occurring after 1 week of traumatic brain injury (TBI) and their recurrence are accepted as post-traumatic epilepsy (PTE). The severity of TBI, age of the patient and genetic factors each have roles in the onset of PTE.

**Method:** This study includes 75 epileptic patients with a history of TBI. Their patient records are retrospectively reviewed and the data about demographic, clinical, electrophysiologic and neuroimaging features is gathered.

**Results:** The mean age of the patients was  $25 \pm 9.9$ . Fifty-seven (76%) out of 75 patients were men. The onset of epilepsy was in the first year of TBI in 45.3% of patients. Thirty-one patients (41%) were on polytherapy with antiepileptic drugs. The rate of polytherapy did not differ between mild-TBI and severe-TBI groups (43.1% vs 37.5%;  $p = 0.84$ ).

**Conclusion:** This study shows that nearly half of the PTE-patients were on polytherapy with antiepileptic drugs. Further research is needed to delineate drug-resistancy in PTE.

**p0656**

### CLINICAL, NEURORADIOLOGICAL AND EEG FINDINGS OF REFLEX EPILEPSIES

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**Purpose:** Repeating seizures induced by a specific afferent stimuli or patient activity alone or in combination with spontaneous seizures, and/or photo paroxysmal response on Electroencephalogram (EEG) is called reflex epilepsy. We are reviewing clinical, neuroradiological and EEG findings of reflex epilepsies.

**Method:** Records of 1395 follow up patients out of 2027 patients who had been examined at second Epilepsy Outpatient Clinic between July 1995 and January 2015 were analyzed retrospectively.

**Results:** 69 of 1395 patients had reflex epilepsy and 60 patients had seizures induced by visual stimuli. Considering the somatosensory stimuli; eating was determined in one, hot water was determined in 3 patients, both hot water and visual stimuli were determined in another one patient. The average age of seizure onset was 12.6 years. History of febrile convulsion was present in 27.5% and a family history for epilepsy was present in 31 patients. The types of seizures were generalized tonic clonic seizure in 58, absence in 35 and myoclonia in 30 of them. Neurological examination was normal in 88.4% and Magnetic Resonance Imaging of brain or cranial Computed Tomography were normal in 86.9% of them. EEG revealed generalized epileptiform discharges in 31.8% and focal epileptiform discharges in 7.2% of the patients who had pathological EEG findings. Photo paroxysmal response was present in 15 patients (one of them without clinical photosensitivity). Slow wave paroxysm was seen at 5 patients and disorganized background activity was seen at 2 patients. Most frequently prescribed drug was Valproate in 38 patients. 7 patients did not need any antiepileptic drug.

**Conclusion:** In this hospital based study; reflex epilepsy frequency was 4.9% and cranial imaging was mostly found to be normal as in the literature. Pathological EEG finding were determined at highest rate in hot water epilepsy.

**p0658**

### ICTAL MONOPARESIS: 2 SYMPTOMATIC EPILEPSY CASES

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Ictal paresis is a rare manifestation of epileptic seizures. It is sometimes difficult to differentiate from other neurological disorders such as migraine, transient ischemic attacks and psychogenic paralysis. Video EEG is useful to make diagnosis. Here we described 2 patients with ictal monoparesis whom had a tumour and the other had a head trauma due to traffic accident. Case 1: 38 year-old woman was admitted to our emergency department with seizures. She had seizures since 2 years. The seizures presented with awareness and left arm monoparesis, the duration is approximately 2–4 minutes and it repeats once a week. On examination after the seizure was normal. She had an operation history due to brain tumour in 1992. She had no family history. She is taking levetiracetam 3000 mg/day and valproate 1000 mg/day. Brain MRI revealed a slight bilateral frontotemporal subdural effusion and right frontal encephalomalacia. The EEG showed right frontocentral epileptiform activity. Case 2: 34 year-old man admitted to outpatient clinic with seizure history. He had a traffic accident and had right cerebral hemorrhagia history 6 months

ago. After the accident his seizures began. The seizure begins with left monoparesis and evolves to secondary generalised tonic clonic seizures. The EEG showed right centroparietal epileptiform activity. There was an encephalomalacia in the right frontal lobe in the brain MRI. He was taking phenytoin 300 mg/day and levetiracetam 1500 mg/day.

**Discussion:** Ictal paresis is a rare phenomenon of epileptic seizures. There are two probable pathophysiological hypothesis. If the negative motor areas located anterior to the primary or supplementary sensorimotor areas affected it occurs or if the epileptic activities in the sensorimotor areas activated an inhibitory system it may be occurs. Our both patients had lesion on the sensorimotor areas so these lesions may be the reason of ictal paresis.

**p0659**

### DE NOVO TOURETTE'S SYNDROME: A CASE REPORT WITH EPILEPSY

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**Introduction:** Tourette's syndrome (TS) is a childhood-onset neuropsychiatric disorder characterized by multiple motor and vocal tics with at least 1 year duration. Age of onset before 21 together with waxing and waning clinical course of symptoms are typical. Tics are defined as involuntary, sudden, non-rhythmic movements and vocalizations. Comorbid conditions such as obsessive-compulsive disorder (OCD) and attention-deficit disorder (ADHD) are more common in TS patients than normal population. Although the underlying pathophysiological mechanism of TS is unknown, it most likely involves basal ganglia and frontocortical circuits. Any pathological condition that causes damage on basal ganglia and its connections may lead to de novo TS presentation. We describe a case of acquired Tourettism after an arteriovenous malformation (AVM) operation. **Case:** A 15 year old man with sudden, brief head-ache and loss of consciousness, was evaluated for symptomatic epileptic seizures. He developed tics and behavioural changes 2 years after his AVM operation. He had secondarily generalized tonic-clonic seizures and well responded to carbamazepine and lamotrigine treatment. Although he had no tic disorder prior to surgery, he developed motor and vocal tics. He complained of memory loss attributed to attention deficiency. On his psychiatric evaluation obsessive-compulsive disorder and psychotic findings were detected.

**Discussion:** TS is a rare disease but has an important impact on the health related quality of life. While the typical definition of the syndrome posits it as developing with a neuropsychiatric disorder, neuroanatomic and neurotransmitter changes can also cause TS symptoms as in the case we described. Better understanding de novo TS will guide furthermore investigations to unravel the mechanism of TS.

**p0661**

### PARTIAL AND SECONDARY GENERALIZED SEIZURES INDUCED BY DECISION MAKING: A CASE REPORT

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**Introduction:** Reflex seizures are defined by the International League Against Epilepsy (ILAE) as "objectively and consistently demonstrated to be evoked by a specific afferent stimulus or by activity of the patient" (Blume et al., 2001). We want to present a case with seizures evoked by decision making. **Case report:** A 52 years old otherwise healthy patient with no family history, presented at the epilepsy polyclinic at the age of 17 years, with 1 year history of seizures. His seizures start with an anxious feeling, perspiration and are followed by a tonic activity and a

tingling on the right hand, extending to the right arm and the right side of his face, causing elevation of the right arm over the head. The patient keeps conscious and aware but he sometimes gets a speech arrest. During some of the seizures he feels like he has to urinate and defecate, but never loses sphincter control. Visual, auditory or tactile stimuli do not trigger his seizures. But all of the seizures, except for a small percentage which are spontaneous and usually occur in the evening, are triggered with 'decision making', as he claims. He experienced 2 secondary generalized seizures in his whole life, one at the age of 17 and the other at the age of 29 (after withdrawal of his treatment). His physical examination is normal as well as his repeated cranial Magnetic Resonance Imaging (MRI)'s. His interictal electroencephalogram (EEG)'s showed a left parieto-temporal focus which sometimes extended to the homologue part of the right hemisphere and occasional diffuse bilaterally synchronous theta activity. We obtained partial response to treatment with Levetiracetam 3000 mg/day, Phenytoin 400 mg/day and Phenobarbital 100 mg/day (1–2 partial seizures/month).

**Conclusion:** Considering the lack of specific guidance regarding broader definitions of reflex seizures and reflex epilepsies we want to describe this rare clinical phenomena we observed.

#### p0662

##### SEIZURE ASSOCIATED WITH HEPATITIS A VIRUS

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**Background:** Hepatitis A virus (HAV), which causes acute hepatitis, is transmitted by the fecal-to-oral route. It is known that rarely involves the CNS. We present two cases of patient who had HAV infection with generalized seizure. **Case 1:** A 25-year-old female, with history of fever and general weakness for 3 days admitted. Body temperature was 38.4°C and no neurologic deficit was found. In blood tests, leukopenia and elevation of ALT and AST were found. Serum IgM HAV Ab was detected. On the 4<sup>th</sup> day, deterioration of consciousness and neck stiffness were found and generalized seizure followed. CSF pressure was 235 mmH<sub>2</sub>O, but pleocytosis was not present. Generalized delta activity was observed on EEG. After conservative care, mental status was gradually improved and follow up EEG was interpreted as normal. **Case 2:** A 34-year-old man was transferred to neurology department after generalized convulsion a day ago. 6 days ago, he had mild fever and general weakness. He was alert and only showed neck stiffness. Serum AST, ALT and total bilirubin levels were elevated. HAV IgM Ab was detected and other viral markers were negative. CSF revealed 182 mmH<sub>2</sub>O of opening pressure with WBC 28/mm<sup>3</sup>. CSF HAV IgM Ab and PCR were positive. EEG revealed diffuse slowing and brain MRI showed normal findings. With conservative care, he discharged without recurrence of seizure.

**Discussion:** The etiology of seizure with HAV infection is not well understood. One possible mechanism is a disturbed detoxification process by liver damage. Another is the direct invasion to CNS. In case 1, normal CSF result revealed and the seizure might be from toxic metabolites. But case 2 showed CSF pleocytosis with HAV IgM Ab and PCR, supporting the viral invasion to CNS. Although some cases were reported, HAV-associated seizure is a rare disorder and the diagnosis may be difficult without a clinical suspicion.

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#### p0665

##### MEDIUM-CHAIN TRIGLYCERIDE DIET IMPROVES SEIZURE CONTROL IN EPILEPTIC DOGS

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**Purpose:** Epilepsy is the most common chronic neurological disorder in dogs as it is in people. Approximately one-third of people and dogs with epilepsy continue to seizure despite adequate antiepileptic treatment. There continues to be a need for new treatment strategies to improve the welfare of epileptic patients.

**Method:** A 6-month prospective, randomised, double-blinded, placebo controlled crossover dietary trial was designed to compare a medium chain triglyceride ketogenic diet (MCTD) to a standardised placebo diet in chronically treated dogs with idiopathic epilepsy, which had  $\geq 3$  seizure(s)/3 months prior enrolment. Dogs were fed either MCTD or placebo diet for 3 months followed by a subsequent respective switch of diet for a further 3 months. Seizure frequency, clinical and laboratory data were collected prospectively and evaluated for 21 dogs completing the study.

**Results:** Seizure frequency was reduced when dogs were on MCTD (2.31/month, 0–9.89/month) in comparison to placebo diet (2.67/month, 0.33–22.92/month,  $p = 0.0195$ ); 3 dogs achieved seizure freedom, 7 dogs had  $\geq 50\%$  reduction in seizure frequency, 5 had an overall reduction in seizures and 6 showed no response. Number of days with seizures were also significantly reduced when dogs were on the MCTD (1.63/month, 0–7.58/month) in comparison to placebo diet (1.69/month, 0.33–13.82/month,  $p = 0.0216$ ). There were no significant changes in serum concentrations of glucose ( $p = 0.9027$ ), phenobarbital ( $p = 0.4223$ ), potassium bromide ( $p = 0.4037$ ) and weight ( $p = 0.2997$ ) between groups.

**Conclusion:** In conclusion the data shown are in accordance with other studies, showing anti-seizure properties of a MCTD, and provides evidence for the implications of the MCTD as a therapeutic option for treatment in epilepsy.

#### p0666

##### EPILEPSY IN KOREAN TRADITIONAL MEDICINE: A HISTORICAL REVIEW

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**Purpose:** "Korean Medicine" based on Korean traditional medicine exists in parallel with "Medicine" based on western modern medicine in the Korean health care system. People with intractable diseases including epilepsy often seek traditional medicine. We aimed to understand the perspective of Korean medicine on epilepsy by reviewing medical textbooks of medieval Korea, which might have had a major influence on contemporary Korean Medicine.

**Method:** We reviewed "Classified Assemblage of Medical Prescriptions (醫方類聚)" (1445–1477) and "Treasured Mirror of Eastern Medicine (東醫寶鑑)" (1610) and abstracted their records associated with epilepsy. The Joseon Dynasty supported their publication to create standard medical textbooks. The "Classified Assemblage of Medical Prescriptions" compiled vast quantities of prescriptions from East Asia that existed prior to the early 15th century with citations. The "Treasured Mirror of Eastern Medicine" interpreted this information in a more system-

atic fashion and re-classified the diseases, establishing originality to Korean Medicine.

**Results:** Since the 14th century, the concepts of 'Jeon' (癲) and 'Gan' (癎) approximated the modern concepts of epilepsy or seizure. They described their differential diagnosis from stroke, psychosis or syncope. The cause of epilepsy was classified as inborn, environmental, and food related. The pathophysiology was explained on the basis of obstruction or turbulence of energy flow within the brain, startle response, or pathological hyperactivity. Attempts were made to classify seizures based on semiology: 'Jeon' (癲) were seizures with psycho-behavioral symptoms and 'Gan' (癎) were convulsive seizures. There was documentation of acute and chronic states, suggesting that three or more seizures could be considered chronic epilepsy. Medicine, food, physical therapy, meditation, and acupuncture were all introduced as methods of treatment. Formulation methods for the medications were described in detail.

**Conclusion:** Epilepsy was an area of extensive research in medieval Korea. Appreciating traditional medicine can provide new insight in developing novel treatment methods for epilepsy.

#### p0667

### DO CIRCADIAN PREFERENCES AND SLEEP QUALITY DIFFERENT ACCORDING TO EPILEPSY CLASSIFICATION?

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**Purpose:** To evaluate the circadian preference and sleep quality in patients with partial epilepsy (PE) and generalized epilepsy (GE) and to investigate whether circadian preferences and sleep quality differ according to epilepsy classification.

**Method:** We enrolled the consecutive 170 patients (age 20–49; PE, n = 127; GE, n = 43) who were diagnosed more than 1 year before and were taking antiepileptic drugs for more than 6 months. Subjects with mentally retarded (IQ < 80), serious medical and psychiatric diseases including depression, and habitual use of hypnotics (≥ 3 nights/w) for last 4 w, short sleeper (≤ 5 h/d), and shift worker were excluded. All completed morningness-eveningness questionnaire (MEQ), Pittsburg sleep quality index (PSQI), and Epworth sleepiness scale (ESS). Epilepsy history and seizure frequencies for the last 1 year were obtained from medical records.

**Results:** GE was younger (30.3 year) than PE (33.9 year, p = 0.015). The most common circadian pattern was neither type in both groups (74.0 and 79.1%), however, the proportion of evening type was significantly higher in GE (20.9%, n = 9) than PE (6.3%, n = 8, p < 0.001). GE reported more sleepy (ESS 7.5) than PE (6.0, p = 0.022). Overall PSQI scores and each question scores were not different between GE and PE although more than half in each group were poor sleepers (PSQI ≥ 5). Compared to good sleepers, poor sleepers had more frequent seizures (8.0 vs. 22/y in PE, 1.8 vs. 15.8/y in GE). Poor sleepers with GE (n = 28) showed the lowest MEQ scores and the highest ESS.

**Conclusion:** Younger age of GE may be related to higher frequency of evening circadian preference than PE. In both group, evening people with poor sleep quality had more frequent seizures and more sleepy, which suggests the importance of sleep on seizure control regardless of epilepsy classification.

#### p0670

### VITAMIN D, PARATHORMONE AND CALCIUM LEVELS IN ADOLESCENTS UNDER ANTIEPILEPTIC DRUG TREATMENT

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**Purpose:** In patients with epilepsy side effects can occur due to long term use of anti-epileptic drugs. In many researches it is shown that due to use of anti-epileptic drugs vitamin D3 levels drop off. In our research vitamin D3 levels in adolescent patients with epilepsy has been investigated.

**Method:** Our research included 30 adolescent patients, 20 of whom are girls and 30 of whom are boys. The patients were using the same anti-epileptic drug regularly at least for 6 months. They did not have any endocrinologic or metabolic disorders. They were not taking extra calcium and vitamin D. The patients' levels of vitamin D3, parathormone (PTH), and Ca were analysed.

**Results:** The age interval of the patients was 9–18, and the age average was  $13.9 \pm 2.85$ . The mean values of anti-epileptic drug doses were between the recommended daily dose intervals. The Ca values of the patients were found to be  $9.7 \pm 0.33$  mg/dl, that is within normal limits. PTH has been found to be higher than above normal levels in two patients ( $18.45 \pm 4.41$  ng/ml). The patients' vitamin D3 level interval was found to be 11.3–72.75 ng/ml and their vitamin D3 level average was found to be  $34.71 \pm 17.4$  ng/ml. In 11 patients medium level of vitamin D3 deficiency ( $18.45 \pm 4.41$  ng/ml) was found. In 19 patients, 52.63 percent of whom were girls, optimal vitamin D3 levels were found ( $43.79 \pm 15.56$  ng/ml). The lowest vitamin D3 level was found to be  $28.84 \pm 14.4$  ng/ml in patients who were treated with polytherapy.

**Conclusion:** Vitamin D3 deficiency is much more significant in the long-term anti-epileptic drug treatment and in girl patients. This research has been submitted as a preliminary study showing that it is important to follow up adolescent patients with epilepsy in whom bone formation is high.

#### p0671

### SEMIOLOGIC AND HEMODYNAMIC FEATURE OF CONVULSIVE SYNCOPE: HEAD-UP TILT TEST WITH VIDEO MONITORING

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**Purpose:** Convulsive syncope can be confused with epilepsy. We aimed to demonstrate the semiologic signs during the syncopal attack and to characterize eye signs of syncope.

**Method:** All patients underwent head-up tilting table test (HUT) and video recording simultaneously, which includes another video setting for eye observation. We investigated the video of the patients with positive results and syncope during HUT, especially focusing on the convulsive features and eye ball deviations. Furthermore, we estimated a certain correlation between these semiologic findings and the hemodynamic changes including heart rate and blood pressure.

**Results:** Of 541 patients with HUT, 84 (15.5%) patients experienced syncope during the test. Among these syncope patients, 49 (58.3%) patients showed eye opening with eyeball positioning or movements dur-

ing the syncopal attack. Out of eyeball manifestations, conjugate eyeball deviation to upward in 35 patients (41.7%) is common position. Twenty four (28.3%) patients revealed head drop. Forty four (52.4%) patients showed seizure mimicking movements in their arms or legs, including myoclonic, tonic, or clonic phase. Interestingly, patients with head drop and eye opening showed significant decrease of systolic blood pressure and heart rate during syncopal attack ( $p = 0.031$ ).

**Conclusion:** We reported that head drop with eye opening state during syncope can be the sign of more profound degree of cardiohemodynamic dysfunction.

**p0672**

### EFFICACY OF KETOGENIC DIET CAN BE IMPROVED WITH HIGH POLYUNSATURATED FATTY ACID CONTENT

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**Purpose:** The ketogenic diet (KD) is used to treat persons with uncontrolled epilepsy. One proposed mechanism of KD is the elevation of polyunsaturated fats (PUFA) resulting in increased resistance to seizures in ketotic brain tissue. However, a high PUFA-enriched KD may achieve a better seizure control than a classical KD. Trials to date with high PUFA KD have shown equivocal results.

**Method:** This was an open, non-blinded study of 50 patients of age 11 months to 14 years (mean = 7 years) on KD who had inadequate seizure control. They were changed to high PUFA KD. KD consisted of 37.5% PUFA while PUFADK consisted of 73% PUFA.

**Results:** A total of 17 patients had more than 90% reduction (Of these 13 had 100% reduction) with a responder rate of 46% (23 patients >50% reduction).

**Conclusion:** PUFA KD could be tried successfully in those who fail the KD. The earlier trials were not successful either due to small sample size or short period of trial. A randomised control trial comparing KD and PUFADK may help further elucidate this hypothesis.

**p0673**

### DIFFERENT ETIOLOGICAL FACTORS AND CLINICAL COURSE OPSOCLONUS-MYOCLONUS-ATAXIA SYNDROME: REPORT ON THREE PEDIATRIC CASES

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**Purpose:** Opsoclonus-myoclonus-ataxia (OMA) syndrome is a rare neurological disorder of acute/subacute onset characterized by multi-directional chaotic saccadic eye movements, accompanied by myoclonus and cerebellar ataxia, as well as sleep disturbance, cognitive dysfunction, and behavioral disruption. OMA syndrome is commonly related to a paraneoplastic process, specifically neuroblastic tumors in children. However, OMA syndrome may occur in association with infectious agents, and genetic predisposition. The pathophysiology of OMA syndrome is not well understood. It is postulated dysfunction of the humoral and cell-mediated immune mechanism.

**Method:** We describe three children with OMA syndrome, occurring with different etiological factors and clinical course.

**Results:** The first patient, a 2-years-old boy, developed a sudden onset of OMA, and eventually diagnosed with posterior mediastinal ganglioneuroma. The second patient, a 2-years-old girl, experienced ataxia and opsoclonus with a mild degree of myoclonus associated with an adrenal gland neuroblastoma. The third patient, a 2.5-years-old boy, who presented with ataxia and myoclonus without opsoclonus. Opsoclonus occurs after 5 months, and it became clear OMA syndrome. The patient diagnosed with idiopathic OMA syndrome based on normal laboratory examinations and imaging results.

**Conclusion:** We emphasize that three components of OMA syndrome may not be occur at the same time or one of these can be obscure, therefore comprehensive systemic investigations should be made in patients with suspected OMA syndrome.

**p0674**

### CLINICAL PRESENTATION OF EPILEPTIC SEIZURES IN A CHILD WITH DIAGNOSIS OF ATRIAL FIBRILLATION: A PEDIATRIC CASE REPORT

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**Purpose:** Many cardiovascular disorders may result blackouts accompanied by abnormal movements attributable to generalized brain hypoxia. In some cases it may be difficult to distinguish between cardiac and epileptogenic causes. Misdiagnosis of epilepsy and unnecessary antiepileptic medication are common in these patients. Although rare in children atrial fibrillation may cause loss of consciousness. These disorder is strong associations with underlying cardiovascular diseases and male gender.

**Method:** We describe a *previously healthy* 13-year-old female patient who presenting with urinary incontinence and generalized tonic-clonic convulsions.

**Results:** The patient diagnosed with atrial fibrillation based on physical examination and ECG findings.

**Conclusion:** Cardiovascular disorders should be considered in patients presenting with loss of consciousness and seizure-like symptoms. We emphasize that complete physical examination, and ECG recording in necessary cases are important for correct diagnosis of patients.

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**p0675**

### TREATMENT OF INFANTS WITH EPILEPSY: COMMON PRACTICE ACROSS THE WORLD

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**Purpose:** There is currently a lack of high quality data to guide the development of treatment recommendations for infants with epilepsy. The aim of this study was to develop global understanding of the preferred use of treatment interventions and to identify inter-regional differences.

**Method:** An electronic survey was distributed to chapters of the International League Against Epilepsy (ILAE), the International Child Neurology Association (ICNA) and various regional child neurology associations. Questions were focused on current clinical practice including drug and non-drug treatment interventions. Inter-regional comparisons were then identified and analysed using the relevant statistical analysis.

**Results:** 733 unique responses were captured from 96 different countries. The survey found that overall most regions have a similar practice for first line interventions. There were, however, statistically significant differences identified in North America where more Levetiracetam was prescribed and in sub-Saharan Africa where there is a large amount of variability in drug preference. Furthermore, it was also noted that phenobarbital was used for generalised and focal seizures in both resource-poor and resource-equipped regions. For second and third line interventions the ranges of choices were diverse, often with little correlation across regions. In terms of alternative therapies, overall previous experience with vagal nerve stimulation and epilepsy surgery significantly increases the preferred use of these therapies once seizures have been diagnosed as medically refractory.

**Conclusion:** The results from this survey highlight the lack of global consistency in the management of infants with epilepsy. These findings further justify the need for more randomized controlled trials within this population group to guide the development of more useful treatment recommendations. Lastly, the identified differences in global prescribing practices may provide a useful platform for further investigation into the issues surrounding the management of infants with epilepsy.

p0676

### DEVELOPMENTAL OUTCOME IN CHILDREN OF INFANTILE SPASMS WITH FOCAL CORTICAL DYSPLASIA

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**Purpose:** We investigated developmental and epilepsy outcome in infantile spasms patients with focal cortical dysplasia, and analyzed clinical factors related to the developmental outcome in these patients, retrospectively.

**Method:** This is a retrospective chart review of 47 children who diagnosed with infantile spasms and focal cortical dysplasia. We included the children treated with diverse modality of treatments, antiepileptic drugs, ketogenic diet and epileptic surgery at Severance children's hospital from January, 2008 to December, 2014. We reviewed patients' characteristics and outcomes of treatment, and sorted them into good outcome and poor outcome groups. With comparing the clinical factors of two groups, we analyzed predicted factors for better developmental outcomes in these patient group.

**Results:** Among 47 children, 12 of them (25.5%) were treated only with AEDs and 24 children (51.1%) tried on ketogenic diet. Children who underwent epileptic surgery and pathologically confirmed cortical dysplasia were 11(23.4%). Good outcome group (Social quotient >70) were 15 (31.9%) and poor outcome group (Social Quotient <70) were 32 (68.1%). And shorter epilepsy duration (from clinical onset of spasm to seizure cessation), good initial neurodevelopmental status and unilobar focal cortical dysplasia distribution were possible predicted factors for better neurodevelopmental outcomes in this study.

**Conclusion:** Etiologic diagnosis and providing early and active appropriate therapy can lead to shorter epilepsy duration and it can prevent children from functional declining and may contribute to better developmental outcome.

p0677

### THE CLINICAL AND DEMOGRAPHIC CHARACTERISTICS OF CHILDREN WITH LATE FEBRILE SEIZURE

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**Purpose:** The goal of this study was to assess the clinical and demographic characteristics of children with late febrile seizure on Jeju Island, South Korea.

**Method:** We reviewed retrospectively patients whose FS occurred after 5 years of age (defined as late FS) who visited the Jeju National University Hospital between March 2007 and December 2014. We excluded patients with evidence of intracranial infection.

**Results:** Eighty-four (53 boys and 31 girls) of a total of 448 patients with FS were diagnosed with late FS. A family history of FS and epilepsy was found in 30/83 (35.7%) and 2/83 (2.3%), respectively. Thirty-eight (45.2%) patients were diagnosed with complex FS. Subsequent non-febrile seizures were observed in 29/84 (34.5%) patients. Abnormal EEG findings were observed in 46/78 (58.9%) patients. The 84 patients were classified into two groups based on the onset of the first FS (before and after 5 years of age, n = 54 and 30, respectively). Two variables were significantly more prevalent in the group with the first FS before 5 years of age: family history of FS and complex FS. Analysis was performed to compare the patients grouped according to the absence or presence of late FS (n = 364 and 84, respectively). Three factors were significantly more prevalent in the group with late FS: neurodevelopmental delay, subsequent nonfebrile seizure, and EEG abnormalities.

**Conclusion:** Patients with late FS had a significantly higher frequency of EEG abnormalities and subsequent nonfebrile seizures compared with patients whose last FS developed before 5 years of age. Among patients with late FS, the group of patients who had their first FS before 5 years of age had a higher prevalence of family history of FS and complex FS compared with the group of patients whose first FS occurred after 5 years of age.

p0679

### CHILDHOOD-ONSET EPILEPSY IN JAPANESE PATIENTS WITH DOWN SYNDROME

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**Purpose:** A retrospective review of patient histories was conducted to clarify the clinical features of epilepsy in children with Down syndrome.

**Method:** Based on records in our hospital database entered between 1981 and 2013, we identified 25 patients (14 males) with childhood-onset (<18 years) epilepsy associated with Down syndrome. The patients were classified into two groups according to seizure type at onset: epileptic spasms (ES) and non-ES groups. We compared the clinical manifestations and outcomes of epilepsy between the groups.

**Results:** The study included 13 patients in the ES group and 12 in the non-ES group. Spasms developed at the mean age of 7 months (range

## Abstracts

3–15 months) in the ES group, whereas at 10.5 years (1 month–17 years) in the non-ES group. Congenital heart diseases were the most common comorbidity in both groups. There were no significant differences in clinical features (e.g., gender, gestational week, birth weight) between the two groups. At the last follow-up, all patients of both groups had severe mental retardation. All except 2 patients in the ES group could walk without support. Most (12/13) children in the ES group achieved seizure control. In contrast, 7/12 patients in the non-ES group had intractable seizures.

**Conclusion:** In our study, patients with epilepsy associated with Down syndrome classified as ES had more favorable seizure outcomes as compared with those who had non-ES seizures.

## p0680

#### DIFFERENT AMBULANCE CALL-OUT RATES FOLLOWING PROLONGED ACUTE CONVULSIVE SEIZURES BUT SIMILAR AVAILABILITY OF RESCUE MEDICATION AND TRAINED PERSONNEL AT HOME AND AT SCHOOL IN A EUROPEAN SURVEY OF CHILDREN WITH EPILEPSY

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**Purpose:** To explore rescue medication administration and ambulance use in children with epilepsy who experience prolonged acute convulsive seizures (PACS).

**Method:** Practices in Emergency and Rescue medication For Epilepsy managed with Community-administered Therapy 3 [PERFECT-3]) enrolled non-institutionalized children (aged 3–16 years) who had been diagnosed with epilepsy ≥ 12 months previously, had experienced ≥ 1 PACS within the last 12 months, and had currently prescribed rescue medication(s) for PACS. Patients' parents/guardians completed web-based questionnaires.

**Results:** According to 258 patients' parents in Germany (n = 87), Italy (n = 74), Spain (n = 72) and the UK (n = 25), 171/253 (67.6%) had their most recent PACS at home, 32/253 (12.6%) at kindergarten/nursery/school and 50/253 (19.8%) elsewhere. Of these, 69.0%, 75.0% and 82.0% received rescue medication, and an ambulance was called for 19.9%, 56.3% and 14.0%, respectively. Overall, rescue medication was always carried by 42.4% of children and by an accompanying adult for 44.0%, with separate supplies often kept at home (84.9%) or school/kindergarten/nursery (73.3%). Most children's parents (81.0%), school staff (72.5%) or relatives (63.6%) were trained to give rescue medication. Most patients' schools (63.0%) had a documented PACS care process. The majority of parents (54.3%) were very or extremely confident that their child would receive rescue medication promptly following PACS at school. Of the remainder, 48.7% reported that the school protocol was always to call an ambulance, 28.6% that school staff were not trained to administer and 21.8% that school staff were unwilling to administer rescue medication.

**Conclusion:** For most but not all surveyed children with epilepsy, their prescribed PACS rescue medication and people trained in its administra-

tion were available at home and at school. Ambulance utilization following PACS was high, especially at school. These findings confirm the need for improved community training in PACS management.

Study funded by ViroPharma (part of the Shire Group of Companies)

## p0681

#### PSYCHOSOCIAL ISSUES OF ADOLESCENTS WITH EPILEPSY IN JAPAN

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**Purpose:** Transitional youths in epilepsy care have gathered attention worldwide recently, as they face specific psychosocial problems that need to be incorporated in their treatment. However, only a few studies investigated these issues in Japan. This study aimed to explore youth's multi-dimensional aspects of psychosocial issues in relation to epilepsy.

**Method:** A mixed-methods study design was utilized to better understand the impact of epilepsy on adolescents and their level of psychosocial adjustment. The study included 11 adolescents with epilepsy (12–18 years old) and their parents in our epilepsy monitoring unit. Quantitative self-report instruments were first administered to both parties to assess psychiatric and behavioral issues, and quality of life (QOL). Semi-structured interviews were then conducted separately. Quantitative data were analyzed to generate key issues in order to explore more contextual information from interviews.

**Results:** Quantitative data indicated youths with psychiatric and behavioral issues tend to perceive a large negative impact from social issues (i.e., stigma, lack of social support, interpersonal relationship). Three youths were indicated for possible depression, whose issues extended to behavioral and social aspects. Of those, 2 youths reported a history of medication overdose and self-harm episodes, and one was referred for psychiatric care after the discharge. Semi-structured interviews revealed 36% of the adolescents having experienced stigma, bullying, and friendship issues during secondary school. However, no youths indicated significant impact of epilepsy on their QOL. Furthermore, reporting gaps existed between youths and their parents in terms of emotional issues.

**Conclusion:** Findings indicated adolescents with epilepsy perceive environmental issues as significant barriers than their health perception itself, which subsequently impact their emotional well-beings. Reporting gaps between adolescents and parents may be suggestive of youths in transitioning phase into independent adulthood. This provides future implication to emphasize on psychosocial assessment and educational intervention for self-management.

## p0683

#### FEATURES OF HOT WATER EPILEPSY IN HUNGARY AND COMPARISONS WITH CASES FROM EUROPE

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**Purpose:** Hot water epilepsy (HWE) is a rare form of reflex epilepsies, characterized by seizures precipitated by warm bath. Only small series of patients have been reported outside of India, Turkey and Japan. We

present 13 cases of HWE and compare their clinical features with HWE cases published from Europe.

**Method:** Retrospective chart review. Student's t-test and chi-square test were used.

**Results:** At the time of first seizure the patients age ranged from 1 week to 10 years (11 younger than 14-month). Most commonly complex partial seizures presented soon after immersion into a normal temperature bath. 8 patients suffered seizures not related to bath, too. Interictal EEG revealed focal epileptic discharges in 7. Brain MRI revealed various abnormalities in 3 children. 7 patients had a family history of epilepsy. After a mean follow-up period of 9.5 years, 10 patients became seizure free with changes in bath habit and antiepileptic medications. 6 patients suffer comorbid developmental disorder. We compared our patients with other 38, published from Europe. Age at onset was lower and developmental disorder was more frequent in our cohort, however these differences were not significant. Further comparisons were made after merging our patients with those from Europe, and grouping them based on the presence or absence of family history of epilepsy. Non-bathing-related seizures and developmental disorder were more common in HWE patients with family history of epilepsy. When groups were formed on the basis of the absence or presence of developmental disorder, a younger age, non-bathing seizures and the family history of any seizure were found to be more common in the latter group.

**Conclusion:** Characteristics of 13 new HWE patients from Hungary are similar to those in Europe. Further analysis of the merged groups suggests, that some features may outline a subgroup of patients within HWE.

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p0686

### STUDY ABOUT PREVALENCE OF FEBRILE SEIZURE IN CHILDHOOD EPILEPSY

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**Purpose:** To determine the prevalence of febrile seizure before the onset of afebrile seizures in childhood epilepsy.

**Method:** Children between 1 to 14 years of age with idiopathic, cryptogenic epilepsy and other rare epilepsy syndromes were included in the study. Children with acute symptomatic seizures or epilepsy due to identifiable acquired lesion like granulomas etc were excluded from the final analysis. Of the 100 cases 49 were localization related, 48 were generalized and in 3 cases the syndromes was undetermined.

**Results:** Seizures provoked by fever had occurred before the onset of afebrile seizures in 15 of 100 cases studied. 7 of these later developed generalized epilepsy syndromes 6 developed localization related epilepsy syndromes and in 2 cases it was undetermined. In our study 4% of the cases had cryptogenic localization related epilepsy. Of these 3% were semiologically complex partial seizures of temporal lobe origin. Of the 6 children with absence epilepsy 2 children (33%) had febrile seizure preceding onset of absence seizures. Of the other idiopathic generalized epilepsy cases 2 children had a family history of febrile/afebrile seizures and also prior history of febrile seizures qualifying the criteria of generalized epilepsy with febrile seizures plus (GEFS+) syndrome. In one of our cases febrile seizures started at 6 months of age and had continued till presentation to us at 5 years of age. In the second patient febrile seizure occurred at 3 years of age and later the child had two afebrile seizures at 9 and 13 years of age. We had 3 cases of other symptomatic generalized epilepsy (50%) with prior history of febrile seizures.

**Conclusion:** Febrile seizures preceded epilepsy in 15% of our patients. Two patients of these had GEFS+ syndrome, a genetic syndrome linked to the sodium channels. Febrile seizures were also found preceding childhood absence epilepsy and cryptogenic localization related epilepsy especially in children with complex partial seizures.

p0687

### ANTI GAD POSITIVE AUTOIMMUNE EPILEPSY IN CHILDREN: A REPORT OF 3 CASES

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**Purpose:** To study the clinical profile of anti-GAD positive autoimmune epilepsy in children.

**Method:** Case series.

**Results:** Anti-glutamic acid decarboxylase antibodies act against an enzyme that catalyzes the conversion of glutamate to GABA. These antibodies are sometimes associated with epilepsy, often involving temporal lobe. Anti-GAD positive epilepsy in children is rarely reported. In a pediatric case series by Suleiman J et al., out of 13 cases of suspected autoimmune epilepsy, only one case of anti-GAD positivity was reported. We suspected autoimmune epilepsy in 20 children over last 1 year and we found three anti-GAD positive cases. Here, we report three children with anti-GAD positivity with varied clinical presentations. First patient is a 4 year girl who presented with single episode of right focal seizure. MRI brain showed left temporo-occipital gyral swelling. EEG showed left temporal epilepsy. She was anti-GAD positive and was successfully treated with immunotherapy. MRI changes reversed over 6 month period. Second patient is an 8 year old girl who presented with fever followed by aggressive behavior and altered sensorium. Child developed refractory status epilepticus not responding to high dose barbiturate infusion. MRI brain showed medial temporal lobe signal changes suggestive of autoimmune encephalitis. Anti-GAD antibody was positive. Patient expired in spite of immunotherapy. Third case is an 8 year old girl, a known case of shunted early onset hydrocephalus with intellectual disability, presented with recent onset cognitive decline and behavioral problems for 2 months. MRI brain was showing shunted hydrocephalus without ooze. Sleep EEG was revealing continuous spikes and waves during slow-wave sleep. Anti-GAD antibody was strongly positive. She responded to methyl prednisolone therapy showing improvement in behavior and cognition and CSWS pattern resolved in EEG.

**Conclusion:** These cases highlight the spectrum of anti GAD positive epilepsy in children and immunotherapy can prove beneficial in such conditions.

p0690

### EFFECTIVENESS AND TOLERABILITY OF RUFINAMIDE IN KOREAN CHILDREN WITH LENNOX-GASTAUT SYNDROME

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**Purpose:** Rufinamide is known to be effective for children with Lennox-Gastaut syndrome (LGS). The aim of this study is to evaluate its efficacy and tolerability in Korean children with LGS.

**Method:** This is a single center, open label, retrospective study. The subjects with LGS who had received rufinamide as an adjunctive therapy were enrolled in this study. Their baseline clinical characteristics, the

percent change in the seizure frequency per 4 weeks and adverse events were evaluated.

**Results:** Thirty two children (20 males and 12 females, aged  $11.3 \pm 6.6$  years) were enrolled in the study. Half of the subjects suffered from symptomatic causes and 72% of them had almost daily head drops and tonic seizures despite the administration of multiple antiepileptic drugs. After 1 month of rufinamide trial, seizure freedom was achieved in two patients (6.3%),  $\geq 50\%$  reduction in seizure frequency was shown in ten (31.3%) and not effective in eight children (25%). After 6 months of rufinamide trial, twenty patients showed a satisfactory response (seizure free in one,  $>50\%$  seizure reduction in ten, and  $<50\%$  seizure reduction in nine). Adverse events were noted in nine children (28.1%), which include somnolence, aggressive behavior, drooling, etc.

**Conclusion:** The study suggests that rufinamide can be considered to be an efficacious and safe AED for children with intractable epilepsies such as LGS.

p0691

#### EVALUATION OF ETIOLOGY AND PROGNOSTIC FACTORS OF THE DEVELOPMENTAL OUTCOME IN NEONATAL SEIZURES

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**Purpose:** The purpose of this study was to investigate the clinical features of neonatal seizures and to identify prognostic factors of neurodevelopmental outcome in term infants who experienced clinical seizures.

**Methods:** A retrospective analysis was performed on 153 full term and preterm infants with seizures from January 2008 to December 2013. Binary logistic regression analysis was applied to assess risk factors associated with neurological adverse outcomes using variables that were found to be significant on univariate analysis.

**Results:** During the study period, 102 term (66.7%) and 51 preterm infants (33.3%) were enrolled. The main cause of neonatal seizures was hypoxic ischemic encephalopathy (24.5%) in term infants and intracranial hemorrhage (74.5%) in preterm infants. The most common type of seizure was the focal clonic seizure, but the generalized tonic seizure was more common observed in preterm than in term infants. Totally 39 out of 56 term infants with at least 12 months of neurologic follow-up showed normal outcomes compared with only one preterm infant with normal development. Prognostic factors related to adverse neurodevelopmental outcomes in term infants were perinatal history of fetal distress, etiology of hypoxic ischemic encephalopathy, a moderately or severely abnormal EEG, evidence of hypoxic ischemic encephalopathy on brain magnetic resonance imaging and the need for multiple antiepileptic drugs for seizure control.

**Conclusion:** Preterm infants showed poor neurodevelopmental outcomes compared with term infants. The etiology of seizures, treatment response, neuroimaging and electroencephalographic findings were important in predicting the developmental outcome in term infants with seizures.

p0692

#### SEIZURE OUTCOME AND ELECTROENCEPHALOGRAPHIC FEATURE CHANGES AFTER CORPUS CALLOSOTOMY IN PATIENTS WITH LENNOX-GASTAUT SYNDROME

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**Purpose:** To evaluate two-year seizure outcome of Corpus Callosotomy (CC) in children with Lennox-Gastaut syndrome (LGS) and to investigate whether specific electroencephalographic (EEG) features relates to surgical outcome.

**Method:** Forty one children (23 boys and 18 girls) with LGS who underwent CC at Severance Children's Hospital between 2009 and 2012 were included in the study. We reviewed EEG before CC and at 3 months, 1 year and 2 years after CC. We rated hemispheric lateralization ratio (generalization, 6:4, 7:3, 8:2, 9:1, and complete lateralization) of epileptiform discharges (EDs). We also categorized severity of EEG into three (mild, moderate, and severe) based on the background EEG and frequency of EDs.

**Results:** All patients except five (two 8:2 and three 7:3) showed near generalized EDs before CC. After 3 months post-CC, twenty-nine patients (71%) had favorable seizure outcome (Engel class I and II). Three patients (7%) showed close to normal EEG on both hemispheres. Twenty patients (49%) showed improved laterality (over 7:3 ratio) whereas eighteen (44%) showed no lateral improvement. After 2 year post-CC, seven patients (17%, three had further resection) showed near complete remission of EDs. Twenty five patients (61%) remained Engel class I or II. Seven patients underwent subsequent resective surgery after CC (mean  $1.0 \pm 0.7$  year) and six showed favorable seizure outcome. While inspecting EEG features, six patients had higher than 7:3 ratio right before surgery but it did not necessarily predict improved EEG patterns.

**Conclusion:** This study confirms that CC is an effective surgical treatment in patients with LGS. We also showed that complete remission of EDs can be achieved by CC only in a small number of patients. When planning a further resective surgery, background EEG patterns and frequency of EDs as well as the lateralization ratio need to be thoroughly inspected to achieve favorable outcome.

p0694

#### COMBINATION TREATMENT WITH ACTH +MAGNESIUM SULFATE VERSUS ACTH MONO OHTAHARA SYNDROME THERAPY

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**Purpose:** This study compared the efficacy and tolerability of ACTH + magnesium sulfate (MgSO<sub>4</sub>) versus ACTH monotherapy for the treatment of OS (Ohtahara Syndrome).

**Method:** This 30-week, randomized, open-label follow-up study enrolled male and female infants with OS. Patients were randomly assigned to receive ACTH 20 U/d + MgSO<sub>4</sub> 0.25 g/kg/d, or ACTH 20 U/d only (control), intravenously for 3 weeks. Efficacy was assessed over a period of 30 weeks based on seizure Frequency and EEG changes. Tolerability was assessed by monitoring for adverse events using laboratory analysis and clinical evaluation.

**Results:** 10 OS were enrolled (7 male, 3 female; median age, 1.5 months; 5patients per group). At 12 weeks, 3 patients (60%) who received ACTH + MgSO<sub>4</sub> and 2 patients (40%) in the control group were seizure free. At 30 weeks, seizurefree rates were 4 (80%) in the ACTH + MgSO<sub>4</sub> group and 3 (60%) in the control group. On EEG, 3 patients (60%) in the ACTH + MgSO<sub>4</sub> group achieved complete recovery (normalized EEG), 1 (10%) attained partial improvement (multifocal spike wave),and 1 (10%) had no improvement burst suppression. At 4 weeks, in the control group, 1 patients (10%) achieved complete recovery, 2 (25%) achieved partial improvement, and 3 (60%) had no improvement. Of the 3 patients who were seizure free at 30 weeks in the ACTH + MgSO<sub>4</sub> group, 4 (80%) had complete recovery (normalized EEG); this

rate was 3 of 5 (60%) in the control group. In the control group, the difference before and after treatment was nonsignificant.

**Conclusion:** In this study in OS, the proportions of patients who were seizure free from 4 to 30 weeks were significantly greater in the ACTH + MgSO<sub>4</sub> group compared with the ACTH monotherapy group.

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p0695

### EPILEPTIC ENCEPHALOPATHIES OF CHILDREN ABOUT 113 CASES

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**Introduction:** Epilepsy is a public health problem in Senegal and Africa because of its severity and its social importance. It occurs at any age sparing no sex. It can influence the sexual life and vice versa. The objective of this work is to study the effects of antiepileptic drugs on the sex lives of women with epilepsy, the influence of these drugs on pregnancy and when breastfeeding.

**Methods:** This prospective study was conducted in the month of March in the month of August 2011 in the neurological clinic teaching hospital Fann Dakar Senegal and is directed only at women with epilepsy.

**Results:** We collected, 120 patients aged 16–64 years with a mean age of 30.58 years, 45% married, 44.16% were uneducated preponderant All patients were taking antiepileptic drugs, 89.16% was alone. 55% of our patients had epilepsy for at least 6 years. 45.83% had generalized epilepsy, 44.17% of partial seizures. In our cohort, 64.16% were under phenobarbital, 69.16% had good adherence. As side effects of drugs 90% had sexual problems. 75% enjoyed an active sex life, was noted a decrease in the number of sex per week for the disease [31/55 = 56.66%]. In addition, 51.17% were using contraception, including 38.7% of oral kind. 64.86% had noticed an increase in seizure frequency during their pregnancies. Of the 74 women who had contracted a pregnancy, 41.89% had premature infants, 16.21% have made abortions. 61.17% had psychosocial life affected.

**Discussion and conclusion:** People with epilepsy often experience sexual problems that may be caused by epilepsy, antiepileptic and/or reactions of the partner and the other facing the diagnosis of epilepsy.

**Keywords:** epilepsy, reproductive health, pregnancy, antiepileptic, Senegal

p0696

### PANAYIOTOPOULOS SYNDROME: A REPORT OF 44 CASES

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**Purpose:** The purpose of the study was to evaluate the electro-clinical features of patients with Panayiotopoulos Syndrome (PS) in detail.

**Method:** An analysis of patients with Panayiotopoulos Syndrome between 1994 and 2014 was performed.

**Results:** Forty-four patients were included in the analysis. Twenty-three of them (52.3%) were female and 21 patients (47.7%) were male. Mean age was 22.3 ± 4.4 (15–33) currently. Age of seizure onset was 7.2 ± 3.2 (1–12). The number of seizures per patient was 1–3 in 22 patients (50%), 4–10 in 15 patients (34.1%) and >10 in 7 patients (15.9%). Amongst our patients we defined 36 types of clinical features some of which were atypical for this syndrome. The most common clinical features were nausea (52.3%), vomiting (47.7%), pallor (47.7%), deviation of head and eyes (45.5%), generalized seizures (38.6%), ictal syncope (31.8%) and stomach ache (25.0%). Visual manifestations were observed in 16 patients (36.4%). The most common negative manifestation was amaurosis (18.2%) whereas the most common positive manifestation was flashes of colourful lights (15.9%). Autonomic status epilepticus were detected in 9 patients (20.5%). The timing of the seizures was following awakening (65.9%), during daytime(awake) (13.6%), both during nocturnal sleep and daytime(11.4%) and during nocturnal sleep (9.1%). The interictal scalp EEG was abnormal in all patients. Epileptiform discharges were recorded from right, left or bilateral occipital lobes independently and sometimes they occurred on different sides of the same patient. Thirteen patients (29.5%) received antiepileptic drugs. The antiepileptic drugs used in our series were oxcarbazepine (15.9%), carbamazepine (9.1%), valproate (2.3%) and levetiracetam (2.3%).

**Conclusion:** Although PS is a benign and common syndrome, diagnosis of this syndrome may be missed due to atypical features or autonomic features suggesting mainly other non-epileptic conditions. We conclude that our detailed data might contribute to the awareness of PS.

p0700

### A SYSTEMATIC CLINICAL AUDIT OF THE EPILEPSY CARE OF CHILDREN AND YOUNG PEOPLE WITH NEURODISABILITIES ATTENDING SPECIAL SCHOOLS: PRELIMINARY RESULTS

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**Purpose:** The investigation, diagnosis and management of the epilepsies is challenging but especially so in children and young people (CYP) with neurodisabilities due to difficulties in compliance with investigations and confounding factors such as co-existing non-epileptic movement disorders. The purpose of this clinical audit was to assess the epilepsy care provided, using an adaptation of the UK Epilepsy 12 national audit.

**Method:** This was a retrospective case note-based clinical audit. A data collection sheet was devised to allow collection of anonymised clinical information from each child's school health records and electronic hospital records. 16 performance indicators were devised, based on Epilepsy 12 methodology with additional information relevant to CYP with neurodisabilities. Inclusion criteria were children attending one of two special schools for CYP with profound and multiple learning disabilities, on one or more antiepileptic drug for treatment of epilepsy, resident in the area for past 5 years. Exclusion criteria were all seizure episodes were febrile, all seizures were acute symptomatic.

**Results:** To date 19 patients have been identified and notes reviewed. 95% (18/19) had at least 1 neurodisability diagnosis; 74% (14/19) had 2 or more neurodisability diagnoses. Performance indicators (PIs) that scored well included seizure classification, written seizure care plan and input from a paediatrician with expertise in epilepsy (all 100%). PIs highlighting areas for improvement were the discussion of risk of dying (0%), risk of SUDEP (1 patient, 5%) and epilepsy syndrome classification (26%).

**Conclusion:** CYP with significant neurodisabilities are at increased risk of having epilepsies and have other complex needs in addition, making

appropriate assessment and management a clinical challenge. Our audit identified areas of high quality practice and areas for improvement in practice, in particular around documentation of important discussions such as the risk of death and SUDEP. Further data will be presented in September.

**p0702**

### FAMILY AND ADAPTATION OUTCOMES OF CHILDREN WITH EPILEPSY: THE ROLE OF SEIZURE CONTROL AND CONDITION SEVERITY

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**Purpose:** To compare children in different seizure control (achieved vs. non achieved) and severity groups (low vs. moderate/high) with regard to psychosocial and clinical indicators: family functioning, perceived stigma, adaptation outcomes (health-related quality of life (HRQOL), psychopathology), and adherence to treatment.

**Method:** The participants were 196 children (50.5% males;  $M = 12.10$  years old) with epilepsy and one of their parents (84.7% mothers), recruited consecutively in three Portuguese neuropaediatric units. Inclusion criteria consisted of:

- (1) epilepsy diagnosis for at least 9 months;
- (2) children aged between 8 and 20 years old
- (3) absence of significant developmental delays or other non-neurological conditions requiring daily prescriptions.

Most of the children (88.3%) were on medication and had achieved seizure control (65.8%). Children and parents completed questionnaires on general and condition management related family functioning, perceptions of stigma, HRQOL and psychopathological symptoms. Neuropaediatricians assessed seizure control status, severity of epilepsy and adherence to treatment.

**Results:** No differences were found between the two seizure control groups. Regarding epilepsy severity, results showed that children within the moderate/high severity group, reported lower levels of HRQOL, higher levels of psychopathology and perceived stigma, and showed worse levels of adherence to treatment, in comparison to children within the low severity group. Parents in the former group also perceived higher levels of family functioning difficulties related to epilepsy management and perceived stigma. No interaction effects between severity and control were observed.

**Conclusion:** Epilepsy severity, but not seizure control, significantly influenced the psychosocial indicators assessed. Results suggest that within neuropaediatric services, a routine assessment of family factors and children's adaptation is warranted, especially among children with more severe epilepsies. Moreover, interventions designed to promote positive family interactions, tackle family related difficulties regarding epilepsy management, discuss stigma related issues alongside emotional and behavioural problems, may lead to improved family and child adaptation outcomes.

**p0704**

### ELECTROCLINICAL PREDICTORS OF OUTCOME IN WEST SYNDROME & ITS RELATIONSHIP TO TRACTOGRAPHIC ABNORMALITIES

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**Purpose:** To study tractographic abnormalities in West Syndrome (WS) in relation to electroclinical characteristics and etiology.

**Methods:** From the prospectively maintained database of an epilepsy centre in Kerala, India, children with a diagnosis of WS with a minimum followup of 1 year were selected. In addition to their electroclinico-radiological data, DTI parameters were statistically compared between control data published in literature and two etiological groups.

**Results:** Forty-five children with available DTI sequences were included in the study (19-cryptogenic; 26- symptomatic). Duration of follow up varied from 14 months–7 years. The two groups were comparable in age at the time of DTI study, age at onset, spasm frequency, hypsarrhythmia pattern, developmental quotient at last followup. Sustained seizure freedom was noted in 4 patients (21.1%) in the cryptogenic group and 1 in symptomatic group (3.8%), evolution into LGS in comparable proportions ( $p = 0.404$ ). ROI based DTI analysis for 4 mm voxels revealed mean fractional anisotropy (FA) values to be significantly lower over the pre-frontal regions in cryptogenic group as opposed to symptomatic group ( $0.220 \pm 0.025$  vs.  $0.321 \pm 0.072$ ) [ $p = 0.016$ ] corresponding to increased mean diffusivity (MD in  $10^{-6} \text{ mm}^2/\text{s}$ ; ( $1469 \pm 206$  vs.  $1204 \pm 940$ ) [ $p = 0.024$ ]. No differences were noted in FA, MD values over the parietal, temporal, occipital white matter, thalamus, putamen, posterior limb of internal capsule, upper brain stem, and posterior cerebellar hemispheres. Both groups demonstrated reduced FA and increased MD in comparison to age-matched values from literature ( $p < 0.001$ ) for all areas except thalamus and internal capsule. No correlation was found between age at seizure onset, developmental age and spasm frequency with these values.

**Conclusion:** The study quantified impairment of white matter integrity in the subcortical regions in West syndrome, predominating over the frontal regions in cryptogenic group. These abnormalities could potentially represent an epiphenomenon of epileptogenesis in West syndrome and can be used in etiological subgrouping as well.

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**p0705**

### DISORDERS OF EARLY LANGUAGE DEVELOPMENT IN DRAVET SYNDROME

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**Purpose:** Aim of the study is investigating DS patients with specific assessments of language development in the first years of life, in order to try to highlight mechanisms underlying language disorders and possibly to provide new tools to improve their outcome.

**Method:** Thirteen patients with typical findings of Dravet syndrome, followed in the Child Neurology Unit of Catholic University in Rome (Italy) were enrolled in the study. Full clinical observation including neurological examination and long monitoring EEG were serially performed till a maximum of 7 years of life and detailed epileptic history was collected in each case. Furthermore, development, cognitive and language assessments were performed with different tests according to age (Griffiths: WPPSI: WISC III; First language evaluation, Axia 1995; Language evaluation at pre-school age, Cianchetti and Sannio Fanciello, 2003).

**Results:** Beside the cognitive decline a characteristic language impairment was found. With a relative preservation of receptive abilities (comprehension) and a strong impairment of productive (phonetic and phonological) skills.

**Conclusion:** The defect in sensorimotor integration of verbal processing together with the well known analogue defect of visual processing shapes a neuropsychological phenotype in DS patients at the beginning of devel-

opment, highlighting a possible mechanism underlying cognitive decline and providing information useful to a targeted treatment strategy.

**p0707**

### FOCAL EPILEPSY IN CHILDREN WITH PERINATAL BRAIN INJURY

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**Purpose:** Study of focal epilepsy and the effectiveness of its treatment in patients with the consequence of perinatal brain injury.

**Method:** We studied 160 patients with focal epilepsy due to perinatal brain injury. Inclusion criteria: perinatal brain damage, neurological/cognitive deficits, changes on MRI, originating in the perinatal period, focal epilepsy, non-progressive neurological deficit due perinatal encephalopathy. All the patients were divided into two groups: I group – the focal epilepsy of perinatal etiology (FEPE) without Benign Epileptiform Discharge of Childhood (BEDC) on EEG (94 cases), II group – the FEPE with BEDC on EEG (66 patients).

**Results:** We analyzed the effectiveness of antiepileptic therapy. Complete remission of seizures was achieved: in the total group in 55.6% cases; in I group – 35.1%, in patients with FEPE with BEDC on EEG – 84.8%. Reduction of seizure frequency  $\geq 50\%$  was achieved in 31.9% in the total group; in I group – 43.6% cases, in II group – 13.7%. Effect is not observed in the total group in 12.5%; in I group – 21.3%, in II group – 1.5%.

**Conclusion:** We consider that patients with FEPE with BEDC on EEG represents original epileptic syndrome. It is characterized by the following features: 1) The SGTCS, hemiclonic and occipital seizures occur almost always during falling asleep or upon awakening. Usually they are not frequent and disappear by puberty spontaneously or by treatment, 2) BEDC on EEG, 3) structural changes in the brain are diffuse cortical atrophy, and not a specific focus. For this form of epilepsy, we suggest using a new term – Focal Epilepsy with Brain Lesion and Benign Epileptiform Discharges of Childhood.

**p0708**

### EXPERIENCE MEDICAL CORRECTION OF SPEECH DISORDERS IN CHILDREN

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**Purpose:** Estimate the efficiency of the therapy of children's speech disorders (CSD) depending on more probable leading disfunction of the neurotransmitter metabolism.

**Method:** An open non-comparative study of 72 children from 2 to 6 years old was carried out. Their middle age of the initial research was 38 months, with different CSD: senso/motor alalia, variants of disarthria. Besides the clinical-neurological examination, the research of genealogical anamnesis, logopedic testing, the continual video EEG including a day sleep. The period of observation was from 2 months to 3 years.

**Results:** 27 (37.5%) children showed epileptic etiology of CSD [Mukhin K.U.co-auth, 2011 ], the efficiency of treatment was estimated from 24, three of them refused from the treatment. Antiepileptic therapy in mono and duo-therapy, gave positive dynamics of development of speech. Out of 15 (20.8%) children with CSD and concomitant Attention-Deficit/Hyperactivity disorder, 11 (73.3%) are successfully treated by noradrenergic inhibitor of reuptake by Atomoxetine [Aikardi G. 2013], three refused from the treatment. 21 (29.2%) with "acetylcholine" CSD were successfully treated with medicines, that had an influence on metabolism of acetylcholine directly or indirectly. The psychogenic CSD showed to 2

(2.8%), a positive dynamics was found when treating by Thioridazine. As it was known, the pathology of neurotransmitter system is on the basis of anxiety-depressive defects, particularly in serotonergic [Gurieva V.A. 1996]. The rest of the children have other reasons of CSD: 6 (8.3%) have autism and 1- surdomutism. They were excluded from the estimation of efficient therapy. Also in 34 (91.9%) of the 37 surveyed identified CSD from various relatives.

**Conclusion:** The therapy of CSD from the point of the most probable leading neurotransmitter disorders is efficient and has good perspectives in case of lowering of investment in treatment. But it demands the follow-up detailed research and evidence. When making treatment decisions should take into account heredity.

**p0709**

### PERAMPANEL EFFICACY AND SAFETY IN SEVERE EPILEPTIC ENCEPHALOPATHIES OF CHILDHOOD

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**Rationale:** To evaluate the efficacy and tolerability of Perampanel (PER) in children with severe epileptic encephalopathies.

**Methods:** Twenty children (mean age: 8.2 years, range: 2–15 years, male: 10) with severe epileptic encephalopathies (EE) have been prospectively followed for 3–24 months since initiation of adjunctive treatment with Perampanel (PER). EE were classified as Dravet syndrome (n = 2), Lennox-Gastaut syndrome (n = 5), EE associated with PCDH19 mutations (n = 5), FIRES (n = 1), EE in non-ketotic hyperglycinemia (n = 1) and EE without known etiology (n = 6). PER doses varied from 2 to 12 mg/d (mean 5.2 mg/d). Three patients dropped out from the study after 1 month (2 - lack of efficacy, 1 - side effects) and were not included into final evaluation. The clinical efficacy and tolerability have been assessed in 17 children during the entire study period and at the end of follow up.

**Results:** The complete seizure control was achieved in 4/17 patients (23.5%), lasting 17–21 months. More than 50% reduction of seizures was observed in 10 patients (58.8%), three children (17.7%) experienced <50% reduction of seizure frequency. PER efficacy was highest in EE associated with PCDH19 mutations (3/5 - seizure-free, 2/5 - >50% seizure reduction) and Lennox-Gastaut syndrome (4/5 patients - >50% seizure reduction). As regards seizure types, PER was mostly efficacious against tonic, focal motor and generalized tonic-clonic seizures, whilst had minimal or no influence on the frequency of myoclonic, atonic seizures and epileptic spasms. Adverse events (tiredness, aggressiveness, somnolence, vomiting) were reported in five patients (29.5%), mostly mild-moderate, with remission spontaneously or with decreasing the PER dosage. The occurrence of adverse events led to PER withdrawal only in one patient.

**Conclusions:** These preliminary data suggest that PER may be a therapeutic option in childhood EE. Further studies are needed to determine its syndrome-specific efficacy.

**p0710**

### FEVER IN THE ONSET OF PANAYIOTOPOULOS SYNDROME: UNDERRECOGNIZED TRIGGER

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## Abstracts

**Purpose:** To assess the prevalence of fever-triggered seizure onset of Panayiotopoulos syndrome, to emphasize the lack of rapid diagnosis in these cases, and to clarify prognostic role of fever in the onset of PS.

**Method:** Thirty five patients with PS aged from 2 to 10 years were included in this retrospective study, divided into two groups: with febrile onset (FO) and afebrile onset (AO). Age, seizure types, prevalence of status epilepticus, history of febrile seizures, precipitating factors were studied. All patients were followed up for 2–5 years to establish the remission.

**Results:** We identified 12 patients with PS whose first seizures were observed during fever episode (34%). The mean age of onset in this group was 4.5 years, compared to 6 years in AO group. Seizure semiology was similar in both groups (mostly versive and autonomic). Status epilepticus was seen in 58% in FO group and (52%) in AO group. Two children in FO group and three children in AO group had simple febrile seizures before the occurrence of PS. Fever was associated with respiratory infections, urinary tract infections and in one patient seizure was precipitated by overheating during sunbathing. Correct diagnosis at onset was made only in three patients in FO group and in 65% in AO group. The most common false diagnosis were encephalitis and meningitis (nine patients), gastroenteritis (one patient), migraine (one patient) and intoxication (one patient). Remission was achieved in all children.

**Conclusion:** Fever triggered seizures in 34% of new-onset seizures in PS. There is a tendency to earlier age of seizure onset in patients with fever trigger. Long term prognosis and clinical course were similar in both groups. Our study showed no link of febrile seizures with prognosis in Panayiotopoulos syndrome. Misdiagnosis is quite common in cases of febrile onset seizures in PS.

## p0712

### MYOCLONIC EPILEPSY OF INFANCY: PHARMACO-RESPONSIVE BUT WITH RISK OF NEUROPSYCHOLOGICAL IMPAIRMENT

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**Purpose:** Myoclonic epilepsy of infancy (MEI) accounts for <1% of all epilepsies, with approximately one case in 40 000 children. Although previously termed “benign”, the risk of adverse neuropsychological outcome may be higher following MEI despite adequate seizure control.

**Method:** We retrospectively reviewed our patients with MEI, who were neurodevelopmentally normal at the time of diagnosis. All 11 patients had the diagnosis confirmed with generalized spike-waves or polyspike-waves, together with epileptic myoclonic jerks that were recorded on video-EEG and surface muscle electrodes, in the presence of normal background for age.

**Results:** The onset of seizures was between 8 months and 3.5 years. Two patients had prior history of febrile seizure. Two had family history of epilepsy. During the EEG recording, photosensitivity was demonstrated in four patients (36%). Seizure control was achieved in nine patients with monotherapy using valproic acid at a dose range of 20–50 mg/kg/day. Two others required the addition of levetiracetam to achieve seizure control. In eight patients who were successfully weaned off all medications and remained seizure-free for more than 4 years, two has attention deficit hyperactivity disorder (inattentive type), one has dyslexia, and one has central auditory processing deficit.

**Conclusion:** Although MEI is generally associated with good prognosis, the neuropsychological and behavioral outcome may be less favourable, as is suggested by our case series. This may occur despite early treatment and good seizure control, indicating that other factors play important roles affecting the neuropsychological outcome.

## p0713

### THE MEDIATING EFFECT OF DISTRESS IN THE RELATIONSHIP BETWEEN ILLNESS PERCEPTIONS AND QUALITY OF LIFE IN ADOLESCENTS WITH EPILEPSY

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**Purpose:** The link between illness perceptions (IP), distress and Quality of Life (QoL) in adolescents with epilepsy remains inadequately investigated. We aimed to explore the mediating effect of distress in the relationship between IP and QoL.

**Methods:** Interviews using the KIDSCREEN-27 Questionnaire, the Brief Illness Perceptions Questionnaire and the Revised Children's Anxiety and Depression Scale were conducted in 100 patients ( $M_{age} = 13.9$ ,  $SD = 2.21.41\%$  girls). A mediation analysis was performed.

**Results:** Most patients (91%) were well controlled on antiepileptics; 3% had infrequent seizures; 6% were pharmacoresistant. There was a significant negative association between IP and QoL ( $b = -0.27$ ,  $P < 0.001$ ) and a significant negative relationship between distress and QoL ( $b = -0.47$ ,  $P < 0.001$ ). The relationship between IP and distress was significant ( $b = 0.39$ , 95% CI: 0.79; 0.91). Results from bootstrapping showed a significant mediation effect of distress on QoL ( $b = -0.08$ ,  $CI_{BCa}: -0.25; -0.13$ ). The relationship between IP and QoL remained significant after including the mediator ( $b = -0.18$ ,  $P < 0.05$ ).

**Conclusion:** Threatening perceptions regarding epilepsy were associated with worse QoL. When distress was added in this relationship it acted as a partial mediator. Our findings highlight the importance of self-reported psychological distress in the relationship between IP and QoL.

## p0714

### EFFECTS OF TOPIRAMATE ON EPILEPTIFORM DISCHARGE IN HIPPOCAMPAL SLICE OF IMMATURE RAT

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**Purpose:** Mechanism of Topiramate is not understood very well and optimal dose of efficacy in animal models is not determined yet. In order to elucidate the action mechanism and optimal concentration of TPM, we observed ictal and interictal discharges from immature-rat-hippocampal-slices in  $Mg^{2+}$ -free, 4-aminopyridine (AP) added artificial-CSF with various-TPM-concentration.

**Method:** We divided rats into 5-groups, control-group ( $n = 12$ ), 4TPM-groups; divided by concentration of TPM, 6 ( $n = 11$ ), 20 ( $n = 7$ ), 60 ( $n = 10$ ) and 200 ( $n = 14$ )  $\mu M$ . Brains were cut into 400  $\mu m$ -hippocampal-slices. Slices of control-group were soaked in 200  $\mu M$  4-AP added  $Mg^{2+}$ -free, then extracellular recordings were performed in hippocampal CA1-pyramidal-region. Slices of TPM-groups were soaked in solution containing 6, 20, 60, 200  $\mu M$ .

**Results:** 1) Interictal-discharges were observed in control-group and 6, 20  $\mu M$ - group but frequency was decreased as concentration of TPM increases, 90% in 60  $\mu M$ -group, and 35.7% in 200  $\mu M$ -group. Amplitude of TPM-group was much smaller than control-group. Latency to first interictal-discharge after 4-AP addition was 52.7 second in control-group, but was 290.2 second in 60  $\mu M$ -group,

568 second in 200  $\mu\text{M}$ -group. Duration of interictal-discharge was 64.6 second in control-group, but was prolonged to 141 second in 60  $\mu\text{M}$ -group.

2) Ictal-discharges were observed in control-group and 6  $\mu\text{M}$ -group, but frequency was decreased as concentration of TPM increases, 55.6% in 60  $\mu\text{M}$ , 28.6% in 200  $\mu\text{M}$  group. Amplitude of TPM-group was much smaller than control-group. Latency to ictal-discharge after 4-AP addition was 141 second in control-group, but increased as concentration of TPM increases, 431.8 second in 60  $\mu\text{M}$ , 627.8 second in 200  $\mu\text{M}$ -group. Duration of ictal-discharge was 1534.7 second in control-group, but decreased as concentration of TPM increases, and the-shortest in 60  $\mu\text{M}$ -group, 155.2 second.

3) Status-epilepticus was seen in 58.3% of control-group and 27.2% of 6  $\mu\text{M}$ -group.

**Conclusion:** TPM suppresses the frequency, latency, and duration of epileptiform discharge induced by  $\text{Mg}^{2+}$ -free, 4-AP added artificial-CSF in immature-rat-hippocampal-slices, starting from 20  $\mu\text{M}$ -concentration and reaching maximal effect at over-60  $\mu\text{M}$ . This finding is presumably due to TPM enhancing of GABA-receptor currents and/or  $\text{K}^+$  channel conductance in response to TPM.

## Paediatric Epileptology 11 Monday, 7th September 2015

p0715

### UNIQUE AND RARE SEMIOLOGIES: ICTAL SMILE AND GELASTIC SEIZURES

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**Purpose:** Gelastic seizures are characterized by epileptic laughter and have most commonly been associated in patients with hypothalamic hamartomas. Although, different localizations have been reported including temporal, frontal and parietal lobes. Ictal smile is an uncommon manifestation which presents a tonic deviation of the mouth or other tonic-clonic movements and it is localized on temporal, parietal and frontal regions and lateralized more frequently to right hemisphere. This case series were performed to analyze the different localizations and lateralizations of gelastic and smiling seizures.

**Method:** We investigated gelastic and smiling seizures from Gazi University School of Medicine Pediatric Video-EEG Monitoring Unit between 2011–2014 as retrospectively. Detailed seizure semiology, EEG and neuroimaging were evaluated.

**Results:** Ten children (6–15-year-old) were found having either gelastic or smiling seizures. 6 of 10 patients had ictal smile, four patients had gelastic seizures. Among the patients with gelastic seizures, the epileptic foci were located in the hypothalamus as hamartoma (four patients). In patients with ictal smile, the localization of the epileptogenic region revealed FCD in left frontal lobe, dysembryoplastic neuroepithelial tumor in right orbitofrontal, FCD in left cingulate, FCD in left supramarginal gyrus, pachygyria-heterotopia in left hemisphere and one patient had unknown origin.

**Conclusion:** Gelastic seizures and ictal smiles are unique and rare semiology. All our patients with gelastic seizures had hypothalamic hamartomas. Ictal smile may originate from frontal lobe, cingulate gyrus and supramarginal gyrus. Beyond right hemispheric involvement, we found left hemisphere may also be responsible for ictal smile different from the current literature. As supported our findings, the differential diagnosis of gelastic and smiling seizures require detailed electrophysiological, radiological and pathophysiological work up especially in case of non lesional patients.

p0716

### COBALAMIN C DEFICIENCY WITH INFANTILE SPASM AND CUTANEOUS FINDINGS: A UNIQUE CASE

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**Introduction:** Cobalamin C (cblC) deficiency is a rare disorder of vitamin B12 metabolism which results from impaired conversion of both its active forms methylcobalamin and adenosylcobalamin. Early onset cblC deficiency typically presents in the first year of life with hypotonia, lethargy, seizures, microcephaly, hydrocephalus, developmental delay and other multisystem involvement including hematologic, ocular, renal, hepatic and cardiac symptoms. We report a case of a female infant with cblC deficiency who presented with seizures, developmental delay and hypopigmented cutaneous lesions.

**Case:** A 4-month old previously healthy, female infant born to non-consanguineous parents was referred to our pediatric neurology department with one month history of loss of eye contact and smile. She also had failure to feeding, slowing of movements and spasms. She was lethargic, pale and hypotonic. On physical examination, her weight and head circumference were below the 10th percentile, there were hypopigmented macules in her chest, arm and abdomen. MRI of the brain showed significant cerebral atrophy and delay of myelination. Urine methyl malonic acid level was 4923 mmol/mol cr (0), plasma homocystein 109  $\mu\text{mol/l}$  (5–14), significantly elevated and methionine was 9  $\mu\text{mol/L}$ , (9–29) low. Genetic testing revealed a single copy of a previously identified pathogenic mutation, c.394 C>T, in the MMACHC gene and confirmed a diagnosis of a cblC deficiency. After treatment her mental status improved and seizures were controlled with antiepileptic drug therapy.

**Conclusion:** In conclusion, any infant presenting with seizures, developmental delay and cutaneous findings, disorders of cobalamin metabolism should be considered in differential diagnosis and the role of cblC deficiency should be identified in aetiology of skin pigmentation.

p0717

### PHARMACO-RESISTANT EPILEPSY IN CHILDREN WITH NEONATAL HYPOGLYCEMIA

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**Purpose:** To report on long-term clinical course in patients with symptomatic epilepsy secondary to neonatal hypoglycemia.

**Method:** We retrospectively reviewed the medical records of patients with neonatal hypoglycemia who have been followed at Gazi University Faculty of Medicine Pediatric Neurology Department between 2008–2014. Patients with perinatal asphyxia were excluded. Thirty three patients (range 6 months–15 years) with a history of neonatal hypoglycemia were included the study.

**Results:** Epilepsy developed in 24 (72%) patients and 14 of them had intractable epilepsy. Other neurologic problems included neurodevelopmental delay (n:21), autism spectrum disorders (n:3), microcephaly (n:4) and visual disturbance (n:4). Two patients did not have any neurological disability during follow-up. Two of 14 patients with intractable seizures had hyperinsulinism. Their seizures have been controlled after pancreatectomy. Two patients had vagal nerve stimulator and showed a partial response to treatment.

**Conclusion:** Our findings demonstrate that neonatal hypoglycemia can influence neurodevelopmental outcome and epilepsy secondary to neonatal hypoglycemia is mostly intractable during childhood. They

show poor response to antiepileptic drug therapy. Therefore, early diagnosis and treatment of neonatal hypoglycemia can prevent future neurological sequelae and may prevent drug resistance.

**p0718**

### CLINICAL AND IMAGING CORRELATES OF EEG PATTERNS IN PEDIATRIC PATIENTS WITH ACUTE ENCEPHALOPATHY

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**Purpose:** We aimed to study the relationship between clinical, electrophysiological and imaging findings of pediatric patients with acute encephalopathy.

**Method:** Electroencephalographic reports of children from January 2012 to march 2015 were retrospectively analyzed at Neurophysiology Laboratory, Department of Pediatric Neurology at Gazi University Medical Faculty. All electroencephalograms (EEGs) consistent with encephalopathy between January 2012 and March 2015 were identified. Clinical and imaging data were collected from charts of patients with encephalopathy. EEGs were classified according to five predefined patterns: Isolated continuous slowing of background activity (theta, theta/delta and delta activity) and patterns with slowing background activity with episodic transients [i.e., triphasic waves (TWs) or frontal intermittent delta activity (FIRDA)]. Clinical characteristics, type and frequency of the disorders and neuroimaging data were documented.

**Results:** We identified 37 EEGs consistent with encephalopathy pattern from a total of 5125 EEGs. EEGs were performed because of a history of altered mental status, seizure, headache. Three patients had encephalopathy due to encephalitis, one due to limbic encephalitis. One patient has ADEM. One of the patients had recurrent encephalopathy periods and was diagnosed with H1N1 associated RANBP2 mutation. Three patients had hepatic encephalopathy. One patient had a vasculopathy due to varicella infection. Two patients had head trauma. The theta pattern was present in 18.6% of patients, 27.1% had theta/delta, 10.2% delta, 3.4% TWs, and 3.4% presented with FIRDA. The most common imaging abnormalities were oedema (15.3%), white matter changes (66%), brain atrophy (7.5%). Theta was associated with brain atrophy, theta/delta with infectious and metabolic disorders, FIRDA with otoimmun encephalitis, TWs with liver or renal failure.

**Conclusion:** In encephalopathic patients, well-defined EEG patterns are associated with specific pathological conditions, suggesting that mechanistic hypotheses underlie these abnormal EEG patterns and these patterns can be correlated to cerebral imaging findings.

**p0719**

### EXPRESSION PATTERNS OF MICRORNAS -146A, -34A, -132, -134 AND -184 IN PEDIATRIC EPILEPSY PATIENTS

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**Purpose:** Epilepsy is one of the most common brain disorder in children. Dysregulation of immunologic and inflammatory systems have been considered to play role in the pathogenesis of epilepsy. The regulation of these systems has been shown to be related to microRNAs. MicroRNAs are small non-coding RNAs which have been known to be an important

controller of post-transcriptional gene expression. The aim of this study is to investigate the expression patterns of microRNA-34a, -132, -134, -146a and -184 in peripheral blood mononuclear cells of patients with drug-resistant and drug-controlled epilepsy.

**Method:** We enrolled 49 epilepsy patients (25 drug-controlled, 24 drug-resistant) and 24 healthy control subjects. Quantitative analysis of microRNAs were performed using specific stem loop primers followed by real-time polymerase chain reaction.

**Results:** Fourty-nine epilepsy patients (mean age  $11.00 \pm 4.36$ ) and 24 healthy controls. The expression levels of microRNA-34a and -184 were significantly decreased in epilepsy patients as compared to control subjects ( $0.79 \pm 0.69$  vs.  $1.07 \pm 0.45$ ,  $p = 0.000$ ;  $0.60 \pm 0.45$  vs.  $1.44 \pm 1.31$ ,  $p = 0.000$ ). There was no significant difference between epilepsy and control groups regarding expression levels of microRNA-132, -134 and 146a. The patients who were mentally deficient had significantly lower microRNA-146a, -132, -184, -134 expression levels ( $p = 0.001$ ;  $p = 0.026$ ;  $p = 0.004$ ;  $p = 0.009$ ). The patients with motor deficiency had significantly lower microRNA-146a expression levels ( $p = 0.043$ ).

**Conclusion:** MicroRNAs are emerging key controllers of gene expression which may play role in epileptogenesis. There are conflicting reports about the effects of microRNAs in pediatric epilepsy patients. Alterations of microRNAs may shed new light on pathogenesis and new treatment choices in pediatric epilepsy patients.

**p0720**

### EFFECTIVENESS OF METHYLPREDNISOLONE AND DIAZEPAM FOR CONTINUOUS SPIKE WAVES DURING SLOW WAVE SLEEP

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**Purpose:** Epilepsy with continuous spike-waves during slow wave sleep (CSWS) is an age related condition characterized by heterogeneous seizure types, neuropsychological and behavioral impairment and a typical EEG pattern that shows "significant activation of epileptiform discharges by sleep". We describe a patient with CSWS who had been previously diagnosed as benign childhood epilepsy with centrotemporal spikes (BCECTS). She benefited well from combination of steroid and diazepam.

**Case report:** This 7.5-year-old girl was born at 37 weeks with no perinatal problem. Her psychomotor development was appropriate for her age. She had been previously diagnosed BCECTS when she was 5-years-old and was treated with levetiracetam and carbamazepine. She had frequent hemiclonic seizures involving right side of the body with jerking of eye lids, mouth and upper limb during the sleep. EEG revealed left frontocentrottemporal spikes which became more frequent during sleep. We ended levetiracetam due to side effects; and ended carbamazepine because of worsening of EEG discharges during sleep. Her seizures stopped with combination of valproic acid and clobazam. After one seizure-free year, she was admitted with ataxia, right hand weakness and deterioration of cognitive functions. EEG demonstrated pattern of continuous spike and wave during slow wave sleep. She did not response to sulthiame treatment and she was started methylprednisolone and high dose diazepam. After 2 weeks, dramatic improvement in clinical and EEG findings were observed. Methylprednisolone and diazepam was tapered at 3th month of the medication and outpatient follow up showed sustained improvement.

**Conclusion:** The current case showed that combination of methylprednisolone and diazepam is an effective treatment for continuous spike and wave during slow wave sleep related to BCECTS.

p0721

**EXPERIENCE FROM A FIRST SEIZURE CLINIC FOR CHILDREN: ALL THAT SEIZES IS NOT EPILEPSY**

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**Purpose:** Report on the experience of a first-seizure clinic for children (Birth to 16 years) based on a triaging system to reduce wait times for a neurological assessment.**Method:** We established and implemented a triaging system with the aid of a Nurse Case Manager. An early telephone interview with families upon receipt of referral by the Nurse. Coordinator enabled the neurologist with information to apply the triaging system on a case-by-case basis. Objective outcome measures included; wait times for evaluation, investigations, return visits, discharge as well as final diagnoses established.**Results:** A total of 368 referrals received during the period of study. There were 186 males and 182 female participants. The triaging system helped reduce wait times from a mean of 179 days (38–312 days) in the pre-study period to a mean of 88 days (5–239 days) during the study. Age ranges of patients (n) included: 1–5 years (85), 6–10 years (96), 11–15 years (80), 16–20 years (107). Only 159 (43%) patient referrals to the program were actually diagnosed with epilepsy, 24 (7%) with a single or first epileptic seizure, while 140(38%) patient referrals were given an alternate diagnosis. Eleven % of referrals missed or cancelled appointments, 1% could not be given a specific diagnosis within the time frame of the project. Conditions presenting as a first seizure in children included; syncope with reflex anoxic seizures (12%) psychogenic non-epileptic seizures (PNES 10%). Anxiety disorder (3%), breathholding spells (2%), behavioral inattention (3%), tics (3%), GE reflux (1%), sleep disorders (1%), migraine and migraine equivalents (2%), while narcolepsy, jitteriness, cyclical vomiting, congenital nystagmus, and spasmus nutans made up the remainder (n of 1 each).**Conclusion:** Over a third of new patient referrals to the First Seizure Clinic did not to have epilepsy. A search for alternative diagnosis in first seizure presentations by referring physicians could reduce referral volumes and wait times for patients with epilepsy.

p0723

**CLINICAL CLASSIFICATION OF INFANTILE SPASMS USING VIDEO EEG FOR INITIAL DIAGNOSIS: TO HAVE HYPSSARRYTHMIA WILL BE WORSE PROGNOSIS?**M.F. Rios Pistoia, M. Avesratury, B. Comas, N. Espinosa, W. Silva  
Universidad de Buenos Aires, Buenos Aires, Argentina**Purpose:** To classify the video EEGs with IS according to the Delphi West group classification and analyze outcome.**Method:** Observational retrospective study that included 33 video-EEGs of infants with IS, performed between January 2010 and December 2014. To simplify the analysis, we grouped West with HWIS (hypssarrythmia) and ISSV with IS (without Hypssarrythmia).**Results:** The median of age was 6.1 months, 18 (%) were female. According to the classification, we observed: 19 (57.57%) had West, 2

(6.06%) HWIS, 6 (18.18%) ISSV and, 6 (18.18%) IS cluster without hypssarrythmia. Twenty four patients had symptomatic epilepsy and seven cryptogenic. EEG findings: 21 (63.6%) presented hypssarrythmia, 27 (81.81%) multifocal paroxysms and 6 (1.81%) unifocal paroxysms. 17 of the 21 (80.95%) patients with hypssarrythmia, had symptomatic epilepsy. Two patients were lost to follow-up, so we analyzed 31 patients. 8 (25.8%) were preterm. 23 (74.2%) had a normal neurological exam before seizures started, but 15 (49.5%) worsened or acquired developmental delay. One patient died. The median duration of the spasms was 4 months (IQR 1.5–9), 5.56 months in patients with hypssarrythmia and 3.83 months in patients without hypssarrythmia. When we analyzed outcome, we observed that; 10/31 developed a refractory epilepsy. Of this subgroup, 7/10 had symptomatic epilepsy and 5/10 hypssarrythmia. Five of the twelve patients that lost patterns neurodevelopmental in the moment to diagnosis (=12 patients/5 had not normal exam previously): 10 had hypssarrythmia and not have exam before the spasms started.

**Conclusion:** In our population, we observed a higher prevalence of patients with hypssarrythmia. We found that hypssarrythmia itself is not a predictor of refractory epilepsy, as if it would be the symptomatic etiology. The duration of infantile spasms would be higher in patients who associate hypssarrythmia.

p0724

**LACOSAMIDE POPULATION PHARMACOKINETICS IN CHILDREN FROM 6 MONTHS TO 17 YEARS OF AGE**J. Winkler\*, R. Schoemaker\*, A. Stockis†  
\*SGS Exprimo, Mechelen, Belgium, †UCB Pharma, Braine-l'Alleud, Belgium**Purpose:** Lacosamide is approved as monotherapy (USA only) and adjunctive therapy of partial-onset seizures in adults with epilepsy (maximum maintenance dose of 400 mg/day). The purpose was to develop a pediatric population pharmacokinetic model for lacosamide considering the effects of demographic variables and concomitant antiepileptic drugs, and perform simulations supporting pediatric dosing adaptations.**Methods:** Two studies (SP0847, SP1047) were conducted in children with epilepsy in which sparse plasma samples were collected for lacosamide determination. A population pharmacokinetic model was developed using the nonlinear mixed effects method. The structural model had a single compartment with first order absorption and elimination. Plasma clearance was modelled using allometric scaling on body weight with a freely estimated allometric exponent, while volume of distribution (V) used a fixed theoretical allometric exponent. Residual error was modelled using additive and proportional error terms.**Results:** Lacosamide plasma concentration-time data (n = 402) were available from 79 children, with a balanced distribution of 14, 22, 25, and 18 subjects in age groups 6 months to <2 years, 2 to <6 years, 6 to <12 years, and 12 to <18 years, respectively. Body weights ranged from 6–76 kg. Covariate search did not evidence significant effects for race, sex, age, renal function or co-administration of valproate on lacosamide plasma clearance, but an increase by co-administration of carbamazepine, phenobarbital and phenytoin was observed. Different pediatric dosing adaptations were simulated with the aim of reaching the range of concentrations obtained in adults receiving lacosamide 400 mg/day. This was achieved with a dosing scheme of 12 mg/kg/day in children weighing <30 kg, 8 mg/kg/day from 30 to <50 kg, and 400 mg/day in children weighing ≥50 kg.**Conclusion:** A population pharmacokinetic model was developed that adequately describes the plasma concentration of lacosamide in children. Weight-based dosing adaptations could be selected to guide subsequent pediatric development. UCB Pharma-Funded.

## Psychiatry 2 Monday, 7th September 2015

p0725

### RIGHT SELECTIVE HIPPOCAMPECTOMY AND PERSISTENT GENITAL AROUSAL DISORDER

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**Introduction:** Persistent Genital Arousal Disorder (PGAD) refers to the experience of persistent sensations of genital arousal that are unprovoked, intrusive and unrelieved by one or several orgasms. It is often mistaken for hypersexuality since PGAD often results in a high frequency of sexual behaviour. At present little is known with certainty about the etiology of this condition.

**Case presentation:** We describe a 37 year-old single woman with typical PGAD symptoms. She had had drug resistant temporal lobe epilepsy for 17 years until right hippocampectomy because of right mesial temporal sclerosis. After 6 years from the surgery, she had obsessive compulsive neurosis and hypersexuality. These persistent feelings of sexual excitation were not associated with epileptic (ictal) sexual manifestation. There was no epileptic abnormality in her EEGs and she had no seizures after the surgery. She is still on oxcarbazepine 900 mg/day. The patient's symptoms resolved briefly after psychotherapy and risperidon 2 mg/day, paroxetine 30 mg/day treatment.

**Conclusions:** PGAD can be tremendously distressing, adding significant burden onto a woman who may already be suffering from anxiety. The proposed etiologies of PGAD are plentiful and may involve a range of psychological, pharmacological, neurological, and vascular causes. Our aim is to discuss and draw attention to PGAD following epilepsy surgery. Successful treatment requires a multidisciplinary approach and consideration of all reversible causes as well as cognitive therapy.

p0726

### EMOTIONAL AFFECTIVE DISORDERS IN ELDERLY PATIENTS WITH POST-STROKE EPILEPSY

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**Introduction:** Ninety six patients post-stroke sequelae were studied. In 55 patients, the course of disease was complicated by symptomatic epilepsy.

**Study objectives:** To study the structure of non-psychotic mental disorders in elderly patients with post-stroke epilepsy and to assess the impact of the disorders on the patients' quality of life.

**Materials and methods:** Two patient groups (96 persons) were studied. Group 1 (55 patients: 31 men 24 women) included patients whose stroke was complicated by the development of epilepsy; Group 2 (41 patients: 21 men and 20 women) included post-stroke seizure-free patients. The average age in Group 1 was  $63.0 \pm 2.0$  years; in Group 2:  $62.5 \pm 2.5$  years.

**Results:** The leading symptoms were depressive and anxiety disorders: depression was found in 68.96% of the patients with epilepsy and in 21.4% of the seizure-free patients, whereas anxiety disorder was found in 21.4% and 64.3% of the patients, respectively. Average scores in Group 1 and Group 2 on the BDI scale were  $34.81 \pm 2.73$  and  $28.57 \pm 3.07$ , respectively; on the HRDS scale,  $21.84 \pm 1.50$  and  $13.79 \pm 1.36$

( $p \leq 0.01$ ), respectively. The Global Severity Index (GSI) in Group 1 and Group 2 was 1.21 and 0.70, respectively. Quality of life (QL) indices were significantly lower in the patients with epilepsy. According to the QOLIE-31, the overall scores QL in Group 1 was 82.27, which is lower than the norm ( $p < 0.001$ ). A comparative analysis of SCL-90-R and QOLIE-31 constructs has provided us with findings on the impact of psychopathological factors on the QL domains.

**Conclusion:** The peculiarity of psychopathological syndromes in elderly patients with post-stroke epilepsy consists in the predominance of depressive disorders over anxiety. The clinical manifestations of psychopathological symptoms correlate with the indices of QL domains. Emotional affective disorders play an important role in the formation of the QL of elderly patients with epilepsy and require additional rehabilitation interventions.

p0727

### NON-EPILEPTIC PSYCHOGENIC SEIZURES IN EPILEPSY PRACTICE

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**Purpose:** Non-epileptic psychogenic seizure (NEPS) is a condition which is frequently encountered in epilepsy practice, composes differential diagnosis and treatment problems. In this study, we searched NEPS incidence in the patients with epilepsy diagnosis who are directed to our epilepsy department that is a tertiary healthcare center.

**Method:** Thousand hundred and fourty patients who were followed in epilepsy department of neurology clinic in Antalya Training and Research Hospital between July 2011 and January 2015 were examined retrospectively. All patients with NEPS were recruited into the study.

**Results:** Total 70 patients were examined; 54 of them were female (77.1%) and 16 of them were male (22.9%). The age average was 35.49; the youngest one of patients was 18 years old and the eldest one was 74 years old. Average epilepsy terms were  $12.38 \pm 11.38$  years. There were 24 patients having only NEPS (34.3%) and 46 patients having combination of epilepsy and NEPS (65.7%). While 43 (61.4%) of the patients used antidepressant, 6 (8.6%) patients did not use any antiepileptic, 35 (50%) patients took antiepileptic monotherapy, 29 patients (41.4%) took antiepileptic polytherapy. The diagnosis of NEPS was established in 8 (11.4%) patients in clinic, in 32 patients (45.7%) with induction EEG, in 24 patients (34.3%) with history, in 6 patients (8.6%) with video EEG monitoring. When educational levels were examined, it was noted that 1 (1.4%) patient took private education and 10 (14.3%) patients graduated from the university.

**Conclusion:** The most important stage in diagnosis of non-epileptic psychogenic seizures is the formation of clinical suspicion. It should be definitely taken into account that non-epileptic psychogenic seizures accompany with actual seizures. NEPS should be definitely kept in mind in patients who were diagnosed with epilepsy, for whom antiepileptic treatment was started and refractory epilepsy was considered.

p0728

### BEHAVIOURAL FEATURES OF PATIENTS WITH PSYCHOGENIC NON-EPILEPTIC SEIZURES (PNES)

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**Purpose:** This retrospective study in patients with nonepileptic seizures (PNES), with epilepsy (PWE), and both conditions (PNES+PWE) evaluated whether the groups can be differentiated by use of a German clinical personality questionnaire (FPZ), which is routinely used in

epilepsy and which originally had been designed for patients with CNS pathologies.

**Method:** Groups of 58 PNES, 207 PWE and 70 PNES+ were selected and evaluated on the basis of having answered a questionnaire on personality (FPZ) which assesses Neuroticism, Organic psycho syndrome, Intra/extra-version, and Addiction via 22 sub-scales with 98 questions. Subgroups had received neuropsychological testing and additional scales for depression (BDI), anxiety (SAS), and quality of life (German modified QOLIE-10)

**Results:** All questionnaires indicated greater behavioural problems in PNES and PWE+ as compared to PWE. A profile with greater emotional lability and aspects of an organic psychosyndrome was indicated in PNES. PNES patients showed a trend of more frequent somatisation, poorer reward learning, greater impulsivity, and communication problems when compared to PNES+. Cluster analysis of the FPZ revealed 4 clusters, two being associated more with epilepsy, (C11. mild psychosyndrome and depression, CL3. emotional stable and non-depressed), two being associated more with PNES (C12. strong neuroticism, psychosyndrome, and depression CL4. neuroticism and not depressed). Cognitive problems were indicated in each group with a non-significant trend to be poorest in PNES+.

**Conclusion:** Patients with PNES and PNES+ share common behavioural features with increased neuroticism and behaviours reminding of a fronto-medial dysfunction. Cluster analysis identifies clinical subgroups which may turn out to have a different aetiology or prognosis. A prospective study taking this as well as seizure semiology into consideration has been initiated.

p0729

#### DEPRESSION IN PERSONS WITH EPILEPSY: RELATED TO PERCEPTION OF ADVERSE EFFECTS AND ADHERENCE?

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**Purpose:** Depression has a high impact on quality of life and might affect factors for a successful treatment with antiepileptic drugs (AEDs) as adverse effects and adherence. The purpose of this study was to investigate the correlation between symptoms for depression and patients' perception of adverse effects and adherence.

**Method:** Prospective data from an anonymous questionnaire answered by patients admitted at the National Center for Epilepsy, Norway in 2014 were used. Data regarding symptoms for depression (Beck Depression Inventory/BDI), current AED medication, perception of adherence and adverse effects in the Adverse Event Profile (AEP) were collected. For further analysis patients with a BDI-score >14 were considered to have relevant symptoms for depression and an AEP score >44 was used as a cut-off to label patients with a severe adverse effect load. Questions regarding adherence dealt with intentional and unintentional non-adherence occurring occasionally or often. The project was approved by the local ethics committee.

**Results:** Questionnaires from 158/184 patients were analysed. The patients' mean age was 36 years (18–78 years). Age at seizure onset was 21 years (0–78 years). 62% of the patients used AED polytherapy. 30% of the patients scored 15 or higher in the BDI. 37% of patients reported a severe adverse effect load. 30% of the patients reported to forget AED, whereas 12% reported to intentionally take AED differently than prescribed occasionally or often (an additional 40% respectively 10% would do so rarely). We found highly significant

correlations between symptoms for depression and a severe adverse effect load ( $p < 0.001$ ), unintentional ( $p < 0.01$ ) and intentional non-adherence ( $p < 0.005$ ).

**Conclusion:** There is a high prevalence of symptoms for depression in epilepsy that is highly correlated to perception of adverse effects and poor adherence. This is important regarding a need for better communication and understanding to improve the treatment outcome.

p0730

#### EPILEPSY AND AED INDUCED DECREASED LIBIDO - THE UNASKED PSYCHOSOCIAL COMORBIDITY

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**Purpose:** Epilepsy is the 4<sup>th</sup> leading neurologic condition with a lifetime prevalence of 3.8%. Quality of life in epilepsy (QOLIE) is inversely related to both seizure frequency and severity of psychosocial comorbidities. Treatment gap in epilepsy is defined as percent of all patients with epilepsy who receive subtherapeutic and/or no antiepileptic drug (AED) treatment. Since QOLIE also reflects severity of psychosocial comorbidities, perhaps true treatment gap should include the percent of all patients with epilepsy who receive subtherapeutic and/or no treatment for psychosocial comorbidities. An important psychosocial comorbidity associated with epilepsy and AED treatment is decreased libido. This paper addresses whether "libido" is questioned with/without utilizing federally mandated electronic medical record (EMR) by epilepsy, pain management and psychiatry clinicians.

**Method:** Quality improvement initiative at an academic medical center (AMC) was employed.

**Results:** This AMC utilized a federally mandated EMR in outpatient epilepsy/pain/psychiatry clinics. The EMR Review of Systems (ROS) GU section included libido only for male patients in these clinics. Clinicians from each outpatient service were directly questioned regarding use of EMR (100%), use of EMR ROS-GU section (66.67% pain/25% epilepsy/20% psychiatry), whether libido was directly asked of all patients (0% pain/0% epilepsy/20% psychiatry), awareness that epilepsy and AEDs both can induce decreased libido (33.33% pain/25% epilepsy/20% psychiatry), and whether this survey will increase future review of libido (100%).

**Conclusion:** Treatment gap of epilepsy-induced and/or AED-induced decreased libido in patients with epilepsy/psychiatric/pain disorders may be related to both lack of education and efficacy of EMR. Education of clinicians is indicated.

p0731

#### TO WHAT EXTENT DEPRESSIVE MOOD INFLUENCE ON QUALITY OF LIFE IN PEOPLE WITH DRUG RESISTANT EPILEPSY. AN ARGENTINE STUDY

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**Purpose:** The aim of this study was to determine if the quality of life (QoL) is differentially affected in patients with drug resistant epilepsy (DRE) with and without depression, in an epilepsy reference center of Buenos Aires, Argentina.

**Methods:** Patients with DRE who were admitted to the monitoring video EEG unit during the period 2010–2013 underwent a standardized psychiatric assessment using (SCID I and BDI). QoL was evaluated using GAF (Global assessment of functioning) and QlesQ (Quality of life enjoyment and satisfaction questionnaire). Two groups were compared according to the presence of current affective disorders (depression) codified in axis I of DSM IV and the lack of affective disorders (absence of depression and/or a psychiatric disorder according DSM IV). Statistical tests used were student t test, ANOVA, Chi square test ( $\chi^2$ ) and Pearson. SPSS for Windows was used.

**Results:** Eighty one patients with DRE were included, 40 men (49.4%) y 41 women (50.6%). Forty four patients (54.32%) had depression criteria, and were compared with 37 (45.67%) patients without depression. No significant differences in age and sex were found between the groups. The total score of QoL was significantly lower in depression group (p0.005). The most affected areas were physical health (p0.039), mood (p0.01), leisure activities (p0.04), and social activities (p0.041). GAF did not show significant differences.

**Conclusion:** Depression is the most frequent psychiatric co morbidity in epilepsy and this study showed a worst QoL in DRE patients with depression compared with DRE patients without depression. Therapeutic approach should be interdisciplinary (neurology, psychiatry, psychology) in people with DRE and should also address mood to improve QoL.

#### p0732

### THE RELEVANCE OF CLINICAL RECOGNITION AND DIFFERENTIAL SEMIOLOGY TO FACILITATE A QUICK ACCESS TO VIDEO-EEG IN PATIENTS WITH PSYCHOGENIC NON EPILEPTIC SEIZURES

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**Purpose:** In this work we compared the seizure semiology in PNES and in Temporal Lobe Epilepsy TLE patients recorded during VEEG. The aim was to detect specific clinical signs which will allow the clinician to suspect the PNES diagnosis, and accelerate the access to VEEG for diagnosis confirmation.

**Method:** VEEG records were reviewed and seizures were analyzed and classified according to the presence of: aura, lack of responsiveness, hypermotor, automatisms and motionless. All patients had a psychiatric evaluation (Structured Clinical Interview for DSM-IV I and II). Results were compared between PNES and TLE groups. For the statistical analysis student test and chi square were used with SPSS for windows.

**Results:** Twenty one patients with PNES (age:  $35 \pm 11$  years) and 21 with TLE (age:  $34 \pm 13$  years) were included. Seizure's duration was of  $1.44 \pm 0.5$  minutes in TLE and of  $6.7 \pm 8.8$  minutes in PNES (p < 0.05). Absences of Lack of responsiveness and hypermotor seizures were more frequent in PNES (p < 0.05) and automatisms were more frequent in TLE (p < 0.05). Age of seizure onset was lower in TLE (p < 0.05) and females prevailed in PNES group (p < 0.05). The

presence of aura and motionless was similar in both groups. Inside the psychiatric evaluation the PNES group presented a higher frequency of depression (p < 0.05) and personality disorders (p < 0.05).

**Conclusion:** In the present study we found differences that may orientate the differential diagnosis between PNES and TLE. Even though VEEG is the gold standard in PNES diagnosis, clinical semiology may help to speed up the access to VEEG and therefore the differential diagnosis, which delays the instauration of the correct mental health treatment.

#### p0733

### CALBINDIN DISTRIBUTION IN DENTATE GYRUS LAYERS OF PATIENTS WITH DEPRESSION AND RESISTANT TEMPORAL LOBE EPILEPSY

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**Purpose:** The aim of this study was to determine the immunoreactivity for calbindin (expressed in post-mitotic new generated cells during synaptogenesis), in dentate gyrus layers of patients with resistant TLE (temporal lobe epilepsy) and hippocampal sclerosis (HS) with and without depressive disorders. Both depression and TLE have been linked to abnormalities in hippocampal neuroplasticity but pathogenic mechanisms are still unclear.

**Method:** Patients with HS and TLE were evaluated according clinical, neurological and psychiatric assessment protocols before surgery. For psychiatric diagnoses, Structured Clinical Interviews for DSM IV disorders (SCID-I and -II), were determined. After surgery selected hippocampal sections from patients with and without depressive disorders and archival material from normal post-mortem hippocampus were processed using immunoperoxidase with antibody anti-calbindin. Reactive area for calbindin, number of positive cells per field (20X), and MGv (mean gray value), were measured by computerized image analysis (Image J). ANOVA Test was determined.

**Results:** Hippocampal sections of eight patients with TLE and depression (TLE+D), eight patients with TLE without depression, and five matched postmortem controls were included. Calbindin immunoreactivity (Calbindin IR) was found in granule cells layers of both controls and patients. A significant reduction in the total number of calbindin IR cells per field was found in patients, more intense in TLE +D (p < 0.01). Many reactive cells in TLE dentate gyrus have larger somas with more staining intensity reaction: these findings were stronger in TLE +D (p < 0.01).

**Conclusion:** Calbindin-IR cells in dentate gyrus are reduced in HS as was previously reported. These alterations were more prominent in patients with TLE+D comparing to TLE and controls, suggesting a most important compromise of hippocampal neuroplasticity in these patients. Deeper studies using double immunostaining should be performed to confirm these preliminary findings.

## Social Issues 2

Monday, 7th September 2015

#### p0734

### HOW2TELL - THE COLLABORATIVE DEVELOPMENT OF AN EVIDENCE-BASED RESOURCE FOR SELF-DISCLOSURE STRATEGIES FOR PEOPLE WITH EPILEPSY: INTERIM RESULTS

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**Purpose:** To generate evidence-based information about the strategies that adult people with epilepsy (PWE) use in the process of telling others about their epilepsy. To design a self-management APP/multimedia resource based on PWE's experiential knowledge of self-disclosure that will support PWE in social, personal and work situations.

**Method:** Using grounded theory approach, in-depth interviews explored PWE's first-hand experiences of self-disclosure (or not) and grounded theory methods of data analysis were used to identify core strategies. To account for maximum variation within the sample, adult PWE with different life experiences and situations relating to (a) support group, (b) family relationship, (c) personal relationship, and (d) work status were included. Given the many variables and psychosocial issues associated with epilepsy, demographic details and validated measures including Coping Inventory of Stressful Situations, QOLIE-10-P and Patient Health Questionnaire were used to profile participants.

**Results:** Twenty-nine adults with epilepsy participated. Participants reported using a range of different strategies: calculating need-to-know; selecting 1st confidant; using humour; making it "ordinary"; seeding hints for disclosure; disclosing gradually depending on level of interest; and, tailoring the message to audience needs. For example, in employment situations, participants presented information to employers in a structured, factual format that addressed work performance and safety management issues. Whereas in social situations, telling friends involved a more casual approach, and information was presented in a way that was designed to educate, reassure and also to maintain social relationship.

**Conclusion:** PWE use multiple and varied strategies in the process of self-disclosure about their epilepsy to others. These strategies will inform the development of *How2tell* multi-media educational resources, including an APP, on self-disclosure for practical use in everyday social and life situations. The *How2tell* study is funded by Epilepsy Ireland/HRB (Grant No. MRCG/2013/6)

#### p0735

### ETHNIC DIFFERENCES IN CULTURAL AND SPIRITUAL PERCEPTIONS AND COPING STRATEGIES IN FAMILIES WITH EPILEPSY

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**Purpose:** To determine factors emerging from cultural and spiritual background of different ethnic groups, which could influence perception and management of epilepsy in children.

**Method:** Retrospective questionnaire based survey in families whose children have epilepsy. Data were collected when families attended epilepsy clinics at Luton & Dunstable University Hospital, United Kingdom (UK) and when visited by the Epilepsy Specialist Nurse in the community. We extracted data on ethnic origin, religion or spiritual belief, concepts of epilepsy, stigmatisation, degree of influence of religion and cultural beliefs and use of non-medical therapies. We compared Caucasian and Asian families. Data were analysed using Fisher's exact test and Chi-square test.

**Results:** A total of 70 families participated in the survey. 28 were of Caucasian, 30 of Asian, 6 of African and 6 of mixed ethnic origin. There were 34 Muslims, 29 Christians, 6 Atheists and 1 unspecified. Significantly more Asian families had the belief that epilepsy was influenced by non-medical causes like fate or destiny (50%) or spirit related (43%) than

Caucasian families (0%). There was no difference in perception of stigmatisation between Caucasian and Asian families. Influence on treatment and management of epilepsy by family, religion or culture was significantly more common in Asian compared to Caucasian families ( $p < 0.001$ ). Non-medical therapies (use of traditional healers, prayers, complementary therapies) were used in significantly more Asian compared to Caucasian families ( $p < 0.001$ ).

**Conclusion:** Non-medical influences on perception of cause and on treatment of epilepsy were more common in Asian compared to Caucasian families. Since the UK has a diverse population, consisting of a wide range of spiritual and cultural beliefs, clinicians should strive to understand all different viewpoints in order to develop a better rapport with families. This will allow for a more holistic healthcare provision, and may improve patient outcomes.

#### p0736

### PERCEPTION OF EPILEPSY IN LUBUMBASHI, DEMOCRATIC REPUBLIC OF CONGO: FINDINGS FROM PUBLIC OPINION POLL

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**Purpose:** The purpose of the present study was to investigate the public opinion on the perception of epilepsy in Lubumbashi, an urban city in the Democratic Republic of Congo.

**Methods:** We conducted a cross-sectional study using a household survey questionnaire specially designed to collect information on people perception of epilepsy. Community clusters from Lubumbashi were randomly selected for heterogeneity. A total of 885 households were interviewed.

**Results:** Of the 885 respondents in the survey, 45.5% were female and 54.5% were male. It was reported that the majority of the respondents have either high school or higher education level (94.70%). All the respondents believe in God, of which 82.67% were Christians. 28.8% of the respondents reported that they have heard about epilepsy at school, whereas 21.8% in mental health centers. Only 49.4% have heard about epilepsy on public media such radio and television. The majority of the respondents (61.8%) refused to marry an epileptic person. Less than a quarter (18.3%) reported to have visualized a seizure. More than half of the respondents believe that epilepsy is a disease with both mystical and religious component (73.0%) and only 33.1% of the respondents believe that epilepsy can be treated by the neurologists.

**Conclusion:** Findings from this survey suggested that the majority of the population in Lubumbashi still believe that epilepsy is a mystical-religious disease, though most of the interviewed had a level of education higher than secondary school. In this respect, one would expect that the perception of epilepsy is more scientific than metaphysical. More studies are needed to better understand the community perception of neurological diseases in an African setting.

#### p0738

### HEALTHCARE COSTS AMONG PATIENTS WITH POST-STROKE SEIZURE

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**Purpose:** Stroke is commonly considered as one of the major causes of epilepsy in adults, and accounts for almost half of all cases of epilepsy

with identifiable etiologies. The incidence of post-stroke epilepsy ranges from 3% to 67% across various studies in different populations. Our aim in this study is to determine the burden of post-stroke epilepsy by evaluating readmissions, and medical expenditure during the first year after acute stroke under the National Health Insurance (NHI) program in Taiwan.

**Method:** We conducted this nationwide retrospective cohort study by using claim data about new incidence of stroke obtained from a subset of the National Health Insurance Research Database (NHIRD), which contains the data of all medical claims from 2002 to 2009 of 1 million randomly sampled NHI enrollees in Taiwan, with a 1-year follow-up duration. Early-onset post-stroke seizure was defined as onset of seizures within 14 days of the stroke index date, whereas late-onset post-stroke seizure was defined as onset of seizures more than 14 days after the stroke index date. The total amount of the first-year hospitalization medical expenditure of patient with late-onset post-stroke seizure was assessed and compared to the expenditures of stroke patients without post-stroke seizure.

**Results:** Of 3502 stroke patients, we identified 72 patients with early-onset post-stroke seizure and 76 patients with late-onset post-stroke seizure. Overall, 2.21 late-onset post-stroke seizure incidence occurred per 100 person-year and a cumulative incidence of 4.23%. The first-year hospitalization medical expenditure was NT\$ 631, 344 and NT\$ 920 831 for patients with early-onset post-stroke seizure and patients with late-onset post-stroke seizure, respectively. This is significantly higher compared to stroke patients without post-stroke seizure (NT\$ 465 655).

**Conclusion:** Our study suggests that patients with post-stroke seizure had a significantly higher medical expenditure than without seizure, especially in late-onset post-stroke seizure.

p0739

### AN EXPLORATORY STUDY OF THE SOCIAL WORK NEEDS AND OUTCOME OF ADULTS WITH EPILEPSY

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**Purpose:** The objective of this study is to explore the social work needs of adults with epilepsy and the benefits derived from social services (outcome), to establish whether outcome and needs match.

**Method:** A structured questionnaire was sent to 100 clients and a focus-group of social workers was used to interpret the results of the questionnaire. The results were mapped in three categories: supporting and stabilizing guidance (SSG), practical and informational services (PIS) and chance-oriented and competence-based guidance (CCG).

**Results:** In total, 48 clients (48%) took part. 76% had SSG needs, 80% PIS needs and 67% CCG needs.

1. The main SSG needs were: to "stand one's ground" (81%) and to share emotions (54%). The outcome was: emotional support (62%) and being heard (68%).

2. The main PIS needs were: work-related issues (59%) and insight into statutory provisions (34%). The outcome was: ability to organize things by themselves (28%), referral to other agencies (26%) and work-related questions were answered (26%).

3. The main CCG needs were: self-esteem issues (61%) and dealing with the daily consequences of epilepsy (61%). The outcome was: ability to set boundaries (42%), learning to deal with daily consequences (30%), acceptance (24%) and increased self-esteem (24%).

A small group (27%) found the outcome to be unsatisfactory, but the provision of social services for this group is still ongoing.

**The focus-group showed::** 1. There are many work-related issues, but few opportunities in the current labour market. Solution-oriented services and management of expectations can be the key to increase the benefits in this area.

2. Further empowerment of adults with epilepsy is a challenge for the future.

**Conclusion:** The outcome of the social services appears to relate to the needs of adults with epilepsy. On a critical note, outcomes could be improved, especially on work-related questions and empowerment.

p0741

### "I AM NOT MUCH OF A MAN" - A QUALITATIVE RESEARCH PROJECT WITH FOCUS ON SEXUALITY OF THE MALE ADULT EPILEPSY PATIENT

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**Purpose:** The aim of this project was to clarify, analyze and discuss the experience of sexuality in the male epilepsy patient. In this context sexuality is seen as a multidimensional issue.

**Methods:** The project is carried out within the framework of a qualitative research interview based on a phenomenological and hermeneutical approach. Literature theories on *men*, *masculinity*, and *life quality* contributed individually to an understanding of the statements of the male epilepsy patients.

**Results:** The project shows that sexuality has a big influence on the identity of the male epilepsy patients and their self awareness and body integrity. The interviews shows that sexuality is experienced as a multidimensional concept, when dealing with life quality. Themes like *identity* and *self awareness* appear to be closely connected and impossible to separate.

**Conclusion:** Sexual problems can generate feelings of *inadequateness*, *guilt* and *shame* in the men. Those feelings very much affect the experience of masculinity. It is however in this context also noticeable that the feeling of being a "real man" is depending on their ability to control their epilepsy. Furthermore the interviews showed that the relationships can be challenged by change of roles within the partnership which again can accumulate a feeling of inferiority in the sexual relation. Finally the project highlighted that taboos arises when sexuality as a theme has to be articulated. The taboo is thus not only from patient and his partner but also exists in the health professionals such as the nurse and the doctor. This taboo seems to produce an underestimation of sexual issues in the epilepsy patients in clinical practice and should be taken further into consideration when dealing with the epilepsy adults patients.

## Status Epilepticus 2 Monday, 7th September 2015

p0743

### NON-INTRAVENOUS MIDAZOLAM VERSUS INTRAVENOUS OR RECTAL DIAZEPAM FOR THE TREATMENT OF EARLY STATUS EPILEPTICUS: A SYSTEMATIC REVIEW WITH META-ANALYSIS

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**Purpose:** To determine if non-intravenous (non-IV) MDZ is as effective and safe as intravenous or rectal diazepam (DZP) in terminating early status epilepticus (SE) in children and adults.

**Method:** We searched CENTRAL, ClinicalTrials.gov, and MEDLINE for randomized controlled trials comparing non-IV MDZ with DZP (by any route) in patients (all ages) with early SE, defined as seizures lasting >5 minutes or as seizures at arrival in the emergency department. Following outcomes were assessed: seizure cessation within 15 minutes of drug administration; serious adverse effects; time interval to drug administration; time from arrival in the emergency department to seizure cessation. Outcomes were assessed with random-effects Mantel-Haenszel meta-analyses to calculate risk ratio (RR) and mean difference (MD) with 95% confidence intervals (95% CIs).

**Results:** Nineteen studies with 1933 seizures in 1602 patients were included. 1573 patients were younger than 16 years. For seizure cessation, non-IV MDZ was as effective as DZP (any route) (RR: 1.03; 95% CIs: 0.98–1.08). No difference in adverse effects was found between non-IV MDZ and DZP by any route (RR: 0.87; 95% CIs: 0.50–1.50). Buccal MDZ was more effective than rectal DZP in terminating SE (RR: 1.78; 95% CIs: 1.11–2.85). Time interval between arrival and seizure cessation was shorter with non-IV MDZ by any route than with DZP by any route (MD: -3.67 minutes; 95% CIs: -5.98 to -1.36); a similar result was found for time from arrival to drug administration (MD: -3.56 minutes; 95% CIs: -5.00 to -2.11).

**Conclusion:** Non-IV MDZ is as effective and safe as intravenous or rectal DZP in terminating early SE in children. Times from arrival in the emergency department to drug administration and seizure cessation are shorter with non-IV MDZ than with intravenous or rectal DZP, but this does not necessarily result in higher seizure control.

p0744

#### NON-CONVULSIVE STATUS EPILEPTICUS - THERAPEUTIC APPROACH

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**Purpose:** Non-convulsive status epilepticus (NCSE) is a common disorder comprising at least 1/3 of all cases of status epilepticus (SE). Although including a great diversity of syndromes, these forms of SE share two important features: the diagnostic difficulty and uncertainty about the best treatment approach. We evaluate the therapeutic approach and its effect in NCSE outcome.

**Method:** All consecutive cases of NCSE according to Beniczky et al. 2013 criteria, seen in an unselected hospital cohort, between January/2012 and December/2014, were identified and the files reviewed. Therapeutic approaches were identified retrospectively and related to outcome.

**Results:** A total of 42 patients were found, 23 females, mean age 72 years (24–90). The subtypes of NCSE were: complex partial SE in 33 patients, NCSE in coma in 7, simple partial SE in 2 patients. 29 were provoked NCSE. NCSE was treated with one antiepileptic drug (AED) in 10 patients, with two AED in 14 patients, with three in nine patients, with four in four patients and coma was induced in five patients. NCSE resolved when a BZD was started in 1/23 patients, PHT in 6/15 patients, VPA in 9/25, LEV in 20/33, CBZ in 1/1 and propofol/midazolam in 2/5. 10 patients died, three without NCSE resolution. At discharge only 12 patients were treated with >1 AE.

**Conclusion:** Therapeutic approaches were heterogeneous reflecting the absence of NCSE treatment guidelines. Despite that, success rate with AED was high and coma induction was rarely needed. In the majority of patients  $\geq 2$  AED were necessary to treat NCSE, but once treated the underlying factor and outdated the acute phase, AED discontinuation does not seem to be related with a high risk of recurrence. In our series mortality was high but essentially related with the underlying etiology and medical complications.

p0745

#### NON-CONVULSIVE STATUS EPILEPTICUS: CLINICAL PRESENTATIONS AND EEG PATTERNS

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**Purpose:** Non-convulsive status epilepticus (NCSE) is classically characterized by changes in behavior/awareness caused by continuous or very frequent epileptiform activity. However, its clinical manifestations can be very heterogeneous and attributable to a non-epileptic etiology, being the EEG fundamental for its definitive diagnosis. We describe the clinical presentation and EEG patterns in a cohort of patients with EEG confirmed NCSE.

**Method:** We identified all consecutive patients admitted to our hospital (1/2012 to 12/2014) with EEG criteria for NCSE (1 hour video-EEG); their clinical presentation was retrospectively evaluated.

**Results:** 38 patients were identified (21 female, mean 73 years-old, 24–90), 13 with known epilepsy. Most presented with behavioral (58%) or consciousness abnormalities (stupor/coma, 27%); visual impairment or aphasia were the only clinical manifestation in two patients. Before EEG confirmation, the diagnosis of NCSE was only considered in nine patients, in all following an isolated generalized tonic-clonic seizure; in 59% of the remaining patients, the clinical changes were attributed to a medical cause (metabolic, infectious) or acute CNS injury (stroke/trauma). In the initial EEG, the most commonly patterns were epileptiform discharges >2.5 Hz (42%) or  $\leq 2.5$  Hz (40%), in these with the definitive diagnosis of NCSE made by registration of electro-clinical seizures (subtle eye versions, myoclonus, 16%), EEG/clinic response to intravenous benzodiazepines (16%) or by demonstrating ictal dynamic EEG changes (11%). In four patients, all with initial EEG showing less epileptiform activity and dominated by slow rhythmic activities, occasionally with recruitment features, the definitive diagnosis of NCSE was only made in subsequent EEG's (2–4, mean 2.7).

**Conclusion:** The diagnosis of NCSE should be considered in patients with behavior/awareness changes, even in those without previous epilepsy or with a medical/neurological condition that could justify the clinic presentation. Its EEG patterns are variable and dynamic, often being necessary pharmacological manipulations/ repeated EEG to make a definitive diagnosis.

p0748

#### INDICATIONS AND DIAGNOSTIC YIELD OF EMERGENCY ELECTROENCEPHALOGRAPHY (EEG) IN AN "ERA" OF ELECTRICAL STATUS EPILEPTICUS

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**Purpose:** The electroencephalogram (EEG) is a unique and valuable measure of the brain's electrical function. The use of EEG in emergent conditions have been boosted with the definition of electrical status epilepticus (ESE), however the precise role and value of EEG in emergent conditions have yet to be clearly defined. Therefore, our objective was to determine the indications and the yield of EEG in an emergency setup.

**Method:** A descriptive cross sectional study, 20 minutes standard digital EEGs (10–20 system) were performed. Individual bias was minimized by independent reporting done by two. Authors retrospectively reviewed the reports of eEEGs performed over a period of 12 months.

**Results:** A total number of 1028 were performed, out of which 166 (16.1%) through emergent requests, nullified 11 due to inadequate information. The mean age of eEEG was 22.0 years, no significant difference compared to routine-EEG (rEEG), Sex-male 57.8% for eEEG, 48.2% for rEEG ( $p < 0.05$ ). The commonest clinical indication for eEEGs was altered level of consciousness 78(46.9%). None suspected ESE on clinical grounds. The sensitivity of eEEGs for positive yield was 27.1%. Twenty-one had inter-ictal-epileptiform discharges (14 = focal), 16 had background slowing (12 = diffuse), only 04 had ESE (diffuse discharges). Moreover, 02 had burst-suppression, 01 spindle-coma and 01 periodic-lateralized-epileptiform-discharge. Majority (68.2%) with reduced level of consciousness had background slowing; only 01 had ESE. There was no significant difference between the sensitivity of eEEG versus rEEG ( $P > 0.05$ ).

**Conclusion:** Reduced level of consciousness is the commonest indication for eEEG, only a minority had ESE. Sensitivity of eEEG for a positive yield is the same as of routine EEG.

p0749

#### PANORAMA OF QUANTITATIVE EEG (QEEG) MONITORING IN ICU: OUR EXPERIENCE IN PSMCMC, RIYADH

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**Purpose:** To understand concepts of quantitative EEG in trend display and to evaluate the diagnostic accuracy of seizure (Sz) probability, rhythmic run detection and display (R2D2), color density spectrogram (FFT), burst-suppression patterns and amplitude-integrated EEG (aEEG).

**Method:** The trending study was made by using Cadwell machines (32 channels, sampling frequency of 250 Hz) and Persyst 12 software. A total of nine comatose patients (4M+5F) age ranged 17–78 years have 160–4320 minutes recordings. The size of the files for visual analysis ranged from 800 pages to 21 600 pages at 12 second/page (Mean = 8488 pages). These CEEG records were frequently read by our five readers independently by visual analysis. The EEG background, electroclinical seizures and artifacts were identified and discussed for their correction. All of them were subsequently subjected to Trend analysis at a rate of 1 hour recording/page.

**Results:** Seven of our nine patients were elderly (74–78 years). All the electrographic seizures identified by visual analysis were identified by combined trends (100% sensitivity) with the exception of seizure probability detection trend alone. The small amplitude slowly evolving Sz's are missed by trends and thereby produces high false positive results. However, using all trends, the distinctive SZ detection frequency was 76 Sz's/hour in one of our young patients with intractable Sz.

**Conclusion:** The study showed higher sensitivity in identifying seizures and focal/generalized slowing, burst-suppression patterns while using the seizure signature of all the above trend tools than others (Stewart C.P. et al, 2010). The study also reveals the simplicity and reliability of the program for analysis. However, the trend data must be checked by opening the raw data for further confirmation and a single trend for seizure analysis should be avoided. A future study using Persyst 13 with artifact reduction technique (a step forward in clinical Neurophysiology after Digital EEG) will continue.

p0750

#### NON-CONVULSIVE STATUS EPILEPTICUS WITH UNILATERAL EEG CHANGES IN AN ELDERLY PATIENT

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**Purpose:** Altered mental status is a very common presentation in the elderly causing from different etiologies. As they have the same clinical presentation, it is difficult to diagnose non-convulsive status epilepticus. It has been determined that about 16% of patients older than 60 years with confusion of unknown origin have non-convulsive status epilepticus.

**Method:** We report a 84 years-old patient who diagnosed of non-convulsive status epilepticus with continuous unilateral EEG changes. She had chronic left middle cerebral artery infarct. After preparation of colonoscopy, she had developed confusion and then unconsciousness. The clinical state of the patient and EEG changes of non-convulsive status epilepticus was refractory to diazepam. She had been taking levetiracetam so we administered her levetiracetam infusion. Because of no response to antiepileptic drugs, the patient treated with midazolam infusion and her status had been undercontrolled. After administration of the drugs, PLEDs on the left hemisphere had continued for a while.

**Conclusion:** We present this case because of the non-convulsive status epilepticus with unilateral EEG changes. We assumed that it's important to be careful about any kind of interventional procedures in an elderly patient, especially who had brain lesion.

p0753

#### EARLY INTRODUCTION OF KETOGENIC DIET MAY IMPROVE THE OUTCOME IN SEVERE REFRACTORY STATUS EPILEPTICUS OF FEBRILE INFECTION-RELATED EPILEPSY SYNDROME (FIRES)

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**Purpose:** To evaluate the therapeutic outcome of Ketogenic Diet (KD) in the intensive care setting in severe refractory status epilepticus of febrile infection-related epilepsy syndrome (FIRES).

**Method:** This retrospective observational study (2011–2014) included children who were initiated on KD for refractory status epilepticus of FIRES. Those with previous history of seizures were excluded. Baseline characteristics, fever and status epilepticus onset, ketogenic diet initiation, efficacy, and side-effect profile were analyzed.

**Results:** Fourteen children were initiated on KD for status during this period. Of these, five were excluded from final analysis due to various reasons. Of the remaining nine children (M: F = 4: 5), age at presentation varied from 1 to 15 years (median 7 years). Fever to status interval was 1–9 days (median 4 days). All were on multiple (4–7) AEDs prior to KD (median 5). Six were on anesthetic infusions at initiation of KD. The interval from status onset to KD initiation was 5–86 days (median 11 days). Five patients were on 3:1 diet, while the other four were on 4:1 diet. Hypoglycemia was noted in three children, necessitating diet withdrawal in one child. Two other children discontinued the diet due to other reasons. In the remaining six patients, KD was effective within 0–4 days (median 1 day) of onset of ketonuria and 1–12 days (median 6 days) after diet initiation. Complete seizure freedom was achieved in three children; one showed >90% and two showed 50–80% reduction in

seizure frequency. Of the three children, who discontinued KD, one became seizure free; other two expired due to persistent seizures and systemic complications. The outcome was relatively better for patients with early introduction of KD.

**Conclusion:** Ketogenic diet can be instituted safely and effectively in the ICU setup for children with FIRES in refractory status epilepticus. Early introduction of ketogenic diet may have a more favorable outcome.

## Women's Issues 2 Monday, 7th September 2015

p0754

### ANTENATAL CARE AMONG PREGNANT WOMEN WITH EPILEPSY IN A DEVELOPING COUNTRY: A RETRO-PROSPECTIVE SURVEY IN CHINA

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**Purpose:** The aims of this study were to investigate the implementation of antenatal care among pregnant women with epilepsy (WWE) in China and to identify its potential correlations with selected sociodemographic and clinical factors.

**Method:** A detailed survey was conducted in China using a structured questionnaire from December 2013 to January 2014. Information on the awareness and implementation of antenatal care, as well as selected sociodemographic and clinical characteristics, were collected from 206 pregnant WWE. Descriptive and logistic regression analyses were applied in this survey.

**Results:** Among the enrolled subjects, 2.9% suffered ionising radiation exposure 3 months before pregnancy. And 62.3% exposed to antiepileptic drugs (AEDs), almost half of whom were under polytherapy. Only 30.1% of them knew the exact effects of folic acid, and 73.8% had taken folic acid at some point during periconception. About 45.1% obtained continuity of care throughout the antenatal period. Majority of the subjects performed malformation directed ultrasound (88.3%) and Down's screening (81.6%). Minority performed chorionic villus sampling (3.9%) and amniocentesis (5.8%). But still 7.3% of the subjects knew little about antenatal care. Pregnant WWE with higher education levels, those with a planned pregnancy, or those who live in urban areas were more likely to know about and implement antenatal care during pregnancy.

**Conclusion:** The extent of awareness and implement of antenatal care among pregnant WWE remains insufficient in China. More efforts are needed to promote antenatal care for WWE, especially those with low education levels and those who live in rural areas.

p0756

### THE FREQUENCY OF SEIZURES IN PREGNANT WOMEN WITH EPILEPSY

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**Purpose:** We aimed to investigate seizure frequency in pregnant women with epilepsy.

**Method:** We evaluated 175 pregnant women with epilepsy from 1996 to 2015. Total 216 pregnancy were investigated retrospectively and

prospectively. The patients whose pregnancy were terminated and who have not enough information were excluded. All the patients had taken folic acid during pregnancy. Seizure frequency 1 year before pregnancy, first trimester, during pregnancy and after pregnancy were recorded respectively.

**Results:** The mean pregnancy age of patients was  $27.05 \pm 4.66$  years. The etiology of epilepsy in patients was idiopathic (78.7%) or symptomatic (21.3%). Seizures types were primary generalized epilepsy, partial epilepsy or mix type epilepsy and the frequencies were 34.2%, 10.25 and 55.6% respectively. The percentage of patients who were followed up during pregnancy without therapy, monotherapy or polytherapy were 16.3%, 69.3%, and 14.4% respectively. 216 pregnancies ended with 77 normal delivery, 105 cesarean section, 17 abortus and 17 curettage. Before pregnancy there was no seizure in 101 (46.8%) and there was at least one seizure in 115 (53.2%) patients. The pregnancies which were terminated or ended with abortus or curettage were excluded to investigate seizure frequency during pregnancy and postpartum stage. The frequency of seizures decreased 25.3%, increased 12.1% and unchanged 62.6% of patients in first trimester. The frequency of seizures decreased 15.4%, increased 24.2% and unchanged 60.4% of patients during pregnancy. The frequency of seizures decreased 20.3%, increased 19.8% and unchanged 59.9% of patients after pregnancy.

**Conclusion:** In literature most of the investigations revealed that the frequency of seizures is not increased in perinatal period of pregnancy, either during or after, and our results are consistent with this information.

p0757

### THE FREQUENCY OF MALFORMATION IN PREGNANT WOMEN WITH EPILEPSY

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**Purpose:** We aimed to investigate malformation frequency in pregnant women with epilepsy (WWE).

**Method:** We evaluated 175 pregnant WWE from 1996 to 2015. Total 216 pregnancy were investigated retrospectively and prospectively. All the patients had taken folic acid during pregnancy. Malformation frequency was investigated.

**Results:** The mean pregnancy age of patients was  $27.05 \pm 4.66$  years. The etiology of epilepsy in patients was idiopathic (78.7%) or symptomatic (21.3%). Seizures types were primary generalized epilepsy, partial epilepsy or mix type epilepsy and the frequencies were 34.2%, 10.25 and 55.6% respectively. The percentage of patients who were followed up during pregnancy without therapy, monotherapy or polytherapy were 16.3%, 69.3%, and 14.4% respectively. 216 pregnancy were end with 77 normal delivery, 105 cesarean section, 17 abortus and 17 curettage. 11 babies had congenital malformation. These malformations and the drugs which mothers used were cleft lip and palate (three babies, valproate (VPA) 1000 mg/day, phenobarbital 200 mg/day, phenytoin (PHT) 300 mg/day as monotherapy), hypospadias (three babies, VPA 1200 mg/day, carbamazepine (CBZ) 400 mg/day as monotherapy, and topiramate (TPM) 200 mg/day, levetiracetam 1500 mg/day, CBZ 800 mg/day as polytherapy), sacral teratoma (one baby, VPA 500 mg/day and TPM 50 mg/day), renal malformation (one baby, CBZ 400 mg/day), cutaneous hemangioma (one baby, CBZ 1200 mg/day), atrial septal defect (one baby, PHT 300 mg/day), spina bifida (one baby, VPA 500 mg/day, lamotrigine (LTG) 200 mg/day, TPM 50 mg/day). Three pregnancies were terminated due to renal cists (LTG 100 mg/day), meningomyelocele (CBZ 400 mg/day), trizomie 18 (CBZ 400 mg/day) respectively and one pregnancy was finished with abortus due to omphalocele (CBZ 600 mg/day).

**Conclusion:** The seizures and teratogenic effects of AED are risk factors for pregnancy in WVE. Carbamazepine was found associated with malformations mostly in this study results and our results are consistent and comparable with literature data.

**p0758**

### ETHICAL ASPECTS OF EPILEPSY TREATMENT IN ONE OF THE MOST VULNERABLE GROUPS OF PATIENTS - WOMEN OF THE REPRODUCTIVE AGE

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**Purpose:** Women of the reproductive age who suffer from epilepsy constitute one of the most vulnerable groups of patients. Along with classical ethical principles, a physician must adhere to the special principle of bioethics - protection of future generation. Study of physicians' motivation to apply ethical principles to woman epilepsy treatment.

**Method:** Twenty five years of experience of teaching Bioethics to students of Moscow Medical Schools, teaching biomedical and professional ethics to graduate medical students and physicians attending continuous education courses and certificate courses on Neurology and Epileptology; personal experience of participating in expert committees of various levels. Sociological surveys, self-administered questionnaires, interviews of 211 epileptologists.

**Results:** Sixty percent of respondents start treatment after receiving the patient's informed consent; 57% of respondents are guided in their practice by the principle of respecting the patient's autonomy and dignity; and 53% of the respondents adhere to the partnership and contract model. The physicians' motivation to apply bioethical principles to the treatment process is very importance. The index of motivation (IM) was calculated as a ratio of 1:10. The IM of physicians-epileptologists was rather high: 0.8–0.95. In comparison, the IM of medical graduate students was 0.8–0.9. Over 97% of the respondents among these groups try to follow the principles of Bioethics in their medical practice and research. At the same time, 29% of respondents had difficulty identifying the type of model they use in their work. 70% of epileptologists admitted to a significant deficit in their knowledge in the field of bioethics and its applications.

**Conclusion:** Bioethics as it is currently taught in medical schools is insufficient for an ethically informed treatment process. The bioethics classes should be moved to the curricula of the upper level students and included in the system of the continuous medical education.

**p0759**

### EMILIA ROMAGNA STUDY ON PREGNANCY AND EXPOSURE TO ANTIEPILEPTIC DRUGS (ESPEA): A POPULATION-BASED STUDY IN AN ITALIAN REGION

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**Purpose:** To assess the prevalence of Antiepileptic Drug (AED) exposure in pregnant women with or without epilepsy and the comparative risk of terminations of pregnancy (TOPs) and major congenital malformations (MCMs) following intrauterine AED exposure in the Emilia Romagna region (RER), Northern Italy (4 million inhabitants).

**Method:** Data were obtained from official regional registries: Certificate of Delivery Assistance, Hospital Discharge Card, reimbursed prescription databases and Registry of Congenital Malformations. We identified all the deliveries, hospitalized abortions and MCMs occurred between January 2009 and December 2011. The following active substances were considered: Phenobarbital, Primidone, Phenytoin, Ethosuximide, Clonazepam, Carbamazepine, Oxcarbamazepine, Rufinamide, Valproic Acid, Vigabatrin, Tigabine, Lamotrigine, Felbamate, Topiramate, Gabapentin, Levetiracetam, Zonisamide, Pregabalin, Lacosamide.

**Results:** We identified 145243 pregnancies: 111284 deliveries (112845 live births and 279 stillbirths), 16408 spontaneous abortions and 17551 induced terminations of pregnancy (TOP). Six hundred and eleven cases (0.42% 95% CI: 0.39–0.46) were exposed to AEDs. Twenty-one per cent of pregnancies ended in TOP in the AED group versus 12% in the non-exposed (OR: 2.24; CI 1.41–3.56). Three hundred fifty-three babies (0.31%, 95% CI: 0.28–0.35) were exposed to AEDs during the first trimester. The rate of MCMs was 2.3% in the AED group (2.2% in babies exposed to monotherapy and 3.1% in babies exposed to polytherapy) versus 2.0% in the non-exposed.

**Conclusion:** The prevalence of AED exposure in pregnancy in the RER was 0.42%. The rate of MCMs in children exposed to a single AED in utero was almost superimposable to the one of the non-exposed, however polytherapy carried a slightly increased risk. The rate of TOPs was significantly higher in the exposed women. Further studies are needed to clarify whether this high rate reflects a higher rate of MCMs detected prenatally or other more elusive reasons.

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**p0762**

### VALPROIC ACID USE DURING PREGNANCY: OUTCOMES IN REAL CLINICAL PRACTICE

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**Purpose:** Recently important data emerged on valproic acid (VA) effects related to pregnancy outcome and subsequent physical and mental development of the child, however according to EURAP data, VA is still the 3<sup>rd</sup> most frequently used antiepileptic drugs during pregnancy.

**Method:** Six clinical situations of pregnancy were examined in **focal epilepsy** (FE): (a) VA continued; (b) VA discontinued after stable remission for the last 2–3 years; (c) VA discontinued, but infrequent focal seizures (FS) observed without secondary generalized tonic-clonic seizures (SGTCS); (d) VA discontinued, infrequent FS and single SGTCS; (e) VA discontinued, frequent FS and SGTCS; (f) VA discontinued, FS and SGTCS increased versus before treatment. Six clinical situations of pregnancy were examined in **juvenile myoclonic epilepsy** (JME): (a) VA continued; (b) VA discontinued after stable remission verified clinically and by EEG testing for the last 5 years; (c) VA discontinued, but duration of remission is 1–3 years only, and previously the patient had generalized tonic-clonic seizures (GTCS) predicted by increased absences and myoclonic seizures (MS); (d) VA discontinued, no GTCS, but infrequent MS and absences are present; (e) VA discontinued, asynchronous MS, absences and infrequent GTCS; (f) VA discontinued, all types of seizures increased versus before treatment. All clinical situations may burden by self-cancellation of VA by pregnant women at I-st trimester of pregnancy.

**Results and conclusion:** Best pregnancy outcomes were observed, when the following conditions were met:

- (1) VA gradually discontinued 9 months before pregnancy;  
 (2) continued VA use during the 1st trimester in daily dose not exceeding 800 mg.

However in case of five and more GTCS during the 1st trimester, pregnancy discontinuation was recommended. At the 2nd trimester, the daily dose of VA was usually increased from 800 mg, or VA was combined either with levetiracetam (in FE or JME) or pregabalin (only in FE).

### p0763

#### SEIZURE OCCURRENCE, PREGNANCY OUTCOME AMONG WOMEN WITH EPILEPSY; ONE YEAR PROSPECTIVE STUDY

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**Purpose:** To determine the prevalence of epilepsy, seizure frequency and the outcome of pregnancy amongst a cohort of pregnant women attending antenatal clinic (ANC) at two tertiary hospitals.

**Methods:** An observational cohort study conducted at the University of Maiduguri Teaching Hospital and State Specialist Hospital, Northeast Nigeria. Pregnant women attending antenatal care were screened for previous history of active convulsive epilepsy, and recruited consecutively according to a specified protocol. A standardized questionnaire was administered to record pregnancy history, nature of epilepsy and treatments received. They were followed-up during the course of the pregnancy based on the ANC schedule up to delivery. The outcome of pregnancies was recorded.

**Results:** A total of 7 063 pregnant women were screened, from which 103 (1.46%) subjects had at least a past history of seizure. Seventy-eight (1.10%) had a past history of seizure(s) from eclampsia and 23 (0.33%) pregnant subjects recruited were identified to have active convulsive epilepsy. The unadjusted prevalence of epilepsy in pregnant women was found to be 3.33 per 1000 (95% CI: 2.1–4.8). Subjects who had a history of head injury and encephalitis were more likely to have seizures during pregnancy. ( $P = 0.013$  and  $P = 0.041$ ). Those who had recurrent seizures within the last 6 months before recruitment were more likely to have a negative pregnancy outcome ( $P = 0.043$ ).

**Conclusion:** Our study found a prevalence of active epilepsy of 3.33 per 1 000 among pregnant women, with about one percent having a past history of seizure from eclampsia.

## Adult Epileptology 7 Tuesday, 8th September 2015

### p0764

#### CIRCADIAN CHANGES OF EPILEPTIFORM DISCHARGES IN GENETIC GENERALISED EPILEPSIES

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**Purpose:** We sought to study the circadian patterns and sleep-specific epileptiform abnormalities in genetic generalised epilepsy (GGE).

**Methods:** The diagnosis of GGE was established according to International League against Epilepsy criteria. All patients had 24-hour ambulatory electroencephalograms recorded according to a standard protocol. The duration of all epileptiform discharges were measured manually using a software tool and details of all discharges were entered into an electronic database. The details included time of discharge, state of arousal and duration. Generalised epileptiform discharges lasting  $\geq 2$  second were classified as paroxysms and  $< 2$  seconds as fragments. Spikes overlapping with K-complexes (epileptiform K-complexes) and sleep spindles (epileptiform spindles) were identified as sleep-specific epileptiform abnormalities. We plotted a histogram of the frequency of epileptiform discharges against 24-hour time scale followed by cluster analysis to study circadian patterns.

**Results:** Out of 120 patients who participated, 107 had abnormal EEGs which were analysed. The cohort consisted of 37 (34.6%) males and 70 (65.4%) females with mean age of  $28.5 \pm 10.7$  years (range, 13–58). Epileptiform K-complexes were more frequent (66.7%) than epileptiform spindles (10.5%). Amongst syndromes, epileptiform K-complexes and spindles were more commonly seen in juvenile myoclonic epilepsy (71.4%) and juvenile absence epilepsy (70.6%). Generalised fragments and focal discharges were more frequently seen during non-REM sleep whilst paroxysms were more in wakefulness. Overall, 67% of epileptiform discharges occurred in non-REM sleep, whilst 33% occurred in wakefulness. The cluster analysis showed four clusters of epileptiform discharges around 2 am, 7 am, 2.30 pm and 10 pm confirming the impression from the histogram.

**Conclusion:** Our study demonstrates epileptiform K-complexes occur in the majority of GGE indicating the importance of arousal in the generation of epileptiform discharges. Furthermore, the study shows that epileptiform discharges are more likely to occur at certain times of the day, probably reflecting circadian rhythms of epileptogenicity.

### p0765

#### DEVELOPMENT AND EVALUATION OF A CLINIC-BASED DECISION SUPPORT SYSTEM FOR EPILEPSY SELF-MANAGEMENT IN THE USA

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**Purpose:** Decision support electronic tools (“e-tools”) to improve self-management of patients with epilepsy are being developed by member organizations of the CDC-sponsored Managing Epilepsy Well (MEW) Network in the USA. This presentation will describe the development and evaluation of the Management Information & Decision Support Epilepsy Tool (MINDSET).

**Method:** The stepped Intervention Mapping framework informed MINDSET development including to create a logic model of the problem and expected change (Steps 1 & 2), plan and produce MINDSET (Steps 3 & 4), and to implement and evaluate MINDSET (Steps 5 & 6). A 9-month RCT of MINDSET (Version 3.1) compared to a usual care only condition was conducted with 42 adult patients at three participating neurology specialty clinics in Houston, Texas to determine impact of MINDSET on patient self-management.

**Results:** MINDSET, mounted on a Windows-based Dell tablet, provides real-time self-management decision support to patients ( $> 18$  years) and their providers in the context of the clinic visit. Patients input data on seizure, medication, and lifestyle management using embedded validated surveys including the Epilepsy Self-Management Scale, the Neurological Disorders Depression Inventory for Epilepsy (NDDIE) Screening Tool, and the Epilepsy Adverse Events profile. A tailored management action plan is printed for review by the patient and provider. RCT preliminary results indicate significant between-group difference for self-efficacy for

management of lifestyle issues ( $p < 0.05$ ). Between-group behavioral impact was not demonstrated. Study challenges included cross-contamination, small sample size, and variable number of patient return visits.

**Conclusion:** Decision support to assess patient epilepsy self-management behavior and provision of a tailored action plan is consistent with approaches from other chronic diseases. RCT findings suggest MIND-SET's potential to impact lifestyle behaviors, often ignored in patient-provider discussions. However, results indicate modifications to further engage providers and a more rigorous RCT to overcome study design challenges.

**p0766**

### EEG, HALLUCINATORY SEIZURES AND SOCIOCULTURAL IMPLICATIONS IN AN AFRICAN COUNTRY: SENEGAL

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**Purpose:** Hallucinatory seizures are partial seizures with strong subjective connotation. They are difficultly or awkwardly reported by the patients and/or their relatives. This study is one part of a research long term project comprising four sections (electrophysiological, socio-psychiatric, ORL and ophthalmologic). We try to understand these hallucinatory manifestations knowing origin and cultural impregnation of our patients.

**Method:** Prospective study during 5 months in our Neurophysiological unit in 2014. It concerns all patients refer for hallucinatory seizures, isolated or associated with others types of seizures. Patients did an interview with the neurologist and after psychiatry, ORL and ophthalmologist for eliminating organic troubles can explain hallucinations.

**Results:** We found 31 patients, including 76.9% old from 20 to 50 years, and a sex-ratio of 1.38 in favor of the men. Patients had a low level instruction. 25% had done their first seizure before 5 years old and 39% after 18 years. Hallucinations manifestations was mainly visual (19 cases) and were isolated or associated especially with convulsive seizures. Auditive hallucinations concerned 14 patients against five cases gustative and psychosensorial (intrapyschic) hallucinations. EEG were mainly (17 cases) normal or with focal abnormalities, mainly in pariéto-temporal seat (90% of abnormal cases).

**Conclusion:** Hallucinatory seizures have a large share of subjectivity and critical polymorphism. Their dissociation from a particular psychological state and cultural influences, make more difficult their interpretation. And then, sociocultural correlations are very hard because of variable origin and different interpretations of hallucinations toward ethnics. Anatomico-electroclinic correlations are also difficult because they are in the borders between frontal, parietal, temporal, and occipital lobes. EEG helps to specify the localization of the discharge and its propagation. Our study shows in 42% of cases parieto-temporal discharges with posterior propagation.

**p0767**

### ICTAL CHANGES IN PARASYMPATHETIC TONE: CAN THEY PREDICT POST-ICTAL OXYGEN DESATURATION?

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**Purpose:** To measure changes in parasympathetic tone before, during and after temporal seizures, and to determine whether changes in high-frequency heart rate variability are correlated with post-ictal oxygen desaturation. Seizures with desaturation could be associated with a higher decrease in parasympathetic tone, which could explain the increased risk of sudden death in patients with epilepsy.

**Methods:** Retrospective review of 55 partial seizures, with or without impairment of consciousness but without secondarily generalization, including recordings of ECG and oxygen saturation during seizures. We calculated a high-frequency variability index (HFVI, based on the variability of RR intervals at high frequencies) as a marker of parasympathetic tone for periods of 20 minutes (centered on seizure onset). We then compared HFVI values in seizures with and without post-ictal hypoxemia.

**Results:** At the onset of seizures, HFI decreased rapidly, reached its minimum value at the end of the seizure and then gradually returned to its pre-ictal value. Changes in parasympathetic tone were more intense and longer-lasting in older patients with a longer duration of epilepsy. The HFVI was significantly lower during seizures with hypoxemia, and remained significantly lower five minutes after the end of the seizure. The change in the HFVI's slope over the first 30 seconds of the seizure was predictive of post-ictal oxygen desaturation.

**Conclusion:** We show a strong link between the presence of oxygen desaturation and duration of impairment of ANS during partial seizures. Seizures with desaturation are associated with a more prolonged disturbance of ANS, with a delay in the recovery of parasympathetic basal tone. This prolonged impairment of parasympathetic tone could predispose to a higher risk of sudden death.

**p0768**

### OPTIMIZING CARE DELIVERY FOR PATIENTS WITH EPILEPSY: OUTCOMES FROM A CANADIAN SINGLE SEIZURE CLINIC

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**Purpose:** To determine if a single seizure clinic (SSC) is superior alternative to standard care for people with epilepsy (PWE). Care for PWE is fragmented and there is a lack of evidence to support specific care delivery platforms.

**Methods:** A prospective study of all patients ( $n = 200$ ) referred to our SSC for first seizure evaluation. Demographic, clinical, and paraclinical variables were analyzed against a historical cohort. Binary logistic regression analysis was conducted to predict impact of dichotomized variables on epilepsy. Diagnostic concordance between epilepsy nurses and epileptologists was assessed.

**Results:** Mean patient age was 42.1 years. Referral sources were emergency department physicians and general practitioners. A diagnosis was established at first-contact in 80.9% of cases while 16.1% of patients required a second a visit. 41% of patients ( $n = 81$ ) were diagnosed with epilepsy. The most common non-seizure diagnosis was syncope (24.5% of cases). Mean wait-time for first assessment was significantly reduced by 71% (23.6 SSC vs. 80.1 days standard care). Mean wait-time for an EEG was 4.0 days (37.1 days standard care). 63 patients were started on anti-epileptic drugs (63.50% starting lamotrigine, 7% levetiracetam, 5% phenytoin, and 5% topiramate). In 18% of cases driving restrictions were initiated by the SSC. An abnormal EEG was found in 63% of patients diagnosed with epilepsy. Presence of EEG abnormalities increased the odds of epilepsy diagnosis (OR=2.00–12.75). Patients stratified as high (OR=4.29) or medium risk (OR=3.57) for seizure recurrence, had imaging abnormalities

(OR=2.00), reported being amnesic (OR=3.11), had limb stiffening (OR=2.52), tongue trauma (OR=6.31), or incontinence (OR=4.62) were at higher risk for epilepsy. There was only moderate correlation between SSC epilepsy nurses and physicians ( $\kappa=0.54$ ;  $p < 0.001$ ). Physicians were significantly more likely to diagnose epilepsy (likelihood ratio of 32).

**Conclusion:** The SSC, under supervision of epileptologists, reduces wait-times, improves patient access, and streamlines care.

p0769

### ETIOLOGY OF CONVULSIVE AND NONCONVULSIVE SEIZURES IN PATIENTS WITH SEVERE TBI

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**Background:** There are insufficient data about incidence of convulsive and nonconvulsive seizures (Sz), convulsive and nonconvulsive status epilepticus (SE) in traumatic brain injury (TBI) patients. According to different studies the incidence of convulsive SE and nonconvulsive SE is 8–48%, convulsive Sz and nonconvulsive Sz is 3–10%.

**Objective:** To evaluate the incidence of convulsive SE and nonconvulsive SE, convulsive and nonconvulsive Sz in patients with severe TBI (GCS 4–8).

**Methods:** Consecutive 24 cohort with TBI were evaluated by EEG monitoring, MRI, CT and followed for 3 months or until death.

**Results:** Seizures were detected in 13 (54%) patients, including nine patients with convulsive Sz, two with nonconvulsive Sz and two with SE. Convulsive Sz occurred immediately in two cases, within 7 days in three cases and after 7 days in three cases (12–70 days after TBI) and one patient had early and late seizures. In patients with subdural hematomas (SDH), epidural hematomas (EDH), diffuse axonal injury (DAI) the proportion of patients with Sz and without Sz were almost equal - about 50%. However, patients with multiple brain injury (MBI) were prone to seizures (80% with seizures, including two nonconvulsive Sz). Nonconvulsive SE and convulsive SE occurred in two patients: in one patient - convulsive SE and in one patient - were both convulsive SE and nonconvulsive SE. The mortality rate in all patients was 41% (10/24), among 10 died patients, 7 (70%) were with Sz and SE.

**Conclusion:** The pilot study demonstrate importance of detection convulsive Sz and nonconvulsive Sz, convulsive and nonconvulsive SE in patients with TBI and confirms the negative prognostic significance in patients with Sz.

p0770

### CLINICAL PROFILE OF PATIENTS WITH MALFORMATIONS OF CORTICAL DEVELOPMENT

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**Purpose:** Cortical dysplasia of various types, reflecting abnormalities of brain development, have been closely associated with epileptic activities.

The aim of the study was to elucidate the clinical-radiological profile of patients with malformations of cortical development.

**Method:** This observational study was conducted at Izmir Tepecik Educational and Research Hospital, Department of Neurology, Epilepsy Outpatient Unit. The diagnosis of “Malformations of cortical development” was based on clinical-radiological data. Details of clinical symptoms and treatment were reviewed.

**Results:** Thirty-six cases (17 women and 19 men) of “Malformations of cortical development” were identified. The mean age was  $34.14 \pm 10.9$  years. The commonest malformations were focal cortical dysplasia (26/36), polymicrogyria (4/36) and lissencephaly (3/36). agyria-pachygyria, schizencephaly, and heterotopias were the other malformations seen. Developmental delay was seen in 8 (22.2%) patients. All patients had seizures; being as presenting symptom in majority of patients. All patients were taking anti-epileptic drugs and none of them had surgery. Thirteen patients (36.1%) were seizure free and 13 (36.1%) patients were having <2 seizures per month. Drug resistant epilepsy was seen in 10 patients (27.8%).

**Conclusion:** The present study provides data on the pattern of malformations of cortical development seen in a Epilepsy Outpatient Unit. It emphasize that in most of the patients with malformations of cortical development, seizures may be controlled with anti-epileptic drugs.

p0772

### MYOCLONUS EPILEPTIC STATE AS A RARE CLINICAL MANIFESTATION OF RING CHROMOSOME 20 SYNDROME

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**Purpose:** Ring Chromosome 20 has a remarkable association with refractory epilepsy and frequent nonconvulsive status epilepticus. Continuous myoclonus has been infrequently reported during the clouding of consciousness periods. The aim of this study is the electroclinical description of two patients with Myoclonus epileptic state and Ring Chromosome 20 syndrome.

**Methods:** Two women (Patient 1: 60 and Patient 2: 37 years old) with pharmacoresistant epilepsy were admitted in our hospital. They suffered from tremor states with impairment of consciousness several times a week. Both patients had mild cognitive impairment. They underwent long term Video EEG monitoring. After video EEG findings, karyotyping was performed.

**Results:** Daily long periods of rhythmic 4–5 Hz clonic axial movements with a state of fluctuating consciousness were recorded in both patients. They lasted up to one hour in patient 1 and until six in patient 2. These states were precipitated by the drowsiness in patient 1 and they appeared in patient 2 while she was awake. The response to parenteral diazepam was better in patient 1. Ictal recording showed bilateral rhythmic slow activity with changing in frequency and a peak of 4–5 Hz, intermixed with spikes. This activity had higher amplitude in fronto temporal areas in patient 1 and in central areas in patient 2. The duration of the muscle activity was 120 msg and was synchronous in the agonist antagonist muscles. This activity was accentuated by touch and during postural holding. Karyotyping revealed 46, XX/46, XX r(20) in both patients with mosaicism of 15% in Patient 1 and 20% in Patient 2.

**Conclusion:** Our findings support the existence of continuous rhythmic myoclonus at 4–5 Hz during the confusional long states in patients with ring chromosome 20. Recognition of this type of seizure could contribute towards a better diagnosis of Ring Chromosome 20 syndrome.

p0773

**CARDIAC ARRHYTHMIAS DURING OR AFTER EPILEPTIC SEIZURES***M. van der Lende\**, †, *R. Surges*‡, *J.W. Sander\**, §, *R.D. Thijs\**, †\**Stichting Epilepsie Instelling Nederland, Heemstede,*Netherlands, †*Leiden University Medical Center, Departement of Neurology, Leiden, Netherlands,* ‡*University of Bonn Medical Center, Department of Epileptology, Bonn, Netherlands,* §*NIHR University College London Hospitals Biomedical Research Centre, Department of Clinical & Experimental Epilepsy, London, UK***Purpose:** Seizure-related cardiac arrhythmias are frequently reported and have been implicated as potential pathomechanisms of Sudden Unexpected Death in Epilepsy (SUDEP). We attempted to identify clinical profiles associated with various (post)ictal cardiac arrhythmias.**Method:** We conducted a systematic search from the first date available to July 2013 on the combination of two terms: “cardiac arrhythmias” and “epilepsy”. Databases searched were PubMed, Embase (OVID version), Web of Science and COCHRANE Library. We attempted to identify all case reports and case series.**Results:** We identified seven distinct patterns of (post)ictal cardiac arrhythmias: ictal asystole (103 cases), postictal asystole (13 cases), ictal bradycardia (25 cases), ictal AV-conduction block (11 cases), postictal AV-conduction block (two cases), (post)ictal atrial flutter/atrial fibrillation (14 cases) and postictal ventricular fibrillation (three cases). Ictal asystole had a mean prevalence of 0.318% (95% confidence interval 0.316–0.320) in people with refractory epilepsy who underwent video-EEG monitoring. Ictal asystole, bradycardia and AV-conduction block were self-limiting in all but one case and seen during complex partial seizures. Seizure onset was mostly temporal (91%) without consistent lateralization. Postictal arrhythmias were mostly found following convulsive seizures and often associated with (near) SUDEP.**Conclusion:** The contrasting clinical profiles of ictal and postictal arrhythmias suggest different pathomechanisms. Postictal rather than ictal arrhythmias seem of greater importance to the pathophysiology of SUDEP.

p0774

**VALUE OF VIDEO MONITORING FOR NOCTURNAL SEIZURE DETECTION IN EPILEPSY RESIDENTIAL CARING HOMES: AN INTERIM ANALYSIS***M. van der Lende\**, †, *J.W. Sander\**, ‡, *R.D. Thijs\**, †\**Stichting Epilepsie Instellingen Nederland, Heemstede,*Netherlands, †*Leiden University Medical Center, Departement of Neurology, Leiden, Netherlands,* ‡*NIHR University College London Hospitals Biomedical Research Centre, Department of Clinical & Experimental Epilepsy, London, UK***Purpose:** Following a case of SUDEP at a residential care unit, the Dutch care inspectorate requested the use of video monitoring (VM) at such unit. All those residents with a clinical suspicion of unwitnessed nocturnal convulsions are now monitored. We audited whether VM resulted in an increase in the reporting of seizures needing clinical intervention.**Methods:** The unit cares for 340 individuals. Acoustic detection systems cover all and 37 people also have a bed motion sensor (Epicare, Danish Care). As a result of the request of the care inspectorate, 46 people with possible nocturnal seizures are monitored by VM regardless whether a bed motion sensor had been evaluated. We analyzed the seizure charts for a two month period. Care providers were asked to report which device/system alerted them of suspected seizure and to indicate if it lead to an intervention (repositioning; emergency medication; activation vagal nerve stimulator).**Results:** Four hundred and sixty five seizures in 31 individuals were reported. Eleven of the 31 had an additional bed motion sensor. The total number of reported seizures was higher in those with versus those without a bed motion sensor (295 vs. 170). The proportion of seizures that were reported to be seen only on video footage differed per seizure type: 14/158 tonic clonic seizures; 58/125 tonic seizures; 4/11 complex partial seizures; 18/103 myoclonic seizures; 0/1 simple partial seizures and 18/67 “unclassified” seizures. Of 97 seizures requiring intervention, 16 were reported only to be seen on video. This proportion was lower for people with (6/64) than for those without (10/33) a bed motion sensor.**Conclusion:** VM may increase the identification of nocturnal seizures, especially in those without other detection devices.**Adult Epileptology 8  
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p0775

**GENITAL AUTOMATISMS: RARE OR UNDERESTIMATED SYMPTOM OF FOCAL SEIZURES?***H.O. Dede*, *N. Bebek*, *L. Baysal*, *C. Gürses*, *B. Baykan*,*A. Gökyigit**Istanbul University Istanbul Faculty of Medicine, Neurology, Istanbul, Turkey***Purpose:** Genital automatisms (GAs) are rare clinical phenomena during or after epileptic seizures. They are defined as repeated fondling, grabbing, or scratching of the genitals. The anatomic correlates of GAs have been discussed controversially. The aim of this investigation was to assess the localizing and lateralizing value of GAs.**Methods:** Three hundred and fifty one consecutive patients with intractable seizures referred to our University Hospital for presurgical evaluation between 2009 and 2014 were investigated. We evaluated the incidence of these behaviours, the clinical semiology, the associated symptoms/signs with the corresponding ictal EEG findings and their potential role in lateralizing the epileptogenic zone.**Results:** Eleven (3.2%) of 351 patients showed GAs. GAs occurred more often in men than in women (M/F: 8/3). GAs were associated with unilateral hand automatisms as postictal nosewiping or manipulating movements in 8 (%72.7) of 11. Seven of eleven patients (63.7%) were affected by temporal lobe epilepsy and four of them (36.3%) were affected by frontal lobe epilepsy. Epileptic focus lateralized to the left hemisphere in seven patients, lateralized to the right hemisphere in three patients and just a patient had bilateral frontal focus in scalp EEG. The surface EEG showed ipsilateral seizure pattern in six of 11 seizures (% 54) at the onset of GAs. All patients had amnesia for the performance of GAs.**Conclusions:** GAs appear in the ictal or postictal period with impaired consciousness. Men exhibit GAs more often than women. GAs do not localize or lateralize per se. Our results indicate that ictal genital automatisms are slightly more frequent in seizures originating from temporal lobe and they can be seen in frontal lobe seizures too.

p0776

**INVESTIGATION OF NEURONAL AUTO-ANTIBODIES IN MESIAL TEMPORAL LOBE EPILEPSY WITH HIPPOCAMPAL SCLEROSIS***E.N. Vanli-Yavuz\**, †, *E. Tuzun*‡, *C. Ulusoy*‡, *E. Ekizoglu\**,*L. Baysal Kırac\**, *N. Bebek\**, *C. Gürses\**, *A. Gokyigit\**,*B. Baykan\**

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**Purpose:** There is increased awareness of autoimmune factors in the etiology of epilepsy. Our aim is to investigate the antibodies developed against various neuronal proteins in a large series of mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS) and to elucidate the relationships between these neuronal auto-antibodies and clinical findings.

**Method:** We studied eight different anti-neuronal antibodies by RIA, ELISA and cell based assays in sera of 111 consecutive adult patients diagnosed with MTLE-HS according to clinical and MRI criteria. The clinical and laboratory features of antibody positive patients were investigated with a standard form, after their consent. The patients with dual pathology and without neuropathological confirmation of HS after the operation were excluded.

**Results:** We found antibodies against voltage-gated potassium channel (VGKC)-complex in five patients, contactin-associated protein2 (CASPR-2) in four, glycine receptor (GLY-R) in one and N-methyl-D-aspartate receptor (NMDA-R) in one patient with MTLE-HS, making a total of 9.9% seropositivity in the study group. Their current ages were 40.63 years ( $\pm 11.76$ ) and follow-up periods were 97.18 months ( $\pm 64.63$ ). Two of them had bilateral HS, other two had status epilepticus episodes and five patients had febrile seizure history. Except two patients (diagnosed with SLE and Hashimoto) none of the others had a history of autoimmune disorders. Four of nine patients with drug-resistant course were operated ending up with Engel 1–2 in the first year. Two patients had a history of psychotic attacks; one of them became seizure-free spontaneously, indicating a fluctuating course. Glutamic acid decarboxylase (GAD), leucine rich glioma inactivated 1 (LGI1),  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPA) and GABA receptor antibodies were not detected in any patients' sera.

**Conclusion:** We showed that 9.9% of MTLE-HS patients harbored various anti-neuronal antibodies with heterogeneous clinical characteristics. These antibodies, mostly against potassium channels should be screened for enlightening the etiology and immune treatment possibilities.

#### p0777

### A BIOSENSOR FOR TRACKING SEIZURES: LINKING A WRIST ACCELEROMETER TO AN ONLINE SEIZURE DATABASE

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**Purpose:** Because patient and caregiver reports of seizures are unreliable, there is a critical need for improved accuracy and reliability of tracking seizures. Both clinical management of epilepsy and current anti-convulsant and epilepsy device trials rely on paper diaries with self-reported seizure frequency as the primary outcome. This is the first study addressing the feasibility of detecting and recording convulsive seizures through a biosensor to an online seizure database.

**Method:** This prospective trial was conducted in the video EEG (vEEG) Epilepsy Monitoring Unit. Epilepsy patients wore a wristwatch accelerometer (SmartWatch, SmartMonitor©) that detected and transmitted events via Wi-Fi to a bedside electronic tablet with an online portal. The watch recorded the date, time, audio, duration, frequency and amplitude of convulsive events. Events logged by the watch were compared to vEEG to determine device sensitivity and specificity to detect and record convulsions to an online database.

**Results:** Twenty-one patients were enrolled, 41 epileptic seizures were recorded on vEEG: 10 convulsive and 31 non-convulsive. The watch cap-

tered 8/10 convulsive seizures. One patient was not wearing the watch at the time of convulsion. Of the remaining nine convulsions, watch sensitivity was 88.9% (8/9): one short duration myoclonic seizure was not detected. Watch audio recordings demonstrated seizure activity in 7/9 (77.8%). The watch recorded 77 false positives and 38 patient-initiated cancellations (49% specificity). False positives were easily explained on vEEG as non-epileptic repetitive movements such as teeth brushing. Patients and caregivers reported 5/41 (12.2% sensitivity) seizures but zero seizures were recorded on paper logs.

**Conclusion:** Through a biosensor, automatic detection and recording of tonic clonic seizures to an online database is feasible and should be employed in for clinical decision making and future clinical drug and device trials to improve accuracy of seizure counts and characteristics.

#### p0781

### ANTI-NMDA RECEPTOR ENCEPHALITIS: CLINICAL CHARACTERISTICS, PREDICTORS OF OUTCOME AND THE KNOWLEDGE-PRACTICE GAP IN SOUTHWEST CHINA

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**Purpose:** This study aimed to analyze the clinical profiles and outcomes of patients with anti-NMDAR encephalitis in China.

**Method:** We reviewed the clinical data of patients who received a definitive diagnosis of anti-NMDAR encephalitis between June 2011 and June 2014. Clinical information was obtained, and we compared the patients who initially presented with seizure with those who initially presented with psychiatric symptoms. We also analyzed the predictors of poor outcome.

**Results:** A total of 51 patients with a definitive diagnosis of anti-NMDAR encephalitis were included in this study. Four of them were surgically confirmed to have a neoplasm. Thirty-two patients, among whom 24 were female, presented with psychiatric disorder as the initial symptom, whereas 14 patients, only five of whom were female, presented with seizure as the initial symptom ( $p = 0.011$ ). Older patients and those with an extended hospital stay, memory deficits, decreased consciousness, central hypoventilation, complications, positive CSF results, or elevated creatine kinase levels were more likely to have a poor outcome ( $p = 0.041, 0.016, 0.031, 0.019, 0.011, 0.027, 0.049, \text{ and } 0.028$ , respectively). It typically took three weeks before these patients were admitted to our hospital and another two weeks before the correct diagnosis was made. The misdiagnosis rate was 56.86%, and 58.8% of the patients experienced at least one type of complication.

**Conclusion:** The treatment of anti-NMDAR encephalitis in China continues to face many challenges. Increasing the awareness of this disorder and reducing the interval to diagnosis and the rate of complications are essential and practical measures to improve the prognosis of afflicted patients.

#### p0783

### IS TEMPORAL LOBE EPILEPSY A PREDISPOSING FACTOR FOR SLEEP APNEA?

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**Purpose:** The interaction between epilepsy and sleep is known. It has been shown that patients with epilepsy have more sleep problems.

## Abstracts

However, there is no recent study that compares the frequency of sleep disorders in groups with medically refractory Temporal lobe epilepsy (TLE) and Extratemporal lobe epilepsy (ETLE). The main purpose of this study was to investigate sleep disorders in two subtypes of epilepsy by using sleep questionnaire forms.

**Method:** One hundred and eighty-nine patients from 215 who were monitored for refractory epilepsy were followed by the video EEG monitoring unit, divided into TLE and ETLE groups. The medical outcome study-sleep scale (MOS-SS), Epworth sleepiness scale (ESS) and sleep apnea scale of the sleep disorders questionnaire (SA/SDQ) were completed after admission to the video EEG monitoring unit. The total scores in the TLE and ETLE groups were compared.

**Results:** TLE was diagnosed in 101 (53.4%) (45 female) and ETLE was diagnosed in 88 (46.6%) (44 female) patients. Comparison of MOS-SS and Epworth sleepiness scale scores in the two subgroups did not reveal significant differences. In the TLE group SA/SDQ scores were significantly higher compared to the ETLE group.

**Conclusion:** Temporal lobe epilepsy patients have higher risk of OSA according to their reported symptoms. Early detection of OSA in epilepsy patients by using questionnaire forms may decrease the risk of ictal or postictal respiratory related "Sudden Unexpected Death in Epilepsy" (SUDEP).

p0785

#### ASSOCIATION BETWEEN INTERLEUKIN 1 BETA (IL-1 $\beta$ ) GENE VARIATION AND TEMPORAL LOBE EPILEPSY WITH HIPPOCAMPAL SCLEROSIS

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**Purpose:** We attempted to demonstrate a positive association between a polymorphism in the promoter region of the IL-1 $\beta$  gene resulting in enhanced gene transcription and the clinical phenotype of temporal lobe epilepsy with hippocampal sclerosis (TLE+HS).

**Method:** We determined the frequency of a single nucleotide polymorphism (SNP) that results in a C>T transition 511 base pairs five prime to the transcription start site of the IL-1 $\beta$  gene in a group of 21 patients with TLE+HS patients, 21 patients with temporal lobe epilepsy without hippocampal sclerosis (TLE-HS) and 23 healthy volunteers.

**Results:** The frequency of the -511T allele was 11/21 in TLE-HS, 13/21 in TLE+HS and 12/23 in normal control groups. Chi squared analysis of genotype and allele distribution showed no significant difference between patients with TLE+HS, TLE-HS and controls.

**Conclusion:** The results of the current study fail to document an association between the -511/C>T SNP variation and TLE+HS.

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p0786

#### HISTOPATHOLOGICAL CHARACTERISTICS OF CORTICAL TUBERS IN PATIENTS WITH TUBEROUS SCLEROSIS COMPLEX - A COMPREHENSIVE SEMI-AUTOMATED TISSUE ANALYSIS

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**Purpose:** Tuberous Sclerosis Complex (TSC) is a rare pediatric genetic syndrome frequently associated with severe intractable epilepsy. In some of the patients epilepsy surgery can be conducted as treatment option if the epileptogenic zone can be located to one lesion. On histopathology the lesions contain dysmorphic neurons, brightly eosinophilic giant cells and white matter alterations. The aim of this study was to generate a lesion classification system based on semi-automated histological quantification and find clinically significant correlations.

**Method:** We studied 29 cases of TSC with representative cortical tubers and eight matched samples of peritubular cortex in relation to an age- and region matched control group (n = 12). The following panel of cellular features were assessed: mTOR activation, amount of neurons, dysmorphic neurons, calcification, gliosis, giant cells, vessels, inflammation, myelin content and amount of oligodendroglia. An Olympus whole slide scanning system (BX53) was used to obtain images for further processing on the ImagePro software package (MediaCybernetics, USA). Field fractionation and smart segmentation was applied to analyze the data. The thresholds were kept the same throughout the analysis.

**Results:** With regard to the lesion severity (assessed by presence of calcifications, dysmorphic neurons and giant cells) were strong correlations with inflammation, neuronal cell loss, reduction in myelin content, mTOR activation, TSC mutation, age of epilepsy-onset and duration of active epilepsy.

**Conclusion:** On basis of the available set of data and the clinical implications we propose a three-tiered classification system: A: presence of giant cells  $\leq 10$  cell/mm<sup>2</sup>. B: giant cells  $> 10$  cell/mm<sup>2</sup> OR presence of dysmorphic neurons  $> 5$ /mm<sup>2</sup>. C: giant cells, dysmorphic neurons and calcifications. This histopathological classification system provides consistent objective criteria for a better definition of the clinico-pathological features of cortical tuber variants and may represent the basis to further explore imaging, functional and molecular features, and postsurgical seizure outcome.

p0787

#### BRIVARACETAM DOES NOT MODULATE THE MAJOR IONIC CONDUCTANCES IN NEURONS

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**Purpose:** Brivaracetam (BRV) is a selective, high affinity ligand for synaptic vesicle protein 2A (SV2A) and recently demonstrated positive Phase III results as adjunctive treatment for partial-onset (focal) seizures

in adults with epilepsy. BRV binds SV2A with 10- to 30-fold higher affinity than levetiracetam (LEV), but its exact mechanism of action is not known. Electrophysiological investigations were performed to determine whether BRV modulates the major ionic currents activated in neurons. Previous pharmacological studies of BRV, which explored its effect on low-voltage activated (LVA) and high-voltage activated (HVA)  $\text{Ca}^{2+}$  currents<sup>1</sup> and on fast  $\text{Na}^{+}$  voltage-gated currents ( $I_{\text{NaF}}$ )<sup>2</sup>, are summarised and supplemented with the results of further investigations performed on voltage-gated  $\text{K}^{+}$  ( $I_{\text{K}}$ ) and persistent voltage-gated  $\text{Na}^{+}$  ( $I_{\text{NaP}}$ ) currents.

**Method:** Voltage-clamp experiments were performed under whole-cell patch-clamp configuration. LVA  $\text{Ca}^{2+}$  currents, HVA  $\text{Ca}^{2+}$  currents, voltage-gated  $\text{K}^{+}$  currents and voltage-gated  $\text{Na}^{+}$  currents were investigated in isolated dorsal root ganglia neurons from 1- to 2-month-old rats, in dissociated CA1 hippocampal neurons from 14-day-old rats, in primary cultures of mouse hippocampal neurons (10–21 DIV) and in CA1 neurons from adult rat hippocampal slices, respectively.

**Results:** In isolated neurons, BRV (0.1  $\mu\text{M}$ –1 mM) did not affect LVA and HVA  $\text{Ca}^{2+}$  current properties, with respect to maximal amplitude, voltage-dependence and activation/inactivation kinetics. In primary hippocampal cultured neurons, BRV tested at 1, 10 and 100  $\mu\text{M}$  did not alter the amplitude of the non-inactivating outward  $\text{K}^{+}$  current. Finally, perfusion of BRV did not modify the amplitudes of  $I_{\text{NaF}}$  (300  $\mu\text{M}$ ) and  $I_{\text{NaP}}$  (2–20  $\mu\text{M}$ ) recorded in CA1 neurons.

**Conclusion:** These results suggest that the molecular mechanism of BRV does not involve major ionic voltage-dependent conductances in rodent neurons. UCB supported.

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#### p0788

### EFFECT OF ANTIOXIDANT MNTMPYP ON ELECTROENCEPHALOGRAPHIC ACTIVITY DURING EXPERIMENTALLY INDUCED STATUS EPILEPTICUS BY LI-PILOCARPINE, 4-AMINOPYRIDINE OR KAINIC ACID IN IMMATURE RAT

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**Purpose:** An oxidative stress has been convincingly shown to be an important contributor to neuronal and mitochondrial damage observed after status epilepticus in both adult and immature brain. We have shown recently that acute treatment with cell-permeant SOD mimetic manganese (III) tetrakis(1-methyl-4-pyridyl)porphyrin (MnTMPYP) protects brain against excessive production of superoxide during status epilepticus. The purpose of the present study was to assess an effect of the MnTMPYP on the electrographic epileptiform activity during status epilepticus induced in immature rat.

**Method:** To record EEG activity during status epilepticus four epidural silver wire electrodes were bilaterally implanted above sensorimotor cortex. Reference and ground electrode were placed in the occipital bone above cerebellum. Status epilepticus was induced after postsurgical recovery in immature 12-day-old male Wistar rats by substances with a different mechanism of action, namely 4-aminopyridine (bilateral i.c.v., 100 nmol/side,  $n = 8$ ), Li-pilocarpine (i.p., LiCl 127 mg/kg at P11 and the next day pilocarpine 35 mg/kg,  $n = 13$ ) or kainic acid (i.p., 6 mg/kg,  $n = 8$ ). A water soluble antioxidative agent MnTMPYP was applied (3 mg/kg i.p.) in two time points, 30 minutes before and 30 minutes after application of the convulsant. The control group obtained adequate volume of saline. The EEG was continuously recorded for 120 minutes covering whole period of the experiment. Number and frequency of spikes and power spectra were obtained using Matlab software.

**Results:** Application of all convulsants consistently led to both behavioral and electrographic seizure activity. The treatment with MnTMPYP did not affect latency nor severity of behavioral seizures induced by all three convulsants. Similarly, spike analysis did not revealed significant alterations in spike frequency and count after the treatment.

**Conclusion:** The present study has shown that protective effect of MnTMPYP during status epilepticus is likely to its antioxidative action. The study was supported by grant project no. 15-08565S from Czech Science Foundation.

#### p0790

### DIFFERENTIAL PROTEOME ANALYSIS DURING EPILEPTOGENESIS: FOCUS ON INFLAMMATION

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**Purpose:** Excessive inflammatory signaling is considered as a major contributing factor to epileptogenesis. Differential proteome analysis can provide comprehensive information about the sequential alterations in inflammatory signaling cascades during epileptogenesis. Expected data sets can suggest novel target and biomarker candidate.

**Method:** Epileptogenesis was triggered by electrical stimulation of the basolateral amygdala and induction of status epilepticus in Sprague Dawley rats. Hippocampus and parahippocampal cortex tissue has been collected at three different time points reflecting the early post-insult phase, the latency phase and the chronic phase with spontaneous recurrent seizures. Development of seizures was monitored by a 2 week video-EEG recording. Samples were subjected to a liquid chromatography tandem mass spectrometry (LC-MS/MS) proteomics profiling approach based on label-free quantifications.

**Results:** Parahippocampal cortex data sets revealed a higher number of differentially expressed proteins as compared to the hippocampus. The most pronounced regulation of protein groups linked with immune and inflammatory responses was observed during the latency phase. The functional categories comprised proteins associated with leukocyte transendothelial migration, Toll-like receptor signaling, prostaglandin synthesis and regulation, heat shock protein regulation, and heat shock factor interaction. In the early post-insult phase, proteins associated with signaling of transforming growth factor beta proved to be differentially expressed. In the chronic phase findings from the parahippocampal cortex demonstrated a regulation of proteins associated with integrin signaling.

**Conclusion:** In-depth bioinformatic analysis of the proteomic data sets rendered novel information about the time course of expression regulation of inflammation-associated proteins. Moreover, the findings point to previously unknown players in the disease-associated inflammatory interactome, which are co-regulated along with other proteins already known to be regulated during epileptogenesis. Future studies are necessary validating novel target and biomarker candidates.

#### p0793

### COGNITIVE DEFICITS AND ASTROCYTIC MYO-INOSITOL (MINS) PREDICT EPILEPSY DEVELOPMENT IN A RAT MODEL OF STATUS EPILEPTICUS

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**Purpose:** We evaluated cognitive deficits and astrocyte activation during epileptogenesis to explore whether they represent predictive biomarkers of epilepsy development and neuropathology.

**Method:** Animal randomization and blinding procedure for data analysis were applied. Status epilepticus (SE) was induced by lithium+pilocarpine in 21 day-old Sprague-Dawley male rats (n = 27) to provoke epilepsy only in ~60% of rats. Rats were exposed longitudinally to <sup>1</sup>H-MRS (7 Tesla) at day 1, 2, 3, 7, 9, 22 and 75 post-SE, to encompass epileptogenesis preceding spontaneous seizure onset in this model. We measured mIns (a metabolite specifically induced in activated astrocytes) in the hippocampus, a key epileptogenic area in this model. Rats were tested in the Morris water-maze at 15 and 65 days post-SE. Thereafter, all rats were electrode-implanted and EEG recorded for 2 weeks (24/7) at 7 months post-SE to identify animals with or without spontaneous seizures. A *post-hoc* analysis of learning ability and mIns level measured during epileptogenesis was done in these two groups. Age-matched controls (lithium+saline, n = 18) were exposed to <sup>1</sup>H-MRS and behavioral test.

**Results:** SE severity and duration were similar in all animals, as quantified behaviorally in MRI-exposed animals and by EEG analysis in a parallel cohort of electrode-implanted rats. Our data show: (a) an irreversible learning deficit at 15 and 65 day-post SE (2-fold longer latency to reach the platform) only in rats later developing epilepsy; (b) ~40% increase in mIns levels at 7 and 9 days post-SE (p < 0.01 vs. control); mIns increase persisted up to 75 days only in rats later developing epilepsy, whereas it returned to control level in non-epileptic rats. Brain histology will assess if behavioral changes and mIns levels predict the extent of neurodegeneration in rats.

**Conclusion:** Our results identify putative biomarkers for predicting epilepsy development in individuals at-risk using approaches readily translatable to the clinic.

#### p0794

### ROLE OF MATRIX METALLOPROTEINASE-9 (MMP-9), RHO KINASE (ROCK II) AND GLYCOGEN SYNTHASE KINASE-3 $\beta$ (GSK-3 $\beta$ ) IN THE PROTECTIVE EFFECT OF CURCUMIN IN PENTYLENETETRAZOLE (PTZ)-INDUCED KINDLING IN RATS

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**Purpose:** We have recently demonstrated anti-epileptic effect of curcumin. Matrix metalloproteinase-9 (MMP-9), rho kinase (ROCK II) and glycogen synthase kinase-3- $\beta$  (GSK-3 $\beta$ ) have been implicated in pathogenesis of epilepsy. In the present study, the effect of curcumin on the expression of MMP-9, ROCK II and GSK-3 $\beta$  in pentyletetrozole (PTZ)-induced kindling was evaluated.

**Method:** PTZ (30 mg/kg, i.p.) was administered on alternate days up to day 43 or until seizure stage 5 on two consecutive trials was achieved, whichever was earlier. Curcumin, suspended in 0.1% carboxymethylcellulose (CMC), was administered daily per orally (p.o). The animals were randomly divided into five groups (n = 6). Group I (Normal control) received no active treatment. Group II (vehicle control) was administered 0.9% saline i.p. and CMC p.o. Group III (PTZ group) was injected PTZ, i.p on alternate days. Group IV was pre-treated with curcumin in a dose of 300 mg/kg in addition to alternate day PTZ. In this group, curcumin was administered 30 minutes before PTZ administration on the days of PTZ injection. Group V (*per se*)

was administered curcumin, 300 mg/kg, p.o daily. Western blot analysis was performed to study the expression of MMP-9, ROCK II and GSK-3 $\beta$ .

**Results:** Curcumin caused significant increase in development of kindling, latency to myoclonic jerks as well as latency to GTCS and decrease in number of myoclonic jerks as compared to PTZ group. PTZ-induced kindling in rats caused significant increase in the expressions of MMP-9, ROCK II and GSK -3 $\beta$  which were prevented by curcumin. Curcumin *per se* did not alter MMP-9, ROCK II and GSK -3 $\beta$  expressions.

**Conclusion:** This study demonstrates a possible role of MMP-9, ROCK II and GSK -3 $\beta$  in the antiepileptic effect of curcumin in PTZ-induced kindling in rats.

**Acknowledgement:** The work was supported by Institute Research Grant to Dr KH Reeta.

#### p0796

### UPSTREAM AND DOWNSTREAM MTOR PATHWAY HYPERACTIVATION IN FOCAL CORTICAL DYSPLASIA TYPE II

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**Purpose:** FCD II are malformation of cortical development frequently associated with intractable epilepsy and characterized by cortical dyslamination and abnormal cells including dysmorphic neurons (DNs) and balloons (BCs). The downstream mediators of the mTOR pathway - important network involved in multiple functions during development and maturational stages - are abnormally activated in both DN and BCs, suggesting a role in the pathogenesis of FCD II, but less is known about upstream activators. Aim of this work is to clarify the contribution of the upstream compartment PI3K-Akt to mTOR pathway activation in surgical specimens presenting FCD II.

**Method:** We analyzes, in surgical samples from patients with FCD II (19 cases) and Rasmussen Encephalitis (RE- three cases used as comparison tissue without developmental malformation), the expression pattern of pS6 (downstream target), pPDK1 and pAkt (upstream targets). We also perform a cell count and a plotting analysis of BCs and DN positive for mTOR markers. Moreover, immunofluorescence experiments were made combining mTOR markers with GAD, VIM and SMI (to identify interneurons, BCs and DN).

**Results:** In FCD II, DN and BCs express upstream and downstream targets. pS6 is detected in almost all abnormal cells, conversely, pPDK1 and pAkt, distributed in the same spatial areas of pS6, are observed in a less proportion of DN (respectively in 41% and 25%) and BCs (respectively in 87% and 63%). In contrast, in RE cases, the rare DN are pS6 positive but pPDK1 and pAkt negative.

**Conclusion:** In FCD II, the PI3K-Akt compartment is only partially responsible to the mTOR hyperactivation; therefore, as in acquired epilepsy (RE), additional mechanisms, for example linked to epileptic activity or inflammatory mechanisms might be involved.

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p0797

### UPHOLDING WAG/RIJ RATS AS A MODEL OF EPILEPTOGENESIS: PHARMACOLOGICAL EFFICACY

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**Purpose:** WAG/Rij rats display spontaneous absence-type seizures that are accompanied by generalized SWDs similar to human absence seizures and represent a validated animal model of absence epilepsy[1]. Recently, WAG/Rij rats have been indicated as a relevant model of genetically determined epileptogenesis[2]. WAG/Rij rats, as well as GAERS, are genetically prone to develop spontaneous absence seizures during their lifespan with only few early immature EEG-SWDs, which increase in number and duration with ageing also changing their morphology to become fully matured and expressed in all rats only after 2–3 months of age. In this light, both strains can be considered models of epileptogenesis where an early intervention can modify the underlying process and future development of seizures[2, 3].

**Method:** We have reviewed all scientific articles on antiepileptogenic treatments in WAG/Rij rats.

**Results:** The first article demonstrating that an early drug intervention has antiepileptogenic effects in WAG/Rij rats was published at the end of 2007 by Blumenfeld, et al.[2]. Ethosuximide was demonstrated to suppress the development of SWDs. In the same year, we demonstrated that fetal exposure to ethanol had similar effects [4]. Subsequently, antiepileptogenic effects were demonstrated for levetiracetam, zonisamide, vigabatrin, rapamycin, statins, fluoxetine, duloxetine, clomipramine and etoricoxib while no effects were observed for carbamazepine, haloperidol, risperidone and quetiapine.

**Conclusion:** WAG/Rij rats may represent a good opportunity to study genetically determined epileptogenesis. Molecular studies are needed to better define the process underlying seizure development in this strain. Finally, the recent study by Berg et al.[5] supporting that ethosuximide might have disease-modifying effects in childhood absence epilepsy has confirmed the data obtained in this model.

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p0798

### THE BLOOD-BRAIN BARRIER INTEGRITY AND EPILEPTOGENESIS IN GENETIC ABSENCE EPILEPSY OF WAG/RIJ RATS WITH CORTICAL DYSPLASIA

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**Purpose:** Absence epilepsy appears with age in WAG/Rij rats. This study investigates the effects of cortical dysplasia (CD) on the blood-

brain barrier (BBB) integrity and epileptogenesis in genetic absence epilepsy model of WAG/Rij rats.

**Method:** Pregnant WAG/Rij rats with genetic absence epilepsy were exposed to 145 cGy of gamma-irradiation on embryonic day 17 to induce CD. In the offsprings of the pregnant animals, EEG was recorded and horseradish peroxidase (HRP) was used as the BBB tracer.

**Results:** A massive cortical atrophy indicating cerebral cortex loss was shown in WAG/Rij rats with CD. There is a significant decrease in the number and duration of spike-and-wave discharges (SWDs) and an increase in the frequency of SWDs in WAG/Rij rats with CD when compared to the properties of SWDs in the intact WAG/Rij rats ( $p < 0.05$ ). Ultrastructurally, frequent vesicles containing HRP reaction products were observed in the cytoplasm of capillary endothelial cells in the cerebral cortex and thalamus of WAG/Rij rats with CD prominently more in the intact WAG/Rij group. Tight junctions were ultrastructurally intact in animals in both groups.

**Conclusion:** In conclusion, CD could play an important role both in the formation and duration of SWD and also in the frequency patterns of this wave in WAG/Rij rats. Our data also demonstrated that the induction of CD exacerbated BBB disruption that was observed in the WAG/Rij rats.

p0800

### WHITE MATTER PATHOLOGY IN PEDIATRIC EPILEPSY SURGERY SPECIMEN - A QUANTITATIVE HISTOLOGICAL ANALYSIS

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**Purpose:** Focal Cortical Dysplasia (FCD) can be found in 42% of children with medically refractory seizures. It is characterized by: disruption of cortical lamination (Type I), balloon cells and/or dysmorphic neurons (Type II) or can be associated with other principal lesions (Type III). Specific histopathological features characterize each subgroup and quite recently white matter alterations have been identified.

**Aim:** The aim of this study was to evaluate the degree of white matter pathology and give insights into underlying causes.

**Methods:** An immunohistochemical analysis of cortical white matter sections for oligodendroglial and myelination markers in 80 pediatric patients ([mean age 11 years], lesional and perilesional regions was performed in: cortical tubers, focal cortical dysplasia, complex cortical malformations, mild malformations of cortical development and controls). Stained sections were digitalized in high resolution, followed by a standardized quantitative image analysis, utilizing a ImageJ based macro for full automatic processing of whole region specific staining. Correlations and linear regression models were performed using SPSS (Version 22.0).

**Results:** Immunoreactive responses (CD3, CD68) were seen in all lesions compared to perilesional areas. Evaluation of oligodendroglial staining (Olig2) identified an increased amount of oligodendroglial cells in FCD type Ia and IIa compared to perilesional regions and controls. In contrast, two populations were identified in FCD type IIb, showing either increase or decrease of Olig2-positive cells. These populations signifi-

## Abstracts

cantly correlate with the degree of myelin pathology (MBP, CNPase). Immunofluorescence double staining identified a slight increase in proliferating oligodendrocytes (Olig2, Ki67) compared to samples with lower expression.

**Conclusion:** The myelination pathology in all FCD lesions shows a continuous spectrum ranging from increase in oligodendroglia up to severe myelin and oligodendrocyte loss suggesting a regenerative process due to intractable epilepsy.

## p0801

### CYCLIC GABA CONFORMER AND GLYCINE AS NATURAL ENDOGEN AGONISTS OF GABA-BENZODIAZEPINE-RECEPTOR COMPLEX

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**Purpose:** The aim of the present work is searching for natural endogen agonists of GABA-benzodiazepine's receptors and synthesis of new anticonvulsants (Ac) on the basis of their structural similarity.

**Method:**

We studied:

1. Molecular geometry and quantum chemistry of the barbiturates and benzodiazepines pharmacophores, main GABA conformers (linear, cyclic, scoop) and glycine using molecular mechanics approximation with the use of the MM2 force field;
2. Effect of introventricular injection of GABA and glycine on the cerebral neurophysiological activity in rats (EEG analysis);
3. Anticonvulsant activity of different one-valence salts of glycine and GABA using strychnine, picrotoxin, pentylenetetrazol and maximal electro seizure models.
4. Activity of the chlorine ionic channels was studied using the patch-clamp method on rat glioma cell cultures of C6 line.

**Results:** 1. Molecular geometry of the derivatives of barbiturates, benzodiazepines and glycine reminds that of cyclic GABA-conformer.

2. Introduced in same dosage glycine produces more pronounced and prolong inhibition of the brain cortex bioelectrical activity as GABA.

3. Using the main convulsive models (pentylenetetrazol and maximal electro seizure) there was revealed a pronounced anticonvulsant activity of the glycine Li salt,

4. It is believed that GABA-scoop conformer and glycine open chlorine ionic channels; Li salt of glycine has an ability of passing through BBB using a channel with strong inside field (11-th Eisenman's sequence).

**Conclusion:** 1. GABA-cyclic conformer and glycine act as natural endogen agonists of GABA-a-benzodiazepines receptor complex in CNS, while barbiturates and benzodiazepines act as their artificial agonists.

2. GABA-scoop conformer and glycine act like biotic endogen agonist GABA-benzodiazepine-receptor complex.

3. Developing new antiseizure drugs incorporating glycine pharmacophore in their structure (like Li salt of glycine) might be a promising direction in antiepileptic neuropharmacology.

## p0805

### EFFECT OF THE ENDOCANNABINOID RECEPTOR AGONIST WIN-55 212-2 ON EARLY ELECTROGRAPHIC CHANGES IN A POST-STATUS MODEL OF EPILEPTOGENESIS

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**Purpose:** This study was performed to investigate whether stimulation of endocannabinoid system early after status epilepticus (SE) could prevent or modify the subsequent epileptogenesis. We studied the effect of an agonist of endocannabinoid receptors, WIN-55 212-2, on electrographic features during the latent period of post-SE epileptogenesis in rats.

**Method:** The study was carried out on the lithium-pilocarpine model of temporal lobe epilepsy (TLE). Rats were treated with LiCl (127 mg/kg) 24 hour before administration of pilocarpine (25 mg/kg). SE lasted for 90 minutes and was stopped by injection of pentobarbital (25 mg/kg). WIN-55 212-2 (5 mg/kg) or vehicle (DMSO) was administered 4 hour after the end of SE. Cortical and hippocampal electrographic activity was recorded in awake freely moving rats using NeuroLogger (TSE Systems). Behavior was video-recorded. Data of video-EEG monitoring were analyzed offline; the first 34 hour after SE and two 30 hour records made during the period from day 7 to day 12 after SE were included in the analysis.

**Results:** During the first 34 hour after SE, recurrent generalized seizures appeared on EEG. These seizures included both convulsive seizures and ones without obvious motor manifestations. In the period 7–12 days after SE, such generalized seizures did not occur; however, short (1–3 second) 5 Hz cortical spike-and-wave discharges were observed. These discharges were not associated with motor seizures. Administration of WIN-55 212-2 significantly reduced the total duration of convulsive seizures during the first 34 hour after SE and in addition, suppressed the following development of cortical 5 Hz discharges.

**Conclusion:** Administration of the potent agonist of endocannabinoid receptors WIN-55 212-2 had an anticonvulsive effect during the first 34 hour after SE and suppressed further development of non-convulsive cortical spike-and-wave discharges during the early latent period of epileptogenesis. This study was supported by the Russian Foundation for Basic Research, project no. 14-04-01184.

## p0806

### VOXEL-BASED MORPHOMETRY IN THE EPILEPTIC BABOON

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**Purpose:** There is conflicting data regarding structural imaging and histopathological findings in people with genetic generalized epilepsies (GGE). The epileptic baboon represents a natural model for GGE, electroclinically resembling juvenile myoclonic epilepsy. We evaluated structural MRI differences between epileptic baboons and asymptomatic controls using voxel-based morphometry (VBM). We intend to correlate these abnormalities using functional neuroimaging and histopathological findings.

**Methods:** Twenty-eight, adult baboons (14 EPI/14 CTL;  $12 \pm 5$  years) underwent standard anatomical (MP-RAGE) MRI scanning on a 3T Siemens TIM Trio (Siemens, Erlangen, Germany); each baboon was sedated using intravenous ketamine (5–6 mg/kg/hour) and paralyzed with vecuronium (0.1–0.3 mg/kg) throughout the scan. Data processing and analysis were performed using FSL's VBM toolbox, in which each baboon's scan underwent

- 1) brain extraction,
- 2) tissue segmentation,
- 3) study-specific gray matter baboon template creation,
- 4) non-linear image registration to the baboon brain template.

Each baboon's spatially normalized scan was then used to assess voxel-wise differences between the EPI and CTL groups.

**Results:** Significant ( $p < 0.05$ ) increases in gray matter volume (GMV) were noted bilaterally in the anterior medial frontal and occipital, lateral frontoparietal, as well as cingulate cortices (Figure 1). Significant decreases in gray matter volume were noted in the thalami, midline cerebellum and pontomedullary brainstem.

**Conclusions:** Similar to human studies of GGE, the epileptic baboons with GGE demonstrated (GMV) decreases in the thalami, cerebellar midline and brainstem suggesting secondary injury due to chronic epilepsy. Cortical GMV, on the other hand, is increased diffusely, but sparing the medial frontoparietal and basal temporal cortices. Increased cortical GMV in human GGE is thought to reflect developmental abnormalities. In summary, this preliminary VBM study indicates suspected developmental and acquired GMV changes in the epileptic baboon, which need to be confirmed with cerebral histopathology.

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p0808

### ALTERATION OF THE GABA-A RECEPTOR $\alpha 1$ SUBUNIT EXPRESSION IN DIFFERENT TYPES OF INTERNEURONS OF THE HUMAN EPILEPTIC HIPPOCAMPUS

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GABAergic inhibition is known to play a complex role in the pathomechanism of epilepsy. Beside the interneuron loss and fiber reorganization, other factors like changes in the subunit composition of certain transmitter receptors also contribute in the pathological changes affecting the function of the preserved interneurons. In this study we examined the changes of the expression of GABA-A receptor  $\alpha 1$  subunit ( $\alpha 1$ ) in different functional types of interneurons. Surgically removed hippocampi of drug-resistant temporal lobe epileptic patients were examined and compared with control samples. We analyzed the density and synaptic coverage of the  $\alpha 1$ -immunopositive interneurons. The coexpression of  $\alpha 1$  and calcium binding proteins - parvalbumin (PV) and calbindin (CB) - in interneurons was studied using immunofluorescent double labeling. In control,  $\alpha 1$ -positive cells were found throughout the entire hippocampus with largest densities in the CA1 region and the hilus. The density decreased in the hilus of patients with hippocampal sclerosis. In the CA1 region an increased density of immunoreactive cells was found, which may be partially explained by the tissue shrinkage. The percentage of  $\alpha 1$ -positive-neurons also expressing CB is reduced significantly in the sclerotic CA1. In the hilus, the percentage of  $\alpha 1$ -positive neurons containing CB increased, and significantly more CB-positive interneuron showed  $\alpha 1$ -expression. In contrast, a decreased amount of PV-positive cells expressed the  $\alpha 1$  subunit in the hilus of epileptic patients. Electron microscopic examination showed that both asymmetric- and symmetric synaptic coverage of  $\alpha 1$ -positive dendrites was increased in the sclerotic epileptic samples, probably reflecting the sprouting of excitatory pathways and inhibitory cells. These data suggest pronounced differences of coexpression of  $\alpha 1$  with interneuron-markers in sclerotic epileptic human hippocampal tissue, as well as regional differences between the hilus and CA1 region. Changes in the subunit composition can lead to an altered response to GABAergic inputs and influence the sensitivity to certain drugs.

p0809

### INFLAMMATORY MEDIATORS IN HUMAN EPILEPSY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Purpose:** The mechanisms underlying epileptogenesis and seizures are incompletely understood. Accumulating evidence suggests a link between inflammation and epilepsy. The objective of this systematic review is to provide an overview of studies that investigated the involvement of inflammatory mediators, in human epilepsy.

**Methods:** A systematic literature search was conducted in MEDLINE, EMBASE and Cochrane databases. Original studies reporting inflammatory mediator levels in serum, cerebrospinal fluid or brain tissue of patients with epilepsy were included. Only studies comparing patients to controls were included in an aggregate meta-analysis.

**Results:** The search yielded 3.980 articles, of which 66 articles reporting on 1934 patients were eligible for inclusion. IL-1ra, IL-1 $\beta$ , IL-6, IL-10, IFN- $\gamma$  and TNF- $\alpha$  were the most extensively investigated proteins and results concerning their significance are equivocal. Elevated levels for IL-1ra, IL-1 $\beta$  and IL-6 were reported in several different epilepsy etiologies and media, while other proteins were specifically increased for one etiology. In brain tissue IL-22, -25, -27, TGF- $\beta$ , CCL 2, 3, 4, 5, 19, 22, CXCL 19, S100- $\beta$  and COX-2 were reported significantly elevated. In a meta-analysis combining the results of 27 studies including serum and CSF data of 664 epilepsy patients, we found a significant difference in inflammatory protein levels between patients and controls for serum IL-6, IL-17 and CSF IL-1 $\beta$  and IL-10.

**Conclusion:** The results of this systematic review confirm that inflammatory pathways are involved in epilepsy. The inflammatory response in epilepsy can be divided in a systemic response and a focal (brain) response, as reflected by the different inflammatory profiles that we found. Future studies may further clarify the role of inflammation in epilepsy and may prove the potential of anti-inflammatory treatment.

p0811

### SEIZURES, SLEEP-WAKE STATES AND JET LAG: DOES MELATONERGIC ANTIDEPRESSANT HELP TO RESTORE INTERNAL SYNCHRONY?

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**Purpose:** Rhythmic occurrence of absence seizures in WAG/Rij rats, a validated animal model of childhood absence epilepsy, is determined by the circadian timing system. Stable phase-relationship between seizures and sleep-wake states is maintained in the 12:12 light-dark cycle. Rapid, unexpected changes in the photoperiod, e.g. caused by long-distance air travels, result in a loss of the synchrony. Re-synchronization

## Abstracts

was found to be accelerated by melatonin and its agonists. The aims of the present study were to investigate the re-adaptation of the various sleep-wake states and absence seizures to an 8 hour phase delay and to assess the effect of the melatonergic antidepressant agomelatine on the speed of re-synchronization of the different electroencephalographic (EEG) states.

**Method:** Simultaneous EEG and electromyographic (EMG) recordings were made in adult, male WAG/Rij rats, a strain endowed with hundreds spike-wave discharges (SWDs) daily, to assess the effect of various doses of agomelatine on sleep-wake states and absence seizures (acute study, 3 days) and to investigate the effect of the compound on the process of re-synchronization after the phase delay (chronic study, 11 days).

**Results:** Agomelatine showed neither an effect on sleep-wake parameters in the acute study, nor affected SWDs and re-synchronization in the chronic study. Internal desynchronization between various rhythm was observed, however, some rhythms remained coupled (active wakefulness and deep slow-wave sleep, SWDs and light slow-wave sleep). A post-shift increase in passive wakefulness and a reduction in deep slow-wave sleep resulted in an aggravation of epileptic activity.

**Conclusion:** Different speed of re-entrainment and coupling between various rhythms suggests that SWDs and light slow-wave sleep are controlled by common circadian mechanism distinct from that for active wakefulness and deep slow-wave sleep. The increase in the number of seizures after the phase shift may be of significant importance for people with epilepsy planning transmeridian flight.

## p0812

#### EXPRESSION OF INFLAMMATION RELATED MICRORNAS MIR21, MIR146A AND MIR155 IN TUBEROUS SCLEROSIS COMPLEX CORTICAL TUBERS AND THEIR MODULATION IN CULTURED HUMAN ASTROCYTES

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**Purpose:** Tuberous sclerosis complex (TSC) is a genetic disease characterized by cortical tubers, giant cell astrocytomas and sub-ependymal nodules in the brain. Seventy to 90% of people with TSC have epilepsy, often unresponsive to anti-epileptic drugs. The innate inflammatory response is thought to play an important role in TSC pathology. Recent studies suggest that microRNAs (miRNAs), specifically miR21, miR146 and miR155, may function as crucial regulators of inflammatory pathways linked to epileptogenesis. The aim of the present study was to characterize the expression of the inflammation-related miRNAs miR21, miR146a and miR155 in TSC and control brain tissue and the effect of their modulation on inflammatory signaling in IL-1 $\beta$  stimulated astrocyte cultures.

**Method:** Expression and localization of miR21, miR146a and miR155 was studied in human TSC and control brain tissue using qPCR (n = 20 TSC/13 controls) and in situ hybridization (n = 7 TSC/6 controls) respectively. Expression of miRNAs and their targets under inflammatory conditions was mimicked by IL-1 $\beta$ -stimulation of human astrocyte cultures (n = 6). Furthermore, the effect of overexpression or knock-

down of miRNAs on inflammatory signaling by transfection of astrocytes with miRNA mimics or antisense molecules was examined (n = 4).

**Results:** Expression of miR21, miR146a and miR155 was increased in TSC tubers compared to control and perituberal brain tissue. Expression was localized in dysmorphic neurons, reactive astrocytes and giant cells. IL-1 $\beta$  stimulation of cultured astrocytes strongly induced intracellular miR21, miR146a and miR155 expression, as well as miR21 extracellular release. Preliminary results showed that overexpression of miR155 increases pro-inflammatory signaling, while overexpressing miR146a tends to dampen inflammatory signaling after IL-1 $\beta$  stimulation.

**Conclusion:** These data suggest that the studied miRNAs are associated with TSC and epilepsy. Inflammatory pathways underlying epilepsy pathology can be regulated in vitro by modulating miRNAs.

## p0813

#### INCREASED EXPRESSION OF CONSTITUTIVE ( $\beta$ 1, $\beta$ 5) AND IMMUNOPROTEASOME ( $\beta$ 1i, $\beta$ 5i) SUBUNITS IN EPILEPSY ASSOCIATED HUMAN FOCAL LESIONS

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**Purpose:** The proteasome is a multisubunit enzyme complex involved in protein degradation, which is essential for many cellular processes. During inflammation, the constitutive subunits are replaced by their inducible counterparts, resulting in the formation of the immunoproteasome, which has been suggested to play a role in epilepsy.

**Method:** Immunohistochemical analysis of  $\beta$ 1,  $\beta$ 1i,  $\beta$ 5 and  $\beta$ 5i subunits was performed in a cohort of surgical specimens from patients with drug-resistant epilepsy: hippocampal specimens with hippocampal sclerosis (HS, n = 20; ILAE type 1) and without (n = 16), cortical specimens of patients with focal cortical malformations, including Mild Malformations of Cortical Development (mMCD, n = 6), Focal Cortical Dysplasia (FCDIIa, n = 5; FCDIIb, n = 6) and cortical tubers from patients with Tuberous Sclerosis Complex (TSC, n = 6); as well as in autopsy controls (n = 14).

**Results:** In temporal lobe epilepsy,  $\beta$ 1,  $\beta$ 1i,  $\beta$ 5 and  $\beta$ 5i expression increased in hippocampal neurons and reactive astrocytes and was most pronounced in HS. In HS, neuronal  $\beta$ 1,  $\beta$ 5 and  $\beta$ 5i expression was positively correlated to seizure frequency. Neuronal  $\beta$ 1i and  $\beta$ 5i expression was positively correlated to epilepsy duration. In the cortex, expression in mMCD was not different from controls. In FCD, the expression of  $\beta$ 1,  $\beta$ 1i,  $\beta$ 5 increased in dysmorphic neurons, balloon cells and reactive astrocytes and was most pronounced in FCDIIb. The most prominent changes were observed in TSC: the expression of all subunits increased in dysmorphic neurons, giant cells and reactive astrocytes. In TSC,  $\beta$ 1 and  $\beta$ 5 expression in dysmorphic neurons and  $\beta$ 1i in giant cells was correlated to seizure frequency.

**Conclusion:** These observations suggest that dysregulation of the proteasome system represents a common pathologic hallmark of human focal lesions associated with drug-resistant epilepsy. Since the expression of the (immuno)proteasome is associated with the severity of pathologi-

cal alterations and epilepsy, this system may represent an interesting novel target for drug treatment in epilepsy that deserves further investigation.

**p0814**

#### ***MBD5*/M*BD5* DEPLETION VIA CHRISPR/CAS9 AFFECT NEURAL DEVELOPMENT THROUGH EPIGENETIC MODIFICATION IN A ZEBRAFISH MODEL**

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**Purpose:** Recent progress support that *MBD5* heterozygous deficiency causes epilepsy in comorbid with ASD and other neurological disorders with the mechanisms behind are unclear. To further elucidate the mechanistic relevance between *MBD5* deficiency with disease etiology, manifestation, as well as the role of *MBD5* in regulating neural development in vivo, we created a Zebrafish model with CRISPR/Cas9 that abolishes the expression of fish homologue gene *mbd5* subjected for phenotypic/molecular characterization.

**Method:** To create the *mbd5*<sup>-/-</sup> fish, we hired the CRISPR/Cas9 system with sgRNAs targeting at two independent *mbd5* genomic sites that completely abolished the endogenous expression of *mbd5*. Transgenic lines were then subjected for social behavioral, electrophysiological, and pathological analysis. To investigate how *mbd5* deficiency was involved in disease progress we also compared the profile of gene expression and DNA methylation between wildtype and *mbd5*<sup>-/-</sup> fish, with RNA sequencing and pyrosequencing.

**Results:** The *mbd5*<sup>-/-</sup> fish manifested dysmorphism particularly in the head, in together with developmental delay and elevated sensitivity to PTZ, a chemical compound used for inducing seizure in animal model. Immunohistochemistry indicated brain malformation, a phenotype caused probably by down-regulation of genes involved in neural development based on the RNA sequencing data. Besides, the genomic loci with perturbation in DNA methylation also partially overlapped with the dysregulated genes in mutant animal.

**Conclusion:** Knocking-down of fish *mbd5* expression created similar phenotypic characteristics with patient carrying *MBD5* mutation supporting this fish model can be used to investigate the molecular mechanisms of a type of neural disorders including epilepsy and ASD. Our preliminary studies suggested a model of *mbd5*/*MBD5* in regulating gene expression involved in proper neural development probably through affecting epigenetic modification.

**p0817**

#### **WAVELET ENTROPY ANALYSIS OF DIGITAL EEG FOR CHILD ABSENCE EPILEPSY**

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**Purpose:** The individual-scale and integral wavelet entropy of digital electroencephalogram (EEG) are employed to investigate the dynamical complexity mechanism of central nervous system and evaluate the damage of epileptic discharge to the central nervous system function in child absence epilepsy (CAE).

**Method:** Comparing the individual-scale and integral wavelet entropy of ictal and interictal EEG for child absence epilepsy with that of normal control. A total of 15 patients with CAE and 12 healthy, age- and gender-matched children were enrolled. EEG signals of 15 CAE patients and 12 normal children were recorded. Epileptic discharge signals during clinical

and sub-clinical seizures were collected 10 and 20 times, respectively. All the digital EEG signals collected from 21 leads were decomposed into 30 scales components by continuous wavelet transform (CWT). The individual-scale and integral wavelet entropy of EEG was computed to measure the dynamical complexity measure of central nervous system and evaluate the damage of epileptic discharge to the central nervous system and its function.

**Results:** The integral wavelet entropy of EEG for CAE is significantly lower than that of normal control. The integral wavelet entropy of ictal EEG is lower than that of interictal EEG for CAE. The individual-scale wavelet entropies of ictal EEG from 2 to 5 Hz are much higher than that of normal control. The individual-scale wavelet entropies of ictal EEG from 0.01 to 1 Hz and from 7 to 100 Hz are much lower than that of normal control. The individual-scale wavelet entropy of interictal EEG from 5 to 50 Hz is lower than that of normal control.

**Conclusion:** The individual-scale and integral wavelet entropy of digital EEG can be considered as a quantitative index for evaluating dynamical complexity of central nervous system. The epileptic discharge of CAE can reduce the integral wavelet entropy and damage the central nervous system function.

## **Clinical Neurophysiology 4 Tuesday, 8th September 2015**

**p0818**

#### **PATIENT TOLERABILITY OF CONTINUOUS CARDIOVASCULAR AND RESPIRATORY PHYSIOLOGICAL RECORDINGS IN A TELEMETRY UNIT**

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**Purpose:** Current studies suggest epileptic seizures can be associated with autonomic changes which are thought to contribute to the risk of sudden unexpected death in epilepsy (SUDEP). Furthermore, some have suggested ictal autonomic changes may be a SUDEP marker. We aimed to assess the tolerability of continuous and simultaneous non-invasive recordings of multiple autonomic variables in epilepsy patients.

**Method:** This is a pilot study examining pre-surgical epilepsy patients in a telemetry unit at King's College Hospital. Physiological parameters were studied via continuous measurement of heart rate (Medifit Ltd), blood pressure (Portapres<sup>®</sup>), respiratory effort (Smart Belt<sup>™</sup>), oxygen and carbon dioxide levels (TCM4 series) and electroencephalography (Ambu/Unimed/AD-TECH<sup>®</sup>). At the end of the monitoring each patient assessed the tolerability of the devices using a standardized form.

**Results:** Fifteen subjects underwent autonomic monitoring for variable lengths of time, ranging from two hours and forty minutes to forty-five hours and twenty minutes. The durations varied for different reasons but the main factor was the patient's tolerance for the equipment. Each patient rated each device as comfortable or uncomfortable and whether they would have the monitoring repeated with that device. The Portapres<sup>®</sup> unit was rated uncomfortable by up to 57% of the participants, along with the system used to monitor heart rate (36%) and electroencephalography (29%). Only 14% of the subjects did not wish to undergo continuous monitoring of blood pressure and/or respiration in further studies.

**Conclusion:** The Portapres<sup>®</sup> device was the most uncomfortable. The equipment used for heart rate and electroencephalography monitoring (both core components of telemetry) were identified as being uncomfortable in a substantial number of subjects. If ictal autonomic measures are to be studied continuously further development in device technology is required. This is particularly so if parameters recorded including blood

pressure or baroreflex sensitivity are found to be biomarkers for SUDEP risk.

**p0819**

### DOES LONG-TERM VIDEO-EEG RECORDING PREDICT SEIZURE DEVELOPMENT AFTER STROKE IN CRITICAL CARE PATIENTS?

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**Purpose:** Seizures are not an infrequent complication after stroke. Although there are numerous publications related to EEG findings in these patients, few investigators have examined the predictive role of EEG in the early post-stroke period. In this study, we investigated whether video-EEG monitoring (VEEGM) results of stroke patients in our neuro-intensive care unit (NICU) could predict seizure development and survival.

**Method:** Fifty patients (23M, 27F; age:  $66 \pm 14$ ; 37 ischemic, 13 hemorrhagic stroke) hospitalized in our NICU between 2009–2014, were included in the study. Follow-up information regarding development of seizures and survival was obtained from patient charts and telephone calls. We tried to determine whether the presence of epileptic discharges or ictal patterns in EEG correlated with the above measures of outcome.

**Results:** Twenty nine (58%) patients developed seizures during follow-up ( $26 \pm 16$  months). Of these, 18 (62%) patients had early ( $\leq 1$  week), and 11 (38%) patients had late ( $> 1$  week) seizures. Thirteen patients (26%) developed recurrent seizures (i.e., epilepsy). The risk of epilepsy was significantly higher in the late seizure group ( $p < 0.001$ ). We did not find a correlation between type of stroke and seizures ( $p = 0.72$ ). Epileptic discharges were detected in 17 (34%) patients. In two of them discharges were periodic (PED). Non-convulsive status epilepticus (NCSE) was detected in 3 (6%) patients. Overall, the presence of epileptic discharges did not correlate with seizure development ( $p = 0.6$ ) or survival ( $p = 1$ ), as was the case with NCSE. However both patients with PEDs developed seizures and died within one year after stroke.

**Conclusion:** Almost 2/3 of our study cohort developed seizures. In agreement with the literature, late seizures were a risk factor for epilepsy development. VEEGM results did not correlate with the occurrence of seizures or survival. However, more studies with larger patient populations are needed to better clarify this issue, especially regarding PEDs.

**p0820**

### CYCLIC ALTERNATING PATTERN AND INTERICTAL EPILEPTIFORM DISCHARGES IN CHILDREN WITH ABSENCE EPILEPSY

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**Purpose:** Cyclic alternating patterns (CAP) represent sleep instability in the NonREM. These patterns are related to learning, neurodevelopmental processes and epileptiform activity. Controversy about the microstructure of sleep and the presence of epileptiform generalized interictal discharges and their implication in clinical aspects of patients exists. In the setting of patients with childhood absence epilepsy (CAE), the challenge between how the difficulties found in cognitive processes are related to epileptic activity and in what extent this is due to external factors other than the seizure activity per se. This study pretends to explore the relationship of interictal activity (spike-slow wave) in CAE and sleep microstructure in terms of CAP assessment, as one of the associated factors to impairment of cognitive processes CAE.

**Methods:** 24 hour-Polygraphic studies of patients with CAE were performed and assessed their sleep pattern, we analyzed the interictal epileptiform activity and their CAP

**Results:** patients were between 9 and 12 years, all patients had seizures during the wake period, one of them had no treatment. 93 interictal epileptiform activity of spike-slow wave paroxysms. 60 (64.51%) were during CAP-A1, while seven presented in CAP-B and only two presented during a NonCAP period. The mean duration of Interictal discharges (ID) was 4.94 second in CAP-A1, 5.6 second in CAP-A2 and 0.58 second in the Non-CAP period. ID were more frequent in CAP-A1 than other sleep stages. The CAP-A1 is an important feature of sleep microstructure have been close related to learning processes, attention and behavior. This results suggests that attention, execution and scholar performance of patients with absence epilepsy might have a multi factorial origin, not only related to the seizures but to the impairment of sleep architecture, that is strongly associated to cognitive function, behavior and learning consolidation.

**p0821**

### CHARACTERISTICS OF ALTERED CORTICAL EXCITABILITY IN PATIENTS WITH GENERALIZED OR FOCAL EPILEPSY

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**Purpose:** We used transcranial magnetic stimulation (TMS) to investigate the difference of cortical excitability between patients with IGE or PE and normal controls.

**Methods:** We consecutively recruited 55 drug-naïve patients with epilepsy (IGE 35, PE 25, mean age 28.5 years) and 32 age- and sex-matched normal subjects. Epileptic focus was lateralized into right ( $N = 7$ ) or left hemisphere ( $N = 8$ ) in PE patients. We measured TMS parameters including resting motor threshold (RMT), motor evoked potential (MEP) amplitudes, cortical silent period (CSP), intracortical inhibition (ICI) and facilitation (ICF) during seizure free more than 24 hours.

**Results:** In both epilepsy patient and control groups, the CSP was lengthened approximately linearly with increases of stimulus intensity in both hemispheres. In IGE patients, interhemispheric differences of CSP were not found in any stimulus intensity ( $p > 0.05$ ). However, the mean CSP was longer in IGE patients compared with normal controls at all stimulus intensities ( $p < 0.05$ ). In PE patients, TMS parameters were compared between 1) ipsilateral hemisphere to epileptic focus (IH) versus contralateral one (CH), or 2) IH or CH versus normal controls, and 3) IH or CH versus IGE patients. The mean CSP was significantly shorter in IH than that in CH at 120% ( $p = 0.028$ ) and 140% of RMT ( $p = 0.003$ ). Mean CSP duration in CH was significantly longer at the stimulus intensities 120–150% of RMT and that in IH was longer only at 120% of RMT than that of normal controls ( $p = 0.005$ ). Between PE and IGE patients, there were no significant differences of CSP at any stimulus intensity.

**Conclusion:** These findings suggest that the CSP may have a lateralizing value in partial epilepsy by shorter CSP in the epileptic hemisphere. Prolonged CSP in epilepsy patients compared to normal subjects may indicate the abnormally increased interictal cortical inhibition.

**p0822**

### DETECTION OF EPILEPTIC ACTIVITY IN ABSENCE OF EEG INTERICTAL EPILEPTIFORM DISCHARGES

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**Purpose:** Currently there are not reliable bio-markers of active epileptogenicity in the individual patient.

**Aim:** to assess if the EEGs of epileptic patients without any detectable spikes contain the voltage epileptic map, specific of the individual patient.

**Methods:** Fifteen patients with pharmaco-resistant focal epilepsy were included. Six minutes of EEG with spikes and six minutes without any detectable spikes were selected from long-term monitoring recording during wakeful resting state (EEG 31-channels, ref: FCz). Resting-state EEG from 48 healthy control subjects were also recorded and corrected for artifacts. For the EEG of each patient, we calculated the averaged spike and its voltage map. We fitted the spike map on i) EEG of patient with visible spikes ii) EEG of the same patient without any visible spike and iii) EEGs of the 48 controls. The amount of presence of the voltage epileptic map was characterized using two criteria: mean correlation and Global Explained Variance (GEV). For these criteria statistical differences between 1) controls and EEG with spikes, and 2) controls and EEG without spikes were evaluated using z-scores.

**Results:** The patient-specific epileptic voltage map was significantly more represented in the spike-free EEGs of patients than in EEGs of healthy controls (GEV  $p = 0.029$ ; mean correlation  $p = 0.032$ ). This difference was more accentuated for the patient EEGs containing spikes (GEV  $p = 0.001$ , mean correlation  $p < 0.001$ ).

**Conclusions:** Scalp EEGs of patients with pharmaco-resistant epilepsy contains the epileptic voltage map (index of epileptic activity), even in absence of any detectable interictal epileptic discharges. This finding suggests that epileptic voltage map could be a new epileptic bio-marker (SPUM grant 140332 and 141165).

#### p0823

### SCALP HFOS AND BILATERAL SYNCHRONOUS SPIKE AND WAVE IN FOCAL AND IDIOPATHIC GENERALIZED EPILEPSY

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**Purpose:** Localizing the epileptic focus in patients with secondary bilateral synchrony and differentiation from generalized epilepsy is challenging. High Frequency Oscillations (HFOs) opened a promising research area for localizing the epileptogenic zone. We evaluated if scalp HFOs lateralize the origin of secondary bilateral synchrony, if HFOs are detectable in idiopathic generalized epilepsy (IGE) and if their distribution differs between focal and generalized epilepsy.

**Method:** We analyzed 30 minutes of 18 scalp EEG recordings (300 Hz filtered, 1000 Hz sampled) characterized by bilateral synchronous discharges of patients with focal (Focal Group: 11) and generalized (Generalized Group: 7) epilepsy. Spikes and ripples (at least four consecutive oscillations above 80 Hz) were visually marked. We calculated the ripple rate (number of ripples co-occurring with spikes over spiking duration) for each channel, each hemisphere and in anterior and posterior head regions. The higher ripple rate hemisphere was called prevalent and the higher ripple rate head region was called predominant. Prevalent/non prevalent hemisphere and predominant/non predominant head region ripple rates were compared using t test ( $\alpha < 0.05$ ) within group and between groups.

**Results:** Ripples co-occurring with spikes occurred in nine patients of the focal group and in three of the generalized group. Eight of the nine focal patients had a clinical lateralization, which was always concordant with the prevalent ripple hemisphere. All three generalized patients showed a prevalent hemisphere. The ripple rates comparison in prevalent/non prevalent hemisphere and predominant/non predominant head region showed no difference between focal and generalized patients but significant difference within each group ( $p < 0.01$  and  $p < 0.05$  respectively)

**Conclusion:** Ripples do not help in the differentiation between focal epilepsy with secondary bilateral synchrony and IGE but, if we suspect a focal origin, HFOs help the lateralization of the focus. This is the first report of ripples in IGE.

#### p0824

### COGNITIVE EVOKED POTENTIALS P3 IN PATIENTS WITH IDIOPATHIC EPILEPSY

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**Purpose:** The goal of this four-year prospective study was to investigate and determine whether there are cognitive changes in patients with idiopathic epilepsy (IE) detected with cognitive evoked potential P3 compared to the results obtained in the healthy population of the same age and sex characteristics. The secondary goal was to determine whether there is a connection between certain demographic (age, gender) and clinical (type of epilepsy, duration of disease, frequency of the seizures, severity of the interictal EEG changes, antiepileptic therapy, duration of treatment, etc.) characteristics of patients with IE with possible cognitive changes. We compared the obtained results with the PASAT test and determine the correlation between these two tests.

**Method:** The study was conducted on 82 patients with IE in age from 18–65 years, who were treated at least one year and in 82 healthy subjects, that were control group of the appropriate age, sex, education and other demographic characteristics. P3 were recorded in all study subjects using sound paradigm. For further analyse we used values of latency of P1, N1, P2, N2, P3 and P3 amplitude. We have also studied the localization of P3. All study subjects underwent PASAT test whose values were compared with values obtained from P3. Interictal EEG were recorded in patients with IE, and we analysed data related to the underlying disease: type of epilepsy, duration of epilepsy, seizure frequency, type of AED and EEG changes.

**Results:** Patients with IE have significantly extended latency of N2 and P3 and also decrease of P3 amplitude compared with healthy subjects. Changes of cognitive evoked potentials P3 characteristics correlate with changes of PASAT testing.

**Conclusion:** On the results of the both tests affect auditory attention, so we assume that the brain regions, that are activated when performing these tasks, are equal or at least overlap.

#### p0825

### SLEEP DEPRIVATION EEG FOR INCREASING EEG YIELD IN EPILEPTIC PATIENTS

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**Purpose:** First routine EEG is unlikely to detect interictal epileptiform abnormalities in 30%–50% of patients with epilepsy. Sleep deprivation (SD) is an important activation method for diagnosis of epilepsy-like

intermittent photic stimulation and hyperventilation. In this study, we assess the usefulness of SD-EEG in terms of diagnosis and type of epilepsy.

**Method:** From among the 896 adult patients undergoing SD-EEG in 2004–2015, we retrospectively and prospectively selected for analysis only those: (a) with epilepsy or suspected epilepsy; (b) with a normal/non-specific routine EEG; (c) using or not using antiepileptic drugs at the time of SD-EEG and routine EEG; (d) with previous MRI; (f) with at least 1 year of follow-up. SD was applied for at least 24 hour, while partial SD was applied for less than 24 hour. EEGs were reported as being normal or non-specific and abnormal, with abnormalities defined as the presence of epileptiform abnormalities, focal or generalized. We analyzed epileptic interictal abnormalities (IIAs) defined as spike, sharp, spike and wave discharge complexes.

**Results:** Two hundred fifty-eight patients fulfilled the inclusion criteria. SD-EEG revealed IIAs in 34.8% (n = 90) and supported diagnosis of epilepsy in patients with suspected epilepsy. Focal epilepsy was diagnosed in 68% (n = 61) of subjects and generalized epilepsy in 25% (n = 23), while no epileptic syndrome could be identified in 7% (n = 6). Of the 61 patients with focal epilepsy, 84% (n = 51) exhibited localized epileptic interictal abnormalities and 8% (n = 5) patients lateralized IIAs, while 8% (n = 5) exhibited generalized IIAs. Of the 23 patients with generalized epilepsy, 13% (n = 3) exhibited generalized, bilateral and asymmetric IIAs and 87% (n = 20) exhibited generalized, bilateral and symmetric IIAs.

**Conclusion:** The use of SD-EEG will help clarify diagnosis of epilepsy and epileptic syndrome in patients with normal/non-specific routine EEG. We suggest that SD EEG records should include both wakefulness and sleep in order to identify IIAs.

#### p0826

##### TESTING PATIENTS IN THE EPILEPSY MONITORING UNIT

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Interacting with the patients during seizures in the Epilepsy Monitoring Unit (EMU) is essential for evaluation of the semiological signs, for accurate classification and, for focal seizures for localization of the symptomatogenic zone. Although many publications addressed the value of various semiological signs, there are no published standards on the protocol for testing the patients during seizures in EMUs. Since 2009, the EMU at the Danish Epilepsy centre has implemented a standardized protocol for patient testing. The protocol focuses on highlighting cognitive changes, attention, memory and speech alterations. Our results show that the protocol is feasible and provides the semiological information necessary for seizure classification and for localization. A standardized patient testing protocol should be implemented in all EMUs.

#### p0827

##### USEFULNESS OF ELECTROENCEPHALOGRAPHY IN DEMENTIA

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**Purpose:** To determine the correlation between the type of dementia, the cognitive impairment and the electroencephalographic abnormalities and to evaluate the usefulness of systematic EEG in a dementia.

**Methods:** A retrospective study including 543 patients with dementia (276 Alzheimer's disease, 70 vascular dementias, 91 mixed dementias, 17 Fronto-temporal dementias, 20 Lewy body dementias and 69 other dementias) followed up in the department of Neurology at Razi Hospital

for a year (2008–2009). An EEG was systematically practiced in all patients. A patient file was developed, including epidemiological data, clinical MMSE, radiological, EEG and therapeutic data.

**Results:** The mean age of onset of cognitive impairment was 60.19 years. 285 patients were female (52.5%). Dementia was moderate in 49% of cases and severe in 37% of cases. The EEG was normal in 72%. Diffuse slowing of background activity was present in 17% of cases with mild dementia, 16% of cases with moderate dementia and 35% in cases of severe dementia. Paroxysmal abnormalities were observed in 59 patients (11%), eight of them presented clinical epilepsy.

**Conclusion:** In our series, a slowing of background activity was correlated with the severity of dementia. The EEG was not decisional for diagnosis. It remains useful in cases of specific orientation such as Creutzfeldt-Jakob disease or associated epilepsy.

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#### p0830

##### FUNCTIONAL CONNECTIVITY IN JUVENILE MYOCLONIC EPILEPSY: MEG-BASED NETWORK AND ANALYSIS

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**Purpose:** To investigate the functional connectivity between patients with juvenile myoclonic epilepsy (JME) and healthy controls using magnetoencephalography (MEG) investigations. We test the hypothesis that Motor functional connectivity is altered in JME compared to healthy controls.

**Method:** Seventeen epileptics with JME and fourteen age-matched and sex-matched healthy controls performed audio-motor tasks during MEG examination. We selected region of interests including motor area (M1), sensory area (S1), supplementary motor area (SMA), default mode network (DMN), frontoparietal control network (FPC) and dorsal attention network (DA). MNE (minimum-norm estimate) software was used to analyze and map the functional connectivity between patients and healthy controls.

**Results:** The coherence values had significantly increased in alpha and beta band between left M1 and left SMA in patients with JME compared to controls. Also the coherence values had significantly increased in the left M1 and S1, in the right M1 and DMN in beta band. There was no significant difference among M1, the FPC and the DA.

**Conclusion:** Motor functional connectivity is altered in JME compared to healthy controls. In JME, functional connectivity increased coactivation in M1 and SMA after perform finger movement compared to controls. There is stronger connectivity in motion and sensory network. Furthermore, we found impaired the deactivation of the default mode network.

#### p0831

##### ELECTRO-CLINICAL ANALYSIS OF ICTAL KISSING AUTOMATISM

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**Purpose:** Ictal kissing automatism (IKA) is a rarely seen ictal phenomenon. We aimed to study electro-clinical characteristics of this complex ictal behaviour.

**Method:** The clinical and imaging data and video – EEG recordings (when available) of 23 patients with IKB from five different centers were reviewed.

**Results:** Eighteen patients (11 females) were included. The mean age of the patients were 33.2 years (20–51 years). Seizure onset was 12.8 years (5–23). Fourty-eight ictal video-EEG obtained from 16 patients were reviewed. In 24 of them, IKA was observed during the seizure. All of 24 seizures revealed temporal lobe (TL) involvement during the kissing episode with seizure onset at TL in 12 patients (10 right, 2 left), at occipital in one patient. MRI showed hippocampal sclerosis in 10 (8 right, 2 left), parietal cortical developmental malformation and occipital lesion in 2 patients where it was normal in 6 patients. Different types of kissing (hands, arm, cheek, and blowing kisses) were seen during the ictal events.

**Conclusion:** Ictal kissing is a very rare automatism during epileptic seizures. There were only nine patients reported in the literature which four of them are from our series. In this study EEG and MRI revealed right side in 12, left side in three patients. Three other patients with negative MR showed bilateral EEG findings which disabled the delineation of epileptogenic zone. In conclusion, IK is a complex behavior usually related to right, nondominant temporal lobe although involvement of the other side is also possible.

#### p0832

### COMPARISON OF THE EFFECT OF TRANSCRANIAL DIRECT CURRENT STIMULATION BETWEEN FOCAL AND GENERALIZED EPILEPSY SYNDROMES

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**Purpose:** Transcranial direct current stimulation (tDCS) is a non-invasive and safe method tried in drug-resistant epilepsies. Our aim was to compare the effect of t-DCS between Lennox-Gastaut syndrome (LGS) and temporal lobe epilepsy with hippocampal sclerosis (TLE-HS) which are two well-known drug-resistant epileptic syndromes differing from each other by causing generalized versus focal seizures and EEG findings.

**Method:** Twelve LGS patients (mean age: 15.5; six males) and 14 TLE-HS patients (mean age 35.5; six males) diagnosed with their typical clinical, EEG and MRI findings were included after signed consent. All patients received cathodal stimulation. TLE-HS group were stimulated over the concordant MRI and EEG foci whereas LGS patients were stimulated over Cz region. Five patients from LGS group and all patients from TLE-HS group also received sham stimulation (60 seconds stimulation gradually decreased in 15 seconds). All were followed up by standard seizure diaries.

**Results:** Eleven patients (78%) among TLE-HS group had more than 50% decrease in their seizure frequencies by cathodal stimulation whereas three patients also showed positive sham effect. Among LGS patients, two patients (16%) had more than 50% decrease in their seizure frequencies by cathodal stimulation. However sham stimulation of these patients did not show any change in seizure frequency. Interestingly both of the responders with LGS had prominent additional focal EEG findings when compared to non-responders. No adverse effect has been reported.

**Conclusion:** Our small series suggested that cathodal t-DCS may be used as an additional option in focal epilepsies with significant EEG findings. It may be tried in TLE-HS patients rejecting epilepsy surgery or even with ineffective surgery results. However t-DCS is not effective enough in generalized refractory epilepsies such as LGS unless there are prominent focal EEG abnormalities. More studies are needed with large series of patients.

#### p0833

### EFFECT OF CATHODAL TRANSCRANIAL DIRECT CURRENT STIMULATION IN PATIENTS WITH TEMPORAL LOBE EPILEPSY – PRELIMINARY RESULTS

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**Introduction:** Temporal lobe epilepsy is a chronic condition characterized by recurrent, unprovoked epileptic seizures. Pharmacological treatment may be relatively effective in about 2/3 of the patients; for the other 1/3 surgical resection of the epileptogenic region is usually successful. Video-EEG monitoring in the epilepsy monitoring unit (EMU) is part of the presurgical evaluation. Transcranial direct current stimulation (tDCS) is a non-invasive, safe, painless stimulation technique, offering the possibility to induce prolonged excitability alterations in different cortical areas. Early animal experiments have revealed that cathodal tDCS reduces spontaneous firing rates of cortical cells, most likely by hyperpolarizing the cell body. tDCS allows diagnostic applications and offer a potential therapeutic use in neurorehabilitation, chronic pain, focal epilepsy and neuropsychiatric disorders. There is limited evidence on the efficacy of tDCS in epilepsy.

**Objective:** To detect the possible therapeutic effect of cathodal tDCS due to reduction of the epileptiform activity on the EEG/ reduction of the seizure frequency.

**Materials and methods:** Patients (age > 18 years) affected from drug resistant temporal lobe epilepsy, undergoing to EMU recordings, were recruited (planned 20 patients). Cathodal tDCS was delivered through a pair of rubber electrodes positioned over the epileptogenic focus. Current intensity was 1.0 mA; current duration: 20 minutes. For control stimulation we used sham stimulation. The effect of tDCS was measured on EEG, by quantifying the percentage of the epileptiform discharges by Brain Electrical Source Analysis program at least 4 hours before and after stimulation.

**Results:** Our preliminary data shows that the effect of tDCS is mainly in reducing propagation of the epileptiform discharges.

p0834

### POLYGRAPHIC FEATURES AND CLINICAL COURSE IN POST-ANOXIC MYOCLONUS (LANCE-ADAMS SYNDROME)

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**Purpose:** Post anoxic myoclonus is a severe condition resulting from coma and myoclonic status caused by prolonged anoxic insult. Poor prognosis has been associated with occurrence of myoclonic status and absence of SSEPs (Wijdicks et al., 2006). We describe the polygraphic features and clinical course in a patient with severe post-anoxic myoclonus.

**Method:** We investigated clinically and neurophysiologically a 18 years old girl who developed post-anoxic myoclonus after an episode of severe brain anoxia for 15 minutes. Prolonged coma and refractory status epilepticus followed the anoxic insult. Therapeutic hypothermia and antiepileptic drugs (levetiracetam, phenytoin, sodium thiopental, midazolam, lacosamid) were used. SSEP in the 3rd day were normal.

**Results:** 1 month post-anoxia, she shifted from vegetative to minimally conscious state. After 3 months she recovered consciousness completely. Brain MRI showed ischemic changes in basal ganglia, and mild brain atrophy. Seven months post-insult she displayed cognitive dysfunction in several domains, severe action myoclonus and myoclonic seizures. After 11 months she had mild cognitive deficits, action myoclonus and myoclonic seizures, treated with clonazepam, zonisamid, levetiracetam, valproic acid. Polygraphic recordings showed two patterns of myoclonic activities:

(1) massive jerks that occurred with a rostro-caudal muscular recruitment, isolated or in brief rhythmic (12–15 Hz) bursts, associated with EEG spikes, facilitated by voluntary movement.

(2) myoclonic bursts without EEG correlates, showing an activation pattern starting from sternocleidomastoideus and spreading upward to orbicularis oris, masseter and downward to deltoid, consistent with subcortical myoclonus. MEP showed prolonged central conduction time bilaterally, consistent with a central dysfunction of motor pathways.

**Conclusion:** Our patient with post-anoxic myoclonus showed a good outcome in spite of initially prolonged coma and refractory status epilepticus. We provide neurophysiological evidence that action myoclonus results from a mixture of cortical and subcortical myoclonia, associated with a central dysfunction of motor pathways.

p0835

### THE RELATION BETWEEN INTERICTAL EPILEPTIC SPIKES AND RIPPLES IN SURFACE EEG

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**Purpose:** Ripples (80–250 Hz) have been shown to be a more specific biomarker for the epileptogenic zone than epileptic spikes in intracranial EEG and even in surface EEG. Ripples often co-occur with spikes, but we do not know whether one evokes the other. We investigated the spatiotemporal relation between spikes and ripples, and the differences between spikes that do and do not co-occur with ripples.

**Method:** We marked 50 time points with spikes in bipolar surface EEG during NREM sleep in patients with focal or multifocal epilepsy. We marked ripples that occurred within 400 ms of these time points. We calculated several parameters relating spikes and ripples: the duration, amplitude and slope of spikes, the timing of the start of ripples compared to spikes and the proportion of overlap.

**Results:** In total 219 ripples and 5995 individual spikes were marked in 31 patients. Spikes with ripples were on average significantly shorter, had higher amplitude and higher slope than spikes without ripples, although there was no clear cut-off. 64% of ripples started before spikes started. The proportion of ripples before, during the first and second slopes and after spikes was on average 26%, 37%, 30% and 7%. Spikes occurred on a median of 13 (5–26) channels per patient, and ripples on 3 (0–14) channels, which were also spike channels.

**Conclusion:** Ripples precede rather than follow spikes, so ripples are unlikely to result from spikes. Ripples and spikes seem not one-on-one couples, but certain states of the brain can accommodate both.

p0836

### AUTOMATIC IDENTIFICATION OF THE EPILEPTOGENIC ZONE BASED ON HIGH FREQUENCY OSCILLATIONS IN MEG

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**Purpose:** High frequency oscillations (HFOs, >80 Hz) are a biomarker for the epileptogenic zone (EZ). Our final goal is to automatically localize the HFO region using magnetoencephalography (MEG).

**Method:** Fifteen minutes of resting state MEG data were selected in 12 patients. We increased the signal to noise ratio in MEG recordings by computing spatial filters using beamforming, and used this technique to reconstruct time series (virtual sensors, VS) for a priori defined brain regions. As a first step we placed VS around the epileptic spikes (affected region) and in the contralateral hemisphere. We manually marked HFOs and spikes in MEG in the time domain in these VS. The time points with HFOs in VS were reviewed in the physical sensors. The next step will be to use a detector to automatically identify HFOs for all brain regions (a task which is too time-consuming to do manually) and to generate a 3D map to reveal regions with HFOs.

**Results:** We identified 575 HFOs in VS, at 78 points in time, in eight patients. 513 HFOs were in the affected region. HFOs could not be visually identified in physical sensors for 61 of the 78 time points that showed HFOs in VS. These manually marked HFOs will be used to optimize an automatic detection algorithm.

**Conclusion:** Beamformer-based VS analysis can help to identify HFOs that are not discernable in physical MEG sensors. This step eases the automatic detection of the HFO region. These findings are a preliminary step towards our goal: to automatically localize the HFO region in patients with focal epilepsy using MEG. This map can be used to tailor epilepsy surgery.

## Comorbidities 4 Tuesday, 8th September 2015

p0837

### COMORBID DISEASES IN EPILEPSY PATIENTS

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**Purpose:** Epilepsy is a chronic disorder that may be associated with various comorbid diseases. In this study, we aimed to evaluate the comorbid diseases detected in our patients with epilepsy.

**Method:** We analyzed 365 patients who were followed up in the epilepsy department between 2011 and 2014 retrospectively. Besides demographic and clinical findings of the patients, neurological, psychiatric, systemic and other comorbid diseases were recorded.

**Results:** Mean age of total 365 patients was  $30.9 \pm 13.9$  (10–83) years and 182 (49.9%) were female, 183 (50.1%) were male. Age at seizure onset was between the 1st year of life and 80 years. Mental retardation was detected in 13.7% of the patients. The most common comorbidities were psychiatric diseases (21.1%), headache (11.2%), hypertension (4.7%), thyroid diseases (4.7%), anemia (4.1%), gastrointestinal problems (3%), coronary artery diseases (2.5%), cerebrovascular accidents (2.2%), diabetes mellitus (2.2%), hyperlipidemia (1.9%), asthma (1.6%), genito-urinary diseases (1.4%) and cancer (0.8%). Depression and anxiety disorders were the most common psychiatric comorbidities. Other psychiatric comorbidities consisted of psychosis, obsessive compulsive disease, agitation, behavioral problems, autism, panic and conversion disorders. Amongst headache comorbidity, migraine was more common than tension-type headache. Smoking in 63 (17.3%) and alcohol consumption in 14 (3.8%) patients were recorded. EEG revealed pathological patterns in 247 (67.7%) patients. MR/CT investigations were abnormal in 40.8% of the patients and the most common pathological finding was encephalomalacia.

**Conclusion:** Psychiatric, neurological and other systemic disorders may be together with epilepsy. Especially psychiatric comorbidities and epilepsy have a bidirectional relationship. Comorbid diseases may contribute to functional disability of epileptic patients and may complicate epilepsy treatment. The diagnosis and treatment of comorbid diseases is necessary for the improvement of life qualities of epilepsy patients.

#### p0838

### IMPROVED MATERNAL CARE OF FOSTER WISTAR MOTHER EARLY IN DEVELOPMENT REDUCES SEIZURE ACTIVITY, ANXIETY AND DEPRESSION-LIKE COMORBIDITY IN ADULT WAG/RIJ RATS WITH GENETIC PREDISPOSITION TO ABSENCE EPILEPSY

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**Purpose:** WAG/Rij rats are a valid genetic animal model of absence epilepsy with comorbid depression. Adult WAG/Rij rats at the age of 6–8 months exhibit depression-like behavioral symptoms and seizure activity characterized by spontaneous generalized spike-wave discharges (SWDs) in the EEG. We have recently found that WAG/Rij dams in addition to depression-like behavior display reduced maternal care in comparison with Wistar controls. We have hypothesized that impaired early rearing environment in WAG/Rij rats may contribute to the expression of seizure activity and depression-like comorbidity later in life. To test this hypothesis, a cross-fostering procedure has been used.

**Method:** Rat pups of “depressive” WAG/Rij and “normal” Wistar dams were cross-fostered on postnatal day 2. Control rats remained with their birth mother. EEG and behavior in the light-dark choice, open field, elevated plus-maze and forced swimming tests were assessed in the offspring of “depressive” WAG/Rij and “normal” Wistar rats reared by their own or foster mothers at the age of 7–8 months.

**Results:** WAG/Rij rats reared with improved maternal care of “normal” Wistar dam exhibited less seizure activity (a decreased SWDs number, duration and index), reduced depression-like behavior in the forced

swimming test and anxiety in the elevated plus-maze in comparison with age-matched WAG/Rij rats reared under abnormal maternal care of their own “depressive” dam. Adoption by WAG/Rij dam didn’t exert a significant effect on EEG and behavior in the forced swimming test in “normal” Wistar rats.

**Conclusion:** Results suggest that an epigenetic factor such as maternal care early in development reduces epileptogenesis and expression of depression-like comorbidity in the WAG/Rij rat model of genetic generalized absence epilepsy. We propose that the improvement of early caregiving environment can be used as disease-modifying treatment to prevent or ameliorate the process of epileptogenesis and behavioral comorbidities in people with genetic predisposition to absence epilepsy.

#### p0839

### SLEEP DISORDERS IN PATIENTS WITH EPILEPSY: A SYSTEMATIC REVIEW

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**Introduction:** Sleep and epilepsy interact on many levels. The prevalence of sleep disorders and their impact on epilepsy has been addressed by several studies with significant heterogeneity in observations. We appraised the evidence to assess the relationship between sleep and epilepsy.

**Methods:** We searched Embase and Medline databases for publications in English until December 2014, using MeSH headings and keywords related to “epilepsy,” “seizure,” and various sleep disorders. We included articles describing original data on adult patients with sleep disorders and epilepsy. Two reviewers independently reviewed abstracts and selected articles which fulfilled eligibility criteria. We analyzed data descriptively.

**Results:** From 2778 citations 19 articles were included. Nine studies were questionnaire based and six polysomnography (PSG) based. A total of 2070 patients (38% women, mean age 35.3 years) were included. Most studies investigated excessive daytime somnolence (EDS; n = 773 patients), insomnia (n = 218) and obstructive sleep apnea (OSA; n = 849) and reported increased prevalence (upto 38.6%) in patients with epilepsy (PWE). However, three studies found no significant difference in the occurrence of OSA in PWE and controls. Only three (n = 541) focused on epilepsy diagnosis. Overall, 62.5% patients had focal epilepsy. On PSG assessments, all sleep related parameters were worse in PWE, including sleep latency, sleep efficiency, total sleep time and EDS. In four studies (n = 153) looking at the impact of CPAP therapy on seizure control, more than 50% of patients improved in seizure control. One study concluded that subjective sleep complaints improved after epilepsy surgery.

**Conclusions:** There is increased prevalence of sleep disorders including EDS, insomnia, OSA and RLS in PWE as compared to normal controls, and treatment of OSA with CPAP therapy improves seizure outcomes. Successful epilepsy surgery may lead to improvement in subjective sleep parameters. No studies look at the relationship of the epilepsy syndrome or localization and the type of sleep disorder.

#### p0840

### LACK OF HEART RATE VARIABILITY (HRV) DURING APNEA IN DRUG NAÏVE PATIENTS WITH TEMPORAL LOBE EPILEPSY: A MARKER OF SUDEPUS?

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**Purpose:** There is lack of literature about heart rate variability (HRV) during apnea among patients with temporal lobe epilepsy (TLE). The

aim was to characterize the heart rate variability (HRV) during the peri-apneic period in TLE.

**Method:** Overnight-PSG on 10 patients of drug-naïve TLE (M:F = 6:4; age:  $22.8 \pm 4.1$  years) and 10 TLE on carbamazepine (CBZ) (M:F = 6:4; age:  $20.5 \pm 4.3$  years) were performed and compared with 10, age ( $p = 0.205$ ) and gender ( $p = 0.271$ ) matched healthy controls (M:F = 5:5; age:  $24.3 \pm 5.03$  years). EC approval and consent was obtained. The time/frequency domains and non-linear HRV indices were analyzed for two minutes before and after apnea/hypopnea termination and analyzed using paired t-test. Changes in HRV parameters in the peri-apnea/hypopnea period were compared among three groups using one-way ANOVA followed by post hoc comparison.

**Results:** Among controls, there was an increase in SD of RR interval (SDNN) ( $p = 0.010$ ), very low frequency (VLF) ( $p = 0.001$ ) and long term HRV (SD2) ( $p = 0.004$ ) parameters, along with a decrease in low frequency (LF) component ( $p = 0.011$ ) in the post-apneic period compared to the pre-apneic period. Conversely, in drug naïve TLE, all the HRV parameters, including nonlinear measures were comparable during the pre and post-apneic period. However, patients on CBZ showed a decrease in LF ( $p = 0.010$ ) and increase in high frequency component (HF) component ( $p = 0.001$ ) in the post-apneic period compared to the pre-apneic period. Finally, comparison of HRV changes in the peri-apnea/hypopnea period among healthy controls, drug naïve TLE and on CBZ TLE showed significant differences in SDNN ( $p = 0.021$ ), VLF ( $p = 0.002$ ), LF ( $p = 0.017$ ) and SD2 ( $p = 0.004$ ).

**Conclusion:** This study, first of its kind, showed a lack of apnea mediated HRV changes in patients with drug naïve TLE, suggesting possible alteration in reflex baroreceptor activation, and was partially reversible with carbamazepine.

#### p0841

### COMPARISON OF THE EFFECTIVENESS OF SERTRALINE, VINPOCETINE AND SEVERAL CONVENTIONAL ANTI-EPILEPTIC DRUGS TO INHIBIT THE EPILEPTIFORM EEG ACTIVITY INDUCED BY 4-AMINOPYRIDINE IN THE RAT

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**Background:** Depression is a major comorbidity in patients with epilepsy. Previously we found that the anti-depressive, sertraline (a novel non-FDA-approved agent for seizures), effectively inhibits presynaptic  $\text{Na}^+$  channels permeability, and thus, may have anti-seizure potential. Herein, we compared the epileptiform EEG activity induced by 4-aminopyridine (4-AP) for sertraline (0.75 & 2.5 mg/kg), vinpocetine (2.5 mg/kg), and several conventional antiepileptic drugs (AEDs): CBZ & TOP (25 mg/kg only), and PHT, LTG, OXC, (latter 3 at 2.5 & 25 mg/kg), VPA & LEV (100 mg/kg only).

**Methods:** 59 Wistar rats, avg wgt =  $315 \pm 3$  g were used. All animal experiments were carried out in compliance with the "Guidelines for Animal Experimentation" and had Institutional approval. The control group ( $n = 10$ ) and each of 9 drug/AED groups ( $n = 3-5$  rats), had 4-AP administered i.p. at a convulsive dose of 2.5 mg/kg. Following 4-AP, EEG cortical activity (highest peak amplitude value [EEG-hpav], in  $\mu\text{V}$ ) was monitored (Nihon-Kohden Neuropack IV Mini (MEB-5304 K) system)  $\times$  1 hour. EEG-hpav  $\mu\text{V}$  changes at 10, 20 & 30 minute post-baseline were analysed via ANOVA.

**Results:** Results show a marked increase in the EEG amplitude ( $\mu\text{V}$ ) near 20 minute following 4-AP, reaching maximum at 30 minute in all

rats. Sertraline and vinpocetine (2.5 mg/kg dose) statistically significantly prevented this epileptiform EEG activity induced by 4-AP ( $p < 0.05$ ). Likewise, PHT, LTG and OXC were ineffective at 2.5 mg/kg, but were effective at 25 mg/kg; CBZ was effective at 25mg/kg. TOP, LEV and VPA all failed to prevent the epileptiform EEG activity induced by 4-AP.

**Conclusions:** Sertraline and vinpocetine are effective and potent anti-seizure drugs in this model, perhaps due to their action on cerebral presynaptic ionic channels permeability. Secondly, 4-AP is a powerful experimental tool to investigate the anti-seizure mechanism of action of AEDs.

#### p0842

### ATHEROSCLEROSIS DISEASE RISK IN EPILEPSY PATIENTS

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**Purpose:** Chronic epilepsy has been linked with vascular atherosclerotic disease. Previous studies have correlated increased common carotid artery intima-media thickness (CCA-IMT), an index of carotid artery atherosclerosis, with chronic epilepsy and prolonged anti-epileptic drug (AED) usage. The aim of our study was to evaluate the association between increased CCA-IMT and the factors regarding epilepsy and its treatment.

**Method:** We included epilepsy inpatients and outpatients who attended the epilepsy clinic during an 1 year period. Inclusion criteria were a definite diagnosis of epilepsy of >1 year duration and AED treatment. We assessed demographic and clinical characteristics regarding epilepsy and vascular risk factors. Patients' CCA-IMT was measured using a B-mode ultrasound examination of both carotid arteries.

**Results:** We evaluated a total of 116 patients with epilepsy (mean age  $34 \pm 14$  years, 52% men, mean BMI  $26 \pm 4$   $\text{kg/m}^2$ ) treated with antiepileptic drugs (median number of drugs: 2, interquartile range: 1-3; median duration of antiepileptic treatment in years: 6, interquartile range 3-13). The mean CCA-IMT in the study population was  $0.61 \pm 0.18$  mm. Patients receiving more than two AEDs had higher CCA-IMT values than patients under single or dual antiepileptic treatment ( $0.69 \pm 0.22$  mm vs.  $0.59 \pm 0.22$  mm;  $p = 0.013$ ). Duration of antiepileptic treatment correlated positively with mean CCA-IMT (Pearson's correlation coefficient: 0.257;  $p = 0.007$ ). The use of >2 AEDs was independently associated with greater CCA-IMT values (standardized linear regression coefficient: 0.250; 95%CI: 0.012-0.182;  $p = 0.026$ ) in multiple linear regression models adjusting for demographic characteristics (age, sex, BMI) vascular risk factors (hypertension, diabetes mellitus, hypercholesterolemia, atrial fibrillation, coronary artery disease, hypercholesterolemia, current smoking) and duration of antiepileptic therapy.

**Conclusion:** Our study showed increased atherosclerotic disease risk in epilepsy patients on long-term treatment, in accordance with previous studies, and in patients taking more than two AEDs. These patients should be closely monitored and treated for vascular risk factors in order to prevent vascular disease progression.

#### p0843

### COMPARISON OF THE EFFECT OF VALPROATE AND LEVETIRACETAM MONOTHERAPY ON SUBJECTIVE AND OBJECTIVE SLEEP PARAMETERS IN PERSONS WITH EPILEPSY

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**Purpose:** Sleep disturbance and its consequences are a comorbidity in persons with epilepsy (PWE). Almost every antiepileptic drug (AED) impacts sleep. Valproate (VPA) and levetiracetam (LEV) are two common agents used in the treatment of generalised epilepsies. The aim of this study was to document prospectively changes in the subjective and objective aspects of sleep and its resultant effects in PWE receiving these two AEDs.

**Method:** 52 consecutive PWE on monotherapy with VPA and 58 PWE on LEV were included in this study conducted from 2012–2014. A minimum 12 months of seizure freedom was the entry criteria. Parameters documented were BMI, metabolic syndrome criteria (IDF), adverse event profile by LAEP, depression by PHQ-9, physical activity assessed by IPAQ, sleepiness by ESS, insomnia by ISI. Overnight PSG was done on the somnomedics system.

**Results:** Majority of the patients were women (69). Most had JME (94), age range was  $28 \pm 6$  years. Physical activity was significantly more impacted in those on VPA so did they have higher BMIs. Sleep architecture changes in REM and stage 3 were significant. Sleep efficiency was significantly reduced in the LEV versus VPA group ( $80.33 \pm 2.00$ , vs.  $91.98 \pm 3.12$  respectively;  $p < 0.01$ ), the number of times of that the patients awoke was increased in the LEV group ( $5.20 \pm 2.86$  vs.  $2.65 \pm 1.50$ ,  $p < 0.01$ ). Patients on treatment for more than 1 year had in the VPA group an AHI of  $19 \pm 15$  versus LEV group who had a AHI of  $7 \pm 2$  this was significant. Those on VPA higher than 800 mg were more likely to have higher AHIs.

**Conclusion:** VPA results in significantly more PWE having snoring, OSA, hypersomnia, increased BMI, impaired daytime performance. PWE on LEV were significantly more likely to have insomnia and its consequences. Informed choice of the possibility of these comorbidities must be discussed before prescribing these AEDs.

p0845

#### FACTORS ASSOCIATED WITH HOSPITAL ADMISSION AND INJURY IN PEOPLE WITH EPILEPSY

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**Purpose:** People with epilepsy (PWE) have an increased risk of accidents and injuries. The cause of injuries have been studied before but the results are diverse. There is a high frequency of hospital admission due to various factors. It is important to determine the cause of injuries and hospital admissions since preventing them may increase the quality of life in PWE, and reduce costs.

**Method:** Consecutive follow up patients over a 10 month period attending a London epilepsy clinic were included. All patients completed a self filling questionnaire including questions about injury and/or hospital admissions that had occurred since their last appointment, Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) and adverse event profile (AEP). Other information including about seizures and treatment were obtained from clinical records. Multivariate analyses of the potential predictors of injury or hospital admission were performed

separately. Descriptives and multivariate regression analysis were performed using SPSS for Windows 17.0.

**Results:** 448 participants with confirmed diagnosis of epilepsy were included. Patients with missing data ( $n = 36$ ) were excluded. Among the remaining 407 patients (243 female) mean age was 43.09 years (SD: 15.75 year). NDDIE-total (OR: 1.085; 95%CI: 1.032–1.140,  $p = 0.001$ ) and presence of seizures (OR: 6.777; 95%CI: 2.641–17.389,  $p = 0.000$ ) were independently associated with injury in multivariate model. Injury (OR: 2.134; 95%CI: 1.194–3.814,  $p = 0.011$ ) and presence of seizure (OR: 2.495; 95%CI: 1.301–4.787,  $p = 0.006$ ) were independently associated with hospital admission in multivariate model.

**Conclusion:** Presence of seizures is an important determinant for risk of injuries and hospital admissions of PWE. Unexpectedly, a significant association between depression and injuries was also identified. Although a frequent comorbidity in PwE, and strongly associated with QoL, depression is often missed. Individuals presenting with injuries should be a trigger for mood screening, and treatment where appropriate. Further prospective studies are needed to ascertain whether depression maybe a determinant for injury or a consequence.

## Drug Therapy 8 Tuesday, 8th September 2015

p0846

#### THE ROLE OF LACOSAMIDE AS ADJUNCTIVE THERAPY FOR PARTIAL-ONSET SEIZURES

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**Purpose:** Lacosamide (LCM) is a newly registered antiepileptic drug with dual mechanisms of action. It has been found effective on uncontrolled partial epilepsy for reducing seizure frequency as add-on therapy. We aimed to investigate retrospective data of our patients on LCM.

**Method:** We performed a retrospective medical record review of 63 patients with uncontrolled partial epilepsy who received LCM as add-on therapy for at least 6 months. Data included demographics, LCM dosing, concomitant AED therapy and seizure activity.

**Results:** 32 patients were female and 31 patients were male. The mean age of patients were 33,7611,17 years. The mean onset of seizures were 16,2610,72 years. The median of seizure frequency in a month was 5 (1–300). The median number of AED before LCM was 3 (1–5). The median dose of LCM was 200 mg/day (50–400 mg/day). The mean duration of onset of LCM was 9.85 (6–39) months. 61.9% of patients had decreased seizure frequency in 1st month but in 6 months or after 6 months 54% of patients had decreased seizure frequency. The mean percent reduction in seizure frequency was  $35.82 \pm 36.23\%$  in 1st month and  $31.25 \pm 35.90\%$  in 6 or after 6 months. Three patients had gastroenterological side effects, two patients had diplopia, two patients suffered from blurred vision and two patients had itchy skin. In three patients LCM treatment was stopped (one patient had side effect and LCM was ineffective in two).

**Conclusion:** In literature median percent reduction in seizure frequency was 18.4% for placebo, 33.3% for LCM 200 mg/day, and 36.8% for LCM 400 mg/day. These results are consistent with our results. But we found that the reduction in seizure frequency decreased in some patients after 1 month. Prospective, randomized, placebo controlled, multicenter studies which include more patients are necessary to investigate the role of LCM on add-on therapy in patients with partial seizures.

p0849

**EFFECT OF ESLICARBAZEPINE ACETATE ON SERUM LIPID PROFILE**

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**Purpose:** The increase in cholesterol level is a well-known side-effect of enzyme inducers antiepileptic drugs (EIAEDs) such as carbamazepine (CBZ). Our objective was to analyze if ESL, a milder inducer agent, modifies or not serum lipid profile.

**Method:** Serum lipid profile (total cholesterol, HDL-C, LDL-C and triglycerides) before and 6 months after the beginning of ESL treatment were compared.

**Results:** 45 patients (28 women) were included. Age ranged from 16 to 82 years (mean: 52.82 years). In 14 patients (31.11%) ESL was added to baseline AED medication; in 27 (60%) one AED was switched to ESL (12 of them stayed in monotherapy with ESL when the other AED was withdrawn); in 4 (8.93%) ESL was started as monotherapy. The mean number of concomitant AED was 0.84 per patient. Dose of ESL ranged from 400 to 1200 mg/day (mean 897.78 mg/day). In the total group, serum lipid parameters did not change significantly after the introduction of ESL. Only two patients with basal total cholesterol levels under 220 mg/dL experienced an increase of this value over 220 mg/dL at the end of the follow-up. None of them were concomitantly being treated with EIADs. Patients switched from CBZ to ESL (n = 8) experienced a significant decrease of cholesterol levels. No significant change was observed when oxcarbazepine was switched to ESL. Five patients were under statin treatment at the beginning of the study. No change in their serum lipid profile with the addition of ESL was observed

**Conclusion:** ESL does not seem to modify serum lipid profile. When CBZ is switched to ESL, a decrease in the cholesterol levels can be observed.

p0850

**EFFICACY AND SAFETY OF OXCARBAZEPINE ORAL SUSPENSION IN PEDIATRIC PATIENTS AGED 2–5 YEARS WITH PARTIAL SEIZURES AND/OR GENERALIZED TONIC-CLONIC SEIZURES IN ROUTINE CLINICAL PRACTICE IN CHINA**

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**Purpose:** The efficacy of Oxcarbazepine (OXC) for seizure control has been confirmed by many international studies. However, there are few reports about treatment with its oral suspension, of young pediatric patients in real-world clinical practice, especially in China. Our study aimed to assess efficacy and safety of OXC oral suspension in pediatric patients aged 2–5 years with partial seizures (PS) and/or generalized tonic-clonic seizures (GTCS) in real-world clinical practice in China.

**Method:** This 26 week, single arm, multicenter, observational study recruited pediatric patients aged 2–5 years. OXC oral suspension was administered as per physicians' discretion. Study parameters were captured at baseline and four follow up visits conducted at 4, 8, 13 and 26 weeks. The efficacy endpoints were to assess the change in frequency of seizures at the end of study compared to baseline. Safety endpoints mainly included incidence of adverse events (AEs) and severe adverse events (SAEs). Dosing strategy in clinical practice was also recorded.

**Results:** A total of 606 pediatric patients were enrolled and majority of the subjects (531; 87.6%) completed the study. After 26 weeks of treatment, 93.3% subjects had achieved reduction in seizure frequency  $\geq 50\%$ , and 81.8% had achieved complete seizure control compared to baseline. Among different seizure types, OXC was found to be effective in all subjects with simple PS type. Mean initial dose was 192.6 mg/day and mean maintenance dose was 454.8 mg/day. AEs were observed in 49 (8.1%) subjects. Only two cases namely rash and hypersensitivity were severe. Skin and subcutaneous tissue disorders were the most frequently reported AEs and had 19 (3.14%) occurrences. Only 17 subjects discontinued due to AEs.

**Conclusion:** This study, reporting the real-world data, further confirms the efficacy and good safety profile of OXC oral suspension in Chinese pediatric patients aged 2–5 years with PS and/or GTCS.

p0851

**EFFICACY AND SAFETY OF ADJUNCTIVE BRIVARACETAM FOR PARTIAL-ONSET (FOCAL) SEIZURES: POOLED RESULTS FROM THREE FIXED-DOSE, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE III STUDIES**

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**Purpose:** To assess the efficacy and safety of adjunctive brivaracetam (BRV), a selective, high-affinity SV2A ligand, for the treatment of partial-onset (focal) seizures (POS).

**Method:** Data were pooled from three studies (NCT00490035, NCT00464269, NCT01261325) of adult patients with POS uncontrolled by 1–2 antiepileptic drugs (AEDs) receiving BRV 5, 20, 50, 100, or 200 mg/day or placebo. Efficacy population: patients from primary efficacy analyses, not receiving concomitant levetiracetam. Safety population: patients taking  $\geq 1$  dose study drug, with/without levetiracetam. This analysis reports data for the proposed dose range 50–200 mg/day, for which approval is being sought.

**Results:** Patients (efficacy population; n = 1,160) were 50.6% female; 72.5% white; 24.3%, 38.3% and 37.4% took 0–1, 2–4 and  $\geq 5$  previous AEDs, respectively. Most common concomitant AEDs: carbamazepine (41.0%), lamotrigine (25.5%) and valproate (22.9%). Baseline median (IQR) POS frequency/28 days was 8.9 (5.5–17.3), 50 mg/day; 8.9 (5.5–

20.6), 100 mg/day; 9.3 (5.5–18.8), 200 mg/day and 9.6 (5.5–24.3), placebo. Across the groups, 90.1%–94.7% completed the studies. Percent reduction over placebo (95% CI) in baseline-adjusted POS frequency/28 days was 19.5% (8.0%, 29.6%), 50 mg/day (n = 161); 24.4% (16.8%, 31.2%), 100 mg/day (n = 332); 24.0% (15.3%, 31.8%), 200 mg/day (n = 249). The  $\geq 50\%$  responder rate was 34.2% (50 mg/day), 39.5% (100 mg/day), 37.8% (200 mg/day) versus 20.3% (placebo). Median percent reduction in POS frequency from baseline was 34.7% (50 mg/day), 37.6% (100 mg/day), 35.6% (200 mg/day) versus 17.2% (placebo). In the safety population (n = 1,262), 68.0% (BRV, n = 803), 62.1% (placebo, n = 459) reported treatment-emergent adverse events (TEAEs). Serious TEAEs were reported by 3.0% (BRV), 2.8% (placebo); three patients on BRV and one on placebo died. TEAEs reported in  $\geq 5\%$  patients taking BRV were somnolence (15.2% vs. 8.5%), dizziness (11.2% vs. 7.2%), headache (9.6% vs. 10.2%) and fatigue (8.7% vs. 3.7%) for BRV versus placebo, respectively.

**Conclusion:** In a pooled analysis of adults with POS, adjunctive BRV (50–200 mg/day) was effective and generally well-tolerated. UCB-supported.

### p0852

#### QUANTITATIVE ANALYSIS CONFIRMS THE POTENTIAL OF THE PHOTOSENSITIVITY MODEL TO PREDICT THE CLINICALLY EFFICACIOUS AED DOSE

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**Purpose:** The Photosensitivity Model (testing suppression of Photo-Paroxysmal EEG Response [PPR]) is a useful tool to *qualitatively* predict newly developed anti-epileptic drug (AED) efficacy as proof-of-concept (PoC) (Kasteleijn-Nolst Trenité DGA, *Epilepsy Res* 1996; Schmidt B. *Neurotherapeutics* 2007). Some researchers (Yuen, *Seizure* 2014) have retrospectively attempted to *quantitatively* compare the doses used in AED PoC photosensitivity trials with the eventual AED doses used in clinical epilepsy. The average ratio of AED minimum effective dose (MED) to clinically effective dose (ED<sub>50-100</sub>) was 0.95 (95% CI = 0.6–1.30). Herein, we substantially expand on those initial observations, by quantitative analysis of PoC AED rank-potency versus rank-dose for epilepsy.

**Method:** Our retrospective analysis preliminarily includes #10 AEDs in #10 publications. Dose ranges for efficacy in the treatment of epilepsy and for suppression of EEG in the photo-sensitivity paradigm were obtained from literature. Dose-ranges were then ranked by the mean of the range (If tied, the ranks involved were averaged). Spearman's rank correlation coefficient was calculated from a conventional formula (Myers JL 2003).

**Research design & statistical analysis:** [2<sup>nd</sup> edition]. Lawrence Erlbaum, Editor. pg 508). Separate analyses were performed for those AEDs studied in Phase 2/3, in double-blind trials, and for all data combined.

**Results:** We identified the AED dose used in every PoC trial, ranked it, and compared it with the mg dose used clinically (by rank) for all data combined; the Spearman rank correlation coefficient (SRCC) = 0.9634; 2-tailed *p* value <0.01. Similar SRCC values were seen for ranked data from double-blind trials or Phase 2 trials.

**Conclusion:** The AED dose utilized in the human Photosensitivity Model accurately and very strongly predicts the AED dose eventually used in clinical epilepsy. We confirm Yuen's quantitative analysis of the utility of the photosensitivity model to aid dose selection for newly-developed AEDs in early AED development.

### p0854

#### ANTICONVULSANT EFFECT OF NEURAL REGENERATION PEPTIDE 2945 ON THE PRODUCTION OF DARK NEURON IN THE THE HIPPOCAMPUS OF PENTYLENETETRAZOL-INDUCED MODEL

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**Purpose:** Neuron regeneration peptides (NRPs) are small synthetic peptides that stimulate neural proliferation, migration, and differentiation with no apparent toxicity and high target specificity in CNS. The aim of this study was to investigate the effect of NRP2945 on seizure activity induced by pentylenetetrazol (PTZ) in rats.

**Method:** Using behavioural assessment and electrocorticographical recordings, the effects of different doses of NRP2945 (5–20 µg/kg) were tested on seizure attacks induced by PTZ injection. In addition, the effect of NRP2945 was evaluated on the production of dark neurons in the hippocampus of the rat brain.

**Results:** Intraperitoneal injection of NRP2945 at 20 µg/kg prevented seizure attacks after PTZ injection. NRP2945 at doses of 5 and 10 µg/kg significantly decreased the total duration of seizure attacks and reduced the amplitude, duration and latency of epileptiform burst discharges induced by PTZ. In addition, the peptide significantly inhibited the production of dark neurons in the hippocampus of epileptic rats.

**Conclusion:** This study indicates that NRP2945 is able to prevent the seizure attacks and neuronal injuries induced by PTZ.

## Drug Therapy 9 Tuesday, 8th September 2015

### p0856

#### PRESCRIBING AEDS IN A PEDIATRIC NEUROLOGY CLINIC IN MALTA

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**Purpose:** The selection of appropriate antiepileptic drugs (AEDs) in paediatric populations depends on seizure type, available drugs, possible drug interactions, and susceptibility to drug toxicity. This study aimed to investigate the prescribing patterns of AEDs in a population of children presenting to a paediatric epilepsy clinic.

**Method:** Clinical records were reviewed retrospectively from the 31st December 2013 to the date of first presentation of each patient to hospital services for the management of epilepsy.

**Results:** Following the application of inclusion and exclusion criteria, the final study population comprised 76 children, ages 0–16 years, 32

girls and 44 boys, whose mean age at diagnosis was of 4.54 years and whose main duration of the epilepsy had been of 8.7 years. The most common type of epilepsy was generalised tonic clonic seizures only (28.95%), childhood absence epilepsy (19.74%) and BECTS (14.47%). Valproate was the most commonly prescribed AED overall (40.8%). Lamotrigine was the most commonly prescribed newer AED (19.7%). The use of older AEDs exceeded that of newer ones, suggesting clinician confidence with working with time-tested drugs. The most commonly prescribed AED combination was valproate with lamotrigine. 48.7% of children were receiving AEDs as monotherapy, similar to studies from other countries. Around a third of the children (35.5%) were off AED therapy on the 31st December 2013 since they were in seizure remission. In 55.3% of cases the first AED started at diagnosis remained unchanged. AED selection was not affected by gender or comorbidity.

**Conclusion:** This study identified prescribing trends in a cohort of children with epilepsy in Malta. Results regarding demographic findings and selection of drug therapy are comparable to findings from studies from other countries. This study may serve as a basis for further pharmacoepidemiological and pharmaco-economic studies which could guide local drug-related policy.

p0857

#### BRIVARACETAM AND TOPIRAMATE INTERACTION STUDY IN HEALTHY SUBJECTS

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**Purpose:** Brivaracetam is a high-affinity synaptic vesicle protein 2A ligand that is under review as adjunctive treatment for adults with partial-onset (focal) epilepsy. The objective of this study was to investigate the effects of steady-state brivaracetam concentration on topiramate pharmacokinetics in healthy subjects.

**Method:** This was a phase I, single-centre, open-label study. All participants received brivaracetam 200 mg twice daily on Days 5–17 and single-dose topiramate 200 mg on Days 1 and 14. Trough plasma brivaracetam was measured on Days 7, 10, 13, 14 and 16; plasma topiramate was measured pre-dose and up to 96 hours post-dose on Days 1 and 14. Geometric least squares means ratios (Day 14:Day 1) and 90% confidence intervals (CIs) were derived from analysis of variance for topiramate maximum plasma concentration ( $C_{max}$ ), area under the plasma concentration versus time curve to last measurable concentration (AUCt) and extrapolated to infinity (AUCinf). Time to  $C_{max}$  ( $t_{max}$ ) was analysed using Wilcoxon's signed ranks test. Safety assessments included adverse events, physical examinations, laboratory tests, vital signs and electrocardiograms.

**Results:** All 14 participants [male:female 6:8, mean (SD) age 33 (8) years, body weight (SD) 70 (9) kg] completed the study. Topiramate plasma concentration versus time profiles were similar on Days 1 and 14. Geometric means ratios (90% CI) of topiramate with brivaracetam versus without brivaracetam were 0.98 (0.93, 1.03) for  $C_{max}$ , 0.95 (0.89, 1.01) for AUCt, and 0.94 (0.88, 0.99) for AUCinf. All CIs were within the acceptance range (0.80, 1.25). Median topiramate  $t_{max}$  was 3 hours with and without brivaracetam; median difference [Day 14–Day 1] (90% CI) was  $-0.5$  ( $-3.5$ ,  $0.2$ ). Brivaracetam was well tolerated.

**Conclusion:** Brivaracetam 200 mg twice daily did not significantly alter topiramate pharmacokinetics. UCB supported.

p0858

#### BRIVARACETAM AND LAMOTRIGINE INTERACTION STUDY IN HEALTHY SUBJECTS

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**Purpose:** Brivaracetam is a selective, high-affinity synaptic vesicle protein 2A ligand that is under FDA and EMA review as adjunctive treatment for adults with partial-onset (focal) epilepsy. The objective of this study was to investigate the effects of steady-state brivaracetam on lamotrigine pharmacokinetics in healthy subjects.

**Method:** This was a Phase I, single-centre, open-label study. All participants received brivaracetam 200 mg twice daily on Days 5–17 and single-dose lamotrigine 25 mg on Days 1 and 14. Trough plasma brivaracetam was measured on Days 7, 10, 13, 14 and 16; plasma lamotrigine was measured pre-dose and up to 96 hours post-dose on Days 1 and 14. Geometric least squares means ratios (Day 14:Day 1) and 90% confidence intervals (CIs) were derived from analysis of variance for lamotrigine maximum plasma concentration ( $C_{max}$ ), area under the plasma concentration versus time curve to last measurable concentration (AUCt) and extrapolated to infinity (AUCinf). Time to  $C_{max}$  ( $t_{max}$ ) was analysed using Wilcoxon's signed ranks test. Safety assessments included adverse events, physical examinations, laboratory tests, vital signs and electrocardiograms.

**Results:** Fourteen male participants [mean (SD) age 26 (5) years, body weight (SD) 73 (8) kg] completed the study; 13 were evaluable for pharmacokinetic assessments. Lamotrigine plasma concentrations appeared to be slightly higher when co-administered with brivaracetam. Geometric means ratios (90% CI) of lamotrigine with brivaracetam versus without brivaracetam were 1.10 (1.03, 1.17) for  $C_{max}$  and 1.17 (1.09, 1.25) for AUCt. Both CIs were within the acceptance range (0.80, 1.25). AUCinf could not be accurately estimated for some participants as the extrapolated part exceeded 20%. Median lamotrigine  $t_{max}$  was 3 hours with and without brivaracetam; median difference [Day 14–Day 1] (90% CI) was  $-0.5$  ( $-1.75$ ,  $0.75$ ). Brivaracetam was well tolerated.

**Conclusion:** Brivaracetam 200 mg twice daily did not significantly alter lamotrigine pharmacokinetics. UCB supported.

p0859

#### BRIVARACETAM AND CARBAMAZEPINE INTERACTION STUDY IN ADULT PATIENTS WITH EPILEPSY

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**Purpose:** Brivaracetam is a selective, high-affinity synaptic vesicle protein 2A ligand that is under review as adjunctive treatment for adults with partial-onset (focal) epilepsy. The objective of this investigation was to assess the effects of steady-state brivaracetam on the pharmacokinetics of carbamazepine (CBZ) in patients with epilepsy, in the presence and absence of the epoxide hydrolase inhibitor valproate (VPA).

**Method:** In this Phase I, open-label, dose escalation study, brivaracetam was administered during successive 1-week periods at dosages of 50, 100, 200 and 400 mg twice daily (bid) to adult patients with epilepsy chronically treated with  $\geq 600$  mg/day CBZ alone ( $n = 9$ ) or  $\geq 600$  mg/day CBZ and  $\geq 500$  mg/day VPA ( $n = 9$ ). Dosages of CBZ and VPA must have been stable for at least 3 months. Trough plasma concentrations of brivaracetam, CBZ, CBZ metabolites (CBZ-E, CBZ-diol) and VPA were determined on Days 1, 8, 15, 22 and 29. Safety assessments included adverse events, laboratory tests, vital signs and electrocardiograms.

**Results:** Thirteen male and five female patients with median (range) age of 46 (20–62) years and body weight of 74 (59–124) kg were enrolled and completed the study. In the presence of CBZ alone, brivaracetam dose-dependently increased mean trough levels of CBZ-E from 1.38  $\mu\text{g/mL}$  at baseline to 2.16  $\mu\text{g/mL}$  (+57%), 2.72  $\mu\text{g/mL}$  (+98%), 3.02  $\mu\text{g/mL}$  (+120%) and 2.67  $\mu\text{g/mL}$  (+94%) on Day 8 (50 mg bid), Day 15 (100 mg bid), Day 22 (200 mg bid) and Day 29 (400 mg bid), respectively. In the presence of CBZ and VPA, CBZ-E increased from 1.98  $\mu\text{g/mL}$  at baseline to 2.72  $\mu\text{g/mL}$  (+37%),

3.53 µg/mL (+78%), 4.43 µg/mL (+124%) and 3.22 µg/mL (+63%), respectively. There was no trend for changes in CBZ, CBZ-diol or VPA levels. Brivaracetam levels increased linearly with dose. Brivaracetam was well tolerated.

**Conclusion:** These findings are consistent with a dose-dependent and reversible inhibition of microsomal epoxide hydrolase by brivaracetam. The effect was similar in presence of valproate. UCB supported.

#### p0860

### RUFINAMIDE AS ADJUNCTIVE TREATMENT FOR ADULTS WITH LENNOX-GASTAUT SYNDROME: SUBGROUP ANALYSIS FROM A PHASE III TRIAL

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**Purpose:** Rufinamide is a triazole derivative, structurally unrelated to other antiepileptic drugs, approved for adjunctive treatment of seizures associated with Lennox-Gastaut syndrome (LGS) in patients aged  $\geq 4$  years. LGS often persists into adulthood, or may have late onset in adulthood. Management of LGS in adulthood is challenging; seizures are often intractable and most patients have from moderate to severe cognitive impairment. A post-hoc subgroup analysis of data from a Phase III trial was conducted to investigate efficacy of rufinamide in adults with LGS.

**Method:** A randomised, double-blind, placebo-controlled trial was conducted in patients with LGS, aged 4–37 years, with multiple seizures types (including drop-attack seizures and atypical absence seizures) and a minimum of 90 seizures during a 28-day baseline period. During a 14-day titration phase plus 70-day maintenance period, patients received double-blind treatment with either rufinamide (titrated to approximately 45 mg/kg/day maximum) or placebo. In a post-hoc subgroup analysis, efficacy in adult patients ( $\geq 18$  years) was assessed as median percentage change from baseline in monthly frequency of all seizures and drop-attack seizures during double-blind treatment.

**Results:** Adults with LGS were randomised to adjunctive treatment with rufinamide ( $n = 21$ ; 15 male, 6 female) or placebo ( $n = 10$ ; 5 male, 5 female). Mean (standard deviation [SD]; range) age was 25.2 (4.7; 18–35) and 29.3 (7.1; 18–37) years in the rufinamide and placebo groups, respectively; mean (SD; range) time since LGS diagnosis was 18.5 (8.9; 0–33) and 25.5 (8.1; 8–34) years. Median change from baseline in seizure frequency was  $-31.5\%$  for rufinamide versus  $+22.1\%$  for placebo ( $p = 0.008$ , Wilcoxon Rank Sum test, unadjusted) for all seizures and  $-54.9\%$  versus  $+21.7\%$  ( $p = 0.002$ ) for drop-attack seizures.

**Conclusion:** Rufinamide demonstrated favourable efficacy, compared with placebo, when used as adjunctive treatment for adults with LGS. Study and abstract supported by Eisai.

#### p0864

### PERAMPANEL IN FOCAL EPILEPSY: A FRENCH COHORT

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**Purpose:** Perampanel (PER) was introduced in France in May, 2014 as add-on in drug-resistant focal epilepsy (DRFE). All patients newly treated with PER have been prospectively added to an ad hoc database in two

tertiary epilepsy clinics (Montpellier and Marseille), in order to assess efficacy (with at least 3 months of follow-up) and tolerability of PER in a practical setting.

**Method:** Patients were reviewed at 3 month intervals and were encouraged to manifest at shorter intervals in case of problems. We recorded all personal and epilepsy data, and actively looked for side-effects and all parameters of clinical efficacy at each contact.

**Results:** As of February 25, 2015, we have treated 218 DRFE patients with PER (101 M, 117 F, mean age 42.5 years, range 11–83; mean duration of epilepsy: 26.6 years, range 1–67). All had DRFE (symptomatic: 137, cryptogenic: 81) with a least one seizure per month (up to several per day) and were receiving a mean of 3.1 drugs (range 1–6). 24 patients stopped PER within 2 months because of at least one intolerable side-effect: seizure aggravation 9, psychiatric side-effects 6, dizziness/ataxia 3, fatigue/somnolence 2, headache 2, skin rash 2, abdominal pain 2; 110 were evaluated after at least 3 months: 21 (19.1%) were seizure-free, 14 (12.7%) had  $\geq 90\%$  seizure reduction,  $10 \geq 75\%$  (9.1%),  $28 \geq 50\%$  (25.5%), and 39 (35.5%) no worthwhile improvement; 8 patients stopped PER after 3 to 6 months due to side-effects (7 with seizure aggravation); 8 patients reported (independently of seizure control) a noticeable feeling of well-being, which may point to a positive side-effect.

**Conclusion:** Although the follow-up is still short at this time, a large cohort has enabled us to use PER with a major benefit for 40% of patients with DRFE, an outstanding result in our experience.

#### p0865

### DO ANTIPILEPTIC DRUGS AFFECT LIPID PROFILE?

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**Purpose:** Several studies have reported that commonly used antiepileptic drugs such as phenytoin, phenobarbital and carbamazepine increase low density lipoprotein-cholesterol profile, but others couldn't find any relationship between antiepileptic drug usage and hyperlipidemia. The present study was planned to assess and compare serum lipid profile of epileptic patients on antiepileptic drugs.

**Method:** 830 patients with epilepsy who admitted to the hospital of BEU, Faculty of Medicine for the last 8 years were screened retrospectively. Patients with stroke, chronic renal/hepatic failure, hypo- or hyperthyroidism, diabetes mellitus and patients on medication which were known to change the lipid profile were excluded. So 205 patients with epilepsy who were taking the same antiepileptic drug(s) for at least 3 months were taken into account. Lipid profile (total, HDL-, LDL-cholesterol, triglyceride, apolipoprotein B/apolipoprotein A) on the last visit were extracted from chart reviews. Age and sex matched 31 healthy volunteers were taken as the control group.

**Results:** 126 patients out of 205 were on monotherapy (on phenytoin = 16, carbamazepine = 40, oxcarbazepine = 17, valproic acid = 22, levetiracetam = 25, others = 6). Lipid profile wasn't statistically significant different between the patient and control groups. Furthermore there wasn't any difference between patients on monotherapy and polytherapy as for the lipid profile.

**Conclusion:** Although it is suggested that antiepileptics, especially CYP enzyme inducers is strongly associated with increased levels of cholesterol, our study didnot confirm this. It could be due to our strict exclusion criteria, which allowed us to study the solitary effect of antiepileptic drugs on lipid profile. Because of our subgroups being small, other studies with larger groups are needed.

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p0866

### UNEXPLAINED LAMOTRIGINE TOXICITY- EVIDENCE OF NONLINEAR KINETICS IN SELECT INDIVIDUALS

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**Purpose:** To report acute lamotrigine (LTG) toxicity after minor or no change in LTG dose.

**Method:** We searched our database for patients with LTG levels of  $\geq 25$  mcg/mL and analyzed medication changes that preceded the elevated serum concentration. We also reviewed clinical correlates of elevated LTG level.

**Results:** 40 patients had a serum LTG concentration measurement of  $\geq 25$  mcg/mL (range 25–40.3). The previous measured concentration was above 15 mcg/mL in 25 of the patients (mean 16.5), and there was a relative mean increase of 150%. In 29 patients, the increase in LTG concentration was not preceded by any change in dose and had no explanation. In two patients, the increase was related to addition of valproate, despite some concomitant reduction in LTG dose. In the remaining nine patients, there was a 164% mean increase in LTG concentration in response to a 12% mean increase in dose. Clinical manifestations of toxicity were seen in 29 patients and included tremor, light-headedness, vertigo, ataxia, lethargy, confusion, agitation, delirium, nausea and vomiting. 11 patients had no clinical toxicity.

**Conclusion:** LTG may follow nonlinear kinetics at elevated concentrations in select individuals, and a large increase in concentration may be seen with a small change or even no change in dose. Close monitoring of LTG serum concentration is warranted for symptoms consistent with LTG toxicity, particularly when the baseline serum concentration has been above 15 mcg/mL.

p0867

### VALPROIC ACID-INDUCED HYPERAMMONEMIC ENCEPHALOPATHY IN A PATIENT WITH CONCOMITANT USE OF LEVETIRACETAM AND ZONISAMIDE

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Hyperammonemic encephalopathy is a rare but potentially fatal complication of valproic acid (VA) treatment. The mechanism by which VA induces hyperammonemia remains incompletely understood but is likely to relate to deficiencies in the uric acid cycle. Frequently encountered symptoms of VA-induced hyperammonemia are lethargy, impaired consciousness, focal neurological signs, increased number of seizures and rarely coma. A mentally and motor retarded 44-year old female with a history of generalized tonic clonic seizures since 4 years old was admitted for altered state of consciousness and an increased number of seizures for 5 days. The patient has been on levetiracetam (1000 mg/day) carbamazepine (400 mg/day) and zonisamide (300 mg/day) treatments for more than a year. Carbamazepine treatment has been gradually tapered and changed to valproic acid (250 mg/day) a week ago in a local hospital. On admission, she was unresponsive with reactive pupils and normal vital signs. Routine blood chemistry including hepatic functions, urine analysis and computed tomography were normal. Electroencephalography was consistent with moderate to severe encephalopathy. VA was therapeutic at 80  $\mu\text{g/dL}$ ; (50–100  $\mu\text{g/dL}$ ) whereas serum ammonia level was elevated at 130  $\mu\text{g/dL}$  (20–50  $\mu\text{g/dL}$ ). VA was immediately discon-

tinued and the patient was admitted to the intensive care unit where she recovered completely. Concomitant use of levetiracetam and/or zonisamide might have promoted hyperammonemic encephalopathy. Any suspected patient even if receiving very low doses of VA with normal liver functions, should be sought rigorously.

p0868

### ZONISAMIDE TREATMENT FOR REFRACTORY IDIOPATHIC GENERALIZED EPILEPSY: PRELIMINARY RESULTS OF AN OBSERVATIONAL STUDY

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**Purpose:** The efficacy of zonisamide (ZNS) for the treatment of patients with refractory idiopathic generalized epilepsy (IGE) was analyzed retrospectively.

**Method:** Fourteen patients with different types of IGEs with at least two generalized tonic clonic seizures per month were regarded as patients with refractory IGE. Patients who were treated with ZNS were identified. Efficacy was assessed at 3 month intervals after ZNS treatment. Response was defined as a 50% or greater reduction in seizure frequency according to the patient and caregiver reports.

**Results:** Mean age was 25.5 years. Mean daily dose was 228.6 mg (range 100–300 mg/day). Mean follow-up period was 9.8 months (range: 2–19 months). ZNS was effective for all patients except one patient, who discontinued ZNS due to a major depressive disorder. Response was achieved in 11 (78.6%) patients whereas 9 patients (64.3%) were seizure free. Retention rate was found as 92.9%.

**Conclusion:** Despite limitations, including the small sample size of patient population and the short follow-up period, according to the results of this observational study, ZNS might be regarded as a promising anti-epileptic drug for patients with refractory IGE.

p0869

### LACOSAMIDE AS ADJUNCTIVE THERAPY IN ADULT PATIENTS WITH RESISTANT PARTIAL EPILEPSY

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**Purpose:** Lacosamide (LCM) is a novel antiepileptic drug (AED). Its efficacy as adjunctive therapy for focal seizures is confirmed in adult placebo controlled trials with >50% reduction in seizure frequency in up to 50% patients. We aimed to investigate efficacy and tolerance of LCM as adjunct therapy in treatment of adult patients with resistant partial epilepsy (RPE).

**Method:** The study was performed between May 2013 and January 2015. In the current study, 17 with RPE (age 22–51 years) who had failed two or more antiepileptic drugs and in whom LCM was used as an add-on drug was enrolled. LCM was given a dose of 50 mg for 1 week followed by 100 mg twice daily for the remaining period. Total dose of LCM as 150 mg was given to twice daily up two patients. Efficacy and tolerability evaluation was performed monthly three times at beginning and follow-up visits at three monthly intervals. Electrocardiogram and liver function tests were also performed before enrollment and at the end of 3 months of LCM therapy.

**Results:** Seventeen patients with RPE were followed. The mean age was  $35.23 \pm 10.36$  years; 8 patients (50%) were men. Twelve patients were responded of 50%–90%. One patient left the study because of side

effects. There was no response to treatment even the dose increased to the effective levels in three patients. The agranulocytosis appeared in a case. Three patients had weakness, dizziness and nausea. One of them left the treatment. In the remaining two patients all symptoms disappeared spontaneously in the following 2 weeks.

**Conclusion:** It seems that LCM is a well-tolerated AED with RPE in adults in 94.1% (16 cases). Frequency and severity of seizures were reduced in cases of 70.5% (12 cases). LCM may be useful in treatment of RPE in adults.

#### p0870

### SAFETY AND TOLERABILITY OF LONG-TERM TREATMENT WITH ADJUNCTIVE BRIVARACETAM FOR PARTIAL-ONSET SEIZURES

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**Purpose:** To assess long-term safety/tolerability of brivaracetam (BRV) for adjunctive treatment of partial-onset (focal) seizures (POS).

**Method:** Data were pooled from two Phase II (NCT00175929, NCT00175825), six Phase III (NCT00490035, NCT00464269, NCT00504881, NCT01405508, NCT01261325, NCT01653262) and associated long-term follow-up (LTFU) studies (NCT00175916, NCT00150800, NCT01728077, NCT01339559). Adults (≥16 years) with epilepsy received BRV 5–200 mg/day. Treatment-emergent adverse event (TEAE) monitoring and safety/laboratory assessments were performed at protocol-specified time points until 17 January 2014.

**Results:** Of 2388 patients who received BRV (Europe 46.2%; North America 20.7%; Asia Pacific/other countries 20.0%; Latin America 13.1%), treatment is ongoing in 943 (39.5%), 1293 (54.1%) discontinued treatment in core or LTFU studies and 152 (6.4%) completed core studies but had not entered LTFU. At baseline, patients (mean [SD] age 37.0 [12.6] years; 50.3% male) most frequently had POS (97.1%); other seizure types 2.9%. Most common concomitant AEDs (≥20%): carbamazepine (42.0%), lamotrigine (27.3%) and valproate (24.2%). Exposure to BRV was 5558.0 patient-years in total; 1740, 1363, 923, and 569 patients were exposed for ≥6, ≥12, ≥24 and ≥60 months; some received BRV for >8.5 years. Altogether 84.8% patients reported TEAEs (55.0% drug-related); 14.1% patients discontinued due to TEAEs. The most common TEAEs (≥10%) were headache (20.9%), dizziness (17.3%), somnolence (15.2%), nasopharyngitis (12.7%), fatigue (11.5%) and convulsion (10.5%). Serious TEAEs (SAEs) were reported in 18.1% patients (4.4% drug-related), most commonly convulsion (2.5%), status epilepticus (0.8%); pneumonia, epilepsy, grand mal convulsion, suicidal ideation and suicidal attempt (0.5% each). There were 34 (1.4%) deaths, of these five (0.2%) were considered possibly related to study drug. Vital signs, electrocardiograms and laboratory assessments did not reveal any clinical concerns.

**Conclusion:** Pooled long-term safety data show that treatment with adjunctive BRV for up to 8.5 years was generally well tolerated, with a low incidence of TEAEs, drug-related TEAEs and SAEs. UCB supported.

#### p0871

### DAYTIME SLEEPINESS AND SLEEP QUALITY IN PATIENTS TREATED WITH PERAMPANEL

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**Purpose:** The purpose of this study was to evaluate the effects of perampanel (PER) as adjunctive therapy on daytime somnolence and sleep quality in adult patients with focal onset epilepsy.

**Method:** Multicenter prospective study performed during 6 months, assessing daytime somnolence by means of the Epworth Sleepiness Scales (ESS) before and 3 months after starting treatment with PER. Sleep quality by using Pittsburgh Sleep Quality Index (PSQI) was also recorded when available. Demographic and clinical data were considered to analyze the results.

**Results:** Of 67 patients included at baseline visit (Age 43, range 17–75 years; 60% Female), 49 completed the study evaluation at 3 months with ESS, and 34 with PSQI.

PER was used as ≥3rd AED in all patients. The average seizure frequency at baseline was 49 per months, which was reduced to 38 at follow-up ( $p = 0.007$ ). The responders rate (>50%) was 30%, with a median PER doses of 4 mg (range 2–8 mg). The retention rate at follow-up was 73%, drug withdrawn was due to lack of efficacy (12%) or side effects (15%). Most common treatment emergent adverse events were somnolence (20%) and dizziness (18%). Average baseline ESS (6) score was within normal limits and PSQI (8) was considered abnormal in the sample. At follow-up, daytime sleepiness was not impaired by PER treatment (ESS = 6). However, the quality of sleep improved significantly by two points in the PSQI ( $p = 0.004$ ). Sleep improvement was independent from demographic variables, seizure response and PER doses.

**Conclusion:** PER is an effective and safe antiepileptic drug, which can improve the sleep quality without impact in the daytime somnolence in patients with epilepsy.

#### p0873

### VITAMIN D SUPPLEMENTATION COULD BE INSUFFICIENT FOR OSTEOPOROSIS PREVENTION IN PERSONS WITH EPILEPSY ON ANTIEPILEPTIC DRUGS

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**Purpose:** Antiepileptic drugs (AED) as carbamazepine (CBZ), phenytoin (PHT) and valproic acid (VPA) are strongly related to disturbances in bone metabolism in persons with epilepsy, and can lead to a premature osteoporosis. Vitamin D supplementation (VD) has been recommended but dosage is still not clear. The aim of our study was to determine if VD administration as performed in everyday clinical practice is related to a better outcome on densitometry parameters in patients on chronic AEDs.

**Method:** We conducted a prospective observational study on adult epileptic outpatients from the Epilepsy Unit of Arrixaca's Hospital (Murcia, Spain), on stable monotherapy with AEDs, either classical or new (levetiracetam (LEV), eslicarbazepine (ESL), lacosamide (LCM)), that were going to start VD (cholecalciferol 400 UI/calcium carbonate 1500 mg). A similar sample of patients not taking VD was collected as control group. Bone mineral density (BMD) at lumbar level and neck of left femur was studied by dual energy X-ray absorptiometry at the beginning of the study and after 6 months.

**Results:** 26 patients on VD and 38 controls were studied. Mean age was  $45.27 \pm 14.74$  years in VD group (16 men, 13 on LEV, 5 on CBZ, 5 on

## Abstracts

VPA and 3 on PHT), and  $39 \pm 14.20$  years in control group (26 men, 17 on LEV, 13 on VPA, 4 on ESL, rest on CBZ, PHT and LCM). Differences between basal and follow-up lumbar and femoral BMD values were not significantly different in patient group than in control group ( $0.016 \pm 0.541 \text{ g/cm}^2$  versus  $-0.004 \pm 0.063 \text{ g/cm}^2$ , and  $0.021 \pm 0.115 \text{ g/cm}^2$  vs.  $-0.010 \pm 0.045 \text{ g/cm}^2$ , respectively). No difference was found when adjusted to sex, age, AED and other confounding factors.

**Conclusion:** VD at low doses could be an insufficient measure to prevent BMD disturbances in patients on AEDs. Guidelines are needed to establish an accurate management of bone disease in our patients.

p0875

#### EPILEPSY OUTCOME IN WEST SYNDROME AT 4 YEARS OF LIFE FOLLOWING TREATMENT WITH ACTH OR PREDNISOLONE AS FIRST LINE THERAPY: PRELIMINARY FINDINGS FROM A RANDOMIZED CLINICAL TRIAL

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**Purpose:** West syndrome is a devastating epileptic encephalopathy associated with significant mortality and morbidity. Majority evolve to different epilepsy syndromes in later life. Descriptions on late outcomes are very limited.

**Method:** Ninety seven children with previously untreated West Syndrome were randomized to receive ACTH (48) and Prednisolone (49) according to the UKISS protocol. They were prospectively followed at different time points. This abstract describes epilepsy outcome at 4 years of life.

**Results:** There were 43 children completing 4 years by 28.02.2015. Only 25 presented for the 4 year evaluation; seven died before this date and eleven did not respond. All the deaths were in ACTH arm, but were unrelated to epilepsy or drug side effects. Out of 25 reviewed, eighteen children (72%) were spasm free by their 4th birthday. Nine children were completely free of any form of seizures (36%). There were 16 experiencing ongoing epilepsy. These epilepsies included epileptic spasms only in 3 (18%), spasms  $\pm$  other seizure type/types in balance thirteen. A clear evolution into a focal epilepsy occurred in 4 (25%). Multiple seizure types were noted in 9 (55%) and this included one child with definite Lennox Gastout syndrome (6%), and another with focal plus reflex (photic) epilepsy (6%). The likelihood of spasm freedom at 4 years was not affected by the initial treatment method ( $p = 0.2$ ). Likelihood of evolving into other type of epilepsy was also equal ( $p = 0.56$ ). However, better seizure control (Engels class 1 or 2) in those with ongoing epilepsy, was seen in those treated with prednisolone ( $p = 0.02$ ).

**Conclusion:** Preliminary findings in this clinical trial on outcome at 4 years indicate that treatment with steroids as first line resulted in sustained spasm freedom in 72%. Irrespective of treatment type, 52% evolved to different seizure types. Overall epilepsy outcome was better if initially treated with prednisolone.

p0876

#### EFFICACY AND SIDE EFFECT PROFILE OF LACOSAMIDE IN REFRACTORY FOCAL ONSET EPILEPSY PATIENTS

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**Purpose:** To evaluate efficacy and safety profile of Lacosamide.

**Method:** 30 adult patients (>18 year) who are on Lacosamide were retrospectively and randomly selected from our electronic database. Each patient's epilepsy/AED history and seizure control were reviewed before and after Lacosamide introduction.

**Results:** Of 30 patients (mean age 41 years, 53% women, mean epilepsy duration 18 years, 1/3rd Learning disability), 63% had Complex partial seizures. Commonest epilepsy syndrome was Symptomatic/Cryptogenic partial epilepsy (43%) followed by Idiopathic partial epilepsy. 40% were on 4 AED, 30% on  $\geq 5$ AEDs, 20% on 3 AED, 10% on 2 AED. <50% seizure reduction was seen in all patients on  $\leq 2$  AED and 84% on  $\geq 3$  AED. None reported  $\geq 75\%$  seizure reduction. Following introduction of Lacosamide (mean treatment duration 25 months; mean daily dose 345 mg), commonest side effect was dizziness and cognitive/behaviour change (10% each), ataxia (9%) and increase in seizure frequency (7%). 20% stopped Lacosamide due to adverse events, 7% due to increase in seizure frequency; all who stopped were on 3 or more AED. Those who reported side effects did so in first few months of starting Lacosamide. Lacosamide showed  $\geq 75\%$  reduction in seizure frequency in 50%. 25% showing 50%–75% reduction; 7% had >2 years of seizure freedom.

**Conclusion:** Lacosamide is effective in reducing seizure frequency significantly or achieving seizure freedom (7%) in refractory focal onset epilepsy patients. 7% reported increase in seizure frequency. Significant adverse events or increase in seizure frequency are noted especially in those on 3 or more AEDs before addition of Lacosamide and early on during Lacosamide treatment. There may be a justification to introduce Lacosamide as a 2nd add-on AED in focal onset epilepsies, in order to improve seizure control with less side effect profile for the patient.

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p0877

#### THE ADVERSE EFFECTS OF ANTIEPILEPTIC DRUGS

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**Purpose:** Epileptic patients should use long-term antiepileptic drugs (AEDs). Side effects are common with immediate and long-term usage. We aimed to raise awareness on the side effects of AEDs and to compare these adverse effects of old and new generation drugs

**Method:** We evaluated retrospectively the type and frequency of the side effects of old and new generation AEDs in 189 patients with epilepsy who were followed up in our clinic.

**Results:** The age range of 79M:110F patients was 7–82 years ( $26.9 \pm 13.8$ ). Idiopathic epilepsy was diagnosed in 104 patients (55%), symptomatic in 57 (30%) and cryptogenic in 28 (15%). Monotherapy was applied in 129 patients whereas polytherapy in 60 patients. The frequency of side effects was 50% and 46% of them were in monotherapy. Both in monotherapy and polytherapy, the most frequent AED was valproate (52%). Valproate had the highest frequency

of side effects; weight gain, tremor, hair loss and drowsiness. Carbamazepine was the second common drug (16.1%) with the side effects of liver enzymes increase, drowsiness and weight gain. Levetiracetam was the third frequent and the side effects were irritability and dizziness. The frequency of side effects in the old generation AED's was 69.9%, in the new generation 21.5%.

**Conclusion:** It is important to follow up the frequency and type of side effects of AEDs as well as the seizure frequency of patients and the side effects seems to be less frequent in new generation drugs.

#### p0878

### RATIONALE AND STUDY DESIGN FOR A NOVEL PHASE 3, RANDOMIZED, DOUBLE-BLIND TRIAL OF ADJUNCTIVE LACOSAMIDE IN PATIENTS WITH IDIOPATHIC GENERALIZED (GENETIC) EPILEPSY AND UNCONTROLLED PRIMARY GENERALIZED TONIC-CLONIC SEIZURES

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**Purpose:** SP0982 is a Phase 3 study designed to evaluate the efficacy and safety of oral lacosamide as adjunctive therapy for uncontrolled primary generalized tonic-clonic seizures (PGTCS) in patients ( $\geq 4$  years) with idiopathic generalized (genetic) epilepsy (IGE). It will utilize a novel "time to nth PGTCS" primary endpoint. This differs from traditional outcomes which assess reduction in seizure frequency and require a high Baseline PGTCS frequency. Post-hoc analysis of a lamotrigine trial comprising patients with low PGTCS frequency (French et al. *Epilepsia*. 2007; 48[Suppl.6]: 77) demonstrated statistical separation from placebo for "time to third PGTCS." Clinical experience in patients ( $\geq 16$  years) with focal epilepsy indicates that an effective adjunctive lacosamide dose would be achieved more rapidly than with lamotrigine, suggesting that "time to second PGTCS" would be an appropriate primary endpoint in SP0982.

**Methods:** This international, double-blind, placebo-controlled study will randomize up to 250 patients to achieve 125 events, defined as a patient experiencing  $\geq 2$  PGTCS. Patients taking 1–3 AEDs and experiencing  $\geq 3$  PGTCS during the 16-week Baseline (12-week Historical/4-week Prospective) will be randomized (1:1; stratified by age and seizure frequency) to receive placebo or lacosamide (target: up to 12 mg/kg/day or 400 mg/day). Treatment continues for up to 24 weeks (6-week Titration Phase and up to 18-week Maintenance Phase), or until the patient completes  $\geq 6$  weeks' treatment with  $\geq 2$  PGTCS. All patients may enter the open-label extension study (EP0012).

**Results:** Recruitment planned to begin Q2 2015.

**Conclusion:** SP0982 will pioneer a "time to second PGTCS" primary endpoint to evaluate lacosamide efficacy in adult and pediatric patients with IGE and uncontrolled PGTCS. This design facilitates entry of patients with a range of seizure frequencies, representative of the broader IGE patient population, and enables patients experiencing ongoing PGTCS to complete the trial early, therefore minimizing their exposure to potentially suboptimal treatment.

**Disclosures:** UCB Pharma-funded.

#### p0879

### EVIDENCE FOR A DIFFERENTIAL INTERACTION OF BRIVARACETAM AND LEVETIRACETAM WITH THE SV2A PROTEIN

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**Purpose:** The synaptic vesicle protein 2A (SV2A) represents the molecular site of action for the antiepileptic drugs brivaracetam (BRV) and levetiracetam (LEV). In animal models of epilepsy, BRV has a higher potency and more complete seizure suppression than LEV (Matagne et al, BJP 2008), suggesting different interactions with the SV2A protein. We recently identified a compound that modulates the confirmation of the SV2A protein (Daniels et al, BJP 2013). We have therefore investigated the effect of this allosteric modulator on the binding of [ $^3$ H]-LEV and [ $^3$ H]-BRV to the human SV2A protein.

**Method:** Saturation binding studies in membranes (25  $\mu$ g per well) from HEK 293 cells expressing human SV2A protein (Daniels et al, BJP 2013) were incubated for 120 minute at 4°C in 0.2 mL buffer. Data were analysed in GraphPad PRISM and are mean  $\pm$  SD (n = 3).

**Results:** Both [ $^3$ H]-LEV and [ $^3$ H]-BRV bind to single apparent binding sites. The modulator produced a 2–3 fold increase in affinity, Kd (nM), for [ $^3$ H]-LEV (2500  $\pm$  180 to 900  $\pm$  28) and a 2-fold increase in Bmax (pmoles/mgPr: from 67  $\pm$  3 to 140  $\pm$  3). On [ $^3$ H]-BRV binding, the modulator produced a 10-fold increase in affinity, Kd (nM), from 190  $\pm$  3 to 20  $\pm$  2 and a 0.7–0.8 fold increase in Bmax from 130  $\pm$  5 to 170  $\pm$  3.

**Conclusion:** We have previously suggested that the SV2A allosteric modulator alters the confirmation of the SV2A protein producing differential effects on SV2A ligands. The differential modulation of the binding of [3H]-LEV and [3H]-BRV suggests that their antiepileptic effects derive from distinct interactions with the SV2A protein. In the absence of a functional assay or an understanding of the function of the SV2A and the role of conformational states, the consequence of this differential interaction remains unknown. This warrants further studies, including assessing whether these effects are seen in native tissue such as human cortex. UCB supported.

#### p0881

### EFFECTS OF ANTIEPILEPTICS ON BODYWEIGHT

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**Purpose:** To point on the effects of antiepileptic medications on body-weight.

**Method:** We screened 362 follow up patients in Haydarpaşa Research and Training Hospital Epilepsy Outpatient Clinic.

**Results:** We had 137 valproate, 95 carbamazepine, 22 phenytoin, 81 levetiracetam and 19 topiramate users. There were 42 patients with various weight gain complaints. 38 of them were using valproate, 3 of them were carbamazepine users and 1 of them were levetiracetam user. 8 patients were presented with weight lose. 2 of them were using levetiracetam and 3 of them were using topiramate.

**Conclusion:** Weight problems affect continuity and adherence to long term drug treatments such as epilepsy treatments. Weight gain also has effects on health conditions and psychology. Weight changes should be questioned for antiepileptic users to maintain health, stability and medication adherence.

#### p0882

### ANTIOXIDANT STATUS AND THE EFFECT OF SINGLE OR MULTIPLE ANTIEPILEPTIC DRUG USE TO OXIDATIVE STRESS IN PATIENTS WITH EPILEPSY

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**Purpose:** Oxidative stress has been implicated in various disorders including epilepsy. The aim of this study was to investigate the antioxidant status of patients with epilepsy using antiepileptic drugs (AEDs) regularly and to compare them with healthy subjects.

**Method:** We investigated the plasma catalase, malondialdehyde (MDA), glutathione peroxidase (GSH-Px), superoxide dismutase (SOD), and xanthine oxidase (XO) levels in 58 epilepsy patients using AEDs and 25 healthy controls. Patients were divided into polytherapy (n = 17) or monotherapy (n = 41) groups and antioxidant status was compared with the two groups and controls.

**Results:** Catalase and SOD levels were significantly lower in patients with epilepsy than the control group ( $p < 0.01$ ). Malondialdehyde, GSH-Px and XO levels were significantly higher in patient group ( $p < 0.01$ ). High level of GSH-Px is likely to have increased as a compensatory response to low catalase level and oxidative stress. Increased MDA level is associated with an increase in lipid peroxidation. Increased XO level is associated with increased degradation of nucleotides, meanwhile oxidative stress is augmented by high XO and low catalase levels. There was no statistically significant difference between the monotherapy and polytherapy groups in terms of serum catalase, MDA, GSH-Px or SOD levels while XO level was higher in the monotherapy group ( $p < 0.01$ ). Although serum XO level was significantly lower in polytherapy group than monotherapy group ( $p < 0.01$ ), was significantly higher than control group ( $p < 0.01$ ).

**Conclusion:** Our results showed that antioxidant status was significantly lower in patients with epilepsy using AEDs than the healthy control group. Whereas polytherapy has not considerably affected oxidative stress parameters. Therefore we believe that the oxidative stress caused by epilepsy itself rather than the antiepileptic drugs. Recommendation of antioxidant replacement may be helpful for patients with epilepsy.

#### p0883

### THE EFFECT OF LEVETIRACETAM AND CURCUMIN ON GENE EXPRESSION OF INFLAMMATION AND IMMUNE RESPONSE IN HIPPOCAMPAL BRAIN TISSUES OF KAINATE-INDUCED POST-STATUS EPILEPTICUS WISTAR RATS

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**Purpose:** To evaluate the effect of levetiracetam and curcumin on gene expression of inflammation and immune response in hippocampal brain tissues of kainate-induced post-status epilepticus (SE) wistar rats.

**Method:** SE was induced in Female Wistar rats with 10 mg/kg kainic acid. Only rats achieved stage 4 and 5 limbic seizures were used and treated intraperitoneally with levetiracetam 100 mg/kg, curcumin 100 mg/kg and vehicle 50% DMSO respectively, for 1 week. After the treatment, the rats from each group were decapitated and RNA was extracted from hippocampus tissues for microarray analysis.

**Results:** A list of 59 genes related with inflammation and immune response was differentially expressed based on fold change more than

two in either direction and p value less than 0.05 by ANOVA analysis. Kainic acid up-regulated the pro-inflammatory cytokines included *Il18* and *Ifngr1*, which played an important role in neuroinflammation. Kainic acid also up-regulated a class II major histocompatibility complex, *Cd74* and complement component, *C3*. Despite of treatment given, pro-inflammatory cytokines was remained up-regulated in the kainate-induced status epilepticus rodents (levetiracetam: *Il18*, *Ifngr1*, *Ccl2*, *Ccl3*, *Ccr5*, *Cx3cr1*; curcumin: *Cx3cr1*, *Cx3cl1*). In addition to pro-inflammatory cytokines, anti-inflammatory cytokines was also up-regulated by both levetiracetam (*Il10rb*, *Tgfb1*, *Cxcl16*) and curcumin (*Il10rb*, *Cxcl16*, *Cxcl17*), but not by kainic acid treatment. Levetiracetam was potentially modulating the inflammation process during epileptogenesis via up-regulation of *Tgfb1* as well as up-regulation of *Il10rb* and *Cxcl16*. Curcumin may be potentially exert anti-inflammatory activities via up-regulation of anti-inflammatory cytokines, such as *Il10rb*, *Cxcl16* and *Cxcl17*.

**Conclusion:** Both levetiracetam and curcumin may be involved in activation of anti-inflammatory factors, which was likely to contribute in counteracting neuroinflammation induced by kainic acid.

#### p0884

### ANTI-EPILEPTIC DRUGS IN EPILEPSY WITH FEBRILE SEIZURES PLUS: EFFICACY AND THE RELATIONSHIP WITH SCN1A MUTATIONS

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**Purpose:** To explore the proper medical strategies on early stage of epilepsy with febrile seizure plus (EFS+) and their relationship with *SCN1A* mutations.

**Method:** The data of anti-epileptic drugs (AEDs) treatment in 202 patients with EFS+ searching for *SCN1A* mutations were collected. The seizure control at different levels were compared in each AED administered to patients with EFS+ and further compared between patients with *SCN1A* mutations and those without *SCN1A* mutations.

**Results:** A total of 9 AEDs used in more than 10 cases were identified, including Valproate, Topiramete, Clonazepam, Phenobarbital, Levetiracetam, Lamotrigine, Carbamazepine, Oxcarbazepine and Phenytoin. The three highest prescriptions were Valproate, Topiramete and Clonazepam. Combined therapy was predominant (166/202, 82.2%). Compared with other AEDs, the improvement rate was the highest in Valproate (169/187, 90.4%), Topiramete (111/120, 92.5%) and Clonazepam (69/78, 88.5%), and were lowest in Phenytoin and Lamotrigine (0 and 4/45, 8.9%) ( $p < 0.01$ ). The improvement rate of Phenobarbital (58.1%, 25/43) and Levetiracetam (44.7%, 21/47) were intermediate, and no statistical difference between them but had difference with others ( $p < 0.01$ ). The aggravation rats of Lamotrigine (57.8%, 26/45) and Carbamazepine (36.7%, 18/49) were the highest, followed by Oxcarbazepine (33.3%, 15/45) and Phenytoin (26.9%, 7/26). All of them showed statistical difference compared with others ( $p < 0.01$ ). The aggravation rate of Lamotrigine in patients with *SCN1A* mutations (81.3%, 13/16) was significant higher than those without *SCN1A* mutations (44.8%, 13/29), and there was statistical difference between them ( $\chi^2 = 5.607$ ,  $p = 0.018$ ); similarly, the aggravation rates of Carbamazepine, Oxcarbazepine and Phenytoin showed an increase tendency, but no difference compared with other AEDs.

**Conclusion:** Valproate, Topiramete and Clonazepam are relatively proper choices in patients with EFS+ on early stage. Sodium channel blocking AEDs should be avoided in EFS+, especially in the patients with *SCN1A* mutations. The efficacy of Levetiracetam and Phenobarbital in EFS+ remain uncertain.

p0886

### THE EFFECT OF VITAMIN E ON THE SEIZURE FREQUENCY, EEG FINDINGS AND BIOCHEMICAL PARAMETERS OF EPILEPTIC PATIENTS TREATING WITH CARBAMAZEPIN, SODIUM VALPROATE AND LEVETIRACETAM

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This study aimed to evaluate the effect of vitamin E on increasing the effects of antiepileptic drugs.

**Materials and methods:** This double-blind, placebo-controlled clinical trial have done on 66 patients with epilepsy treated with antiepileptic drugs referred to Kashani hospital and private clinics in Isfahan. Non-random simple sampling 33 patients were allocated to intervention and control groups. The intervention group was given daily supplements of 400 IU vitamin E and the control group gave similar pills of vitamin E as placebo. Patients were examined monthly about the seizure frequency and EEG and blood biochemical markers at the end of sixth months. Data were analyzed by SPSS software using chi square test and T-test.

**Results:** The mean of total antioxidant in cases before treatment was  $6.2 \pm 2$  and significantly increased to  $7.7 \pm 2.1$  after treatment ( $p = 0.001$ ), but in controls was increased of  $7.3 \pm 1.9$  to  $7.4 \pm 2.1$  ( $p = 0.91$ ). The mean of catalase in cases was  $14.3 \pm 5.1$  and significantly increased to  $17.5 \pm 5.4$  after treatment ( $p < 0.0001$ ), in controls was  $17.5 \pm 5.2$  and increased to  $17.4 \pm 6$  ( $p = 0.44$ ). The mean of glutathione in cases after treatment was significantly increased compare to before treatment ( $13.6 \pm 6.1$  to  $18.5 \pm 8.2$ ,  $p < 0.0001$ ), in controls ( $16.4 \pm 5.7$  to  $16.3 \pm 5.4$  respectively,  $p = 0.88$ ). malondialdehyde decreased but was not statistically significant in case ( $p = 0.1$ ),but in control don't decreased( $p = 0.53$ ). The mean number of seizure in cases after treatment was significantly decreased compare to before ( $2.25 \pm 0.62$  to  $1.34 \pm 0.83$ ,  $p < 0.0001$ ), but in controls was similar ( $2.36 \pm 1.1$  to  $2.57 \pm 1.2$ ,  $p < 0.0001$ ). Changes in the positive EEG findings in cases observed more than control group (50% vs. 12.1% respectively,  $p = 0.001$ ).

**Conclusion:** Our results showed that vitamin E in addition to antiepileptic drugs improved antioxidant parameters and seizure frequency and positive EEG finding in compare to placebo, but no significant effect on reduced oxidative stress(respect to malon di aldehyd enzyme).

## Epilepsy Surgery 6 Tuesday, 8th September 2015

p0890

### IDENTIFYING FOCAL RESECTIVE SURGERY CANDIDATES IN CHILDREN WITH NONLOCALIZING MRI

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**Purpose:** Presurgical evaluation in individuals with nonlocalizing (normal or nonfocal lesional) MRI requires multimodal evaluations due to lack of an anatomic surgical target. The impact of noninvasive evaluations on surgical candidacy and outcome was assessed in a single institu-

tion, retrospective review of children with medically refractory focal epilepsy and nonlocalizing MRI.

**Method:** Children with nonlocalizing MRI undergoing a standardized presurgical evaluation were identified through the Epilepsy Monitoring Database between 2000 and 2009. Surgical candidacy was based on multidisciplinary epilepsy surgical conference. Surgical outcome was defined as favorable (Engel I and II) or unfavorable (Engel III and IV).

**Results:** Among a total of 135 children, 41 patients (30%) had a single focal ictal scalp-EEG onset. Subtraction ictal SPECT co-registered to MRI (SISCOM) provided additional localization in 43/94 patients (36%) without focal scalp-EEG. Among 73 patients deemed to be surgical candidates, 42 patients (31%) proceeded to surgery or phase II intracranial EEG (iEEG) monitoring. Due to nonlocalizing iEEG, 12 of 24 patients undergoing phase II evaluation were not offered surgery. Surgical candidacy was highly associated with the presence of focal scalp-EEG ( $p < 0.0001$ , OR: 5.6, 95%CI: 2.3–13.3) and concordant focal EEG and focal SISCOM ( $p = 0.02$ , OR: 4.3, 95%CI: 1.2–15.7). Favorable outcome at last follow-up was achieved in 11/30 patients (37%) who had resective surgery and more likely with concordant focal scalp-EEG and focal SISCOM ( $p = 0.03$ , OR: 5.3, 95%CI: 1.35–20.89).

**Conclusion:** Focal ictal scalp-EEG and concordant focal SISCOM were the most useful tests for surgical candidacy in children with nonlocalizing MRI. Favorable surgical outcome was associated with concordant focal scalp-EEG and focal SISCOM. Favorable outcome was seen 11/30 patients (37%) who ultimately underwent resective surgery and in 6/30 patients (20%) who underwent phase II evaluation, demonstrating the challenges in evaluating such children with nonlocalizing MRI for resective surgery.

p0892

### AURA'S PREDICTIVE VALUE IN TEMPORAL LOBE EPILEPSY SURGERY PATIENTS

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**Purpose:** The aura is an epileptic phenomenon, which is frequently observed before the attack. It is seen in 90% of the epilepsy patients. While the aura is a sign of the onset of the focal attack, the symptoms could localize the epileptogenic zone. In TLE, abdominal, emotional and psychic aura are the most commonly observed symptoms.

**Method:** The study included 100 patients with medically refractory TLE undergoing anterior temporal lobectomy (ATL) between 2010 and 2014 in our center. A multidisciplinary preoperative evaluation was performed. We investigated the association of aura with the postoperative seizures, descriptive factors and preoperative tests. Postoperative seizure outcome was evaluated using Engel's outcome classification.

**Results:** The abdominal and emotional aura were among the most frequently observed aura in our patients. In this patients group, the most frequently detected histopathological finding was MTS. In patients with abdominal and emotional aura, the risk factor of febrile convulsion (FK) was more commonly observed. However, any relationships between aura and the lateralization could not be found. In TLE patients with a later onset, the incidence of abdominal and emotional aura and the frequency of FK history were lower. After surgery only in 11 cases, only the aura was maintained, and in 2 of them, the type of aura was changed after the surgery. When the rate of absence seizure were evaluated according to

## Abstracts

Engel classification I, it was detected as 83%, which was considered as sufficient.

**Conclusion:** Our findings were clearly suggested that there were a relationship between FK, MTS and abdominal-emotional aura. However, there was no effect of having abdominal and emotional aura on the prognosis of surgery. Finally, although the aura could be instructive about the onset of the seizure, it did not allow to make a prediction about the seizure free after surgery.

## p0893

### LOCALIZATION OF CORTICAL LANGUAGE AREA FOR PATIENTS WITH REFRACTORY EPILEPSY: A COMPARISON OF A NEW METHOD BASED ON HIGH GAMMA ACTIVITIES WITH ELECTRICAL CORTICAL STIMULATION

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**Purpose:** To localize the cortical language area based on high gamma activities recorded from electrocorticogram for patients with refractory epilepsy and to compare the new method with classic electrical cortical stimulation (ECS).

**Method:** Electrocorticographic signals were recorded during an auditory-language task for eight patients with refractory epilepsy who underwent intracranial recording to localize the epileptogenic zone and language area. The high gamma activities were analyzed with event-related synchronization (ERS) and adaptive directed transfer function (ADTF). The results were compared to that of ECS.

**Results:** The analysis of ERS based on auditory-language task showed the activated cortical areas on all patients. The ADTF analysis provided dynamic information about the connectivity pattern of cortical interaction. Totally, 111 cortical nodal points were identified as the predominant points in the event-related information outflow according to the ADTF analysis, and 76 of the points lied in frontal or central area, 35 lied in temporal area. By contrast, 22 cortical points were positive according to ECS in 7 of the 8 patients (19 in frontal and 3 in temporal area). Additionally, ECS was terminated for continuous after discharges in 21 points in 5 patients and secondary seizures occurred in 7 of these points. Excluding the numbers of one patient without electrodes covering temporal area, the positive numbers of ADTF analysis and ECS were 60 versus 17 in frontal area and 35 versus 3 in temporal area ( $p = 0.059$ ). The positive points were not completely the same between the two methods. The process of recording electrocorticographic signals is quick and safe.

**Conclusion:** The method of ADTF analysis based on high gamma activities may be a useful complement to traditional ECS in the localization of language area for patients with refractory epilepsy. The combination of the method of ECS and ADTF analysis may be a better way.

## p0894

### ANALYSES OF PATIENTS WHO UNDERWENT INVASIVE ELECTROENCEPHALOGRAPHY MONITORING BEFORE EPILEPSY SURGERY

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**Purpose:** Accurate delineation of epileptogenic zone is crucial before epilepsy surgery, however non-invasive presurgical evaluation may not provide adequate data. Therefore invasive electroencephalography monitoring (IEM) is needed in selected patients. In this study, we aimed to investigate electro-clinical characteristics and long-term outcome of our case series with IEM.

**Method:** Patients who were admitted to our Clinical Neurophysiology Division-Epilepsy Unit and underwent IEM between 2003 and 2014 are included in this retrospective study.

**Results:** Sixty patients (32 Males/28 Females) with mean age of  $29.7 \pm 9.6$  (5–50 years) were included. Mean age at seizure onset and time of IEM were  $9.5 \pm 8.3$  and  $24.3 \pm 9.4$  years, respectively. Cranial MRIs of 14 patients were normal, while FDG-PET showed hypometabolism. FDG-PET was normal in two patients, while MRI showed lesions and in four patients both MRI and FDG-PET findings were negative. Subdural electrodes were implanted in 35, depth electrodes in 14, and combined electrodes in 6 patients (data not available (N/A): 5 patients). Apart from non-operated 2 patients, 53 cases underwent lobectomy, one had hemispherectomy (N/A: 4 patients), and 5 cases were re-operated. Eight patients had hippocampal sclerosis, 32 had focal cortical dysplasia (13: type-1, 19: type-2), other etiologies such as polymicrogyria/reactive gliosis were defined in 12 cases (N/A: 6 patients). Postoperative complications including focal neurological deficits/hemorrhage, which were transient observed in nine patients. Antiepileptic drug therapy was discontinued postoperatively in 4 patients (7%) and decreased to monotherapy in 18 patients (31%). Postoperative follow-up was  $6.3 \pm 2.8$  years. On the last follow-up visit, 30 patients are Engel-I (52%), 12 patients Engel-II (21%), 12 cases Engel-III (21%), and 4 patients Engel-4 (7%).

**Conclusion:** Favorable results are still possible in patients, whose epileptogenic zone cannot be described by non-invasive techniques during presurgical evaluation. Majority of our patients, who needed IEM had FCD or were MRI negative. In carefully selected patients with medically refractory epilepsy, IEM provides critical information before surgery and increases success rate.

## p0895

### HIGH FREQUENCY OSCILLATIONS IN THE INTRA-OPERATIVE ECOG TO GUIDE EPILEPSY SURGERY (THE HFO TRIAL): A RANDOMIZED CONTROLLED CLINICAL TRIAL PROTOCOL

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**Purpose:** Intra-operative electrocorticography (ioECOG), based on interictal spikes and spike patterns, is often performed to optimize delineation of the epileptogenic tissue during epilepsy surgery. High Frequency Oscillations (HFOs, 80–500 Hz) have been identified as more precise biomarkers for epileptogenic tissue. Aim of the study is to determine if ioECOG-tailored surgery using HFOs instead of interictal spikes is feasible and will lead to equal or better seizure outcome.

**Method:** A single blinded multi-center randomized controlled trial ("the HFO trial"), includes children (all ages) and adults with refractory focal epilepsy who undergo surgery with ioECOG. Surgery is tailored by HFOs (arm 1) or interictal spikes (arm 2). Primary outcome is post-operative result after 1 year, dichotomized in seizure freedom (Engel 1a&b) versus seizure recurrence (Engel 1c-4). Secondary outcome measures are the volume of resected tissue, neurologic deficits, surgical duration and complications, cognition and quality of life. The study has a non-inferiority design to test feasibility and at least equal performance in terms of surgi-

cal outcome. We aim to include 78 patients within 3 years including 1 year follow-up.

**Results:** Results are expected in 2018.

**Conclusion:** This trial provides a transition from observational research towards clinical interventions using HFOs. We address methodological difficulties in designing this trial. We aim to make a first step in using HFOs to increase the success rate of tailored epilepsy surgery, while minimizing resection volume. This may reduce neurological deficits and yield a better quality of life. Meanwhile, the identification and quantification of HFOs can be automated, resulting in a potential objective surgical tailoring measure that can be readily implemented.

#### p0896

### HIGH FREQUENCY OSCILLATIONS AND FUNCTIONAL NETWORK CHARACTERISTICS IN THE INTRA-OPERATIVE ELECTROCORTICOGRAM IN TEMPORAL LOBE EPILEPSY

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**Purpose:** High frequency oscillations (HFOs; ripples, 80–250 Hz), especially fast ripples (FR, 250–500 Hz), are biomarkers for epileptogenic tissue. Removal of tissue generating HFOs correlates with good surgical outcome. Network studies show that patients with focal epilepsy have pathological highly connected nodes (hubs). Resection of these hubs is associated with good outcome. We investigated the overlap between functional network characteristics and HFOs in subdural intra-operative electrocorticography.

**Methods:** We studied pre-resection electrocorticography recorded at 2048 Hz in fourteen patients with refractory temporal lobe epilepsy. We marked FRs, ripples and spikes in 1 minute of these recordings. Connectivity was assessed in four event-free epochs (2 second) within this minute using the phase lag index. Graphs were constructed, and centrality-measures (eigenvector centrality (ECM), Minimum Spanning Tree-degree (MST-deg), and MST-betweenness centrality (MST-bc) were computed for each channel in the theta, gamma, ripple and FR frequency band. We related percentages of events per channel to centrality-measures using linear regression.

**Results:** We found FRs in 8 patients (mean number: 10, range: 2–32), ripples in twelve patients (mean: 41, range: 1–140), and spikes in 11 patients (mean: 180, range: 13–535). Preliminary analysis showed negative correlations between the percentages of all events and the ECM in the gamma band ( $R_{FR-ECM}$ : -0.133;  $R_{ripples-ECM}$ : -0.141;  $R_{spikes-ECM}$ : -0.159,  $p < 0.01$ ). The percentage of ripples was negatively correlated to MSTdeg and MSTbc in the gamma band ( $R_{ripples-MSTdeg}$ : -0.135;  $R_{ripples-MSTbc}$ : -0.125,  $p < 0.01$ ). The percentage of spikes was positively correlated to MSTdeg and MSTbc in the FR band ( $R_{spikes-MSTdeg}$ : 0.129;  $R_{spikes-MSTbc}$ : 0.131,  $p < 0.01$ ).

**Conclusion:** Areas with high HFO and spike rates are functionally isolated, characterized by low centrality-measures, in the gamma band in subdural temporal lobe recordings. High spike rate areas show high centrality-measures in the FR band. These findings can help improve identification of the epileptogenic tissue and unravel the pathophysiology of epileptogenic networks.

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#### p0897

### A GENOME-WIDE META-ANALYSIS OF AROMATIC ANTI-EPILEPTIC DRUG INDUCED MACULOPAPULAR EXANTHEMA

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**Purpose:** Carbamazepine, lamotrigine and phenytoin are among the world's leading anti-epileptic drugs (AEDs) for treating epilepsy. However, it is estimated that 5%–10% of patients exposed to these aromatic drugs develop an idiosyncratic cutaneous adverse drug reaction (ADR) characterized by a generalized maculopapular exanthematous rash (MPE). The ILAE Consortium on Complex Epilepsies has collected detailed point-of-care phenotypic and genetic information for epilepsy patients across Europe, North America, Australia and China and provides a framework to study ADRs. Alleles in the major histocompatibility locus, *HLA-A\*3101* and *HLA-B\*1502*, have powerful diagnostic value in predicting carbamazepine-hypersensitivity yet these markers do not have complete prognostic sensitivity and markers for lamotrigine-related hypersensitivity remain elusive.

**Method:** We conducted a genome-wide association study of 251 MPE cases and 858 drug-tolerant controls from epilepsy patient cohorts of northern European and Han Chinese descent. Cases were stratified according to the causal aromatic drug; namely carbamazepine, lamotrigine or phenytoin. We imputed genotype data with IMPUTE2 and performed logistic regression of cases versus controls per ancestral cohort, controlling for within-population differences by principal components analysis. Common HLA serotypes were imputed using SNP2HLA. Results from each cohort were then meta-analysed.

**Results:** There were no significant markers for MPE to all aromatic drugs. In the drug-specific analyses, we observed some novel loci with suggestive association warranting further investigation. *HLA-A\*3101* was the most significant marker for carbamazepine-MPE in Europeans ( $p = 1.29 \times 10^{-8}$ , OR = 5.29 [2.69–10.39]) and following meta-analysis with Han Chinese ( $p = 0.009$ , OR = 3.71 [2.04–6.76],  $I^2 = 49$ ).

**Conclusion:** Identification of secure genetic markers for AED-induced MPE will result in more personalized prescribing and is expected to reduce the overall rates of AED discontinuation due to ADRs.

p0898

### MODELING OF FEVER-ASSOCIATED EPILEPSY SYNDROMES CAUSED BY MUTATIONS IN *STX1B* IN ZEBRAFISH

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**Purpose:** Febrile seizures affect 2%–4% of all children and are known to have a strong genetic component (*SCN1A*, *SCN1B*, *GABRG2*). Lately, mutations in syntaxin-1B (*STX1B*) have been identified in several independent large pedigrees with febrile seizure and epilepsy (genetic analysis underlying this research can be found in greater detail in Schubert, Siekierska et al., 2014). In recent years, zebrafish has emerged as a promising *in vivo* model for the functional analysis of novel human disease candidate genes and, more specifically, has been expansively used as a novel experimental model for epilepsy. To clarify the role of *STX1B* in fever-associated epilepsies we established an *in vivo* zebrafish model of *stx1b* knockdown.

**Method:** Functional consequences of an *STX1B* defect *in vivo* were investigated in a *stx1b* knockdown model using morpholino antisense oligomers in zebrafish. Local field potential recordings were performed to investigate abnormal brain activity under normal conditions and hyperthermia. The specificity of the *stx1b* antisense phenotype was confirmed by rescue experiments through CNS-specific Tol2-mediated transgenesis.

**Results:** Video-recording and local field potential analyses of zebrafish larvae using antisense knockdown of *stx1b*, revealed seizure-like behavior and epileptiform discharges that were highly sensitive to increased temperature. The specificity of the knockdown experiment could be proven by a rescue with wild type *STX1B*. Moreover, the loss-of-function character of one of the mutations was demonstrated by its inability to ameliorate spontaneous epileptiform discharges in *stx1b*-knockdown larvae.

**Conclusion:** Our study provides evidence that *stx1b* knockdown in a vertebrate *in vivo* system causes abnormal seizure-like behaviors and “epileptiform” discharges increasing under hyperthermia.

p0899

### STXBP1: CLINICAL AND GENETIC DESCRIPTION OF 39 NEW PATIENTS WITH AN STXBP1 MUTATION AND REVIEW OF LITERATURE

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**Purpose:** To describe the phenotypical spectrum associated with *STXBP1* encephalopathy (*STXBP1-E*) through description of a large cohort of newly diagnosed patients and a review of all *STXBP1-E* patients published to date. To look for possible genotype-phenotype correlations.

**Method:** Newly diagnosed patients with a *STXBP1* mutation were recruited through a European network of collaborating child neurologists. A PubMed search was performed to retrieve all publications reporting *STXBP1-E* patients.

**Results:** We describe 39 new patients with *STXBP1-E*, between the age 10 weeks and 56 years and 31 novel *STXBP1* mutations. We further reviewed available information on 78 reported patients. Two third of all mutations were whole gene deletions or truncating mutations, 1/3 missense mutations. The majority of patients have an epileptic encephalopathy with onset in the 1st year of life, with Ohtahara and West syndrome being the most frequent recognizable syndromes and epileptic spasms the most frequent seizure type. Five percent of patients have childhood onset epilepsy with ID, and 6% ID without epilepsy. More than one third of patients achieved seizure freedom at time of publication. Non-epileptic motor features were seen in more than half of the patients with dyskinesia, tremor and ataxia being the most frequent. All patients had some degree of ID, mostly severe to profound (88%). One patient out of five showed autism or autistic traits. Although MRI’s were normal in the majority of patients, cortical atrophy, delayed myelination and thin corpus callosum were recurrent findings. There was no correlation between mutation type (truncating vs. missense) and presence and severity of epilepsy, or degree of ID.

**Conclusion:** *De novo STXBP1* mutations are one of the most frequent causes of early onset epileptic encephalopathy and the large majority of patients are severely disabled. So far no specific genotypes seem to be predictive of a better outcome.

p0901

### ANGIOTENSIN-CONVERTING ENZYME AND ANGIOTENSIN II TYPE 1 RECEPTOR GENE POLYMORPHISMS IN CHILDREN WITH SUBACUTE SCLEROSING PANENCEPHALITIS

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**Purpose and method:** Subacute sclerosing panencephalitis (SSPE) is a progressive, debilitating, and fatal brain disorder caused by mutant measles virus infection. Although both viral and host factors seem to be involved in SSPE, the exact pathogenesis remains to be determined. Autoimmune demyelination is characteristic of SSPE. The blood angiotensin – converting enzyme (ACE) activity and Angiotensin II (AngII) levels are associated with the ACE gene polymorphism. Proinflammatory effects of AngII may contribute to the development of SSPE. The aim of this study was to investigate whether the ACE and Ang II type I receptor (ATIR) (A1166C) gene polymorphisms were investigated by polymerase chain reaction (PCR) in 43 patients with SSPE and 100 healthy controls.

**Results:** The genotype distribution of the SSPE children and Healthy controls were as follows: DD 58.1% versus 34.0, ID 37.2% versus 48.0%, and II 4.7% versus 18.0, respectively ( $p = 0.012$ ). Allele frequencies of patients and controls were D 76.7% versus 58.0% and I 23.3% versus 42.0% respectively ( $p = 0.004$ ). The frequency of DD genotype and D allele were significantly higher in SSPE children compared with controls ( $p < 0.05$ ). ATIR gene polymorphism distribution was found to be similar in SSPE children and control subjects: AA 55.8% versus 60.7%, AC 37.2% versus 32.1% and CC 7.0% versus 7.2% respectively ( $p > 0.05$ ).

**Conclusion:** The results of this study suggest that the DD genotype of ACE I/D polymorphism may be related to SSPE. Due to small size of this study, further studies with more patients are needed to confirm these results.

p0903

### CHRNA2: THE MISSING GENE TO BE TESTED IN INFANTILE AND NEONATAL BENIGN SEIZURES?

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**Purpose:** The actual mutational screening for Neonatal and Infantile Benign Seizures (BNFS, BFNS and BFIS) includes *KCNQ2*, *KCNQ3*, *SCN2A* and *PRRT2* genes. BNFS and BFNS families are mainly linked to *KCNQ2*, while *PRRT2* represents the major gene for BFIS cases. However, a causative gene is still lacking in about 10% of families. Differently, nicotinic acetylcholine receptor genes (*CHRNA4*, *CHRN2*, *CHRNA2*) are mainly involved in Autosomal Dominant Nocturnal Frontal Lobe Epilepsy (ADNFLE). Despite extensive studies, *CHRNA2* has been reported only in a single family, and never confirmed in large cohorts of patients with ADNFLE.

**Method:** Through a TrueSeq Custom Amplicon (TSCA) sequencing approach we screened 10 ion channel genes in patients with idiopathic epilepsies. *PRRT2* mutations were excluded by Sanger sequencing.

**Results:** TSCA revealed a heterozygous single-nucleotide substitution in *CHRNA2* gene (c.1126 C>T; p. Arg376Trp) that segregated in a family with BFIS (Trivisano et al. *Epilepsia* 2015, *in press*). Based on bio-informatics inspection, the change was predicted to be pathogenic. The investigated family includes parents and their three daughters. Seizures started between 6 and 24 months of age, they were almost in cluster and well-controlled. Outcome was good in all subjects. A second *CHRNA2* gene mutation was found in a 6-month-old girl with normal psychomotor development, diagnosed as sporadic neonatal benign seizures. Differently from the *CHRNA2* mutation associated with ADNFLE, our two mutations fall in the cytoplasmic domain. Bioinformatic structural studies are ongoing to assess to role of cytoplasmic mutations in the pathogenesis of neonatal and infantile benign seizures.

**Conclusion:** Our genetic findings open new chance in the genetic diagnosis of infantile and neonatal benign epilepsy. Further studies on patients negative for *KCNQ2*, *KCNQ3*, *SCN2A* and *PRRT2* are needed to assess the *CHRNA2* role in both neonatal and infantile benign seizures.

p0904

### INHERITED KCNQ2 DUPLICATION IN 3 PATIENTS WITH BENIGN NEONATAL SEIZURES

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**Purpose:** Benign familial partial epileptic syndromes of the 1st year of life are classified into three groups based on the age of seizure onset as neonatal (BFNS) (less than 30 days), neonatal-infantile (BFNE) (1–4 months) and infantile (after 4 months). The majority of typical BFNS families are linked to *KCNQ2* and of BFNS to *SCN2A*. Sporadic forms of BFNS are also linked to inherited or *de novo* *KCNQ2* mutations. We aimed to find genetic etiology in 5 patients with sporadic form of early benign infantile partial seizures with similar clinical and electrophysiological features.

**Patients:** The seizures characterized by apne, peroral cyanosis, stiffing of chin and blank stare occur during breast-feeding or spontaneously. The age of onset is within first 2 week for three patients and 35 and 70 days for the other two, respectively. Ictal EEG showed temporal onset in one neonate. Interictal abnormalities were in the temporal regions in all patients.

**Method:** Candidate gene screening including *SCN2A*, *KCNQ2* and *PRRT2* genes were conducted with Sanger sequencing. Patient samples were also analyzed by array CGH using a custom array targeting *KCNQ2*, *KCNQ3*, *SCN2A*, and *PRRT2* at exon resolution. *KCNQ2* qPCR assay were employed for patient and parental samples to validate CGH results.

**Results:** *SCN2A*, *KCNQ2* and *PRRT2* genes were negative for point mutations in all patients. Array CGH analysis showed inherited *KCNQ2* gene duplication in three patients with neonatal onset of seizures and the duplication was validated by *KCNQ2* qPCR.

**Conclusion:** The genetic etiology is highly correlated with the age onset of seizures but not the clinical and electrophysiological features. Though majority of reported *KCNQ2* mutations are single nucleotide alterations, there are several deletions and duplications leading to BFNS. *KCNQ2* deletions/duplications are also associated with *KCNQ2*-related neonatal epileptic encephalopathy with intellectual disability. Pathogenicity of *KCNQ2* duplication is under further investigation.

p0905

**COPY NUMBER VARIANTS IN A HOSPITAL-BASED COHORT OF CHILDREN WITH EPILEPSY***D.R.M. Vlaskamp\**, *P.M.C. Callenbach\**, *P. Rump†*, *C.M.A. van Ravenswaaij-Arts†*, *O.F. Brouwer\***\*University of Groningen, University Medical Center Groningen, Department of Neurology, Groningen, Netherlands, †University of Groningen, University Medical Center Groningen, Department of Genetics, Groningen, Netherlands***Purpose:** Copy number variants (CNVs), detected with chromosomal microarray, have been shown to cause or predispose to epilepsy. We aimed to evaluate the diagnostic yield of microarray in a large cohort of children with epilepsy and to identify novel genes and regions for epilepsy.**Method:** From a single university hospital-based cohort of children below 18 years who were treated for epilepsy, diagnosed after 2000, we included all children who had undergone microarray before May 2014. Oligonucleotide array Comparative Genome Hybridization or Single Nucleotide Polymorphisms array was performed to report CNVs of at least 4 consecutive probes on chromosome 1–22 or X. CNVs that were found in <1% of healthy controls and comprised protein-coding genes were evaluated for their pathogenicity.**Results:** Microarray had been performed in 226 of 1100 (21%) children with epilepsy. In 66% of them, symptomatic focal epilepsy was diagnosed, 60% had intellectual disability (ID), and 48% had facial dysmorphisms. In 181 children, 408 CNVs were evaluated for their pathogenicity. Twenty-seven CNVs that are known to cause or predispose to epilepsy were found in 26 (12%) children. All these children had developmental or behavioral problems, and two-third had focal epilepsy. In five children, novel CNVs comprised *NRX3* (n = 2), *SCN4B*, *MYT1L* and *UNC5D* as potential candidate genes for epilepsy.**Conclusion:** In our cohort, we found a 12% yield of microarray resulting in CNVs that cause or predispose to epilepsy, which is much higher than the 5% yield in an American cohort of 805 epilepsy patients (Olsen, 2014). This variability is probably due to the way how children are selected for microarray, based on their additional features. We identified novel CNVs with four genes of major interest for further evaluation of their role in epilepsy.**Genetics 5  
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p0906

**THE HEREDITARY FEATURES OF EPILEPSIES WITH SCNIA MUTATIONS***J. Wang\**, *H. Xu\**, *H. Meng\**, *†, L. Yu\**, *W. Liao\***\*Institute of Neuroscience and The Second Affiliated Hospital of Guangzhou Medical University; Key Laboratory of Neurogenetics and Channelopathies of Guangdong Province and the Ministry of Education of China, Guangzhou, China, †Department of Neurology, The First Affiliated Hospital of Jinan University, Guangzhou, China***Purpose:** *SCN1A* mutations have been identified in both familial and sporadic cases with epilepsy. In the majority of cases, generalized epilepsy with febrile seizures plus (GEFS+) is a familial disorder, whereas severe myoclonic epilepsy in infancy (SMEI) is mostly sporadic cases, suggesting that the phenotypes may be associated with hereditary features. We want to investigate the hereditary features and identify a possible genotype-inheritance correlation in epilepsy patients with *SCN1A* mutations.**Method:** We systematically reviewed all *SCN1A* mutation-related publications and established a database that includes 1,248 *SCN1A* mutations associated with epilepsy (<http://www.gzneurosci.com/scn1adatabase/>). A further analysis was performed to investigate the hereditary feature of each phenotype and identify a possible genotype-inheritance correlation.**Results:** This study demonstrated a negative correlation between phenotype severity of and the frequency of familial cases caused by *SCN1A* mutations; familial cases represented 83.7% of mild cases with GE (generalized epilepsy) and/or FS (febrile seizures), 62.8% of PE (partial epilepsy) and PEFS+ (partial epilepsy and febrile seizures plus) cases, 23.3% of epileptic encephalopathy cases, but only 9.8% of SME cases. Missense mutations frequency was higher in familial cases, whereas destructive mutations occurred more frequently in individuals with severe phenotypes. For different phenotypes, the penetrance of *SCN1A* mutations in GE and/or FS, PE&PEFS+ and SME was 91.0%, 94.0% and 92.2%, respectively. While the penetrance of *SCN1A* mutations for different genotypes of missense, splice-site, truncating and genomic rearrangements was 91.3%, 88.9%, 100% and 100%, respectively.**Conclusion:** The frequency of inherited mutations is related to genotype and phenotype in familial cases. The hereditary features of epilepsies with *SCN1A* mutations differed in each phenotype, and the penetrance of which didn't differ among phenotypes or genotypes. However, incomplete penetrance was associated with missense and splice-site mutations, but was not associated with truncating mutations or genomic rearrangements. These results have implications for clinical genetic counseling.

p0907

**GENETIC EVALUATION OF INTRACTABLE EPILEPSY PATIENT WITH A CUSTOM DESIGNED SCREEN PANEL REVEALED NEW PATHOLOGICAL MUTATIONS IN EPILEPSY GENES***Y. Wang, X. Xu, W. Yan, Y. Wang**Children's Hospital of Fudan University, Shanghai, China***Purpose:** Epilepsy of unknown etiology (particularly in children) posts a major challenge in clinical diagnosis and treatment. However, numerous disease relevant mutations have been detected through next generation sequencing, making custom-designed and cost-efficient target sequencing as a possible solution for clinical diagnosis. To test this feasibility we have designed a panel containing selected candidate epilepsy genes subjected for sequencing potential pathological mutations in a group of patients prone to have genetic origin in their disease onset.**Method:** A custom-made NimbleGen SeqCap EZ Choice Library (Roche NimbleGen, Madison, USA) was designed to capture the exons, splice sites and the immediately adjacent introns of 407 candidate genes selected with the key words such as epilepsy, seizure, and etc. 75 unrelated Chinese individuals (34 females, 41 males) diagnosed as epilepsy (48 IS, 9 CAE, 4 CFS, 5 EE, 1 FLE, 2 LGS, 1 PSE, 5 EP) from our hospital and their family members were studied. Data was then processed with standard analytical protocol to generate a mutation list.**Results:** 25 mutations were detected in 12 patients and validated by traditional Sanger sequencing. Among them, a number of mutations were detected for the first time for well-known epilepsy genes such as *SCN1A* (3), *CDKL5*, *STXBPI*, *POLG*, and *TSC2*. Besides, we also find mutations that are predicted to be damage to encoding protein's proper function in candidate epilepsy genes.**Conclusion:** The data indicated that, custom-designed panel sequencing is capable of identifying potential pathological genetic mutations in epilepsy patients. Besides, the data also expanded the mutation spectrum of epilepsy. In long run, it would be worth to test the behavior of the panel sequencing in large cohort.

p0908

### IDENTIFICATION AND FUNCTIONAL ANALYSIS OF MULTIPLE ISOFORMS OF EPILEPSY RELATED PROTEIN FMRP

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**Purpose:** 20% of Fragile X syndrome (FXS) patients suffer seizures during lifetime. Fragile X mental retardation protein (FMRP) is a global regulator of translation in neurons and an important factor in synaptic plasticity, absence of which results in epileptogenesis. Distinct FMRP isoforms may have important differences in their expression and function, lead to various susceptibility of epilepsy.

**Method:** We identified the transcript isoforms in the brain tissue of FVB inbred embryonic mice (E18) and adult mice (P28) respectively and compared their frequency of utilization with each other. We constructed plasmids of fusion protein coupling V5-tag with isoform proteins, analyzed the distribution of exogenous mFMRP isoforms in N1E-115, Neuro-2A and HEK-293 cell lines, observed the affection of these isoforms structure for distribution, and explored the latent function and regulation mechanism of mFMRP.

**Results:** In the whole brain tissues of E18 and P28 mice, there were five patterns of sequence alternative splicing which formed seven different mFmr1 transcript isoforms base on GT-AG rule. The mFmr1 transcript isoforms distributed diversely in different stages of neurodevelopment, which might lead to diversity of the recognition and binding functions between FMRP and RNA sequences, suiting the special features in individual developmental periods. Individual mFMRP isoform had specific characters in expression among different types of cell lines whilst all mFMRP isoforms had diversity in distribution in same cell line as well. Varying location of V5-tag in the fusion protein (either at N-terminal or at C-terminal) affected the expression and distribution of related protein isoforms.

**Conclusion:** We identified seven mFmr1 transcript isoforms lacking some important functional elements, in which it was also confirmed the diversity of distribution and expression, and the isoform six was detected for the first time. It suggested that the difference of FMRP structure contributed to the difference of its distribution and expression.

p0909

### SIMULTANEOUS IMPAIRMENT OF NEURONAL AND METABOLIC FUNCTION OF GEPHYRIN IN A PATIENT WITH EPILEPTIC ENCEPHALOPATHY

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**Purpose:** Using whole exome sequencing on a cohort of patients with epileptic encephalopathies (EE) and their unaffected parents we identified a *de novo* heterozygous missense mutation in the gene *gephyrin* (*GPHN*): c.1124G>A, p.Gly375Asp. Gephyrin directly interacts with and clusters GABA<sub>A</sub> and glycine receptors and is thereby indispensable for normal functioning of inhibitory synapses. Additionally, gephyrin catalyzes the synthesis of the molybdenum cofactor (Moco) in peripheral tissue. In this study we further wanted to explore the functional consequences of this mutation and search for extra mutations in the gene.

**Method:** We performed various functional assays to characterize the effect of this novel *GPHN* mutation and to gain further insights in the underlying pathomechanisms leading to epilepsy. We also used different targeted resequencing technologies aiming to identify additional mutations in *GPHN*.

**Results:** We showed that the mutation abolishes both functions of gephyrin without affecting the structure and folding of the protein: (a) mutant gephyrin exerts a dominant negative effect on gephyrin clustering and significantly reduces postsynaptic GABA receptor clustering and (b) the mutant protein is unable to synthesize the molybdenum cofactor which is vital for the function of molybdo-enzymes.

Genetic screenings of *GPHN* in follow-up cohorts of patients with different types of EEs did not lead to the identification of additional mutations.

**Conclusion:** We present the first patient with an infantile onset EE and a heterozygous *de novo* missense mutation in the *GPHN* gene. This alteration disrupts both functions of the protein. We suggest that the identified defect at GABAergic synapses is the mechanism underlying the patient's severe phenotype. Our findings strengthen previous associations of

*GPHN* with epilepsy and other neurodevelopmental disorders and expand the spectrum to an infantile onset EE.

#### p0910

### THE MEMBRANAL EXPRESSION LEVEL AND FUNCTIONAL ALTERATION OF *SCN1A* TRUNCATION PROTEINS ARE CORRELATED WITH EPILEPSY WITH FEBRILE SEIZURES PLUS

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**Background and purpose:** *SCN1A* mutations have been identified in patients with epilepsies with antecedent febrile seizures plus, which mainly comprise Dravet syndrome (DS), partial epilepsy with febrile seizures plus (PEFS<sup>+</sup>) and generalized epilepsy with febrile seizures plus. Our recent study has showed that the *SCN1A* truncation mutations were not only occurred in DS, but also in PEFS<sup>+</sup>. Therefore, we suspected that the membranal expression level and functional alteration of *SCN1A* truncation proteins might correlate with severity of vary phenotypes. We studied the membranal expression and the electrophysiological function in six truncated Na<sub>v</sub>1.1 mutants, which included H1848fsX1861, R1874fsX1944, R542X and W280X originated from four DS patients, respectively, and M145fsX148, S662X originated from two PEFS<sup>+</sup> patients, respectively.

**Methods:** We engineered H1848fsX1861, R1874fsX1944, R542X, W280X, M145fsX148 and S662X in the human Na<sub>v</sub>1.1 cDNA and studied their membranal expression level and the electrophysiological function by transfecting HEK293 cell lines.

**Results:** We found all of six truncation proteins can expressed on HEK293 cells membrane and cytoplasm, and the membranal expression quantity of which obviously decreased compared with wildtype Na<sub>v</sub>1.1 protein ( $p < 0.05$ ). The expression quantity on membrane of truncation protein originated from both PEFS<sup>+</sup> patients was less than that from DS ( $p < 0.05$ ). According to electrophysiological records, the shorter truncation proteins which included R542X, W280X, M145fsX148 and S662X, lead to the loss of function, while the truncation proteins with longer (H1848fsX1861 and R1874fsX1944) lead to partial loss of function.

**Conclusions:** We concluded the membranal expression level and functional alteration of *SCN1A* truncation proteins were correlated with epilepsy with febrile seizures plus.

#### p0912

### EXOME SEQUENCE IDENTIFIES A NEW MUTATION OF *PKHD1L1* IN A CHINESE FAMILY WITH CORTICAL TREMOR AND EPILEPSY

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Autosomal dominant cortical tremor and epilepsy (ADCTE) is a hereditary myoclonic epilepsy syndrome. The core symptoms of this syndrome are adult-onset hand tremor with the electrophysiological features of cortical reflex myoclonus (giant sensory evoked potential [g-SEP] and long latency reflex), myoclonus and/or generalized tonic-clonic seizures and a rather benign course. In this study, we used whole-exome sequencing to screen potentially novel causal mutations in a Chinese with ADCTE.

Two cases and one family control were subjected to exome sequencing. By a. filtering out synonymous mutations that do not affect the function of the genes, only retaining the mutation that affect the function of the genes such as non-synonymous mutations and splice site mutations; b. filtering out common mutations carrying out by normal people in the public genetic mutation database (dbSNP), the normal individual mutations that have been published, and the mutations carrying out by the control who subject exome sequencing in the experiment; then making intersection of the mutation set of the two patients, we reduce the number of candidate pathogenic mutations. By the candidate pathogenic region on chromosome 8q23.3–q24.11, we further reduce the number of the candidate pathogenic genes. And then using the software that can predict the affection the mutations can make to the function of the protein, we further filter to identify the possible mutation/gene of ADCTE. Using PCR sequencing methods, we validate the mutation identified by exome sequencing in the family to observe whether the disease phenotype is caused by the mutation. Using real-time quantitative PCR method, we test the expression difference of the pathogenic gene between ADCTE patients and normal controls. In conclusion, we identified a heterozygous mutation in underlying causal gene *PKHD1L1* in this family with ADCTE.

#### p0913

### FUNCTIONAL CORRELATES OF SEVERITY IN GLUCOSE TRANSPORTER 1 (GLUT1) DEFICIENCY

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**Purpose:** We investigated the function of *SLC2A1* variants from patients with mild and severe forms of epilepsy to develop an understanding of how combined genetic and functional assessment can be used to reveal pathophysiological mechanisms and develop precision diagnostics. *SLC2A1* accounts for approximately 1% of genetic generalised epilepsy patients and encodes the glucose transporter 1 (GLUT1) protein found in glia and the epithelium of the blood brain barrier. Very severe GLUT1 deficiency disorders, such as De Vivo disease, are associated with complete loss of GLUT1 function. However, the association between mutation severity and phenotype is less clear in the milder epilepsies harbouring GLUT1 mutations.

**Method:** A *Xenopus laevis* oocyte glucose uptake assay was employed to measure the kinetics and affinity of expressed GLUT1 transporter with a minimum  $n = 5$  for each group. This characterisation was undertaken in GLUT1 mutations from control cases and patients with two grades of clinical severity. “Unaffected” is comprised of variants found in the control population, “mild” is treatment responsive epilepsy and “severe” is characterised by refractory epilepsy and/or mild intellectual disability.

**Results:** A total of 20 variants were analysed with 11 from the mild cohort, 5 from the severe and the remaining 4 from unaffected cases. Although there was a spectrum of functional change within each group, with overlapping  $V_{max}$  and  $K_m$ 's of unaffected ( $V_{max} M = 21.35$ ,  $SEM = 2.841$ ,  $K_m M = 47.38$ ,  $SEM = 3.435$ ) with mild ( $V_{max} M = 14.18$ ,  $SEM = 2.426$ ,  $K_m M = 41.26$ ,  $SEM = 7.421$ ) and severe ( $V_{max} M = 4.417$ ,  $SEM = 2.484$ ,  $K_m$  not ascertainable), population analysis showed an overall correlation of molecular dysfunction with clinical severity (Unaffected vs. Mild  $r^2 = .826$ , Unaffected vs. Severe  $r^2 = .011$ ).

**Conclusion:** The functional genotype-phenotype correlation found in GLUT1 testing suggests that a risk model for acquiring GLUT1 disorders

could be developed by the functional profiling of a patient's variant. A better understanding of the relationship between clinical severity and GLUT1 function will provide a foundation for building our understanding of the neurobiology of GLUT1 disorders critical for diagnosis and targeted therapy.

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p0916

### USE OF FMRI TO DETERMINE LANGUAGE AND MEMORY LATERALIZATION IN EPILEPSY SURGERY CANDIDATES

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**Purpose:** Wada test is the gold standard for language lateralization, however its routine use is limited due to invasiveness. Functional magnetic resonance imaging (fMRI) is a non-invasive alternative. However standard fMRI procedures for lateralization are not established.

**Method:** We developed standardized language and memory paradigms activating language comprehension and verbal/non-verbal memory encoding via scanning healthy individuals. Until now we tested five epilepsy (two left handed) surgery candidates with left temporal lobe epilepsy to determine language and memory lateralization.

**Results:** Left handed patients had right lateralized language and memory functions. In all right handed patients we found left language dominance, however memory was lateralized to left in one patient, to right in the second one and lateralization could not be determined due to equal activation in both temporal lobes in the third patient. fMRI results were also compared with neuropsychological test battery findings.

**Conclusion:** fMRI is a safe and non-invasive alternative to Wada test. These preliminary findings suggest that it could also be efficient method for language and memory lateralization.

p0917

### CURRENT EUROPEAN PRESURGICAL DIAGNOSTIC PROCEDURES IN EPILEPSY SURGERY CENTERS

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**Purpose:** In January 2014 the E-PILEPSY project, a European Union funded project, was launched to improve awareness of, and accessibility to, epilepsy surgery across different countries in Europe. We compared the use of presurgical imaging and source localization procedures between participating centers and with guideline recommendations.

**Methods:** A survey was distributed through the E-PILEPSY consortium to collect data regarding the use of MRI, PET, SPECT with corresponding post-processing procedures, and EEG/MEG source localization in pediatric and adult epilepsy surgery patients.

**Preliminary results:** Twenty centers were included. Eighteen centers performed epilepsy surgery both on children and adults, two centers focused on either adults or children. Of the 20 centers 65% utilized a 3T MRI scanner, 35% had only access to a 1.5T system. In only 21% of adult

and 26.3% of pediatric centers all guideline recommended MRI sequences, with correct angulation and resolution, were included in the MR protocol. These recommendations include 3D T1 GRE (resolution:  $\leq 1$  mm), T2 and FLAIR axial and coronal (resolution:  $\leq 3$  mm). Use of additional sequences (mostly fMRI and DTI) is reported by 89.5% of centers. MRI post-processing (e.g. VBM/SPM, image reformatting) is performed by 65% of centers. PET is performed by 94.8% of adult and 73.7% of pediatric centers, and PET post-processing by 72.2% and 85.7% of those, respectively. SPECT is performed by 90% of centers, of which 89% perform post-processing. MEG is utilized by 45% of centers. Only 40% perform EEG source localization.

**Discussion:** There is much variation in the presurgical diagnostic work up between epilepsy surgery centers in Europe. A minority follow all MRI protocol guideline recommendations. These findings could be explained by differences in healthcare/reimbursement policies, clinical experience or expert opinion among centers. Harmonization in pre-surgical diagnostics is needed to improve selection of candidates for epilepsy surgery across Europe.

p0918

### THE EFFECT OF MEDICATION WITHDRAWAL ON EEG RELATED FMRI CONNECTIVITY PATTERNS IN FOCAL EPILEPSY

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The effect of anti-epileptic drugs (AEDs) most likely is reflected in functional brain activity recorded with EEG and fMRI. These effects may cause substantial inter-subject variability in studies where EEG correlated functional MRI (EEG-fMRI) is used to determine the epileptogenic zone in epilepsy surgery candidates. In the present study the effects on resting state fMRI measures are quantified due to withdrawal of AEDs. EEG-fMRI data were obtained of 10 patients in the condition that the patient was on the maintenance doses of AEDs as prescribed (condition A) and after withdrawal of AEDs (condition B), at the end of a video-EEG seizure monitoring session. EEG-fMRI data were analysed using both the general linear model (GLM) approach and independent component analysis. The epileptic independent component (ICE) was identified by selecting the component with the largest overlap with the EEG-fMRI correlation pattern (van Houdt et al., Brain Topogr. 2014). A similar procedure was used to select the well-known resting state networks (RSNs) (Shirer et al., Cereb Cortex 2012). Next, the difference in resting state functional connectivity (rsFC) between conditions A and B was quantified by using a GLM approach applied to the concatenated time series of the RSNs, including the ICE. EEG-fMRI correlation analysis was successful in 30% and 100% of the cases in conditions A and B, respectively. Spatial patterns of ICEs appeared to be comparable in conditions A and B, except for one patient for whom it was not possible to identify the ICE in condition A, while the global rsFC of all selected resting state components was significantly increased after withdrawal of AEDs. The results indicate that both the higher sensitivity of EEG-fMRI and the increased rsFC might be related to an increased excitability of the brain what makes resting state fMRI potentially a new biomarker for investigating AED effects.

p0919

### RAPAMYCIN TREATMENT RESTRAINS MODIFICATION OF WHOLE-BRAIN FUNCTIONAL NETWORK BACKBONE TOPOLOGY DURING TEMPORAL LOBE EPILEPTOGENESIS IN THE KAINIC ACID RAT MODEL

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**Purpose:** Focal epilepsy affects global structural and functional brain network topology. Whether these topological changes already occur during epileptogenesis and might be halted at this early stage is unknown. Rapamycin, an inhibitor of the mammalian target of rapamycin, is one of the few drugs known to reduce epileptogenesis. We aimed to determine whether rapamycin treatment modulates global functional network topological changes from serial fMRI measurements during epileptogenesis of focal epilepsy in rats.

**Method:** Temporal lobe epileptogenesis was induced with the kainic acid-based status epilepticus model in adult male rats ( $n = 12$ ; 350–450 g). The brain's functional status was longitudinally assessed with resting-state blood oxygenation level-dependent (BOLD) fMRI at days  $-7$ , 1, 4, 8, 21 and 48, in twelve rats with status epilepticus Racine's scores class IV–V. Four rats were treated with rapamycin starting 4 hours after status epilepticus (GroupRAP; 6 mg/kg i.p. daily every 24 (first week) or 48 hours). Eight rats received saline at similar intervals (GroupSALINE). Functional connectivity between various brain regions was calculated from correlation of low-frequency BOLD fluctuations. Whole-brain network backbones, based on functional connectivity values, were quantified using minimum-spanning-tree metrics. At day 48, seizures were quantified using video monitoring.

**Results:** Backbone hierarchy and leaf number significantly dropped, while network diameter increased, at day four and eight in the GroupSALINE, but not in GroupRAP, relative to the pre status epilepticus networks. Eccentricity increased from day 4–21 in the GroupSALINE. Reduced eccentricity was found in the GroupRAP at day 48. The median daily seizure frequencies ( $\pm$ interquartile range) were GroupSALINE:  $2.7 \pm 3.23$  and GroupRAP:  $0 \pm 0.3$ .

**Conclusion:** Network topology changes during epileptogenesis in rats. Rapamycin treatment diminishes these effects and directionality of these changes. Rapamycin-induced seizure reduction is associated with functional network modulation. Further research should elucidate whether this is caused by anti-epileptogenesis or seizure-load reduction.

p0920

### INFLUENCE OF SEIZURE FREQUENCY ON LONGITUDINAL MEMORY PERFORMANCE AND T2 RELAXOMETRY IN PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY AND HIPPOCAMPAL ATROPHY

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**Purpose:** To evaluate the role of seizure frequency on longitudinal memory performance and T2 relaxometry in patients with Mesial Temporal Lobe Epilepsy (MTLE) and Hippocampal Atrophy (HA).

**Method:** We performed two MRI acquisitions and neuropsychological assessments in 20 MTLE patients with frequent seizures and 24 MTLE patients with infrequent seizures. Frequent seizures were considered as, at least, one discognitive seizure per month. Infrequent seizures were considered as three or less discognitive seizures per year and no event evolving to a bilateral convulsive seizure. All images were acquired in a 3T scanner. We used a control group for T2 relaxometry comparisons. Neuropsychological assessment included: Wechsler Adult Intelligence Scale-Revised; Wechsler Memory Scale-Revised and Rey Auditory Verbal Learning Test. We performed statistical analyses in SPSS 21<sup>®</sup>, using General Linear Model for repeated measures on longitudinal analyses.

**Results:** There was a significant longitudinal increase in the mean of T2 values on the side of HA in the infrequent seizures group ( $p = 0.022$ ). However, in the frequent seizures group, the mean of T2 values was higher than the infrequent seizures group from the baseline, although there was not longitudinal difference, probably due to a “floor effect.” There were no differences related to the contralateral hippocampus. Comparing the second versus first neuropsychological assessment, the frequent seizures group had better longitudinal scores in Visual Reproduction I ( $p = 0.047$ ). The mean interval between evaluations was  $23.55 \pm 8.65$  months. Infrequent seizures group showed better longitudinal scores in general memory ( $p = 0.005$ ), delayed recall ( $p = 0.035$ ) and Visual Reproduction I ( $p = 0.042$ ). The mean interval between evaluations was  $25.75 \pm 8.99$  months.

**Conclusion:** Longitudinal increase of T2 values in infrequent seizures group suggests progressive hippocampal damage despite the low seizure frequency and better longitudinal scores on memory performance, suggesting that the frequent seizure group had a decreased ability of familiarity/learning in the second neuropsychological assessment.

p0921

### PHOTOSENSITIVITY IN IDIOPATHIC GENERALIZED EPILEPSIES: AN EEG-FMRI STUDY

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**Purpose:** The presence of reflex traits in idiopathic generalized epilepsies (IGEs) is largely known. In this study we identified the hemodynamic maps of generalized spike-and-wave discharges (GSWDs) recorded in IGE patients with photosensitivity respect with the one detected in IGEs without reflex traits. We aim to reveal differences that might be linked with the presence of photosensitivity and hence improve the knowledge of its pathogenesis.

**Method:** 34 IGEs (26 females) who underwent an EEG-functional MRI (EEG-fMRI) study with the recording of GSWDs were selected. Based on the electro-clinic data, the population recruited was divided into Group(1): IGEs with photosensitivity and Group(2): IGEs without photosensitivity. Within each IGEs sub-group, a random effect group analysis was performed, comparing Group(1) and Group(2) with a two-sample T-test.

**Results:** Group(1) included 18 patients, Group(2) 14 cases. Group(1) random effect analysis showed positive BOLD changes at the thalamus, basal ganglia, the motor cortex bilaterally and the right temporal-parietal cortex. At the group level, Group(2) showed a thalamic, left orbito-frontal cortex and bilateral occipital cortex BOLD signal increases. A two-sample T-test random analysis revealed the involvement of the motor cortex bilaterally and the right temporal-parietal cortex time-locked with GSWDs in the reflex traits group compared with the not-reflex group.

**Conclusion:** Our results showed that the GSWDs recorded in patients with photosensitivity involve distinctive cortical networks (motor

cortex). This finding might explain the different clinical features (myoclonus) observed in these patients.

**p0922**

### BRAIN MORPHOLOGY IN JUVENILE MYOCLONIC EPILEPSY AND ABSENCE SEIZURES

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**Purpose:** We evaluated the differences in brain morphology among patients with juvenile myoclonic epilepsy according to the occurrence of absence seizures.

**Method:** Twenty-one juvenile myoclonic epilepsy patients with ( $n = 6$ ) and without ( $n = 15$ ) absence seizures were enrolled. We analyzed whole-brain T1-weighted MRI using FreeSurfer 5.1. Measures of cortical morphology, such as thickness, surface area, volume, and curvature, and the volumes of subcortical structures, the cerebellum, and cerebrum were compared between the groups. Moreover, we quantified correlations between clinical variables and each measures of abnormal brain morphology.

**Results:** Compared to normal controls, patients without absence seizures demonstrated thinning of the cortical thickness in the right hemisphere, including the post-central, lingual, orbitofrontal, and lateral occipital cortex. Compared to normal controls, patients with absence seizures had more widespread thinning of the cortical thickness, including the right post-central, lingual, orbitofrontal, and lateral occipital cortexes as well as the right inferior temporal cortex. Additionally, the volume of cerebellar white matter in patients without absence seizures was significantly smaller than that in normal controls. Patients with absence seizures had a much smaller cerebellar white matter volume than normal controls or patients without absence seizures. Moreover, there was significantly positive correlation between age of seizure onset and the volume of cerebellar white matter in patients with JME.

**Conclusion:** We demonstrated that there were significant brain morphology differences in patients with juvenile myoclonic epilepsy according to the presence of absence seizures. These findings support the hypothesis that juvenile myoclonic epilepsy may be a heterogeneous syndrome.

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**p0924**

### AUTOMATIC SEGMENTATION OF DEPTH ELECTRODES IMPLANTED IN EPILEPTIC PATIENTS: A MODULAR TOOL ADAPTABLE TO MULTICENTRIC PROTOCOLS

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**Purpose:** Automating the localization of implanted depth electrodes, as well as their visualization in three-dimensional (3D) space, can greatly decrease the amount of resources needed for planning, executing and validating resection in epilepsy surgery. We present an integrated and automated image processing modular research tool that uses pre-operative

MR and post-operative CT images to accurately detect the position of each implanted electrode.

**Method:** First, an initial segmentation of different brain structures is carried out, followed by a CT to MRI rigid registration. Then, electrode contacts are segmented using a watershed transform-based algorithm followed by different image processing steps allowing for correct feature classification. Meshes of all segmented structures are generated for visualization with Slicer. An interactive tool may be used in case any mistakes in the segmentation process have been found. Finally, the MRI is normalized to the MNI space to automatically calculate the anatomical label for each contact and visualize the results on coregistered subject images.

**Results:** Data from ten patients (from two centers) have been used. The method was able to automatically detect all the electrodes in most patients, allowing an interactive refinement when the automatic approach was not totally accurate. The whole process takes around 10 minutes for each patient, in contrast to the multiple hours that an operator would take to manually localize all the contacts. Software was easily used by operators without prior image processing experience.

**Conclusion:** We propose an easy to use, novel research tool for accurately segmenting and visualizing depth electrodes in 3D space on epileptic patients. Although the method is yet to be validated, first results are promising and feedback from operators is encouraging. A connection with a tool for electroencephalography monitoring is being developed. Unlike manual localization procedures, our algorithm achieves excellent results without time-consuming and difficult judgments from an operator.

**p0925**

### 1H-MRS IN MESIAL TEMPORAL LOBE EPILEPSY WITH AND WITHOUT HIPPOCAMPAL ATROPHY

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**Purpose:** To investigate changes in proton magnetic resonance spectroscopy (1H-MRS) in relation to response to antiepileptic drugs (AED) and hippocampal atrophy (HA) in patients with mesial temporal lobe epilepsy (mTLE). We analyzed myo-inositol/creatine (Ins/Cr+PCr), N-acetyl aspartate+N-acetyl-aspartate-glutamate/creatine (NAA+NAAG/Cr+PCr), and glycerophosphocholine/creatine (GPC/Cr+PCr) as markers of cellular structural and functional alterations.

**Method:** 1H-MRS were acquired using a PRESS (Point Resolved Spectroscopy) sequence with repetition time (TR) = 2000 msec and echo time (TE) = 35 msec in a 3.0T Philips MRI scanner with a single voxel placed in the anterior portion of hippocampi. Individuals with unilateral HA or non-lesional mTLE on MRI were divided according to AED response:

- (1) *refractory with HA;*
- (2) *refractory non-lesional;*
- (3) *responders with HA,*
- (4) *responders non-lesional, and compared to*
- (5) *healthy controls.*

Metabolite were quantified ipsi- and contralateral to the EEG lateralization using LCModel. All patients with HA had concordant EEG lateralization. Metabolites from controls were defined as the mean values of right+left hippocampi. We performed statistical analyses with SPSS (Version 22.0) using MANCOVA co-varying for age with Bonferroni post hoc comparisons.

**Results:** We found a relative increase of Ins/Cr+PCr, a marker of astrocytes, in groups *refractory with HA* and *refractory non-lesional*, in the ipsilateral hippocampus, when compared to the other groups ( $p < 0.0001$ ,  $p = 0.001$  and  $p = 0.024$ ). Moreover, NAA+NAAG/Cr+PCr, a marker of neuronal damage, was reduced in group *refractory with HA* in the ipsilateral hippocampus compared to all other groups ( $p = 0.028$ ,  $p = 0.048$ ,  $p = 0.041$  and  $p < 0.0001$ , respectively). In addition, GPC/Cr+PCr, a

product of choline metabolism, was increased in the group *responders* with HA in the contralateral hippocampus compared to group *responders non-lesional*, although this finding needs further investigation.

**Conclusion:** Our findings indicate that 1H-MRS changes in mTLE appear to be related to the presence of HA rather than the pattern of AED response.

#### p0926

### MAPPING AND VOLUMETRY OF HESCHL'S GYRUS BY VBM 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 versus 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 nine patients without seizures, the HG was disrupted completely by more than two-third its volume (mean pre- vs. post-surgery volume, 2.02 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.

#### p0927

### WHITE MATTER ABNORMALITIES IN PATIENTS WITH HOT WATER EPILEPSY REVEALED BY DIFFUSION TENSOR IMAGING ANALYSIS IN A VOXEL WISE APPROACH

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**Purpose:** We investigated changes of White Matter (WM) integrity in patients with Hot water epilepsy (HWE), and their relationships with epilepsy-specific clinical factors by comparing the fractional anisotropy (FA) and the mean diffusivity (MD) maps between patients and the controls.

**Method:** We performed diffusion tensor imaging (DTI) in 100 patients with HWE and 57 controls matched for age and gender. Between-group, comparisons of DTI parameters were carried out in a whole-brain voxel-wise manner using tract-based spatial statistics (TBSS). In addition ROI based evaluation of both, FA and MD was correlated with epilepsy-specific clinical variables.

**Results:** Compared to controls, patients with HWE had significantly reduced FA and increased MD in both hemispheres, mainly in the frontal lobes, cingulum, and forceps major and minor, anterior thalamic radiation, superior longitudinal fasciculus, uncinate fasciculus, cortico-spinal tract, and inferior fronto-occipital fasciculus. HWE subgroup with family history had higher FA values in bilateral anterior thalamic radiation, cingulum (hippocampus), forceps major, inferior fronto-occipital fasciculus, right inferior longitudinal fasciculus, superior longitudinal fasciculus and uncinate fasciculus. Subgroup with frequent seizures had lower FA values in left -anterior thalamic radiation, superior longitudinal fasciculus, cingulum, inferior fronto-occipital fasciculus, uncinate fasciculus and forceps minor. Drug naïve HWE subgroup had lower FA values in bilateral anterior thalamic radiation, corticospinal tract, hippocampal, cingulate gyrus, uncinate, inferior fronto-occipital fasciculus, inferior longitudinal fasciculus, superior longitudinal fasciculus, forceps major and minor. On ROI based evaluation, MD value of the superior longitudinal fascicle and the splenium of the corpus callosum had a positive co-relation with age at onset of seizure.

**Conclusion:** Relative to healthy controls, hot water epilepsy subjects showed aberrations in several major inter-and intra-hemispheric tracts. Patients with family history of epilepsy had increased connections in the right hemisphere. The frequency of seizure, the age at onset of seizure and treatment influenced the DTI parameters.

#### p0929

### RESTING-STATE FUNCTIONAL CONNECTIVITY IN THE BABOON MODEL OF GENETIC GENERALIZED EPILEPSY

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**Purpose:** The baboon provides a natural model of genetic generalized epilepsy (GGE) that closely resembles juvenile myoclonic epilepsy. This study uses a data-driven approach to determine the intrinsic connectivity networks of epileptic (EPI) and healthy control (CTL) baboons using resting-state fMRI and assess any group-wise functional connectivity (FC) differences.

**Method:** Twenty baboons, matched for age and weight, were classified into two groups (10 EPI, 10 CTL) on the basis of scalp EEG findings. Each animal underwent one MRI session—one 5-minute resting state (rs-fMRI) and one anatomical MRI. All images were pre-processed using the most current rs-fMRI techniques. Using independent component analysis (ICA), we identified 14 unique components (i.e. networks) which were then used to characterize each network's functional connectivity. We utilized a data-driven approach to evaluate functional connectivity so that our results would not be influenced/limited by our seed selection. Each network mask was then thresholded ( $|z| > 2.3$ ), then used to assess group-wise FC differences using cluster analysis.

**Results:** Similar to human studies of GGE, the epileptic baboons demonstrated significant FC decreases in the anterior cingulate and insular cortices as well as FC increases in the network's associated with the mid-cingulate and thalamic regions. We also found significant FC increases in the motor and default mode networks. Additionally, we identified that the sensitivity (i.e. strength) and specificity (i.e. size) of the two groups' functional connectivity maps were significantly different in the visual, motor, thalamic, insular, and default mode networks.

**Conclusion:** This is the first study (using rs-fMRI) to demonstrate FC differences between EPI and CTL baboons that resemble the network differences observed in human GGE patients. However, this data-driven approach may be used to assess the effects anti-epileptic drugs on a medication naïve patient population. This approach may also inform the targeting of neurostimulation therapies in GGE patients.

### p0930

#### GRAY MATTER VOLUME REDUCTION AND ITS RELATED FACTORS IN TEMPORAL LOBE EPILEPSY

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**Purpose:** This study aimed to estimate the difference in gray matter volume (GMV) in patients with mesial temporal lobe epilepsy (MTLE) using a voxel-based morphometry (VBM), and to determine whether these changes correlate with their clinical features.

**Method:** VBM analysis of brain magnetic resonance imaging using statistical parametric mapping software (SPM8) was performed to 60 MTLE patients (30 left-sided and 30 right-sided) and 30 age- and gender-matched healthy volunteers. We also analyzed the correlations between GMV changes and clinical features of MTLE patients. We also measured entire hippocampal volumes in all patients and healthy controls.

**Results:** No significant differences between right and left MTLE groups were observed in demographic characteristics except epilepsy durations and seizure frequencies. Left MTLE patients showed significant GMV reductions in the hippocampus ipsilateral to the epileptic focus, and bilateral thalami, and putamen contralateral to the epileptic focus. More extensive GMV reductions were seen in the bilateral hemispheres of the right MTLE patients, including bilateral hippocampi, thalami, caudate nuclei, putamens, ipsilateral uncus, insula, inferior temporal gyrus, and contralateral frontal gyrus. GMV reduction in parahippocampal gyrus and middle temporal gyrus negatively correlated with seizure onset age in the right MTLE (uncorrected  $p < 0.001$ ). In the left MTLE, in contrast, only positive correlation was observed between presence of febrile seizure and GMV reduction in superior temporal gyrus (uncorrected  $p = 0.001$ ). Total hippocampal volume negatively correlated with the epilepsy duration in the right MTLE group ( $p = 0.004$ ,  $r = -0.505$ ).

**Conclusion:** Our VBM analyses revealed GMV reduction in not only hippocampi, but also extra-hippocampal regions such as thalamus and basal ganglia in MTLE patients. Epilepsy duration was related to the total hippocampal volume.

### p0932

#### ACCURACY OF ARTERIAL SPIN-LABELED MRI PERFUSION IN DETECTING THE EPILEPTOGENIC ZONE IN PATIENTS WITH DRUG-RESISTANT NEOCORTICAL EPILEPSY: COMPARISON WITH ELECTROPHYSIOLOGICAL DATA, STRUCTURAL MRI, SISCOM AND FDG-PET

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**Purpose:** Locating the epileptogenic zone (EZ) in patients with neocortical epilepsy presents major challenges. We aimed to assess the accuracy of arterial spin-labeling (ASL), an emerging noninvasive MRI-perfusion technique, in locating the EZ in patients with drug-resistant neocortical epilepsy.

**Method:** 25 consecutive patients with neocortical epilepsy referred to our presurgical epilepsy unit underwent a standardized evaluation including video-EEG monitoring, structural MRI, subtraction ictal SPECT co-registered to MRI (SISCOM), and FDG-PET studies. We included an ASL sequence in the MRI studies. We classified areas of hypoperfusion or hyperperfusion on ASL into 15 anatomic-functional cortical regions, comparing these regional CBF maps with the EZ determined by the other tests, and assessing the strength of concordance with the kappa coefficient. We used the EZ determined after the overall consensus from the different non-invasive evaluations (electrophysiological data, structural MRI, SISCOM and FDG-PET) to calculate the sensitivity, specificity and accuracy of ASL.

**Results:** Of the 25 patients (16 (64%) women; mean age, 32.4 [ $\pm 13.8$ ] years), 18 (72%) had lesions on structural MRI. ASL abnormalities were seen in 15 (60%) patients (nine hypoperfusion, six hyperperfusion). ASL had a very good concordance with FDG-PET ( $k = 0.84$ ), a good concordance with structural MRI ( $k = 0.76$ ), a moderate concordance with video-EEG monitoring ( $k = 0.53$ ), and a fair concordance with SISCOM ( $k = 0.28$ ). ASL had 71.43% sensitivity, 100% specificity, and 76% of accuracy, when compared with the overall consensus.

**Conclusion:** ASL might help to determine the location and extent of the EZ in the presurgical workup of patients with drug-resistant neocortical epilepsy.

### p0933

#### COMPLEX NEUROVASCULAR REACTIVITY IN PATIENTS WITH PARTIAL EPILEPSY

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**Purpose:** Complex neurovascular activation by transcranial Doppler (TCD) is not presented at the moment in patients with partial epilepsy. The objective of this study is to assess the neurovascular activation to complex visual stimulation of patients with partial epilepsy during inter ictal period.

**Method:** Twenty-four patients with partial epilepsy at least 10 days later after last epileptic attack and 75 healthy subjects were screened for this study during the last year in our Neurosonology laboratory. We performed transtemporal TCD recordings from the P2-segments of both posterior cerebral arteries (PCA) simultaneously during complex visual stimulation. The individual reactivity was defined with a relative increase of the blood flow velocities as a percentage change of the baseline values.

**Results:** Most of the patients have an epileptic focus on the temporal lobe documented by the EEG. The Doppler data of the epileptic sides and non-epileptic sides were analysed separately in patients. The complex visual reactivity was significantly higher at the epileptic side in the patients (52.5%) from those of the controls (43.6%) ( $p = 0.034$ ), although the difference between the non-epileptic side of the patients (40.1%) and controls (46.0%) was not significant ( $p = 0.14$ ).

**Conclusion:** In contrast to the earlier reports of the studies which was found diminished neurovascular reactivity to simple visual stimulation using TCD, our study showed the temporal and occipital region perfused by PCA of the patients with partial epilepsy have hyperactive neurons at the epileptic side during the inter ictal period when comparing with the healthy subjects.

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p0934

### CAN T2/ FLAIR SIGNAL INTENSITY RATIOS OF THE HIPPOCAMPUS WITH THAT OF IPSILATERAL INSULAR, CINGULATE AND FRONTAL CORTICES OBVIATE THE NEED FOR T2 RELAXOMETRY IN EVALUATING TLE?

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**Purpose:** To find out, if the signal intensity ratios of the hippocampus with ipsilateral insular cortex, cingulate gyrus and the frontal cortex have a positive correlation with elevated T2 relaxometry values in histopathologically proven cases of unilateral hippocampal sclerosis.

**Methods:** MR Images of 44 consecutive patients with histopathologically proven unilateral hippocampal sclerosis, who had undergone ATL after pre surgical work up from Jan 2008, were retrospectively analyzed. Signal intensity ratios on FLAIR and T2 coronal sequences were determined for the hippocampus with the respective ipsilateral cingulate gyrus, insular cortex and frontal cortex. Similar signal intensity ratios were obtained on the contralateral side (normal) which acted as controls. These ratios were compared with T2 relaxometry values of the hippocampus on each side at the same level.

**Results:** Mean hippocampal signal intensity ratios on FLAIR sequences of the abnormal side with the cingulate, insula and frontal cortex were 1.24, 1.21 and 1.39 respectively. The same on the normal side were 1.07, 1.05 and 1.21. On T2 weighted sequences the signal intensity ratios of the abnormal side were 1.36, 1.29 and 1.56 and the normal side were 1.1, 1.08 and 1.27. Statistically significant difference was noted on both T2 and FLAIR sequences between the normal and abnormal sides ( $p < 0.0001$ ). Mean T2 relaxometry values were 138.4 ms and 110.3 ms for the abnormal and normal sides respectively. Pearson correlation coefficient of 0.46 was noted with the T2 relaxometry values on FLAIR and 0.49 on T2 in the abnormal sides.

**Conclusion:** The insula and the limbic structures have higher signal intensity compared to neocortex, due to differences in cortical lamination. Signal intensity ratios help in diagnosis of hippocampal sclerosis, and with moderate positive correlation to T2 relaxometry values, may be used instead of the time intensive relaxometry sequence in evaluating TLE.

p0935

### FDG-PET AND MRI COREGISTRATION IN MRI-SUBSTRATE NEGATIVE REFRACTORY EPILEPSY

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**Purpose:** Utility of F-18 Fluorodeoxyglucose (FDG) Positron Emission Tomography (PET) and MRI coregistration for detection of the epileptogenic zone in MRI-substrate negative (SN) refractory epilepsy (RE).

**Methods:** 35 patients undergoing pre-surgical evaluation for RE with non-localizing/ normal MRI were included in the study. The pre-surgical evaluation in these patients included resting brain FDG-PET and FDG-PET/MRI fusion in all. Hypometabolism was visually interpreted on both studies and compared with the presumed epileptogenic zone on

electroclinical studies including vEEG and MEG. The MRI was then reviewed by the neuroradiologist for lesion definition corresponding to the area of focal hypometabolism. 15 patients with concordance for localization of epileptogenic zone on electroclinical and fusion PET/MRI further underwent surgery and were followed up for 1 year.

**Results:** Hypometabolism on FDG-PET and PET/MRI coregistration was identified in 24 (68.5%) patients. Hypometabolism detected by PET/MRI was located in the same hemisphere as indicated by the electroclinical study in 62% (15/24) of patients and localized to the same focus in 37.5% (9/24) patients. Re-evaluation of MRI in these patients subsequently revealed abnormality in 41.6% (10/24) of patients. Surgical outcome was evaluated at 1 year post-op for the 15 patients undergoing epilepsy surgery-70% had an Engel 1 outcome, 20% Engel 2 and 10% Engel 3.

**Conclusion:** PET/MRI coregistration is a useful non-invasive investigation that can be included in the pre-operative evaluation of intractable epilepsy, especially in MRI SN cases. Subsequent surgery in these cases is associated with good surgical outcomes.

p0938

### UTILIZATION OF FMRI IN PATIENTS WITH EPILEPSY AND RIGHT HEMISPHERIC DOMINANCE

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**Purpose:** fMRI and Wada findings are discordant in 40%–51% in right sided or bilateral language lateralization. Our aims were: A) To evaluate the concordance of language lateralization between fMRI and Wada tests in patients with epilepsy and right sided language. B) To compare the distribution of language activation and contralateral language representation as detected with fMRI and Wada.

**Method:** Medical charts of patients with intractable epilepsy who underwent Wada and fMRI to evaluate language dominance were reviewed. Patients with right hemispheric language dominance as determined with Wada test were included. Data included demographics, past medical history, information about Wada and fMRI results, intraoperative cortical mapping findings and outcomes of surgery.

**Results:** Eight patients (6 male, 2 female, age range: 21–46 years) had right hemispheric language dominance as detected with Wada and underwent fMRI. Five patients had right-handedness, two had left-handedness, and one was ambidextrous. Wada language protocol consisted of naming, comprehension, reading, and repetition tests. Mutism, aphasia, and paraphasia with right sided amygdala injection was recorded. fMRI protocol to evaluate language included category fluency and word generation tasks. Regions of activation in the inferior and middle frontal gyri, temporal and parietal lobes were included in the evaluation of laterality. Of the six patients with right hemispheric language lateralization with Wada test, four showed bilateral frontal activation with right dominance on fMRI and two showed right sided activation.

**Conclusion:** The results of fMRI compared to Wada was concordant in all cases. fMRI results however were not similar to that of Wada, functional maps revealed activation in contralateral language areas that was undetected with Wada. These regions might represent non-critical areas or provide more information about language distribution. Concurrent use of fMRI and Wada in language assessment has potential to enhance surgical planning and prediction of postoperative language changes.

p0939

### RELATING COGNITIVE ADVERSE EVENTS OF ANTI-EPILEPTIC DRUGS TO FUNCTIONAL NETWORK EFFICIENCY

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**Purpose:** Cognitive adverse events (CAE), such as mental slowing, often arise when antiepileptic drugs (AEDs) are prescribed to treat patients with epilepsy. To get more insight in the mechanisms of these adverse events, the relation between graph theoretical measures derived from resting state fMRI, AED use, and cognitive function was investigated.

**Method:** Two groups of patients with epilepsy with a different risk at developing CAE were included: a “low risk” group (30 patients using lamotrigine or levetiracetam) and a “high risk” group (17 patients using topiramate or phenytoin). A Computerized Visual Searching Task was used to measure mental slowing. The results were compared with norm scores based on age, sex, and global cognitive performance, resulting in a dichotomous variable “with” or “without” problems (CAE score). Brain connectivity was assessed using 3.0T resting state fMRI scans. Linear regression analysis was applied to test whether graph measures (normalized clustering coefficient and global efficiency) can be associated with AED use and cognitive functioning, with as covariates risk group, CAE score, the interaction between risk group and CAE score, age, and epilepsy severity score.

**Results:** CAE were observed in 43% of the low risk group and in 53% of the high risk group, hinting at a survivor effect in the high risk group. The clustering coefficient was lower in patients with than without CAE ( $p = 0.03$ ), and also lower in high risk compared with low risk patients ( $p = 0.04$ ). No significant associations were found between the global efficiency and risk group or CAE score. Results were robust over a sparsity range of 0.1–0.6.

**Conclusion:** Both CAE and the use of AEDs with a high risk on CAE can be associated with decreased brain network efficiency. Further research is needed to better characterize the relationship between AED use, network efficiency and cognitive adverse events.

p0940

### DISTINCT WHITE MATTER INTEGRITY IN GLUTAMIC ACID DECARBOXYLASE AND VOLTAGE-GATED POTASSIUM CHANNEL-COMPLEX ANTIBODY-ASSOCIATED LIMBIC ENCEPHALITIS

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**Purpose:** Autoantibodies against glutamic acid decarboxylase (GAD) and the voltage-gated potassium channel (VGKC)-complex are associated with distinct subforms of limbic encephalitis (LE) regarding clinical presentation, response to therapy, and outcome. Volume and signal changes of mesiotemporal structures are well-known characteristics on MRI. However, studies investigating white matter changes in LE are lacking. We aimed to assess these changes by means of diffusion tensor

imaging (DTI) in LE associated with GAD antibodies (GAD-LE) and LE associated with VGKC-complex antibodies (VGKC-LE).

**Method:** DTI data was obtained in 14 patients with GAD-LE and 16 patients with VGKC-LE and compared with age- and gender-matched control groups. Voxelwise statistical analysis of fractional anisotropy (FA) and diffusivity parameters was carried out using tract-based spatial statistics (TBSS). Results were furthermore compared with those of 15 patients with unilateral histologically confirmed hippocampal sclerosis (HS).

**Results:** We found widespread changes of FA and all diffusivity parameters in GAD-LE, whereas no changes were found in VGKC-LE. The changes observed in GAD-LE were even more extensive compared to the HS group, although the disease duration was markedly shorter in GAD-LE. Tract-specific FA analysis revealed the most prominent changes in the uncinate fasciculus in GAD-LE.

**Conclusion:** The present study provides further evidence that LE features clearly distinct imaging characteristics depending on the associated antibody by showing widespread white matter changes in GAD-LE and preserved white matter integrity in VGKC-LE. Furthermore, our results contribute to a better understanding of the specific pathophysiological properties in these two LE subforms by indicating that GAD-LE shows widespread affections of gray and white matter across various regions of the brain, whereas in VGKC-LE, the inflammatory process seems to be more localized, primarily affecting mesiotemporal gray matter.

p0941

### SOURCE STRENGTH OF HIGH-FREQUENCY OSCILLATION IS A POTENTIAL IMAGING BIOMARKER OF SEIZURE SEVERITY IN ABSENCE EPILEPSY

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**Purpose:** The discovery of high-frequency oscillations in the brain has had a profound impact on our understanding of epilepsy. The objective of this study was to quantify the clinical correlates of interictal and ictal brain activities from low- to very-high-frequency ranges in childhood absence epilepsy (CAE).

**Methods:** Twelve patients with clinically diagnosed drug-naïve CAE were studied with a 275-channel whole head magnetoencephalography (MEG) system. MEG data were digitized at 6000 Hz and analyzed in nine frequency bands: delta (1–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta (12–30 Hz), low-gamma (30–55 Hz), high-gamma (65–90 Hz), ripple (90–200 Hz), high-frequency oscillation (HFOs, 200–1000 Hz) and very-high-frequency oscillations (VHFOs, 1000–2000 Hz). MEG sources were volumetrically localized with accumulated source imaging.

**Results:** In comparison with interictal neuromagnetic activities, ictal neuromagnetic activities had significantly higher odds of occurrence in the medial prefrontal cortex (MPFC) in bands of 1–4 Hz, 4–8 Hz and 30–45 Hz. This was also seen in the parieto-occipito-temporal junction (POT) in bands of 1–4 Hz, 4–8 Hz, 8–12 Hz and 12–30 Hz. Ictal activity in 30–45 Hz, 55–90 Hz and 200–1000 Hz showed a trend of elevation as compared with interictal activity. There were significant correlations between the number of daily seizure episodes and source strength of ictal activity in bands of 4–8 Hz ( $r = 0.587$ ,  $p < 0.05$ ), 90–200 Hz ( $r = 0.640$ ,  $p < 0.05$ ) and 200–1000 Hz ( $r = 0.734$ ,  $p < 0.01$ ).

**Conclusion:** The results suggest that neuromagnetic HFOs (200–1000 Hz) are a potential neuroimaging biomarker of clinical seizure

severity. The magnetic sources support that there are focal cortical areas responsible for absence seizures.

**p0942**

### MULTI-FREQUENCY NEUROMAGNETIC ANALYSIS REVEALED THE DEFAULT MODE NETWORK IMPAIRMENT IN ABSENCE EPILEPSY

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**Purpose:** The default mode network has been shown to be selectively impaired during epileptic seizures associated with loss of consciousness. This study aimed to characterize neuromagnetic signatures and clinical correlates of interictal and ictal brain activities from low- to very-high-frequency ranges in childhood absence epilepsy (CAE).

**Methods:** Twelve patients with untreated clinically diagnosed CAE were studied with a 275-Channel high sampling rate MEG system. Neuromagnetic data were systematically analyzed in nine frequency bands: delta (1–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta (12–30 Hz), low-gamma (30–55), high-gamma (65–90 Hz), ripple (90–200 Hz), high-frequency oscillations (HFOs, 200–1000 Hz) and very-HFOs (VHFOs, 1000–2000 Hz). MEG sources were volumetrically localized with accumulated source imaging.

**Results:** The peak 2–3 sources were mainly localized in the medial prefrontal cortex (MPFC), the precuneus (PC) and the parieto-occipito-temporal junction (POT), which were the well-known nodes of the default mode network. In comparison with interictal neuromagnetic activities, ictal neuromagnetic activities had significantly higher odds of occurrence in the MPFC in bands of 1–4 Hz, 4–8 Hz and 30–45 Hz. This was also seen in the POT in bands of 1–4 Hz, 4–8 Hz, 8–12 Hz and 12–30 Hz.

**Conclusions:** CAE has significantly focal aberrant brain activity that can be noninvasively detected. The interictal and ictal activities in CAE are spatially concordant in high-frequency ranges (>90 Hz). The nodes of default mode network was selectively impaired in absence seizures. HFOs may help to explain phenotypic variability in CAE patients.

**p0943**

### 7T EX VIVO MRI OF TYPE II FOCAL CORTICAL DYSPLASIA: DIFFERENTIATION BETWEEN LESIONS AND PERILESIONS BY EVALUATION OF T2-WEIGHTED SIGNAL INHOMOGENEITY

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**Purpose:** The effectiveness of epilepsy surgery largely depends on the correct identification and removal of the epileptogenic lesion, but their presurgical identification on MRI is often difficult, especially for Focal Cortical Dysplasia (FCD) type IIa. Our purpose is to verify the potentiality of ex-vivo high-resolution MRI to improve the detection of type II FCD.

**Method:** Surgical specimens from patients with histological diagnosis of FCD type II (IIa, n = 2 or IIb, n = 4), after fixation (PFA 4%) were embedded in 6% agarose. A high-resolution T2-weighted sequence was acquired by a 7T-MRI scanner with the following parameters: TE = 60 ms, TR = 6.5 s, NA = 24, resolution: 50 × 50 × 700 mm<sup>3</sup>. Homogeneity and contrast maps were obtained by texture analysis. Regions of interest were manually delineated in lesions and perilesions according to histology. The mean and coefficient of variation (CV) of the signal, and the mean homogeneity and contrast were computed in each region.

**Results:** MRI signal alterations were visible in all the FCD IIb cases and in one FCD IIa case. The mean signal was significantly reduced in FCD IIb cortical lesions compared to cortical perilesions, while WM lesions were generally hyperintense. In IIa cases, only the lesions identified by visual inspection were hypointense. The CV was significantly increased in the cortical lesions of all the cases, even in one specimen where no lesion was identified by visual inspection. The CV was reduced in hyperintense WM lesions and slightly increased in WM lesions without signal hyperintensity. Texture parameters showed no significant difference.

**Conclusion:** While the mean signal intensity allowed to detect only the visually identifiable lesions, the CV was altered also in apparently isointense lesions. These preliminary results, if confirmed by a correlation study including co-registration between MRI and histology, could be translated to clinical practice when a sufficient spatial resolution will be achieved.

## Neuropsychology 3 Tuesday, 8th September 2015

**p0944**

### MEMORIES ARE MADE OF THIS: DETERMINANTS OF IMPAIRED AUTOBIOGRAPHICAL MEMORY IN EPILEPSY

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**Purpose:** Autobiographic memory catalogues the events experienced by an individual across the lifespan, forming the basis of self-identity and psychological wellbeing. Deficits in autobiographic memory are common in patients with epilepsy, and are also associated with psychiatric disturbances such as depression. This study investigates the antecedents of autobiographic memory impairments in epilepsy patients with early (childhood/adolescence) versus late (adulthood) disease onset. It is hypothesised that impairments in people with onset during the critical neurodevelopmental period of childhood/adolescence will be linked to epilepsy-related factors. In contrast, impairments in those with later onset will be more strongly related to psychiatric factors, such as depressive symptoms.

**Method:** Eighty-five adult patients with focal epilepsy were recruited to the study between 2010–2014 from the Comprehensive Epilepsy Programme at Austin Health, with their performances on cognitive and psychiatric measures compared to that of 72 healthy controls. Predictors of autobiographic memory impairment were contrasted between patients with early (n = 43) versus late (n = 42) onset.

**Results:** Epilepsy patients performed significantly worse on indices of both semantic and episodic autobiographic memory and had significantly higher rates of depressive symptoms and disorder than controls ( $p < 0.001$ ). Reduced autobiographic memory in epilepsy patients with early onset was associated with more frequent seizures, young age at onset, and reduced working memory. In contrast, late onset patients' difficulty in recalling autobiographic information was largely associated with depression and the presence of a MRI-identified lesion.

**Conclusion:** This study reveals that autobiographic memory deficits in patients with epilepsy have differing antecedents depending on the timing of disease onset. While neurobiological factors strongly underpin reduced autobiographical recall in early onset epilepsy, psychological difficulties play a role in the impairments of later onset patients. More broadly, these findings support the use of subtyping patients according to distinct clinical characteristics to find individualised predictors of cognitive outcome.

p0945

### SOCIAL COGNITION IN EPILEPSY

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**Purpose:** we aims to evaluate as social cognition can be impaired in Frontal lobe epilepsy (FLE) and Generalized Idiopathic epilepsy (IGE). We evaluate Theory of mind (ToM), as the ability to understand and predict behaviors, intentions and emotions of others, cognitive flexibility, the decision-making and its impact on the quality of life.

**Methods:** this is a case-control study of adults patiens with (FLE) and (IGE), whith IQ > 85 and without relevant comorbidity. Subjects completed a questionnaire about quality of life (QOLIE-31) and ToM task: Faux-Pas, Eyes-Test, understanding of false beliefs, Happé stories, Facial emotion recognition, Iowa-Gambling-Task and Wisconsin-Card-Sorting-Test.

**Results:** we study 100 subjects (30 FLE, 20 IGE and 50 controls). Average age:38 ( $\pm 12$ ) [18–65] years old. FLE patiens showed lower performance in ToM than IGE and controls. (Faux-Pas, Eyes-test, Wisconsin-perseverations:  $p < 0.001$ ; understanding of false beliefs, Happé stories:  $p < 0.001$ ; Facial emotion recognition:  $p = 0.003$ )

We observed a tendency in the concern about the disease and the social cognition as factors of bigger negative impact on the quality of life of FLE as compared with IGE). Women with FLE showed lower performance in the emotional state than IGE ( $p = 0.02$ ) And men concerns about future seizures and driving were the two limiting factors in FLE compared to IGE.

**Conclusion:** FLE patients have higher impairment in ToM and less cognition flexibility the IGE. Concerns about the disease and the social cognition are the most negative impact factors on the quality of life.

p0947

### COGNITIVE FUNCTIONING IN AICARDI SYNDROME

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**Background:** Aicardi syndrome is a rare neurodevelopmental disorder. The main diagnostic features are agenesis of corpus callosum, chorioretinal lacunae, and infantile spasms. The outcome is in general severe, with poor cognitive development and difficult-to-treat epilepsy.

The disorder is only observed in females and in males with chromosome 47, XXY.

**Purpose:** Cognitive investigation of girls with Aicardi syndrome.

Six females aged 7–27 years with the diagnosis of Aicardi syndrome were identified in Norway in an epidemiologic study. Five of these were cognitively investigated.

**Method:** Wineland-II Adaptive Behavior Scales, Survey interview, Bayley Scales of Infant and Toddler Development, WPSSI-R, Weschler Intelligence Scale for Children, fourth edition, and some additional tests were used. The cognitive screening was adjusted to the individual level of functioning.

**Results:** Three were diagnosed with F 73 Profound mental retardation, one with F 71 Moderate mental retardation, and one with F 70 Mild mental retardation (ICD-10). The four with the most severe mental retardation (F 73 anf F 71) all had epilepsy, and the one with mild mental retardation (F 70) did not have epilepsy.

The girls with profound mental retardation gave few communicative responses. They all used wheelchairs and had a gastric feeding tube because of poor food consumption.

The girl with moderate mental retardation used up to three words herself at the age of 6 years and was able to follow simple verbal instructions.

The girl with mild mental retardation could follow normal conversations on a simple level at the age of 13 years, although with short sentences and a limited vocabulary. She could also read and write.

**Conclusion:** The neurocognitive level varied in the group, from profound mental retardation to mild mental retardation. The girl without epilepsy had a far better neurocognitive level of functioning than the girls with epilepsy.

p0948

### EXECUTIVE FUNCTIONS IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): COMPARISON WITH ADHD ASSOCIATED WITH ROLANDIC EPILEPSY OR ROLANDIC SPIKES

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**Purpose:** Attention-deficit/hyperactivity disorder (ADHD) is commonly associated with pediatric epilepsy. Both the high prevalence of epileptiform abnormalities in children with ADHD and prevalent ADHD diagnosis preceding the first seizure in children with epilepsy suggest a bidirectional relationship between these two disorders. We aimed to explore the possible neuropsychological differences between ADHD and ADHD associated with Benign Rolandic Epilepsy (ADHD-BRE) and ADHD associated with Rolandic Spikes (ADHD-RS).

**Method:** Ninety-eight children (25 female), aged between 6 and 12 (mean age:  $8.06 \pm 1.46$ ) years, diagnosed with ADHD according to the DSM-IV-TR criteria were recruited. The neuropsychological data of children diagnosed as ADHD ( $n = 52$ ) with normal EEG were compared to children with ADHD-RS ( $n = 25$ ) and to ADHD-BRE ( $n = 21$ ). All subjects were given a neuropsychological test battery including Wechsler Intelligence Scale For Children-Revised (WISC-R), Wisconsin Card Sorting Test (WCST), Stroop Task, Visual Span subtests of Wechsler scales, Category Naming Test, and Phonemic Verbal Fluency Task.

**Results:** Total, verbal and performance IQ scores of WISC-R were not statistically different between the groups. Vocabulary ( $F = 5.10$ ;  $p = 0.008$ ) and digit span ( $F = 10.80$ ;  $p = 0.000$ ) subtests of WISC-R and failure to maintain set score ( $F = 3.45$ ;  $p = 0.036$ ) of WCST were different between the groups. ADHD cases had a lower Digit Span score (mean $\pm$ SD:  $8.25 \pm 2.03$ ) compared to the children with BRE ( $10.65 \pm 2.52$ ) and RS ( $10.33 \pm 2.82$ ). Children with ADHD had significantly higher vocabulary subtest scores compared to the group with

ADHD-RS (mean±SD 11.32 ± 2.27; 9.75 ± 2.33). Failure to maintain set scores of WCST in ADHD group were higher compared to subjects with ADHD-BRE (mean±1.83 ± 1.55; 0.84 ± 0.96).

**Conclusion:** We found significantly low digit span score in ADHD group compared to patients with BRE or RS. Digit span performance in ADHD was linked to a locus and low digit span performance was suggested to be an endophenotype. ADHD might have a different pathogenetic process compared to the ADHD associated with BRE or RS.

#### p0951

### THE ROLE OF POSITIVE ILLUSIONS IN ADJUSTMENT TO EPILEPSY AND EXPECTATIONS OF SURGERY

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**Purpose:** It is well-established that humans use a complex system of cognitive biases or “positive illusions” that foster emotional wellbeing and subjective quality of life. These include an inflated assessment of one’s abilities and personal control over life events. This study aimed to examine the role of positive illusions in patient adjustment to epilepsy and expectations of surgical treatment. We hypothesised that a failure to generate positive illusions about epilepsy would be associated with poorer adjustment, reflected by lower mood and HRQOL. This, in turn, would increase the gap between patient perceptions of their current life and the life they expect after surgery, leading to inflated expectations of surgery.

**Method:** Participants included 90 patients (58% female; mean age = 41 years, SD = 13; mean FSIQ = 101, SD = 13) with drug-resistant focal epilepsy (76% temporal focus; mean seizure onset = 21.5 years, range = 1–63) admitted to our Comprehensive Epilepsy Program for surgical characterisation. We purpose-built an interactive computer program to comprehensively assess the experience of living with epilepsy and expectations of surgery, and assessed mood and HRQOL using standardised questionnaires.

**Results:** A hierarchical cluster analysis identified 54% of patients with positive illusions about their epilepsy, including believing they could control it and feel proud about it. Patients with no illusions (46%) reported higher levels of depression ( $p < 0.01$ ) and anxiety ( $p < 0.05$ ), and lower levels of HRQOL ( $p < 0.05$ ). They also endorsed increased expectations of post-surgical life relating to personal, social and medical outcomes ( $p < 0.05$ ). Patient groups showed no differences on clinical or socio-demographic variables.

**Conclusion:** Positive illusions can be disrupted in epilepsy, negatively impacting a patient’s sense of self and control over life events, lowering mood and HRQOL. Paradoxically, this can increase expectations of life after surgery and may heighten the risk of post-operative adjustment difficulties, highlighting the need to address psychological processes underpinning patient adjustment to epilepsy before surgery.

#### p0952

### ALTERED SELF-IDENTITY AND AUTOBIOGRAPHIC MEMORY IN EPILEPSY

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**Purpose:** Research suggests that individuals with chronic epilepsy display differences in their self-identity. The mechanisms by which self-

identity is altered, however, are not well understood. Neural networks supporting autobiographic memory retrieval in the mesial temporal (MT) lobe are thought to be fundamental to self-identity processes. Thus, we examined differences in self-identity and autobiographic memory in patients with either MT or non-mesial temporal (NMT) foci with early or late age of habitual seizure onset.

**Method:** Participants included 102 adults; 51 healthy individuals and 51 patients with drug-resistant focal seizures (19 MT, 32 NMT). We used the Ego Identity Process Questionnaire to profile the identity development of participants, and examined how this related to memory function assessed using the Autobiographical Memory Test.

**Results:** Patients and controls had strikingly different self-identity profiles, with early onset MT patients showing the least identity development compared to controls and other patient groups. In contrast, late onset NMT patients showed the highest level of identity development of the patient groups and closely resembled healthy controls ( $p < 0.05$  for all comparisons). For all MT patients, poor autobiographic memory retrieval was correlated with altered self-identity ( $p < 0.001$ ). No associations between autobiographic memory and self-identity were evident in the NMT group.

**Conclusion:** Self-identity in epilepsy may be modulated by the extent to which seizure foci impinge upon the autobiographic memory network and the timing of seizure onset. Early disruption to the autobiographic memory network may constitute a neurocognitive mechanism by which self-identity is altered in chronic focal epilepsy.

#### p0953

### ACCELERATED LONG-TERM FORGETTING, RETROGRADE AUTOBIOGRAPHICAL MEMORY LOSS, AND DEPRESSED MOOD IN GLUTAMIC ACID DECARBOXYLASE ANTIBODY POSITIVE LIMBIC ENCEPHALITIS

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**Purpose:** To describe the course of clinical and neuropsychological symptoms in a patient with previously unrecognized glutamic acid decarboxylase (GAD) antibody related limbic encephalitis.

**Method:** Case report of a 35-year old male patient complaining about severe anterograde and retrograde memory problems after two breakdowns with confusion of unknown etiology who underwent thorough diagnostics and treatment at our epilepsy center after various practitioners and clinics had suggested different etiologies such as a psychosomatic condition, burnout, depression or dissociative amnesia.

**Results:** The patient presented with emotional instability and depressed mood. Retrograde autobiographical memory loss spanned the preceding 3 years and was characterized by loss of emotional attachment and auto-noetic consciousness. Anterograde memory functions were compromised by accelerated long-term forgetting. Standardized neuropsychological assessment indicated selectively impaired figural memory performance. Extended diagnostics confirmed accelerated forgetting of previously learned and retrievable verbal material. Structural MRI revealed bilateral swelling and hyperintensities of temporomesial structures, more prominent in the left hemisphere. Volumetry confirmed an enlargement of the left amygdala. Video-EEG registered a left temporal epileptic focus and a subclinical but no overt seizure. Clinical findings and positive antibody tests in serum and liquor led to the diagnosis of GAD antibody positive limbic encephalitis. Monthly steroid pulses over a 6 month-period led to recovery of subjective memory and to intermediate improvement but subsequent decline of objective material-specific memory performance. During the course of immunotherapy the patient reported de novo paroxysmal non-responsive states which completely remitted under subsequent antiepileptic treatment. At the final visit stepwise vocational reintegration was successfully in progress.

**Conclusion:** Amygdala swelling, retrograde autobiographic memory loss, accelerated long-term forgetting and emotional instability may serve as indicators of limbic encephalitis even in the absence of overt epileptic seizures. The monitoring of such patients calls for a standardized and concerted multilevel diagnostic approach with repeated assessments.

**p0954**

#### HEALTH RELATED QUALITY OF LIFE IN PATIENTS ADMITTED FOR VIDEO-EEG MONITORING DIAGNOSED AS EPILEPSY OR PSYCHOGENIC NON-EPILEPTIC SEIZURES

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**Purpose:** We sought to determine the health related quality of life (HRQL) in patients who are admitted for video/EEG monitoring and diagnosed as epileptic seizures or psychogenic non-epileptic seizures (PNES) according to information obtained from the histories, physical and neurological examinations and investigations for differential diagnosis.

**Method:** Consecutive 125 adult patients admitted for video/EEG monitoring and diagnosed as epilepsy (64) or PNES (54) were assessed using The World Health organization quality of life (WHOQOL)-BREF questionnaire. Additionally, psychiatric comorbidities were diagnosed using structured clinical interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV). Seven patients were excluded (3 because of diagnosed as both epilepsy and PNES and 4 because of diagnosed as syncope).

**Results:** The two groups were similar in terms of age, personal and family history, marital status, educational level and vocational features. Patients with epilepsy and PNES were found to have similar HRQL in physical, psychological, social and environment domains. However, the percentage of concomitant psychiatric disease diagnosis was higher in patients with PNES than patients with epilepsy (68.5%, 18.1%, respectively;  $p < 0.05$ ).

**Conclusion:** This study suggests that HRQL is affected in patients with PNES as in patients with epilepsy, however, the concomitant psychiatric disease is more frequently encountered in PNES group. We think that a better understanding of the impact of PNES manifestations and epilepsy would help to provide appropriate clinical, psychological and social care.

## Others 5

**Tuesday, 8th September 2015**

**p0955**

#### TLAZOLTEOTL THE AZTEC GODDESS OF EPILEPSY

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**Purpose:** The historical allure of epilepsy transcends academic circles and serves as fascinating critique of the state of the times. For centuries the different medical beliefs in epilepsy through different cultures have been an indication of the relationship between the disease and the supernatural. Our purpose is to present the history of the the Aztec goddess of epilepsy and describe her depictions over time.

**Method:** We performed a comprehensive search for articles published from 1800 to 2015 to identify stories and depictions of Tlazolteotl and the Aztec medicine.

**Results:** The Aztecs believed that illnesses like epilepsy were punishments sent from angry and temperamental god or goddess. In particular, epilepsy was considered in the Aztec culture a “sacred disease” and convulsions were traditionally associated with a deified woman who have died in childbirth. Tlazolteotl was able to give and cure epilepsy from people, in a similar way as other deities such as Shiva and Apasmāra in ancient India and Saint Valentine in Germany. Tlazolteotl is one of the most endearing and complex goddesses of Mesoamerica. Her name is derived from the Nahuatl word for garbage, *tlazolli*, literally old, dirty, which was used to connote filth. The second part of her name, *teotl*, signifies a deity. She was the Goddess of the black fertile and fecund earth that gains its energy from death, and in turn feeds life. Associated with purification, expiation, and regeneration, she embodied fertility and turns all garbage, physical and meta-physical, into rich life.

**Conclusion:** Tlazolteotl, the mystic Mexican goddess represents the supernatural view of the sacred disease in Mesoamerica, where the illness of humanity is always consumed and pardoned by the act of childbirth.

**p0959**

#### DESIGN AND VALIDATION OF A SCALE OF QUALITY OF LIFE FOR CHILDREN AND ADOLESCENTS WITH EPILEPSY IN SPANISH LANGUAGE. ECÁVINAE-LICCE. COLOMBIA

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**Purpose:** To develop and validate a scale to assess the quality of life of children of different ages with epilepsy in the Colombian context, according to different domains that are related to the condition of these patients.

**Method:** Multicenter study; three-stage: A systematic search of the literature, creating scale and validation. Population: 0–17 years diagnosed with epilepsy who consulted Central League Against Epilepsy LICCE and Hospital La Misericordia, Bogotá, Colombia; from 2014–2015.

Sample Calculation for intraclass correlation 0.08 and 0.05 type I error: In total 274 patients, 137 of 0–10 years (divided 0–3 years, 4–10 years) and 137 of 11–17 years.

**Results:** Stage 1: A literature search was conducted.

Stage 2: biological, psychological, social and school / work: A scale with 4 domains was designed. The scale was divided into 2 age groups, a group of 0–10 years to be answered by parents and another group of 11–17 years to be answered by the patients. The survey was conducted with Likert questions.

Stage 3: Using data from surveys of population characteristics were evaluated. Face validity and content validity, construct validity through factorial analysis, reliability analysis using Cronbach's alpha (0.7), intraclass correlation and stability through test-retest (0.99); finding numbers that pass validation.

**Conclusion:** It was designed and validated a scale in Spanish to assess quality of life in children and adolescents with epilepsy in the Colombian context to assess patients at the time of consultation and monitoring of this aspect throughout the intervention.

**p0960**

#### EPILEPSY AND BURNS: REVIEW OF THE BURNT INTENSIVE CARE UNIT BETWEEN 2012-2014

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## Abstracts

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**Introduction:** Epilepsy patients can suffer different injuries, including skin burns. The causes are various, and depend on the type and frequency of the seizure, antiepileptic drug and comorbidities.

**Objective:** To identify the risk factors associated with skin burns in adults patients with epilepsy.

**Methods:** Retrospective study done in the burnt intensive care unit between march 2012 and march 2014. From a total 120 patients, there were only 6 patients that fulfilled the criteria of epilepsy and skin burns (5%); 3 of them were male. The average age was 45.8 years old (40–76). All of them currently treated with antiepileptic drugs: 5 in monotherapy and 1 in politherapy.

**Results:** 5/6 of the patients presented generalized seizures when they suffered the skin burn (83%), in 5 of the cases the accident happened at their houses and 1 at work. 5/6 (83%) recognized partial adherence to the antiepileptic treatment, including forgetting the medication and 2 out of 6 (33%) had alcohol consumption before the skin burn happened. 1 female patient died because of the extent of the skin burns lesions. The average severity index for these patients was 116 (critic).

**Conclusion:** There is a relation between epilepsy and skin burns, with a clear tendency to severe lesions. Physicians should emphasize in selfcare and adherence to antiepileptic therapy in order to minimize the risks of skin burns among other accidents.

## p0961

### LONG-TERM OUTCOMES IN SEIZURE CONTROL AND QUALITY OF LIFE AMONG PATIENTS WITH MEDICALLY INTRACTABLE EPILEPSY TREATED WITH MODIFIED KETOGENIC DIET THERAPY (MKDT) - A 12-MONTH RETROSPECTIVE STUDY

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**Purpose:** Modified ketogenic diet therapy (MKDT) is an effective treatment for intractable epilepsy; however, long-term outcome data remains limited. The aim of this retrospective study was to report outcomes with long-term use of MKDT.

**Methods:** Patients with intractable epilepsy, following MKDT for  $\geq 12$  months between December 2012 and February 2015 were included. Treatment outcomes, measured at baseline, 3, 6, and 12 months, included self-reported change in:

- (1) Seizure frequency ( $< 50\%$  or  $\geq 50\%$  improvement),
- (2) Seizure severity (improved intensity and/or duration),
- (3) QOL (improved mood and/or alertness), and
- (4) Compliance (strict or occasional deviation).

**Results:** Twenty-seven patients were included; 85% were aged  $\geq 18$  years ( $n = 23$ ), 70% were females ( $n = 19$ ).

MKDT resulted in  $\geq 50\%$  improvement in seizure frequency in 74% ( $n = 20$ ), 63% ( $n = 17$ ), and 56% ( $n = 15$ ) at 3, 6 and 12 months, respectively. Additionally, improved seizure severity was reported in 75% ( $n = 15$ ), 82% ( $n = 14$ ), and 87% ( $n = 13$ ) of these patients at each time point. QOL improvements were reported in 90% ( $n = 18$ ), 88% ( $n = 15$ ), and 87% ( $n = 13$ ) at each time point.

A total of 26% ( $n = 7$ ), 37% ( $n = 10$ ) and 44% ( $n = 12$ ) reported  $< 50\%$  seizure frequency improvement at 3, 6, and 12 months, respectively. Interestingly, 57% ( $n = 4$ ), 70% ( $n = 7$ ), and 58% ( $n = 7$ ) reported improved seizure severity, and 57% ( $n = 4$ ), 50% ( $n = 5$ ), and 33% ( $n = 4$ ) reported QOL improvements at each time point.

Among those with  $\geq 50\%$  improvement in seizure frequency, strict compliance was reported in 80% ( $n = 16$ ), 59% ( $n = 10$ ), and 80% ( $n = 12$ ) at 3, 6, and 12 months, respectively.

**Conclusion:** This study demonstrates the efficacy of long-term MKDT for seizure control and QOL among both pediatrics and adults with medically intractable epilepsy. Not surprisingly, strict compliance appears to result in the most benefit. Tolerability of these diets may account for the sustained/long-term benefits. Further, objective research is needed to verify these outcomes.

## p0962

### THE VALUES OF P300 COGNITIVE POTENTIALS IN CASES OF IDIOPATHIC AND SYMPTOMATIC FORMS OF EPILEPSY, TASHKENT MEDICAL ACADEMY

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**Purpose:** At the modern time the methods of cognitive induced potentials (CIP) find their vast application in clinical practice, making possible the objective estimation of the cognitive functions linked with perception and processing of information, and letting us get objective data.

**The aim of the research:** Is to study the peculiarities of cognitive induced potentials in the patients with symptomatic and idiopathic forms of epilepsy.

**Method:** the study was based on the results of examination of 72 patients with epilepsy, among them 38 with symptomatic epilepsy (SE) and 34 with idiopathic form (IE). The average age of the examined patients was  $48.0 \pm 25.3$  years old. The control group included 10 practically healthy people of the appropriate age.

**Results:** The patients with symptomatic and idiopathic epilepsy had characteristic alterations of P300 values, accompanied by more profound alterations in the cases of idiopathic form. It is, possibly, linked with more frequent epileptic attacks, longer term of the disease and, as a result, longer term of anticonvulsants administration. In the cases of idiopathic and symptomatic forms we detected absence of inter-hemispheric asymmetry of P300 wave amplitude, indicating dysfunctional disorders. The values of P300 latent period were increased in the cases of symptomatic epilepsy, different from idiopathic one, reflecting the inhibition of cognitive processes.

**Conclusion:** Thus, the neurophysiological values of cognitive induced potentials of the patients with epilepsy objectively reflect the status of the higher cerebral functions and depend on the form of epilepsy.

## p0963

### INTERRELATION OF COGNITIVE POTENTIALS AND NEURO-IMMUNOLOGICAL VALUES IN THE PATIENTS WITH EPILEPSY. TASHKENT MEDICAL ACADEMY, UZBEKISTAN

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**Purpose:** Nowadays one of the actual problems in epileptology is the study of interrelation of neuro-immunologic values and disorders in cognitive sphere in epilepsy cases. The aim of the research: is to study the interrelation of neuro-immunologic values and cognitive induced potentials P300 among the patients with idiopathic and symptomatic epilepsy.

**Method:** We checked 43 patients with epilepsy aged from 16 to 70 years old (27 men; 16 women), among them 11 had idiopathic epilepsy and 32 patients with symptomatic focal epilepsy. The control group included 16

clinically healthy people. The quantitative definition of serum immune reactivity of antibodies to neuromediators' receptors was performed with the help of ELI-N-test solid phase immune enzyme method (Russia). The study of P300 was performed on four-channel electromyograph "Med-elec."

**Results:** We detected the rise of autoantibodies' level to neuro-specific proteins NF-200, GFAP and OBM together with the decrease of S 100 among the patients with symptomatic epilepsy. The rise of autoantibodies' level to neuro-messengers was characterized by decrease of Chol-R, Glu-R, Da-R, Ser-R, DNA at the same time homogenous values of GABA-R and B2GP in the cases of symptomatic epilepsy and opposite data in the cases of idiopathic epilepsy. On the basis of neuro-physiologic values of CIP we detected the absence of inter-hemisphere asymmetry of P300 wave amplitude testifying dysfunctional disorders. The values of latent P300 period were increased in cases of symptomatic epilepsy, different from idiopathic one, and reflect inhibition of cognitive processes. We detected an inverse dependence of the latent period and amplitude increasing on the presence and explicitness of neuro-immunologic values in the analysis of neuro-immunologic values and P300 interrelation.

**Conclusion:** On the basis of the achieved data we can make a conclusion about inverse dependence of the degree of latent period and amplitude increasing on the presence and explicitness of neuro-immunologic values.

#### p0964

##### IMMUNOLOGICAL PARAMETERS IN EPILEPSY

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**Purpose:** Background. Epilepsy may present as a symptom of many neurological disorders and often an etiological explanation cannot be identified. There is growing evidence that autoimmune mechanisms might have a role in some patients.

**Objective:** To study the levels of autoantibodies (AAB) to brain proteins-antigens (NF-200, GFAP, BMP, and S100 $\beta$ ) in blood serum of patients with idiopathic and symptomatic epilepsies.

**Method:** We studied 52 patients with epilepsy (main group) at the average age of  $36.2 \pm 14.7$  years old. The main group was divided into 2 groups: I group—38 patients with idiopathic epilepsy, II group—14 patients with symptomatic epilepsy. The control group consisted of 16 healthy subjects. Immunological studies were conducted with ELI-Neuro-test by immunoenzymatic analysis. The data obtained were processed using methods of variation statistics

**Results:** We observed significant elevation of AAB to protein S100 $\beta$  in epilepsy patients, greater in idiopathic epilepsy, compared to control ( $54.3 \pm 10.3$ ;  $39.4 \pm 10$  and  $5.8 \pm 1.3$  CU, respectively,  $p < 0.001$ ). The levels of AAB to MBP were high in the first group ( $14.9 \pm 4.9$  CU,  $p < 0.001$ ), while in the second group were low ( $2.6 \pm 4.3$  CU), in comparison with control ( $8.0 \pm 4.7$  CU). The levels of AAB to GFAP were higher in symptomatic epilepsy ( $13.9 \pm 7.9$  CU,  $p < 0.001$ ). Patients with idiopathic epilepsy had higher ( $22.0 \pm 6.7$  CU) levels of AAB to NF-200 vs. patients with symptomatic epilepsy ( $11.4 \pm 6.4$  CU) ( $p < 0.001$ ).

**Conclusion:** Thus, all groups of epilepsy patients differed from control group by as individual levels, as degree of deviations of the studied immunological parameters. Early-initiated immunotherapy may improve seizure outcome in such patients.

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#### p0965

##### REDUCED FREQUENCY OF BLOOD CD8<sup>+</sup> T LYMPHOCYTES EXPRESSING PROINFLAMMATORY CYTOKINES IN MESIAL TEMPORAL LOBE EPILEPSY PATIENTS

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**Purpose:** To compare the proinflammatory and anti-inflammatory cytokine expression profile of CD4<sup>+</sup> and CD8<sup>+</sup> T lymphocytes between drug resistant mesial Temporal Lobe Epilepsy (mTLE) patients and healthy subjects.

**Method:** mTLE patients were enrolled at the Neurology Center of Santa Casa de Misericórdia de Belo Horizonte (SCM-BH) and healthy volunteers were selected at Universidade Federal de Minas Gerais. Individuals from both groups accepted to participate in this study and signed an informed consent. Peripheral blood mononuclear cells (PBMC) were isolated from whole blood using Ficoll/Hypaque followed by flow cytometry analysis. Data analysis was performed using FlowJo.

**Results:** Compared to healthy individuals, mTLE patients showed reduced frequency of CD8<sup>+</sup>

T lymphocytes expressing IFN- $\gamma$ , TNF- $\alpha$ , IL-17 and IL-4. Moreover, mTLE patients presented increased frequency of CD4<sup>+</sup> T lymphocytes expressing IL-6 when compared to healthy volunteers.

**Conclusion:** Epilepsy is the third most common chronic brain disorder. Mesial temporal lobe epilepsy (mTLE) is a major and severe form of epilepsy and 30% of the mTLE patients do not respond to conventional medications. Our data suggest that mTLE patients have distinct immunological profiles that are related to disease pathophysiology.

#### p0966

##### EPILEPSY CARE IN BANGLADESH: THE EXPERIENCE OF FIRST VIDEO-EEG CENTER

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**Purpose:** Video-EEG is a very effective diagnostic tool for differentiation of seizure and pseudo-seizure and to classify various seizure types. In Bangladesh this investigation has been introduced since February, 2014 in our institute. The objective of this study is to evaluate the findings of the Video-EEGs.

**Method:** This is a retrospective study. The electro-clinical information of the patients who had their Video-EEGs performed in our laboratory were collected and reviewed. All patients from February, 2014 to October, 2014 were included in this study. Clinical diagnosis was made by taking the history meticulously and doing clinical examination by the investigator. Video-EEGs were performed for various durations, ranging from 30 min to 24 hours with a view to capture an event and classify it. The seizures were classified following the International League Against Epilepsy classification (ILAE 1989, 1993). The EEG findings were interpreted accordingly.

**Results:** In 09 months total 25 Video-EEGs have been done. The duration of these V-EEGs were 0.5–24 hour. Age of the patients were 5 month–78 year. Male-female ratio was 12:13. In 14 cases clinical events could be captured. Various types of EEG pathology were found

in 20 cases. The final diagnosis is, CPS-T-7, PS with secondary generalization- 4, IGE-2, Symptomatic Gen. Ep.-3, Childhood Absence Epilepsy-2, Juvenile Myoclonic Epilepsy-1, SSPE-1, Status Epilepticus of Atypical Absence Seizure-1(LGS) and Pseudo-seizure-4. EEG was positive in 95% cases in our study. In 56% cases it was possible to capture an event which provided conclusive result of the presenting complain.

**Conclusion:** This result demands wide-spread use of Video-EEG in selected cases by trained experts for the accurate diagnosis and classification of epilepsy and to differentiate seizures from pseudo-seizures.

#### p0967

### EPILEPSY CLINICAL GUIDELINES: A “HOW TO” GUIDE

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**Purpose:** Clinical practice guidelines (CPGs) contain evidence-based recommendations to guide clinical care, policy development and improve quality of care. While CPGs can be a valuable resource, they are not without limitations. There are no universally accepted standards for CPG development, which can negatively impact their quality. A recent systematic review of epilepsy guidelines identified considerable variability in the quality of available guidelines. Although excellent frameworks for CPG development exist (i.e. AAN, SIGN, NICE) systematic processes are not uniformly followed internationally and resources to develop CPGs may be limited in certain settings. An ILAE working group has been charged with proposing methodology to guide the development of future epilepsy-specific CPGs.

**Method:** A comprehensive literature search including grey literature (1985–2014) was performed to identify CPG development handbooks and related articles. Guideline handbooks were included if they were: in English, publicly available, and if CPGs had been developed using the methodology. A table was developed comparing and contrasting identified CPG methodologies. The working group’s expert opinion was also gathered to develop unique CPG methodologies and processes to support future CPG development for the ILAE.

**Results:** Five CPG handbooks (North America, Europe, Australia, and World Health Organization) and additional references were identified to produce evidence-based and consensus-driven methodology for the development of epilepsy-specific CPGs. Key components of CPG development were: Identifying topic and defining scope (including formulating clinical question); establishing working group; reviewing evidence (systematic review and evaluating evidence using GRADE); formulating recommendations and determining strength of recommendations (using GRADE); peer review; dissemination, implementation, and auditing; updating and retiring. A practical toolkit and handbook was developed.

**Conclusion:** The resulting CPG development toolkit should facilitate the development of high quality ILAE CPGs for the care of persons with epilepsy internationally. The resulting CPGs will fill important gaps for healthcare professionals caring for persons with epilepsy.

#### p0968

### CURRENT STATE OF INTERNATIONAL EPILEPSY GUIDELINES

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**Purpose:** The Epilepsy Guidelines Task Force, composed of 13 international members, was commissioned by the International League Against Epilepsy in 2011. The first aim of the task force was to identify, using systematic review methodology, existing international epilepsy clinical care guidelines, to assess the quality of guidelines, and to identify gaps in topics.

**Method:** A systematic review of the literature (1985–2014) was performed in six electronic databases

(eg. Medline, Embase) using a broad search strategy developed to identify published epilepsy guidelines. Six grey literature databases (e.g. AAN, ILAE) were also searched to minimize publication bias. Two independent reviewers screened abstracts, reviewed full text articles and performed the data abstraction. There were no language exclusions. Basic descriptive statistics were generated.

**Results:** The search identified 10,925 abstracts, of which 409 articles were selected for full text review and 63 met our eligibility criteria for a guideline. Of those included, 54 were English and 9 were in other languages. Of all guidelines, 29% did not specify the target age groups, 28% were targeted at adults, and 23% were targeted at children. The included guidelines were most commonly aimed at guiding clinical practice for status epilepticus (n = 7), first seizures (n = 6), drug resistant epilepsy (n = 5), women with epilepsy (n = 4), and febrile seizures (n = 4), among others. Most of the guidelines were diagnostic (n = 16) or therapeutic (n = 35) in nature. The quality of the guidelines on a 1–7 point scale varied and was moderate overall (median/mean = 5 ± 1.0 (SD)).

**Conclusion:** In this internationally-led systematic review of epilepsy clinical care guidelines, significant gaps in topics and issues regarding quality were identified. The findings provide a valuable resource for physicians caring for people with epilepsy and will guide the prioritization, development and dissemination of future epilepsy-related guidelines.

#### p0969

### THE RETROSPECTIVE EVALUATION OF ELEVEN EPILEPTIC PATIENTS WITH A DIAGNOSIS OF TUBEROUS SCLEROSIS COMPLEX

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**Aim:** Tuberous sclerosis complex (TSC) is an autosomal dominant, neurocutaneous disease, affecting multiple organ systems. Epilepsy is the most common neurologic manifestation in TSC. The aim of this study is to evaluate the clinical and laboratory findings of the epileptic patients with a diagnosis of TSC and to determine the factors which may affect the prognosis of the disease.

**Material and method:** Eleven patients with TSC, (7 male and 4 female) followed up because of epileptic seizures between 1996–2014 at Istanbul University, Faculty of Medicine, were assessed with their clinical and laboratory data, retrospectively.

**Results:** Three of TSC patients were familial and the others were sporadic. Neurocognitive impairment was observed in 2 patients and mental retardation in 3 patients. Seizure onset age ranged between 3,5 months–51 years. 5 patients had status epilepticus and 1 patient had infantile spasms. The most common seizure type was focal seizure. 5 patients were without seizures in the last 2 years and two patients had rare seizures (once or two times a year). On MRI, except multiple cortical tubers and subependymal nodules, one patient had giant cell astrocytoma. The most common cutaneous finding was adenoma sebaceum and was found in 7 patients. Besides cranial and skin findings, eye involvement was detected in 1 patient and renal involvement in 5 patients. Two of the patients with renal involvement had the diagnosis of renal cell ca. Interestingly, two daughters of two index familial patients had also renal cell ca.

**Conclusion:** In our study, we showed that TSC patients could have a better seizure prognosis than expected. These patients need a close follow-up and care should be taken about possible malignancies, especially, renal cell ca.

#### p0970

#### MISDIAGNOSIS IN JUVENILE MYOCLONIC EPILEPSY

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**Purpose:** Juvenile myoclonic epilepsy (JME) is a generalized idiopathic epileptic syndrome a prevalence of 5–11% amongst other forms of epilepsy. Despite the certain diagnostic criteria, JME is still misdiagnosed by physicians and even experienced neurologists 1–4. We investigated our cases retrospectively to assess the pitfalls in JME diagnosis.

**Method:** We included 200 patients with JME examined at the epilepsy outpatient clinic. There were 94 (59 female, 35 male) patients who were misdiagnosed. All patients had well-documented diagnoses of JME, based on both clinical and EEG findings. Patients were evaluated demographic and clinical data; type of seizures and age at onset, precipitating factors, family history of epilepsy, neurological and mental examination, initial diagnosis, age at correct diagnosis, duration and causes of delay in diagnosis, EEG findings, neuroimaging findings, initial treatment.

**Results:** The mean age and the mean duration of epilepsy of 94 patients were  $26.7 \pm 8.46$  (12–55) and  $10.7 \pm 7.28$  years (1–35) respectively. The definite diagnosis was delayed by a mean of  $3.0 \pm 4$  years. The most common seizure-precipitating factors were sleep deprivation, photic stimulation, stress, fatigue and menstruation. The typical and pathognomonic epileptic discharges were found in 42.6% of cases. Fifth-teen patients (16%) had focal EEG abnormality. The most common reasons of misdiagnosis are:

(1) most of the patients did not complain of myoclonic jerks and these were revealed only by questioning.

(2) In some cases physicians seemed to be unaware of the syndrome.

(3) Another factor in misdiagnosis may be presence of atypical EEG findings.

**Conclusion:** Whereas in our study from 15 years ago the definite diagnosis was delayed by 5.9 years, in this study it is determined as 3 years. This indicates that there is more knowledge and experience about JME.

#### p0972

#### A DESCRIPTIVE ANALYSIS OF VISUAL SEIZURES SYMPTOMATOLOGY IN PATIENTS WITH OCCIPITAL LOBE EPILEPSY

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**Purpose:** To analyse the characteristics of visual seizures (VS) in occipital lobe epilepsy (OLE) patients, identify the predominant visual phenomena, and differentiate elementary visual hallucinations (E-VH) from complex visual hallucinations (C-VH).

**Method:** We retrospectively studied the ictal characteristics (derived from patients’ and witnesses’ descriptions) of VS in patients with OLE followed in our epilepsy clinic since 1996. We specifically recorded the characteristics of visual hallucinations (VH) such as type (E-VH or C-VH), morphology, coloring, location in the visual field, flashing or movement, and background characteristics. Other ictal symptoms (duration, progression, symptoms other than visual) and postictal characteristics have also being explored. SPSS 22 was used for statistical analysis.

**Results:** There were 76 (36M; 40F) patients with OLE and VS. Their mean age (range) was 23.0 (11–83) years. Forty-nine patients described E-VH with stars, spheres or lights. Almost half of them (46.9%) were multicolored, mainly of white (16.3%), red (6.1%), silver (6.1%) and blue (6.1%) color. The majority (65.3%) were located unilaterally. The remaining 27 patients reported either well-described C-VH (vague shapes or well-organized scenes) or ill-defined VH; in those, when predominant colors reported, these were most often black or blue. C-VH were multicolored (68%) and unilateral (63%). Comparatively, flashing of the illusion was more frequent in E-VH (38.8%) than C-VH (18.5%) and longer (>2 min) duration in C-VH (22.2%) than E-VH (14.3%). In overall, VH movement was more frequently horizontal (21.1%); patients could see through the VH in 36.8%. VS frequently progressed into a generalized tonic-clonic seizure (GTCS) (38.2%); importantly, 59.2% of patients could exhibit GTCS without onset of perceptible visual symptoms.

**Conclusion:** Our study showed that although VH in OLE are not always easily classified into E-VH or C-VH, there are some specific VH characteristics (morphology, type of color, flashing of the illusion and duration) that could differentiate those groups.

#### p0973

#### PEER SUPPORT FOR PERSONS WITH RARE EPILEPSY AND THEIR FAMILIES

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**Introduction:** A disease/disorder is defined rare when it affects less than 5 persons in every 10 000 people. Infantile spasm syndrome, Dravet syndrome, Lennox-Gastaut syndrome and Unverricht-Lundborg disease but also several other epilepsy syndromes are rare, difficult to treat and sometimes life threatening. Rare epilepsies affect not only the patient, but the entire family and community. It has been recommended by the EU that each member state should establish a national program for the development of care, support and research of rare diseases. There is need for

comprehensive care, counselling and peer support. Special information about rare epilepsies, social security, adequate services and disability benefits are also needed. We present some solutions in organizing peer support in a country with special challenges: long distances and a small population.

**Case presentation:** Finnish Epilepsy Association (FEA) has organized restorative weekends for people with rare epilepsies (PWRé) and their families. Furthermore FEA has produced information material about rare epilepsies. When one meets another one with the same rare disease, it helps a lot in finding solutions to cope. Even if diagnosis of a rare epilepsy is the same, there may be differences in the treatment options, prognosis and needed support, yet it is important to share experiences.

Internet offers a great opportunity to share experiences even 24/7. Online peer support groups have emerged spontaneously and with support by FEA. Previous studies have highlighted the significance of sharing personal experiences about the disease and its effects. Online discussion groups support empowering.

**Conclusion:** One of the current strategic goals of FEA is to support PWRé and their families and the means are presented in this poster. In addition, the role of advocacy to improve public services for the PWRé will be described. Both face-to-face and online peer support have their role to support each other.

p0974

#### DEMOGRAPHIC DATA OF PATIENTS WHO HAVE PSYCHOGENIC NON-EPILEPTIC SEIZURES (PNES) AND ITS RELATION WITH SEMIOLOGICAL CHARACTERISTICS OF PNES

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**Purpose:** PNES is a type of somatoform disorder consisting of paroxysmal episodes resembling epileptic seizures (ES) without concomitant Electroencephalographic activity. Distinguishing PNES from ES is important to avoid overdiagnosis of Epilepsy as well as overtreatment of epileptic patients. Backgrounds of patients such as gender, having family history of epilepsy, having epileptic background might have effects on semiological characteristics of PNES. The aim of the study is to analyze demographic data of PNES patients in terms of semiological characteristics.

**Method:** 114 patients (male:female = 44:70) aged 13–67 years, who were diagnosed as PNES with video monitoring EEG between 2010 and 2014, were included in this retrospective study. Patients were divided into groups according to their background data; gender, family history of ES, epilepsy history. Patients were grouped according to common semiological characteristics of non-epileptic seizure which were defined by epileptologist during video monitoring EEG. Chi-square test was used statistically.

**Results:** Age histogram showed two peaks at age 20–23 and 40–43, which was more prominent in female gender. Age 20–23 was peak age for male group. 1–5 min was the most frequent seizure duration. There was no significant relationship between defined semiological characteristics and gender in exception of high concomitance of opisthotonic posture in male patients ( $p = 0,017$ ). There was no significant relation with defined semiological characteristics of seizures in patient with or without epileptic background and having or not having family history of epilepsy.

**Conclusion:** Our results did not show significant relationship between common semiological seizure characteristics, gender, family history of epilepsy and having epileptic background. Male patient percentage was high compared to other studies in literature. High frequency of PNES patients at age 40–43 was also remarkable. Sociocultural characteristics of the population could cause the differences of demographic background from the literature.

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p0975

#### HAND PILL ROLLING TREMOR AND TEMPORAL LOBE SEIZURES

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**Purpose:** To validate and define the Hand PILL-ROLLING tremor (HPRT) as a sign occurring in temporal lobe seizures.

**Method:** From a cohort of patients undergoing video-EEG intensive monitoring, we selected 45 out of 70 seizures in 15 patients with a video recording such as to allow a suitable kinematic analysis of a rhythmic movement of the thumb against the index and medium fingers defined as HPRT.

**Results:** HPRT has frequency around 3.5 sec (range 2–4 sec), onset occurs from 9 to 185 sec after electroclinical seizure onset; duration ranged from 2 to 35 sec with possible interruption and recurrences; topography unilateral or bilateral (simultaneous or not).

**Conclusion:** HPRT is observed as a rare but up to now reliable-albeit ancillary sign of temporal lobe seizures. Since HPRT can be bilateral, its value as a lateralizing sign should be discussed in the light of the presence of different modifiers. The most relevant is the hand tonic contraction contralateral hemispheric seizures side susceptible to block the HPRT and modifying either onset or the end, rendering unilateral a putative bilateral tremor. HPRT related to an epileptic event is a “new entry” in the multifactorial list of “tremors”.

p0976

#### SEIZURES-RELATED FELINE BEHAVIORS IN MAN: HISSING, CLAWING, BITING

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**Purpose:** Description of an unusual behavior occurring during seizures.

**Method:** Retrospective retrieval and analysis of EEG video recorded seizures with hissing, clawing and biting.

**Results:** Hissing can occur as a single or repetitive behavior followed or not by clawing and biting. Clawing aimed unusual to surrounding person, with or without effective contact; biting is the relatively most frequent behavior which can occur either isolated (Tassinari et al. 2005) or associated with previous hissing and clawing. It has been associated with grabbing, with or without successful actual biting.

**Conclusion:** Feline Behavior (FB), commonly occur in relation to experimentally induced seizures involving the “temporo-limbic seizures”. FB, defined as a sequence of the triadic hissing-clawing-biting behavioral sequence is rare occurrence in man. The FB is likely modulated:

- by the functional activity in the relevant limbic-hypothalamic, mammillary bodies circuiting;
- by the interference with either the effective real surrounding and how this surrounding “professional space” is internally “felt” by the patient;
- the evolution in time from the initial events and its effect on various functional structure responsible for the “execution” of the behaviors.

FB is consequently a “vanishing” and modulated behaviors, in intensity and duration, requiring careful analysis for its identification. FB is discussed in an ethological prospective as “a release” of ancient behaviors (Tassinari et al. 2005, 2009).

**p0977**

### FROM GESTURE TO SPEECH: ON RECOVERY FROM SEIZURE INDUCED APHASIA, THE MIRROR NEURONS SYSTEM RE-ENACTS THE MOTOR SEQUENCES OF LANGUAGE EVOLUTION?

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**Purpose:** To describe the pattern of language recovery from aphasic seizures by analysis of video-EEG recordings.

**Methods:** We reviewed our video-EEG database searching for aphasic seizures with an adequate testing of language function. We described the semiological features during the recovery phase.

**Results:** In most patients we identified a common pattern characterized by three distinct phases.

(1) an early phase in which orolimentary “automatisms” are present and the hands go repeatedly to the head and/or face, then to the mouth/lips/tongue;

(2) afterward a series of gestures that can be interpreted as morphemes or sentences (communicative gestures) appear (e.g. the palm of the hand with open finger is flashed toward the requesting examiner signaling “stop asking, I understand. . .wait”; or the hands correctly pantomime the use of the tools that mount is still unable to name);

(3) finally the first phonemes and words are uttered and progressively speech is back.

**Conclusion:** The “mirror neurons system” (MNS), by matching observation and execution in the same motor format and in the same neuronal network, is considered to be the most important substrate for understanding the others without language mediation. For this reason MNS has been proposed as the initial communication system, that - from protospeech - evolved into speech (Rizzolatti and Airbib, 1998). Accordingly, (Gentilucci and Corballis, 2006) “an evolutionary scenario is suggested in which mouth movements primarily used in eating gradually assume dominance over hand movements and were eventually accompanied by voicing and movements of the tongue and vocal tract: thus speech was born”. We suggest that the pattern of language recovery after an aphasic seizure recapitulate in few minutes the same millenary evolutionary process.

**p0978**

### HYPERBARIC OXYGEN THERAPY INDUCED POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME ACCOMPANIED BY CHARLES BONNET’S SYNDROME

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**Introduction:** Posterior reversible encephalopathy syndrome(PRES) is a rare situation whose diagnosis is based on magnetic resonance images and clinical symptoms. It can be confused with acute cerebral infarction. It is characterised by visual disturbances, alterations in consciousness, headache, nausea and vomiting.

Hypertension, chemotherapeutic agents, preeclampsia are the factors included in its aetiology. However, to our knowledge no case report of

PRES induced by hyperbaric oxygen therapy has been reported in the literature.

**Case:** Fifty-one year old male was admitted to emergency room with the complaints of nausea, vertigo and temporary unconsciousness followed by bilateral acute blindness. He had the history of being under hyperbaric oxygen therapy for his chronic wound currently.

Diffusion restriction on cranial MR diffusion images located at bilateral occipitotemporal gyrus, right occipitotemporal lobe’s white matter and at thalamus was observed.

Two days following his admission to neurology clinic he reported seeing abnormal and frightening images which were smaller or bigger than normal size. He was aware of their unreality. In the fourth day, an episode of generalized tonic-clonic seizure beginning from the left side was observed. In following days the seizures continued and antiepileptic treatment was initiated. By time his epileptic seizures could be managed. On control cranial MRI in forty fifth day diffusion restriction was found as resolved and his blindness was almost improved.

**Conclusion:** Our patient did not have the known risk factors such as hypertension, chemotherapeutic agent exposure, nephrotic syndrome etc. for to develop PRES. He was under hyperbaric oxygen therapy. For this reason we concluded that this therapy could induce PRES and, Charles Bonnet’s syndrome might accompany to this radiological and clinical picture.

**p0979**

### THE COMPARISON OF METABOLIC SIDE EFFECTS OF TOPIRAMATE AND LEVETIRACETAM IN PATIENTS UNDERGOING CRANIOTOMY WITH PROPOFOL INFUSION

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**Background:** Antiepileptic agents are commonly used in the perioperative period in neurosurgical patients. Although metabolic side effects of topiramate are well known, there is no study about the metabolic side effects of new generation antiepileptic levetiracetam when it is used for anti-epileptic prophylaxis in patients undergoing craniotomy with total intravenous anesthesia. Propofol is an short acting agent oftenly used for total intravenous anesthesia, and propofol infusion is associated with perioperative metabolic acidosis. Anti-epileptic drugs with propofol infusion could be have an additional effect. To our knowledge there were no study to compare the aforementioned two drugs.

This study was conducted to compare the metabolic side effects of topiramate and levetiracetam in patients undergoing craniotomy with propofol infusion.

**Materials and methods:** After obtaining the written informed consent of the local ethics committee and the patients decision who underwent craniotomy, 80 patients of these were using topiramate with a minimum of 1 month (n = 40) (2 × 100) or levetiracetam (n = 40) (2 × 500) was included in the study. The blood gases, electrolytes, liver and kidney function tests, coagulation tests and lipid profiles were conducted in all patients preoperatively. In patients with metabolic acidosis, topiramate therapy was discontinued, and the anti-epileptic therapy was changed. Before induction of anesthesia and during anesthesia (1, 2, 4 and 6 hours) blood gases and liver, kidney function tests, lipid profile and coagulation tests were tested at preoperative and postoperative period. During the surgery all hemodynamic parameters were recorded at 10 min intervals. Results in the two groups were compared statistically.

**Results:** The demographic characteristics were similar in both groups ( $p > 0.05$ ). In the preoperative period, metabolic acidosis was significantly higher in topiramate group than levetiracetam group ( $p < 0.001$ ). Metabolic acidosis was recorded following propofol and remifentanyl infusion in 24% of patients in topiramate group, and 11% of these patients required treatment. In the levetiracetam group, there were no metabolic changes following propofol and remifentanyl infusion. In both groups, there were no differences in terms of lipid profiles and renal functions during the perioperative period ( $p > 0.05$ ).

**Conclusion:** It was concluded that the patients undergoing total intravenous anesthesia with propofol and remifentanyl, antiepileptic prophylaxis with levetiracetam should be preferred to topiramate due to less metabolic side effects.

**p0980**

#### CLINICAL, NEURORADIOLOGICAL AND EEG FINDINGS OF PATIENTS WITH EPILEPSY AND MALFORMATION OF CORTICAL DEVELOPMENT

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**Purpose:** The purpose of the study was reviewing clinical, neuroradiological and EEG findings of patients with Epilepsy and Malformation of Cortical Development (MCD).

**Method:** Retrospective analysis of medical records of patients of Haydarpasa Numune Education And Research Hospital second Epilepsy Out-patient Clinic.

**Results:** 2027 patients were examined between July 1995 and January 2015. 17 out of 1395 patients who has been followed, had MCD. 10 of the patients were male and 7 female. Time of seizure onset was between 30 months and 39 years (mean 12 years). 11 patients had focal seizures, 10 had generalized tonic clonic seizures, 1 had absence and 1 had tonic-atonic seizures. Syndromic classification revealed 12 patients with symptomatic focal epilepsy, 3 with symptomatic generalized epilepsy, 1 with Dyke-Davidoff syndrome and 1 with juvenile myoclonic epilepsy. Mental retardation was present in 5, Autism in 2 and Tubero sclerosis in 1 of them. Family history of Epilepsy was present in 8, consanguinity in 5, head trauma in 2 and difficulty during delivery in 1 patient. Brain Imaging revealed 7 patients with cortical dysplasia, 4 with heterotopia, 2 with subependymal heterotopia, 2 with schizencephaly, 2 with lissencephaly, 1 with agyria, 1 with pachygyria, 1 with macrogyria, and 1 with polymicrogyria. EEG revealed focal epileptiform discharges in 4 patients, high frequency activity in 2, generalized epileptiform discharge in 1 and diffuse disorganized background activity in 1. The EEG was normal in 7 patients. 3 of the patients were on monotherapy but 14 of them were on polytherapy.

**Conclusion:** The time of seizure onset was in the second decade in majority of our patients, against the known onset time in the early childhood. EEG revealed high frequency activity in some of our patients and the polytherapy was necessary in many patients as expected.

**p0982**

#### VALIDITY AND RELIABILITY OF TURKISH VERSION OF THE EPILEPSY SELF MANAGEMENT SCALE

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**Purpose:** This research has been conducted to determine the validity and reliability of the Turkish version of the Epilepsy Self Management Scale

developed by Dilorio et al. to evaluate self management behaviours of patients with epilepsy.

**Method:** This cross-sectional and methodological study has been carried out among patients attending to an epilepsy outpatient clinic of a university hospital between February and October 2014. The sample consisted of 194 patients with age above 18, able to communicate and having diagnosis of definite epilepsy. Patients seizure-free for two years were excluded from the group. For linguistic validation, an expert panel of nine academics was formed, and the Turkish form was finalized according to their recommendations. The thirty-eight item likert-type scale was applied to a group of ten persons, following language translation and content validation processes, and was implemented following necessary changes. Exploratory and Confirmatory Factor Analysis was performed for construct validity.

**Results:** Twenty items that factor loadings of less than 0.30 were removed from the scale. It was determined that the eighteen-item scale consisted of five factors. Item-total score correlation coefficients of the scale have been determined to be in range of 0.043 and 0.530, and correlation coefficients of sub-scale items and sub-scale total scores to be in range of 0.335 and 0.914. For internal consistency analysis, Cronbach alpha reliability coefficient was determined to be 0.607 for the whole scale and between 0.573 and 0.677 for the sub-scales. The test was repeated to evaluate the invariance of the scale and its sub-scale with respect to time and no difference was determined between two implementations ( $p > 0.05$ ).

**Conclusion:** It was determined that Turkish version of the "Epilepsy Self Management Scale" needs further refinement to be used in studies.

**p0983**

#### CLINICAL AND ELECTROPHYSIOLOGICAL FEATURES IN EPILEPTIC PATIENTS WITH PHENYLKETONURIA

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**Purpose:** Phenylketonuria (PKU) is the most common form of amino acid metabolism disorders with autosomal recessive inheritance. During the early periods of life, brain damage can be prevented by early diagnosis and by a phenylalanine restricted diet. Untreated patients show mental retardation and other cognitive dysfunctions, motor disability and epilepsy. We aimed to present 10 adult epileptic patients with PKU, three of them having reflex-induced seizures.

**Method:** 10 adult epileptic patients with PKU were evaluated retrospectively. The patients' ages at the onset of symptoms and seizures, neurological examination findings, neuroimaging findings, electroencephalography and reflex features were evaluated.

**Results:** The diagnosis of PKU was made between 3.5 months and 12 years. Of those 4 patients had moderate, 5 patients had severe mental-motor retardation (one patient was bedridden). The intelligence level of 1 patient was at the border. 4 patients' parents were cousin. All patients had experienced the first seizure under the age of 15. Focal or generalized seizures were observed. 3 patients had experienced febrile convulsion, 2 patients had myoclonus. 2 patients had developed status epilepticus. There was slow background activity for all patients (except one). 7 patients showed up generalized epileptic discharges. Of those 2 had asymmetric generalized discharges whereas one patient experienced generalized discharges during the hyperventilation. Magnetic resonance imaging (MRI) revealed white matter lesions in 5 patients. One patient had hippocampal sclerosis, one patient had hypointensities in basal ganglia and corpus callosum. 3 patients had reflex features without evidence of EEG findings.

**Conclusion:** To the best of our knowledge, there hasn't been sufficient reports regarding clinical and electrophysiological features of adult PKU

patients. In this study we showed that reflex feature can be observed in this metabolic disease. Furthermore, focal epileptiform anomalies and asymmetries can also assositate in electrophysiological assessment.

**p0984**

### DISCOURSE COMPREHENSION AND PRODUCTION IN RUSSIAN SPEAKERS WITH EPILEPSY

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**Purpose:** The goal of our project is to analyze language comprehension and production in Russian speakers with epilepsy using the Russian Aphasia Test. In the report we will focus on discourse comprehension (DC) and production (DP) results.

**Method:** During the DC subtest patients had to listen a story and answer yes/no questions relating to information in the story. In the DP subtest patients were asked to tell two stories based on two presented pictures. The data of eight patients were analyzed.

**Results:** Preliminary results show that, firstly, language competence in patients with epilepsy depends on age of seizure onset and seizure severity. For example, a patient with late seizure onset and right temporal lobe epilepsy (TLE) showed high scores in all the subtests; while a patient with early seizure onset and right parietal lobe epilepsy (PLE) performed worse on all the tasks. Secondly, location of the epileptic focus is crucial for performance on language tasks. Discourse of the patient with right PLE was characterized by decreased syntactic complexity and syntactic errors, impairment of discourse structure at macro-level. A patient with right frontal lobe epilepsy (FLE) made errors during DC task and provided excessive information during DP. A patient with right TLE also had problems with DC and failed to create logically structured and coherent discourse. Similarly, two out of three patients with left TLE produced inappropriately structured discourses with syntactically simple sentences and deficit in cohesion. No such characteristics were observed for a patient with left FLE.

**Conclusion:** Language competence in patients with focal epilepsy is influenced by both seizure history and location of the seizure focus. According to our preliminary results, language comprehension and production at discourse level is often impaired in patients with right hemisphere epilepsy and left TLE and relatively intact in patients with left FLE.

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**p0986**

### ANTIOXIDATIVE ENZYME POLYMORPHISMS AND THE RISK FOR EPILEPSY AFTER PERINATAL HYPOXIC-ISCHAEMIC BRAIN INJURY

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**Introduction:** Hypoxic-ischemic encephalopathy (HIE), caused by perinatal oxygen deprivation to the brain, represents a major cause of neonatal seizures. 20–30% of these infants develop epilepsy. Important

etiopathogenetic mechanism in brain tissue damage is associated with reactive oxidative species (ROS), which may be important also in epileptogenesis.

**Purpose:** To investigate the impact of decreased capacity for defence against reactive oxidative species (ROS), we analysed selected functional polymorphisms of genes for antioxidative enzymes - GPX1, MnSOD and CAT, in patients with epilepsy after perinatal HIE.

**Methods:** 230 patients with epilepsy and/or hypoxic ischemic encephalopathy (HIE) and 95 healthy controls were included. Clinical data were collected from medical records retrospectively. Real-time PCR based methods were used to genotype *GPX1 rs1050450*, *SOD2 rs4880* in *CAT rs1001179*. Logistic regression was used for statistical analysis.

**Results:** Polymorphisms for *GPX1 rs1050450*, *SOD2 rs4880* in *CAT rs1001179* in 204 epilepsy patients did not correlate with epilepsy in comparison to healthy controls. However, among 64 patients with epilepsy after HIE, more patients had at least one polymorphic *GPX1 rs1050450* allele in comparison to healthy controls, but the difference was not statistically significant ( $p = 0,127$ ). *CAT rs1001179* distribution among patients with epilepsy and HIE was not significantly different than in controls ( $p = 0,337$ ); *SOD2 rs4880* distribution was similar to controls. Although pharmacoresistant epilepsy was significantly more frequent among children with epilepsy after HIE (40/62 pts) in comparison to other etiologies (67/150,  $p = 0,009$ ), the number of patients was not sufficient to demonstrate significant difference in polymorphisms.

**Conclusions:** Polymorphisms of genes for antioxidative enzymes *GPX1 rs1050450*, *SOD2 rs4880* and *CAT rs1001179*, associated with decreased capacity of defence against ROS, do not influence the overall epilepsy risk, but may have an impact to development of pharmacoresistant epilepsy. Larger numbers of patients are needed for further studies.

**p0988**

### COMPARISON OF POLISH PAEDIATRIC PATIENTS WITH AND WITHOUT DIAGNOSED POST-STROKE EPILEPSY

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**Purpose:** Arterial ischaemic stroke (AIS) occurs in approximately 3 per 100, 000 children per year. Several neurological complications (e.g. motor impairment, speech impairment, seizures and intellectual delay) are the consequences of this disease. The prevalence of post-stroke epilepsy is quite high and has great impact on daily activity of little patients.

The aim of the present study was to compare Polish paediatric patients suffering from AIS and post-stroke epilepsy with post-stroke epilepsy-free patients.

**Method:** The study population consisted of 68 children (white Polish Caucasians): 10 patients with post-stroke epilepsy (mean age  $3.50 \pm 2.55$ ; 4 females and 6 males) and 58 children suffering with AIS but epilepsy-free (mean age  $8.96 \pm 5.42$ ; 23 females and 35 males). Data were analyzed using STATISTICA 10.1 and MedCalc softwares.

**Results:** Focal cerebral arteriopathy (FCA) was observed in 90% of patients with post-stroke epilepsy and in 51% epilepsy-free patients (Relative risk 1.74, 95%CI 1.26–2.40,  $p < 0.001$ ). In seven of the participants post-stroke epilepsy evolved from late remote seizures (occurring between 7 days and 2 years after AIS onset) and three of the patients had early post-stroke seizures (occurring up to 7 days after

AIS onset). In 30% of post-stroke cases and in 14% of epilepsy-free patients heart diseases were observed (Relative risk 2.74, 95%CI 0.69–6.83,  $p = 0.183$ ).

**Conclusion:** FCA is risk factor for post-stroke epilepsy in the Polish paediatric patients.

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**p0989**

#### NON-LESIONAL PARTIAL EPILEPSY WITH VESTIBULAR DISTURBANCES IN CHILDHOOD

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**Purpose:** We describe a series of children who share electrical and clinical characteristics of focal epilepsy manifesting as prominent vestibular disturbances, suggesting a temporal-parietal ictal origin.

**Method:** We retrospectively reviewed a database of patients admitted from 2012 to 2014 following these criteria: presence of predominant or exclusive paroxysmal vestibular symptoms, age range between 5–18 years and normal magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) on 3T equipment. Eight patients were finally selected (4 females and 4 males).

**Results:** The symptoms began abruptly as rotational vertigo which lasted several seconds. The complex vestibular symptoms observed were: feeling of floating, turning inside head and walls caving in. The accompanying symptoms were nausea or vomiting, déjà-vu and non-pulsatile tinnitus. The predominant feature on interictal scalp EEG was abnormalities over the temporal-parietal areas. There was an average 3 month period until final diagnosis was established. All patients responded well to antiepileptic medication.

**Conclusions:** The patients described show similar electroclinical features, normal neuroimaging and remain seizure free after treatment. It should be considered as a form of epilepsy within the group of non-lesional focal epilepsies of childhood.

**p0990**

#### VAGUS NERVE STIMULATION FOR PHARMACO-RESISTANT EPILEPSY: A LONG TERM STUDY OF 59 PATIENTS

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**Purpose:** Vagus nerve stimulation (VNS) is thought to have a cumulative effect in time on seizure frequency reduction. In this study we retrospectively reviewed our experience with VNS in pediatric patients with pharmacoresistant epilepsy and described the long-term outcome of the patients who have been followed at least 5 years after VNS implantation.

**Method:** Fifty-nine consecutive children, 26 females and 33 males, with pharmacoresistant epilepsy under the age of 18 years, who were implanted with a vagus nerve stimulator and had at least five years of postimplantation follow-up, were included in the study. A vagus nerve stimulator was implanted in the period January 2000– March 2010. Fol-

low-up ranges from 5 to 15 years (mean 7.1 years). Efficacy was measured as the percentage change in seizure rate during 1 year and then after each year follow-up of VNS compared to 3 months baseline before implantation.

**Results:** Median age at implantation was 11.5 (range 4–17) and median duration of epilepsy 8.0 (2–15) years. At 5 years postimplantation, thirty-five (63.6%) of the 59 patients had a greater than 50% reduction in seizure frequency. Eighteen patients (30.5%) reported a lesser reduction (<50%), 7 had less than 25% reduction. Two patients had no apparent reduction in seizure frequency. Eleven patients became seizure free within 24–120 months. The results, once obtained, were maintained steadily over time without any loss of efficacy during the follow-up. Three stimulators were turned off within 1–2 years after implantation, one because of the absence of clinical benefit; two because of recurrent local infection. Three patients received a new pulse generator when the battery was depleted.

**Conclusion:** Our results demonstrate that adjunctive VNS Therapy in children with pharmaco-resistant epilepsy is an effective long-term therapy to control a patients' seizure frequency.

**p0991**

#### EVALUATION OF PATIENTS WITH TUBEROUS SCLEROSIS COMPLEX ADMITTED TO PEDIATRIC VIDEO-EEG MONITORING UNIT

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**Purpose:** Epilepsy prevalence in Tuberous sclerosis complex (TSC) is very high and seizures are usually intractable. We studied children with TSC admitted to the video-EEG monitoring unit (VEMU).

**Method:** The study included 30 TSC patients admitted to the Hacettepe University VEMU between 2006–2014.

**Results:** 49 episodes of VEMU stay of 30 patients were analysed. Male/female ratio was 15/15. Three patients had a cardiac rhabdomyoma, 4 had renal involvement, 2 had subependymal giant cell astrocytoma (SEGA), 20 had hypopigmented macules, 2 had hemiparesis, and 20 had developmental delay. Main psychiatric comorbidities were hyperactivity and autism. With respect to epilepsy; age at seizure onset was between 1st day and 2.5 years, age at the time of admission was between 15 months and 14.5 years. 15 patients had epilepsy before TSC diagnosis, 2 developed seizures after the diagnosis, 13 had seizures at the time of diagnosis. 26 patients had daily seizures; 12 patients had a history of infantile spasms, 3 had a history of status epilepticus. 12 patients had focal seizures, 7 had generalized seizures, 8 had mixed semiology, and 3 had epileptic spasms. EEG was normal for one patient with focal seizures. Interictal recordings showed slow and irregular background for age. Interictal findings were focal for 20 patients, multifocal for 5, focal + secondary generalization for 4 patients. Ictal EEG recordings were lateralizing in 3, both lateralizing and localizing in 16; not lateralizing or localizing in 10. Two patients underwent corpus callosotomy, 3 resection of tuber, 3 lobectomies (2 temporal, 1 frontal), 1 SEGA excision, and 2 patients had vagal nerve stimulation therapy (one of them following two resective surgeries). After invasive treatments 6 patients became seizure free, 3 had improved conditions, 1 had ongoing seizures.

**Conclusion:** Epilepsy in TSC is a challenging burden affecting quality of life. Epilepsy surgery is a promising treatment for selected patients.

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p0995

### **PATHOLOGICAL LAUGHING AND CRYING AS DIFFERENTIAL DIAGNOSIS OF GELASTIC SEIZURES**

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**Purpose:** Pathological laughing and crying (PLC) is characterized by involuntary and uncontrollable laughing and/or crying episodes incongruent to the patient's mood. The theory most accepted proposes that motor control of emotions is modulated by the cerebellum, which acts as a "gate control." Reduction of the inhibitory input results in disinhibition of the cerebellum, with socially inappropriate emotional expression. Occasionally these episodes may be mistaken for epileptic seizures. The objective of this study was to evaluate systematically the occurrence of PLC in children.

**Method:** This was a retrospective study conducted at the neuropediatric clinic of our University Hospital. Inclusion criteria was age up to 18 years-old and episodes of uncontrollable laughing or crying consistent with PLC. Exclusion criteria were the presence of an underlying mood or personality disorder that could explain the abnormal emotion expression, Angelman syndrome and hypothalamic hamartoma.

**Results:** Sixteen patients met the inclusion criteria, eight boys, eight girls; ages ranging from three to 18 years-old (mean = 8.5 years-old). All patients had pathological laughter; and only four had pathological crying. Neurological examination was abnormal in all patients, and most of them showed developmental delay and cognitive impairment. In most patients the main presenting concern was if the laughing was seizure related. Only three patients needed treatment. Risperidone was highly effective in all of them, with no side effects.

**Conclusion:** We conclude that PLC is not rare in childhood and should be considered more often as a possible diagnosis. When treatment is needed, risperidone is a safe and effective option providing major improvement in quality of life.

p0997

### **VISUAL HALLUCINATIONS IN CHILDHOOD SYNCOPES - NOT ONLY EPILEPSY**

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**Purpose:** While the end-point of syncope is a loss of consciousness, the patient usually describes a progression of symptoms in the prodrome to this, commonly those of visual disturbances such as blurred vision, greying out or "blackouts". Visual hallucinations (VH) are a less documented phenomena in syncope(1) and are more commonly thought of as manifestations of other paroxysmal conditions such as epilepsy and migraine. We would like to share our experience regarding VH among young patients with reflex syncope. We also discuss the significance of the findings and consider a common pathophysiology between visual manifestations in migraine, epilepsy and syncope.

**Method:** 274 patients (145 females; 129 males) with reflex syncope were included. Their mean age was 11.7 years. Each patient reported at least two separate attacks of syncope occurring at least 24 hours apart.

**Results:** Premonitory visual hallucinations during syncopal attacks were identified among 36/274 (13%) patients. This consisted of different colours including white, black, yellow, red, pink, green and blue. 19/36 (53%) patients reported flashing zig-zag lights, and the remaining 17/36 (47%) experienced dots and / or stars of different sizes. Such VH lasted

from seconds to less than 5 min with full reversibility. None of the 36 patients are known to have migraine or epilepsy.

**Conclusion:** Our findings provide further evidence to support the overlapping clinical spectrum of paroxysmal disorders such as epilepsy, migraine and syncope. Syncope shares cerebral hypoperfusion with epilepsy and migraine(2). Therefore it could be hypothesised that there is a common element to the pathophysiology of all three disorders, specifically that of hypoxia/hypoperfusion within the occipital lobe, which could explain the overlapping symptoms seen in our cohort of patients.

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p1000

### **EFFICACY OF MODIFIED ATKINS DIET VERSUS KETOGENIC DIET IN CHILDREN WITH REFRACTORY EPILEPSY AGED 1 YEAR TO 18 YEARS: A RANDOMIZED CONTROLLED TRIAL (RCT)**

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**Purpose:** Around one third of patients with epilepsy are drug refractory, of which only one third are amenable to surgical resection. Dietary therapy in the form of ketogenic diet (KD) and its variants are useful in intractable epilepsy. Modified Atkins Diet (MAD) is a milder variant of KD in terms of composition, tolerability and acceptability. There is no prospective RCT comparing the efficacy of MAD with ketogenic diet in intractable epilepsy.

**Method:** The objective of the current study was to determine the efficacy of MAD (vs.) KD for seizure control at three months follow up in children aged 1–18 years with intractable epilepsy

In this open label RCT, 30 patients received MAD and 30 patients received KD, with unchanged anti-epileptic drug treatment in both groups during the entire study period. Lennox Gestaut syndrome was the most common diagnosis in the study population.

**Results:** Percentage of seizure reduction at 3 months follow up from baseline in MAD group was 47.4 (18.8 to 77.8) and in KD group was 61.9(–182.9 to 100) (p = 0.348). At third month follow up, in the MAD group, seven patients and 9 patients in the KD group achieved more than 50% seizure reduction from baseline (p = 0.341). There were no statistically significant difference in terms of hematological and biochemical parameters between the two groups. Five patients in the MAD group and 2 in the KD group had minor adverse vents in the form of diarrhoea, vomiting and constipation.

**Conclusion:** Thus MAD as add on to ongoing AED therapy is not inferior to KD in terms of percentage seizure reduction from baseline and proportion of patients who achieve >50% seizure reduction from baseline seizure frequency at 3 months follow up. Studies with larger sample size and longer follow up period should be planned in future.

p1002

### **EPILEPSY OF INFANCY WITH MIGRATING FOCAL SEIZURES: CASE REPORT**

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**Introduction:** Migrating partial seizures of infancy (MPSI) is a rare, infantile epileptic encephalopathy, first described by Coppola et al. (1995). This entity is characterized by refractory focal seizures associated with autonomic features, arising independently from both hemispheres, post-natally acquired microcephaly and severe developmental delay. We present the first Colombian case describes with MPSI.

**Case presentation:** Is a 2 years-old boy who was a full-term healthy newborn. He presented with hypotonia, somnolence and poor feeding at three days of age. He developed hypoglycemia and seizures. Blood analysis showed transitional hyperammonemia and metabolic acidosis, lactic-acid was normal. Extensive metabolic investigations and comparative genomic hybridization were all normal. At the age of 2 months he started to have almost continuous migratory focal motor seizures with autonomic features and asymmetric tonic seizures from both sides, refractory to antiepileptic drugs. He has severe developmental delay and microcephaly. Actually he is receiving treatment with LVT-VGB-PB-LCM. He was seizure free for a month when LCM was started; actually his seizure frequency is 2–3/day.

EEG/Video-EEG-recording: multi-focal spikes and background slowing. Electro-clinical seizures from the right and left fronto-central and temporo-parietal areas, with occasional overlapping of consecutive seizures.

Brain-MRI-T2: delayed myelination with hyperintensity of the deep white matter.

MRS: slight increase of lactate peak in the white matter and the slight decrease of N-acetyl aspartate peak. Choline and Creatine peaks were normal.

**Conclusions:** Migrating partial seizures of infancy is a rare early onset epileptic encephalopathy with poor prognosis. Although its prevalence is unknown, approximately 100 cases have been described in the medical literature. This baby-boy fulfill the diagnostic criteria of this entity, characterized for highly pharmaco-resistant seizures. In our case good response was observed when LCM was added. The shifting clinical and EEG pattern of seizures should alert the physician to the possible diagnosis of this devastating infantile epileptic encephalopathy.

### p1003

#### VITAMIN D DEFICIENCY IN CHILDREN WITH NEWLY DIAGNOSED IDIOPATHIC EPILEPSY

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**Purpose:** Vitamin D is a neurosteroid, and similar to the classical neurosteroid, it may positively modulate brain neuromediators and receptors via GABA-A receptors. Several studies have shown a link between vitamin D deficiency and epilepsy

**Method:** This study includes 60 newly diagnosed idiopathic epilepsy patients and 101 healthy controls (between the ages of 5 and 16). Each group was also divided into two subgroups according to seasonal changes in terms of months of longer (vs.) shorter daylight. We retrospectively evaluated the levels of calcium, phosphorus, alkaline phosphatase, parathyroid hormone, and 25-OH vitamin-D3 in the study participants. Levels below 20 ng/ml were defined as vitamin D deficiency and levels of 20–30 ng/ml as insufficiency.

**Results:** There were no significant differences in age, gender distribution and levels of calcium, phosphorus, alkaline phosphatase and parathyroid hormone between the groups. The level of 25-OH vitamin-D3 in the patient group was significantly lower when compared to the control group ( $p < 0.05$ ) ( $14.07 \pm 8.12$  and  $23.38 \pm 12.80$  ng/ml, respectively). This difference also held true when evaluation was made according to seasonal evaluation ( $12.38 \pm 6.53$  and  $17.64 \pm 1.14$  in shorter daylight and  $18.71 \pm 9.87$  and  $30.82 \pm 1.04$  in longer daylight)

**Conclusion:** The mechanism and effect of vitamin D deficiency in seizure is still unknown. We think that screening of vitamin D levels is simple and relatively inexpensive and should be strongly considered in all children with epilepsy. We also suggest that further studies including a larger sample of patients are needed to draw a firm conclusion

Note: This study was published in *J Child Neurol*. 2015 Jan 30. pii: 0883073814566627. [Epub ahead of print]

### p1004

#### MICRODELETION OF CHROMOSOME 1Q21.3 IN FRATERNAL TWINS WITH MENTAL RETARDATION, MICROCEPHALY, EPILEPSY AND DYSMORPHIC FEATURES

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**Purpose:** The development of genomic DNA microarray technology to detect whole genome copy number variations (microarray-CGH) has facilitated the discovery of novel chromosomal phenotypes associated with epilepsy. There is only one study with 1q21.3 microdeletion syndrome until now in which deleted region span about 1.4 Mb with approximate genomic location chr1:152,511,593-153,993,103 (NCBI genome build 36).

**Method:** We report on twins carrying a 1q21.3 microdeletion and exhibiting important common features with earlier reported case like microcephaly and developmental delay together with other clinical signs which have never been described to date in this microdeletion like epilepsy, hypotonia and hyperlaxity in joint. The karyotype analysis was performed. And array comparative genomic hybridization was performed on the patient using an oligonucleotide array.

**Results:** The karyotype was normal 46, XX for both of the cases. Array CGH analyses identified a 2.6 Mb deletion on chromosome 1q21.3 (chr1:153514121-156171335 bp) in case 1 and a 1.6 Mb deletion on chromosome 1q21.3 (chr1:154748365-156358923 bp) in case 2. Both of siblings have common findings like microcephaly developmental delay, epilepsy, distal hypotonia. Deleted region includes DPM3, MUC1, GBA, PKLR, RIT1 and LAMTOR2 genes in both of sibling. However, they have some different clinical findings and different deleted genes from each other. Deleted region in one of our sibling encompasses this region and 21 genes are common between our cases and this patient.

**Conclusion:** To the best of our knowledge, this is the first study that two siblings have 1q21.3 microdeletion in a family with mental retardation, developmental delay, seizures, and dysmorphic features. The identification of etiology with array-CGH screening is very useful when all laboratory and metabolic investigations were normal and the identification of causative genetic background associated with seizures and their related phenotypes is useful for genetic counseling, and possibly for management of the patients.

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p1006

### THE RELATIONSHIP BETWEEN INTER-ICTAL SPIKES AND SPINDLES IN THE IDIOPATHIC FOCAL EPILEPSIES OF CHILDHOOD

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**Purpose:** Research has demonstrated that there may be a link between the generators of spikes and sleep spindles in idiopathic focal epilepsies of childhood (IFE) (Beelke et al., 2000, Kellaway, 2000, Nobili et al., 1999). Therefore, a study exploring the relationship between spikes and sleep spindles could provide the knowledge to further define these mechanisms and add to our understanding of brain function in children with IFEs.

**Method:** Sleep EEGs of children with IFE and controls were analysed visually and by using the hypnospectrogram. Spikes and spindles were counted from a single channel in non-rapid eye movement sleep (NREM) stages two and three. In addition, single isolated spikes and spindles were marked, averaged over time, and morphologically defined. Two relationships were explored, the density of spikes and spindles, and the association between their morphology. To validate these findings were also analysed in context to the child's age.

**Results:** The results conclude that there is evidence of a positive correlation between spike and spindle density. In addition, a positive correlative relationship was found between the morphology of spikes and spindles. The lack of correlation with age reinforces this affiliation.

**Conclusion:** These findings suggest that the generation of spikes and spindles in IFEs have similar mechanisms.

p1007

### POLG1-RELATED EPILEPSY: REVIEW OF REPORTED CLINICAL, NEUROPHYSIOLOGIC AND GENETIC FINDINGS

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**Purpose:** The clinical spectrum associated with POLG1 gene mutations is wide, ranging from non-syndromic epilepsy or mild isolated neurological signs to neurodegenerative disorders. The aim of the present article is to review clinical, genetic, neurophysiological, neuroimaging, therapeutic approach and outcome of all the reported cases.

**Method:** The articles for review were identified through a search of Medline, searching the terms "epilepsy AND POLG1". Sixty-eight articles, including 281 cases of epilepsy due to POLG1 mutations, were found. Thirty-four of them were selected for the review, including 164 cases.

**Results:** This is an underestimated condition as it is rare, not sufficiently documented. Data on its prevalence are lacking. Age at epilepsy onset varies between 0 and 55 years. Two main peaks of age at onset are found: respectively at 1 year and at 13 years. The most frequent seizure type is myoclonic. The occurrence of Status Epilepticus was reported in 48.4% of cases. Most of the reported cases presented developmental delay or psychomotor regression. Epileptiform and slow abnormalities were most frequently seen over occipital regions. Brain MRIs revealed increased T2 signal intensities in thalamic regions.

Many patients developed brain atrophy. Genetic analysis revealed a large number of mutations with a prevalence of A467T, W748S and G848S mutations. A large number of antiepileptic drugs were used and in almost all cases. The use of valproate determined liver dysfunctions. Survival at 5 years was estimated at very low levels, with a better outcome in late onset cases.

**Conclusion:** In this review we included cases with both pediatric and adult epilepsy onset. The analysis of data regarding prognosis showed that survival is related to age at epilepsy onset. Serum lactate and muscle biopsy is not diagnostic. The review of the published cases allowed us to identify and summarize the epileptic phenotype of POLG-related epilepsy.

p1008

### PREVALENCE OF FEBRILE SEIZURES AT CHILDREN IN SIBERIA

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**Purpose:** The study of prevalence of febrile seizures (FS) at childhood population in the Krasnoyarsk city (Siberia, RF).

**Method:** The Krasnoyarsk is a city and the administrative center of the Krasnoyarsk Krai (Russia), located on the Yenisei River. It is the first city in Siberia. The Krasnoyarsk experiences a continental climate with long and very cold winters, and short but warm summers.

The retrospective analysis of official medical records of infectious division of City Children's Clinical Hospital №1 (Krasnoyarsk) held us in 2009 to 2012. For the analyzed period in an infectious hospital 578 children with FS and an acute respiratory virus infection (ARVI) are hospitalized.

**Results:** The prevalence of FS among children aged from newborn to 14 years old was 75-112/100000 childhood population of the Krasnoyarsk city in 2009-2012. Annually the increase in number of the entered patients with FS occurred during the winter and spring period that is bound to lifting of incidence of ARVI and flu. Relation FS around boys and girls was 57.3% (vs.) 42.7%. We showed a dominance of FS around children from 12 to 36 month old (57.6%). The greatest number of FS registered in 2010-177 (30.6%), and the lowest in 2009-130 (22.5%).

Leading place on the frequency of cases of FS among districts of the Krasnoyarsk city take Soviet's district (179 pers.) is as the most multioccupied and big on the area the district of the Krasnoyarsk city, and also Lenin's district (112 pers.) is as the most adverse in social aspect the industrial region.

**Conclusion:** The prevalence of FS in the Krasnoyarsk city exceeds those in the Russian Federation. The conducted research testifies that development and carrying out correcting actions are necessary for decrease in risk of FS development in the studied nursery of childhood population in Siberia.

p1009

### THE IMPACT OF MOTOR-SENSORY DEVELOPMENT AND LEVEL OF DISABILITY ON QUALITY OF LIFE AND MOTHER'S STRESS LEVEL IN CHILDREN WITH EPILEPSY

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**Purpose:** Physiotherapy and rehabilitation reviews are important in epilepsy rehabilitation. This study aims to determine the normal motor

development level in children with epilepsy, explore its impact on the child's activity level and quality of life, and exhibit the potential stress load of the condition on the parents.

**Method:** Demographical data of children and parents included in the study were recorded. The children's sensory-motor development levels were assessed by *The Neurological, Sensory, Motor, Developmental Assessment (NSMDA)* scale, level of disability by *Impact of Childhood Neurologic Disability Scale (ICND)*, disease impact level by *Impact of Pediatric Epilepsy Scale (IPES)* questionnaires, daily living activities and quality of life by the Turkish version of the *Pediatric Outcomes Data Collection Instrument (PODCI)* scale, and stress/depression conditions by the *Parental Stress Scale (PSS)*.

**Results:** The study included 82 children, 53 male (64.64%) and 29 female (35.36%) diagnosed with temporal lobe epilepsy. The mean values of the scales applied on children were  $6.45 \pm 0.67$  for NSMDA;  $47.22 \pm 30.94$  for ICND;  $20.93 \pm 11.4$  for IPES;  $51.38 \pm 7.80$  for upper extremities,  $48.16 \pm 8.15$  for transfer and basic mobility,  $51.15 \pm 7.34$  for sports and physical function,  $48.06 \pm 11.92$  for pain/comfort,  $55.30 \pm 4.41$  for happiness,  $49.86 \pm 8.14$  for global function, which are the subscales of the PODCI scale;  $3.95 \pm 0.80$  for IPES/ICND QoL; and  $40.54 \pm 8.71$  for PSS, respectively. There was a statistically significant correlation between the children's PODCI transfer and basic mobility subscale and PSS ( $r = -0.249$ ;  $p < 0.05$ ).

**Conclusion:** The results indicate the need for more structured and detailed assessment of emotional, intellectual, functional and psychosocial etc. impairments as well as motor-sensory impairments in children with epilepsy. The results suggest that psychosocially supporting both the parents and children in conjunction with all other rehabilitation treatments from the very early phases could positively impact the quality of living of both the parents and children.

#### p1010 THE EVALUATION OF MOTOR DEVELOPMENT LEVEL IN CHILDREN WITH EPILEPSY

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**Purpose:** In our study, we aimed to determine physical disability which include gross and fine motor development levels of children with epilepsy.

**Method:** The level of sensory-motor development of children who between 2–6 years had epilepsy diagnosis are evaluated with "The Neurological Sensory Motor Developmental Assessment (NSMDA)" scale. NSMDA, defined the motor development from birth through the first 6 years of the properties and describe relationship between the system. Motor performance, identifies abnormal or dysfunctional movement components at various ages and problem areas.

**Results:** 53 boys (64.64%) and 29 girls (35.36%) were included in the total of 82 children in our study. The average applied to children NSMDA score is  $6.45 \pm 0.67$ .

**Conclusion:** This study found that although the children were in normal levels for sensory-motor development in the sensory-motor development assessment performed only in cases with temporal lobe epilepsies exhibiting no other neurological diseases, the children were observed to have difficulties and low scores in certain activities in the fine motor, proprioception and tactile sense subscales of the test. This study found that the fall in bottom scores in the sensory-motor assessment was not reflected in the overall score and had a ceiling effect in the overall score, resulting in the requirement of individual assessment of each motor and sensory skill in such children.

#### p1011 INVESTIGATION OF DISEASE IMPACT AND DISABILITY LEVELS IN CHILDREN WITH EPILEPSY AND THEIR FAMILIES

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**Purpose:** In our study we aimed to determine the influences in daily living activities and get over disease in children with temporal lobe epilepsy and their families.

**Method:** We determined the child's disability level by "Impact of Childhood Neurologic Disability Scale (ICNDS)" and to measure the disease efficiency by "Impact of Pediatric Epilepsy Scale (IPES)" survey was performed after obtaining the use permit.

**Results:** The study included 82 children, 53 male (64.64%) and 29 female (35.36%) diagnosed with temporal lobe epilepsy. The mean values of the scales applied on children were  $47.22 \pm 30.94$  (min-max = 11–132) for ICNDS and  $20.93 \pm 11.4$  (min-max = 0–33) for IPES.

**Conclusion:** In harmony with the above findings, this study found that children with temporal lobe epilepsy and their parents were slightly-mildly impacted from the disease according to IPES and that the children's disability levels were close to the upper limit according to ICNDS. Also, in addition to the above result, this study found that the children were weak in their relations with their parents, with poor social interaction, and this finding could be a proof of the negative impact of epilepsy on the child's emotional wellbeing.

#### p1012 THE RELATIONSHIP BETWEEN NORMAL MOTOR DEVELOPMENT AND DISEASE IMPACT-DISABILITY LEVEL IN CHILDREN WITH EPILEPSY

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**Purpose:** In our study, we aimed to determine the impact on the child's illness impact-disability levels of epileptic children's on motor development levels.

**Method:** In our study to determine the child's motor development levels 'The Neurological Sensory Motor Developmental Assessment (NSMDA)' scale, determine to disease the effects-disability levels' Impact of Childhood Neurological Disability Scale (ICNDS) 'and' Impact of Pediatric Epilepsy Scale (IPES) scale was used.

**Results:** In the study 82 children with temporal lobe epilepsy, 53 men (64.64%), 29 were female (35.36%) were enrolled. Motor development levels and assessing NSMDA the score was  $6.45 \pm 0.67$  (min-max = 6–8), disease impact assessing ICNDS score was  $47.22 \pm 30.94$  (min-max = 11–132) and IPES score was  $20.93 \pm 11.41$  (min-max = 0–33), respectively. A significant relationship was found in children between NSMDA and ICNDS score ( $r = -0.097$ ;  $p > 0.05$ ) and between IPES score ( $r = -0.273$ ;  $p > 0.05$ ).

**Conclusion:** This study found that although the children were in normal levels for sensory-motor development in the sensory-motor development assessment performed only in cases with temporal lobe epilepsies exhibiting no other neurological diseases, the children were observed to have difficulties and low scores in certain activities in the fine motor, proprioception and tactile sense subscales of the test. This study found that children with temporal lobe epilepsy and their parents were slightly-mildly impacted from the disease according to IPES and that the children's disability levels were close to the upper limit according to ICNDS.

Children of the assessment to be made in more detail in the motor level is thought to be effective on disability-effect levels.

**p1014**

### OVERREPRESENTATION OF AGE RELATED EPILEPTIFORM DISCHARGES IN CHILDREN WITH HEMISPHERIC EPILEPSY SYNDROMES

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**Introduction/aim:** Few publications have reported rare combinations of age related epileptiform discharges (ARED)/-epilepsies (ARE) with symptomatic focal epilepsies (1–2). However, in one study dealing with children with cerebral palsy and epilepsy after perinatal stroke, higher rates of ARED and ARE were reported(3).

**Methods:** Data from 131 children who had undergone hemispherectomy/hemispherotomy from 1998–2014 were screened for the presence of ARED/ARE. Inclusion criteria for ARED: age of patients >18 months <18 years, typical multi-phasic morphology of spikes, no continuous irregular slow or cortical scars over the area over which spikes were recorded from; facultative: activation of spikes during sleep, cessation of spikes during puberty.

**Results:** Overall 28/131 (21.4%) (16 males) had ARED at some time at pre-, peri-, post-surgery investigations: 15/40 (37%) with porencephalic cysts, 8/70 (11.4%) with developmental lesions (FCD, hemimegalencephaly, polymicrogyria), 5/21 (23%) with miscellaneous lesions. None of the patients had an ARE. Positive family history for epilepsy was found in only 2 of the ARED patients.

**Conclusion:** In accordance with the publication by Wanigasinghe (3), we found a dramatic overrepresentation of ARED in epileptic children with congenital hemiplegia after arterial ischaemic stroke/ porencephalic cysts. The rate of ARED was much lower in the other etiologies but higher than expected. Recognizing additional ARED in symptomatic structural focal epilepsies might have an impact on the management of these patients, e.g. regarding the indication for surgery as well as the selection of antiepileptic drugs is concerned (risk of an aggravation of the ARED- component by drugs acting as sodium channel blockers).

As part of this ongoing study, data are searched for variables explaining the high rate of ARED in patients with porencephalic cysts.

#### References

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3. Wanigasinghe et al.. *Dev Med Child Neurol.* 2010

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**p1015**

### A CASE OF SENSORY (TACTILE) EVOKED IDIOPATHIC MYCLONIC SEIZURE OF INFANCY

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Reflex seizures are originated with a specific afferent stimulus or the patient's self activities. Reflex seizures have a prevalence of 4–7% among patients with epilepsy

Ten months old female patient was referred to our hospital with complaints of upward eye movements that lasted a few seconds for ten to fifteen times a day since 1 month. This seizure could be provoked by tapping the nose of the baby. EEG confirmed a generalized epileptiform discharge. Valproic acid 20 mg/kg was started and the patient was seizure free. The case was diagnosed as sensory (tactile) evoked idiopathic myclonic seizure of infancy. Tactile stimuli given during electroencephalogram may help in diagnosing the patients with this syndrome.

**p1016**

### EARLY PREDICTORS OF CLINICAL AND MENTAL OUTCOME IN TUBEROUS SCLEROSIS COMPLEX: A PROSPECTIVE STUDY

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**Purpose:** We aimed to identify early predictors of pharmacoresistance, mental retardation and autistic spectrum disorder (ASD) in pediatric patients diagnosed with cardiac rhabdomyomas (CR) in pre- and perinatal period. Our goal was to demonstrate significance of standardized protocol for diagnosis and follow-up in patients in high risk of tuberous sclerosis complex (TSC), development of intractable epilepsy and its unfavorable consequences.

**Method:** Clinical, neuropsychological, electrophysiological and neuroimaging data in a group of 22 patients with definite clinical diagnosis of TSC were followed prospectively according to a standardized protocol for patients with pre/perinatal diagnosis of CR developed in our centre. EEG exams from period before the onset of epilepsy, at the time of epilepsy onset and at the end of follow-up period were reevaluated using a specific parametrical protocol. MR studies from period of incomplete and complete brain myelination were reviewed and searched for lesions associated with TSC, including defined features of focal cortical dysplasia (FCD). Barnard's exact test and Kruskal-Wallis test of independence (at  $p < 0.05$ ) were used for statistical evaluation of results.

**Results:** Development of mental retardation was predicted by abnormal neurological exam, early seizure onset, intractability of seizures, higher total number of AEDs used, abnormal EEG background at the end of follow-up, and higher number of both tubers and areas with FCD-like features on MR. Predictors of ASD included abnormal neurological exam, early developmental delay, first-line AED treatment failure; abnormal background, presence of spikes, and their higher frequency on EEG at the end of follow-up, as well as higher number of areas with FCD-like features on MR. Intractable epilepsy at the end of follow-up was predicted by mental retardation; a trend towards intractability in children with earlier seizure onset and higher number of tubers was observed.

**Conclusion:** Early initiation of antiepileptic treatment and prompt seizure control could improve mental outcome and decrease incidence of pervasive developmental disorders in TSC patients. We regard standardized protocol for clinical follow-up and treatment essential in management of patients with pre/perinatal diagnosis of cardiac rhabdomyomas.

p1020

### SYMPTOMATIC WEST SYNDROME: THE ELECTROPHYSIOLOGICAL AND STRUCTURAL FEATURES AND PROGNOSIS

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**Purpose:** Symptomatic etiology has been well recognized as a factor for severity in the long-term prognosis of WS. Impact of different etiological or pathophysiological sub-groups however, is not so much questioned. The aim of this study was to search a relation between the clinical, electrophysiological and structural features in patients with symptomatic WS (sWS) in regards to the long-term course of the disease.

**Method:** Data belonging to a total of 99 patients with sWS recruited since 1991 were included in the study. According to the neuro-developmental and social conditions during the final evaluation, the patients were placed into two categories: Group I: patients with normal or subnormal motor and intellectual outcomes with favorable social status; ambulatory patients receiving special academic and/or physical support to cope with social needs. Group II: Patients with severe motor and/or mental impairment with solely supervised living or patients who were deceased. The EEG findings were reviewed and classified. The cMRI findings were classified as normal, with diffuse cortical and/or subcortical involvement, or with unilateral cortical and/or subcortical involvement.

**Results:** The study population consisted of 61 males and 38 females with a mean follow-up duration of 8 years. The most common etiological causes were perinatal asphyxia and CNS infections. Sixty-three patients suited to Group I and 36 patients were in Group II. We examined a total of 764 video EEG recordings, with a duration of minimum 2 hours. Sixty-two patients had consistently symmetrical, 22 patients asymmetric hypsarrhythmia and four patients unilateral hypsarrhythmia in the EEGs. Asymmetry of hypsarrhythmia showed no correlation with long-term course. Preservation of sleep spindles had a direct and diffuse involvement in the cMRI revealed an inverse correlation with better prognosis.

**Conclusion:** Prognostic consequences of sWS may be partly anticipated by careful examination of the clinical, imaging and EEG data.

p1021

### MEAN PLATELET VOLUME, IRON, FOLIC ACID AND VITAMINE B12 LEVELS IN FEBRILE CONVULSIONS

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**Purpose:** To evaluate mean platelet volume level in patients with simple and complicated febrile convulsions, and also investigating the relationship between convulsions and iron, vitamin B12 and folic acid levels in patients diagnosed with anemia.

**Method:** Total of 83 patients between month 6-age 5 diagnosed with febrile convulsion(FC) were included in the study, and as control group 92 cases with inflammatory diseases without convulsions were included. Hemogram results of all patients in study and control groups were evaluated. Serum iron, total iron binding capacity, plasma ferritin, transferrin saturation, peripheral distribution, folic acid, vitamin B<sub>12</sub> and mean plate-

let volume levels were examined in patients with convulsion and anemia diagnosis.

**Results:** We enrolled 83 patients in this study; 47 (56.6%) boys, 36 (43.4%) girls. Control group had 36 (39.1%) girls and 56 (60.9%) boys who had no history of febrile convulsions. 48 (57.8%) of the patients had simple febrile convulsions(SFC), 35 (34.9) had complicated febrile convulsions (CFC) and 6 (7.3%) had febrile status. 22.8% of the patients had anemia. There was no significant difference between SFC and CFC but also FC and control group for iron, TIBC, transferrin saturation, and folic acid parameters. The mean of level of ferritin in SFC was 30.58 ng/ml, whereas it was 13.78 in CFC. There was a significant difference between two groups ( $p < 0.001$ ). Vitamine B12 level in SFC group was 430.73 pg/ml and 408.75 pg/ml in CFC group. There was a significant difference between two groups ( $p < 0.01$ ). There was no significant difference between SFC, CFC and control group for the level of mean platelet volume.

**Conclusion:** Ferritin and vitamin B12 levels of CFC group were found to be significantly lower with regard to SFC group. This result suggested low ferritin and vitamin B12 levels may be a factor in complicated type febrile convulsion.

p1022

### USE OF ACTH AT HIGH DOSES FOR THE MANAGEMENT OF EPILEPTIC ENCEPHALOPATHY

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**Purpose:** Describe the response in seizure control in patients with epileptic encephalopathy treated with ACTH at high doses.

**Method:** We review the charts of patients who were treated with ACTH between 2005–2014 under the diagnosis of epileptic encephalopathy. We analyze demographic characteristics, seizure control, adverse reactions and follow up.

This protocol of ambulatory administration and weekly follow up, uses a deposit synthetic ACTH with gradual tapering between 12 to 14 months, previously discarding associated pathologies that contraindicate the use of this treatment.

**Results:** 49 patients with a mean age of 7 years [1.3–23 years]: 12 (14%) with Doose syndrome, 8 with Lennox-Gastaut, 7 West syndrome, 10 with focal symptomatic epilepsy; 44% had symptomatic epilepsy. The initial dose of ACTH was 3.3 UI/kg/day (0.1–8 UI/kg/day). The complete time of the protocol was 20.11 months, seizure control 78.9% (0–100%) (IC 68.8–88.9) and 26.2% of patients accomplished 100% seizure control.

Neurodevelopment improved about 33%, with a subjective progress of 70%. 97% presented adverse reactions, 18.4% had severe adverse reactions which lead to discontinue the protocol. 36.6% of the patients continued with complete seizure control after treatment.

**Conclusion:** ACTH can be used as an effective therapeutic strategy in patients with epileptic encephalopathy with poor response to pharmacologic treatment, achieving an improvement of 78.9% in seizures, neurodevelopment and performance, with bearable and treatable adverse reactions.

p1023

### A PREDICTION MODEL TO DIAGNOSE CHILDHOOD EPILEPSY AFTER A POSSIBLE SEIZURE

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**Purpose:** The clinical profile of children who suffered from a possible seizure is heterogeneous and the sensitivity of diagnostic testing is limited. This hampers early and accurate diagnosis. We developed a model to reliably predict diagnosis of epilepsy in children after a possible seizure by combining routinely available information at first consultation.

**Method:** We collected clinical data of 451 children who visited our first seizure clinic between January 2008 and May 2013. The gold standard outcome, classified as epilepsy or no epilepsy, was based on the eventual diagnosis after clinical follow-up. A multivariate logistic regression model was fitted on data from 70% of randomly selected children. Patient characteristics (age, gender), clinical characteristics (age of first seizure, event frequency, developmental status, event description, medical and family history) and standard electroencephalography report were used as predictor variables. Model performance was validated with data from the remaining 30% of children using a receiver operating characteristic (ROC) curve.

**Results:** Overall model performance was excellent, with an area under the ROC curve (AUC) of 0.90 [95% confidence interval (CI) 0.83 to 0.97]. Model performance in a selective sub-population of 177 children with unclear diagnosis at initial consultation was good with an AUC of 0.76 [CI 0.68 to 0.83].

**Conclusion:** This model may prove to be a valuable tool in clinical practice as all predictor variables are routinely available at first consultation. A web-application is provided to facilitate the diagnostic process for clinicians who are confronted with children with paroxysmal events, suspected of suffering from epilepsy.

#### p1024

### TARGETED RESEQUENCING IN EPILEPTIC ENCEPHALOPATHIES: DIAGNOSTIC IMPLICATIONS AND GENOTYPE-PHENOTYPE CORRELATIONS

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**Purpose:** To assess the diagnostic value of NGS target re-sequencing approach for epileptic encephalopathies.

**Method:** The diagnostic tool allows the screening of 20 genes which have been consistently associated with early-onset epileptic encephalopathy (EE): ALDH7A1, PNP0, ARHGEF9, ARX, SLC25A22, PLCB1, TBC1D24, PNKP, KCNT1, KCNQ2, SCN2A, SCN8A, STXBPI, SCN1A, PCDH19, CDKL5, SPTAN1, SLC2A1, ST3GAL3, GRIN2A). NGS have been performed by Ampliseq/Ion Torrent technology of at least 120X. Patients have been classified into 5 phenotypic classes:

- (1) EEs with onset in the first year of life;
- (2) infantile spasms/West syndrome
- (3) Dravet Syndrome
- (4) CSWS/Landau-Kleffner Syndrome
- (5) EEs with onset after the first year of life.

**Results:** Fifty-four patients have been analyzed: class 1, n°26; class 2, n°10; class 3, n°6; class 4, n°4; class 5, n°8. Pathogenetic effects of variants have been attributed according to i) segregation analysis (inherited vs transmitted; putative functional effect (damaging (vs.) benign); state-of-art genotype-phenotype correlations. We identified a total of 23 unreported variants: - n°13 variants were classified as likely pathogenetic (24%) on the following genes: STXBPI (n°2), SCN1A (n°2), SCN2A (n°2), KCNQ2 (n°2), CDKL5 (n°2), KCTN1 (n°1), GRIN2A (n°1), PNPO (n°1). - n° 6 variants were classified of uncertain significance (11%): PCDH19 (n°1); SCN1A (n°1), ARHGEF9 (n°1), KCNQ2 (n°1), SPTAN (n°1), STXBPI (n°1). - n° 4 variants were classified likely benign (7%): ARHGEF9 (n°1), TBC1D24 (n°1), SCN1A (n°1), KCNQ2 (n°1).

**Conclusion:** In about 1/4 of the cases we were able to reach a definite diagnosis. Detailed clinical information is required to interpret genetic findings. The diagnostic yield is particularly high within the group of EEs with onset in the first year of life. SCN1A, SCN2A, STXBPI and CDKL5 show multiple mutations, providing a further confirmation on their pivotal role in the etiology of epileptic encephalopathy.

## Paediatric Epileptology 16 Tuesday, 8th September 2015

#### p1026

### PREVALENCE OF EPILEPSY IN CHILDREN WITH DOWN SYNDROME, TOO HIGH OR TOO LOW?

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**Background:** Down Syndrome (DS) is the most common chromosomal abnormality and may be associated with a variety of complications including epilepsy. Several studies indicate that the frequency of epilepsy in children with DS ranges between 1% and 13%. The prevalence of epilepsy in DS is more than in general population and less than would be expected when compared with other groups of children with learning disabilities. In DS, a bimodal distribution of epilepsy onset has been described: the first peak in early childhood and the second increasing with age.

**Objectives:** To assess change in the prevalence of epilepsy in children with DS and evaluate the type of epilepsy in this population.

**Methodology:** We reviewed retrospectively our cohort of 79 patients with DS, aged 0 to 19 years of age (median age 8 years), 44 males, 35 females. All were followed in our clinic at least once per year. The clinical diagnoses of DS based on typical somatic features was confirmed by cytogenetic analysis in all patients of which 60 had trisomy 21, one translocation and information of the others was limited to "diagnosis confirmed".

**Results:** In our cohort of 79 patients with DS none of them was diagnosed with epilepsy, according to the ILAE criteria.

**Conclusion:** Epilepsy as a comorbidity in DS has an age dependent prevalence. In paediatric population we might consider that the prevalence of epilepsy is decreasing as secondary lesions due to congenital heart anomalies, respiratory distress, metabolic disturbances are diagnosed and treated promptly due to improved medical care before and after the birth in this population.

#### p1027

### PERSISTENT EPILEPTIC SPASMS AND TONIC SEIZURES IN OLDER CHILDREN AND YOUNG ADULTS WITH DRUG RESISTANT EPILEPSY: ARE THERE ANY BIOLOGICAL DIFFERENCES?

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**Purpose:** Epileptic spasms are being increasingly recognised in older children and young adults. We describe the clinical characteristics of patients with persistent epileptic spasms (occurring beyond 2 years of age) in comparison to patients with tonic seizures.

**Method:** Patients with documented spasms or tonic seizures were identified from the EEG database at a tertiary epilepsy centre in U.K. Consecutive patients who presented with persisting epileptic spasms or tonic seizures were recruited. Each group (30 patients) was subdivided into early onset (<2 years) and late onset (>2 years) based on the age at seizure onset. Thirty patients with mixed seizure types were taken as a comparator. Aetiology was divided into structural lesions (including HIE & ABI), genetic and metabolic causes. The response to medication was also analysed.

**Results:** The median age was 17 years (range 2 to 27 years) with a male:female ratio of 1:1.25. The median age of seizure onset was 2 years (range Day 1–12 years). Structural causes were noted in 62.5% (10/16) of early onset spasms and 35.7% (5/14) of late onset spasms [p value 0.028; Fisher's Exact Test, 95% confidence interval]. Genetic aetiology was also more associated with early onset spasms than late onset spasms, 31.3% (5/16) (vs.) 14.3% (2/14). [p value 0.028; Fisher's Exact Test, 95% confidence interval]. When the whole group of spasms was considered, structural aetiologies were higher 50% (15/30) than in the tonic group 33.3% (10/30), but did not reach statistical significance. Patients in both the groups were refractory to treatment.

**Conclusion:** Structural and genetic aetiologies are significantly higher in patients presenting with early onset spasms. Structural lesions are overall commoner in the spasms group than in the tonic group indicating fundamental biologic differences.

#### p1028

##### FEBRILE SEIZURES AND OTHER EPILEPTIC DISORDERS FREQUENCY IN CHILDREN WITH INFECTIOUS DISEASES

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**Purpose:** Our purpose was to establish frequency of febrile seizures and other epileptic disorders in children attending tertiary hospitals with the symptoms of infectious diseases

**Method:** 27 029 patients, aged 0.2–16 years, who were admitted in the tertiary hospitals in 2009–2013 with acute infectious diseases were enrolled. Those who developed seizures one day before the admission, at admission and during the in-hospital stay were thoroughly investigated using lab tests, neurological examination and EEG in all patients and brain ultrasound and MRI if needed.

**Results:** Among 27 029 patients 676 (2.5%) had epileptic disorders. Among these 76.3% (n = 516) had febrile seizures. 16.6% (n = 112) had seizures during the neuroinfection (35 patients with encephalitis and 77 with meningitis); 7.1% (n = 48) had established childhood epilepsy. Among patients with febrile seizures 81.4% (n = 420) had acute respiratory infections and 14.9% (n = 77) had intestinal infectious diseases. 85% of the patients (n = 575) were younger than 3 years old.

**Conclusion:** Epileptic disorders are relatively rare in children with infectious diseases and occur in all forms in 2.5% of the cases. Mainly these seizures appear in early childhood (children younger than 3 years). Majority of these epileptic disorders are febrile seizures (seen in 76.3% of the cases). Infectious respiratory diseases seems to cause febrile seizures more often than all other causes.

#### p1029

##### THE IMPACT OF PROLONGED ACUTE CONVULSIVE SEIZURES ON LEARNING AND SCHOOLING IN A EUROPEAN SURVEY OF CHILDREN WITH EPILEPSY

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**Purpose:** To survey educational needs and the burden of disease in children with epilepsy who experience prolonged acute convulsive seizures (PACS).

**Method:** Practices in Emergency and Rescue medication For Epilepsy managed with Community-administered Therapy 3 (PERFECT-3) was an international, cross-sectional, observational study. Eligible patients were non-institutionalized children with epilepsy (aged 3–16 years) who had experienced ≥1 PACS within the last 12 months and had current prescription(s) for PACS rescue medication. Investigators provided clinical assessments and patients and their parents/guardians each completed web-based questionnaires. Parents/guardians acted as proxies for children unable to complete questionnaires.

**Results:** A total of 286 patients were enrolled in Germany (n = 92 [32.2%]), Italy (n = 75 [26.2%]), Spain (n = 77 [26.9%]) and the UK (n = 42 [14.7%]). Their mean age was 8.9 years (standard deviation [SD], 3.8) and 54.9% were male. In the 12 months before enrolment, patients had experienced 1–400 PACS (median, 4; mean, 23.6 [SD, 59.8]); 54.9% experienced 1–5 and 9.8% experienced ≥51. The majority of patients (52.7%) could not undertake typical day-to-day activities and most (76.9%) had learning disabilities. Of these, 69.9% had severe or moderate learning disabilities, and were unsuited to mainstream school/ kindergarten. Only 108/257 parents (42.0%) reported that their child attended mainstream school. In the patient/proxy survey (n = 251), most children reported that PACS always, often or sometimes interfered with school attendance (60.4%) and their activities at school (62.8%), home (70.0%) and elsewhere (66.4%).

**Conclusion:** This European study of children with epilepsy who had experienced ≥1 PACS in the year before enrolment confirmed that children with epilepsy often face learning disabilities and need specialist education. Most children also had problems with attendance and participation at school.

Study funded by ViroPharma (part of the Shire Group of Companies).

#### p1030

##### NEURONAL ANTIBODIES IN PAEDIATRIC EPILEPSY: CLINICAL FEATURES AND LONG-TERM OUTCOMES

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**Purpose:** Neuronal antibodies (Abs) are now widely accepted as causative in autoimmune encephalitis (AE), and most patients respond well to immunotherapy. In paediatric epilepsy (PE), the implications of a positive test are not yet clear. In this study, a historical cohort of PE patients were tested for neuronal autoantibodies and their outcomes analysed in relation to antibody status.

**Method:** Serum from 178 new-onset PE patients recruited between 1988–1992 as part of the Dutch Study of Childhood Epilepsy and 112 healthy age-matched controls were tested for neuronal-Abs to the NMDAR, AMPAR, VGKC-complex, LGI1, CASPR2, contactin-2 proteins and GAD, using cell-based and radio-immunoprecipitation assays. The results were correlated with the clinical data collected over 15 years.

**Results:** 17 PE patients (17/178; 9.5%) were positive (NMDAR-Ab (7), VGKC-complex-Ab (3), CASPR2-Ab (4), and contactin-2-Ab (3) compared to 3 healthy controls (VGKC-complex (1) and NMDAR (2), 3/112; 2.6%,  $p = 0.03$ ; Fisher's exact test). Ab-positive patients had a significantly higher rate of pre-existing cognitive impairment (9/17 (vs.) 33/161;  $p = 0.0056$ ). 57% (8/14) Ab-positive patients were on AEDs at final contact compared to 31% (44/143) of Ab-negative patients ( $p = 0.07$ , ns); 3/17 of Ab-positive patients were intractable (21% (vs.) 10% in the Ab-negative group,  $p = 0.18$ , ns). At final follow-up, 65% of Ab-positive patients had been seizure free for more than 2 years. Six patients, Ab-negative at epilepsy onset, became Ab-positive within the first year of disease (NMDAR-Ab (2), CASPR2-Ab (3), contactin-2-Ab (1)).

**Conclusion:** Neuronal surface Abs were found more commonly in new-onset PE patients than in controls, and more frequently in patients with pre-existing neurological problems. Given that the majority of patients responded well to standard treatments, and some patients developed Abs after the onset of epilepsy, this study suggests that Abs can arise secondary to brain damage, and are not necessarily the primary cause of epilepsy without encephalitis.

### p1031 EFFICACY OF EVEROLIMUS AGAINST EPILEPSY WITH TUBEROUS SCLEROSIS

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**Purpose:** An investigation of use of everolimus (EL) was conducted in patients to confirm the efficacy against epilepsy with tuberous sclerosis (TS).

**Method:** We investigated changes in epilepsy symptoms and examinations after EL therapy for angiomyolipoma (AML) and subependymal giant cell astrocytoma (SEGA) in 1 male and 2 female patients with TS aged 21, 16, and 13 years, respectively, at the start of EL. All patients had repeatedly received resection or embolization of AML, and one had undergone resection for comorbid SEGA. All patients had epilepsy that had occurred during infancy: partial seizures (PS,  $n = 3$ ) and epileptic spasms in series (ESS,  $n = 2$ ). Before EL, 2 patients had been receiving multiple anti-epileptic therapies to successfully prevent epileptic seizures (ES), and 1 had daily PS accompanying secondarily generalized tonic-clonic convulsions (sGTC) and ESS.

**Results:** Two patients had no seizure recurrence during EL. In the patient with daily PS, sGTC disappeared immediately after introducing EL. PS decreased from daily to weekly basis at two months of EL, and eventually disappeared after one year. No changes in EEG or cortical tubers occurred after EL in any patient. AML became smaller or remained

unchanged, requiring no resection or embolism, and the SEGA tumor size decreased in all cases. All patients experienced rash and stomatitis during EL, and one required treatment suspension. No serious adverse events occurred, including interstitial pneumonia, and all patients continued EL over one year.

**Conclusion:** EL was quite effective against intractable PS in one TS case. Although it currently is not, EL should be indicated for treatment of intractable epilepsy.

### p1032 NEXT GENERATION SEQUENCING ANALYSIS IN NEONATAL / EARLY EPILEPTIC ENCEPHALOPATHY

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**Purpose:** Epileptic encephalopathy (EE) term describes epilepsy syndromes in which seizures and epileptiform electroencephalographic abnormalities are considered to contribute to progressive cerebral dysfunction. A subset of all the EEs that still await an etiological explanation, particularly those with onset of seizures within the first year of life. In this study genetic background of neonatal/early infantile EE was investigated by next generation sequencing (NGS) analysis.

**Method:** Thirty cases who had refractory seizures with neonatal or early infantile onset were prospectively included in this study. Three cases had history of hospitalization in neonatal unit due to meconium aspiration syndrome, and four cases also had cyanosis and/or transient respiratory distress following the labor. All cases had normal metabolic work up including serum lactic acid, pyruvic acid, aminoacid and carnitine levels, biotinidase activity and urine organic acids. Their cranial magnetic resonance imaging findings were normal except cerebral atrophy. Their karyotype analyses were normal. None of them had antequitin gene mutation. Mutations in 16 genes (ARX, CDKL5, CNTNAP2, FOLR1, FOXP1, GRPR, LAMC3, MBD5,MECP2, PCDH19, PNKP, SCN1A, SCN1B, SCN2A, STXBPI, KCNQ2) were examined with NGS method in our cases.

**Results:** All they were born at term except three cases. Their ages were between 6 and 204 ( $62.5 \pm 51.6$ ) months. Parental consanguinity was found in 11 of 30 cases (36%). Their seizures started between 1 and 270 ( $91.7 \pm 80.25$ ) days of life, eleven cases had seizures with neonatal onset. Infantile spasms are the predominant seizure type in our group consisting of 16 of 30 cases. All of them were treated at least two anticonvulsant drugs. Cranial MRI was normal in half of the cases, the reminder had cortical or cerebellar atrophy in different severity. Only one case had T2 hyperintense signal changes in basal ganglia. The results of NGS analysis were discussed with the literature.

## Psychiatry 3 Tuesday, 8th September 2015

### p1035 EPILEPSY AND PSYCHOSIS: PATTERN OF PSYCHOTIC DISORDERS AMONG PERSONS WITH EPILEPSY IN ILE-IFE

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**Purpose:** Psychiatric disorders are common in Persons with Epilepsy and these may have a negative impact on the course of epilepsy.

**Method:** A retrospective case review of 7 persons with epilepsy and psychotic disorder presenting over a 2 year period at the Neurology and psychiatric units of Ile-Ife. In each patient the clinical characteristics, epilepsy variables, use of antiepileptic and antipsychotic drugs were studied.

**Results:** The prevalence of psychosis among the 150 patients in both clinics was 4.6%. There were 7 persons with epilepsy presenting with 8 psychotic episodes comprising 5 females and 2 males. The age ranged between 16 and 40 years with a mean of 28 years. Majority (4) had complex partial seizures and 3 were one of a pair of twins. Most of the episodes were interictal (5). In two of the patients with post ictal psychosis the episode was preceded by poor sleep and status epilepticus. All the patients were on carbamazepine. Only 4 of the episodes were treated with antipsychotics and the outcome was good with all patients discharged to the clinic.

**Conclusion:** Psychotic disorders occurred among persons with complex partial seizures and was more prevalent in females. Post-ictal psychosis is commoner than inter-ictal psychosis. Further studies are needed to find out the predisposing factors to the occurrence of psychotic disorders in PWE.

#### p1036

### VALIDATION TURKISH 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) was developed for the rapid detection of a major depressive episode in people with epilepsy. This study describes the development, validation, and psychometric properties of the Turkish version of the NDDI-E

**Method:** A consecutive sample of 100 outpatients with epilepsy has been assessed using the Beck Depression Scale and the NDDI-E.

**Results:** All patients had no major difficulties in understanding or answering the questions of the Turkish version. Nearly all of the other language validations were performed before 2013 mostly with M.I.N.I. Plus version 5.0.0 which bases on DSM-IV. We used Beck Depression Scale in validation because of changing DSM criteria. Distribution of variables was evaluated with Kolmogorov-Smirnov test, concordance between each test was studied with kappa test and Spearman correlation was used to find out correlation between tests. Results of our statistical analysis were sensitivity of 91%, a specificity of 74%, a positive predictive value of 82.5%, and a negative predictive value of 86.5% of new Turkish version.

**Conclusion:** Dealing with treatment of epilepsy usually shadows diagnosis of psychiatric comorbidities. Depression is the most common psychiatric comorbidity. The validation of Turkish version of this test is necessary for correct diagnosis of depression in patients with epilepsy.

#### p1037

### INTERICTAL DISPHORIC DISORDER: IS IT SPECIFIC FOR PATIENTS WITH EPILEPSY?

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**Purpose:** (1) to assess prevalence of interictal dysphoric disorder (IDD) (Blumer 2000) in patients with epilepsy by comparison to patients with migraine;

(2) to evaluate influence of IDD on quality of life in patients with epilepsy.

**Method:** Adult patients (age range 18–65 years) with definite diagnosis of epilepsy or migraine, of normal intelligence, without any progressive neurological disease or psychotic disorder were included in the study. They were assessed with Interictal Dysphoric Disorder Inventory (IDDI) (Mula M, Trimble MR, 2008). Beck's Depression Inventory (BDI), Beck's Anxiety Inventory (BAI), and QOLIE-31 Inventory (Serbian version) were completed by patients themselves.

**Results:** Study groups consisted of 59 patients with epilepsy (mean age  $42.3 \pm 14.4$ ; female 57.6%), and 49 patients with migraine (mean age  $36.7 \pm 12.3$ ; female: 71.3%). Prevalence of IDDI definite diagnosis in epilepsy group was similar (12%) to migraine group (11%). IDDI affective scores were significantly higher in migraine than in epilepsy patients ( $p = 0.017$ ). IDDI total and partial (labile depressive symptoms, labile affective symptoms and specific symptoms) scores showed strong correlations among themselves in both groups supporting the validity of the IDDI as a construct. In epilepsy group, IDDI total score and IDDI partial affective score displayed a significant positive correlation with BDI and BAI scores. In migraine group only IDDI total score was highly positively correlated with BDI and BAI scores. QOLIE-31 total score was significantly negatively correlated with: IDDI total score ( $r = -0.355$ ), IDDI depressive scores ( $r = -0.276$ ) and IDDI affective scores ( $r = -0.415$ ).

**Conclusion:** IDD represents a homogenous construct that can be diagnosed in a relevant proportion of patients, but it is not typical for epilepsy. In patients with migraine, IDDI affective symptoms are more pronounced and severe than in patients with epilepsy. IDDI total score, especially labile depressive symptoms and affective symptoms have significant influence on quality of life in patients with epilepsy.

#### p1039

### AUTISM SPECTRUM DISORDER ASSESSMENT IN FEMALE EPILEPSY WITH PCDH-19 MUTATION: CLINICAL DATA

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**Purpose:** Epilepsy with PCDH-19 mutation is an X-linked disorder. Intellectual delay and behavioral disturbances especially autistic features are reported in affected females. The aim of our study was to study with a detailed methodology the Autism Spectrum Disorders (ASD) in patients with epilepsy with PCDH-19 mutation.

**Method:** We included eight females aged from 5 to 17 years. Clinical data and history was reviewed. Patients underwent an autism spectrum disorder battery of tests and questionnaires: the Autism Diagnostic Observation Scale (ADOS), ECAR-T, Childhood Autism Rating Scale and Autism Diagnostic Interview-Revised questionnaires and a detailed

interview with child psychiatrist. They also had an assessment of the cognitive area using standardized tools: Wechsler tools (WISC-IV or WPPSI-III) or the Psycho-Educative Profile-III (PEP-III).

**Results:** Age at seizure onset ranged from M4 to M58. 3/8 patients were seizure free and 5/8 presented annual seizures at last visit. One patient had no treatment, others had from 2 to 6 antiepileptic drugs. 6/8 patients presented ASD with 4/8 patients with definite autism and 2/8 with Pervasive Developmental Disorder Non Otherwise Specified. Mainly, patients presented communication and social interaction difficulties while stereotypes and restricted interests features are not predominant. Two groups are emerging: a group of 2 patients with intellectual abilities in the low average and no ASD presenting later seizure onset, another with mental retardation and ASD (6/8). The neurodevelopmental profile is not clearly linked to seizure and treatment on further aspects.

**Conclusion:** The ASD and MR comorbidity is important in our population justifying the importance of behavioral and cognitive evaluations and follow-up. We address the possible causal role of the mutation of the protocadherin 19 protein beyond the seizures per se.

#### p1040

### PERCEIVED STRESS IN PEOPLE WITH EPILEPSY AND ITS PREDICTORS

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**Purpose:** People with epilepsy (PWE) have been reported to be more stressful than those without epilepsy. We investigated perceived stress in PWE and identified its predictors.

**Method:** This was a case-control study. Eligible subjects who consecutively visited epilepsy clinic underwent several questionnaires including the Perceived Stress Scale (PSS), the Revised Stigma Scale (RSS), the Korean version of the Neurological Disorders Depression Inventory for Epilepsy (K-NDDI-E), the Generalized Anxiety Disorder-7 (GAD-7), the Epworth Sleepiness Scale (ESS), and short forms from the Patient-Reported Outcomes Measurement Information System (PROMIS) Sleep Disturbance (SD) and Sleep-Related Impairment (SRI) item banks.

**Results:** Mean PSS score of PWE was not higher than that of people without epilepsy (PWoE). However, that score was significantly higher in patients with poorly controlled epilepsy ( $p = 0.038$ ) or uncontrolled epilepsy ( $p < 0.001$ ) than PWoE. Univariate analyses revealed associations between the PSS score and gender, education, job, household income, driving license, marital state, the number of antiepileptic drug (AED), seizure control, co-administration of psychiatric drugs, AED load, the RSS score, the K-NDDI-E score, the GAD-7 score, the ESS score, and the PROMIS SD and SRI scores. Multivariate analyses indicated that the strongest predictor for the PSS score was the K-NDDI-E score ( $\beta = 0.375$ ,  $p < 0.001$ ), followed by the GAD-7 score ( $\beta = 0.220$ ,  $p = 0.003$ ), and the PROMIS SRI ( $\beta = 0.161$ ,  $p = 0.016$ ) and SD ( $\beta = 0.131$ ,  $p = 0.047$ ).

**Conclusions:** Perceived stress in PWE is more closely related to psychiatric and sleep problems than demographic, socioeconomic, and seizure-related factors.

#### p1041

### PSYCHOGENIC MODULATION OF FOCAL EPILEPTIC SEIZURES: A NON-DESCRIBED PSYCHOGENIC PHENOMENON

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**Purpose:** Psychogenic non-epileptic seizures (PNES) account for up to 30% of referrals for medically refractory epilepsy. PNES appear most often isolated in the context of a personality disorder. However, between 5% and 40% of patients with PNES has concomitant epilepsy. Fortunately, the largest numbers of PNES are clearly distinguishable from seizures of epileptic origin. Therefore, patients can be divided into three groups: epileptic seizures only, PNES only and mixed cases. We have detected a fourth group: patients with post ictal psychogenic modulation (PIPM) of epileptic seizures in which the psychogenic event occur timely related to a focal seizure.

**Method:** We reviewed the files of patients with pharmacoresistant focal epilepsy who underwent long-term video-EEG monitoring (VEEGM) between January 2010 and January 2015. Most of them underwent presurgical evaluation. All clinical files were screened for psychogenic events during VEEGM. All selected patients were individually clustered in one of four groups: only seizures, only PNES, mixed cases and PIPM.

**Results:** 565 clinical records were screened. Four patients with PIPM of focal seizures were found. Two were female patients, with a mean age of 33.2 years (range, 28–47 years). Two presented temporal, one insular and one occipital lobe epilepsy. Two were left- and two right-lateralized. Epilepsy surgery was indicated in 3 cases and was performed in two with excellent outcome. Two patients were studied with SEEG. In all cases psychogenic events occurred immediately after focal seizures without generalization. The EEG/SEEG during the events was normalized.

**Conclusion:** Psychogenic events can appear timely related with true epileptic events. Possibly, the perception of an epileptic seizure in a small group of patients can trigger a psychogenic reaction. This causes additional difficulties in the interpretation of ictal phenomena that could lead to false localization/ lateralization hypothesis. Its occurrence does not preclude the indication of epilepsy surgery.

#### p1042

### TREATMENT CHOICES FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN WITH AND WITHOUT INTERICTAL EPILEPTIFORM ABNORMALITIES

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**Purpose:** The purpose of this retrospective study was to investigate whether interictal epileptiform discharges (IED) recorded at the attention-deficit/hyperactivity disorder (ADHD) assessment influence pharmacological treatment choices for ADHD during 12 months follow-up.

**Method:** Subjects were 517 ADHD children (82.4% male), aged between 6 and 14 years, who were diagnosed between January 2000 and December 2005 with one awake EEG at ADHD assessment. IED were found in 39 cases, 12 of them had previous epilepsy. 39 cases with IED (IED group) were matched on age and gender with 39 patients without IED (non-IED group). We measured initial use of MPH, positive response to MPH after 4–7 weeks, the use of MPH at 12 months, the use of antiepileptic drugs (AEDs), and the use of dexamphetamine and atomoxetine.

**Results:** Of the 39 patients with IED, 36 (92.3%) cases were treated with MPH and initial positive response to MPH was achieved in 83.3%. In the non-IED group, initial positive response was found in 89.2%. There were no statistically significant differences between the groups with respect to MPH use during 12 months. The use of dexamphetamine and atomoxetine were also without differences (2 cases in each group). In contrast, the use of AED significantly differed in children with and without IED

(22 (vs.) 0 cases), regardless of excluding cases with epilepsy. The use of AEDs alone was not sufficient to reduce ADHD symptoms cases with IED.

**Conclusion:** The ADHD children with and without IED differed in using of AEDs regardless of previous history of epilepsy. The use of AEDs alone was not sufficient to reduce ADHD symptoms. The IED-group and non-IED group used MPH, dexamphetamine and atomoxetine similarly during 12 months follow-up.

## Social Issues 3 Tuesday, 8th September 2015

p1044

### EPILEPSY AND DISABILITY

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**Introduction:** Epilepsy is a chronic disease that results in the loss of labor and disability. Despite appropriate medical and surgical treatments patients who experience frequent seizures should be protected by socially. In Turkey by the rules of Social Security Institution patients are entitled to disability retirement if they have more than three generalized tonic clonic seizure in a month or more than two complex partial seizure in a week.

**Method:** According to decisions at the health board of Antalya Education and Research hospital, patients who followed-up by the second stage hospitals or had no follow-up would be followed-up at least 3 months with appropriate and adequate treatment than final decision would be given. In this study we searched retrospectively the patients who applied retirement because of disability between January 2014 and January 2015. All of this patients were evaluated by the experienced neurologists. All demographic characteristics, type of epilepsy, beginning age, frequency of seizures were saved. Patient were followed-up at least three months or monitored at video EEG laboratory.

**Results:** 39 patients (31 male, 8 female) enrolled to the study. The mean age was 41.8 years, duration of epilepsy was  $20.4 \pm 12.6$  years (min 6 months- max. 46 years). At last 7 patients were suitable for disability retirement and 16 were not. 14 patients withdrew applications. Finally understood that two patients have syncope attacks rather than epilepsy.

**Conclusion:** In the follow-up of patients with epilepsy the management of medical therapy is not enough alone, we must educate the patients about their social benefits. Patients who have frequent seizures that obstacle working, should be promoted as social and financial by the social state. However this issue is open to abuse, people who deserve to be determine objectively.

p1045

### ADAPTATION TRAINING AS PSYCHOSOCIAL EMPOWERMENT INTERVENTION IN EPILEPSY

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Epilepsy can have far-reaching psychological and social consequences, which can be more debilitating than the seizures themselves. As a part of the Best Practice Guidelines of Epilepsy in Finland, the Finnish Epilepsy Association has since 1974 implemented adaptation training courses for people with epilepsy and their family members as an interventive measure to improve coping with epilepsy.

**Case presentation:** The purpose of adaptation training is to promote well-being, decision-making and self-management of epilepsy. Thus, the training potentially enables people with epilepsy and their family members to lead as full a life as possible. This is pursued by adopting an empowerment-based, collaborative approach, targeting the real life challenges of living with epilepsy.

Adaptation training is implemented as outpatient and inpatient courses with governmental funding and 350-450 participants yearly. Inpatient courses take 5-10 days. Outpatient group-training takes several weeks and consists of weekly meetings.

The provision of basic facts about epilepsy and individual and peer support are the key components of adaptation training. The peer group provides a forum for the exchange of personal experiences and creates an environment of mutual support. Peer support and collaborate learning help participants develop new skills and boost their confidence and self-esteem.

**Discussion:** The functional goal attainment is evaluated with the Goal Attainment Scaling (GAS) method. GAS includes defining a set of individual goals and evaluating the outcome using a unique scale that reflects concrete activities. Preliminary results from GAS suggest that the outcomes of adaptation training are more positive than expected. Final results will be reviewed in the poster presentation.

Feedback from participants indicates that adaptation training has met their needs and helped them better understand their epilepsy. Furthermore it provides an opportunity for positive peer support. Post-intervention outcome inquiry indicates an overall positive trend in psychosocial empowerment.

p1047

### EPILEPSIES: KNOWLEDGE, SOCIAL REPRESENTATION, PERCEPTIONS AND STIGMA AMONG UNDERGRADUATE HEALTH SCIENCES STUDENTS FROM A BRAZILIAN PUBLIC UNIVERSITY

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**Purpose:** To investigate the knowledge, social representations, perceptions and stigma among students in health sciences (non-medical students) of a Brazilian public university.

**Method:** Students in the first and last year of the courses Physical Education, Physiotherapy, Nutrition, Psychology, Social Work and Occupational Therapy (n = 372) from UNIFESP answered a questionnaire on epilepsy consisting of 53 items sub-divided into seven groups. The Stigma Scale of Epilepsy (SSE) was also used to measure the perception of stigma. Questionnaires and SSE were presented in two versions: one with the term "person with epilepsy", another with the term "epileptic". Knowledge of epilepsy and SSE were graduated from 0 to 100 to compare groups.

**Results:** The mean student's grade showed no significant increase, comparing the first ( $53.0 \pm 15.3$ ) and last ( $57.2 \pm 15.6$ ) years. There was no difference in the scores obtained from questionnaires using the word "epileptic" ( $55.3 \pm 16.2$ ) and "person with epilepsy" ( $55.1 \pm 14.9$ ). The mean SSE of last-year students ( $38.6 \pm 15.4$ ) was lower than the mean of first-year students ( $42.7 \pm 15.1$ ), regardless of the questionnaire presented. Regarding last-year students, 29.23% reported having contact with the subject. There was low performance in items on epidemiology (30.2%), etiology (32.37%) and treatments (39.52%). Regarding the procedure during a seizure, 51.88% did not try to contain a person and 27.96% would not put something in the patient's mouth to avoid suffocation or choking. Almost forty percent of students do not associate epilepsy to mental illness, 15.32% do not consider mental disorders as a cause of epilepsy and 43.28% believe that people with epilepsy often do not have psychiatric disorders. Less than twenty percent of students feel prepared for professional practice.

**Conclusion:** It will be necessary to identify trends and gaps in knowledge to develop strategies to minimize the lack of information and stigma on epilepsy to form more enlightened professionals.

**p1048**

### A RECREATION PROGRAM TO DEVELOP PHYSICAL LITERACY SKILLS IN CHILDREN WITH EPILEPSY

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**Purpose:** The majority of parents using the Epilepsy Support Centre summer camp program described their child with epilepsy as “inactive” or “reluctant” to participate in gym class or community sports. Literature suggests that if children with epilepsy withdraw from physical activity and sports, they turn to more unhealthy choices and become sedentary and isolated. This could result in the development of further medical conditions such as obesity, Diabetes, Depression and heart disease. Therefore, an 8 week physical literacy curriculum was implemented into an existing summer camp. The program was designed based on Active Start and FUNDamentals physical literacy curriculum from Physical and Health Education Canada (PHE). The PHE physical literacy curriculum is evidence based and helps to develop physical coordination, gross motor skills, posture, balance, and confidence.

**Methods:** The program was evaluated using parent feedback, daily observation logs, and standardized skills assessments. The Physical Literacy Assessment for Youth (PLAY) tool was used to assess children’s physical literacy skills pre and post camp. This tool has been validated through Canadian Sport for Life.

**Results:** Thirteen children aged 4–12 were included in the analyses. Preliminary data analysis reveals that on average, object manipulation with the upper body improved the most (40.6%), followed by balance (37.7%), lower body object manipulation (33.3%), locomotor skills (24.1%), and running abilities (21.8%). The biggest challenges for the facilitators was modifying the program to meet the needs of the participants with cognitive and behavioural challenges.

**Conclusion:** Previous research demonstrates that physical literacy teaches children to have the competence, confidence and motivation to apply the fundamental movement and sport skills in new situations. Our study observed on average a 30% improvement in physical skills. We expanded the program and now offer a 2 hour recreation program on Saturday mornings year round.

**p1049**

### THE DIFFERENCES IN BEING DIFFERENT: A NARRATIVE ANALYSIS OF THE NATURE OF EPILEPSY IN ADULTS AND ITS PROBLEMS

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**Purpose:** Epilepsy is not just a medical condition but a social label; successful clinical treatment is therefore only one aspect of epilepsy management. Mismatches between the medical model of “treat the seizures” and the lay model of “learning to manage a life with epilepsy” not only negatively impact on patient expectations and concerns, but also on clinicians’ knowledge and interpretations of patients’ concerns. This scenario can potentially negatively impact on the outcomes of clinician-patient consultations.

**Method:** The voice of the individual living with epilepsy is at the core of this qualitative study. Drawing upon research on illness narratives, I elicited the illness stories of fourteen adults (7 male; 7 female) with

epilepsy to explore how the condition impacts directly or indirectly on daily living and life trajectories, and to re-present the diverse nature and meaning of having epilepsy, including its stigma potential. I conducted in-depth interviews with participants attending epilepsy outpatient clinics. Transcripts were subjected to paradigmatic and narrative analysis in order to examine thematic similarities and differences. Participant stories were identified using Mishler’s theoretical model of “Core Narrative”.

**Results:** What emerged was a discourse of disruption and difference. Epilepsy often imposed barriers to daily living and maintaining a positive sense of self. While the stories told were uniquely individual, collectively a dominant plot emerged. For those with epilepsy in this study the plot takes the individual from a beginning of “discovery and diagnosis”, through the process of “searching for a cause”, “negotiating risk and uncertainty”, and, “striving for control”.

**Conclusion:** Attention to patient stories provides insight into how experience is constructed and evolves over time. Due consideration of such stories by health professionals can offer direction in which intervention (s) can occur to ensure the interests and needs of the individual with epilepsy are holistically considered and met.

**p1050**

### PATIENT’S PERCEPTIONS REGARDING VARIOUS STAGES OF THEIR EPILEPSY ALONG THE EPILEPTO-SEQUENCE TIMELINE

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**Purpose:** Preventing a seizure by developing methods that could discontinue the initiation of an epilepto-sequence would obviously be beneficial for an epileptic’s treatment efficacy and quality of life (QOL). This study aims at describing patient’s perceptions of their epilepsy along the epilepto-sequence timeline in Northeastern Thailand by cross-sectional design.

**Method:** A survey was conducted with people with epilepsy in an epilepsy clinic of university hospital, Khon Kaen, Thailand. This research was based on a cross-sectional design so to evaluate epileptic patients’ knowledge, attitudes and perceptions regarding epilepsy.

**Results:** Two hundred and three epileptic patients were randomly recruited. More than half of the patients in our study (55.2%) had an aura prior to their seizure. Methods such as deep breathing, focusing on a point and mindfulness were used to try and prevent the seizure. Seizures were believed to be triggered by having an illness, hunger, flashing lights and the weather. During seizures, 87.2% of patients knew who and how a person was assisting them during a seizure. However, 82.3% could not describe the characteristics of their seizure. Patients worried about cognitive losses due to seizures, but in general, patients were happy with their medical treatment even when their seizures had not been eliminated.

**Conclusion:** Patient’s perceptions related to their epilepsy may be used to develop individualized regimens to stop a seizure progression before it develops. In addition, patients may be able to improve their QOL by more fully understanding how epilepsy affects them personally.

p1052

### CHANGING THE WAY EPILEPSY CARE IS DELIVERED - AUDIT OF A MULTIDISCIPLINARY EPILEPSY OUTREACH CLINIC TO AN INTELLECTUAL DISABILITY FACILITY SUPPORTED BY AN ELECTRONIC PATIENT RECORD

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**Purpose:** People with an intellectual disability (ID) referred to hospital-based specialist epilepsy clinics face lengthy delays from time of referral, and may experience frustrating delays on the day of clinic leaving them stressed and uncooperative. The delays experienced reduce the numbers of people with severe behavioural problems being referred and the frequent unavailability of key nursing staff attending hospital appointments impacts upon the quality of information available at specialist epilepsy clinics.

**Method:** This study audits a multidisciplinary epilepsy outreach clinic in one ID facility over a 2 year period. This was facilitated by the availability of an electronic patient record (EPR). Follow up care between scheduled appointments was provided by the hospital-based epilepsy nurse telephone service supported by the EPR.

**Results:** The advanced nurse practitioner in epilepsy attended 14 outreach clinics that provided 100 appointments for 40 individual patients (newly referred and existing patients). The consultant neurologist reviewed all newly referred patients at 4 clinics. Five newly referred patients could not have attended hospital-based appointments due to coexisting psychiatric and behavioural problems. Key nursing personnel attended all epilepsy outreach clinic appointments providing good quality clinical information.

Waiting time for first appointments was reduced from 12 months previously to <3 months.

Delays on the day of appointment never exceeded 35 min. The "did not attend rate" was 3% compared to 27% at hospital based epilepsy outpatient clinics.

Preliminary figures show that staff at the ID facility reported that patients were less stressed being seen in a familiar environment. They cited improved continuity of care (75%) increased educational opportunities (82%) and satisfaction with care between appointments (65%) as additional benefits.

**Conclusion:** Changing from a hospital-based epilepsy outpatient clinic to a multidisciplinary epilepsy outreach clinic supported by an EPR enhances the outpatient encounter for patients and staff from both services.

## Status Epilepticus 3 Tuesday, 8th September 2015

p1054

### TIME-DEPENDENT EFFECTS OF LACOSAMIDE, KETAMINE AND COMBINATION KETAMINE AND DIAZEPAM TREATMENT IN A RAT LITHIUM-PILOCARPINE MODEL OF STATUS EPILEPTICUS

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**Purpose:** Time-dependent development of pharmacoresistance to GABAergic benzodiazepines has been reported in the rat lithium-pilocarpine model of status epilepticus (SE). Our objective in this study was to evaluate for time-dependent effects of non-GABAergic agents, lacosamide and ketamine, as well as assess whether the addition of ketamine to diazepam could overcome the time-dependent loss of efficacy seen with benzodiazepines.

**Method:** Wistar rats were implanted with electrodes for EEG recording. After pretreatment with LiCl, SE was induced by intraperitoneal injection of pilocarpine 60 mg/kg. Lacosamide, ketamine, or ketamine + diazepam was administered as either pretreatment (prior to pilocarpine injection), early treatment (at 2nd stage 3 Racine seizure), and/or late treatment (20 min after 2nd stage 3 Racine seizure). Controls received normal saline.

**Results:** Lacosamide 50 mg/kg suppressed onset of SE if given prior to pilocarpine but was unable to suppress SE if administered as early or as late treatment. Ketamine 30 mg/kg did not suppress onset of SE even if administered as pretreatment. After seizure induction, ketamine 30 mg/kg did stop SE in only some pretreatment and early treatment animals. Ketamine at an increased dose of 100 mg/kg was able to consistently stop SE when administered early in all animals tested. Neither dose of ketamine was able to stop SE when administered as late treatment. Early administration of diazepam + ketamine 30 mg/kg did stop SE in most animals, but did not stop SE if administered late.

**Conclusion:** Time-dependent development of pharmacoresistance was observed with all agents and combination of agents tested. If administered early enough, pharmacoresistance may be overcome by increasing an agent's dose as evidenced by our results with high doses of ketamine. However, if administered too late in the time course, neither high doses nor combination of agents could halt SE, supporting the current thought that SE should be treated as quickly as possible.

p1055

### PEDIATRIC STATUS EPILEPTICUS: EVALUATION OF TREATMENT AND PROGNOSIS

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**Purpose:** Status epilepticus is associated with high rates of morbidity and mortality, early diagnosis and proper treatment are of critical importance. In this study, the medical records of one hundred patients between 1 month and 18 years of age were retrospectively revised. The demographic characteristics, treatment protocol and prognosis of patients were evaluated. Thus better management of the future patients was aimed.

**Method:** One hundred patients (35 girls and 65 boys) with a mean age of 60 months (range 1 months–18 years) were evaluated retrospectively. Statistical analysis was performed using the Statistical Package for Social Sciences, version 15. Fisher-Exact test and chi-square tests were used to analyze the data.  $p < 0.05$  was considered statistically significant.

**Results:** Seizures had stopped with the first line treatment (diazepam and/or midazolam) in 29% of the patients, with the second line treatment (phenytoin and/or valproic acid and/or levetiracetam) in 36% of the patients, with the third line treatment (midazolam infusion or thiopental infusion) in 35% of the patients.

**Conclusion:** During the average 36.5 months follow up period while mortality rate was 10%, morbidity rate was 90%. Mortality was significantly much more in the patients with refractory seizure and cerebral palsy ( $p < 0.05$ ). Epilepsy, hemiparesis, spastic tetraparesis and mental retardation developed in seven percent, two percent, two percent and three percent of the patients, respectively. Development of mental retardation was much more higher in the male gender ( $p < 0.05$ ).

p1057

**COGNITIVE FUNCTION AFTER STATUS EPILEPTICUS**

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**Purpose:** Status epilepticus (SE) can be fatal or cause severe sequelae. Cognitive impairment is a feared consequence, but there is a lack of studies systematically investigating this.

Our aim was to conduct systematic cognitive evaluation of patients after SE, with the hypothesis of finding medial temporal lobe dysfunction.

**Method:** Patients were tested when considered clinically recovered from SE. A computerised cognitive test battery (CANTAB<sup>®</sup>) was used. Tests were: Motor Screening Task (MOT), assessing speed and accuracy; Delayed Matching to Sample (DMS), assessing forced choice recognition memory; Paired Associates Learning (PAL), assessing visual memory and new learning; Stockings of Cambridge (SOC), measuring nonverbal planning and execution. Patients with mental retardation, life expectancy <1 year, or progressive neurological illness were excluded. Bootstrap for one-sample t-test was used for analysis.

**Results:** 31 patients were included, mean age 54 years, 25 men, 21 with convulsive and 10 with nonconvulsive SE. Z-scores were compared to norm data for: MOT Mean Latency -0.38,  $p = 0.202$ , DMS Total Correct -0.71,  $p = 0.003$ , DMS Mean Correct Latency -1.12,  $p = 0.001$ , PAL Total Trials Adjusted -1.13,  $p = 0.023$ , PAL Total Errors Adjusted -1.74,  $p = 0.008$ , SOC Mean Initial Thinking time 2 moves -1.03,  $p = 0.009$ , no significant findings for SOC thinking time > 2 moves, for SOC mean moves or for SOC problems solved in minimum moves.

**Conclusion:** Patients performed significantly poorer on tests of memory and early phase problem solving compared to published norms.

In contrast, motor speed and complex executive function was mostly normal. Our findings support the hypothesis of accentuated temporal lobe dysfunction after SE. No significant differences between nonconvulsive and convulsive SE were found.

p1059

**LACOSAMIDE (LCM) IV IN STATUS EPILEPTICUS (SE): SHOULD BE LOADING DOSE ADJUSTED BY WEIGHT?**

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The optimal dosing of LCM for SE is not clearly defined. Some studies reported a better response with higher doses; however it is unclear if the loading dose should be adjusted by weight (as other AEDs).

We aimed to evaluate the relationship between loading dose and the efficacy of LCM in SE.

We performed an analysis of a group of SE patients treated with LCM. We collected demographics, SE type, etiology, response rate, last AED used, line of treatment in which LCM was used, total loading dose and adjusted by weight.

**Results:** 71 SE were evaluated, 47.9% were non-convulsive. Mean age: 62.4 + /-18. 60.6% were men. Regarding the etiology: 39.4% were acute symptomatic, 40.8% delayed symptomatic, 4.2% progressive symptomatic and 14.1% remained as cryptogenic. 66.2% were refractory. The dose used was < / = 200 mg in 32.4%, 300-400 mg in 64.8% and

>400 mg in 2.8%. The adjusted dose was < 4 mg/kg in 32.4%, 4-6 mg/kg in 42.3% and >6 mg/kg in 25.4% (median 5 mg/kg). The response rate was 74.6%, and 53.6% responded within 24 hours. Regarding efficacy, no relationship was observed regarding the dose in mg ( $p = 0.86$ ) or adjusted by weight ( $p = 0.59$ ). The response was similar in all etiologic groups, however in the delayed symptomatic, the response was slightly higher at doses >4 mg/kg, while in the other groups (symptomatic acute, progressive or cryptogenic) a better response was observed using >6 mg/kg. In any case, the differences were not significant. In responders, we found a faster response when LCM was used earlier, but without finding relationship between speed of response and the adjusted dose ( $p = 0.32$ ).

**Conclusion:** In our SE population, with a median dose of 5 mg/kg of LCM, we achieved a response rate of 74.6%. There is no clear relationship between increased efficacy or faster action and the ranges of used doses adjusted by weight.

p1060

**IMPACT OF NONCONVULSIVE STATUS EPILEPTICUS' RECOGNITION ON BRAIN TUMOR PATIENTS MANagements**

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**Purpose:** The prevalence of nonconvulsive status epilepticus (NCSE) in brain tumor patients is unknown. The semiology of NCSE covers a wide range of neurological symptoms, which can be confused with several condition such as tumor progression or edema. Since NCSE has been associated with significant mortality and morbidity, differential diagnosis is essential. This study describes the clinical and EEG characteristics and outcome in brain tumor patients with NCSE.

**Method:** All patients admitted to our neurosurgery department from 2009 to 2014 with a diagnosis of brain tumor were cross-referenced with epilepsy department's database were included. Relevant information from the neurological records of the patients with NCSE was extracted.

**Results:** 981 brain tumor patients were identified, of which 304 (30.9%) had an EEG and 12 (1.2%) had NCSE. The majority of seizures were diagnosed by consulting neurologist although two patients having only subclinical seizures in which detected by EEG recording. Although, five of 12 patients, had grade IV glioblastoma, the NCSE emerged with disease progression, the remaining 7 patients had different pathologies and occurrence of the NCSE were not related with disease progression. In the later group, the NCSE resolved in 6 of the 7 patients with improvement in overall level of function.

**Conclusion:** On one hand, the NCSE in brain tumor patients may associated with tumor progression and decreased survival time, but also in other hand highly treatable in subgroup of patients with significant improvement in quality of life.

p1062

**SUPER-REFRACTORY STATUS EPILEPTICUS (SRSE): CLINICAL CHARACTERISTICS, TREATMENT APPROACH AND PROGNOSIS IN FOUR MEDICAL CENTERS OF BUENOS AIRES**

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**Purpose:** Analyze clinical characteristics, treatment approach and short term prognosis in a group of patients with SRSE.

**Method:** Descriptive, retrospective study of 9 patients with SRSE in 4 Medical Centers of Buenos Aires from June 2012 to June 2014. We analyze demographics, previous history of epilepsy, etiology, type of SE, treatment approach, duration of Intensive Care Unit (UCI) stay, short term prognosis and mortality.

**Results:** The median age was 39 years old. Forty four percent of them had previous history of epilepsy. The etiologies were Anti-NMDA encephalitis (n = 1), hypoxic-ischemic encephalopathy (n = 1), brain tumor (n = 1) and unknown cause (n = 5). Forty four percent were convulsive SE, 33% of them evolved to nonconvulsive SE. Twenty two percent were non convulsive from the onset. The antiepileptic drugs more frequently used were Levetiracetam (89%), Phenytoin (78%), Valproate sodium (78%) and Phenobarbital (68%). The anesthetic drugs used included Midazolam (89%), Propofol (67%), Thiopental (67%) and Ketamine (44%) with more than 2 anesthetic drugs used in 44% of the patients. Sixty seven percent received non pharmacological treatment which included ketogenic diet (n = 3), immunomodulatory treatment (Steroids n = 4, IgIVn=3) and resective surgery (n = 1). The stay in ICU was more than a month long in 67%. Mortality was 22% (n = 2) and the 3 month prognosis was severe disability in 44% (modified Rankin Scale).

**Conclusion:** In our case series more than half of SRSE were of unknown cause and the most frequent onset was as convulsive SE. Levetiracetam was the AED more frequently used and Midazolam the anesthetic drug more indicated. A prolonged stay in ICU was observed in the majority of patients with a high morbidity and mortality.

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p1064

### USEFULNESS OF KETOGENIC DIET (KD) IN THE MANAGEMENT OF SUPER REFRACTORY STATUS EPILEPTICUS (SRSE) IN PEDIATRIC PATIENTS

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KD is a therapeutic choice in Refractory Epilepsy (RE). Studies have demonstrated that 16% of patients become seizure free and 32% experience a seizure reduction greater than 90%, which is a much better response than any other add on antiepileptic drug in RE. It has been reported, as well, its utility in the management of SRSE.

**Purpose:** To analyze the utility of KD in the management of SRSE in pediatric patients.

**Method:** Retrospective review of clinical charts in pediatric patients under control at Clinica Las Condes, in the period January 2007–December 2014, in SRSE patients who underwent through classic KD. Etiology, age at onset of KD, therapeutic response in the acute management, follow up and adverse effects.

**Results:** 7 patients, 4 males, age at onset of epilepsy 10.1 months (median 3 months). Etiology: Epileptic Encephalopathy 6/7. Age at onset of KD 36 months (median 23 months), 3/7 still on KD at cut-off (2 deceased and 2 discontinued because of adverse reactions). With KD 6/7 terminated SRSE in 5 days average. At 3 months follow up, 3 remain seizure free, 3 experienced 50–90% seizure reduction, 1 < 50%, nevertheless was able to wean ventilatory support. Positive ketonuria were achieved before the third day. (n = 6), betahydroxybutyrate between 48 to 96 horas 1.2 mmol/L. No adverse effects were reported concerning KD in the treatment of SRSE.

**Conclusion:** In this group of patients KD was highly effective in the management of SRSE, notably those associated to MRI negative epileptic encephalopathy.

p1067

### USE OF PERAMPANEL (PER) IN TWO CASES OF SUPER-REFRACTORY HYPOXIC MYOCLONIC STATUS

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**Purpose:** Proper treatment of hypoxic myoclonic status is not clearly determined. Induced hypothermia is improving prognosis and a more aggressive treatment might be beneficial in some patients. Among the new options of antiepileptic drugs, Perampanel (PER) is a drug with a novel mechanism and it might be a promising drug for status or as an anti-myoclonic drug.

**Method:** We describe the use of PER in two patients with hypoxic super-refractory myoclonic status.

**Description of cases:: Case 1:** A 51 year-old patient presented an out-of-hospital cardiac arrest due to an acute myocardial infarction. The patient started a clinical and electrical (EEG) myoclonic status at rewarming phase. Several treatments were used, starting with clonazepam, valproate, sedation (midazolam, propofol) and subsequently barbiturate-induced coma with persistent myoclonic status. Finally we decided to try PER (dose: 6–8 mg) through a nasogastric tube, showing a marked improvement of EEG activity and myoclonus decrease. The patient had a progressive clinical improvement, with a CPC (Cerebral Performance Category) scale score of 1.

**Case 2:** A 66 year-old patient presented an out-of-hospital cardiac arrest, and started a clinical myoclonic status confirmed by EEG at rewarming phase. Despite being treated with levetiracetam, valproate and lacosamide, clinical and EEG status persisted; an increasing sedation did not subjugate the situation, therefore we decided to test PER. Myoclonus improved as well as neuronal excitability in the EEG recording. The neurological exploration improved mildly (CPC 3) however, 23 days after admission the patient developed a cardiogenic shock leading to death.

**Conclusion:** These cases might show the usefulness of PER as a therapeutic option in super-refractory hypoxic status. This could raise the possibility of an earlier use even before increasing sedation or inducing barbiturate coma.

p1068

### A PATTERN OF CHANGES IN NEUROTRANSMITTER GENE EXPRESSION CORRELATED WITH EEG STAGES DURING LITHIUM/PILOCARPINE-INDUCED EXPERIMENTAL STATUS EPILEPTICUS

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**Purpose:** Status epilepticus (SE) is a dynamic condition in which EEG patterns and convulsive behavior evolve if seizure activity continues. To better understand the pathophysiology of SE we studied the expression of specific genes associated with selected neurotransmitters in rats at defined EEG stages of SE (Treiman et al., *Epilepsy Res* 5:49–60, 1990).

**Method:** Five days after implantation of epidural screw electrodes, SE was induced in 180 g male Sprague-Dawley rats by injection of LiCl,

3 mmol/kg IP, followed 20 hours later by pilocarpine, 30 mg/kg SC. Control rats were given LiCl plus saline and did not develop SE. Experimental rats were sacrificed 5 minutes after onset of SE EEG stage I, III, V, and V + 4 hours by isoflurane anesthetization and decapitation. Brains were removed and dissected for hippocampus and cortex samples. RNA was extracted, pooled, and then amplified by PCR and analyzed using Qiagen RT<sup>2</sup> Profiler PCR Rat GABA & Glutamate arrays. Statistical significance was set at  $p < 0.05$ .

**Results:** Eighty-four mRNAs were analyzed for each pooled sample. Adenylate cyclase 7, GABA<sub>A</sub>R  $\alpha 6$ , glutamate receptor metabotropic 4, phosphoglycerate dehydrogenase, proline dehydrogenase, solute carrier family 1 member 6, and solute carrier family 1 member 7 all exhibited a similar pattern: reduction in expression compared to controls during EEG Stage I and III, significant increase in expression at EEG Stage V compared to Stage 3, followed by a substantial decrease in expression 4 hours after onset of EEG Stage V. This pattern was noted primarily in genes from hippocampal tissue with only GABA<sub>A</sub>R  $\alpha 6$  from cortical tissue displaying the same pattern.

**Conclusion:** A subgroup of neurotransmitter receptor/transport-associated genes displayed a marked pattern of gene expression changes during the progression of experimental SE through specific EEG changes. The observations from this study may provide further insight into the underlying pathophysiology of SE.

#### p1069

##### POSTICTAL SERUM AMMONIA: A BIOMARKER OF GENERALIZED TONIC-CLONIC SEIZURE?

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**Purpose:** Transient increase in serum ammonia was recently reported in patients following generalized tonic-clonic seizures (GTCS), without sufficient evidence to confirm the epileptic nature of the spells. We wanted to determine if this postictal increase occurs in different types of convulsions (epileptic vs nonepileptic) as confirmed electrographically using continuous video EEG monitoring (cvEEG).

**Method:** Patients older than 18 years-old admitted to the epilepsy monitoring unit were enrolled in this study. Serum ammonia levels were drawn from patients at baseline, within 60 minutes of the first event of interest (epileptic vs nonepileptic) and 24 hours after that event or prior to discharge whichever comes first. Patients were grouped according to the cvEEG result. Descriptive statistics and appropriate parametric/non-parametric methods were used to analyze the data. Mean is used for normally distributed data and median is used for non-normally distributed data.

**Results:** To date, a total of 19 patients with generalized convulsions were enrolled, 11 GTCS and 8 psychogenic nonepileptic spells (PNES). Mean age was  $30.4 \pm 12.2$  years and  $34.8 \pm 10.1$  years, respectively. Mean baseline, median after event, median after 24 hour ammonia levels and median change from baseline were  $43.9 \pm 9.8$   $\mu\text{M}$  (median 39.0  $\mu\text{M}$ ), 83.0  $\mu\text{M}$ , 35.0  $\mu\text{M}$  and 46  $\mu\text{M}$  in GTCS group and  $35.0 \pm 10.6$   $\mu\text{M}$  (median 37.5  $\mu\text{M}$ ), 37.0  $\mu\text{M}$ , 30.5  $\mu\text{M}$  and 1.5  $\mu\text{M}$  for PNES group, respectively. The median change in serum ammonia from baseline after the index event was significantly different between the groups ( $p$ -value: 0.0166).

**Conclusion:** Despite the small number of our patient sample, there was a statistically significant increase in serum ammonia following convulsions in GTCS when compared to PNES group. These preliminary results suggest a possible role for ammonia as a biomarker for electrographic convulsive seizures. Further studies are required to confirm these results and define the time frame within which this test can be utilized.

#### p1070

##### NONCONVULSIVE STATUS EPILEPTICUS IN AN URBAN ACADEMIC TERTIARY MEDICAL CENTER

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**Purpose:** The aim of this study is to characterize cohort of nonconvulsive status epilepticus (NCSE) patients in an urban tertiary academic care center.

**Methods:** We performed a comprehensive retrospective review of electronic medical records and digital EEG or continuous video EEG of patients admitted and treated between January 1st, 2009 and June 30th, 2014. We included patients who had NCSE according to clinical findings and EEG criteria by Beniczky et al., and excluded patients with Creutzfeldt-Jacob disease or anoxic brain injury at presentation. We collected data on demographics, clinical findings at the onset of NCSE, co-morbidities, history of epilepsy, underlying etiology, presence of coma, neuroimaging, duration of NCSE (in days), length of stay (LOS), treatment, presence of sepsis during the course, outcome and disposition. We used Status Epilepticus Severity Score (STESS) to grade the severity of NCSE.

**Results:** The search revealed 188 patients, 45 of which were included. Mean age was  $56.3 \pm 14.9$  years, and 44% were male. All patients had altered mental status (AMS) ranging from confusion to coma and 53% had subtle motor findings. Subtle status epilepticus was seen in 31% of the patients with NCSE. Twenty patients (44%) had acute neurologic pathology. Individual etiologies were epilepsy (40%), infection (13%), intracranial hemorrhage (11%), encephalitis (11%) and medication effect (9%). Twenty-two patients (49%) had STESS >1. Benzodiazepines were first treatment in 62% patients. Intravenous anesthetic drugs were used in 31 (69%) patients. Median length of time to EEG resolution was 1 day (mean:  $2.0 \pm 2.1$  days). Mean LOS was  $21.5 \pm 18.6$  days. In-hospital mortality rate was 29%.

**Conclusion:** We characterized a cohort of patients with NCSE and showed similar findings to previous reports. NCSE has high mortality rate, and presents commonly with AMS and subtle motor findings. History of epilepsy and acute neurologic pathology are most common etiologies.

#### p1071

##### CLINICAL PROFILE OF BULGARIAN PATIENTS WITH STATUS EPILEPTICUS

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**Purpose:** Our purpose was to evaluate the clinical characteristics and outcome of Bulgarian patients diagnosed with status epilepticus (SE).

**Method:** We performed a prospective study of 95 consecutive patients aged 18 years and above, who were admitted in a neuro-intensive care unit and diagnosed with SE over a period of 3 years. Demographics and clinical data concerning established epilepsy and SE were collected. The functional outcome assessment was based on the results from Glasgow Outcome Scale.

**Results:** The mean age of study participants was 50.32 years. Mental retardation had been diagnosed in 13.68% of patients. Existing neurological abnormalities had been found in 44.21%. Convulsive SE was observed in 77.89% of participants. SE etiology included: idiopathic (35.79%), acute symptomatic (8.42%), remote symptomatic (47.37%), and progressive encephalopathy (8.42%). The most common SE trigger factors were poor compliance (29.48%) and alcohol (11.58%). In 41.05%

## Abstracts

SE was treated with a combination of antiepileptic drugs. In 25.31% SE was refractory to 2 antiepileptic drugs and lasted more than 60 minutes. Regarding SE functional outcome, mortality was 5.26%, 34.73% were severely or moderately disabled on hospital discharge, 60% recovered well. SE outcome depended on age ( $P < 0.001$ ), existing neurological abnormalities ( $P < 0.001$ ), mental retardation ( $P < 0.01$ ), etiology of epilepsy ( $P < 0.01$ ), SE etiology ( $P < 0.001$ ), SE type ( $P < 0.05$ ), SE duration ( $P < 0.05$ ).

**Conclusion:** This study makes a detailed clinical profile of patients with SE and emphasizes the role of some clinical and demographic factors for SE outcome.

## p1072

### SIX CASES OF REFRACTORY STATUS EPILEPTICUS IN TERTIARY INTENSIVE CARE UNIT WITH DIFFERENT ETIOLOGIES

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**Purpose:** The aim of this study is to evaluate refractory status epilepticus on six cases with etiology, seizure type, imaging and treatment options.

**Method:** Retrospective data from January 2013 to January 2015 were obtained from records for six refractory status epilepticus patients.

**Results:** Six patients were followed in two years diagnosed as refractory status epilepticus. First case was progressive myoclonic epilepsy that first myoclonic seizure was started at the age of 23, admitted to emergency department with fever and recurrent seizures. Brain MRI including hippocampal region was normal but EEG revealed seriously unorganized background activity with frequently occurring spikemultispikes waves prominent in frontal regions. Refractory status epilepticus was treated with steroid regimen. Second case was admitted with myoclonies on right shoulder and gradually become more frequent. Myoclonies become generalized and almost continuous. Patient was diagnosed as MERRF because of gradually occurring hearing loss, myoclonic seizures, MRI features and history of exercise intolerance and poor night vision history. Third case had refractory complex partial seizures due to limbic encephalitis. Patient was seizure free after intravenous immune globulin, steroid and conventional antiepileptic treatment regimen. Fourth case was diagnosed as tuberous sclerosis when he was 6 months old after his first seizure with typical MRI features. Seizures were terminated with successful antiepileptic regimen including rapamycin and vigabatrin. Fifth case seizures were started after stroke affecting temporal lobe. Patient was seizure free with levetiracetam treatment until urinary infection and secondary sepsis triggered seizures. Sixth case was diagnosed as idiopathic generalized epilepsy and seizures became intractable because of patients insufficient treatment adherence.

**Conclusion:** Refractory status epilepticus is a heterogeneous condition arising as the final common pathway from multiple causes. Early recognition and initiation of specific treatment for underlying pathology leads to a better response and may improve outcomes.

## p1073

### STATUS EPILEPTICUS IN THE ELDERLY IN THE SUPER-AGING SOCIETY: CLINICAL AND EEG FEATURES AND PROGNOSTIC FACTORS

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**Purpose:** We aimed to clarify clinical and EEG features, and prognostic factors of SE in the elderly in the super-aging society.

**Method:** We retrospectively investigated 107 consecutive patients (43 men and 64 women) 65 years or older with SE, who were hospitalized in the comprehensive community hospital from July 2011 to October 2014. SE was defined as either more than 30 minutes of continuous seizure activity, or intermittent seizures without full recovery of consciousness between seizures, and considered refractory when a benzodiazepine and another antiepileptic drug could not discontinue the clinical or EEG seizure activity. Poor outcome was defined as mortality and persistent morbidity at discharge compared to premonitory state, by rating with modified Rankin Scale (mRS).

**Results:** Median age was 80 years (range, 66–98). Median premonitory mRS was 3. 34 patients (31.8%) had been living in nursing homes. Median duration of hospitalization was 16 days. 34 patients (31.8%) had been diagnosed as epilepsy syndrome. Etiology was acute symptomatic in 23 (21.3%), remote symptomatic in 66 (61.7%), and cryptogenic in 18 (16.8%). Acute and remote cerebrovascular disease and dementia were the major cause. Emergent EEG revealed lateralized periodic discharges (LPDs) in 23 (21.5%), generalized or lateralized rhythmic delta activity (GRDA or LRDA) in 10 (9.3%), and conventional seizure patterns without LPDs, LRDA or GRDA in 10 (9.3%). 33 patients (30.8%) had refractory SE (RSE). 41 patients (38.3%) had poor outcome. Univariate analysis showed that poor outcome was significantly associated with no past history of epilepsy syndrome ( $p = 0.003$ ), acute symptomatic etiology ( $p = 0.04$ ), and RSE ( $p < 0.001$ ). RSE remained significant with multivariate analysis ( $p < 0.001$ ).

**Conclusion:** Among the elderly, SE occurred in already disabled people and often further exacerbated activities of daily living. Refractoriness to the initial therapy was common and regarded as significant prognostic factor.