Platform Session: Antiepileptic Drugs 3
Monday, 30th June 2014

001
ANTIEPILEPTIC DRUG WITHDRAWAL IMPROVES INTELLIGENCE AFTER PEDIATRIC EPILEPSY SURGERY: THE TIMETOSTOP (TTS) STUDY

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Purpose: We corrected for other identified predictors of tIQ and dIQ, for timing of assessment was related to tIQ and dIQ, using linear regression analyses. We corrected for other identified predictors of tIQ and dIQ, for timing of latest assessment, and for a compound propensity score that contained previously identified determinants of medication withdrawal (number of drugs at time of surgery, completeness of resection, postoperative effects, multifocal MRI lesions, immediate postoperative seizure freedom, previous surgery, etiology, and type of surgery).

Results: Reduction of AEDs significantly improved tIQ and dIQ (adjusted RC 3.53 [0.37–6.70], p = 0.029, and 3.57 [0.37–6.78], p = 0.029, respectively). Older age at surgery independently predicted higher postoperative tIQ and dIQ (RC 0.14 [0.06–0.22], p < 0.001 and RC 0.14 [0.07–0.21], p < 0.001, respectively). Higher preoperative IQ was independently associated with higher postoperative tIQ (RC 0.83 [0.76–0.90], p < 0.001), and with lower dIQ (−0.14 [−0.20 to 0.08], p < 0.001).

Conclusion: AED reduction significantly and independently improved intelligence after childhood epilepsy surgery.

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002
RESPONSE TO ANTIEPILEPTIC DRUG COMBINATION IN PERSONS WITH DRUG-RESISTANT EPILEPSY AND RELATIONSHIP TO THE ADDED DRUG WHEN MONOTHERAPY IS NOT ENOUGH

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Purpose: To evaluate and compare the response to treatment with dual or triple therapy in persons with epilepsy who have not responded to monotherapy. To evaluate the rate of response to the added drug.

Method: Retrospective study. Patients were classified according to the treatment with 2 or 3 AEDs. Epilepsy syndrome and seizures, disease duration, seizure-free period, treatment failure, tolerance and adverse effects of treatment, the last scheduled drug and duration of the last therapeutic intervention were collected.

Drug responsive epilepsy is defined as the absence of seizures for at least the last year of follow-up.

Results: Eighty-one patients were identified between years 2000 and 2012: 55 patients (67.9%) on 2 AEDs combination therapy and 26 patients (32.1%) in triple therapy. In the group of triple therapy 9 patients (11.1%) out of 26 patients are seizure-free, while 17 patients (20.9%) showed no response. Most used add-on drugs were CLB and LTG.

Conclusion: Facing the most accepted concept that monotherapy should be the ideal choice for all patients with epilepsy, the use of drug combinations can help to reach good seizure control in selected patients. Our results show that a lasting improved seizure control can be achieved with a two-drug combination, in contrast to triple drug therapy.
003  STRUCTURE BASED DRUG DESIGN, SYNTHESIS AND SCREENING OF ADENOSINE A2A ANTAGONISTS AS NOVEL ANTIEPILEPTIC DRUGS
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Purpose: Adenosine receptors (AR) play an important role in chemical signaling in both, peripheral and central nervous systems. Four subtypes of Adenosine Receptors have been identified: designated A1, A2A, A2B, and A3. A2A ARs are found in high density in certain brain regions, such as Striatum, Nucleus accumbens, and Olfactory tubercle. Adenosine exhibits high affinity to A2A ARs, which appear to be tonically activated under physiological conditions. A2A AR antagonists have been proposed as novel therapeutics for Parkinson’s disease.

Methods: Human A2A AR bound to ZM241385 with 1C50 0.22 nM (PDB ID: 3EML) crystal coordinates were downloaded from protein data bank. Energy-optimized pharmacophore was prepared using Schrodinger software. The resulting pharmacophore model contains one hydrogen bond Acceptor (A), one hydrogen bond Donor (D) and three Ring systems (R). Using these features, screened against the public library of compounds (Asinex) to find potential lead compounds.

Results: The compounds which yielded fitness score of more than 1.0 the pharmacophore model were further subjected to Glide HTVS, SP and XP. Glide docking results revealed 33 hits were identified as potential lead molecules. Among them 9 Asinex molecules were selected based on the highest docking score and more number of hydrogen bonds with Ghu169, Asn253 amino acids and Compounds were evaluated in the PTZ induced seizure model in adult Zebrafish (standard 8 min protocol). Furthermore most potent compounds were evaluated for dose response analysis and major toxicities in Zebrafish model.

Conclusion: This study demonstrates that a pharmacophore search using a model based on A2A AR inhibition, and the enzyme’s structural features can be used to screen for new candidates for antiepileptic therapy. Most potent compound to show Anti-epileptic activity was selected and derivatives are synthesized to develop SAR. These have to be validated by using in vitro inhibitory activity.

004  PXR TRANSCRIPTIONAL ACTIVITY INCREASES CYTOCHROME P450 EXPRESSION IN HUMAN EPILEPTIC BRAIN
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Purpose: One of the contributing factors to drug resistance to antiepileptic drugs (AEDs) is cytochrome 450 enzyme activity at the blood-brain barrier (BBB). We explored whether pregnane X receptor (PXR), a known controller of P450 expression in the liver, is involved in the abnormal expression levels of selected P450 enzymes in human epileptic brain. To this end, we used the P450 substrate and PXR inducer sertraline (SRT), a selective serotonin reuptake inhibitor which is often prescribed to epileptic patients to manage depression.

Method: Endothelial cells isolated from drug resistant epileptic brain (EPI-EC) were expanded in standard culture dishes. Human brain endothelial cells (HBMEC) and non-brain endothelial cells (HUVEC) were used as controls. Nuclear receptor mRNA levels were assessed by cDNA microarrays. PXR and CYPs (CYP3A4, 2C9, 2C19, 2D6 and 2E1) involved in hepatic AED metabolism were studied by western blot and siRNA approaches. HPLC-UV was used to quantify sertraline metabolism.

Results: PXR and its downstream targets CYP3A4, 2C9 and 2E1 were overexpressed in EPI-EC compared to control; in contrast, CYP2D6, 2C19 were down-regulated or absent in EPI-EC. PXR expression did not depend on prior SRT exposure (5 mM), suggesting that, in epileptic BBB EC, PXR regulation and activity are altered. SRT conversion to desmethylsertraline was consistently elevated in EPI-EC. SRT upregulated CYP3A4 expression in “epileptic” EC, CYP2D6, 2C19 remained unaltered.

Conclusion: The study suggests that at steady-state PXR transcriptional activity is elevated in drug resistant epileptic BBB cells; this is supported by increased expression of PXR-regulated CYPs. In addition, the chief regulator of multiple drug resistance gene expression (PXR) was insensitive to induction by SRT, suggesting a different mechanism of drug-dependent metabolic enhancement in brain endothelial cell from epileptic brain.

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005  EFFECTIVENESS OF ANTIEPILEPTIC THERAPY IN CATASTROPHIC INFANTILE EPILEPSY: COMPARISON OF PATIENTS WITH SCN1A AND PCDH19 MUTATIONS
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Purpose: The mechanism of epileptogenesis in PCDH19 mutations is not yet clear, but it is thought to be different to SCN1A mutations. Both mutations can cause Dravet syndrome. In both cases epilepsy is highly pharmacoresistant. Here, we compared effectiveness of antiepileptic therapy in both groups.

Method: Retrospective analysis of the effectiveness of antiepileptic drugs assessed after 3 months in 48 patients (24 male, 24 female) with SCN1A mutations aged 2–27 years (mean age: 13.7 years) and 42 patients (all female) with PCDH19 mutations aged 2–21 years (mean age: 10 years).

Results: In patients with SCN1A mutations, best seizure reduction was achieved with CLB (89%), CBR (85%) and VPA (71%). Aggravation was observed in 34 patients (71%), mainly with CBZ (88%), OXC (84%), ZNS (79%), PHT (64%) and LTG (63%). In patients with PCDH19 mutations, best seizure reduction was achieved with CLB (95%), CBR (67%) and VPA (56%). Aggravation was observed in 8 patients (17%), mainly with RFC (17%), OXC (14%), CBZ (9%), PHT (8%) and LTG (5%).

Conclusion: The most effective drug both in patients with SCN1A mutations or PCDH19 mutations was CLB, followed by CBR and VPA. All act via the GABA receptor. Sodium channel blockers like CBZ, OXC, LTG, PHT, RFC or ZNS frequently cause aggravation in SCN1A patients, while there is a surprisingly low rate of aggravation in PCDH19 patients. Based on the observation of differences in response to various anticonvulsant drugs it can be speculated, that, in SCN1A patients, decreased inhibition via altered sodium channels in interneurons causes a susceptibility for aggravation, while in PCDH19 patients, epileptogenesis is caused by a disturbance in brain development due to a deficient structural protein.

006

STUDY OF THE ANTEPIELEPTIC DRUGS TRANSPORT THROUGH THE BLOOD-BRAIN BARRIER IN CHILDREN

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Purpose: To study the impact of the anti-epileptic drugs (AEDs) VPA, STP, CLB and CBZ, on P-glycoprotein (P-gp) and Breast Cancer Resistance Protein (BCRP) efflux transporters function in immature rats. Drug resistant epilepsy remains a major concern in pediatrics despite the different AEDs available. Resistance to AEDs may be related to adaptive mechanisms that oppose their penetration into the brain. Recent research has covered the role of the adult Blood-Brain Barrier (BBB) in this protective mechanism through altered expression of efflux pumps e.g. P-gp and BCRP. In this work we aim to assess modifications of those efflux pumps function that could originate AEDs resistance in immature animals. We will focus on the AEDs used in the Dravet syndrome treatment.

Method: Post-natal day 21 (P21) and P56 rats were treated for 5 days with VPA (400 mg/kg/d) and 350 mg/kg/d, respectively) through subcutaneous osmotic pumps. Changes in BBB transporters P-gp and BCRP function were measured by infusion of P-gp and BCRP substrates (digoxin and prazosin, respectively) and calculation of brain/blood partition coefficients (Kp,brain) in steady-state conditions. Data were analyzed by 2-way ANOVA and considered significant if p < 0.05.

Results: After 5 days, digoxin Kp,brain (mean±SD) increased from 0.070 ± 0.01 to 0.136 ± 0.016 in P21 rats (n = 4) and from 0.042 ± 0.02 to 0.077 ± 0.07 in P56 (n = 4), both differences being statistically significant (two-way ANOVA, p < 0.01). A non statistically significant decrease in prazosin Kp,brain (0.467 ± 0.057 vs. 0.370 ± 0.023) was observed in P21 rats.

Conclusion: P-gp function decreased significantly after VPA treatment in P21 and P56 rats. A trend to increase BCRP function was observed only in P21 rats. Data on mRNA expression and protein levels will be presented to support the effects of VPA on efflux transporters. Further work will unravel the effects of STP, CLB and CBZ on the BBB protective mechanisms.

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007

TREATMENT RESPONSE AND SIDE EFFECTS OF ADD-ON THERAPY WITH PERAMPANEL 1 YEAR EXPERIENCE IN 70 PATIENTS WITH FOCAL-ONSET EPILEPSY

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Purpose: Perampanel (PER) is a noncompetitive AMPA receptor antagonist and has been approved for adjunctive treatment of focal-onset epilepsy in adults by the EMA in 07/2012.

Method: We prospectively collected data of 70 patients (pts) with focal onset epilepsy who received PER since 09/2009 and report treatment response and adverse effects.

Results: Seventy patients (66% women) with focal-onset epilepsy received PER since 09/2012. Mean age was 41.7 years (SD 18.9), mean follow up was 8.2 month (SD 3.3). Thirty-six four patients were in follow up >3 month. At last follow up 46 pts (66%) were still on PER, of whom six pts (11%) were seizure free, six pts (11%) experienced a seizure reduction >50%, 20 pts (30%) experienced no seizure reduction, 50%. Median seizure frequency before add-on therapy with PER was 2.8 [0.1; 80.0], at last follow up 2.0 [0.0; 40.0] seizures per month. Thirty-five pts (50%) experienced adverse effects (AE), of which vertigo was the most common (23/70 pts; 33%), followed by fatigue (8/70 pts; 11%), nausea (4/70 pts; 6%), psychosocial (5/70 pts; 7%) and psychiatric (6/70 pts; 9%) symptoms. Nineteen pts (27%) withdrew medication due to AEs, in 11 pts (15%) dose was reduced by 2 mg due to AEs with remission of AEs. Twenty-nine pts (41%) took a concomitant enzyme inducer (EI); there was no difference in dose (p = 0.249), frequency of AEs (p = 0.283) or treatment response (p = 0.263) if a concomitant enzyme inducer was taken or not.

Conclusion: PER is well tolerated and leads to significant improvement (50–100% reduction) of seizure control in 26% of all patients. AEs – in particular vertigo- are common but can often be avoided, by taking PER immediately before bedtime or by dose reduction. The tolerability did not differ between pts taking concomitant EI and those who do not.
008
BRIVARACETAM POPULATION PHARMACOKINETICS IN CHILDREN WITH
EPILEPSY AGED 1 MONTH–16 YEARS
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Purpose: To develop a population pharmacokinetic model for brivaracetam (BRV) in paediatric patients and provide BRV paediatric dosing adaptations.

Method: A population pharmacokinetic model for BRV was developed using non-linear mixed-effect modelling (single-compartment, first order absorption/elimination, volume and clearance [CL] allometrically scaled using fixed theoretical exponents) and data from study N01263 (open-label, fixed 3-step up-titration study; BRV doses: 0.5/1.0/2.0 mg/kg bid and 0.40/0.8/1.6 mg/kg bid [≤100 mg bid] for patients aged ≤8 and ≥8 years, respectively). Simulations compared predicted BRV steady-state plasma concentrations (C ss) in paediatric patients with values obtained in adults.

Results: Six hundred BRV plasma concentration-time profiles from 96 children were available (1 month–2 years: n = 29; 2–6 years: n = 26; 6–12 years: n = 24 for; 12–16 years: n = 17). Co-administration of phenobarbital/primidone (PB), carbamazepine (CBZ) or valproate (VPA) was associated with changes in CL (PB: +0.035 [±0.012] m M; tri-glycerides change was +0.082 [±1.378] vs. +0.012 [±0.657] m M, and the change in non-fasting glucose levels was +0.044 [±1.199] vs. –0.018 [±0.928] m M. Metabolic parameters reported as treatment-emergent adverse events (TEAEs) in >1% of patients receiving perampanel vs. placebo were: weight increase (39 [3.3%] vs. 6 [1.4%]), decreased appetite (23 [2.2%] vs. 7 [1.6%]) and increased appetite (12 [1.2%] vs. 5 [1.1%]). Further analysis will include breakdown of patients receiving baseline treatment with enzyme-inducing/non-inducing AEDs.

Conclusion: Despite a small weight increase with perampanel, lipid parameters and glucose remained similar over time and across perampanel doses in the pooled Phase III studies with a low incidence of metabolic TEAEs.

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010
EFFECTS OF PERAMpanel ON METABOLIC PARAMETERS IN PATIENTS WITH REFRACtORY PARTIAL-ONSET SEIZURES IN EXTENSION STUDY 307
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Purpose: Assess effects of adjunctive perampanel (up to 12 mg/day) on metabolic parameters in extension study 307.

Method: Patients completing the double-blind studies (304, 305, 306) were eligible to enter the extension, consisting of a 16-week blinded conversion and a 256-week open-label maintenance period. Mean (±SD) change from pre-perampanel baseline to interim data cut-off (December 2010) for cholesterol, triglycerides, glucose (m M) and body weight (kg) is reported (safety analysis set).

Results: Of 1,186 patients, 1,089 (91.8%) and 19 (1.6%) had perampanel exposure >16 weeks, >1 year and ≥2 years, respectively. Overall weight increase was +1.86 (±4.54) kg for patients receiving perampanel (change for 4 mg [n = 15], +4–8 kg [n = 86], +8–12 mg [n = 1,084]: +1.15 [±2.40] kg, +1.46 [±3.11] kg, +1.90 [±4.65] kg, respectively). Change from pre-perampanel baseline to interim data cut-off was +0.002 (±0.644) m M for cholesterol; +0.053 (±0.694) m M for triglycerides, and +0.068 (±0.999) m M for non-fasting glucose. Metabolic parameters reported as treatment-emergent adverse events (TEAEs) in >1% of perampanel-treated patients were: weight increase (n = 81, 6.8%), decreased appetite (n = 39, 3.3%), increased appetite (n = 20, 1.7%) and decreased weight (n = 15, 1.3%). Metabolic TEAEs leading to study/perampanel withdrawal were weight increase (n = 6, <1%), decreased appetite (n = 4, <1%), appetite disorder (n = 1, <1%) and increased appetite (n = 1, <1%). Three patients (<1%) reported serious metabolic TEAEs (hypopnaetriaemia, diabetic ketoacidosis, hypochloroaemia, hypovolaemia).

Conclusion: Despite a small increase in weight with perampanel, metabolic parameters remained stable from pre-perampanel baseline throughout the double-blind studies to the extension study interim cut-off, with a low incidence of metabolic TEAEs.

Acknowledgements: Study sponsor: Eisai Inc. Medical writing support: Choice Healthcare Solutions, funded by Eisai Ltd.
Abstracts

011 EVEROLIMUS LONG-TERM SAFETY AND EFFICACY IN PATIENTS WITH SUBPENETDYMAL GIANT CELL ASTROCYTOMA (SEGA) ASSOCIATED WITH TUBEROUS SCLEROSIS COMPLEX (TSC)
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Purpose: Everolimus, an oral mTOR inhibitor, significantly reduced SEGA tumor volume in an open-label, phase II trial (NCT00411619). Long-term safety and efficacy data for ≥4 years are presented.

Method: Patients ≥3 years of age with a definitive TSC diagnosis and a serial increase in SEGA lesion size (≥2 MRI scans) received everolimus starting at 3 mg/m²/day (titrated to target blood trough levels of 5–15 mg/ml). Measures of efficacy were reductions from baseline in primary SEGA volume.

Results: At the analysis cutoff date (12 December 2012), 23 of 28 (82.1%) patients initially enrolled in the study were still receiving everolimus. The median (range) duration of exposure to everolimus was 57.6 months (4.7–70.5 months). After 48 months of treatment, 58.3% (n = 14/24) experienced SEGA volume reductions ≥50% relative to baseline, and 79.2% (n = 19/24) of patients achieved a reduction ≥30%. Patient-reported seizure frequency (proportion of patients experiencing seizures on a daily basis) was reduced from 26.9% at baseline to 9.5% at month 48. Adverse events (AEs) remained similar to those previously reported for everolimus, and no patient discontinued treatment because of an AE. The most common AEs were infection and stomatitis, which were mostly grade 1 or 2 in severity.

Conclusion: The results of this analysis confirm maintenance of reductions in SEGA volume. Everolimus was well tolerated with prolonged use.

012 HYPONATREA WITH ESLICARBEPINE ACETATE (ZEBINIX) ADD IN THERAPY IN EVERYDAY CLINICAL PRACTICE USING A RETROSPECTIVE MULTICENTRE AUDIT
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Purpose: We report on the frequency of hyponatraemia in relation to add-in eslicarbazepine acetate therapy in routine clinical practice.

Method: A retrospective multicentre audit of outcomes following treatment with eslicarbazepine acetate for localisation-related epilepsy across 7 UK sites (2009–2013). 201 patients with median values for age 42.5 (17.8–85) years; duration of epilepsy 16.5 (0–65) years; 2 (0–4) concomitant AEDs; 12 month (2 days–53 months) duration of treatment and 0–12 (64% ≥2) previous AED exposures. Dosage ranged from 600 to 1,600 mg/day. Baseline seizure types comprised secondarily generalised tonic-clonic seizures (78.2%), complex partial seizures (74.3%) and simple partial seizures (23.8%). Psychiatric comorbidity was reported in 30% of patients, mainly depression and anxiety.

Results: 105 patients (52%) experienced ≥50% seizure frequency reduction. Hyponatraemia was reported (n = 14, 6.9%) and led to discontinuation in 4 patients (2.0%). The hyponatraemia range was 120–131 mEq/l; median range at 125 mEq/l. Hyponatraemia is considered to be uncommon (0.1–1%) based on the summary of product characteristics (SPC) for eslicarbazepine acetate (Zebinix). Although most cases of hyponatraemia were associated with AED polytherapy (median of 2 concomitant AEDs) no specific relationship was found in this study with renal disease, the use of diuretics or concomitant AEDs known to be associated with hyponatraemia.

Conclusion: In the routine clinical use of eslicarbazepine acetate (Zebinix), hyponatraemia was more common than predicted by the SPC. Clinical and biochemical monitoring for hyponatraemia should be considered when initiating eslicarbazepine acetate (Zebinix).

Platform Session: EPILEPTOGENESIS
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013 THE ROLE OF TOLL-LIKE RECEPTOR 3 IN EPILEPSY
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Objective: Effect of Toll-like receptors in the development of epilepsy.

Background: Epilepsy is one of the most prevalent neurological disorders. Despite the development of antiepileptic drugs, 35% of patients cannot be controlled with current pharmacologic therapeutic options. Toll-like receptors (TLRs) are a family of innate immune receptors that mediate neuroinflammatory processes. Inflammation plays a prominent role in the etiology of symptomatic epilepsies that result from traumatic brain injuries, stroke, encephalitis, and status epilepticus (SE). Here we investigated the involvement of TLR3 in the onset, development (epileptogenesis), and severity of epilepsy using mice deficient in TLR3 in the pilocarpine model of epilepsy.

Methods: We utilized mice deficient in TLR3 (TLR3-/-) and their respective wild-type (TLR3+/-) littermates. In both groups, SE was induced using the anti-cholinergic compound pilocarpine. Subsequently, mice were implanted for EEG monitoring with wireless bipolar EEG-electrodes. The electrographic features of SE and chronic seizures are analyzed using a telemetric EEG/video monitoring system (DSI, USA). In addition, all animals were sacrificed for stereological assessment of neuroinflammation in the hippocampus using quantification and morphology assessment of astrocytes (GFAP) and glialis by analyzing the morphology of microglial cells (IBA-1). Furthermore, hippocampal volumetry and quantification of neuronal cell death (NeuN) is performed.

Results: Analysis of Video-EEG recordings of both groups, (TLR3+/−) and wild-type (TLR3+/−) mice developed spontaneous epileptic seizures mainly classified as stage I and II seizures. Histological analysis is still pending but interictal epileptic events and prolonged seizures occurred significantly more frequent in the wild type mice compared with the TLR3 deficient group.

Conclusion: These preliminary results—in a still ongoing study—indicate a central involvement of seizure induction (epileptogenesis) by TLR3 and provide evidence for future research and possibly drug development.
to finally change the treatment paradigm of epilepsy from symptomatic seizure control to curable prevention of seizure development.

014 ACCUMULATION OF IGGS IN HILAR AND CA3 NEURONS AFTER A SINGLE SEIZURE
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Purpose: Autoimmune epilepsies are characterized by autoantibodies against membrane-bound, intracellular or secreted CNS proteins. Histone- and chromatin-specific IgGs are found in the nuclei of cortical neurons and in serum from patients with epilepsy. The mechanism of IgG extravasation is blood-brain barrier (BBB) disruption; but, the trigger of nuclear IgG uptake is unknown. We tested the hypothesis that seizures may cause IgG extravasation and neuronal uptake. We used a genetic mouse model of lupus displaying high levels of anti-histone, anti-chromatin and anti-dsDNA IgGs.

Method: NZBWF1/J mice were given pilocarpine at 170 or 340 mg/kg i.p. Seizures were quantified using the Racine scale. After 2 h, mice were sacrificed and brains processed for immunochemistry. Sections were incubated with an anti-mouse secondary antibody to probe for IgG.

Results: Mice were segregated in three groups based on seizure severity: control, low pilocarpine and high pilocarpine doses. Control mice (no pilocarpine, n = 12) displayed no extravasation of IgG, suggesting that at these disease stages the BBB is intact. Lups mice receiving high doses of pilocarpine and experiencing a Racine IV seizure (n = 5) displayed hippocampal BBB leakage with prominent ingress of IgG in hilar and CA3 neurons. IgG accumulation in neurons followed the mossy fiber territory. Mice treated with low doses of pilocarpine displayed minimal IgG extravasation (n = 12).

Conclusion: These results show that a single seizure allows neuronal accumulation of IgGs extravasated across a leaky BBB. Nuclear accumulation of IgGs comparable to that observed in human epileptic brain was observed in lupus mice. This phenomenon was prominent in regions most susceptible to neuronal cell death. Our results support the use of NZBWF1/J lupus mice to study nuclear autoimmunity and its role in epileptogenesis. Intraneuronal IgG accumulation may be a mechanism of seizure-induced hippocampal sclerosis.

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016 PATHOGENIC POTENTIAL OF ANTIBODIES DIRECTED AGAINST AMPAR AND GABAΔR IN AUTOIMMUNE ENCEPHALITIS
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Purpose: Antibodies directed against AMPAR and GABARΔR subunits have been implicated in forms of limbic encephalitis (LE), a disease characterized by memory loss and seizures. Clinical improvement with immunotherapies in this disease suggests that the disease may have an immune-mediated component and that the associated antibodies may be pathogenic. The potential pathogenic mechanisms of autoantibodies directed against AMPAR and GABARΔR were explored using a series of in vitro experiments.

Method: IgG subclasses, complement fixation and internalization were investigated using human embryonic kidney (HEK) cells transfected with AMPAR and GABARΔR subunits and primary neuronal cultures. GABARΔR antibody IgG was acutely applied to horizontal brain slices, and in vitro recordings were taken in the entorhinal cortex.

Results: Both AMPAR and GABARΔR antibodies showed staining on the surface of appropriately transfected cells and to live primary neuronal cultures. The main antibody subclass for AMPAR and GABARΔR antibodies was shown to be IgG1. Interestingly, on transfected cells only AMPAR antibodies showed C3b staining and therefore had the potential to activate the complement cascade. Application of IgG purified from AMPAR antibody positive patients caused a down regulation of the receptor from the cell surface on transfected HEK cells and primary hippocampal cultures. Changes in UP state duration, and spike rate in the entorhinal cortex following application of purified GABARΔR IgG on brain slices is suggestive of a direct modulation of cortical networks.

Conclusion: These findings suggest that antibodies directed against the AMPAR may mediate their pathogenic effects through activation of the complement cascade or internalization. In contrast, GABARΔR antibodies do not activate complement, but may be causing a direct modulating effect of cortical networks.
017 TRANSITIONAL CHANGES IN AMYLOIDGENIC AND TAU PATHWAYS IN POST-TRAUMATIC EPILEPTOGENESIS IN APP/PS1 MOUSE MODEL OF ALZHEIMER’S DISEASE

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Purpose: To elaborate the role of increased amyloid-β load on post-traumatic epileptogenesis we investigated whether traumatic brain injury (TBI) facilitates epileptogenesis in Alzheimer’s disease mouse model, and whether that associates with long-term changes in the expression of genes involved in amyloidogenic and Tau pathways.

Method: Mild and severe TBI were triggered in APP/PS1 and wild type (Wt) mice to assess TBI ‘dose’ effect and the genotype on functional outcomes. Mice underwent Neuroscore and Morris water-maze (MWM) to evaluate somatomotor recovery and spatial memory. Mice were followed-up for 2 wk (24 h/7d) with video-EEG starting at 6 wk and 14 wk post-TBI. Gene expression profiling of perilesional cortex, ipsilateral thalamus, and ipsilateral hippocampus was performed using Affymetrix microarray.

Results: TBI induced dose-dependent effect on somatomotor performance at 2d and 7d post-TBI in Wt and APP/PS1 groups (p < 0.05). sTBI showed genotype effect on somatomotor recovery 14d post-TBI (p < 0.05), latency to find the target in MWM (p < 0.05), where APP/PS1 had worse outcome then Wt mice.

TBI showed dose-dependent increase in the percentage of APP/PS1 mice with epilepsy (50% of APP/PS1-sTBI vs. 100% of APP/PS1-sTBI, p < 0.01). The effect of genotype on occurrence of epilepsy was present in sham-operated mice (APP/PS1-shams vs. Wt-shams, p < 0.05) and after sTBI (100% of APP/PS1-sTBI vs. 19% of Wt-sTBI mice, p < 0.01).

sTBI induced change in expression of 21 genes in Wt, and 12 genes in APP/PS1 mice out of 133 genes involved in amyloidogenic and Tau pathways. Correlations were observed between motor impairment and cortical expression (p < 0.001) of Clu (r = 0.83), Abca1 (r = 0.78), A2 m (r = 0.76), Apoe (r = 0.70), and Csd1 (r = 0.63).

Conclusion: TBI-induced epileptogenesis and co-morbidogenesis are more severe in APP/PS1 than Wt mice. In both genotypes, TBI causes long-lasting changes in gene expression. Contribution of altered transcripts to the mechanisms of post-TBI epileptogenesis vs. development of other comorbidities is under investigation.

018 AUTOANTIBODIES AGAINST S100B AFTER SUBCONCUSSIVE HITS IN AMERICAN FOOTBALL PLAYERS: A MARKER OF DELAYED NEUROLOGICAL SEQUELAE?

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Purpose: Traumatic brain injury is a well-recognized cause of seizures, but a mechanistic correlation between the early event (trauma) and development of seizures is obscured by a silent period of epileptogenesis. While the effects of major trauma on later risk of seizures have been reported, whether many subconcussive events can mimic the effects of a frank traumatic brain injury remains unknown. The risks for multiple traumatic brain impacts in American football players has prompted studies on the consequences of sub-concussive events. We and others have previously shown that autoimmunity against brain protein is a hallmark of certain epilepsies. To investigate if TBI-related seizures were triggered by head impacts during football games may cause production of brain antigen directed auto-antibodies.

Method: Players from two college football teams were enrolled (total of 33 volunteers). None of the players experienced a concussion. Blood samples were collected before and after games. Auto-antibodies against the astrocytic protein S100B were measured by reverse immunoassays.

Results: Elevated levels of auto-antibodies against S100B were elevated only after repeated sub-concussive events characterized by BBBD.

Conclusion: Even in the absence of concussion, football players may experience delayed serum surges of serum auto-antibodies. This potential marker of epileptogenesis will be further investigated in long-term studies and in populations at risk for posttraumatic epilepsy.

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Platform Session: Genetics
Monday, 30th June 2014

019 IDENTIFYING THE CAUSES OF PHARMACORESISTANT EPILEPSY THROUGH A GENOME-WIDE ASSOCIATION STUDY WITH PATHWAY AND NETWORK ANALYSIS: FROM COMPLEXITY TO COHERENCE TO CENTRALITY

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Purpose: A third of people with epilepsy are pharmacoresistant. As pharmacoresistance is a complex trait, a genome-wide pathway-level approach is likely to prove especially fruitful in its study.

Methods: We performed a genome-wide association study (GWAS) of pharmacoresistant partial epilepsy, with discovery and replication cohorts including, in total, 421 cases and 2,624 normal population controls, and 5,519,310 genotyped and imputed SNPs.

Results: At the single variant level, there was no overlap in the top results of the two cohorts. However, at the gene-set and pathway level, there was clear replication of results between the two cohorts: (i) there was a striking correlation between the discovery and replication cohorts in the gene-set analysis results (Pearson’s correlation coefficient=0.8, one-sided p-value < 2.2x10^-16), and (ii) there was a highly significant overlap between the enriched pathways for the discovery and replication cohorts (hypergeometric distribution p-value < 3.7x10^-17). For the combined “mega-analysis,” there were 71 enriched pathways. We showed using network analysis that these enriched pathways form a highly interconnected network in which each pathway is directly connected, on average, to 8.4 other pathways. The enriched pathways, therefore, form a coherent whole and it can be expected that changes in one pathway in this network will have a cascading effect on the rest of the network. Finally, we identified, using betweenness centrality network analysis, the most important central pathways in this network, for example, signalling by NGF and DSCAM interactions.

Conclusion: We have performed the first ever GWAS of pharmacoresistant partial epilepsy and identified the most central pathways underlying this phenotype.
020 MUTATIONS IN GRIN2B IN WEST SYNDROME AND INTELLECTUAL DISABILITY WITH CHILDHOOD-ONSET FOCAL EPILEPSY

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Purpose: NMDA receptors are tetrameric ligand-gated ion channels permeable to Na+, K+ and Ca2+ composed of two glycine binding NR1 subunits and two glutamate binding NR2 subunits (NR2A, NR2B, NR2C, NR2D) regulating synaptic plasticity.

Mutations in GRIN2A, encoding NR2A have recently been associated with Rolandic epilepsy as well as rare epileptic encephalopathies, such as Landau-Kleffner syndrome and epilepsy with continuous spikes and waves during slow wave sleep (CSWS). Mutations in GRIN2B (NR2B) have been detected in neurodevelopmental disorders but had not been associated with epilepsy to date.

Method: We used a targeted re-sequencing approach to screen patients with epileptic encephalopathies and other epilepsy disorders for mutations in known and putative epilepsy genes.

Results: We describe de novo gain-of-function mutations in GRIN2B in independent individuals with West syndrome and severe developmental delay as well as in patients with childhood-onset focal epilepsy. Via a decreased Mg2+ block, all analysed mutations induced a severely increased influx of Ca2+ and by that may mediate hyperexcitability. The severity of phenotypes correlates with the affected domain and the extent of activation of the receptor. Compared to GRIN2A, the earlier onset of GRIN2B phenotypes is in line with the spatiotemporal expression pattern of both NR2 subunits.

Conclusion: Our observations establish GRIN2B as epilepsy gene and underline the role of dysregulated NMDA signalling in epileptic encephalopathies. These findings reveal promising pharmacologic targets for future therapeutic approaches.

021 MUTATIONS IN DEPDC5 ARE A MAJOR CAUSE OF LESIONAL AND NON-LESIONAL FOCAL EPILEPSY

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Purpose: We set out to find the genetic cause of focal epilepsy in a family with individuals with lesional and non-lesional focal epilepsy, as detectable by MRI analysis. The family showed autosomal dominant inheritance and genome wide linkage analysis had failed to identify a linkage region.

Methods: We carried out exome sequencing on two individuals from the family who were affected with focal epilepsy and analysed the data using an in-house bioinformatic pipeline. Candidate causative genetic variants were validated by direct Sanger sequencing and were analysed for co-segregation with affected status and assessed for likely pathogenicity.

Results: We identified a mutation in DEPDC5 as being causative of lesional and non-lesional focal epilepsy in the family. We then identified two additional families with DEPDC5 mutations who also had mutation-positive individuals with lesional and non-lesional focal epilepsy. DEPDC5-associated malformations include bottom-of-the-sulcus dysplasia (3 members from 2 families) and focal subcortical band heterotopia (1 individual).

Conclusion: We report that mutations in DEPDC5 cause familial cases of focal epilepsy associated with structural lesions. Previously we have found that mutations in DEPDC5 cause familial cases of non-lesional focal epilepsy. We therefore now show that lesional and non-lesional epilepsies can have a shared genetic aetiology. This challenges previous ideas of lesional and non-lesional epilepsy being regarded as distinct entities. DEPDC5 negatively regulates the mTOR pathway which plays a key role in cell growth. The clinical and radiological phenotypes associated with DEPDC5 mutations share features with the archetypal mTORopathy, tuberous sclerosis, raising the possibility of new therapeutic avenues for patients.

022 COMPREHENSIVE NGS BASED DIAGNOSTICS IN OVER 800 PATIENTS WITH EPILEPTIC DISORDERS

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Purpose: Epileptic disorders have a highly heterogeneous background and a strong genetic contribution. Knowing the underlying molecular defect can be very valuable for diagnosis, guiding treatment and estimating recurrence risks. For this purpose we have developed a comprehensive diagnostic panel.

Method: 461 relevant genes were selected from the literature, and subdivided according to their phenotypes. Following customized target enrichment, NGS was performed, followed by bioinformatic analysis. Variants with a global minor allele frequency <5% were selected for evaluation and identified mutations were validated using Sanger sequencing.

Results: In our study, over 800 patients with epileptic disorders were analyzed. 21% of patients had pathogenic mutation(s) and 28% were inconclusive. 51% remained unsolved, mostly due to non-segregation of identified variants, implying complex inheritance or non penetrance. We observed rare variants in 183 different genes, with 69 genes identified as causative only once, emphasizing the advantage of diagnostic panels for very rare conditions.

Conclusion: We have developed a highly reliable and cost-efficient diagnostic NGS panel to analyze the genetic basis of epilepsies. We detected mutations in patients with clear and unspecific epilepsies, as well as in patients suffering from very rare conditions. This enables better...
understanding of genotype-phenotype correlations, and gives new insights into complex modes of inheritance such as combinatorial effects of variants.

023  
GENE DOSE IMBALANCES IN CHILDREN WITH BRAIN MALFORMATIONS AND REFRACTORY EPILEPSY
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Purpose: To study the frequency and the nature of copy number variations (CNVs) in children with brain malformations and therapy refractory epilepsy.

Method: Medical records of all children born between 1990 and 2009 in the epilepsy registry at the Astrid Lindgren’s Children’s Hospital were reviewed and 86 patients with therapy refractory epilepsy and various brain malformations were identified (holoprosencephaly, septo-optic dysplasia, hemimegalencephaly, lissencephaly, heterotopia, schizencephaly, polimicrogyria, focal cortical dysplasia and agenesis/dysgenesis of the corpus callosum). All neuroradiological investigations were re-examined and classified by the same neuroradiologist. Whole genome array-CGH analysis was performed in 76 of the patients.

Results: Pathogenic copy number variations were detected in 7 children (9%). In addition, rearrangements of unclear significance, but possibly pathogenic, were detected in 11 (14%) individuals. In 37 (46%) patients likely benign, but previously unreported, CNVs were detected. Six patients declined participation in the study and 4 (5%) had chromosomal imbalances previously identified by karyotyping or FISH-analysis, which would have been detectable by array-CGH. Thus a large proportion of our patients (74%) had at least one rare CNV. The highest yield was found in the group of lissencephaly/subcortical band heterotopias and polymicrogyria. The diagnostic yield in relation to different malformations will be compared.

Conclusion: Our results suggest that array CGH should be used early in the genetic evaluation of children with cerebral malformations and therapy refractory epilepsy, unless there is a strong suspicion of a specific monogenic syndrome. Genetic studies of children with therapy refractory epilepsy and brain malformations show genetic heterogeneity and expand our understanding of the etiologies.

024  
DIVERSE EFFECTS OF DIFFERENT TYPES OF SCN8A MUTATIONS
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Purpose: To investigate the role of SCN8A mutations in epileptic encephalopathy.

Method: SNP-array and next-generation-sequencing in sporadic patients and their parents to detect possible pathogenic variants, Transfection, western blotting and patch-clamp experiments were used to investigate functional effects of the de novo missense mutation.

Results: One patient carried a de novo missense mutation in SCN8A. Her symptoms were severe with regression after seizure onset at age 8 months and no speech or walking at 3 years of age. Mainly tonic and clonic seizures occurred. This missense mutation reduced protein levels and channel activity. A second effect was an increased response to a slow ramp stimulus. A second patient carried a 13-exon deletion of SCN8A, as well as an inherited rare missense polymorphism in SCN8A. She had mainly absence seizures and seemingly normal development till age of 4, with regression afterwards, resulting in severe delay.

Conclusion: Recent papers have shown a role for SCN8A missense mutations in early-onset epileptic encephalopathy. Probably these mutations alter channel function. Haploinsufficiency, in combination with a milder alteration of protein function, may cause epileptic encephalopathy with a different aetiology. The phenotype of the deletion patient differed from that of the missense patient mainly in the type of seizures and the age at which regression started.

Platform Session: Neuroimaging
Monday, 30th June 2014

025  
ABNORMAL RESPONSE TO PHOTIC STIMULATION IN JUVENILE MYOCLONIC EPILEPSY: AN EEG-fMRI STUDY
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Purpose: Juvenile Myoclonic Epilepsy (JME) is a young onset electroclinical syndrome, characterized by myoclonic, generalized tonic-clonic and possibly typical absence seizures. Intercital EEG displays 3-6 Hz spike/polyspike and wave pattern. Photosensitivity is frequent. Our aim was to explore the BOLD response evoked by a highly provocative photic stimulus in a cohort of people with JME compared to a group of not-photosensitive healthy controls and to investigate the hemodynamic phenomena peculiar of photosensitive JME subjects

Method: We studied 13 JME patients and 18 healthy controls by EEG-fMRI performed during low luminance intermittent photic stimulation (IPS). The BOLD response to IPS was investigated both in JME and control groups. In photosensitive JME subjects we also performed a dynamic evaluation of BOLD signal changes evoked by the Photoparoxysmal Response (PPR) in a time frame ranging from 10 s before the onset of the EEG paroxysm up till 10 s after.

Results: The IPS evoked a positive BOLD response in striate and extrastriate visual areas, lower in JME patients than controls. Moreover, people with JME had a reduced positive BOLD response in frontoparietal areas and putamen and a stronger negative BOLD response in primary sensorimotor cortex (SM1) and in cortical regions belonging to the Default Mode Network (DMN). In JME the dynamic evaluation of BOLD signal changes related to PPR revealed an early positive response in putamen
and SM1, followed by BOLD signal decrements in putamen itself, caudate nuclei, thalamus and SM1.

Conclusion: Our results sustain the hypothesis that people with JME might suffer from an altered interaction between motor circuit and other neuronal networks, with a prominent involvement of basal ganglia circuitry. The PPR could feature the final expression of pathogenic phenomena occurring in the striato-thalamo-cortical system, possibly core of the system epilepsy JME.

026 MR FEATURES OF PROLIFERATIVE OLIGODENDROGLIAL HYPERPLASIA IN EPILEPSY (POGHE) – A NOVEL DIAGNOSTIC ENTITY

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Purpose: From the European Epilepsy Brain Bank, proliferative oligodendroglial hyperplasia in epilepsy (POGHE) has been histopathologically identified recently. This new epilepsy associated pathology differs from tumours by clinical course and histopathology and is conceptualised as mild malformation of cortical development (Coras et al. Epilepsia 2013;54:s3:318). In this multiple case study, MR features of POGHE were evaluated in fully evaluated patients.

Method: In the series of 303 resections at Bethel epilepsy centre between 2011 and 2013, five patients with histopathologically proven POGHE were identified retrospectively (4 m; age range 4–23 years). All patients suffered from pharmacoresistant frontal lobe epilepsy (3 right sided; age of onset 1–12 years) and underwent presurgical 3T MRI (MRI-diagnoses: “FCD”). At 6 months after surgery, MRI was available in 3 patients (3 patients were seizure free at their latest review at 1, 6, and 12 months after surgery, respectively).

Results: All patients had a frontal lobe lesion which had not been detected on prior imaging (location: 2 frontolateral, 2 frontolateral and mesial, 1 frontoorbitolateral; frontal pole involved in 3 cases). In all cases, there was blurred grey white matter interface, not sharply demarcated; more than one gyrus affected in 4 cases. 3 x thickened cortex, 3 x faint transmantle sign. No circumscribed lesions detected on prior imaging (location: 2 frontolateral, 2 frontolateral and mesial, 1 frontoorbitolateral; frontal pole involved in 3 cases). In all cases, there was blurred grey white matter interface, not sharply demarcated; more than one gyrus affected in 4 cases. 3 x thickened cortex, 3 x faint transmantle sign. No circumscribed lesions detected on prior imaging (location: 2 frontolateral, 2 frontolateral and mesial, 1 frontoorbitolateral; frontal pole involved in 3 cases).

Conclusion: Despite significant differences in the cellular composition of POGHE compared to FCD, MR features of POGHE were similar to MR features of FCD. Differentiating clinical features and postsurgical outcome should be clarified in larger studies.

028 FOCAL CORTICAL DYSPLASIA ON 7 TESLA SUSCEPTIBILITY WEIGHTED MAGNETIC RESONANCE IMAGING

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Purpose: Radiological detection of structural abnormalities in focal epilepsy remains a big challenge. Absence of a lesion on MRI has been shown to be a predictor of surgical failure and consequently can be, but not necessarily is, a reason for a patient to be deemed unsuitable for surgery. Focal cortical dysplasia (FCD) is the most prevalent histopathological diagnosis in MRI-negative patients operated for refractory epilepsy. We therefore explored the potential of 7 tesla susceptibility weighted magnetic resonance imaging (SW MRI, SWI) in assisting the detection of FCD.

Method: We retrospectively reviewed pre-surgical 7T MRI scans, acquired between 2009 and 2013, from three patients with histopathologically confirmed FCD. We assessed the presence of features indicative of
FCD and searched for additional characteristics or abnormalities which could aid in lesion detection.

**Results:** SWI showed deeply hypointense signal, suggestive of increased vascular prominence, in the leptomeningeal vascular network overlying FCDs. T1, T2, double inversion recovery and fluid-attenuated inversion recovery sequences showed other, well recognized, features of FCD for all three patients co-localizing with the SWI findings. FCD histopathology could be subdivided in FCD Ib (n = 2) and Ib (n = 1). Surgical samples of one patient showed fibrotic leptomeninges with prominent vessels, which may represent a substrate of the SWI findings. For two patients the leptomeninges were stripped and could not be studied histopathologically.

**Conclusion:** We report a novel MR finding possibly related to FCD. 7T SWI revealed what appears to be an increase in vascular prominence in the leptomeningeal vascular network overlying the dysplastic cortex. Adding SWI sequences to the MRI protocol may increase sensitivity for detection of FCD resulting in a larger proportion of patients to be recognized as potential surgical candidates. Further MRI and histopathological research is warranted to elucidate the nature of these FCD-associated SWI changes.

029
AN FMRI-BASED MODEL FOR PREDICTION OF VERBAL MEMORY DECLINE AFTER TEMPORAL LOBECTOMY (TLE)
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**Purpose:** To study the impact of fMRI verbal memory assessment on post-surgical memory function.

**Method:** 13 pharmaco-refractory patients eligible for TLE were recruited. All patients underwent structural 3T MRI, neuropsychological assessment and memory fMRI before surgery. A risk-assessment score for post-operative memory deficits was calculated including epileptogenic lesion +/-, expected hemisphere dominance (left in all patients) and neuropsychological ratings. Expected fMRI language and verbal memory patterns, expressed as lateralization indices, was defined as left lateralized language and verbal memory lateralized away from the afflicted temporal lobe. Patients with unexpected fMRI results were considered at a higher risk for memory decline than indicated by the comprehensive score. The predictive value was compared to post-surgical memory outcome.

**Results:** 10 patients were rendered seizure-free; 3 had 50–75% seizure reduction. 4/7 patients undergoing left TLE with expected fMRI activation, and 2 patients with moderately atypical fMRI patterns, had no post-operative memory decline. Unexpected post-operative memory decline was seen in one patient with highly atypical fMRI activation results. 3/6 patients undergoing right TLE had expected fMRI patterns and showed no post-operative memory decline. 3 patients with atypical fMRI patterns showed verbal memory decline confirmed by post-operative testing.

**Conclusion:** An unexpected pre-surgical fMRI pattern in verbal memory assessment is predictive for post-operative memory deficits in TLE, a heterogeneous group with expected high rate of atypical language lateralization. Particularly bilateral language activation patterns served as a warning.

030
COMPARATIVE SPIKE MAPPING USING INTRACRANIAL SINGLE-PULSE ELECTRICAL CORTICAL STIMULATION AND INTRACRANIAL EEG-FMRI
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**Purpose:** A number of medication refractory patients with focal epilepsy require invasive monitoring of ical and interictal activity to identify seizure foci and establish surgical candidacy. Single-pulse electrical stimulation of intracranial electrodes allows the assessment of connectivity from evoked responses (cortico-cortical evoked potentials (CCEPs)). This study concerns the comparison of the connectivity patterns revealed by CCEPs to the interictal spiking propagation patterns, complemented by a preliminary comparison to simultaneous intracranial EEG (icEEG) fMRI in a selected case.

**Method:** Five patients were retrospectively selected from the National Hospital for Neurology and Neurosurgery database, each of whom underwent both single pulse electrical stimulation and simultaneous icEEG-fMRI during invasive presurgical evaluation of medically refractory focal epilepsy. All patients had left frontal lobe epilepsy and focal cortical dysplasia, investigated with a combination of grids and depth electrodes. First, spikes and spike propagation were analysed conventionally on icEEG and compared to maps obtained using a new, specifically developed 3D visualisation program for CCEPs evoked from electrode contacts of interest. CCEPs maps were also co-registered with icEEG spike-related BOLD maps in one patient.

**Results:** First and second negative deflections (N1 and N2) and root mean square of evoked potentials showed good correlation with electrodes maximally implicated in the interictal spikes and spike propagation. CCEPs maps illustrated fast non-contiguous propagation in addition to local propagation in three cases after multiple stimulation pairs. Largest evoked responses were typically around stimulation sites, and N2 distribution was greater than N1 distribution. Preliminary visual analysis in a selected patient revealed good concordance between spike associated BOLD responses, spike propagation, and CCEPs.

**Conclusion:** Visualisation of CCEPs with 3D maps is an interesting additional tool for investigating complicated epileptic networks. Combining CCEPs and BOLD changes associated with spike mapping on icEEG may offer further insight into propagative pathways of interictal epileptiform activity.

Platform Session: Neuromodulation Cortical Dysplasia
Monday, 30th June 2014

031
EXPERIENCE WITH THE NEW ILAE CLASSIFICATION ON FOCAL CORTICAL DYSPLASIA IN 60 PATIENTS
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Purpose: Up to 40% of symptomatic childhood onset epilepsies are drug-resistant. About 50% of them are due to malformations of cortical development (MCD). Resective epilepsy surgery has been increasingly performed in these patients, but reported outcomes have been variable and valid outcome predictors are currently not available.

Method: Included were all patients <18 years with drug-resistant epilepsies and histologically proven MCD, who had had epilepsy surgery at the Vienna pediatric epilepsy center and follow-up data of at least 12 months after surgery.

Clinical variables evaluated as possibly associated with outcome after surgery were the following: gender, age at epilepsy onset, age at surgery, duration of epilepsy before surgery, preoperative febrile seizures, preoperative neurological deficits, type of seizure, lesion localization, preoperative seizure frequency, invasive recordings or type of mcd. Classification of MCD was according to the existing classification schemes of Barkovich et al, Palmini et al and the novel ILAE classification of FCDs. Seizure outcome was classified using the ILAE proposal (Wieser et al.).

Results: We included 60 patients. One year after surgery 47/60 (78.3%) patients were seizure-free (class 1a; ILAE). The result remained stable until the last follow-up visit (mean 4.4 ± 3.2 years, minimal and maximal patient ages were one and 14 years, respectively). The decade-long follow-up showed that more than 50% of the patients remained seizure-free following surgery (class 1a) at each annual control visit.

Extended lesion removal showed a statistically significantly better outcome than did tailored resections and partial disconnections (i.e. the best results were achieved with hemispherotomies). The type of MCD did not show significance.

Conclusion: We tried to evaluate the clinical applicability of the new ILAE classification system on Focal Cortical Dysplasia. However, in our patient group the extent of surgery remains the only predictor of seizure freedom.

032 VAGUS NERVE STIMULATION TRIGGERED BY ICTAL TACHYCARDIA-BASED SEIZURE DETECTION, A PROSPECTIVE MULTI-SITE STUDY

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Purpose: Patients treated with VNS Therapy® (VNS) find that using the magnet to activate stimulation near the beginning of a seizure may terminate or decrease severity of the seizure. Magnet use is not always possible due to cognitive impairment, lack of an aura or the disabling effects of the seizure itself. The AspireSTM pulse generator was developed with a cardiac-based seizure detection algorithm to automatically trigger stimulation in response to seizure activity.

Methods: 31 patients with refractory epilepsy were enrolled in trial NCT01325623 to confirm device performance. Patients were monitored using video electroencephalogram and electrocardiogram during an Epilepsy Monitoring Unit (EMU) admission of up to 5 days Patients will be monitored for 2 years to assess device safety and efficacy. Device performance was measured by sensitivity, potential false positive rate and detection latency.

Results: During the EMU phase, 82 focal seizures were recorded. Forty demonstrated heart rate increases in excess of 20% relative to baseline rate. Device sensitivity of 75–100% was observed for ictal tachycardia seizures, (increase of at least 55% or 35 BPM relative to baseline and an ictal rate of at least 100 BPM). Safety profile was comparable to prior VNS epilepsy trials. Six-month data will be presented at ECE.

Conclusion: AspireSR™ performed as intended. Device sensitivity exceeded 80% for more than one programmable algorithm threshold setting, achieving the primary study endpoint. The device delivered acute and timely therapy, providing physicians with a novel enhancement to traditional VNS.

033 FOCAL CORTICAL DYSPLASIA ALTERS FUNCTIONAL CORTICAL HUBS IN THE RESTING-STATE: AN MEG STUDY AT THE SOURCE LEVEL

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Purpose: To test the hypothesis that epilepsy patients with focal cortical dysplasia (FCD) may have different electrophysiological functional cortical hubs (highly central parts of the network) from that of healthy controls.

Method: The resting-state functional networks in the theta, alpha, beta, and gamma frequency bands were evaluated in 35 epilepsy patients with histopathologically verified FCD as a single pathology and 46 age-matched healthy controls.

We investigated the network with nodal efficiency (Enodal) and betweenness centrality (BC) measures at the source level with magnetoencephalography (MEG) signals.

Results: We showed the altered electrophysiological functional cortical hubs in epilepsy patients with FCD compared to healthy controls. The FCD patients had the significant increases in the Enodal of the functional cortical hubs in the left anterior, middle and posterior cortices and medial orbital superior frontal cortex in the beta band. The left posterior cingulate cortex showed the significant increases in the BC in the theta, alpha and beta bands. A negative correlation between the Enodal and age at seizure onset was also found.

Conclusion: Our study for the first time investigated the functional cortical hubs and their alteration in the resting-state functional network in epilepsy patients with FCD using noninvasive MEG signals, providing insight on the different electrophysiological mechanisms of the epileptic FCD brain. A negative correlation between Enodal and age at seizure onset may indicate abnormal brain network development in the epileptic brain with FCD, due to the unfavorable effect of cortical dysplasia on the normal development of the functional network.

034 EFFECTS OF BILATERAL ELECTRICAL STIMULATION OF THE ANT ON NEUROCOGNITION AND QUALITY OF LIFE IN 11 ADULT PATIENTS WITH REFRACTORY EPILEPSY

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Purpose: The SANTE study reported memory and mood disorders as possible adverse events of bilateral electrical deep brain stimulation (DBS) of the anterior nuclei of the thalamus (ANT). We assessed changes in neurocognition, mood and quality of life (QoL) after bilateral DBS of the ANT.

Method: Eleven epilepsy patients (6 female) underwent detailed neuropsychological examination before DBS surgery. Seven patients were re-evaluated 4 weeks after implantation of electrodes, but before onset of stimulation (implantation effects), all 11 patients after 4 months and 6 patients to date after 16 months of stimulation (stimulation effects).

Results: As implantation effects we observed a significant decline of nonverbal encoding, but a significant improvement in psychopathological status and a tendency towards improvement of mood. Four months after stimulation onset we noticed a significant decrease of nonverbal encoding and verbal recognition, but a significant improvement of phobic anxiety and a tendency towards improved general health perceptions. There were no changes in the remaining psychiatric, QoL and cognitive domains. After 16 months of stimulation a significant worsening of verbal encoding could be seen. Disease-specific QoL remained unchanged.

Conclusion: DBS of the ANT had a negative effect on episodic memory, probably because of the involvement of the ANT in the Papez circuit. The effect was reversible in one patient where left-sided stimulation was subsequently turned off. Immediately after implantation we observed a „relief effect”, when patients hope for seizure reduction. In the medium term, this effect disappears and mood, QoL and psychiatric profile in general remain the same.

035

THE LOCATION OF ACTIVE CONTACTS CORRELATES WITH OUTCOME AFTER DBS OF THE ANTERIOR NUCLEUS OF THE THALAMUS IN REFRactory EPILEPSY

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Purpose: DBS of the anterior nucleus of the thalamus (ANT) has been suggested as novel treatment option in refractory focal epilepsy. Unfortunately, detailed anatomical data about the most optimal functional target is currently lacking. In the present prospective study we have studied the outcome after DBS aimed at ANT in 15 patients up to 4 years after surgery. We have especially focused on the correlation between the location of active contacts (a total of 22 treatment trials using different contact pairs) and outcome.

Method: The location of contacts was analyzed on preoperative 3T MRI STIR – postoperative CT fusion images. The location of each contact was classified into 6 identifiable categories accordingly to its location: central ANT, border of the ANT (superior, lateral, inferior), lateral to ANT or inferior to ANT. Each contact pair was evaluated as being responding/non-responding contact pair according to the seizure reduction and potential side effects.

Results: Nine out of ten (90%) stimulation trials using contacts bilaterally in the central ANT or superior/lateral border of ANT were classified as responding contact pairs, whereas stimulation trials using contacts at the inferior border of the ANT or more inferiorly located contacts were classified as non-responding contact pair in all 12 trials out of 12. No differences in age, etiology, epileptogenic zone or seizure onset zone was found between responders and non-responders.

Conclusion: Significantly better results compared to previous studies may be achieved by avoiding inferior parts of the ANT and aiming more central/superior/lateral aspects of the ANT. Better understanding of the optimal antiepileptic “functional target” enables also more accurate surgical planning, selection of the optimal surgical trajectory and more effective postoperative programming.

036

COMbined ex-Vivo 9.4T mri and QuAntitative histOPathological sTUDY in normal and PATHOLOGICAL surgerICAL resections in focAl epiLepsy

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Purpose: Various subtle cortical and white matter abnormalities have been reported on MRI in patients with epilepsy, some may correlate with mild malformations of cortical development (mMCD) or focal cortical dysplasia (FCD) in tissue resections. However varying degrees of reactive or degenerative pathological changes are frequently noted in surgically resected specimens, including gliosis, myelin and axonal loss, inflammation and blood brain barrier breakdown, which could also influence MRI measurements. We aimed to investigate this with high field MRI imaging of resected tissues from patients with epilepsy, correlating this with pathological measurements.

Method: Fourteen lobectomy samples were scanned in a 9.4T MRI scanner. Tissues were subsequently routinely processed and immunostained for SMI94 (myelin), SMI32 (axons), MAP2 (neurones), synaptophysin (neuropil), GFAP (astrogliosis), CD68 (microgliosis) and albumin (blood brain barrier breakdown). MRI images and pathology sections were co-registered and 42 regions of interest (ROI) defined: 24 in the white matter, 18 in the cortex with 33 in pathology-negative and 9 in abnormal regions. Quantitative MR measures (T1, T2, T2 star and MTR) and quantitative histological labelling index (LI) for each marker were calculated for each ROI.

Results: Our findings included a significant correlation between myelin LI and T1 and T2 values over all ROI (p < 0.01); significant correlations were also observed for neuronal LI and MTR and T1 (p < 0.01) but not for axonal or glial LI over all ROI. In pathology-negative ROI, there was a significant correlation with neuronal LI for all MR measurements (p < 0.01) and a trend for a correlation between glial LI and T2 star (p = 0.029). In pathological ROI, MTR values correlated with axonal LI (p < 0.01).

Conclusion: This initial study suggests that myelin and neuronal markers show the strongest correlation with MRI measurements, with less evidence for an influence of the degree of acquired tissue astrogliosis on these measurements.

Platform Session: Seizure Suppression Tuesday, 1st July 2014

037

CHANGES IN CEREBROVASCULAR PDGFRß AND NG2 PERICYTES AFTER SEIZURES

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**Purpose:** The role of cerebrovascular dysfunction in seizure disorders is recognized. Blood-brain barrier (BBB) damage in the epileptic brain has been linked to endothelial and glial pathophysiological changes. Little is known about the involvement of pericytes, a cell type that contributes to BBB function.

**Methods:** Seizures were induced in NG2DS-Red or C57BL/6 mice by intraperitoneal kainic acid. Animals were sacrificed 18 h after kainic acid administration and intracardially perfused with FITC-Dextran to visualize the cerebrovasculature. Control animals did not receive KA and were processed in parallel. NG2DS-Red mice allow for the visualization of NG2+ pericytes. BL6 mice brain sections were stained for the pericyte markers NG2 and platelet-derived growth factor receptor beta (PDGFRβ). Western blot was performed to confirm marker expression. Confocal 3D vessel reconstruction was used to visualize changes in cell morphology and position. We evaluated the expression of PDGFRβ in a cohort of drug resistant human epileptic samples obtained from temporal lobectomies (TLE) and in one control autopic brain from a lung cancer patient.

**Results:** Acute seizures altered the structure and diminished coverage of constitutive NG2+ cells lining the BBB in the temporal cortex and hippocampus. The effect was prominent in animals experiencing severe and repetitive episodes of status epilepticus. Western blot analysis and 3D vascular reconstruction confirmed the changes in NG2 expression. Concomitantly, PDGFRβ+ cells positioning at the BBB was augmented after acute seizures in mice. Analysis of human brain samples revealed perivascular and parenchymal PDGFRβ staining resembling the animal model. Moreover, PDGFRβ+ vascular staining was increased in TLE brain tissues compared to the autopic control.

**Conclusion:** The rearrangement of PDGFRβ+ and NG2+ cells observed after seizures suggests the possible involvement of pericytes in the cerebrovascular response typical of the epileptic brain. Whether targeting pericytes could beneficial to reduce BBB dysfunction and seizures remains to be investigated.

**039**

**THE EFFECT OF DEXAMETHASONE ON ABSENCE SEIZURES OF RATS WITH GENETIC ABSENCE EPILEPSY**

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**Purpose:** Genetic Absence Epilepsy Rats from Strasbourg (GAERS) is a well defined animal model of typical absence epilepsy in human. Recent studies demonstrated a critical role of proinflammatory molecules in absence epilepsy. This evidence can open a perspective for developing anti-inflammatory therapeutic approaches for absence epilepsy. The effect of dexamethasone, an anti-inflammatory steroid drug, was examined on spike-and-wave discharges of adult male and female GAERS.

**Materials and Methods:** Adult male and female GAERS were implanted with bilateral cortical recording electrodes under anesthesia. One week after a recovery period, baseline EEG (PowerLab 8S) was recorded for 3 h in the morning session (9:00–12:00). Animals were treated twice daily with intraperitoneal injection of dexamethasone (3 mg/kg) or saline for 3 days, The EEG recordings for the baseline and after each injection were analyzed for the cumulative duration, mean duration and number of SWDs.

**Results:** In the 3-h-EEG recording after the 3rd injection of dexamethasone, the cumulative duration of SWDs in female GAERS was 2085.9 ± 427.8 s, whereas in the saline group it was 3474.4 ± 490.2 s. This difference was statistically significant (p < 0.05). However, any difference was not observed between the dexamethasone or saline groups in male GAERS. No difference in the number of SWDs in female and male GAERS was shown in the dexamethasone or saline groups.

**Conclusion:** The daily administration of dexamethasone progressively suppressed the cumulative SWDs in female GAERS, whereas no significant effect was found in male GAERS. Preliminary results of the present study suggest a gender difference in the effect of dexamethasone on SWDs in GAERS.

**040**

**ANTICONVULSANT ACTIVITY OF FEEDING RESTRICTION IN ACUTE SEIZURE MODEL INDUCED BY LITHIUM-PILOCARPINE IN ADULT RATS**

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**Purpose:** A variety of observations suggest that changes in the metabolism induced by nutritional challenges, would have an anticonvulsant activity. In this sense, it has been suggested that changes on levels of ketone bodies the principal source of energy in conditions of energy deprivation, can act as neuroprotectors. Because calorie restriction induced
changes in metabolism, we determined whether a feeding restriction model would induce a metabolism shift producing increase of ketone bodies levels and therefore having an anticonvulsant effect. Also, in order to establish that feeding restriction model resemble this metabolism changes such as calorie restriction model, we measured the ketone body \(\beta\)-hydroxybutyrate in blood and hippocampus as well the protein content of phosphorylated AMPK and Akt (components of signaling pathways involved in metabolism regulation), in hippocampus, olfactory bulb and liver.

**Method:** The anticonvulsant activity of the alimentary restriction model was determined in a rat model of acute seizures induced by lithium (3 mEq/kg) and pilocarpine (60 mg/kg) with a previous injection of scopolamine nitrate (1 mg/kg) 30 min before. The efficacy of feeding restriction model was compared with control animals fed ad libitum. Seizure duration, status epilepticus and seizure score were measured in each group.

**Results:** Our results showed that feeding restriction model produce an increase in \(\beta\)-hydroxybutyrate levels (n = 30, \(p < 0.005\)), together with an increase of activity of AMPK signaling pathway (n = 8, \(p < 0.005\)), and a decrease activity of Akt signaling pathway (n = 8, \(p < 0.005\)), resembling the calorie restriction model.

**Conclusion:** Our data demonstrate that feeding restriction model produces an increase in \(\beta\)-hydroxybutyrate levels and therefore have an anticonvulsant effect. Also, in order to establish that feeding restriction model resemble this metabolism changes such as calorie restriction model, we measured the ketone body \(\beta\)-hydroxybutyrate in blood and hippocampus as well the protein content of phosphorylated AMPK and Akt (components of signaling pathways involved in metabolism regulation), in hippocampus, olfactory bulb and liver.

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**041 THE REDOX STATE OF HIGH MOBILITY GROUP BOX 1 (HMGB1) PROTEIN MEDIATES ITS DETRIMENTAL EFFECTS ON SEIZURES AND NMDA-INDUCED CELL LOSS**

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**Purpose:** HMGB1 is a “danger signaling” protein released by glia and neurons following experimental brain injuries, upregulated in human epileptic brain, and with proconvulsive effects in rodents. Since the redox state of HMGB1, as determined by the extracellular milieu, chiefly defines its physiopathologic actions, we investigated the effects of reduced (all-thiol) and oxidized (disulfide) HMGB1 on seizures and cell loss, and the related intracellular signaling in neurons.

**Method:** Seizures were induced by intrahippocampal (ih) kainic acid (KA) injection in C57BL6N adult male mice, and monitored and quantified by EEG analysis. NMDA-induced excitotoxicity was evaluated in hippocampal neuronal cultures by time-lapse single-cell Ca\(^{2+}\) imaging and lactate dehydrogenase release in the medium.

**Results:** Disulfide HMGB1 (5.5 \(\mu\)g ih, 10 min before KA) increased 2-fold the frequency and time spent in seizures whereas non-oxidizable HMGB1 (3S-HMGB1) was ineffective. Transient application of disulfide HMGB1, but not 3S-HMGB1, increased by 50–80% NMDA-induced neuronal Ca\(^{2+}\) influx and the subsequent cell death. These effects were prevented by BoxA, a competitive HMGB1 antagonist, and by LPS-RS, a specific TLR4 antagonist, and abrogated in \(\text{Tir}^4^-\) neurons. These pathologic effects were mediated by Sre-dependent phosphorylation of NR2B subunit which increases NMDA receptor Ca\(^{2+}\) permeability.

**Conclusion:** Our results suggest a contribution of uric acid to ictogenesis and its associated inflammatory response. Further uncovering its role and its mechanism of action may be of value to develop improved therapies for epilepsy in the future.

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**042 ALLOPURINOL REDUCES SEIZURE SEVERITY AND THE INFLAMMATORY RESPONSE IN A MOUSE MODEL FOR STATUS EPILEPTICUS: A POTENTIAL ROLE FOR URIC ACID IN ICTOGENESIS**

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**Purpose:** There is a growing body of experimental and clinical evidence pointing to an active role for brain inflammation in various forms of refractory epilepsy. In this regard, proconvulsant effects of pro-inflammatory danger molecules recently gained a lot of interest. The objective of this study was to investigate the involvement of the danger molecule uric acid in the generation of epileptic seizures and the associated inflammatory response.

**Method:** Mice were injected intraperitoneally with saline or allopurinol (100 mg/kg), an inhibitor of uric acid production. Subsequently, kainic acid or Ringer’s solution was infused intrahippocampally through a microdialysis probe. Dialysates were collected every 50 min to measure uric acid levels in the hippocampus and video-EEG monitoring was done to assess the severity of the kainic-acid-induced status epilepticus. Twenty-four hours after development of seizures, the ipsilateral hippocampi were isolated for RNA-quantification of relevant cytokines using RT-qPCR.

**Results:** Infusion of kainic acid in saline-injected animals increased the median hippocampal uric acid concentration by a 5.7-fold compared to the Ringer’s infused control group. Treatment with allopurinol prior to kainic acid-infusion significantly suppressed this uric acid increase and significantly reduced the total seizure severity score. Moreover, allopurinol treatment attenuated the kainic-acid induced upregulation of TNF mRNA-levels.

**Conclusion:** Our results suggest a contribution of uric acid to ictogenesis and its associated inflammatory response. Further uncovering its role and its mechanism of action may be of value to develop improved therapies for epilepsy in the future.
department before an intended change of medication. The applied Epitrack Plus assesses executive function and verbal memory. The overall drug load was quantified in two ways:

1. Number of concurrent antiepileptic drugs (AEDs) and
2. Total drug load according to the (WHO) daily defined dose (DDD).

Results: Despite the high intercorrelation between both drug load indices ($r = 0.74, p < 0.001$), the cognitive measures showed higher inverse correlations with the number of AEDs (executive function: $r = -0.35, p < 0.001$; memory: $r = -0.22, p < 0.001$) than with the DDD drug load (executive function: $r = -0.24, p < 0.001$; memory: $r = -0.17, p < 0.001$). Reanalysis applying partial correlations to control for differences in age at onset of epilepsy and monthly seizure frequency hardly changed the aforementioned results.

Conclusion: The findings thus demonstrate the adverse effect of an increasing drug load on cognition, especially on executive functions. In this context the more complex calculation of the drug load according to the WHO seems not to be expedient. Future studies with longitudinal designs focusing on the intraindividual changes of drug load and cognitive performance would be appreciated.

044

YKP3089 IN PARTIAL-ONSET SEIZURES: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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Purpose: YKP3089, a tetrazole alkyl carbamate derivative, is a new investigational antiepileptic drug (AED) with a potentially unique mechanism of action and a pharmacokinetic profile suited to once-daily dosing. This randomized, double-blind, placebo-controlled study assessed efficacy and tolerability in patients with refractory epilepsy.

Methods: Adults with partial-onset seizures ($\geq 3$ days in 8-week baseline despite 1–3 AEDs) were randomized to placebo or to adjunctive 200 mg YKP3089 which was titrated over 6 weeks (50 mg increments at 2-week intervals) and maintained for 6 weeks. Primary endpoint was median% seizure reduction from baseline. Secondary endpoints included % patients with $\geq 50\%$ seizure reduction (responder rate); % of study completers with no seizures in maintenance; median% seizure reduction by seizure type.

Results: Patient characteristics were similar at baseline (YKP3089, N = 113; placebo, N = 108). Median seizure reduction (YKP3089 vs. placebo): 56% vs. 22%, p < 0.0001. Responder rate: 50% vs. 22%, p < 0.0001. Seizure-free during maintenance phase: 28% vs. 9%. Significant difference favored YKP3089 over placebo across all partial-onset seizure types. Seizure reduction was observed during titration when patients were receiving 50–100 mg YKP3089. Most common adverse events were somnolence (22% vs. 12%), dizziness (21% vs. 17%), fatigue (11% vs. 6%), headache (11% vs. 11%), nystagmus (10% vs. 0), nausea (8% vs. 1%), tremor (6% vs. 2%), constipation (5% vs. 0), diarrhea (5% vs. 0), vomiting (5% vs. 2%).

Conclusion: YKP3089 was highly effective vs. placebo in reducing partial-onset seizures in patients with refractory epilepsy. No unexpected safety or tolerability issues were identified.

045

FROM EARLY ADD-ON LACOSAMIDE TO MONOTHERAPY CONVERSION: RESULTS OF REALLY STUDY

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Purpose: To evaluate over 1 year the efficacy and tolerability of lacosamide (LCM) in early add-on use and to assess conversion to monotherapy.

Method: REALLY was a multicenter (21 hospitals), retrospective, 1-year, real-life study. The inclusion criteria were:

1. Patients older than 16 years;
2. Diagnosis of partial-onset seizures;
3. Treatment with LCM initiated between September 2009 and January 2012, as add-on therapy on patients that had tried a maximum of 2 antiepileptic drugs (AEDs) prior to LCM.

Results: One hundred and ninety-nine patients were included, 44.7% of patients had tried 1 AED before LCM and 55.3% had tried 2 AEDs. At baseline, 128 patients (64.3%) were taking one concomitant AED and 71 patients (35.7%) were taking 2 concomitant AEDs. At 12 months, 22 patients (11.1%) were on LCM monotherapy, 134 patients (67%) were taking one concomitant AED and 43 patients (21.6%) were taking 2 concomitant AEDs. From the overall population, 44.9% were seizure-free and 76% were responders at 12 months. Side effects were reported by 31.2% of the patients (most common was dizziness) and 7% were severe enough to discontinue. From patients converted to monotherapy, 63.6% of patients had tried one AED before LCM and 36.4% had tried 2 AEDs. In the LCM monotherapy group seizure freedom at 12 months was achieved by 86.4% and 95.5% were responders. At least one adverse event over 1 year was experienced by 36.4% (most common was somnolence), but none of those patients required discontinuation. Patients in whom LCM was the first sodium channel blocker were more probable to be on LCM monotherapy at 12 months (17.5% vs. 4.1%).

Conclusion: LCM was effective and well tolerated on early add-on and conversion to monotherapy setting.
046 STEREOSELECTIVE ANTICONVULSANT AND PHARMACOKINETIC ANALYSIS OF VALNOCTAMIDE, A CNS-ACTIVE DERIVATIVE OF VALPROIC ACID WITH LOW TERATOGENIC POTENTIAL

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Purpose: Valnoctamide-(VCD), a CNS-active chiral constitutional isomer of valproamide, the corresponding amide of valproic acid (VPA), exhibits stereoselective pharmacokinetics-(PK) in animals and humans. The current study comparatively evaluated the pharmacodynamics (PD; anticonvulsant activity and teratogenicity) and PK of VCD four individual stereoisomers.

Methods: The anticonvulsant activity of VCD individual stereoisomers was evaluated in several rodent anticonvulsant models including: maximal electroshock, 6 Hz psychomotor, subcutaneous metrazol and the pilocarpine and soman-induced status epilepticus (SE). The PK-PD relationship of VCD stereoisomers was evaluated following ip administration (70 mg/kg) to rats.

Results: VCD had a stereoselective PK with (2S,3S)-VCD exhibiting the lowest clearance and consequently, a twice-higher plasma exposure than all other stereoisomers. Nerveless, there was less stereoselectivity in VCD anticonvulsant activity and each stereoisomer had similar ED50 values in most models. VCD stereoisomers (258 or 389 mg/kg) did not cause NTD. These doses are 3–12 times higher than VCD-anticonvulsant-ED50 values.

Conclusions: VCD displayed stereoselective PK that did not lead to significant stereoselective activity in various anticonvulsant rodent models. If VCD exerted its broad-spectrum anticonvulsant activity using a single mechanism of action (MOA) it is likely that it would exhibit a stereoselective PD. The fact that there was no significant difference between racemic-VCD and its individual stereoisomers, suggests that VCD’s anticonvulsant activity is due to multiple MOA.

047 LACOSAMIDE CONVERSION TO MONOTHERAPY: EFFECTS ON PARTIAL-ONSET SEIZURE FREQUENCY IN A HISTORICAL-CONTROLLED MULTICENTER, DOUBLE-BLIND, RANDOMIZED TRIAL

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Purpose: To evaluate the efficacy of conversion to lacosamide 400 mg/day monotherapy in patients with partial-onset seizures (POS).

Method: Patients on 1–2 antiepileptic drugs (AEDs) were randomized 3:1 to lacosamide 400:300 mg/day (8-week Baseline, 3-week Titration and 16-week Maintenance Phase [6-week background AED Withdrawal and 10-week Monotherapy Phase]). The primary efficacy variable was the percentage of patients on lacosamide 400 mg/day meeting predefined seizure-related exit criteria by Day 112.

Results: 425 patients (Safety Set; mean age 40.6 years, 48.5% male, median baseline seizure frequency 6.62/28 days) received lacosamide; 271 (63.8%) completed the Monotherapy Phase (201/319 on 400 mg/day and 70/106 on 300 mg/day). The Kaplan-Meier estimate of the percentage of patients on 400 and 300 mg/day meeting ≥50% reduction from Baseline in POS frequency/28 days during the Monotherapy Phase was observed in 41.7% patients on lacosamide 400 mg/day (n = 319) and 44.3% on 300 mg/day (n = 106). For patients who completed the Monotherapy Phase, ≥50% responder rates were 60.7% for lacosamide 400 mg/day (n = 201) and 62.9% for 300 mg/day (n = 70). The most common treatment-emergent adverse events in the 400 mg/day group were dizziness (26.0%), nausea (13.8%), headache (13.2%), convulsion (10.0%), and fatigue (10.0%).

Conclusion: Lacosamide conversion to monotherapy was effective in patients with POS. Supported by: UCB Pharma.

048 MONITORING ANTIPELLEPTIC DRUG CONCENTRATION WITH A DRIED BLOOD SPOT (DBS) TECHNIQUE: COMPARISON OF DBS AND ROUTINE CAPILLARY PLASMA LEVELS IN CHILDREN

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Purpose: To develop a method to facilitate monitoring of AED in children with complicated epilepsy DBS sampling at home by the parents and mailing the DBS may facilitate daily. We have developed a sensitive DBS method to be used at home for simultaneous monitoring of valproic acid (VPA), lamotrigine (LTG) and carbamazepine (CBZ).

Method: A LCMS/MS technique for simultaneous determination of VPA, LTG and CBZ in a single dried blood spot of 30 µl of capillary blood was developed. Children aged 3–18 years of age coming for clinical control of epilepsy and AED levels at the Neuropediatric Clinic, Karolinska University Hospital, Huddinge, Stockholm were enrolled in the study. Capillary DBS (30 µl) samples dried on filter paper (whatman-903 protein saver cards), hematocrit, and an ordinary 500 µikroL capillary sample were collected from each patient.

Results: The LCMS/MS method was fully validated according to guidelines from European Medicines Agency for VPA, LTG and CBZ for DBS samples. The method was linear in the range 0.25–40 µg/ml for CBZ and LTG and 5–300 µg/ml for VPA and well within expected concentration range from patients. We collected pairs of DBS and capillary plasma samples containing VPA (n = 30), LTG (n = 20) and CBZ (n = 30). Preliminary results show a good correlation between LTG, VPA and CBZ concentrations in DBS and in capillary samples.

Conclusion: We have developed a sensitive and reproducible LCMS/MS method for simultaneous assay of VPA, LTG and CBZ in a single 30 µl dried blood spot. Our technique allows development of home based DBS sampling to monitor AED levels of children.
Platform Session: Clinical Neurophysiology Tuesday, 1st July 2014

049 CORTICAL MODULARITY BREAKDOWN IN THE EPILEPTIC BRAIN
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Purpose: Sleep and deprivation of it are known methods to increase the yield of epileptic abnormalities. Whereas neurophysiological mechanisms underlying discharges increase were suggested, less is known of the topographical distribution patterns in wake and sleep. We compared interictal epileptic discharges (IEDs) scalp distribution using 256-channels EEG recordings in wake and sleep in people with pharmaco-resistant temporal lobe epilepsy (TLE).

Method: 14 adults with Right TLE, identified through clinical data, 3T-MRI, PET and electrical source imaging, recorded during a daytime-nap were included. IEDs were identified in wake and S2. A mean of 21 IEDs in wake and 39 in sleep were selected (p = 0.024) and processed to obtain the averaged spike. Digital signals from the averaged wake traces were then subtracted to the sleep ones (Geodesic- EGI, Oregon, USA) and a t-test between the two conditions run.

Results: Single subjects traces localized IEDs over the right temporal regions (rare zygomatic projection), topographically more circumscribed in sleep. EEG digital subtraction showed higher amplitude IEDs limited the temporal mesio-posterior right areas, with a dipole inversion over the contralateral zygomatic leads. Student t-test confirmed a statistically significant signal increase over the same topographic region, with a slight posterior shift on temporal leads (p = 0.039).

Conclusion: This is the first report of a progressive breaking up of cortical modularity during sleep, even S2 stage, in a pathologically hyperactive brain. A similar phenomenon has been previously described (Massimini et al. 2005) using TMS during sleep in healthy subjects. Our data exploit naturally occurring interfering stimuli (IEDs) in a sleeping epileptic brain, demonstrating how they reverberate differently in sleep and wake, with a sleep related amplitude increase. Interestingly, such phenomenon tends to be constrained to a cortical area partially overlapping with the waking one, as to point to the progressive disconnection of integrated areas.

050 HIGH DENSITY EEG IMPROVES DETECTION OF HIGH FREQUENCY OSCILLATIONS ON SCALP EEG
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Purpose: High frequency oscillations (HFO) above 80 Hz are recognized as markers of epileptogenicity in intracranial EEG. Recent publications suggest that HFO can be detected on scalp-EEG. Data from simultaneously recorded intracranial and scalp-EEG suggest that high-density EEG might improve HFO-detection on scalp-EEG. The current study investigates scalp HFOs with varying density of electrodes.

Methods: 17 patients with refractory epilepsy underwent one night of EEG with 128 electrodes prior to intracranial electrodes implantation (sampling rate: 2,000 Hz). Carefully rejecting segments with artefacts, HFOs were marked in 5 min of 80 Hz high-pass filtered sleep EEG first on a bipolar montage (21 contacts) and afterwards on a reference montage in 1–3 Regions of Interest (ROI) per patient, each consisting of 6–22 contacts. ROIs were selected choosing i. areas including contacts adjacent to HFO-showing contacts on bipolar montage ii. an area over the intra-cranially defined seizure onset zone (SOZ).

Results: 4 patients were excluded due to extended artefacts. 13 patients (561 contacts) were analyzed. 12 patients showed HFOs with an average rate of 0.77/min. In 9 patients, HFOs occurred ipsilateral, in 3 only contralateral to the SOZ. Highest HFO-rates were over the lobe of the SOZ in 7 patients within the ROI and in 1 patient on bipolar montage. Compared to bipolar montage, analysis of ROIs revealed additional HFOs in 7 patients.

Conclusion: Our study confirmed the visibility of HFOs on scalp-EEG. HFOs were often visible over the SOZ, but sometimes also occurred contra-laterally. Results suggest that increased density of electrodes improved HFO-identification and -localization.

051 WHAT IS THE ROLE OF THALAMO-CORTICAL SYNCHRONY IN SEIZURE TERMINATION?
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Purpose: The role of synchronized thalamo-cortical networks in focal seizures has not yet been thoroughly studied. Moreover the exact mechanism underlying seizure termination are still unclear. We studied thalamo-cortical connectivity and synchrony in mesial temporal seizures to analyze their role in seizure dynamics.

Method: Twenty-two seizures from ten patients with drug-resistant mesial temporal lobe epilepsy undergoing pre-surgical evaluation were analyzed using intracerebral recordings (stereoelectroencephalography, SEEG). We performed a statistical measure of SEEG signal interdependencies (non-linear correlation), to estimate functional connectivity between thalamus and cortical regions. In addition, an estimation of thalamic “outputs and inputs” connectivity was proposed.

Results: Thalamus was consistently involved in the last phase of all analyzed seizures and thalamo-cortical synchrony was significantly more elevated than background. The analysis of thalamo-cortical connectivity showed a positive correlation (p = 0.001) between synchrony and the degree of outputs from thalamus to cortex. Seven seizures out of twenty-two displayed a particular spike wave pattern (SWP) at the end. They were associated to higher values of global synchrony and outputs from thalamus. In this subgroup, an inverse relation (R = -0.81) between duration of seizure and levels of synchrony was observed.

Conclusion: All mesial temporal seizures analyzed showed a marked increase of thalamo-cortical synchrony at the end of seizure. Moreover, a stronger thalamic involvement and higher levels of synchrony associated with a specific electrical pattern (SWP) seem to play a role in modulating seizure termination.
052 SYNCHRONIZATION AND BRAIN CONNECTIVITY IN PATIENTS WITH FOCAL PERIODIC ACTIVITY IN SCALP EEG: ICTAL FEATURES
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Purpose: Periodic focal activity is usually observed in EEG recordings of patients suffering from acute illnesses and can be caused by different etiologies. Some authors consider previously called PLEDs as an indicator of non-convulsive status epilepticus but there is still no consensus about ictal features of this type of periodic activity. We show the differences in synchronization and connectivity in three groups of subjects: healthy subjects, patients with unequivocal ictal periodic activity and patients with non-ictal periodic activity. The purpose of our study is to provide a new method of EEG-analysis in order to detect qualitative features of ictal periodic activity.

Method: We included 9 healthy patients, 9 subjects with interictal periodic activity and 10 patients with ictal periodic activity considering specific inclusion and exclusion criteria. EEG recordings, selected from daily clinical practice in our hospital, were acquired with a 24-channel machine. In order to analyze synchrony, after establishing a Frequency Band of Interest, we used the synchronization likelihood and time-frequency based phase synchronization methods and then, analyzed the Clustering Index and Path Length parameters. We also described the phase-to-amplitude Cross Frequency Coupling patterns of the oscillatory activity in selected scalp channel involved in periodic activity.

Results: Mean values of synchronization in channels involved by periodic activity showed a significant difference between patients with ictal and non-ictal periodic activity. Significant differences in synchronization between all scalp channels in patients with ictal, non-ictal periodic activity and healthy subjects were also detected and Cross Frequency iterations were also different between ictal and non-ictal periodic activity.

Conclusion: Combining different methods of quantitative analysis of EEG recordings could be a new tool in determining the ictal condition of many periodic activities when clinical signs are equivocal in order to minimize the morbidity and mortality linked to undiagnosed non-convulsive status epilepticus.

053 AUDITORY-VERBAL REMINISCENCE EXPERIENCES SUGGESTING A FUNCTIONAL INTERACTION OF INSULAR-TEMPORAL NETWORKS: CORTICAL STIMULATION DATA IN EPILEPTIC PATIENTS
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Purpose: The epileptic “déjà vu” semiology is characterized by impression of familiarity and multimodal experiential phenomena. The underlying mechanism could involve a functional coupling between rhinal cortex (RC) and hippocampus. Auditory verbal hallucinations (AVHs) are a subjective experience of “hearing voices” in the absence of external stimulations. To our knowledge, the epileptic reminiscences with purely verbal content have been rarely reported.

Method: We analysed the clinical features and anatomic-functional correlates of the reminiscence phenomena evoked by direct electrical stimulations of mesial temporal, lateral temporal or insular structures of a dominant hemisphere in patients undergoing stereoelectroencephalographic (SEEG) recordings in the setting of pre-surgical assessment for drug-resistant epilepsy. Among the 85 SEEG recordings performed in our centre between 2004 and 2013 we selected 32 patients who had left hemispheric implantations that sampled RC, hippocampus, temporal-lateral neocortex and the insula. A total of 21 reminiscence responses were analysed.

Results: 15 stimulations in two patients induced pure auditory-verbal reminiscences (AVR). 6 stimulations in two other patients evoked “classical” déjà vus. All AVR were characterised by non lateralized brief ‘hearing’ of human voices, often with emotional connotation and with a familiarity aspect. Some had also musical component. These phenomena were recognized by patients as parts of their habitual seizures. 7 AVR were induced by stimulation of the inferior insula, 5 – of the superior temporal gyrus (STG) and 3 – of RC. Electrically, the after-discharges, when present after insular or STG stimulations, showed reciprocal involvement of the insula, STG, RC and hippocampus. All RC responses, corresponding either to AVR or to classical déjà vus, correlated with after-discharges strictly limited to RC and hippocampus.

Conclusion: Our data suggest that auditory-verbal reminiscence experiences could depend upon reciprocal functional interaction between the insula, superior temporal gyrus and rhinal cortex as substrates of both memory and auditory processing networks.

054 ICTAL OFFSET PATTERNS AND POST-ICTAL DYNAMICS IN FOCAL EPILEPSIES-A SEEG STUDY
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Purpose: Understanding the mechanism(s) of seizure cessation could create the premises for novel therapeutic breakthroughs (Losher & Kohling 2010). Our study aims at comparing ictal offset and postictal recovery patterns in the seizure onset zones (SOZ) vs. non-SOZ areas.

Method: We selected 15 patients with drug resistant focal epilepsy explored by means of SEEG as part of presurgical work-up. We captured the ictal and postictal activity of 62 seizures. 140 contacts were classified as belonging to SOZ while the others 760 to non-SOZ areas. We analyzed the EEG activity patterns evidenced by plotting time-frequency maps using Matlab (Natick, MA, USA). Degrees of activation, hierarchy and pattern of ictal ending and time to return to base-line rhythms were particularly assessed.

Results: In respect to increase in ictal spectral power compared to pre-ictal baseline, 65% of SOZ contacts had an increase in activation, 30% no increase in power, while 5% exhibited a decrease.

The contacts belonging to SOZ had a strong tendency to exit ictal activity fast (70% in the first third of the whole group) and regained postictal activity slow after flatline (52% in the last third). Variability in the same patient during different seizures was observed.

The ictal offset patterns as well as the postictal return to baseline were mostly determined by the degree of activation at the seizure peak.
Channels displaying higher values evolved with one or multiple sharp transitions. Usually these channels exhibited an ictal ending pattern of burst suppression, or delta brush evolving to flatline or in hyper-slow rhythms. Those with low values evolved with poorly defined transitions directly to the preictal rhythms.

**Conclusion:** Ictal offset patterns are mostly related to the degree of maximum activation at the seizure peak. However areas activated at seizure’s onset do not seem to display a specific ictal ending pattern.

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**Platform Session: Epilepsy and Cognition Tuesday, 1st July 2014**

**055**

**PREOPERATIVE COGNITIVE FUNCTIONS IN PATIENTS WITH LOW-GRADE BRAIN TUMORS WITHIN THE TEMPORAL LOBE**

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**Purpose:** To evaluate the preoperative cognitive profiles of 231 patients with different low-grade brain tumors located in the temporal lobe.

**Method:** The study comprised all patients with refractory temporal lobe epilepsy and low-grade brain tumors (45 grade-I dysembryoplastic neuroepithelial tumors (DNET); 130 grade-I gangliogliomas; 32 grade-I pilocytic astrocytomas (PA), and 24 grade-II astrocytomas) who had undergone epilepsy surgery in the tertiary epilepsy center in Bonn/Germany between 1988 and 2012. Tumor diagnoses were based on histopathological findings. All patients had been evaluated regarding memory, executive and visuo-constructional functions and vocabulary IQ.

**Results:** 61% of all patients had impaired (x < m – 1.5 SD) memory functions (DNET: 44%, ganglioglioma: 46%, grade-I PA: 83%, grade-II astrocytoma: 39%) while executive functions were impaired in 42% (DNET: 35%, ganglioglioma: 38%, grade-I PA: 61%, grade-II astrocytoma: 50%). A minority had impaired visuo-constructional functions (6%) or IQ < 85 (3%). Individual (p = 0.002) and group level (p = 0.02) analyses revealed a significant effect of tumor histology only concerning memory functions due to significantly worse performance of patients with grade-I PA as compared to all other groups (p < 0.01).

**Conclusion:** Memory and executive functions are frequently impaired in patients with low grade temporal lobe tumors. Patients with PA displayed exceptionally poor memory although these tumors behave particularly in patients with low grade temporal lobe tumors. Patients with PA displayed significantly worse performance of patients with PA compared both with HV and CCG. Fear ER deficit was found in 32 out of 36 studies. In 17 studies ER impairment was extended to other emotions with negative value (anger, disgust, sadness); none for happiness. The deficit was independent by the sensory modality tested (visual or auditory). Bilateral and right side MTLE patients seem to have worst performance in ER tasks. Early onset and long duration of epilepsy correlated with impairment in ER performance.

**Conclusion:** ER deficits in MTLE patients are related to specific syndrome features and have some effects on social behaviour. Limits of this review regards the different methodology used in the different studies. Prospective longitudinal studies that evaluate the same TLE patients before and after ATL are needed to improve our knowledge.

**057**

**PARENTAL EDUCATION PREDICTS INTELLIGENCE AFTER EPILEPSY SURGERY IN CHILDREN**


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**Purpose:** To know whether environmental factors – parental education (PE) and socioeconomic status (SES) – are associated with change of children’s intelligence quotient (IQ) after epilepsy surgery.

**Method:** Retrospective cohort study in 118 children (median age at surgery 9.73 years [range 0.47–17.70 years]) who underwent epilepsy surgery between January 1996 and September 2010. Multiple regression analysis was used to identify illness- and environmental predictors of change in IQ after surgery. To enhance interpretation of the results, we applied the same analysis to pre-surgical and post-surgical IQ.

**Results:** Only a model including PE significantly predicted IQ change after surgery (F1,117 = 3.25, p = 0.04, adjusted R² = 0.04). The average difference between lowest and highest levels of PE amounted to 12.18 IQ points (95% CI: 1.20–23.16). Inclusion of SES also significantly associated with IQ change after surgery in the model already containing PE yielded no further contribution to the prediction. A model including PE and socioeconomic status (SES) were included as predictors, confirming the results concerning IQ change.

**Conclusion:** This is the first study that demonstrates effect of environmental variables on IQ change after pediatric epilepsy surgery: IQ increased most in children with highest educated parents or parents with highest socioeconomic status. Children with low PE or SES had smaller IQ increases or even decreases. Further study must disentangle the source (s) of this association.
058
SUDEP DISCLOSURE IN YOUNG ADULTS WITH
EPILEPSY: PATIENTS’ REACTION, PERCEPTION OF
RISK, VIEWS ON TIMING AND BEHAVIOURAL
CHANGE
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Purpose: Sudden Unexpected Death in Epilepsy (SUDEP) occurs in 1 in
every 1,000 persons with epilepsy with peak incidence in young adults.
This study aimed to explore the effects of SUDEP disclosure.

Method: Consecutive adults aged 16–30 years, previously informed
about SUDEP with a Hospital Anxiety and Depression Scale (HADS)
score <11, were invited to participate. Semi structured interviews were
carried out in patients’ homes, recorded, transcribed, and analysed on
Nvivo. The study had full ethical approval.

Results: 27 subjects (15 female) mean age 24, (range 18–29 years) were
enrolled. 12 (44%), reported initial feelings of fear and anxiety after dis-
closure. In the majority this appeared to settle with no long-term distress.
Three expressed anger at not being told at time of diagnosis. 14 (52%),
thought their risk of SUDEP was low, the rest were unsure of their risk.
Of 8 with repeated nocturnal GTCS, 2 believed their risk was low, 5 did
not know, and one believed SUDEP occurred due to alcohol.
22 (81%) thought disclosure important. 17/22 (77%) highlighted the
importance of clinician judgment and family involvement on timing, especially when patients were anxious, depressed or had learning diffi-
culties. 14/22 (64%) thought it should not be done immediately at diagno-
sis, but soon after. 4/22 (18%) personally favoured disclosure at
diagnosis, but did not think this was best for the general epilepsy popula-
tion. 4/22 (18%) thought at diagnosis was best.
Only 9 (33%) thought SUDEP was preventable, 2 did not answer, 1
equivocated.
7 (26%) said their adherence improved after being told about SUDEP.
16 (59%) said it made no different to their behaviour, 3 (11%) altered their
lifestyle in other ways.

Conclusion: Anxiety provoked by disclosure is short lived in most
patients. Most of our patients did not think SUDEP preventable, which
may explain why so few improved their compliance after disclosure.

059
THEORY OF MIND AFTER TEMPORAL LOBE
EPILEPSY SURGERY
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Purpose: Temporal lobe epilepsy (TLE) surgery bears the risk of loosing
memory and language, which may counteract the benefits of seizure con-
trol. Another fearful postoperative complication might be a loss of theory of
mind (ToM) abilities, which are linked to the medial temporal lobe,
superior temporal sulcus, temporoparietal junction, and prefrontal
regions. This study evaluated the postoperative outcome of ToM with the
goal of characterizing its postoperative trend and combination with other
cognitive changes.

Method: Forty patients with medial TLE were evaluated before and
6 months and a year after surgery. Anterior temporal lobe resection were
carried out depending on the extension of the epileptic zone and function-
ally eloquent areas, involving the anterior lateral and medial temporal lobe
encompassing the uncus, amygdala, and part of the hippocampus. The fault
pass recognition test assessed the understanding of epistemic and emotional
mental states. The Tower of London, Short Story, and Boston Naming tests
evaluated executive, memory, and language abilities.

Results: Before surgery patients were impaired in ToM compared with
healthy controls. Repeated analysis of variance, comparing the preopera-
tive and postoperative test scores obtained 6 months and a year after sur-
gery, revealed no significant ToM changes. By contrast, executive,
memory, and language abilities showed different trends relating to the
side of surgery.

Conclusion: These results highlight two main aspects. First, advanced
ToM abilities are not modified by TLE surgery. Medial TLE may impair
ToM not only as a consequence of medial temporal lobe damage but also
due to secondary lesions in the medial and orbital prefrontal regions
which may cause persisting deleterious effects. Second, ToM’s outcome
is dissociated from other cognitive changes, supporting a clear-cut dis-
tinction of these cognitive domains.

060
INTERICTAL EPILEPTIC ACTIVITY INTERFERES
WITH FRONTAL LOBE FUNCTION IN TEMPORAL
LOBE EPILEPSY
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Purpose: Neuropsychological deficits in temporal lobe epilepsy with
hippocampal sclerosis (HS) regularly affect frontal lobe function. The
origins of extra temporal cognitive deficits are multifaceted and include
altered structural connectivity, medication, seizure propagation and
ongoing epileptic discharge. Our study intended to single out the role
of interictal epileptic activity in executive dysfunction.

Method: During presurgical evaluation, 34 patients with unilateral HS
(17 right, 17 left) underwent high resolution MR-imaging, video EEG
and detailed neuropsychological testing. The latter comprised IQ and a
large battery of frontal lobe function tests, such as verbal and non verbal
fluency, Brixton test of spatial anticipation, Wisconsin card sorting and
Stroop test. Hippocampi were segmented via freesurfer. Surface video-
EEG samples during day time and sleep were clinically analyzed for
quantity and scalp distribution of summed spikes and sharp waves (SW).
Only SW ipsilateral to the lesion were sufficiently abundant to calculate
correlations. Their impact on cognitive scores was assessed with partial
correlations, thus correcting for age, age of onset, disease duration and
hippocampal volume.

Results: We found a clear correlation between the number of SW and a
large range of executive functions, notably in patients with left HS. Tem-
poral and temporofrontal SW were correlated with semantic and phonetic
verbal fluency, graphical fluency and Brixton test in patients with left
HS, and with semantic fluency and Wisconsin test in patients with right
HS. In patients with left HS, semantic verbal fluency was well correlated
with SW over the Broca region, whereas in patients with right HS, posterior
temporal SW had greater impact.

Conclusion: Temporal and temporofrontal interictal activity is corre-
lated with diminished performance in a large range of executive func-
tions. We suggest that epileptic discharge has a genuine impact on
cognitive functions beyond the temporal lobe, most likely via alterations
of frontotemporal interplay.

Abstracts

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061
THE USE OF 3D MULTIMODALITY IMAGING IN THE PRESURGICAL EVALUATION OF EPILEPSY
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Purpose: We aim to validate the principle of 3D multimodality imaging in the presurgical evaluation and surgical treatment of epilepsy.

Method: We present a single centre prospective study, describing the use of multimodal 3D neuroimaging in patients undergoing intracranial EEG implantation to plan epilepsy surgery. Implantation planning is divided into designing the overall strategy of implantation and then the precise details of implantation. The multidisciplinary team made decisions on strategy and planning before the disclosure of multimodal models. Any changes in decision making were recorded following disclosure of the multimodal models.

Results: 28 patients had the implantation strategy recorded. Disclosure of 3D neuroimaging led to a change in strategy in 12/28 cases. Changes included addition and subtraction of electrodes, addition of grids, and going directly to resection.

30 patients had surgical planning recorded. 3D neuroimaging led to a change in the strategy in 22/30 cases. 14/14 patients undergoing stereoEEG underwent a change in their planning, with 83/119 electrode trajectories being altered.

Conclusion: 3D multimodality imaging is an important tool in the optimal planning of intracranial EEG electrodes.

062
SEIZURE OUTCOME AFTER RESECTIVE EPILEPSY SURGERY IN INFANCY AND EARLY CHILDHOOD
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Purpose: To describe 2-year and long-term outcomes after resective epilepsy surgery in children operated before the age of 4 years in Sweden 1995–2010.

Method: Data on all patients in Sweden undergoing epilepsy surgery are reported to the Swedish National Epilepsy Surgery Register since 1990 and completely prospectively since 1995. For this study, data on all children undergoing resective epilepsy surgery before the age of 4 years were analysed. Variables studied were: seizure frequency, anti-epileptic drug treatment, neurological deficits, type of surgical procedure, histopathological diagnosis and perioperative complications.

Results: Forty-seven children under 4 years of age underwent resective epilepsy surgery in Sweden 1995–2010. Before surgery they had up to 3,000 seizures per month and used 0–4 anti-epileptic drugs. Thirty had some kind of neurological deficit, including developmental delay. The most common procedures were temporal lobe resection (TLR), frontal lobe resection and hemispherectomy. A majority had malformations of cortical development. Two perioperative complications were registered. At the 2-year follow-up, 21/47 children (45%) were seizure free, 8 of whom were off medication. At the long-term follow-up, 16/32 (50%) were seizure-free, 11 of whom were off medication. Fourteen children were seizure-free at the long-term follow-up and had been so since surgery. TLR and low-grade tumour aetiology were associated with the best seizure outcomes.

Conclusion: A favourable seizure outcome is achievable in a majority of infants and young children undergoing resective epilepsy surgery and the improvement is consistent over time. The findings emphasize the importance and gains of early referral of infants and young children with intractable epilepsy for epilepsy surgery evaluation.

063
TEMPORAL PLUS SEIZURES ARE THE MAIN PROGNOSTIC FACTOR FOR UNFAVOURABLE SURGICAL OUTCOME IN PATIENTS WITH TEMPORAL LOBE EPILEPSY
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Purpose: To retrospectively analyse 190 drug-resistant patients who had undergone temporal lobectomy and identify the variables possibly influencing surgical outcome. Attention was focused on whether temporal plus seizures were associated to worse outcome compared to temporal seizures.

Method: We collected 190 patients from the database of two French Epilepsy Surgery Centres (Grenoble and Lyon) according to the following inclusion criteria: (i) absence of any detectable lesion on MRI, with the exception of hippocampal sclerosis; (ii) Stereoelectroencephalography (SEEG) recordings showing that seizures involved at least mesial and/or lateral temporal lobe (TL) structures or if SEEG was not available, scalp Video-EEG showing that at least the temporal lobe was involved by seizures; (iii) surgery performed according to the results of presurgical evaluation, either invasive or noninvasive, taking into account anatomical constraints and (iv) at least 12 months of post-operative follow-up.

Results: In univariate model, poor seizure outcome was correlated with significant past medical history (i.e neonatal anoxia, traumatic brain injury or central nervous system infection, p = 0.006), occurrence of secondary generalised tonic-clonic seizures (p = 0.005), and diagnosis of “temporal plus” seizures (p < 0.001). Multivariate analyses showed that the only two statistically significant variables predictive of poor outcome were a past medical history (p = 0.046) and the type of seizures, namely “temporal plus” seizures (p < 0.001).

Conclusion: In this study we confirm that risk of surgery failure is greater in patients with “temporal plus” seizures than in those with “pure” temporal seizures. Identifying those of temporal lobe epilepsy cases that
are in fact suffering from temporal plus seizures might help to select candidates to invasive recordings before surgery, and to plan surgical strategies, thus influencing post-operative prognosis.

**064 TIMING OF EARLY AND LATE SEIZURE RECURRENCE AFTER TEMPORAL LOBE EPILEPSY SURGERY**

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**Purpose:** Seizure recurrence after epilepsy surgery has been classified as either early or late depending on the recurrence time after operation. However, time of recurrence is variable and has been arbitrarily defined in the literature. We established a mathematical model for discriminating patients with early or late seizure recurrence, and examined differences between these two groups.

**Method:** A historical cohort of 247 consecutive patients treated surgically for temporal lobe epilepsy was identified. In patients who recurred, post-operative time until seizure recurrence was examined using an ROC curve to determine the best cutoff for predicting long-term prognosis, dividing patients in those with early and those with late seizure recurrence. We then compared the groups in terms of a number of clinical, electrophysiological and radiological variables.

**Results:** Seizures recurred in 107 (48.9%) patients. The ROC curve demonstrated that 6 months was the ideal time for predicting long-term outcome with best accuracy, (AUC=0.761; sensitivity=78.8%; specificity=72.1%). We observed that patients with seizure recurrence during first 6 months started started having seizures at younger age (OR=6.03; 95%CI=1.06–11.01; p = 0.018), had a worse outcome (OR=6.85; 95%CI=2.54–18.52; p = 0.001), needed a higher number of antiepileptic medications (OR=2.07; 95%CI=1.16–9.34; p = 0.013) and more frequently had repeat surgery (OR=9.59; 95%CI=1.18–77.88; p = 0.021). Patients with late relapse more frequently had seizures associated with trigger events (OR=9.61; 95%CI=3.52–26.31; p < 0.001).

**Conclusion:** Patients with early or late recurrence of seizures have different characteristics that might reflect diversity in the epileptogenic zone and epileptogenicity itself. These disparities might help explain variable patterns of seizures recurrence after epilepsy surgery.

**065 EPILEPSY SURGERY IN CHILDREN WITH BENIGN GLIO-NEURAL TUMORS**

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**Purpose:** A consecutive pediatric series of patients with benign glio-neural tumors and refractory epilepsy was retrospectively reviewed to assess the impact of different preoperative and intraoperative variables on outcome.

**Method:** 64 children (median age 7.5 years; range 1–17) underwent surgery; ganglioglioma – in 49 cases, DNET – in 15 cases. In 44 patients tumors were localized in temporal lobe (TL), in remaining 20 patients with extratemporal lesions tumors were localized in: frontal lobe – 8 cases, parietal lobe – 4 cases, occipital lobe – 6 cases and limbic lobe – 2 cases. Median seizure duration before surgery was 2.7 years (range 1 month–17 years). Preoperative evaluation included assessment of clinical history, seizure semiology, video-EEG and MRI. Electroencephalography (EEG) was used preoperatively in 17 patients. Different variables were distinguished and assessed probably to affect the outcome: e.g., seizure duration before surgery, lesion localization, presence of focal cortical dysplasia (FCD) in areas adjacent to excised tumor, inclusion to resect mesial structures within the TL-patients cohort and the usage of ECOG.

**Results:** There was no mortality and the overall morbidity accounted 25% (mild and transient neurological deficit – 5 cases, persistent new deficit – 9 cases, wound infection – 1 case, epidural clot – 1 patient). In 33 cases a type IIIB FCD was detected in brain tissue specimens from areas adjacent to removed tumors. Follow-up is known in 48 patients and ranges from 1 month to 4.5 years (median 1 year). Thirty nine patients are free of seizures (81%), AE-medication was stopped or tapered in 25 of them. No one of variables listed above have impacted significantly the outcome.

**Conclusion:** Surgery is an effective treatment option in children with developmental tumors associated with intractable epilepsy. Lesion gross total resection may render seizure-free more than 80% of patients with acceptable morbidity.

**066 RESECTIVE REOPERATIONS IN SWEDEN 1990–2010 – A NATIONAL PROSPECTIVE OBSERVATIONAL STUDY**

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**Purpose:** To analyse characteristics and results of reoperations following failure of epilepsy surgery in Sweden 1990–2010.

**Method:** Data from the Swedish National Epilepsy Surgery Register were analysed regarding resective epilepsy surgery 1990–2010 and reoperations. Patients who had a 2-year follow up were included and variables analysed were: reoperation or not, location of surgery, histopathology and seizure outcome.

**Results:** During this period 1,055 patients had a resective procedure and 190 of these were reoperations (18%). 890 patients had one resective procedure and of these 57% became seizure-free. Another 17% had ≥75% reduction of seizure frequency compared to preoperative mean. Of the 190 patients who were reoperated 36% became seizure free, and another 15% had ≥75% seizure reduction. 582 patients underwent temporal lobe surgery, 63% became seizure free, and another 17% had ≥75% reduction of seizure frequency. Of the 108 patients reoperated for temporal lobe epilepsy 33% became seizure free and another 19% had ≥75% seizure reduction. 189 patients were operated for neurodevelopmental tumors or cavernous hemangioma and of the 152 who had one resective procedure 84% became seizure free, and another 8% had ≥75% seizure reduction. Of the 37% reoperated for these etiologies 46% became seizure free, and another 16% had a ≥75% reduction of seizure frequency.

**Conclusion:** In this prospective population based study a substantial proportion of the patients who underwent a second resection after having failed surgery for epilepsy had a worthwhile seizure outcome. The reasons for the moderate success rate of reoperation for lesions such as neurodevelopmental tumors and cavernous hemangioma could not be disclosed in this register study but possible explanations might be failure to determine the seizure onset zone irrespective of a visible lesion or vicinity to eloquent cortex.
Platform Session: Epileptic Encephalopathies
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067
THE EMERGING PHENOTYPE OF SCN8A ENCEPHALOPATHY
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Purpose: SCN8A encodes a voltage-gated sodium channel (Na,1.6) that is an important regulator of action potentials in the brain. SCN8A mutations have recently been associated with epilepsy and neurodevelopmental disorders. The aim of this study was to delineate the phenotype associated with mutations in SCN8A.

Method: We used high-throughput sequence analysis of the SCN8A gene in 61 patients with various epileptic encephalopathies (EE). In addition, we ascertained cases with SCN8A mutations from other centers. A detailed clinical history was obtained together with a review of EEG and imaging data.

Results: We identified three de novo heterozygous SCN8A mutations from the initial cohort (n = 61) and collected 14 additional cases. Seizure onset occurred at a mean age of 5 months (range: 1 day–18 months) and in general, were not fever related. 14/17 patients had multiple seizure types including tonic, clonic, myoclonic seizures, epileptic spasms and absences; seizures were refractory to antiepileptic therapy. Development was most often normal but slowed following seizure onset, often with regression. All patients developed intellectual disability, ranging from mild to severe. Motor manifestations were prominent including hypotonia, dystonia, hyperreflexia and ataxia. Following seizure onset electroencephalography (EEG) was abnormal in 15/17 patients, showing moderate to severe background slowing and or focal or multifocal sharp waves or spikes.

Conclusion: Based on the results from this study, SCN8A mutations seem to be contributing to EE and should be considered in the diagnostic workup of patients with infantile EE of an unknown etiology.

068
LONG TERM CLINICAL AND COGNITIVE OUTCOME IN SUBJECTS WITH PCDH19 MUTATION
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Purpose: The role of study is to report the long term clinical and cognitive outcome in 13 females with PCDH19 mutation, and to compare it to the evolution in a Dravet syndrome group.

Method: In this retrospective study we studied 13 females, aging 3–27 years (mean 12 years 6 months), affected by mutations in PCDH19 using longitudinally assessed and detailed clinical, EEG, cognitive and behavioural evaluation. The results were compared to that obtained from a group of 32 subject (16 M, 16 F) affected by Dravet syndrome. All subjects underwent at list three cognitive assessment with neurodevelopmental scales and behavioural observation.

Results: Epilepsy started at mean age of 10.5 months in all PCDH19 subjects, and at mean age of 6.3 months in Dravet subjects; the outcome of seizure was poor in 30/32 DS, while in PCDH19 subjects 6/13 are seizure-free since at least 1 year and one present only occasional seizure.

At the first evaluation (before 18 months of age) in PCDH19 subjects the mean dGQ was 82.5 points (range 32.5–98), while in Dravet group was 103.4 (range 74–119).

Data at follow-up showed a worse development in DS subjects, while in PCDH19 subjects the decline was significantly less severe (at last follow-up for PCDH19 subjects dGQ 67; DS subjects dGQ 49).

Cognitive data showed a different trend between groups: statistical analysis revealed significant effect for Time for all subject (p < 0.001) and for Time*Group between subjects (p < 0.002).

Moreover repeated observation showed a greater significant incidence of psychiatric subjects with PCDH19 disease and behavioural disorders than in DS group.

Conclusion: The outcome of epilepsy in our series of subjects with PCDH19 mutation seems to be better respect to Dravet Syndrome, furthermore the cognitive development showed a different trend, with significantly less severe decline.

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069 AEDS EFFICACY IN THE DRAVET SYNDROME: A CROSS-SECTIONAL STUDY
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Purpose: Dravet syndrome (DS) is a rare epilepsy with seizures’ onset during the first year of life. SCN1A gene abnormalities are detected in about 80% of patients. We aimed to evaluate the efficacy of AEDs in a large series of this pharmacoresistant epilepsy.

Method: This is a cross-sectional study on all our patients with DS and SCN1A mutations who had a visit within 2010–2013. We included 54 patients (32 M and 22 F), aged from 2 to 23 years. We reviewed the characteristics of seizures (age of onset, type, duration, frequency and day/night prevalence) in relation to the AEDs used and patient’s age.

Results: Only 5 patients (9%) were seizure free for more than 1 year. Seizures were mainly febrile seizures. In the oldest patients (>10y) compared to youngers (6–10y), seizures were more often tonic-clonic (86% vs. 36% in each group respectively), shorter (<1 min in 55% vs. 1–5 min in 64%), sleep-related (55% vs. 36%), and rather more frequent (weekly in 55% vs. monthly in 71%).

Fourty patients (74%) received a tritherapy (VPA, STP, CLB), associated with another AED in 30 (74%) of them (TPM, LEV, ZNG, CZP, ketogenic diet, bromide, canabidiol).

Convulsive status epilepticus (SE) disappeared in 48% of patients after the introduction of STP. However, 5 children (9%) still experienced SE after 6 years and one after 11 years, mainly in the context of fever.

Conclusion: Despite the decrease of status epilepticus and long lasting seizures with tritherapy (VPA, STP, CLB), <10% of patients are seizure free and half remain with weekly seizures up to adulthood. These preliminary data suggest that there is still a need for developing and evaluating new AEDs in DS.

070 GENETIC ANALYSIS IN INFANTILE EPILEPTIC ENCEPHALOPATHIES WITH MOVEMENT DISORDER: A SINGLE CENTER STUDY
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Purpose: Recent studies elucidated the role of genetic mutations responsible for infantile epileptic encephalopathies (IEE). The identification of causative mutations associated with IEE and their related phenotypes is useful for establishing diagnostic approach to IEE. This study aimed to investigate the underlying genetic causes for the patients with IEE with involuntary movements and/or hand stereotypies.

Method: Eight patients with IEE with involuntary movements and/or hand stereotypies (Six patients with infantile spasms and two patients with unclassified epileptic encephalopathy) were tested. All patients showed severe developmental delay, cognitive impairments, and involuntary movements such as chorea, ballismus or athetosis, and/or hand stereotypes. Whole exome sequencing was performed in seven patients, and one patient with a SCN2A mutation was examined by high resolution melting analysis.

Results: In six patients with infantile spasms, mutations in CDKL5, SCN2A, CHD2 and TBL1XR1 were identified. In unclassified epileptic encephalopathy patients, mutations of SCN1A and GRIN1 were identified. Five of six mutations were proved to occur de novo. No mutations in known causative gene were found in the remaining two patients.

Conclusion: We could detect presumably pathogenic mutations in six out of eight patients. The underlying causes of IEE patients with involuntary movements and/or hand stereotypes are heterogeneous. More precise evaluations for genotype-phenotype study would be necessary to establish the proper diagnostic approach to IEE.
Conclusion: This meta-analysis suggests superior effectiveness of steroids and surgery in appropriate candidates in ESES syndrome. However, most studies were small and retrospective and heterogeneity allowed analysis of only qualitative EEG or neurodevelopmental outcome data. RESCUE ESES is the first randomized controlled trial in children with ESES comparing treatment with clobazam to treatment with corticosteroids at 20 European centers. Primary outcome is cognition, while EEG effect, seizure frequency, safety and possible predictors are included as secondary outcome measures.

072 DIFFUSION TENSOR IMAGING IN ROLANDIC EPILEPSY
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Purpose: Rolandic epilepsy (RE) is a common childhood epilepsy that is characterised by orofacial seizures with speech arrest. Children with rolandic epilepsy are at high risk of a variety of behavioural and cognitive deficits including attention and reading impairments (Smith AB et al. Epilepsia 2012;53:705–11). The objective of this study was to compare structural connectivity in adolescents with RE with that of healthy controls using diffusion tensor imaging (DTI).

Method: 32 uniformly distributed diffusion-weighted volumes (b = 1,300 s/mm²) were acquired from 24 participants with RE (median 11 years; interquartile range 2 years) and 21 healthy controls (13:1) in addition to 4 non-weighted (b0) volumes. Each volume was acquired with isotropic (2.4 x 2.4 x 2.4 mm) voxels. Further processing was performed using FDT (FMRIb’s Diffusion Toolbox) as implement in FSL (Jenkinson M et al. NeuroImage 2012;62:782–90). Fractional anisotropy (FA) and mean diffusivity (MD) was compared between RE and control groups within a mean white matter skeleton generated by Tract Based Spatial Statistics (TBSS; Smith SM et al. NeuroImage 2006;31:1487–1505), by permutation testing (n = 5,000) with an age covariate. Participants also completed a battery of neuropsychological instruments.

Results: The RE group had lower scores than controls for word reading, word reading efficiency, and coordination (p ≤ 0.05 uncorrected). Diffuse, bilateral decreases in FA were observed for the RE group, in particular in the corpus callosum (p ≤ 0.05 uncorrected). There were no significant differences in MD between the two groups. There were positive correlations between FA and word reading scores and FA and sentence comprehension scores (p ≤ 0.05 uncorrected).

Conclusion: Our findings suggest diffuse and in particular interhemispheric reductions in structural connectivity in RE; we shall seek replication in a larger cohort. FA and MD should be quantified within individual white matter tracts to facilitate the investigation of specific impairments.

073 DOSE-DEPENDENT TERATOGENICITY OF VALPROATE IN MONO- AND COMBINATION THERAPY
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Purpose: To study the risk of major congenital malformations (MCM) in association with maternal use of valproate (VPA) in monotherapy or adjunctive therapy and to analyze dose-dependency.

Method: We used data from EURAP, a registry enrolling antiepileptic drug (AED) treated women in early pregnancy, where the primary outcome is presence of MCM at 1 year after birth. Exposure was defined as type and dose of AEDs at time of conception. The present analysis focused on outcomes in pregnancies with exposure to VPA by different dose categories at conception. A comparison was made between three exposure types: (i) VPA monotherapy (n = 1,224); (ii) VPA combined with lamotrigine (LTG) (n = 159); (iii) VPA combined with any other AED than LTG (n = 205).

Results: The rate of MCM at 1 year after birth was 10.0% in VPA monotherapy, 11.3% among those exposed to VPA and LTG, and 11.7% in the group exposed to VPA+ other (non-LTG) AEDs. Regardless of treatment group, the MCM rate increased with dose of VPA, being highest at doses >1,500 mg/day. In group 1, the mean VPA dose was 991 ± 491 mg/d in pregnancies resulting in MCMs vs. 794 ± 359 mg/day among those without MCMs. The corresponding figures were 1,216 ± 656 vs. 817 ± 477 mg/day in group 2, and 1,275 ± 106 vs. 988 ± 462 mg/day in group 3.

Conclusion: The risk of MCM associated with VPA treatment increases with increasing VPA dose both in the presence and in the absence of concomitant use of other AEDs.

074 FRACTURES IN PEOPLE WITH A DIAGNOSIS OF EPILEPSY: A POPULATION BASED STUDY
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Purpose: Bone fractures can have important health implications and a number of factors may contribute to an increase risk of fractures in people with epilepsy. We performed a large retrospective study to compare the incidence of fractures in people with and without epilepsy and to investigate the risk by age group and socioeconomic status.

Method: We analysed linked electronic primary care and emergency department health care records in Wales, UK between 2005 and 2012.
using the secure anonymised information linkage (SAIL) database. We identified people who had attended a hospital emergency department with a primary diagnosis of a bone fracture; recording their age, gender, socioeconomic status (as measured by an index of multiple deprivation) and if they had epilepsy (defined as a recorded diagnosis of epilepsy and co-prescription of an anti-epileptic drug). We used Poisson regression analysis to calculate crude and adjusted fracture incident rate ratios.

Results: There were 60,565 fractures in 10,002,098 patient years of records – an incident rate of 606/100,000/year. There were 1,397 fractures in people with epilepsy (1.168/100,000/year) and 59,150 fractures in people without epilepsy (598/100,000/year). The crude fracture incident rate ratio (IRR), of people with epilepsy vs. people without epilepsy, was 1.95 (95% CI 1.85–2.06) the corresponding ratio adjusted for age, sex and socioeconomic status was 1.81 (95% CI 1.71–1.91). Fracture rates decreased slightly with decreasing socioeconomic deprivation-IRR 0.964 (95% CI 0.962–0.967). Subgroup analysis by age revealed adjusted IRR which were significantly increased for the age groups 0–5; 6–15; 16–24; 25–64; 65–69; 70+. However, the adjusted IRR for the age groups 6–12; 13–18 and 19–25 were not significantly increased.

Conclusion: People with epilepsy have an increased risk of fractures – an adjusted incident rate ratio of 1.84 (1.74–1.94). Increased attention should be paid to measurements aimed at improving bone health in adults with epilepsy.

075 EXPERIENCE AND RESULTS OF REPEITIVE TRANSCRANIAL MAGNETIC STIMULATION APPLICATION ON REFRACORY TEMPORAL EPILEPSY

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Purpose: The study was designed to evaluate the therapeutic effect of new technology of low-frequency repetitive transcranial magnetic stimulation which was combined with minimal therapeutics doses of anticonvulsants.

Method: Forty-eight patients with epilepsy (mean age 27.6 ± 0.99 years) were studied (EEG before and after 1, 5, 10 rTMS procedures and then every month; neuropsychological tests, QOLIE-31, SSQ before and after rTMS course every month during 1 year). Low intensity rTMS (1 Hz) was performed during ten consecutive days over the temporal lobe projection.

Results: Seizure frequency per week after 10 rTMS decreased following rTMS treatment compared with baseline period (2.3 vs. 0.17 per week; p = 0.016) which corresponds to 82.9% reduction. There were no seizures to end of third month in 66.8% and to termination of sixth month in 27.8% of patients (p < 0.05). Presence of paroxysmal EEG activity disappeared at 40% of patients during 1 month after combined therapy (p < 0.05). Antidepressive and antianxious effect was obtained at 46% of depressive subjects direct after rTMS course (p < 0.004) and continued during 2 months. The common QOLIE-31 point significantly increased during 3 months after rTMS (59.5 vs. 70.2; p = 0.0001). SSQ points improvement was registrated during 6 months (2.7 vs. 1.1; p < 0.05).

Conclusion: New technology of low-frequency and low intensity rTMS delivered into temporal lobe and combined with minimal therapeutics doses of anticonvulsants had a determining function and leads to significant prolonged antiepileptic effect, improves the psychological condition and quality of life of patients with refractory epilepsy what can help to avoid of side AEDs effects.

076 AVAILABILITY OF ANTIEPILEPTIC DRUGS ACROSS EUROPE

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Purpose: There is a pronounced diversity in economic status and political, educational and healthcare systems in Europe. Data from WHO show major gaps in quality of epilepsy care across Europe. The purpose of this study was to investigate the availability and accessibility of antiepileptic drugs (AEDs) in different European countries.

Method: An electronic questionnaire was submitted in 2012 to all 43 ILAE chapters in Europe. The questions concerned availability of AEDs for epilepsy and non-epilepsy disorders, availability of generics, reimbursement rules, and reasons for shortcomings. The countries were divided into high income, upper and lower middle/low income countries, according to the World Bank. The AEDs were divided into older, newer and newest drugs.

Results: Chapters from 34/43 (79%) countries (22 high-, 6 upper-middle and 6 low-middle/low-income) replied. One or more of the newest AEDs (eslicarbazepine acetate, lacosamide, rufinamide, stiripentol) were not available in 43% of high-income countries and in none of the upper-middle and low-middle/low-income countries. Lamotrigine has regulatory approval for psychiatric indications and pregabalin/gabapentin for neuropathic pain in almost all countries. Reimbursement by national healthcare systems was available in 75% of high-income countries in contrast to 30% and 10% of upper-middle and low-middle/low-income countries, respectively.

Conclusions: There are important AED accessibility gaps across Europe, especially for the newest AEDs and mostly due to lack of regulatory approval, high cost and reimbursement restrictions. The reimbursement of AEDs vary from no to full reimbursement. These results raise major concerns related to quality of treatment in epilepsy across Europe, as patients in different countries do not have equal opportunities for optimal treatment.

077 USE OF CHANGE IN EEG PHOTO-PAROXYSMAL-RESPONSE (PPR) TO PREDICT CHRONIC AED EFFICACY: DOES THE SURROGATE ENDPOINT MODEL WORK? A DOUBLE BLIND PLACEBO CONTROLLED STUDY OF LAMOTRIGINE VS. VALPROATE MODELLERED IN JME

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Purpose: The EEG Photo-Paroxysmal-Response (PPR) during Intermittent Photic Stimulation (IPS) correlates with tendency to epileptic seizures. Single dose studies show that reduction in EEG PPR correlates with AED effect. There are no published chronic dose AED studies reporting usefulness of this as an efficacy marker. Early indication of AED efficacy could shorten treatment duration before efficacy is inferred. Female JME patients might particularly benefit from this.

Method: We designed a 20 week 1:1 randomised double blind 1-way cross-over parallel-group study comparing valproate and lamotrigine
monotherapy in JME patients. At four weekly visits; trough AED concentrations, seizure frequencies and types, PPR during IPS and adverse effects were recorded. Only grade 3 or 4 PPR’s were included. IPS testing was carried out and standardised to ‘SPR’ utilising the Kasteleijn-Nolst Trenite et al (2012) protocol.

Results: 74 JME patients were identified. All gave informed consent. Ethics approval was obtained prospectively. 40 were taking valproate monotherapy. 17 valproate treated patients agreed to enter (M:F = 13:4), nine had PPR’s on previous EEG. At study entry four exhibited persistent PPR’s. At study end two valproate treated patients still had PPR’s and four lamotrigine treated patients had PPR’s. All the lamotrigine PPR’s were higher than baseline. In the lamotrigine group the PPR had risen but trended down again as dose was increased. In the lamotrigine group myoclonic seizures had increased markedly but returned to baseline levels by study end associated with progressive lamotrigine dose increases.

Conclusion: Lamotrigine initially suppressed PPR less effectively than valproate but a dose-response effect of lamotrigine on the PPR was identified. Efficacy of lamotrigine for all types of JME seizures was inferred, with a dose-response relationship. Increased lamotrigine doses appeared to overcome transient worsening of myoclonus.

Change in PPR did correlate with lamotrigine effect and may be utilised as an early indicator of efficacy.

Conclusions: Current prescribing of newer AEDs to women of child-bearing age is not based on evidence of fetal neurodevelopmental safety as research is limited and large methodological differences are present.

078 META-ANALYSIS OF NEURODEVELOPMENTAL OUTCOME FOLLOWING PRENATAL EXPOSURE TO ANTI-EPILEPTIC DRUGS
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Purpose: A Cochrane Systematic Review was undertaken to assess the neurodevelopmental effects of prenatal exposure to commonly prescribed antiepileptic drugs (AEDs).

Methods: Searches were undertaken in MEDLINE (Ovid), EMBASE, Pharmline, Reprotox and the Cochrane Central Register of Controlled Trials (March 2013). Predetermined inclusion criteria were defined by study methodology, AED type, control group and outcome. Data were analysed in RevMan (version 5.2) using standardised mean difference for continuous data and risk-ratios for dichotomous data. The results of global cognitive ability for AED vs. AED comparisons are reported here.

Results: Six published and one unpublished prospective observational study contributed data to the meta-analyses. In younger children (<3 years), there was no significant difference in global cognitive ability for CBZ (n = 148) vs. PHT (n = 71) or for CBZ (n = 210) vs. VPA (n = 160) but a significantly higher mean was found for PHT (n = 80) vs. VPA (n = 108) (7.04, 0.44–13.65, p = 0.04). In older children, significant mean IQ reductions were found for children exposed to VPA (n = 99) vs. CBZ (n = 178) (−8.43, −5.18 to −11.69, p < 0.00001) and for VPA (n = 74) vs. LTG (n = 84) (−10.79, −14.41 to 7.16, p < 0.00001). No significant difference was demonstrated for the comparisons CBZ vs. PHT or CBZ vs. LTG. No other comparisons were possible due to limited data or heterogeneity between study methodologies.
080 MOLECULAR IMAGING OF INFLAMMATION REVEALS DIFFERENCES BETWEEN DRUG-RESISTANT AND DRUG-SENSITIVE ANIMALS IN A CHRONIC MODEL OF TEMPORAL LOBE EPILEPSY


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Purpose: Activation of glia cells can promote icotogenesis and can affect the functional state of antiepileptic drug targets. Thus, we hypothesized that imaging of inflammation might render a basis for the development of biomarkers of drug resistance.

Method: PK11195 is a ligand of the translocator protein 18 kDa (TSPO), which has been frequently used as a molecular marker of microglia activation. PET studies using [11C]PK11195 were performed in the chronic phase of an electrically-induced post-status epilepticus model. In post-mortem tissue sampled from all animals groups TSPO expression was analyzed by immunohistochemistry.

Results: Subgroups of phenobarbital responders and non-responders were selected based on continuous seizure monitoring (video/EEG). In phenobarbital responders (R)-[11C]PK11195 brain uptake rates did not differ from those in control animals. In contrast, enhanced [(R)-[11C]PK11195 brain uptake was evident in different brain regions including the hippocampus, occipital cortex, parietal cortex, and caudate putamen. Standardized uptake values of [(R)-[11C]PK11195 showed no correlation with seizure frequencies during the last 72 h before PET scanning.

Conclusion: Our findings indicate that TSPO PET imaging might help to predict the response to antiepileptic drugs and might, thus, guide individualized therapeutic management decisions in the future. Studies are planned to further assess the suitability using a high affinity TSPO ligand tracer in longitudinal studies during epileptogenesis in the post-status epilepticus model.

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081 EXPRESSION OF INFLAMMATION MEDIATORS IN A MOUSE MODEL OF TEMPORAL LOBE EPILEPSY (TLE)

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Purpose: TLE is one of the most represented forms of epilepsy in human. Immune system cells and their mediators have been implied in epileptogenesis and seizure occurrence in TLE. To shed a light on these interplays, we studied changes in inflammatory mediators at gene and protein levels in an experimental model of kainic acid (KA)-injected mice treated with Lipopolysaccharide (LPS).

Method: Mice were unilaterally injected with an intrahippocampal dose of KA. Chronically-epileptic animals were injected with an intraperitoneal dose of LPS to mimic peripheral infection. EEGs were performed to assess frequency and duration of epileptic seizures after LPS administration. Hippocampi were explanted 4 and 24 h after LPS and used for microarray and RT-qPCR gene expression analysis. Immunofluorescence microscopy was used to observe inflammatory mediators expression in hippocampal tissues, meanwhile multiplex and standard ELISA tests were performed to evaluate their concentrations in sera and hippocampal protein extracts.

Results: EEG showed an increased frequency of recurrent seizures in LPS-treated mice in comparison to controls. RT-qPCR analysis confirmed microarray data, showing that KA + LPS treatment exacerbated the expression of chemokines and interleukins already observed in KA or LPS-treated hippocampi. Microscopy observations, multiplex and standard ELISA tests showed that inflammatory mediators increase at protein level in several cellular subpopulation in epileptic tissues, sera, and hippocampal protein extracts.

Conclusion: These data suggest that LPS-mediated inflammatory insult may strengthen the expression of inflammatory mediators that occur during chronic epilepsy, and that these molecular changes are associated with an enhanced propensity to spontaneous seizures.

082 ROLE OF TRANSFORMING GROWTH FACTOR BETA SIGNALING ON THE UPREGULATION OF THE EXTRACELLULAR MATRIX PROTEIN TENASCIN C IN THE RAT HIPPOCAMPUS IN CHRONIC SEIZURE MODEL


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Purpose: Seizures have been shown to upregulate the expression of numerous extracellular matrix molecules. The aim of this study was to evaluate the role of TGF-β signaling pathway on TNC upregulation.

Method: We used male rats (n = 4 each), which were injected with saline or pilocarpine (350 mg/kg) to induce status epilepticus and killed 24 h, 3 and 7 days post-pilocarpine injection. For evaluating biochemical changes, we measured protein content of TNC, TGF-β1 and phospho Smad2/3 by semi-quantitative Western blot and immunohistochemistry for localization of TNC in coronal brain hippocampus at 24 h, 3 and 7 days after pilocarpine-caused status epilepticus. To assess the role of TGF-β signaling on the overproduction of TNC, rats were injected with TGF-β inhibitor SB-431542 (10 mg/kg) dissolved with dimethyl sulfoxide i.p 30 min before the pilocarpine injection and sacrificed 24 h after status epilepticus.

Results: We found a statistically significant increase of TNC protein content in hippocampal homogenates after 1, 3, and 7 days of pilocarpine-caused status epilepticus, together with an enhancement of TNC immunoreactivity in several hippocampal layers and the dentate gyrus field where more dramatic changes occurred. We also observed a statistically significant enhancement of protein content of both
TGF-β1 and the critical downstream transduction effector pSmad 2/3 throughout the chronic time-course. Interestingly, animals injected with SB-431542, a TGF-β type 1 receptor inhibitor, decreased the TNC content in cytosolic fraction and diminishing pSmad2/3 content in both cytoplasmic and nuclear fraction compared with pilocarpine vehicle-injected.

Conclusion: These findings suggest the participation of the TGF-β signaling pathway on upregulation of TNC which in turn support the idea of its misregulation could overproduce extracellular matrix proteins to produce morphological changes which might be involved in the formation of recurrent excitatory circuits that contribute to epileptic seizures.

083

APOPTOSIS THROUGH DEATH RECEPTORS IN TEMPORAL LOBE EPILEPSY-ASSOCIATED HIPPOCAMPAL SCLEROSIS

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Purpose: Several seizure models have demonstrated that neuroinflammation and neurodegeneration are preponderant characteristics of epilepsy. Among a number of activated cytokines TNF emerges as a prominent effector/mediator of both events. Through its two receptors, TNF can play a dichotomous role in animal seizures: programmed cell death activation (via TNFRSF1A) or cell survival actuation (via TNFRSF1B), through nuclear factor kappa B (NFκB) activation. Considering the lack of clinical studies, our aim is to investigate the TNF pathway in temporal lobe epilepsy (TLE) associated with hippocampal sclerosis (HS) patients – TLE(HS).

Method: In an array expression assay, we evaluated 44 genes associated with apoptosis through death receptors in resected hippocampal tissue samples from 14 TLE(HS) patients and compared them to four post-mortem controls. TNFRSF1A and TNFRSF1B were labelled by immunohistochemistry and its relative mRNA expression levels were measured by RT-qPCR. Two reference genes were used: HPRT1 and the geometric mean of ENO2 and TBP.

Results: Our results identified 15 upregulated genes and showed that TNFRSF1A and TNFRSF1B were upregulated in the patients (p < 0.01 and p < 0.04, respectively). Moreover, double immunostaining revealed that both receptors were colocalized and overexpressed in the patients’ tissues.

Conclusion: Our data suggests that the overactivation of the TNF pathway is associated with the inflammatory and neurodegenerative components of TLE(HS). Furthermore, since TNFRSF1A is a key factor in the death receptor signaling canonical pathway, we infer that this via plays a crucial role in TLE hippocampal neurodegeneration. There is still some controversy on the role of TNFRSF1B. Its increase could be related to a survival mechanism because of the inferred NFκB system action; however, there is evidence that TNFRSF1B may reinforce TNFRSF1A action. Our results point out the TNF pathway as an important target for pharmacological studies regarding the benefits of an anti-inflammatory therapy in these patients.

084

ROLE OF ADENOSINE RECEPTORS IN CORTICAL POSTICTAL REFRACTORYNESS IN IMMATURE RATS

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Purpose: Adenosine might be taken as an endogenous anticonvulsant taking part in arrest of epileptic seizures. Postictal refractoriness represents overlasting activity of mechanisms arresting seizures, therefore we started to test drugs affecting adenosine receptors on this phenomenon.

Method: Experiments were performed on rats 12 and 25 days old, i.e. animals exhibiting immature and mature postictal refractoriness, respectively. Epileptic afterdischarges (ADs) were elicited by low-frequency stimulation of sensorimotor cortex in rats with implanted electrodes. First AD was followed after 1 min by the second stimulation, then the drugs were administered and 10 min later the paired stimulation was repeated. Duration of ADs was evaluated off-line.

Results: The second stimulation failed to elicit AD in control 25-day-old rats. In contrast, 12-day-old animals exhibited the second AD of longer duration than the first AD. High doses of caffeine (75 and 150 mg/kg) tested only in 25-day-old rats attenuated refractoriness, the second stimulation induced also AD but of shorter duration than the first one. Specific antagonist of A1 receptors DPCPX moderately suppressed and agonist CCPA did not significantly change the refractoriness in this age group whereas neither agonist CGS 21680 nor antagonist ZM 241385 of A2A adenosine receptors affected postictal refractoriness. Failure of postictal refractoriness in 12-day-old rats was affected by the agonist of A1 receptors CCPA – it was able to suppress partially the second AD. Surprisingly, an A1 receptor antagonist exhibited similar action but it was probably due to extreme prolongation of the first postdrug AD. Postictal refractoriness could not be corrected by any drug affecting A2A receptors.

Conclusion: Adenosine receptors of the A1 but not of A2A type play an important role in postictal refractoriness after cortical epileptic afterdischarges.

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Platform Session: Epidemiology and Prognosis

Wednesday, 2nd July 2014

085

PROGNOSIS AND MORTALITY OF EPILEPSY IN A RURAL DISTRICT OF VIETNAM

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Purpose: Epidemiological and long-term follow up studies of epilepsy from developing countries are scarce. We have therefore conducted a survey on epileptic patients previously diagnosed from a population based project (Tuan, N.A., et al. Epilepsia 2008; 49: 1634–1637) with the overall objective to determine the prognosis and mortality of seizures and epilepsy in a representative region of the country.

Method: A field survey was carried out in the Bavi District in northern Vietnam between January and December 2005, 206 fulfilled the criteria for active epilepsy, yielding prevalent cases. At these end of follow-up period, 197 persons with epilepsy were interviewed by a questionnaire to determine their AED compliance and seizure conditions. The relatives of those who had died during that period were interviewed to understand the causes of death.

Results: Out of 197 interviewed, 63(32%) got at least a seizure within a year and 14 (7.1%) had died. Among those who got seizures last year, 40 (63.5%) were with ongoing treatment of AEDs. 12 out of 14 patients who
had died, were with partial seizures and 9 (75%) were partial secondary
generalized seizures. The most frequent causes of death were co-existing
diseases 5 cases and unknown etiology (possible SUDEP) 5 cases.

**Conclusion:** After 7 years since diagnosed, 32% of patients with epi-
lepsy still got seizures and 7.1% had died. The most frequent causes of
death were co-existing diseases and unknown etiology.

**086**

**LONG-TERM PROGNOSIS OF JUVENILE MYOCLONIC EPILEPSY**

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**Purpose:** To evaluate long-term prognosis and related risk factors of
patients affected by Juvenile Myoclonic Epilepsy (JME).

**Method:** This is an observational, open-label, long-term study. Patients
affected by JME in regular follow-up by our Centers since 1993 were
recruited. The minimum follow-up was of 12 months. Statistical analysis
were performed using discriminant analysis as multivariate analysis.

**Results:** 53 patients affected by JME were recruited [29 F, mean age
29.3 ± 8.2 y (range 16–53)]; in 4 cases JME was an evolution of Child-
hood Absence Epilepsy. 43 (81%) patients showed generalized tonic-clon-
ic seizures (gtcs) and 19 (36%) absence seizures. Mean follow-up was 95 ± 60 months (16–239). 40 (75%) patients resulted seizure-free for at least 2 years; a higher likelihood of refractori-
ness of JME was associated to: family history of epilepsy and febrile con-
vulsions, gts and absence seizures, focal abnormalities and photosensibility on EEG, earlier age at epilepsy onset. 21 (39%) patients, after seizure-freedom, withdrew treatment, at a mean age of 22.9 ± 9 y (15–49); seizures relapse was observed in 20 (95%) cases and the patient who remained seizure-free was the only one who withdrew drug treat-
ment after the fourth decade of life (49 y).

**Conclusion:** Our study confirms the good prognosis of JME and its tight
relation to drug therapy, which should be maintained long-term. Among
the potential prognostic factors, focal abnormalities and photosensibility on EEG seem to be related to the difficulty in achieving seizure control.

**087**

**PREDICTING DRUG-RESISTANCE IN GENERALIZED
EPILEPSY IN AN ADULT POPULATION: A CASE-
CONTROL STUDY**

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**Purpose:** To identify risk factors for development of drug resistant epi-
lepsy (DRE) in an adult cohort of patients with generalized epilepsy. The identification of specific risk factors would allow patients to receive ear-
lier and more specifically individualized treatment plans.

**Method:** Nested case-control study. From a database of 800 patients
with epilepsy, 118 patients with generalized epilepsy (GE) between the
ages of 18 and 75 were identified. We used the definition of DRE (2010) and the guidelines to classify syndromes and seizure types by the ILAE
(1989). Odds ratios and confidence intervals were calculated.

**Results:** 43 (37%) patients fulfill the definition of DRE (cases), 74
(63%) patients were not intractable (controls). Cases of DRE were signifi-
cantly younger than controls at the onset of epilepsy (6.5 vs. 18.8 p < 0.001). Significant variables on univariate analysis were: epilepsy diagnosed prior to 12 years OR 11.75, CI 4.75–29.1, p < 0.001, status
epilepticus OR 15.6, CI 3.3–73.4, p < 0.001, frequent generalized spike
waves on first EEG OR 3.2, CI 1.39–7.5, p = 0.005, developmental delay
OR 13.5, CI 5.3–34.4, p < 0.001 and cryptogenic epilepsy OR 10, CI
3.7–26.8, p < 0.001. Presence of developmental delay and more than one
seizure profile remained statistically significant in a logistic regression
multivariate analysis.

**Conclusion:** Presence of more than one seizure profile and the presence
of developmental delay are significantly associated with DRE. Some risk factors identified in our study are similar to pediatric cohorts, however
our study is specifically tailored to adult patients with generalized epi-
lepsy.

**088**

**DEVELOPMENT OF EPILEPSY IN PATIENTS WITH
POSTERIOR REVERSIBLE ENCEPHALOPATHY
SYNDROME (PRES)**

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**Purpose:** Seizures are common in patients with posterior reversible encephalopathy syndrome (PRES), with a reported incidence of up to
70–80%. Patients are frequently started on antiepileptic drugs (AEDs)
which are continued on an outpatient basis. There is paucity of data to
support continuation of AEDs after resolution of PRES or to guide the
duration of treatment. The purpose of this study was to quantify the risk
of developing epilepsy in patients with PRES in order to determine
whether AED therapy is justified upon hospital discharge.

**Method:** We performed a chart review of 117 consecutive patients diag-
nosed with PRES, based on clinical features (headache, vision changes,
encephalopathy, seizures) and imaging characteristics, with documented
reversibility.

**Results:** 117 patients, age 50.2 ± 17.2 years were included in the analy-
sis of which 80 were women (68%). The most common clinical associa-
tions were hypertension (74%) and immunosuppression (21%). Seventy-
five patients (64%) had seizures (33 focal, 42 generalized) and 12 (10%)
of these presented with status epilepticus. EEG was performed in 57 of
75 (76%) patients. Findings included: 1) generalized slowing (60%), 2)
epileptogenic activity (23%) and 3) focal slowing (9%). Median duration
of follow up was 3.5 years (IQR 3 months–6.8 years). Median duration
of treatment with AEDs was 4 (IQR 2–12) months. AEDs were never dis-
continued in 14 (19%) patients. During the follow up period, 20 (17%)
patients had provoked seizures from various factors lowering the seizure
threshold of whom 7 were on AED therapy. Only 3 (2.5%) patients had unprovoked seizures of whom none were on AED therapy. These patients
were considered to have developed epilepsy.

**Conclusion:** The risk of recurrent unprovoked seizures is very low in
patients with PRES. The vast majority of seizures associated with PRES
occur within 24–48 h of initial presentation. Treatment with AEDs
beyond 2–4 weeks may not be warranted.
Purpose: To evaluate the differences in cardiovascular risk factors between people with epilepsy (PWE) and referents without epilepsy (RWE) who had died from cardiovascular causes.

Method: We identified all 1,386 PWE seen at the neurology clinic of University Hospital of Oulu during 1996 and 1997, with comparison against a population-based reference cohort matched for age and gender. Cardiovascular deaths up to 2008 were identified from Statistics Finland. A survey material was combined from three sources: 1) review of medical records, 2) death certificates and 3) the National Prescription Register data. Logistic regression analysis assessed differences in risk factors between PWE and RWE with odds ratios (OR) and corresponding 95% confidence intervals (95% CI).

Results: During the follow-up, 84 (6.1%) PWE and 61 (4.1%) RWE died of cardiovascular causes, corresponding to 51 and 55 percent of all deaths, respectively. The mean age at death was 69.5 (67.0–72.1) in PWE and 72.1 (68.8–75.3) in RWE. However, significant difference on age at death between PWE and RWE was not found. The most common causes of death were ischemic heart disease (51% in PWE and 55% in RWE) and cerebrovascular disease (29% in PWE and 21% in RWE). Statin treatment (OR = 0.48, CI = 0.22–1.06) and use of loop-diuretics (OR = 0.51, CI = 0.26–1.00) were slightly lower in group of PWE. We found also that PWE had higher MCV values (OR = 1.07, CI = 1.01–1.14) on last reported laboratory tests.

Conclusion: In our explorative study, the mean age at death was similar in PWE and in RWE. We found little differences in underlying risk factors between PWE and RWE who had died of cardiovascular diseases. Epilepsy was associated with lower use of loop-diuretics and statins, and with higher MCV values.

089 DIFFERENCES IN CARDIOVASCULAR RISK FACTORS BETWEEN PATIENTS WITH EPILEPSY AND REFERENCES DECEASED OF CARDIOVASCULAR CAUSES – AN EXPLORATORY ANALYSIS OF A COHORT STUDY

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Purpose: A systematic review and meta-analysis on mortality risk in patients with epilepsy with emphasis on epilepsy-related clinical characteristics.

Method: A systematic literature review covering 15 electronic databases, complemented with browsing reference lists of potentially relevant articles and direct author contact. We included cohort studies reporting mortality in representative epilepsy populations relative to the general population mortality rates, with exclusion of cohorts of highly selected subpopulations, such as epilepsy surgical series. Random effects meta-analyses were used to pool the estimates.

Results: Mortality was threefold (relative risk 3.33, 95% CI 2.83–3.92) in 38 epilepsy cohorts including 165,879 patients. In a meta-regression analysis, differences in age distributions determined 42% (R²; p < 0.001) of the variability between estimates. Among incident cases, idiopathic epilepsies did not associate with materially increased mortality (RR 1.29, 95% CI 0.75–2.20; 4 studies), whereas mortality was almost twofold in cryptogenic epilepsy (1.75, 1.20–2.54; 5 studies), highly elevated in patients with symptomatic epilepsy (4.73, 3.27–6.83; 12 studies) and in epilepsies due to congenital or developmental causes (10.3, 4.03–26.2; 2 studies). Newly diagnosed patients who attained seizure freedom did not have elevated mortality (0.97, 0.73–1.30; 2 studies).

Conclusion: Epilepsy-associated excess mortality was highly attributable to the etiology of epilepsy in all ages. In patients without neuroradiological abnormalities or other identifiable cause of epilepsy, risk of death depended on the differentiation between idiopathic epilepsy and cryptogenic epilepsy.

Platform Session: Genetics and Epilepsy Syndromes
Wednesday, 2nd July 2014

091 A GENETIC BASIS FOR RESPONSE TO THE KETOGENIC DIET

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Purpose: The Ketogenic Diet (KD) is an alternative treatment option for people with drug-resistant epilepsy. It reduces seizures by ≥50% in approximately 40% of patients, but it is resource-intensive and may cause adverse side effects. Predictors of response, in the absence of specific metabolic disorders, are unknown, but would improve patient selection and may enhance our understanding of its anti-epileptic mechanisms. The aim of this study is to determine whether there is a genetic basis for variability in KD response.

Method: After informed consent, blood was taken for DNA extraction from individuals following the KD, or who had previously followed the KD for epilepsy. 45 individuals with an extreme response to the KD had whole exome sequencing. Those with ≥75% seizure reduction maintained over ≥12 months were classed as responders; those with no change or with increased in seizure frequency and who discontinued the diet at or before the 3-month point were classed as non-responders. Following quality control filtering, single-variant, gene-based and pathway-based association tests were conducted in PLINK/SEQ with 22 non-responders and 14 responders.

Results: Only one significant (gene-based) result was obtained, from the c-alpha test. Another gene reached suggestive significance in the burden test, which assumes a uni-directional effect of variants: 14 non-responders.
Abstracts

glyceride biosynthesis” reached suggestive significance for association with favourable KD response.

Conclusion: Little is known about the candidate gene and so it is difficult to interpret how it may influence KD response. Other genes and pathways highlighted are biologically plausible and are of interest for follow-up studies. A larger sample size is needed.

092
JOINING FORCES TO IDENTIFY NOVEL GENES FOR EPILEPTIC ENCEPHALOPATHIES
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Purpose: We aim to explore the genetic spectrum of two subtypes of epileptic encephalopathies (EEs): infantile spasms (IS) and Lennox-Gastaut syndrome (LGS). Given their severity, most patients present as isolated cases and therefore we hypothesize that the disorders are mainly due to heterozygous de novo mutations. Current knowledge however shows that the genetic landscape for IS and LGS is so heterogeneous that each gene explains only a fraction of patients.

Method: In order to increase our chances of identifying novel genes, we set up a collaborative study of three large epilepsy consortia to study almost 400 IS and LGS patients. Using a trio-based whole exome sequencing (WES) approach we searched for novel EEs genes.

Results: We identified four interesting genes not previously linked to EEs with de novo mutations in at least two unrelated patients. In one of these genes we even identified five mutations. Combined with literature we provide major evidence for a causative role of this gene in EEs. The three others genes are good candidate genes for EEs. Furthermore, we identified de novo mutations in 13 genes known to cause epilepsy.

Conclusion: The advent of WES has led to an explosion of genetic data, which we will be able to unravel the genetic architecture of monogenic diseases such as the EEs.

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LONG-TERM PROGNOSIS OF NOCTURNAL FRONTAL LOBE EPILEPSY (NFLE): A COHORT STUDY
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Purpose: To evaluate the prognosis of NFLE in terms of 5-year seizure freedom (SF).

Methods: Cohort study with both retrospective and prospective criterion. We included consecutive patients attending our Institute, diagnosed with NFLE on clinical and video-polysonmographic (VP SG) criteria. To evaluate cumulative time-dependent probability of achieving a 5-years remission from NFLE onset, patients with follow-up (F-U) ≥ 5 years were selected and 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: Among 165 NFLE patients (M/F:103/62) we included 158 patients (M:62.7%; 41 median age at last F-U) with F-U ≥ 5 years (median F-U duration 27 years, range 5–81). Mean age at epilepsy onset was 14.7 ± 10.56 years (median 13; range 1–56). According to VPSG records, hyperkinetic seizures were the most common (40.5%); 47% of patients experienced subjective sensations preceding motor manifestations. At last assessment, 39 patients (25%) had been SF for ≥5 years (56% without therapy; mean age of seizure disappearance: 35.3 ± 17.1 years), 15% of patients were SF for <5 years while the remaining 60% had seizures.

Cumulative 5-year-SF rate was 21% after a 25-year F-U. At logrank test, age at onset <13 years (median age), and pathological neurological examination (NE) considered alone or in association with positive MRI and intellectual disability (ID) correlated significantly with no 5-year remission (p = 0.002 and 0.003). ID, febrile seizures and positive MRI showed a trend toward a negative association with remission. At Cox model, early age at seizure onset and ID + positive NE and MRI were associated with a doubled (OR 2.0; p = 0.047) and quadrupled (OR 4.5; p = 0.014) risk of not achieving 5-year-SF, respectively.

Conclusions: Only about 25% of NFLE patients achieved 5-years remission after a long period of disease. Early age at onset and the association of ID, structural brain abnormalities and positive NE are independent negative predictors.

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MORPHOMETRIC AND FUNCTIONAL MRI CORRELATES IN EYELID MYOCLOSION WITH ABSENCES
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Purpose: In some epilepsies, EEG paroxysms are related to the closure of the eyes. This phenomenon is termed eye-closure sensitivity (ECS). Eyelid Myoclonia with Absences (EMA) is the ideal model for studying the ECS. Here, we investigated the presence of functional and structural brain abnormalities underlying ECS in EMA, by means of a simultaneous recording EEG and functional MRI study (EEG-fMRI) and a Voxel Brain Morphometry analysis (VBM).

Method: Fifteen EMA and 16 Controls underwent to the same EEG-fMRI and VBM protocol. The following EEG events were identified and the relative fMRI maps obtained:

1. Eye-closure (EC) times;
2. Spontaneous blinking;
3. Spontaneously fluctuating EEG alpha power.

For each condition, a random effect analysis was performed comparing EMA and Controls with a two-sample T-test.

Results: In the EMA group compared to controls we found:

1. Higher BOLD increases over the visual cortex, the anterior cingulate and mid-frontal gyrus related to the EC state;
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INVESTIGATION OF GENETIC CAUSES OF EPILEPSY IN CHILDREN WITH NON-SPECIFIC INTELLECTUAL DISABILITY USING ACGH-BASED TECHNOLOGY

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Objective: Epilepsy is a genetically complex disorder, affecting up to 3% of the population. Many chromosomal syndromes include, beside intellectual disability, malformations and other manifestations, as well as epileptic seizures. Previous studies of aCGH have described chromosomal abnormalities in epilepsy, especially in cases with complex phenotypes. In this paper, we present our experience regarding the investigation of genetic abnormalities in children with non-specific intellectual disability and epilepsy using aCGH-based technology.

Material and Methods: 18 children with non-specific intellectual disability and epilepsy were investigated. The clinical evaluation included data about psychomotor development, IQ, behavior, neurological signs, dysmorphic features, and epilepsy history (age of onset, type of seizures, response to treatment). All children were evaluated by EEG, imagistic studies (CT, MRI), biological studies. aCGH was performed in all patients, in order to identify genetic entities that may be causative for epilepsy and intellectual disability.

Results: In 13 children, different microdeletions/microduplications were identified. All detected CNVs included confirmed genes for neurodevelopmental disorders; 9 of these CNVs harbored, also, confirmed genes for epilepsy, such as: CDKL3 and ARX genes in a girl with Xp22.3 duplication, CHRNA2 gene in a patient with 8p21.2 deletion, ZEB2 gene in a boy with 2q22.3 deletion, CLCN2 gene in a patient with 3q26.3 duplication, MFSDS gene in a boy with 4q28.2 deletion.

Conclusions: Our results demonstrate the usefulness of aCGH in identification of genetic mechanisms of epileptic seizures in children with intellectual disability.

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INFECTIONS IN STATUS EPILEPTICUS: A RETROSPECTIVE 5-YEAR COHORT STUDY

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Purpose: For medically refractory cases of status epilepticus, optimal supporting care is of great importance and often involves mechanical ventilation and intensive care unit (ICU) admission. Infections can complicate SE and must be factored in when weighing the risk of ICU admission. Recently an observational study demonstrated an association between infections and poor outcome of SE in a cohort of severely ill patients with high mortality due to hypoxic-ischemic encephalopathy.
We asked if infections were as common in a cohort of patients with SE of less severe aetiology.

**Method:** We performed a retrospective observational study and included all patients with a diagnosis of SE during 2008–2012 at a Swedish tertiary referral centre. In Sweden, neurologists do typically not care for patients with hypoxic-ischemic encephalopathy.

**Results:** The cohort consisted of 103 patients. The mortality was <2% and 70% of the patients where discharged home after resolution of the SE. The most common aetiologies were uncontrolled epilepsy (37%) and brain tumours (16%). A total of 39 patients suffered infections during their hospital stay. Presence of infection was associated with mechanical ventilation as well as poor outcome, and duration of SE was significantly longer in patients with infection.

**Conclusion:** We conclude that the previously described association between infections and SE severity seems valid across different cohorts of SE of different etiologies. Causation regarding SE and infections is probably bi-directional. Nonetheless, the findings illustrate that infections must be taken into account in management of all SE patients.

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**ETIOLOGY, CLINICAL COURSE AND RESPONSE TO THE TREATMENT OF SUPERREFRACTORY STATUS EPILEPTICUS IN CHILDREN: A 15-YEAR A SINGLE CENTER EXPERIENCE**

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**Purpose:** Evaluation of etiology, clinical course and response to the treatment of superrefractory status epilepticus (SuperRefSE) in children.

**Methods:** The study included children aged 0.2–18 years with SuperRefSE treated in our Institute in the period from 1998 to 2012. SuperRefSE is defined as status epilepticus (SE) that continues or recurs 24 h or more after the onset of anesthetic therapy, including those cases that recur on the reduction or withdrawal of anesthesia. Etiology was summarized according to Shinar's classification. Almost all patients were treated according to the same hospital protocol. The drug was defined as effective if seizure stopped within 1 h, without recurrence within next 6 h.

**Results:** The study included 43 SuperRefSE episodes in 23 children with mean age of 4.14 years. Etiology was heterogeneous: progressive encephalopathies (24), remote symptomatic (12), acute symptomatic (5) and cryptogenic (2). Continuous midazolam infusion (mean dosage 0.39 mg/kg/h) was effective in 17 of 30 (56.6%) episodes, while others, thiopental (44%), propofol, ketamine and lidocain were less effective. Adverse effects were common (60.5%), frequently requiring intensive therapy (76.7%). Corticosteroids infusion was beneficial in decreasing seizure recurrence after midazolam/thiopental withdrawal. Leviterac-tam was effective (3/3), but in one case with neuronal lipofuscinosis caused severe bradycardia. Eleven episodes were resistant to all drugs; five patients continued seizing until death. Case-fatality rate was 21.3%.

**Conclusion:** SuperRefSE is particular type of SE characterized by progressive encephalopathy as most common etiology, poor response to anticonvulsive drugs, common adverse effects frequently requiring intensive therapy and high mortality. The treatment of SuperRefSE is very challenging and those patients require a particular therapeutic approach.

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**PROGNOSIS OF NON-COULSIVE STATUS EPILEPTICUS (NCSE): RELATIONSHIP BETWEEN SE DURATION AND SUBSEQUENT DEVELOPMENT OF EPILEPSY**

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Many questions have arisen of how aggressive AED treatment should be in NCSE, and its influence on prognosis. We aimed to study the prognosis of SE de novo and which factors may influence the subsequent development of epilepsy.

**Method:** We evaluated all NCSE patients without previous history of seizures admitted at our hospital (February 2011–January 2014). The complete assessment included demographic data, etiology, number of AEDs, duration of SE, mortality and the occurrence of seizures during follow-up.

**Results:** 89 NCSE patients were evaluated. Median age was 70 years old (25–75). Regarding the etiology, 71 patients were considered acute
101 STATUS EPILEPTICUS PROGNOSIS: A 4-YEAR RETROSPECTIVE ANALYSIS IN A TERTIARY CENTER
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Purpose: Evaluate the influence of clinical, electroencephalographic and neuroimaging variables in the early outcome of a status epilepticus (SE) population.

Method: Retrospective analysis of consecutive adult patients admitted in Intensive Care Units of a tertiary Hospital during 4 years. Demographic, clinical, electroencephalographic and neuroimaging data were collected. Outcome was considered at discharge using modified Rankin (mRankin) and Glasgow outcome scale (GOS). Descriptive statistical analysis, (non)parametric and regression tests were performed as appropriate.

Results: We have 102 cases corresponding to 96 patients (62 female). Mean age: 62.38 ± 1.61 years old. The majority were nonconvulsive. Approximately 50% of patients had multiple factors contributing to the SE. Etiology is not statistically different between the different types of SE and did not predict the final mRankin or GOS. The admission EEG disclosed focal epileptiform discharges in more than 50%, with no impact on outcome. Those with brain lesion(s) had poorest mRankin at discharge and GOS, independently of the location. The initial antiepileptic (AED) was different between types of SE (diazepam used more frequently in convulsive SE and did not predict the final mRankin or GOS. The admission EEG was classified as follows: no changes, burst-suppression (BS) pattern and diffuse theta-delta activity.

Conclusion: In patients with RSE, KE-induced BS pattern during EEG monitoring predicts a good clinical response to both S and racemic KE.

Platform Session: Neurogenesis and Network Reorganisation
Thursday, 3rd July 2014

102 CONTINUOUS EEG RECORDING IS USEFUL TO PREDICT RESPONSE TO IV KETAMINE IN CHILDREN WITH REFRACTORY CONVULSIVE STATUS EPILEPTICUS
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Purpose: To determine the EEG characteristics induced by ketamine (KE) infusion, and their correlation with KE efficacy in children with refractory convulsive status epilepticus (RSE).

Methods: We evaluated the EEG characteristics of 11 consecutive patients with RSE, who were admitted to our Hospital between November 2009 and December 2013, and treated with IV KE. Continuous KE infusion was always preceded by 2 boluses of KE at dosages of 2–3 mg/kg. EEG changes were analysed after each bolus, and during KE infusion. EEG response was classified as follows: no changes, burst-suppression (BS) pattern and diffuse theta-delta activity.

Results: Fifteen consecutive RSE episodes were studied in 11 children (6 female; age range, 2 months–10 years and 5 months). A total of 1,927 h of video-EEG monitoring recordings were analysed. An BS pattern was obtained in all five RSEs that resolved after S(+) KE (by Pfizer), at a dosage of 20–55 µg/kg/min (mean 34.4; median 30). Racemic KE mixture (by Molteni SpA) was administered in the remaining 10 RSE episodes at mean infusion dosage of 38.8 µg/kg/min (range 8–60; median 45). A BS pattern was observed in all eight RSE responders. In S/BS, KE infusion dosage of 8–60 µg/kg/min (mean 47.6; median 60). In the remaining 3/10 RSEs, KE infusion dosage of 26 µg/kg/min (range 20–40; median 20) induced a transitory BS pattern that was followed by diffuse delta activity. No EEG changes occurred in the remaining two non-responder RSE, either after boluses or during KE infusion of 10 and 60 µg/kg/min. EEG changes were not related to the EEG features prior to KE infusion and the add-on of anaesthetics.

Conclusions: In patients with RSE, KE-induced BS pattern during EEG monitoring predicts a good clinical response to both S and racemic KE.
mental situation to compare how similar brain insults lead to an identical endpoint – epilepsy – via different network reorganizations.

Method: During the first days after pilocarpine-SE in mice and rats, we assessed neuronal excitability with PTZ seizure thresholds in vivo. Additionally, we measured EPSCs and IPSCs in mice ex vivo and compared the data with our earlier study in rats (El-Hassar et al., J. Physiol. 2007, 578:193–211).

Results: Although in our model both species develop epilepsy, the PTZ threshold was increased in mice (1–2 days post SE), whilst the opposite was seen in rats. Electrophysiological analysis also revealed differences: Whereas the frequency of GABAergic currents was decreased in both species, AMPA events were significantly enhanced in mice and decreased in rats. Furthermore, amplitude and current kinetics were altered.

Conclusion: The opposing changes after SE could be accounted to different network reorganizations in rats and mice: As a protective mechanism, the brain can be more resistant to seizures due to increased inhibition; however, it is also conceivable that the brain is even more susceptible, caused by a decreased GABA synthesis or a shift in GABA reversal-potential, which will be investigated next.

Supported by a grant (Lo 247/11-2) from the German Research Foundation (Bonn, Germany). S. Bröer was funded by a Boehringer Ingelheim travel grant to perform the experiments at the INSERM Marseille.

104 EFFECT OF EXPERIMENTAL FEBRILE SEIZURES ON DENDRITOGENESIS OF NEWBORN HIPPOCAMPAL DENTATE GRANULE CELLS

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Purpose: Febrile seizures (FS) are fever-triggered convulsions, occurring in 3% of children under the age of 5 years that may increase the risk for epilepsy. Previously, we have shown that experimental FS increase the survival of dentate granule (DG) cells, born after seizures. Furthermore, DG cells show increased sensitivity to GABA, a decreased spontaneous inhibitory post-synaptic current frequency, and an increased spontaneous inhibitory post-synaptic current amplitude. Newborn DG cells are therefore hypothesized to contribute to the development of a hyperexcitable hippocampal network and to play a role in the development of temporal lobe epilepsy.

Method: The aim of the present study was to analyze whether experimental FS alter the morphology of newborn DG cells. To this end, we used an established model where FS are induced in 10-day old rat pups by subjecting them to heated air (FS+). Controls consisted of normothermia (NT) littermates and animals that did not display seizure behaviour upon hyperthermia treatment (FS-). Newborn DG cells were labelled 1 day after treatment by a stereotactic injection of GFP expressing retroviral particles in the dentate gyrus. After 1, 4 and 8 weeks, animals were sacrificed. Confocal Z-stacks were acquired from 40 μm coronal sections allowing morphological analyses of GFP positive DG cells. Dendritic length and arborisation complexity were quantified using Image-J.

Results: Preliminary results indicate that 1 week after FS, dendritic length is significantly increased compared to controls (p < 0.01). Also, an increased complexity of the dendritic branch, indicated by an increase in branching points was found 1 week after FS (p < 0.05).

Conclusion: From these data we conclude that experimental FS can alter dendritogenesis in post-FS born DG cells. These changes are expected to result in an increased connectivity of the hippocampal network.

This study was financially supported by a Grote Bijzonder Onderzoeksfonds grant from Hasselt University.

105 INHIBITION OF MICROGLIAL ACTIVATION VIA CX3CR1/FRACTALKINE SIGNALING PATHWAY DIMinishES STATUS EPILEPTICUS-INDUCED HIPPOCAMPAL NEURODEGENERATION AND NEUROGENESIS IN THE ADULT RAT

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Purpose: Ongoing hippocampal neurogenesis in adult brain can be increased by brain pathology such as an epileptic seizure. However, role of these new neurons is not clearly known. Neuroinflammation, one of the hallmarks of mesial temporal lobe epilepsy induces long-term microglial activation that can modulate the production, survival as well as integration of these new neurons into the existing circuits. Further, it can contribute to the hippocampal pathology including neurodegeneration. Here, we aim to investigate the role of CX3CR1/fractalkine signaling pathway that mediates neuronal/microglial interactions, in hippocampal neurogenesis and neurodegeneration induced by status epilepticus (SE).

Method: Male SD rats were infused anti-CX3CR1 antibody, recombinant rat fractalkine or vehicle into the lateral ventricle through an osmotic pump for a week following electrically-induced SE.

Results: Anti-CX3CR1 antibody treatment led to a significant reduction in the number of Iba1-positive microglia as compared to vehicle-treated rats in granule cell layer of the hippocampus. In addition, it led to altered microglial morphology with greater number of ramified cells and reduced intermediate/round cells in the granule cell layer as well as the molecular layer. Fractalkine treatment did not modulate either the microglial number or morphology in the hippocampus. Anti-CX3CR1 antibody-induced changes in microglial activation were associated with a reduced hippocampal neuroblast production as indicated by a significant reduction in number of doublecortin and Ki67-positive cells. Further, anti-CX3CR1 treatment also led to a reduced SE-induced neurodegeneration, indicated by significant reduction in numbers of Fluoro-Jade-positive cells in dentate hilar region.

Conclusion: These findings suggest a role for CX3CR1/fractalkine signaling pathway in SE-induced neurodegeneration and that blocking the CX3CR1 receptors could diminish SE-induced neuronal degeneration and the seizure-induced increase in hippocampal neurogenesis. Further research on potential role of modulating this pathway during survival and integration of adult born neurons as well as development of spontaneous recurrent seizures is warranted.

106 ADULT NEUROGENESIS AND BRAIN INFLAMMATION AS POTENTIAL BIOMARKERS OF EPILEPTOGENESIS

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**Purpose:** Synapsins – a family of abundant pre-synaptic vesicle phosphoproteins have been linked to the pathogenesis of epilepsy through associations between synapsin gene mutations and epilepsy in humans. Deletion of the synapsins causes an excitatory/inhibitory imbalance exemplified by the epileptic phenotype of synapsin knockout mice. These mice are behaviorally seizure free until 2 months of age after which they then begin to develop handling-induced seizures that worsen with age. Hence, these mice provide an opportunity to study epileptogenesis. In this study, we aimed to investigate potential biomarkers of epileptogenesis, before the occurrence of behavioral seizures using Syn2−/− mice as a model system. We focused primarily on adult neurogenesis, brain inflammation and synaptic proteins.

**Method:** We performed immunohistochemical and biochemical analyses to characterize the pathological environment in pre-symptomatic (1 and 2 months) and symptomatic phase (3.5 months).

**Results:** Immunohistochemical analyses of doublecortin (DCX) and Ki67 – markers of immature neuroblasts and proliferating cells, respectively, revealed significant alterations in the granular cell layer of the hippocampal dentate gyrus at both 1 and 2 months. At 3.5 months, a seizure-induced increase in neuroblast production was evident. Analyses of microglial morphology suggested microglial activation already in the pre-symptomatic phase with a significant decrease in the percentage of ramified microglia and an up-regulation of intermediate morphology at both 1 and 2 months, similar to 3.5 months, The expression of gephyrin, an inhibitory post-synaptic scaffolding protein, was however not altered during the pre-symptomatic phase.

**Conclusion:** In conclusion, our results indicate both adult neurogenesis and brain inflammation as potential signaling pathways for biomarker discovery of epileptogenesis.

107 DIFFERENTIAL VULNERABILITY OF INTERNEURONS ALONG THE SEPTOTEMPORAL AXIS OF THE HIPPOCAMPUS IN EXPERIMENTAL EPILEPSY

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**Purpose:** Loss of interneurons is considered as a reason for hyperexcitability of the hippocampus in temporal lobe epilepsy (TLE). Here we used a focal mouse model for TLE to characterize the vulnerability of interneurons along the septotemporal axis of the hippocampus and to record epileptic activity in corresponding areas.

**Method:** Adult C57Bl6 mice received a unilateral injection of kainate into the septal hippocampus which induced recurrent epileptic seizures, hippocampal sclerosis and granule cell dispersion (GCD). We implanted four electrodes along the septotemporal axis of the hippocampus to measure local field potentials. In situ hybridization for glutamate decarboxylase 67 (GAD67) mRNA and immunolabeling for parvalbumin, neuropeptide Y (NPY) and GAD65 was used to characterize changed inhibition in the whole hippocampus.

**Results:** We show that epileptiform activity is not strongest at the injection site with most prominent cell death and GCD but in the intermediate hippocampus which seems histologically less affected. Quantification of GAD67 mRNA-positive cells revealed a significant loss of inhibitory interneurons close to the injection site and a reduction in the intermediate hippocampus. Yet, different interneurons populations showed differential vulnerability: Parvalbumin-positive cells were lost on a substantially larger extent than NPY-positive interneurons. Remarkably, granule cells showed a compensatory reaction to epileptiform activity characterized by an upregulation of GAD67 mRNA in cell bodies, GAD65 protein in mossy fiber synapses and NPY in mossy fibers.

**Conclusion:** Together with our previous study on neurogenesis (Häussler et al., Cerebral Cortex 2013, 22(1):26–36) these data indicate that the intermediate hippocampus comprises a network with higher epileptogenicity than the dorsal, sclerotic hippocampus. This might be due to a shifted excitation-inhibition balance originating from the reduction in inhibitory interneurons and the addition of newborn, hyperexcitable granule cells.

**Acknowledgements:** Supported as part of the Excellence Cluster “BrainLinks-BrainTools” by the German Research Foundation, grant EXC1086, Scientific Society Freiburg.

108 PHASE COUPLING OF NEURONAL FIRING TO HIPPOCAMPAL NETWORK RHYTHMS IS PRESERVED UNDER EPILEPTIC CONDITIONS

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**Purpose:** In mesio-temporal lobe epilepsy (MTLE) the hippocampal network is pathologically restructured resulting in the emergence of epileptiform activity (EA). EA occurs transiently and alternates with putatively “normal” activity patterns.

In healthy animals, hippocampal activity is dominated by network oscillations that couple information transfer between hippocampal subregions and shape the firing probability of single neurons.

Previously we showed phase-shifted coupling of the theta-rhythm between the medial entorhinal cortex (MEC) and the sclerotic dentate gyrus (DG) in epileptic mice. Whether phase-shifted oscillations are accompanied by shifted neuronal firing across hippocampal fields or locally with respect to ongoing network oscillations is investigated here. Both conditions would severely alter information processing in the epileptic hippocampal formation.

**Method:** We recorded local field potential rhythms and multi-unit activity in freely behaving epileptic animals using the intrahippocampal kainate mouse model of MTLE. We chronically implanted multi-site silicon electrode arrays sampling the whole entorhinal-hippocampal (EC-HC) loop.

**Results:** We show that neurons in all investigated substructures of the EC-HC loop fired phase-coupled to theta and gamma oscillations. Coupling to theta rhythm was comparable in strength and phase-angle across healthy and epileptic groups. Furthermore, coupling properties of neurons recorded in the weakly-sclerotic DG, a region showing highest epileptogenicity, were comparable to those in the non-sclerotic DG.

While the phase-coupling of neurons persisted in epileptic mice, the average firing rate of cells from the DG and parahippocampal region was increased.

**Conclusion:** Hippocampal neuronal firing is modulated with the local theta-rhythm. Thus, a phase-shift between the theta-rhythms of the MEC and DG implies a mismatch of neuronal firing across these structures that...
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could tune the hippocampal network towards seizure susceptibility via pathological plasticity.

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Antiepileptic Drugs 1
Monday, 30th June 2014

p109
A RETROSPECTIVE EVALUATION OF RETIGABINE IN PATIENTS WITH HIGHLY THERAPY-RESISTANT EPILEPSY
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Purpose: To evaluate retrospectively the efficacy and tolerability of retigabine (RTG) in inpatients of the long-stay department of the Bethel epilepsy centre.

Method: All patients (N = 20; M = 13, F = 7; mean age 31.8, range 18–54 years) started on RTG between May 2011 and March 2012 were included.

Evaluation was carried out after 6 and 12 months. Changes in seizure frequency were measured as the number of seizures during 3 months on RTG compared to a 3 months baseline period. Tolerability was assessed using information provided by the patient, staff, and the neonologist in charge. All but one patient had symptomatic (structural), one patient: metabolic) or cryptogenic focal or multifocal epilepsy. All had therapy resistance grade III and cognitive deficits of different degrees.

Results: The retention rate was 60% after 6 months and 35% after 12 months. The 12 months rates of seizure reduction were: >90%; 1 patient; >50%–50%; 1 patient; 25–50%; 4 patients; >50%; 1 patient. Reasons for discontinuation were: adverse effects (6); lack of effect (6); both (1). Dizziness and cognitive or emotional changes were the side effects most frequently reported. The 7 patients still on RTG had dosages between 400 and 1,200 mg/day combined with 1–3 antiepileptic co-medications (most frequently lamotrigine and oxcarbazepine, 4 each).

In summer 2013, a red hand letter by the manufacturer informed about newly emerged RTG side effects (mainly pigment changes of retina, lips and nails). As a consequence, the 7 remaining patients on RTG were re-examined. One patient had a moderate blue-gray finger coloring. Ophtalmological changes were not discovered. Overall, shared re-assessment of the benefit-risk relation led to discontinuation of RTG in 3 patients. From there, only 4 patients are currently left on RTG (20% retention rate).

Conclusion: RTG proved to be useful only for a small minority of patients in a sample of above-average difficult-to-treat patients.

p110
ZONISAMIDE IN THAI CHILDREN AND ADOLESCENTS WITH INTRACTABLE SEIZURES: EVALUATION OF EFFICACY AND SAFETY
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Purpose: To determine the efficacy and safety of zonisamide in Thai children and adolescents with intractable seizures.

Method: Medical records of patients aged under 18 years who received zonisamide for treatment of epilepsy at the Department of Pediatrics, Ramathibodi Hospital, Faculty of Medicine, Mahidol University between November 1, 2010 and June 30, 2011 were reviewed. These data collected including the underlying illness, etiology of epilepsy, seizure types, previous and concomitant antiepileptic drugs, dosage, and adverse effects of zonisamide. Efficacy was evaluated on the seizure reduction. Adverse reactions were descriptively analysed. Student’s t-test and chi-square analysis were applied for continuous variables and discrete variable analysis respectively.

Results: Twenty four patients (13 male, 11 female) with age-range 2–18 years (median 11.5, mean 10.4) were included into this study. At final evaluation, 7 patients continued taking zonisamide (29.1%). Ranges of zonisamide were 3.1–18.8 mg/kg/day (mean 9.9, median 10.1). Seizure free was noted in one patient and the other six had favorable seizure control (50% or >50% seizure reduction). Median duration of treatment of these patients was 23.75 months (range 20.5–25). Among 17 children who did not have favorable seizure control; the median duration of zonisamide therapy was 3.5 months (range 0.5–15.5). Adverse effects were reported in 41.6% of patients during the first 3 months of zonisamide therapy. Four patients discontinued zonisamide due to diarrhea and loss of appetite. There were no serious adverse effects observed.

Conclusion: Zonisamide is an option for the treatment of intractable seizures with favorable seizure control in children and adolescents. Minor adverse reaction is expected during first 3 months.

p111
AN AUDIT OF THE TREATMENT OF DRUG-RESISTANT PATIENTS WITH LACOSAMIDE IN AN EPILEPSY CLINIC
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Purpose: To investigate the results obtained from adjunctive treatment with lacosamide in patients with drug-resistant epilepsy attending an epilepsy clinic.

Method: Record review.

Results: The patient group comprised 70 patients of age 18–80 years who had failed to become seizure-free on at least two anti-epileptic drugs (AEDs). The mean number of AEDs used prior to lacosamide was 7.4. Two patients (3%) became fit-free and 19 patients (27%) responded favourably to lacosamide. Outcome remained uncertain in 7 patients (10%). Lacosamide was withdrawn in 42 patients (60%) owing to lack of efficacy in 24 or due to adverse side-effects in 18.

Conclusion: Lacosamide proved beneficial in 30% of a group of 70 patients who had previously proved drug-resistant to a wide range of AEDs.
Purpose: To determine the efficacy and safety of a once-daily extended-release topiramate formulation, USL255, in adult patients with refractory partial-onset seizures (POS).

Methods: In this double-blind phase 3 study (PREVAIL), patients taking 1–3 concomitant antiepileptic drugs (AEDs) were randomized to placebo (n = 125) or USL255 (n = 124), titrated over 3 weeks (50 mg/week), and maintained at 200 mg/day for 8 weeks. The primary endpoint was median percent reduction in weekly POS frequency and the key secondary was 50% responder rate. Efficacy endpoints were also analyzed in various concomitant-treatment subgroups. Safety measures included adverse event (AE) reporting, which was analyzed at different intervals throughout the trial.

Results: USL255 resulted in significantly greater reduction in POS frequency (39.5% USL255 vs. 21.6% placebo, p < 0.001) and 50% responder rate (37.9% vs. 23.2%, p = 0.013) vs. placebo. Over the entire trial, the percentage of patients with any treatment-emergent AE was 66% USL255 vs. 50% placebo (p = 0.015). AE incidence decreased from titration to the first 4 weeks of maintenance and further decreased over the last 4 weeks of the maintenance phase. Individual neurocognitive and neuropsychiatric AEs were reported in fewer than 3% of patients in both treatment groups, with the exception of disturbance in attention (2.4% USL255 vs. 3.2% placebo). Serious AEs occurred in 1.6% of patients in each group; none were deemed USL255 related.

Conclusion: The PREVAIL trial demonstrated that once-daily USL255 (200 mg/day) significantly improved seizure control, was well tolerated with a favorable neurocognitive AE profile, and may benefit patients with epilepsy.

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p115 PRESCRIBING PATTERNS OF ANTIPILEPTIC DRUGS AND INTERACTION RISK IN GENERAL PRACTICE

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Purpose: The aims of this study were: to analyze the prescribing pattern of newer and older antiepileptic drugs (AEDs); to assess the exposure to potential drug-interactions in a general practice setting.

Patients and Methods: On a population of 150,000 individuals we identified patients who received AED prescriptions during 2005–2011. One-year prevalence and incidence of use and global AEDs consumption were calculated. The risk of drug interactions was calculated as overlapping days between the exposition days of AEDs and interacting drugs. Interacting drugs have been identified according to the Drug Interaction Fact.

Results: Prevalence of older AED use slightly increased during the study period, while a strong increase of newer AED use was observed until 2006, followed by a deep fall in 2011. Among older AEDs, phenobarbital and valproate were the most widely used in 2011, accounting for 21.2% and 16.2% of total AED consumption. In the same year, oxcarbazepine and lamotrigine were the most used new AEDs (10.9% and 10.8% respectively), while gabapentin and pregabalin exhibited the higher incidence of use. The main indication of use was epileptic disorders for older AEDs and neuropathic pain for newer AEDs. A high number of patients treated with older AEDs, received co-prescription at clinically relevant interaction risk. Among newer AEDs, topiramate showed the highest annual rate of possible interactions.

Conclusion: Significant differences were shown in the prescribing pattern of newer and older AEDs. A not negligible patients exposition to potential clinically relevant drug-interactions was shown. The co-prescription of drugs at risk of interaction with AEDs should be evaluated with caution or avoided, if possible.

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Purpose: To evaluate in a real life-setting efficacy, tolerability and dosage-response with lacosamide (LCM) considering patients on a LCM dose ≤400 mg.

Method: LACO-EXP was a multicenter (13 hospitals), retrospective, 1-year, real-life study. The inclusion criteria were:

1. Patients older than 18 years
2. Partial-onset seizures;
3. LCM initiated between September 2009 and November 2011 as add-on therapy;
4. At least 1 partial seizure/year.

In this subanalysis patients on a LCM dose ≤400 mg were studied and a dose-response analysis was performed. The population was divided into two groups: low dose group (LDG) those that received a LCM dose of ≤200 mg and high dose group (HDG), those given doses of >200 mg to 400 mg.

Results: In total 474 patients (≤400 mg LCM dose) were studied. Retention rate was 96% (3 months), 88% (6 months) and 83% (12 months) and 7.2% added a new antiepileptic drug (AED). The responder rate was 44.7% (3 months), 53.6% (6 months) and 57.3% (12 months) and seizure-free rate was 16.5% (3 months), 16.2% (6 months) and 15.5% (12 months). LCM-related adverse events (AE) occurred in 39.5% (9.7% led to discontinuation). The most frequent AE was dizziness (19.4%). Regarding the dose-response analysis, seizure-free rate at 12 months was 33.0% (LDG) and 10.3% (HDG) (p < 0.001) and responder rate was 59.4% (LDG) and 56.7% (HDG) (p = 0.61). LCM-related AE occurred in 43.1% (LDG) and 38.3% (HDG) (p = 0.35). In the LDG there were more patients that had tried up to 2 AED before LCM (42.4%) than 3 or more AED (19.7%).

Conclusion: The addition of LCM ≤400 mg in patients with partial-onset seizures was effective and well tolerated over 1 year. Efficacy and tolerability profile was good regardless of the dose. A tendency to use lower dosage in less refractory patients was observed.

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EFFECTS OF OCXARBAZEPINE AND LEVETIRACETAM AS A MONOTHERAPY ON CALCIUM AND VITAMIN D METABOLISM

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Purpose: To determine changes in calcium, ionized calcium and vitamin D concentrations induced by monotherapy treatment with oxcarbazepine and levetiracetam.

Method: Serum calcium, ionized calcium and vitamin D concentrations were studied in 48 patients who had been receiving oxcarbazepine or levetiracetam monotherapy for at least 6 months and 42 healthy individuals. In patients groups, the duration of drug use, daily drug dosage, also evaluated.

Results: In patients receiving oxcarbazepine, serum calcium, ionized calcium and vitamin D concentrations were lower than in those receiving levetiracetam and control group. Patients who are receiving levetiracetam, serum calcium, ionized calcium and vitamin D concentrations did not differ from the control group. However levetiracetam daily dosage was found to have a significant effect on ionized calcium.

Conclusion: Our results suggested that oxcarbazepine affects serum calcium, ionized calcium and vitamin D concentrations, but levetiracetam monotherapy has no negative influence on serum calcium and vitamin D metabolism. Therefore we suggest that bone metabolism should be monitored in patients receiving especially oxcarbazepine monotherapy.

p118
LEVETIRACETAM AS ADD-ON DRUG IN INTRACTABLE EPILEPSY: A TUNISIAN MULTICENTER STUDY

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Purpose: Levetiracetam has been authorized for use in Tunisia as an add-on therapy for intractable epilepsy since 2011. The aim of the present retrospective study is to document its effectiveness for this indication in a cohort of Tunisian and Libyan patients with intractable epilepsy in two epilepsy centers.

Method: The medical files of 38 patients aged 6–82 years (mean, 34.2 years) were reviewed. All received levetiracetam as add-on therapy following a failure to respond to at least 2 anti-epileptic drugs.

Results: Patients (62%) had partial epilepsy and the remainder had generalized epilepsy. The epilepsy was symptomatic in 57%, idiopathic in 26% and cryptogenic in 14%. Average age at first seizure was 14.1 years. In 45% of patients, the number of seizures was reduced by half with levetiracetam treatment; 11.5% of the cohort achieved complete remission. The drug was well tolerated. The most common adverse effects were irritability and impulsiveness, in 20% of patients.

Conclusion: Levetiracetam is an effective and tolerable add-on agent for use in most epileptic patients who fail to respond to at least 2 antiepileptic drugs and should be the treatment of choice in this setting.

p119
ADJUNCTIVE PERAMPANEL IN HIGHLY DRUG-RESISTANT LOCALIZATION-RELATED EPILEPSY – A PROSPECTIVE AUDIT

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Purpose: When a new antiepileptic drug (AED) is licensed, the only available information on its use comes from placebo-controlled, randomized clinical trials. This interim analysis explores initial outcomes from a prospective audit with perampanel (PER), a novel, highly selective, non-competitive AMPA-type glutamate receptor, as adjunctive treatment in drug-resistant localization-related epilepsy.

Method: After 12 weeks on stable AED dosing, PER was introduced and titrated in patients with ongoing seizures despite AED treatment. Review took place every 6–8 weeks until 1 of 4 end-points was reached: seizure freedom for ≥6 months on a given PER dose; ≥50%, or ≤50% seizure reduction over 6 months compared with baseline on the highest tolerated PER dose; withdrawal of PER due to lack of efficacy, side effects, or both.

Results: To date, 22 of 41 recruited patients (28M: 13F, age range 23–65 years [median 48 years]) have reached an endpoint. At baseline, monthly seizure frequency was 1–60; [median 4], and patients received a median of 2 (range 1–4) AEDs, having previously tried 1–
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INFLUENCE OF ANTIEPILEPTIC DRUGS IN THE LIPID PROFILE OF VASCULAR EPILEPSY
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Purpose: This study aims to describe differences in the lipid profile, between patients with vascular epilepsy taking classic (c-AED) and new generation antiepileptic drugs (n-AEDs).

Method: We retrospectively recruited 200 patients with vascular epilepsy who had been on stable AED treatment for 1 year or longer, in whom the lipid profile was determined. Patients were classified as c-AEDs, when taking CBZ, VPA, PHT or PB in mono- or polytherapy, and n-AEDs when taking some of the other AEDs.

Results: The average age was 59.5 years, range from [16 to 91], 60% were men. The causes were ischemic strokes 58%, arteriovenous malformations 17%, hemorrhages 16% and cavernomas 8%. The average total cholesterol was significantly higher in patients treated with c-AEDs (204.7 mg/dl) than in the group of n-AEDs (191.6 mg/Dl) (p < 0.02). Same observation was seen for Low-Density-Lipoprotein-Cholesterol (c-AED: 126.1 mg/dl vs. n-AED: 113.3 mg/dl) (p = 0.02). When these findings were adjusted considering confounding factors such as age, background lipid lowering drugs and sex, patients treated with n-AEDs remained with lower total cholesterol and LDL-c levels than the group of c-AED (p < 0.05). No significant differences were found in the triglyce-rides or HDL levels.

Conclusion: Newer AEDs are associated with a better lipid profile than the classic AEDs, fact to take into consideration in a special population such as the vascular epilepsy patients.

p121
MECHANISM OF HYPOURICEMIA INDUCED BY CARBAMAZEPINE IN A GIRL WITH ROLANDIC EPILEPSY
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Purpose: Previous reports have described hypouricemia in epileptic patients treated with phenytoin and carbamazepine (CBZ), but the underlying mechanisms remain uncertain. Serial case studies are indicated to clarify the mechanisms of CBZ-induced hypouricemia.

Method and Results: A 10-year-old girl with rolandic epilepsy was referred to our outpatient clinic. She had been treated with CBZ for 3 years. Decreased serum urate levels (1.9 mg/dl; normal range, 3.9–7.2 mg/dl) and increased urate excretion rate (15.72%; normal range, 4.0–12.3%) had been identified in routine blood chemical examinations and urinalysis; however, she was asymptomatic and therefore received no treatment. At 13 years old, rolandic discharges disappeared on electroencephalography, and no epileptic fits had been seen after the introduction of CBZ. Medication with CBZ was subsequently ceased. Serum urate level and urate excretion rate normalized to 3.4 mg/dl and 9.22%, respectively.

Conclusion: We encountered a 13-year-old girl with rolandic epilepsy who showed hypouricemia during treatment with CBZ. Hypouricemia disappeared after discontinuation of CBZ, in association with normalization of the increased fractional excretion of uric acid (FE-UA). The mechanism of CBZ-induced hypouricemia may thus involve increased FE-UA and CBZ-induced hypouricemia appears reversible. As this evidence for the mechanism of CBZ-induced hypouricemia involved only a single case, a prospective study is warranted to clarify this potential mechanism.

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p123
SENSORINEURAL HEARING LOSS AFTER ADMINISTRATION OF SODIUM VALPROATE
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Purpose: To describe ototoxicity related to administration of sodium valproate for the treatment of epilepsy.

Method: This report describes a 9.5 year-old girl with Jeavons syndrome without evidence of pre-existing hearing disorder and normal speech and language development, who presented with sensorineural hearing impairment after sodium valproate administration. Absences were fully controlled at a dose of 18.5 mg/kg/day of the sustained release formulation (serum level 45 μg/ml) and myoclonic jerks were significantly reduced at 34.8 mg/kg/day (serum level 115 μg/ml). Seven months after treatment onset, a sensorineural hearing impairment was diagnosed that was bilateral and of a significant degree. A thorough investigation, including neuroimaging, ruled out various etiologies of hearing loss in this age group. Valproate toxicity was among the rare causes of acquired hearing loss and a change of antiepileptic treatment was deemed necessary.

Results: Two months after discontinuation of valproate and its replacement by levetiracetam, a significant improvement of hearing was ascertained through repeated audiometric studies. The patient remains under close F/U.

Conclusion: Ototoxicity may be rarely associated with valproate, considering the extensive use of this drug in the treatment of epilepsy and psychiatric disorders. It has been rarely reported before (in two adults >70 years old, with pre-existing presbyacusia and a 9 year-old child with severe congenital hearing deficit). It may be severe and reversible. Yet, the role of the epilepsies in altering hearing thresholds has not been clarified.

p124
TOLERABILITY AND EFFECTIVENESS OF PERAMPANEL IN TREATMENT OF PATIENTS WITH PHARMACORESISTANT EPILEPSY
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Purpose: Since September 2012 Perampanel is available in Germany as adjunctive therapy in partial epilepsy. We report our experiences with Perampanel with respect of effectiveness and tolerability in treatment of pharmacoresistant epilepsy.

Method: 60 consecutive Patients were treated with Perampanel on an open label, combined in-and outpatient base. 50 Patients (28 men, age 24−68, mean 40.0 years), with a follow up of more than 26 (mean 51) weeks were included in the analysis.

All patients suffered from pharmacoresistant epilepsy (41 partial, 5 IGE, 4 LGS, 1 PME). 45 had antiepileptic polytherapy (2 or more AEDs), 19 had VNS, when Perampanel was titrated as recommended (2 mg/2 weeks or slower) add-on, the mean therapeutic dose was 6.8 mg/day (range 2−18 mg/day).

Results: 28 Pat. had no change of seizure frequency, 10 had a 25%-reduction, 7 of 50%, 5 of 75%, 1 Patient became seizure free.

Side effects occurred in 22 Pat. 14 reported a cerebellar toxic syndrome (thereof 8 within 1 h after drug intake), in 5 patients disturbances of behaviour or weight were reported. 3 had a marked increase of body weight. Co-medication with an enzyme inductor (CBZ, PB, PHT, 18 Pat.) had no influence on frequency or type of side effects.

Conclusion: Perampanel was mostly well tolerated even in patients with polytherapy. Enzyme-inductors in comedication seemed not to have a marked effect on the tolerability, despite of reported fluctuations of Perampanel-serumlevels when enzyme-inductors are taken.(Gidal 2013) No serious side effects were seen (mean follow-up 51 weeks).

13 of 50 Pat. (26%) showed a response of more than 50%. This is near the results of blinded studies with Perampanel. In our open-label study we also were able to prove favourable effects in patients with IGE, LGS and in 1 Patient with Progressive Myoclonus-epilepsy.

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PERAMPANEL AND RUFINAMIDE SHOW COMPARABLE INITIAL EFFECTIVENESS AND TOLERABILITY IN PEDIATRIC PATIENTS WITH REFRACTORY EPILEPSIES – FIRST EUROPEAN EXPERIENCES AFTER MARKETING
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Purpose: In the past we have conducted two non-sponsored observational surveys with a parallel design, concerning initial effectiveness and tolerability of rufinamide (RUF) and perampanel (PER) in pediatric patients with refractory epilepsies, after the marketing of these drugs. Here, we compare the data of these two new drugs.

Methods: The surveys were conducted through collaborations with multiple centers in Germany, Austria and Denmark, and collected retrospective data on the first pediatric patients treated with PER and RUF. Initial dosage and titration schedule were at the discretion of the treating physician according to medical need.

Effectiveness was evaluated by comparing the seizure frequency between baseline and a 4-week-period 3 months after initiation. Adverse effects were evaluated by the treating physician.

Results: The study populations comprised 59 patients for PER (mean age: 10.6 years; range: 2–17 years) and 60 patients for RUF (mean age: 14.5 years; range: 1−50 years, including 15 adult patients), suffering from various refractory epilepsies.

The response rates (≥50% seizure reduction) were 32% (19/59) for PER and 47% (28/60) for RUF. Complete seizure control was achieved in 10% (6/59) with PER and in 8% (5/60) with RUF. In the subgroup of idiopathic epilepsies, there was a significant difference between the response rates (PER 2/11, RUF 4/5; p < 0.05, Chi-square).

Adverse effects were reported in 49% (29/59) for PER and 58% (35/60) for RUF. Most adverse effects, however, were mild-moderate, remitting spontaneously or with dose reduction.
**Conclusion:** In these heterogeneous groups of therapy-refractory epilepsy cases, PER and RUF show similar effectiveness and tolerability. In the subgroup of idiopathic epilepsies, RUF might show superior effectiveness.

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**EFFICACY AND TOLERANCE OF PERAMpanel IN PHARMACORESISTANT EPILEPSY IN CHILDREN AND YOUNG PEOPLE**

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**Purpose:** To study the efficacy and tolerance of Perampanel in pharmacoresistant epilepsy in children.

**Method:** Retrospective observational study of eighteen children with pharmacoresistant epilepsy who were treated with Perampanel as an add-on. The data was collected by case note review and telephonic interviews.

**Results:** Eighteen children were treated with Perampanel as an add-on antiepileptic drug (AED). 11 were male and 7 were female. The age range was 4–19 years, with a mean age of 17 years and mode of 14 years. The age of onset of epilepsy ranged from 1 to 10 years with a mean of 2.7 years. 9 had structural/metabolic, 8 had unknown etiology of their epilepsy and 1 had identified genetic etiology. At the time of adding Perampanel, the mean number of concurrent AEDs was 2.7. Five patients had VNS, four were on Ketogenic diet in the past. These patients had a mean exposure to Perampanel for 3.7 months (range 1–7 months). 2/18 (10%) became seizure-free. 8/18 (45%) achieved more than 50% seizure-reduction. 1/18 had <50% reduction in seizure-frequency. 6/18 had no change in seizure-frequency or severity. One patient reported increased seizures; however, this patient has a progressive epilepsy and continues to have increased seizures even after stopping Perampanel. 10/18 patients reported no side-effects, four reported dizziness which resolved with lowering of dose. 2 were more sleepy which improved spontaneously and 1 had behavioral change. 2/18 patients discontinued Perampanel either due to adverse effects or lack of efficacy (worsening).

**Conclusion:** In our cohort, Perampanel appears to be an effective AED in pharmacoresistant epilepsy in children and is well-tolerated. It is effective in focal and generalized epilepsy. Relatively short duration of follow-up and retrospective nature of our study are some obvious limitations but initial results seem promising.

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**EFFICACY AND TOLERABILITY OF ZONISAMIDE AS AS FIRST ADD-ON THERAPY TO VALPROATE IN INDIAN ADULT POPULATION: A SUBANALYSIS**

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**Purpose:** Zonisamide as first add-on therapy to valproate in epilepsy - an efficacy and tolerability evaluation in Indian adult population.

**Method:** In this prospective, open-label, non-comparative, multicentric, observational study, zonisamide (100–400 mg) was given as first add-on to valproate for 24 weeks in patients having partial, generalized or combined seizures. Seizure frequency, CGART and PGATT were assessed every 4 weeks. Primary outcome was reduction in seizure frequency and secondary outcomes were responder rate and seizure freedom over 24 weeks. Friedman’s test was used to analyse the change in seizure frequency from baseline.

**Results:** 97 out of initially enrolled 110 patients completed the study. After using zonisamide as first add-on, a progressive and significant decrease (p < 0.0001) was seen in seizure frequency at each subsequent follow up visit, compared to the baseline, with maximum decrease seen at week 24 (mean change from baseline = −4.31; 95% CI −5.54 to −3.09; change −93.68). 24 week seizure freedom and responder rate was seen in 33.64% and 95.45% patients respectively. 86.6% patients showed excellent to good response (CGART) and 91.76% showed excellent to good tolerability (PGATT) to zonisamide therapy at week 24. Most common adverse events were weight loss (5/110 patients), loss of appetite and sedation.

**Conclusion:** Zonisamide as once daily dosing and minimal drug interaction with valproate improves compliance and is an effective treatment option to be used as a first add-on therapy to valproate in treatment of partial, generalized and combined seizures.

**p128**

**TRANSIENT LESION IN THE SPLENIUM OF THE CORPUS CALLOSUM ASSOCIATED WITH CARBAMAZEPINE: A CASE REPORT**

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**Purpose:** Although focal lesions in the splenium of the corpus callosum registered with brain MRI are relatively rare, they have been reported in patients with epilepsy, but also in non-epileptic patients after administration or rapid discontinuation of predominantly conventional antiepileptic drugs. Pathogenesis of this transient, asymptomatic and isolated lesions is still unclear. Different pathophysiologic hypotheses have been suggested, as toxicity of AEDs, the effects of the AEDs on the arginin-vasopressin and fluid-electrolyte imbalance by rapid AED discontinuation and possible cytotoxic edema secondary to seizure spread.

**Method:** We present a 27-year-old male patient who started getting complex partial seizures of lateral temporal lobe origin without secondarily generalisation at the age of 26. Initially carbamazepine (CBZ) at the dose 800 mg twice daily was prescribed. Seizures persisted with frequency of once per month. MR imaging showed oval lesion in the splenium of the corpus callosum which was hypointense on FLAIR and T2 – weighted MR images.

**Results:** Due to hepatal lesion caused by CBZ, the therapy was switched to 1,200 mg of oxcarbazepine (OXC) and 200 mg of lamotrigine (LTG). A few weeks afterwards AEDs control MR imaging was performed and previously identified lesion of the splenium had disappeared.

**Conclusion:** We report our first case in Croatia of transient lesion of the splenium corporis callosi after several months of carbamazepine administration with complete regression after introduction of OXC and LTG.
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EFFICACY OF CONCURRENT APPLICATION OF CARBAMAZEPINE AND OXCARBAZEPINE IN THE TREATMENT OF PHARMACORESISTANT EPILEPSY PATIENTS – A RETROSPECTIVE STUDY
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Purpose: Carbamazepine (CBZ) and oxcarbazepine (OXC) are mainly voltage-dependent sodium channels blockers, however from the pharmacodynamic’s and pharmacokinetic’s point of view they are not identical medications. Therefore, their simultaneous application should be considered in pharmacoresistant patients. We performed a retrospective study with the aim of determining the efficacy, optimum doses and safety of concurrent application of CBZ and OXC in the treatment of pharmacoresistant patients with complex partial seizures with or without secondary generalisation.

Method: 24 patients were included in the period from 2009 to 2013, 13 men and 11 women. All patients had pharmacoresistant partial epilepsy, with or without secondary generalization. The mean age of the patients was 40.39 ± 15.97 years, the average duration of illness was 23.65 ± 17.62 years, and the mean follow up period was 23 months, with first efficacy evaluation after 6 month of drugs administration. The average CBZ dose was 800 mg and of OXC 1,000 mg.

Results: Statistical analysis was done by using the STATISTICA program package. Reduction in number of seizures for ≥50% was registered in 8 patients, 3 of them were seizure free, in 8 patients reduction for ≤50% was noted and 8 patient showed no improvement. Statistically significant relation was found between the higher OXC doses and higher percentage of seizure reduction.

Conclusion: Our study has demonstrated the efficacy and safety of combined CBZ and OXC therapy, notably in pharmacoresistant partial epilepsy with significant reduction of seizures in 66.7% patients, i.e. the reduction of seizures from 25% to 100%. The application of lower doses, which leads to better tolerance of both drugs enables the avoidance of side effects.

p130
OUR EXPERIENCE OF LACOSAMIDE FOR DRUG RESISTANT EPILEPSY AT THE BURDEN CENTRE – A TERTIARY NEUROPSYCHIATRIC SERVICE
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Purpose: Lacosamide is an AED used as an adjunct for partial onset seizures approved by the EU in 2008. It is thought to act through enhancing voltage-dependent sodium channels blockers, however from the pharmacodynamic’s and pharmacokinetic’s point of view they are not identical medications. Therefore, their simultaneous application should be considered in pharmacoresistant patients. We performed a retrospective study with the aim of determining the efficacy, optimum doses and safety of concurrent application of CBZ and OXC in the treatment of pharmacoresistant patients with complex partial seizures with or without secondary generalisation.

Method: We assessed a neuropsychiatric consultant caseload by analysing those prescribed Lacosamide as service evaluation for:

Seizure type, Intellectual Disability (ID), Gender, Total years of Epilepsy, dosage, seizure control, length of treatment, Emergency admissions.

Results: Of 50 patients on Lacosamide, highlights included:

1 Seizure type: CPS (92%), GTS (34%), Absence (22%), Tonic (20%)
2 ID: 58% Male 42% Female 40%
3 Mean years of epilepsy: 32
4 Maximum (average) dosage: 300 mg daily
5 Graph of post-treatment seizure reduction
6 Mean treatment: 28 months
7 Emergency admissions past year: 10%

Conclusion: Most patients had complex partial seizures. Just over half had ID. Gender was evenly balanced and most patients had a longstanding history of epilepsy.

Dosages prescribed were within therapeutic range and tolerated for over 2 years (average).

Our experience suggested that although seizure freedom was not achieved, seizure reduction occurred in many patients. A minority needed emergency hospital admission in the previous year.

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EFFECTIVENESS AND TOLERABILITY OF HIGH DOSE ESLICARBZEPINE
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Purpose: To determine the efficacy and safety of high dose eslicarbazine in pharmacoresistant epileptic patients.

Method: Data was collected from a retrospective registry of patients with partial epilepsy, with and without secondary generalized seizures, who were resistant to treatment. These were divided into two groups – one receiving normal dosage of eslicarbazepine and the other with high doses (≥1,600 mg/día), both with a 6 month follow up.

Results: 34 patients received normal dosage of eslicarbazepine with a mean age of 40.9 years, 61.8% (21) were women, and a mean time period of disease of 21 years. Before starting treatment the mean seizure frequency was 8.9/month and after 6 months of treatment reduced to 5 seizures/month. The commonest side effect was somnolence (5.9%). Ten patients were treated with high dose, with a mean age of 45.4 years, and mean time period of disease 21.4 years. 70% were men. Previous to starting treatment the mean seizure frequency was 11.1/month and after 6 months was 6.2, signifying a 56% reduction in seizure frequency. The commonest side effect was also somnolence (10%), with other side effects not warranting drug withdrawal. The reduction of seizure frequency was statistically significant (p = 0.012) in patients receiving high dose eslicarbazine.

Conclusion: The use of high dose eslicarbazine in pharmacoresistant patients with partial epilepsy was shown to be effective and safe, with few side effects which were mostly mild and tolerable.

p132
GALCICO STUDY: 6 MONTHS EXPERIENCE WITH LACOSAMIDE FOR FOCAL EPILEPSIES IN GALICIA, SPAIN
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doi: 10.1111/epi.12675
Purpose: Lacosamide (LCM) is a sodium channel blocker approved as adjunctive treatment for refractory focal epilepsies in 2008. Efficacy has been shown in addiction to non-channel blockers and classical channel blockers, however its adverse effects are higher in this second group.

Method: Prospective observational study performed in 10 hospitals in Galicia (Spain) from November 2012. We analyzed demographic characteristics, efficacy (reduction of >50% of seizures), concomitant AEDs and safety of patients treated with LCM after 6 months. Statistical analysis was performed with SPSS 19.0. A value of $p < 0.05$ was considered significant.

Results: From 183 patients, $N = 174$ completed the 6 months follow-up. Mean age was 44.8 ± 17.3 years old. 55.7% were males. Mean duration of epilepsy was 18.4 ± 15.4 years. 34.1% had cryptogenic epilepsy. Predominant location was temporal (47.5%). Median monthly seizure frequency before LCM was 2.3 [1, 5]. 43.1% of patients were being treated with 2 AEDs and 29.8% with one. The most frequent combination was a sodium channel blocker and a non-sodium channel blocker (32.7%). Mean number of AEDs previously tried was 4.1 ± 2.5. After 6 months, 64.9% of patients were responders and 33.9% were seizure free. 20.2% of patients referred adverse effects being dizziness (9.8%) and instability (3.8%) the most frequently reported. $N = 172$ patients (98.9%) continue with LCM. Concomitant AEDs were significantly reduced from 2.1 ± 1.0 to 1.8 ± 0.8 ($p < 0.001$). Dosage was also significantly diminished for CBZ, ESL, LMT, OXC, PHT, CLB, LEV, ZNS and VPA ($p < 0.05$).

Conclusion: LCM is safe and efficient in patients with refractory epilepsy. High percentage of responders may be due to a less refractory population (seizure frequency, previous and concomitant number of AEDs). Thus it could be considered an early medical treatment for focal refractory epilepsies. Longer follow-up is needed to certify this early response to LCM.

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Abstracts

(32.3%). Adverse events (AE, n = 31) occurred in 18 patients (7 serious AE in 5 patients). The most commonly reported AE were headache and fatigue; bodyweight loss was reported only for one patient. Seizure-freedom over the observation period was high and reported for 43.6% of the patients.

Conclusion: These findings support the view that ZNS is well tolerated and efficacious as only add-on with a high retention rate in clinical practice.

p135
LIMITED BENEFIT OF PERAM PANEL IN INSTITUTIONALIZED COGNITIVELY IMPAIRED PATIENTS WITH HIGHLY THERAPY-RESISTANT EPILEPSY
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Purpose: The aim was to evaluate the efficacy and tolerability of Perampanel in cognitively impaired patients with highly therapy-resistant epilepsy.

Method: Retrospective evaluation including all in-patients (N = 26, aged 21–54 years) treated with Perampanel since its introduction in September 2012. Most have borderline intelligence or mild cognitive impairment. Most suffer from a focal epilepsy. Perampanel was administered as additional treatment with 2 or more other AED.

Evaluation was carried out after 6 month of treatment with Perampanel.

Evaluation parameter for efficacy was the monthly seizure frequency in a 3 month treatment period after 3 month of titration compared with a 3 month baseline period. Tolerability was analyzed by clinical data. Additionally the clinical global impression scale (CGI) was applied.

Results: By key date (15 December 2013) 17 patients were evaluable, 9 started treatment after 15 June 2013. The Perampanel dose ranged from 4 to 10 mg (median 6 mg) per day. The retention rate after 6 months was 53% (9/17). In the majority of these cases there was no change (6) or an increase in seizure frequency (1) after 6 months of treatment. 2 patients (12%) were responders (>50% seizure reduction and a very good effect on CGI). Reasons for discontinuation were psychological adverse effects in 4 patients and an increase in seizures in 3 patients, one patient had both. Psychological symptoms which led to terminate treatment were acute suicidal tendency (2), depression with suicidal ideation (1), mood instability (1) and agitation (1). Other side effects reported were dizziness (5), feeling unwell (1) and blurred vision (1).

Data on all of the 26 patients will be presented in Stockholm.

Conclusion: In this highly selected population the benefit of Perampanel was moderate, the high rate of psychological side effects was remarkable.

p136
EFFECTS OF PRENATAL ANTIEPILEPTIC DRUG EXPOSURE ON NEWBORN BRAIN ACTIVITY
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Purpose: Prenatal exposure to antiepileptic drugs (AEDs) is associated with an increased risk of neurodevelopmental problems, however the underlying mechanisms are poorly understood. This study was designed to investigate whether prenatal AED exposure affects the quality of neonatal brain activity measured by EEG.

Method: Pregnant women (n = 48) with epilepsy treated with AEDs were recruited in the Helsinki area. Fullterm babies from these pregnancies born between 4/2010 and 9/2013 were compared to a cohort of newborns (n = 54) unexposed to AEDs or other neurotoxic drugs. The EEG was recorded during daytime sleep at 41–42 weeks of conceptional age. The EEG was assessed both visually and by using a custom-scripted detection algorithm. We focused on measuring the known neonatal oscillatory activities (bouts) at theta (temporal [TT] and frontal [FT] areas) and alpha (frontal [FA]) frequencies during active sleep. We counted their number visually, while computerized analysis defined the average duration of single bouts and their proportional duration within the record.

Results: Both the visual and automated analysis showed that the oscillatory bouts at theta frequency (TT, FT) were comparable in the study groups, and visual analysis found no difference in alpha range either. However, the average duration of FA bouts was slightly but significantly (p = 0.035) longer in the newborns exposed to AEDs (mean 0.47 ± 0.017s [SEM]) as compared to the control newborns (mean 0.44 ± 0.013 s).

Conclusion: The use of AEDs during pregnancy has very little effect on the oscillatory activities in the neonatal brain. The mechanisms or physiological significance of frontal alpha frequency activity in the newborn is unknown, hence the upcoming follow-up of this cohort may offer insights into the neurodevelopmental significance of frontal alpha oscillation in newborns.

p137
EFFECTIVENESS AND TOLERABILITY OF PERAM PANEL IN PATIENTS WITH REFRACTORY PARTIAL EPILEPSY IN A TERTIARY EPILEPSY CENTRE
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Purpose: Perampanel was licensed in the UK in October 2012 and has been studied in several placebo controlled phase 3 studies. We present our own experience from our specialist epilepsy service which usually differs from controlled studies.

Method: Retrospective analysis of the safety and efficacy of perampanel in 60 patients with refractory partial epilepsy seen in a tertiary epilepsy centre.

Results: 60 patients (35 males, 25 females) treated with perampanel between October 2012 and December 2013 were included with median age 40 year (18–77 year), median age of epilepsy onset 10.5y (0–55 year), median epilepsy duration 24 year (3–76 year). Common comorbidities included learning disability (19%) and depression (15%). The median number of concomitant AEDs was 3 (range 1–5), most frequently levetiracetam and lacosamide. The number of previous AEDs ranged from 2 to 12 (median 5). The daily perampanel dose range was 2–12 mg (median 6 mg). 31/60 (52%) patients experienced secondary generalised seizures (SGTS). The median duration of treatment was 150 days (14–418 days) retention rate 75%. Ten patients (17%) became seizure-free (min follow up 3 months). Seizure frequency was reduced by ≥50% in 16/60 (27%) of all patients. In the SGTS subgroup, 27% of patients experienced ≥50% reduction of SGTS. In those with partial seizures only ≥50% reduction in seizure frequency was seen in 27%. Adverse events were reported by 37% of patients, most commonly dizziness (27%), unsteadiness (17%), behavioural disturbance (8%). Clinical global impression was one of improved seizure control in 29/60 (48%) of patients.
Conclusion: Our cohort provides an insight into the role of perampanel in refractory chronic partial epilepsy following a failure of multiple previous AEDs. Perampanel rendered 17% of these patients seizure-free and has been associated with a clinical patient improvement in almost 50% of our cases. This study was supported by an unrestricted educational grant from Eisai Ltd.

Method: Preliminary data is presented on 36 patients the three epilepsy centres in South Wales using a standardised evaluation tool.

Results: The combined cohort numbered 36 patients with refractory epilepsy, with a mean duration of 22 years, mean concomitant AED medication of 2.1 and previous AED mean of 5.8. Mean duration of perampanel use was 134 days (range 6–431). Titrations commenced at 2 mg every 2 weeks across the centres. Patients experiencing adverse effects (AE) could opt to slow titration further. In one centre, all patients were maintained on 4 or 6 mg for at least 4 weeks. There were no withdrawals from perampanel in this centre. The overall retention rate in our study was 75% with a 66.7% responder rate (>50% total seizure reduction). The remaining 27 patients have a mean duration on perampanel of 141 days. Of the 9 patients who withdrew drug, 5 reported AE and 4 reported either lack of efficacy or a perceived increase in seizures. Overall 16 patients to date (44%) have reported AE including 48% of those who remain on perampanel.

Conclusion: In this real-life evaluation we found high rates of retention of perampanel (100%) in the slowest titration group. The evidence suggests that slow titration may be advantageous in maintaining patients on perampanel. Despite high reports of AE, the majority of patients opt to continue perampanel suggesting patients become tolerant to AE. Preliminary efficacy data is encouraging. The evidence suggests perampanel may be a useful adjunctive AED in refractory epilepsy.

Method: Adult patients with uncontrolled POS under antiepileptic monotherapy for whom the physician had independently decided to initiate ESL add-on therapy were offered participation in this non-interventional study upon providing informed consent. The results of an interim analysis of the open-label non-interventional study EPOS presented.

Results: The mean age was 45.3 ± 16.5 years; 59.6% were male. The median time since first diagnosis of epilepsy was 9.5 years. The median of seizure frequency over 3 months prior to baseline was 6.0. At 6-months, retention rate was 82.6%. The mean ESL daily dose after titration was 907.1 mg/ml 16 h after the last dose.

Conclusion: ESL as add-on to antiepileptic monotherapy is retained and well-tolerated by the majority of adult patients in a real-life population.
p141
PERAMPANEL AND CORTICAL EXCITABILITY: A TRANSCRANIAL MAGNETIC STIMULATION STUDY
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Purpose: Perampanel is a new antiepileptic medication that acts on the α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) glutamate receptor. We used Transcranial Magnetic Stimulation (TMS) to assess the effect of perampanel on cortical excitability in people with epilepsy.

Methods: Four people with epilepsy were tested with TMS before and after initiation of perampanel. All patients were taking 2 or more concurrent antiepileptic medications, which were unchanged during the testing period. Intracortical facilitation was measured; a subthreshold TMS pulse to the motor cortex is given 10–15 ms before a suprathreshold pulse. The resulting motor evoked potential is facilitated compared to that evoked by a single pulse. This process is known to be mediated by glutamate receptors.

Results: Three of four patients showed a statistically significant reduction in intracortical facilitation following introduction of perampanel (p < 0.05, paired, one-tailed T test) while one showed only a trend in this direction.

Conclusion: These results support perampanel’s proposed mechanism of action on AMPA receptors, and show that it has a measurable effect on cortical excitability in people with epilepsy, which may be useful for drug-based studies, including pharmacogenomics.

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p142
EPILEPSY CO-MORBIDITY IN ADULT PATIENTS
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Object: Thirty-five patients with epilepsy in coexistence with other pathologies as their complication or not, whose were admitted in the last year at our service of Neurology or as outpatient diagnosed, aged from 16 to 89 years (mean of 39 years), from whom 24 female 68.6% and 11 male 31.4% were analyzed retrospectively. Beside one patient presenting at an acute comorbid condition and others two with subacute of monthly duration, all remained patients reported chronic diseases of years duration from 2 to 45 years (mean approximately of 20 years) coincidental with epilepsy.

The common coexistence diseases were joined in two major branches; in systematic co morbidities and in neuropsychiatric co morbidities. Among the first group, seizures co occurred with rheumatologic disorders in 20% (14% LED, 3% AR, 5% mixed collagenosis) or hematologic disease in 8% (LLA, KID, NHL), metabolic pathologies as Fahr disease in 6%, neuroinfection of cysticercosis and atraumatic vertebral fractures in osteoporosis with 3% respectively.

Among the neuropsychiatric co morbidities; 29% presented other neuropsychiatric disorders; 11% headache, Parkinson and Multiple Sclerosis with 6% correspondingly or HSMN and Sturge Weber as well with 3%. Whereas the remained 31% with psychiatric specialties they were diagnosed with 8.5% Bipolar disorders, MR and major depression correspondently with 6%, schizophrenia, interictal psychotic disorder, Down or ADHD with 3% retrospectively.

As for the type of coexistent epilepsy; 16.5% TLE, 26% FLE, 26% generalized epilepsy with immediate onset, 20% posterior epilepsy secondary generalized, 8.5% opercular epilepsy (1 SE), 3% NCSE with hemi facial myoclonic seizures.

Conclusion: The systematic co morbidities were less occurred with epilepsy mostly the former as their complication in 40% of cases, compared to other neuropsychiatric disorders 60% (neurologic 29%; psychiatric 31%). FLE and generalized epilepsy were the most reported types whilst female were most affected than man.

p143
SPREADING DEPRESSION ENHANCES NEUROGENESIS IN HIPPOCAMPUS AND DENTATE GYRUS OF WAG/RIJ RATS
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Purpose: Spreading depression (SD) known by transient loss of spontaneous and evoked neuronal activity and changes in ionic, metabolic and hemodynamic characteristics of the brain. SD plays an essential role in some neurological disorders including migraine with aura, epilepsy, and cerebrovascular disease. Neuronal damage followed by SD, supposed to have a dramatic impression on SD-derived pathologic conditions. We aimed to determine whether SD is able to stimulate persistent neurogenesis in WAG/Rij rat as a model for absence epilepsy.

Method: WAG/Rij rat (60–80 g) randomly chosen and 3 m KCl injected for induction of SD. Four weeks after the first injection, all rats were decapitated and the brains removed. The density of mitotic cells, divided cells, and new neurons in the pyramidal cell layer of hippocampal CA1 and CA3 and granular cell layer of dentate gyrus was assessed. We also detect the DNA during the S phase using Bromodeoxyuridine (BrdU).

Results: A remarkable increase occurred in the number of BrdU-labeled cells in hippocampal region, detected by immunohistochemistry method. The density of mitotic cells, divided cells, and new neurons in hippocampal CA1 and CA3 and granular cell layer of dentate gyrus also increased.

Conclusion: We conclude that Spreading depression potentiates to trigger persistent neurogenesis in hippocampus of rat model of absence epilepsy.

p144
ENVIRONMENTAL ENRICHMENT RESTORES CA1 HIPPOCAMPAL LTP AND REDUCES SEVERITY OF SEIZURES IN EPILEPTIC MICE
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Purpose: Environmental enrichment (EE) improves hippocampal-dependent memory in both physiological and pathological conditions. The CA1 hippocampal region plays a major role in this restorative action. We have analyzed the effects of EE in a seizure-prone mouse model in which the genetic disruption of the presynaptic protein Bassoon (bsn) function leads to structural and functional alterations in the hippocampus and causes early spontaneous seizures mimicking human neurodevelopmental disorders characterized by epilepsy and mental retardation.

Method: Mice lacking the central region encoded by exons 4 and 5 (Bsn/Ex4/5) of Bassoon protein were generated as previously described (Altrock et al., 2003); age-matched wild type (WT) littermates were used as controls. At the beginning of the experiment, animals were 2 months old, and their weight ranged from 23 to 28 g.

Results: EE preserved CA1 LTP in epileptic mutant bsn mice. This effect was associated to a normalization of paired-pulse synaptic responses following repetitive stimulation and a prevention of spine density and dendrite branching abnormalities. The preservation of CA1 long-term potentiation was also concomitant with a reduction of seizure severity in epileptic mice. Conversely, EE failed to reverse alterations of AMPA/NMDA ratio and rectification of AMPA-mediated currents as well as the impairment in hippocampal-dependent non-spatial memory in mutant mice.

Conclusion: Multiple hippocampal adaptive processes underlie therapeutical effects of EE. The mutant bsn mouse represents a possible model to investigate the role of the hippocampus in early onset epilepsy.


p145
MEMORY IMPROVEMENT AFTER APPLICATION OF AMPA RECEPTOR ANTAGONIST DURING REPETITIVE SPREADING DEPRESSION IN JUVENILE RATS

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Purpose: Cortical spreading depression (CSD) is bio-electrical wave in central nervous system which propagates through the gray matter in the brain and cause several effects such as neural depolarization and ionic disturbances. This phenomenon plays a role in many neurological disorders like epilepsy, migraine aura, brain injury and cerebrovascular disease. The excitatory effect of glutamate receptor on the brain seems to be correlated with neural injuries. We examine the hypothesis that could we prevent the histopathological damage of CSD wave propagation in the brain by using excitatory neurotransmitter antagonism. In this study KCl-induced rat used as model of CSD and AMPA-type glutamate receptors antagonist, DNQX, was selected for evaluating possible therapeutic effect. In our study, we administrated DNQX in an optimized dose (1 mg/kg) intraperitoneally in juvenile rats. The efficacy was correlated with memory improvement during early stage of growth.

Method: SD was induced by KCl in 20 Wistar rats (60–80 g). At the same time recording of SD wave were done to prove SD initiation and propagation, then DNQX solution was applied through intra-peritoneal injection and their behavior related to memory was studied by T-Maze test.

Results: We observed that induction of SD could cause brain damage and Blockade of AMPA receptors have ability to improve memory function through protect the brain from cell death by preventing excitotoxicity of glutamateergic neurons during SD.

Conclusion: Our investigation showed that DNQX is potentiated for treatment solutions and have neuroprotective effects after brain disorder and it can provide possible therapeutic strategy against SD-related neurological disorders.

p146
PTZ ADMINISTRATION DISCLOSED POST TRAUMATIC ENHANCED SEIZURE SUSCEPTIBILITY FOLLOWING A NEW FOCAL BRAIN INJURY MODEL
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Purpose: Traumatic brain injury as a predisposing factor may result in Post Traumatic Epilepsy after inestimable latent period. To examine whether our new established focal brain injury model elevates seizure susceptibility, this study was designed.

Method: 48 male Wistar rats randomly assigned in Sham, PTZ, TBI + saline and TBI + PTZ groups. Each group divided into ECoG and behavioral analysis subgroups. After electrode implantation, TBI was induced in right parietal bone by weight drop device (except PTZ and sham groups). 14 days after TBI a subconvulsive dose of PTZ (a GABA inhibitor, 30 mg/kg) was injected (i.p) and during next hour score, frequency and latency of seizures in behavioral subgroup animals were determined (Racine scale). In ECoG subgroups, EOcG for 1 h following PTZ administration was recorded in anesthetized animals and frequency, latency and amplitude of seizure were extracted.

Results: Score (4.2 vs. 0 in sham) and duration of seizures in TBI + PTZ group significantly increased, while latency to onset of first tonic-clonic seizure diminished compared to all other groups. In 83% (5/6) of animals of TBI + PTZ group seizure progressed to tonic-clonic generalized stage. Based on ECoG interpretation, frequency, amplitude and duration of epileptiform discharges significantly elevated in TBI + PTZ group and latency to first epileptiform activity reduced compared to all other groups (>20 vs. 60 min in sham).

Conclusion: Findings of both behavioral and ECoG analysis indicate new focal brain injury model initiates an epileptogenesis process which enhances seizure predisposition within 2 weeks after trauma. This latent period could be optimal opportunity for identification of involved epileptogenic mechanisms and development of prophylactic treatments.

p147
A CHAMBER FOR THE PERFUSION OF IN VITRO TISSUE WITH MULTIPLE SOLUTIONS

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Purpose: The manipulation of the ionic environment of neural tissue is a widely used seizure model. Modification of the solution perfusing part of a tissue slice would provide a model for the study of the propagation of electrographic seizure activity into tissue in a physiological solution – relevant to the study of focal epilepsy and seizure generalisation. For this purpose, we developed a chamber that allows extended regions (>5 mm²) of acute tissue slice to be exposed, in isolation, to changes in ionic conditions (Thomas MG et al. J Neurophysiol 2013;110:269–277).

Method: Microstereolithography, a rapid direct digital manufacturing technique was used to produce the chamber. Inflow channels were designed to minimise the Reynold’s number of perfusing solutions. As a result, solution flow over tissue in the chamber was laminar, this mini-
The chamber was effective in allowing extended regions of neural tissue slice to be perfused, in isolation, with different solutions. The width of the interface between the two perfusing solutions (25–75% change in concentration) was 0.4 ± 0.1 mm. Gas chromatography mass spectrometry was used to test for contamination of the perfusing solutions with the resin used to manufacture the chamber. This put an upper limit on contamination of 2 ppm by volume.

### Conclusion
Microstereolithography can be used to rapidly (<12 h) manufacture chambers bespoke for experiments. The chamber effectively allows the local manipulation of the ionic environment of extended regions of tissue.

### Method
Adult, male Sprague–Dawley rats received bilateral PPS lasting 8 h as described previously (Norwood et al., JCN, 2010). Immediately after PPS, bilateral mechanical lesion of the entorhinal cortex was performed with a microknife. Animals were continuously video-EEG monitored for spontaneous seizures. Controls were treated identically, but received sham surgery (skull trephination, no microknife insertion, recording electrode reimplantation).

### Results
Entorhinal cortex lesions did not prolong the latent period. Interestingly, electrographic seizure activity was dampened, e.g., smaller amplitude epileptiform discharges, in lesioned animals, but seizure behavior was not obviously altered.

### Conclusion
These data demonstrate that entorhinal cortex lesioning does not significantly affect epileptogenesis. Consequently, the hypothesis that the entorhinal cortex kindles the hippocampus, eventually culminating in epilepsy, was sought to test this hypothesis by removing entorhinal cortex input to the hippocampus immediately after pro-epileptogenic PPS.

### Purpose
Following perforant pathway stimulation (PPS) in awake rats for 8 h, a seizure-free “latent period” is observed that lasts ~3 weeks. Continuous recording during the latent period from the dentate gyrus revealed spontaneous events that resembled low-frequency PPS. This led us to hypothesize that, during the latent period, input from the entorhinal cortex kindles the hippocampus, eventually culminating in epilepsy. We sought to test this hypothesis by removing entorhinal cortex input to the hippocampus immediately after pro-epileptogenic PPS.

### Method
Epileptic MAM-PILO rats were analyzed respectively 3–5 days (early chronic stage -EC) and 3–6 months (chronic stage) after the onset of epilepsy. Spontaneous recurrent seizures were assessed by video-monitoring. Age-matched MAM/pilocarpine rats not experiencing either SE or spontaneous seizures were used as controls. In all rat groups we performed morphologic and molecular analysis.

### Results
Our findings indicate that the process triggered by SE and subsequent seizures in the malformed brain is steadily progressive, deeply altering neocortical and hippocampal morphology, with atrophy of neocortex and CA regions and progressive increase of granule cell layer dispersion; changes dramatically the fine morphology of neurons in neocortex and hippocampus, by increasing cell size and decreasing both dendrite arborization and spine density; induces reorganization of glutamatergic and GABAergic networks in both neocortex and hippocampus, favoring excitatory vs. inhibitory input; and activates NMDA regulatory subunits.

### Conclusion
Taken together, our data indicate that, at least in experimental models of brain malformations, severe seizure activity, i.e., SE plus recurrent seizures, may lead to a widespread, steadily progressive architectural, neuronal and synaptic reorganization in the brain. They also suggest the mechanistic relevance of glutamate/NMDA hyperactivation in the seizure-related brain pathologic plasticity.
but not clonus (264.00 ± 35.89 s) and tonic extension (438.00 ± 52.87 s) was significantly prolonged. Pretreatment of GYKI 52,466 (12.5 mg/kg, i.p.), a non-competitive AMPA receptor antagonist, significantly delayed the onset of all the phases of convulsions but not death induced by AMPA (4 mg/kg, i.p.).

Conclusion: These data indicate that AMPA-induced seizure model could be explored further for testing novel antiepileptic molecules for the treatment of neonatal seizures. AMPA receptor antagonists may be useful for the treatment of neonatal seizures in clinics.

Basic Science 2
Monday, 30th June 2014

p151 AUTOANTIBODIES TO THE N-METHYL-D-ASPARTATE RECEPTORS AND SEIZURE SUSCEPTIBILITY IN MICE

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Purpose: Autoantibodies to neuronal surface proteins are found in adult seizure-related disorders such as anti-N-methyl-D-aspartate receptor antibody (NMDAR-Ab) encephalitis and limbic encephalitis. We have previously shown, in new-onset childhood epilepsy, that CNS autoantibodies are also found in a proportion of these patients. We aimed to determine whether these antibodies are pathogenic and epileptogenic in vivo.

Method: IgG from three patients with NMDAR-Ab encephalitis and two healthy controls was purified for passive transfer. Wireless electroencephalogram (EEG) transmitters were implanted into 15 mice. Nine of these mice were injected intracerebroventricularly with IgG from NMDAR-Ab positive patients and six mice with IgG from controls. IgG was coded before injection to avoid experimenter bias. 5 days of continuous electrophysiology recordings were used to detect spontaneous and induced epileptiform activity. A library of signature events was created to analyse the EEG recordings of all mice. Seizure susceptibility was tested 48 h after injection with a subthreshold dose of the pro-convulsant pentylenetetrazole. Seizures were scored according to a modified Racine scale:

1 non-epileptic behavioural change,
2 partial clonus,
3 generalised clonus, and
4 lethal seizure.

Results: Mice injected with NMDAR-Ab positive IgG had increased seizure susceptibility, with all having stage 3 seizures compared with only half of the control-IgG injected group (p = 0.04). The number of stage 3 seizures was also significantly higher (7.7 ± 8.4 vs. 0.8 ± 1.0; p = 0.003), as was the total seizure score calculated at the end of 60 min of observation (38 ± 29.5 vs. 7.5 ± 4.1; p = 0.003). Preliminary analysis of the post-mortem tissue shows human IgG in the hippocampi of the NMDAR-Ab injected but not in control-IgG injected mice.

Conclusion: Successful passive transfer of NMDAR-Ab positive IgG shows the epileptogenic potential of these antibodies. EEG analysis and investigation of the underlying pathogenic mechanism in ex vivo slices is in progress.

p152 EFFECTS OF SYSTEMIC KAINIC ACID PERFUSION ON LIMBIC NETWORK SYNCHRONIZATION IN ISOLATED BRAIN PREPARATION

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Purpose: Systemic administration of kainic acid (KA) into the brain is a widely used model of temporal lobe epilepsy. We investigated the effect of arterial KA perfusion in isolated guinea pig brain preparation, in order to study mechanisms of seizure generation and propagation.

Method: Epileptiform activity was induced by the perfusion of KA (6 μM, 7 min) into the basilar artery of isolated brain. Simultaneous extracellular recordings were carried out with micropipettes filled with 0.9% NaCl and double-barrel K+ sensitive capillaries, bilaterally from CA1 hippocampal areas and medial entorhinal cortices. In separate experiments, the P2X7R antagonist, A438079 (100 μM), was perfused for 40 min, starting 5 min before KA application. Electrophysiological recordings were analyzed with a FFT-based power spectrum (PSD) analysis, over 15 min, starting from KA perfusion.

Results: Isolated brain resting state is characterized by ongoing theta-alpha background activity. PSD analysis showed that systemic KA perfusion induced a simultaneous shift of activated frequencies towards beta-activity in all analyzed areas with disappearance of lower frequencies. In CA1 areas, an increasing recruitment of faster frequencies, leading to ictal-activity, was observed within 215.1 ± 14.8 s (n = 8). Seizures consisted into a single ictal episode involving mainly hippocampal (CA1 region) and spreading bilaterally, with a duration of 148.7 ± 27.7 s (n = 8). Beta-activity persisted after seizure termination and spontaneously resolved. A biphasic extracellular K+ rise, was associated with beta- and ictal-activities.

Pre-administration of A438079 resulted into an altered synchronous recruitment of frequencies towards beta-activity, which was associated with a slower biphasic-trend extracellular K+ rise. Ictal-activity was prevented by A438079.

Conclusion: KA-induced epileptiform activity is associated with an increase of extracellular K+ efflux and with a synchronization of limbic network. Administration of P2X7R-antagonist A438079 resulted into a slower and/or lower efflux of extracellular K+, prevented synchronization of the network and counteracted ictal-activity generation.

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p153 A MODIFIED ANIMAL MODEL OF SYMPTOMATIC INFANTILE SPASMS

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Purpose: Infantile spasms (IS) is one of the most severe epileptic encephalopathy in infancy and early childhood. An informative animal model would provide insights into the pathophysiology of this syndrome and form the basis for the development of innovative therapies. Different approaches have been used including genetic (Down syndrome, ARX mutation) and acquired (multiple hit, TTX, CRH, betamethasone-NMDA) models. However most patients of IS are symptomatic such as in hypoxic-ischemic encephalopathy (HIE). So we report here the modified animal model of symptomatic IS.

Method: On gestational day 15 (GD 15), pregnant rats were injected betamethasone for priming. A rat model of HIE was created by completely severing the right common carotid artery, followed by inducing hypoxia (8% oxygen) at postnatal day (PD) 7. On PD 15, pups were placed in observation cages on a heated pad and tested the susceptibility
to develop spasms after NMDA administration (15 mg/kg/ip). Behavioral and cognitive functions were investigated by weekly open field tests from postnatal week (PW) 3 to PW 7 and by daily testing using the Morris water maze test at PW 8 in the control, HIE only, NMDA only, and HIE + NMDA groups.

**Results:** The HIE + NMDA group was more prone to seizures induced by NMDA. The HIE + NMDA and NMDA only groups showed mild anxiety behavior in the open field test. The Morris water maze test revealed a decline in cognitive function in the HIE + NMDA and HIE only groups compared to the control and NMDA only groups.

**Conclusion:** Our findings suggest that HIE + NMDA model is more clinically relevant for the symptomatic IS. These findings may have understanding in developing brain for provide insights into the pathophysiology of IS and form the basis for the development of innovative therapies for this syndrome.

**Abstracts**

p154

**CHARACTERIZATION AND MODIFICATION OF THE FOCAL KAINATE MODEL IN MICE AS A SUITABLE MODEL FOR STUDIES ON ANTI-EPILEPTOGENESIS**

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**Purpose:** Symptomatic epilepsies, particularly temporal lobe epilepsy, can be induced by a variety of brain insults, including status epilepticus (SE). In the latent period after the initial insult multiple molecular and functional changes, called epileptogenesis, progress in the brain, leading to spontaneous recurrent seizures (SRS). An important unmet clinical need is to find antiepileptogenic strategies that prevent the development of SRS after brain insults such as SE.

**Method:** Post-SE models in rodents are highly recommended for antiepileptogenesis studies. In the widely used focal kainate model, the neurotoxic glutamate analogon kainate is injected into specific brain regions of the limbic system to induce a SE.

**Results:** Focal kainate application in mice leads to the development of frequent SRS in the EEG shortly after the initial SE, which is the major advantage of this model. The drawbacks of this model are that there is almost no seizure-free period after SE, which is essential for antiepileptogenic studies. Furthermore, mice do often not show a clinical correlate to seizures in the EEG. The goal of this project is to modify this model to obtain a longer latent period after SE, which still leads to the development of frequent SRS preferably with clinical correlates. Therefore several strategies are pursued, such as reducing the injected dose of kainate, using different mouse strains and changing the localisation of the recording electrodes.

**Conclusion:** First data indicate that neither a different mouse strain nor reduced doses of kainate lead to a clear latent period. The next step is to inject kainate into the amygdala instead of the hippocampus.

p155

**UTILITY OF PENTYLENETETRAZOL AND MAXIMAL ELECTROSHOCK SEIZURE MODELS IN RODENTS FOR PREDICTING ANTI-EPILEPTIC DRUG EFFICACY IN HUMANS**

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**Purpose:** Animal models in epilepsy typically apply a chemical or electrical stimulus to induce a seizure. Doses of antiepileptic drugs (AEDs) that suppress seizures in 50% of animals (ED50) are used as an endpoint for screening in drug development and in the prediction of clinically efficacious doses. The aim of the current research is to conduct a literature-based evaluation of the preclinical to clinical translation of pentylenetetrazol (PTZ) and Maximal electroshock (MES) rodent efficacy models to human efficacious doses.

**Methods:** A literature search was undertaken to include articles describing PTZ and MES experiments in rodents conducted with approved AEDs. ED50 were recorded and rodent exposures at these ED50 were calculated based on known pharmacokinetic (PK) properties of the AEDs. Human exposures at the minimally efficacious doses (MEDs) were also calculated based on known PK properties. Comparison of the preclinical to clinical exposures was summarised.

**Results:** Data for 11 and 13 AEDs are presented for the PTZ and MES models, respectively. The ratios of MED (human) to ED50 (mouse) unbound exposures averaged (±SD) 0.9 (6.5) and 0.8 (7.2), for the PTZ and MES models, respectively. PTZ models have been known to be more predictive of generalised epilepsy whilst MES models for partial epilepsy. The results showed no difference in ratios between drugs used for partial vs. generalised epilepsy, nor for drugs with different mechanisms of action. Data from mice tended to overpredict human efficacy, whilst data from rats tended to underpredict, although by similar amounts.

**Conclusion:** PTZ and MES rodent seizure models can reasonably predict human efficacious doses in epilepsy. This can be a useful tool in screening and prioritisation of compounds in early drug discovery, and can also be used as an early predictor of human efficacious doses.
SISCOM showed temporal lobe hyperperfusion and frontal lobe hyperperfusion during temporal lobe seizures, comparable with mesial temporal lobe epilepsy in humans. Our main finding was that SISCOM perfusion patterns were comparable across the different seizures stages. The network involved in the generation of seizures as measured by SISCOM appears to be activated early in the process of kindling. Factors responsible for the electrophysiological evolution of seizures within this network during kindling remain to be established.

**p158**

**REDUCTION OF THE NMDA RECEPTOR NR2B SUBUNIT EXPRESSION IN CORTICAL AND SUBCORTICAL AREAS OF WAG/RJ RATS**

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**Purpose:** Glutamatergic NMDA receptors modulation could affect the synchronization of spike discharges in WAG/Rij rats, a valid genetic animal model of absence epilepsy. In present study, we describe the alteration of NR2B subunit of NMDA receptors expression in WAG/Rij rats in different somatosensory cortical layers as well as in hippocampal CA1 area.

**Method:** Experimental groups were divided into four groups of six rats of both WAG/Rij and Wistar strains with 2 and 6 months of age. The distribution of NR2B receptors was assessed by immunohistochemical staining in WAG/Rij and compared to age-matched Wistar rats.

**Results:** The expression of NR2B subunit was significantly decreased in different somatosensory cortical layers in 2- and 6-month-old WAG/Rij rats. In addition, the distribution of NR2B in hippocampal CA1 area was lower in six-month-old WAG/Rij compared to age-matched Wistar rats.

**Conclusion:** The reduction of NR2B receptors in different brain areas points to disturbance of glutamate receptors expression in cortical and subcortical areas in WAG/Rij rats. An altered subunit assembly of NMDA receptors may underlie cortical hyperexcitability in absence epilepsy.

**Clinical Epilepsy 1**

**Monday, 30th June 2014**

**p160**

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

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**Purpose:** To develop a novel primate kindling animal model of temporal lobe epilepsy (TLE).

**Method:** Rhesus monkeys received repeated intramuscular injection of Coriaria lactone (CL) at subthreshold dosage (0.75, 1.50, and 3.00 mg/kg, respectively) or normal saline (NS). Behavioral and electroencephalographic monitoring was performed. Seizure number, intensity (the Racine grade for seizures), and duration were recorded from the video recording and further used for the comparison of anti-epileptic drugs (AEDs) effects. CL-induced pathological change of hippocampus were studied by Hematoxylin-eosin staining, electron microscopy and immunohistochemistry of glial fibrillary acidic protein.

**Results:** Repeated CL injection at subthreshold dosage elicited partial seizures that culminated in secondary generalized tonic-clonic seizures. The sequence of events and features of behaviors observed in this model simulated that in human TLE. Electroencephalogram monitoring revealed the temporal lobe origins of epileptiform potentials, which were consistent with the behavioral changes observed. A total of 7 rhesus monkeys (78%) were kindled with a median of 48 (41–60) CL injections. Both of the seizure-induction rate and the mortality are dose-dependent. CL injection at 1.50 mg/kg obtained the lowest animal mortality (0%) and highest seizure-induction rate (100%). Extensive kindling by CL injections with a median of 97 injections (over-kinding) ultimately resulted in the recurrence of spontaneous seizures in rhesus with frequency patterns similar to those of human TLE. The application of valproate and carbamazepine lacked a satisfactory seizure control. While levetiracetam and zonisamide treatment decreased the duration, numbers and intensity of seizures significantly. Rhesus subjected to large numbers of kindling stimuli display mitochondrial damage and activation of astrocytes in a pattern that is similar to the neuropathological changes characteristic of the human TLE.

**Conclusion:** A kindling TLE model of rhesus, a primate animal model of epileptogenesis, was established for the first time by using Coriaria lactone repeated intramuscular injection.

**p159**

**NEUROPROTECTIVE EFFECTS OF KETOGENIC DIET IN KAINIC ACID-INDUCED SEIZURE MOUSE MODEL**

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**Purpose:** Although the ketogenic diet (KD) is now an established treatment of refractory epilepsy, its antiepileptic mechanisms are still obscure. Kainic acid (KA)-induced seizures are known to cause hippocampal neuronal damage. This study was designed to investigate the neuroprotective effects of the KD on hippocampal neuronal damage after KA-induced seizures in mice.

**Method:** Normal male ICR mice were used for all the experiments. For 4 weeks, the KD group was fed a KD, whilst the normal diet (ND) group was fed a standard rodent chow (each n = 10). Thereafter, seizures were induced by KA (25 mg/kg, i.p.) in both groups. Two days following KA administration, mice were sacrificed and their brains were removed. In each brain sample, the first section was stained with cresyl violet and the second one was used for TUNEL staining.

**Results:** In the KD group, the KA-induced seizure onset time was delayed compared with the ND group. The cresyl violet-stained hippocampus showed that most of the pyramidal layers of the CA1 and CA3 of the ND-fed mice were disrupted and filled with pyknotic cells. On the contrary, well-preserved pyramidal layers were observed in the KD group. The mean neuronal-loss score was decreased by the KD from a control value of 2.5 ± 0.17 to 0.8 ± 0.25 (p < 0.0001) in the CA1 and from 2 ± 0.3 to 0.4 ± 0.16 in the CA3 (p < 0.001). Numerous TUNEL-positive cells were also observed in the CA1 and CA3 of the ND-fed mice, but the KD-fed mice showed less severe apoptotic neuronal damage.

**Conclusion:** In this study, we found that the KD delayed the KA-induced seizure onset time and prevented hippocampal neuronal damage in mice. These findings suggest that the KD may have neuroprotective effects against seizure-induced neuronal damage.
Purpose: The objective of our study was to investigate the structure and features of ES at patients with moderate and severe HI.

Material and Methods: We conducted the prospective analysis of clinical and instrumental examinations and surgical treatment outcomes at 181 patients with moderate and severe HI (Glasgow Coma Scale from 4 to 13 scores). The cerebral contusion of moderate severity was seen in 136 (75.1%) patients and severe cerebral contusion – at 45 (24.9%) patients. We operated 60 (33%) patients and 121 (67%) patients were treated conservatively.

Results: ES was seen at 32 (17.7%) patients with HI. Immediate seizures (developed within the first 24 h after injury) were reveal in 14 of 181 patients (7.7%), early seizures (from 1 to 7 days after trauma) – 9 cases (5%) and delayed seizures (>7 days) – in 6 cases (3.3%).

Most often ES mentioned in patients with: acute and subacute subdural hematoma (n = 46) – 7 patients (15.2%), with multiple brain injuries (n = 14) – 4 (28.6%), intracerebral hematomas and cerebral contusions located in the frontal and temporal lobes (n = 6) – 4 (66.7%).

Frequency of early and delayed ES increased in case of progression of the dislocation syndrome in patients with TBI (p < 0.05).

Conclusion: ES developed in 17.7% patients with moderate and severe TBI. 7.7% of the patients were recorded immediate ES, 5% – early ES and 3.3% – delayed ES.

Risk factors for immediate and early ES: <60 years old, the presence of brain damage, accompanied by the development of acute dislocation syndrome and cerebral contusions located in the frontal and temporal lobes.

Risk factors for delayed ES development: origin of ES within first 7 days after trauma, increase of leukocytes amount in CSF more than 100 cells per 1 μl.

p162
POST-STROKE EPILEPSY AND EPILEPSY ASSOCIATED WITH SMALL VESSEL DISEASE ARE DISTINCT NOSOLOGICAL ENTITIES. AN EPILEPTOLOGICAL PERSPECTIVE

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Purpose: To study clinical, neurophysiological and radiological correlations in patients with epilepsy and cerebrovascular disease.

Method: Two hundred and thirty-eight subjects with epilepsy and cerebrovascular disease were consecutively seen in our Centres from January 2000 to September 2013. Inclusion criteria: history of one or more epileptic seizures and presence, at neuroimaging, of one or more vascular lesions, compatible with large or small vessel disease. Exclusion criteria:

Results: One hundred and sixty-four subjects were included: 85 had PSE, 79 ESVD. At univariate analysis, abnormal EEG and frontal localization were associated with a lower probability of ESVD (odds ratio [OR] 0.39, 95% confidence interval [CI] 0.18–0.83 and OR 0.22, 95% CI 0.09–0.55, respectively), while temporal localization was associated with a higher probability of ESVD (OR 2.5, 95% CI 1.3–4.8). At multivariate analysis including temporal or frontal localization, all three variables confirmed to be independent predictors.

Conclusion: While in PSE epileptogenic focus is related to the large vessel lesions, temporal lobe epilepsy predominates in ESVD. In these subjects, the causal relationship between vascular lesions and epilepsy is not straightforward, and the role of adjunctive factors needs to be elucidated.

p163
EPILEPSY DIAGNOSTIC TOOL BY OPTICAL DISC RECORDING OF THE TEXTBOOK ABOUT NEUROLOGICAL EXAMINATION, DEFINITIONS AND CLASSIFICATIONS OF SEIZURES AND EPILEPTIC SYNDROMES, THEIR LOCALIZATIONS, CAUSES, CHROMOSOMAL ABNORMALITIES, AND LISTING DIFFERENTIAL DIAGNOSES ARE PRESENTED AS DATABASE OF WORKING KNOWLEDGE

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Purpose: To design handy device for making preliminary correct diagnosis at bedside.

Method: Case study. The 60-year-old man was admitted to neurological unit having been diagnosed as suffering from chronic tonic convulsions. This patient had been carrying out hyperpnea in attempt to produce a seizure. His eyes then turned to the right and upward. Head turned to the right. In the Chapter of Definitions we did a search of the words “deviation of eyes and head”. As result, we have found “Adversive epileptic seizures. It is caused by neuronal discharge in the frontal or temporal zone or in the supplementary motor area (H. Gastaut)”. In the chapter of Classifications we are finding causes of epilepsy presenting at late adult age: vascular disease, trauma, tumor, or cerebral degeneration. MRI investigation was showed the cyst of left frontal lobe. The textbook of epilepsy are containing of semeiological definitions, EEG patterns, listing seizures with related epilepsies and seizure localizations, causes of epilepsy, chronological onset, chromosomal focus, and neuroanatomical or neuropathological defects.

Results: By using the optical disc recording of the textbook with personal laptop preliminary correct diagnosis are made at bedside in 90%.

Conclusion: This device may be used as clinician’s diagnostic tool at clinical practice.

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THE LATERALIZING VALUE OF ASYMMETRIC SEIZURE TERMINATION IN SECONDARY GENERALIZED TONIC-CLONIC SEIZURES OF TEMPORAL LOBE EPILEPSY

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Purpose: We assessed the lateralizing value of clonic Asymmetric Seizure Termination (AST) in TLE patients.

Method: We retrospectively reviewed the medical records of patients admitted to the EMU between 2005 and 2007. Patient with the diagnosis
of TLE were selected and those who had GTC were ascertainment. All patients had interictal EEG, video EEG for ictal EEG and clinical semiology, and brain imaging part of phase 1 presurgical evaluation. The EEG and clinical semiology were assessed for the side of epileptogenic focus and the last clonic activity of GTC seizures.

**Results:** Out of 68 patients with TLE, 38 developed secondary GTC seizures. There were 21 females mean age 40 years, (range 19–72 years) and 17 males mean age 38.6 years, (range 22–76 years). Thirteen patients had right TLE (7 ipsilateral AST, 2 contralateral AST and 4 bilateral) and twenty-five had left LTE (5 ipsilateral AST, 13 contralateral AST and 7 bilateral). Twelve out of 38 (35.3%) patients had clonic AST ipsilateral to the TLE focus, 15 patients (39.5%) had contralateral AST and 11 patients (22.5%) had bilateral simultaneous termination of seizures. There was no significant difference between the groups. The seizures duration ranged between 4 and 54 years (mean 22.63 years) in the ipsilateral group, between 5 and 56 years (mean 24.9) in the contralateral group, and between 21 and 49 years (mean 30.25) in the bilateral group. Seizure duration was significantly longer in the bilateral seizure termination group compared to the ipsilateral group.

**Conclusion:** This study demonstrates that clonic AST in TLE patients has no reliable lateralizing value. Furthermore there is a tendency towards a significant relationship between bilateral simultaneous termination of clonic seizure activity and prolonged history of seizure duration. Further studies are warranted to reconcile conflicting findings.

**p166**

**VISUAL EPILEPTIC PHENOMENA: SEMIOLOGY AND CLINICAL IMPLICATIONS**

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**Purpose:** Describe the clinical implications of visual epileptic phenomena according to different semiological characteristics in adult patients.

**Method:** We recruited during 1 year patients who had visual semiology as a major epileptic symptom. All patients underwent neuroimaging. Visual semiology was classified as follows: (i) Simple hallucinations; (ii) Visual illusions; (iii) Vision loss; (iv) Complex visual hallucinations.

**Results:** We recruited 78 patients. Mean age: 44.5 (16–97) years. 52% Male.

Partial epilepsy represented 97% of patients, 28% pharmacoresistant. The most common causes of symptomatic cases (63%) were vascular (36%) and tumors (9%). Lesions were localized in the occipital lobe (24%); parieto-temporo-occipital region (23%); fronto-temporal (9%); parietal (4%) and dual pathology (4%).

The 59% of patients reported visual phenomena exclusively as preceding other ictal semiology (auras), 22% combined visual auras and isolated visual seizures and 19% had isolated visual seizures.

The coexistence in the same subject of visual seizures and other ictal semiology observed in 26% of patients, was associated with a higher risk of pharmacoresistance (p = 0.012).

The visual symptoms were: simple hallucinations (55%), illusions (24%), vision loss (6%) and complex visual illusions (14%).

Occipital origin lesions were related to simple ictal hallucinations (p = 0.002). Complex hallucinations were not reported in occipital epilepsy. Visual illusions and vision loss were reported in all localizations.

**Conclusion:** Ictal visual phenomena present mostly as epileptic auras. The visual phenomena associated to occipital lobe seizures are most likely simple hallucinations. Other visual semiologies, such as complex hallucinations are observed in several cerebral epileptic sources anterior to the occipital lobe. The association with other types of seizures is related to pharmacoresistance.

**p165**

**SEMILOGICAL ETIOLOGICAL ELECTROENCEPHALOGRAPHIC FINDINGS IN FLE**

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**Purpose:** Semiological etiological electroencephalographic findings in FLE.

**Objects:** Thirty eight FLE patients, aged from 17 to 73 years (median 43 years), 13 M; 25 F of epilepsy duration from 1 month to 30 years (median 7.59 years) were evaluated.

**Results:** Previously 35% reported nothing, 24% had trauma, neuroinfections, natal hypoxia, stroke or atrial fibrillation in 8% respectively. Surgery, Tension Type headache, Arterial Hypertension and Febrile Convulsions in 3% respectively. Heredity was positive in 10%, whilst rare in 40%, monthly or daily equally reported in 24%, weekly in 11%.

**Diagnosis:** Non-lesional 34% (hereditary FLE 1%), tumoral (meningeoma, hydrocephaly from carcinomatos meningitis (24%); 1%), post-traumatic and cortical traumatic hemispheric edema (11%; 1%), post-stroke 11%, natal hypoxia 3%, cerebral palsy and cicatricial lesions in 3% respectively. Lastly dementia, cortical hematoma, pinéal cyst and operated abcess in 8% or in one case respectively. AEDs used as monotherapy than as polytherapy (87%; 13%).

**Conclusion:** Immediate GTCs, versive, partial motor seizures onset in semiology; non lesional, tumoral, post-traumatic, vascular and natal hypoxia in etiology; and bilateral anterior IEDs in EEG prevailed more.
Purpose: The basal ganglia form circuits with frontal and temporal neocortices. Among established ictal extrapyramidal motor symptoms (EPMS) are dystonic limb posturing and gyral movements. We investigated order and duration of new ictal EPMS to elucidate seizure propagation pathways in frontal- (FLE) and temporal lobe epilepsy (TLE).

Method: Videos of 38 patients with medically refractory TLE or FLE referred to the epilepsy monitoring unit at the Department of Neurology, Medical University of Innsbruck between 1 January 2001 and 1 August 2002 were analysed for the new ictal EPMS “dystonia with tremor” and “tonic extension after figure-4-sign” (TEAF4).

Results: Aura symptoms preceded more often seizures with temporal than frontal lobe origin (p = 0.000). Dystonia (p = 0.002) or seizure propagation from dystonia to version (p = 0.038) were predominantly observed in seizures with temporal lobe origin. Forced blinking (p = 0.034) and making a grimace (p = 0.002) were exclusively documented in FLE. Immobile limbs (p = 0.028), dystonia with tremor (p = 0.012) and TEAF4 (p = 0.014) were exclusively documented in seizures with temporal lobe origin. Preferred seizure propagation pathways exclusively documented in TLE were aura to head turn (p = 0.028) or dystonia to a generalized seizure (p = 0.005).

Conclusion: Ictal dystonia with tremor and TEAF4 were exclusively documented in our TLE subgroup. The basal ganglia tend to be an important propagation pathway in our TLE group as documented by the different semiological signs following dystonia in TLE, but not in FLE.

More prospective studies are required to elucidate basal ganglia involvement in seizure propagation pathways and establish ictal EPMS as semiological signs with distinct localizing value.
Case: A 50-year-old man visited our hospital because of altered consciousness and high fever. On physical exam, a deep drowsy mentality and neck stiffness were found. On laboratory exam, mild elevated liver enzymes and cerebrospinal fluid abnormalities, including lymphocyte dominant pleocytosis and elevated protein levels were observed.

On the 2nd admission day, his mental state was deteriorated. EEG recordings showed rhythmic delta activities (RDA) with progressive change in both hemisphere which disappeared at 5 min after 2 mg lorazepam iv injection. These findings were compatible with NCSE. MRI showed high signal intensity in left thalamus and corpus callasum splenium with vasogenic edema suggestive of Japanese encephalitis. He was responsive to valproate 1.500 mg/day and levetiracetam 1,000 mg/day. The JE IgM antibody was also detected on the 20th admission day. His mentality was almost recovered to normal state 3 weeks after admission.

Conclusion: Mental changes in JE are usually associated with thalamic involvement and post ictal state. However we also keep in mind that NCSE can rarely occur and can cause sustained mental change in a patient with JE. The diagnosis of NCSE with use of EEG recording should be considered in JE patients with mental changes and focal neurologic deficits.

Methods: We retrospectively selected 149 patients surgically treated at Policlinico Umberto I from 2003 to 2013, for a histologically diagnosed high-grade glioma, showing a disease recurrence. In all cases the extent of tumor resection was evaluated through an early post-operative MRI. After surgery, patients were treated with combined radiotherapy (60 Gy/30 fractions/6 weeks) and chemotherapy (temozolomide 75 mg/m²) and then with chemotherapy alone (Temozolomide 200 mg/m² for 5 of 28 days/cycle). Follow-up included monthly clinical/MRI evaluation carried out 30 days after radiotherapy and repeated every 3 months. In case of onset of seizures/focal neurological deficits, the following MRI was anticipated.

Results: Thirty-five of 149 patients developed at least one seizure after surgery. In 8/35 the tumor was partially resected. In 6/35 recurrence was identified on MRI before seizure occurred. Of the 21 patients without residual disease, 7 had MRI evidence of tumor relapse immediately after seizure onset, whereas 14/21 (67%) developed seizures months before recurrence was detected through neuroradiological investigations (2–19 months).

Conclusion: Seizures are frequently reported in high-grade gliomas and can occur at any time of the disease progression. Our data suggest that seizures might also develop in “apparently” recovered patients preceding—even by several months—MRI evidence of tumor recurrence. Considering the limitations of neuroimaging (presence of pseudoprogression/difficult distinction between recurrence and radionecrosis), the occurrence of seizures in radically treated patients should be considered an important tool to “tailor” MRI follow-up, with relevant therapeutic and prognostic implications. Indeed, by allowing the early identification of ongoing brain disease, “heralding” seizures could contribute to optimize oncological and even surgical management of these patients.

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HIGH-GRADE GLIOMAS: ARE EPILEPTIC SEIZURES MORE SENSITIVE THAN NEUROIMAGING IN PREDICTING DISEASE RECURRENCE?
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Purpose: 30–50% of patients with high-grade gliomas experience epileptic seizures which may have a prognostic relevance. The aim of this study is to evaluate the occurrence of seizures after neurosurgery and possibly correlate them with the disease stage.

Methods: We retrospectively selected 149 patients surgically treated at Policlinico Umberto I from 2003 to 2013, for a histologically diagnosed high-grade glioma, showing a disease recurrence. In all cases the extent of tumor resection was evaluated through an early post-operative MRI. After surgery, patients were treated with combined radiotherapy (60 Gy/30 fractions/6 weeks) and chemotherapy (temozolomide 75 mg/m²) and then with chemotherapy alone (Temozolomide 200 mg/m² for 5 of 28 days/cycle). Follow-up included monthly clinical/MRI evaluation carried out 30 days after radiotherapy and repeated every 3 months. In case of onset of seizures/focal neurological deficits, the following MRI was anticipated.

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Conclusion: Seizures are frequently reported in high-grade gliomas and can occur at any time of the disease progression. Our data suggest that seizures might also develop in “apparently” recovered patients preceding—even by several months—MRI evidence of tumor recurrence. Considering the limitations of neuroimaging (presence of pseudoprogression/difficult distinction between recurrence and radionecrosis), the occurrence of seizures in radically treated patients should be considered an important tool to “tailor” MRI follow-up, with relevant therapeutic and prognostic implications. Indeed, by allowing the early identification of ongoing brain disease, “heralding” seizures could contribute to optimize oncological and even surgical management of these patients.

p173
CLINICAL AND HISTOPATHOLOGICAL CHARACTERISTICS OF TEMPORAL LOBE EPILEPSY PATIENTS MANIFESTING WITH HYPERMOTOR SEIZURES
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DYSPLASIA IN THE RIGHT TEMPORAL LOBE
CASE PRESENTATION OF 26-YEAR OLD WOMAN

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Purpose: To present diagnostic difficulties in a patient with initially MRI negative neocortical temporal lobe epilepsy.

Results: Seizure description: The aura affected right leg; she experienced her right leg being pulled downwards, which was very frightening. The aura was followed by loss of consciousness and stereotype movements of the right leg or arm. In few occasions, generalized seizures appeared. Two MRI were considered normal. Multiple EEG showed epileptic activity over frontal and temporal lobes of the right hemisphere. During video-EEG the semiology was described as follows: Initially she had a motionless stare. Early head turn to the left followed by pedaling of right leg and stereotype movements in right hand, later turning of head and body to the right and speech arrest. Ictal EEG with intracranial recording: Seizure activity starting over a widespread area of the right temporal lobe with spreading to the ipsilateral and contralateral frontal lobes. Intercital epileptiform activity was most pronounced in right temporal area. Dipole analysis demonstrated that the irritative zone included most of right temporal lobe and insula. Ictal SPECT/SISCOM showed hyperperfusion in the neocortical area of right temporal lobe. Control MRI showed a 10 × 3 mm abnormality in right middle temporal gyrus, suspected to be a focal cortical dysplasia. A lesionectomy was performed in December 2013 and after 1 month observation no seizures have occurred. In January she experienced aura in her right arm, however it was milder than preoperatively.

Conclusion: Isolated aphasia is associated with the final diagnosis of seizures mimicking stroke. Cardiobembolic diseases, high cholesterol and high D-dimer are associated with the final diagnosis of ischemic stroke. The model with demographic and initial clinical presentation has an acceptable capacity to identify seizures mimicking stroke from real ischemic strokes.
Results: Bitemporal lobe epilepsy patients had more frequently different seizure semiology (100% vs. 40%; p < 0.001) and significantly more often lateralizing seizure phenomena pointing to bilateral seizure onset compared to patients with unilateral TLE (42% vs. 11%; p < 0.01). The sensitivity of identical vs. different seizure semiology for the identification of bilateral TLE was high (100%) with a specificity of 60%. Lateralizing seizure phenomena had a lower sensitivity (42%) but a higher specificity (89%). The combination of lateralizing seizure phenomena and different seizure semiology showed a low sensitivity (41%) and high specificity (94%).

Conclusion: The analysis of seizure semiology including lateralizing seizure phenomena adds important clinical information to EEG and imaging in the selection of patients considered for resective temporal lobe epilepsy surgery.

p177 AUTOMATISMS IN POSTERIOR CORTEX EPILEPSIES: A STEREO-ELECTROENCEPHALOGRAPHY STUDY
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Purpose: We aimed to explore the correlation between the automatisms occurring during seizures originating in the posterior cortex and the epileptogenic networks involved.

Method: We retrospectively reviewed the records of 19 patients with drug-resistant focal epilepsy originating in the posterior cortex and explored through stereo-electroencephalography (SEEG) as part of presurgical evaluation. Sixteen patients were investigated in the University Hospital of Rennes and three patients were added from the University Hospital of Bucharest. We reviewed a mean of 3 seizures/patient (ranging from 1 to 12). Based on the seizure onset zone location, the patients were divided into a Parietal supra-calcarine group, comprising 11 patients and a Temporo-Occipital group, including 8 patients. We compared the two groups regarding the incidence of various automatisms and the networks involved.

Results: The mean duration of the seizures was 66 s (ranging from 10 to 170 s). We have been able to delineate the following main categories of automatisms: gestural (26.3%), manual or pedal (27.7%), smiling (26.3%), oro-alimentary (22.2%), vocal (5.5%) and verbal (5.5%). No significant difference between seizure duration and time of automatism occurrence was found in the two groups (Fisher’s exact test, p < 0.05).

Conclusion: The seizures originating in the posterior cortex are relatively poor in automatisms. Seizures originating in the infra-calcarine territories exhibit more complex automatic behavior comparing with the supra-calcarine ictal events. This manifestations mainly arise when the ictal activity has spread to the temporal regions.

p178 INTERICTAL EPILEPTIFORM DISCHARGES IN NEW-ONSET EPILEPSY IN THE ELDERLY
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Purpose: In September 2013, the elderly population of Japan included 31.86 million individuals. The aging rate reached 25%, the highest in the world. The incidence of epilepsy is high in older patients and increases with age; however, there are few reports of interictal epileptiform discharges (IEDs) in new-onset epilepsy in the elderly. We investigated the rate of IEDs in elderly patients with new-onset epilepsy.

Method: We reviewed the interictal electroencephalography (EEG) features of elderly patients with new-onset epilepsy treated between April 2005 and December 2011 at a tertiary referral center. Both outpatients and inpatients were included in this study. We defined elderly patients as the patients who developed epilepsy at the age of 65 or older. Epilepsy was diagnosed on the basis of clinical history, physical findings, scalp-recorded electroencephalogram, and 3.0-T magnetic resonance imaging (MRI)/computed tomography (CT). The classification of epilepsy and seizures, and age of onset were also reviewed.

Results: One hundred twelve patients (58 males and 54 females) were included in this study. The mean age of seizure onset was 73.5 ± 6.7 years [mean ± standard deviation]. IEDs were detected in 82 patients (73.2%). Temporal lobe epilepsy (Odds ratio [OR] = 6.3, p = 0.004) and complex partial seizure (OR = 8.0, p = 0.033) were correlated with IEDs.

Conclusion: IEDs were present in 73.2% of the elderly patients with new-onset epilepsy in our cohort, which was higher than the rate that was reported previously. Temporal lobe epilepsy was most frequent in the IED-positive patients.

p179 A SURVEY OF PEOPLE WITH EPILEPSY LIVING IN ELDERLY WELFARE SERVICE FACILITIES IN TOTTORI PREFECTURE
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Purpose: The incidence of epilepsy in the elderly has increased. The purpose of this study was to describe the actual condition of people with epilepsy (PWE) living in elderly welfare service facilities.

Method: A questionnaire asking about the type, number of users of the facilities, the number of PWE and seizure frequency of PWE in the facilities, and the training for management of epilepsy for staff members was distributed to 40 geriatric long-term care insurance facilities and 53 group homes for elderly people with dementia in Tottori prefecture in 2012, and a total of 53 responses (57.0%) were collected.

Results: The total number of users of the facilities was 2,750. We found 59 PWE living in the facilities. The rate of prevalence for epilepsy in the
facilities was estimated to be 21.5 per 1,000 (95% confidence interval 16.0–26.9/1,000). Concerning seizure frequency, 6 PWE had more than 1 seizure per month, 22 had more than 1 seizure every year, and 29 had been seizure free for over 1 year. There were 7 facilities (13%) in which the training for the management of epilepsy had been carried out for staff members.

Conclusion: The prevalence of epilepsy in elderly welfare service facilities was rather high compared to the general population. However, there were few facilities that offered staff training for the management of epilepsy. It is recommended that training for the management of epilepsy should be a part of the curriculum for staff members in elderly welfare service facilities.

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TRENDS IN THE UTILIZATION OF ANTIEPILEPTIC DRUGS IN THE ELDERLY IN NORWAY
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Purpose: To investigate changes in prescriptions of antiepileptic drugs (AEDs) in the elderly (>60 years) compared to younger people (<60 years) in Norway during 2004–2012.

Method: Data regarding all AED prescriptions from the Norwegian Prescription Database were utilized. The study was approved by the National Institute of Public Health.

Results: During 2004–2012 utilization of AEDs increased in the elderly (85%) and younger patients (59%) from totally 18.5 to 32.1 DDD/1,000 inhabitants/day. AEDs were increasingly used for other indications than epilepsy; psychiatric disorders (lamotrigine) and neuropathic pain (pregabalin/gabapentin), accounting for 50% of the total use in 2012. The elderly were more often prescribed AEDs in pain and the younger adults AEDs in psychiatry. The elderly used older AEDs more frequently than younger patients. The prevalence of psychotropic co-medication was 27% and 22%, in elderly and younger patients with epilepsy, respectively, with 2 CNS-active drugs. The most frequently used AEDs with a potential for significant interactions were phenytoin and carbamazepine in the elderly and lamotrigine and valproate in younger patients.

Conclusions: Lamotrigine is increasingly used in psychiatry and pregabalin/gabapentin in neuropathic pain with an age-related difference in prescriptions. Elderly patients used older AEDs more extensively with an increased potential for adverse effects and interactions and polytherapy with other CNS-active drugs. Documentation regarding changes in drug prescriptions contributes to increased focus and thus, improved treatment of elderly patients with epilepsy.

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IS ALL WHAT I FORGET ON A DEGENERATIVE BASIS? TRANSIENT AMNestic EPILEPSy IN A COHORT OF MILD COGNITIVE IMPAIRMENT PATIENTS: A HIGH DENSITY EEG STUDY
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Purpose: Mild cognitive impairment (MCI) converts in up to 80% of patients diagnosed with in Alzheimer’s disease after a few years of diagnosis. The identification among such a population of a rare form of epilepsy (transient epileptic amnesia [TEA]), characterized by mixed anterograde and retrograde amnesia with apparent preservation of other cognitive functions, excessively rapid decay of newly acquired memories, and loss of memories for salient personal events of the remote past, strongly affects prognosis and medical treatment. Our aim was to define the clinical utility of routine high-density electroencephalography (EEG) in MCI patients.

Method: 76 consecutive patients with a diagnosis of MCI (Petersen and Negash, 2008) were included and evaluated with hematological screening, neuropsychological testing (Modified Deterioration Battery, Carlesimo et al., 1996), 3T MRI and 256 channels EEG. After collective case revision, final diagnosis of TEA plus accelerated long-term forgetting, as demonstrated by the Rey memory test scores, was made for 3 patients, according to Butler’s diagnostic criteria (2007). The same diagnosis is plausible for a fourth patient, which was more likely at the beginning of her history, followed by a true multiple domain MCI.

Results: Using high-density EEG (256 channels), we were able to single out 3 cases of TEA previously misdiagnosed as MCI in this cohort. Antiepileptic treatment effectively stopped the acute episodes of memory loss. The diagnostic yield of high-density EEG recording in these patients instead of standard EEG increased by 0.75, with a diagnostic accuracy of 1.

Conclusion: To our knowledge, this is the first report of an incidence of 4% of TEA recorded in an MCI cohort. Antiepileptic treatment effectively stopped the acute episodes of memory loss. The diagnostic yield of high-density EEG recording in these patients instead of standard EEG increased by 0.75, with a diagnostic accuracy of 1.

p182
A CASE OF ANTI-GLUTAMIC ACID DECARBOXYLASE ANTIBODY ASSOCIATED LIMBIC ENCEPHALITIS WITH TEMPORAL LOBE EPILEPSY
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We report a patient with anti-glutamic acid decarboxylase (GAD) antibody positive acute limbic encephalitis showing temporal lobe epilepsy and brain lesion on MRI. Limbic encephalitis is a condition characterised by an acute or sub-acute onset of memory disorder, seizures or psychiatric manifestations. Clinical presentation may be variable and the diagnosis may be problematic. A 57-year-old male was admitted to our hospital with onset of sudden amnesia and seizures that then persisted for 1 month. The patient repeated epileptic attacks starting with orofacial and right manual automatisms, right sided clonic and tonic seizures accompanied with loss of consciousness, and was refractory to valproic acid and carbamazepine. EEG showed rhythmical slow spike-wave
activity over the right temporal region spreading both hemispheres. Brain MRI showed hyperintense lesion with contrast enhancement in predominantly right mesial temporal lobe and hippocampus. After admission, attacks disappeared through the administration of higher doses of carbamazepine (1,200 mg) and intravenous immunoglobulin therapy. Serum was positive with high titers of anti-GAD antibody. The patient completely recovered to an alert state with no seizures but the abnormal MRI lesions is not totally disappeared in the fifth month of the onset of the disease. Recently, anti-GAD antibodies have been reported as implicated in cerebellar ataxia, palatal myoclonus, refractory epilepsy and limbic encephalitis. Epilepsy associated with the anti-GAD antibody is mostly pharmacoresistant and the case suggests that anti-GAD antibodies could contribute to unexplained encephalopathy with brain MRI lesions and symptomatic mesial temporal lobe epilepsy in the elderly.

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p183 DIAGNOSTIC TEST ACCURACY OF EEG IN THE IDENTIFICATION OF EPILEPSY AFTER A FIRST UNPROVOKED SEIZURE: A SYSTEMATIC REVIEW AND META-ANALYSIS

**Purpose:** Our purpose was to examine the diagnostic test accuracy of routine EEG in identifying adults and children with epilepsy after a first unprovoked seizure.

**Method:** We searched Ovid MEDLINE, Ovid Embase, PubMed and Web of Science CPCI-S using a search strategy designed in consultation with a medical librarian. In addition, we manually searched the bibliographies of included studies, published reviews and conference abstracts. Eligible studies included participants of all ages who presented with a first unprovoked seizure, had a routine EEG and were followed for seizure recurrence for at least 1 year. The QUADAS-2 quality assessment tool was used and results were pooled using a bivariate mixed effects regression model.

**Results:** We reviewed 2,588 records and 18 studies were included in the analysis. Among studies of adults, the pooled estimates of sensitivity and specificity (95% CI) were 19.7% (9.2, 37.0) and 95.3% (73.2, 99.3) with positive and negative likelihood ratios of 4.2 (0.8, 22.4) and 0.8 (0.7, 1.0), respectively. Among studies of children, the pooled estimates of sensitivity and specificity were 58.4% (50.3, 66.1) and 68.7% (56.9, 78.4) with positive and negative likelihood ratios of 1.9 (1.4, 2.5) and 0.6 (0.5, 0.7), respectively.

**Conclusion:** Epileptiform abnormalities on routine EEG after a first unprovoked seizure are more likely to rule in epilepsy among adults than among children. These findings are particularly relevant given the recently proposed operational definition of epilepsy which highlights the need for objective methods to determine a ≥75% risk of recurrence after a first unprovoked seizure.

p184 CAPABILITY OF MAGNETOENCEPHALOGRAPHY AND SIMULTANEOUS EEG TO DETECT INTERICTAL EPILEPTIC DISCHARGES IN THE DANISH PRESURGICAL EPILEPSY EVALUATION

**Purpose:** Magnetoencephalography (MEG) is increasingly used in the non-invasive evaluation of patients with refractory focal epilepsy. MEG records the changes in magnetic fields generated by the activity of the neural networks in the brain. EEG and MEG supplement each other in localizing the epileptic focus, because MEG detects epileptic sources tangential to the scull and EEG detects both tangential and radial sources. The magnetic field recorded by MEG is not distorted by the brain, tissue, skull or scalp. This preliminary status of an ongoing project outlines how often interictal epileptic discharges are detected by MEG or EEG.

**Method:** MEG (Elekta Neuromag® TRIUX™) 306 channels and simultaneous EEG (60–70 channels) were recorded in 26 consecutive patients with focal epilepsy, referred for epilepsy surgery. Recording duration was 1 h in resting conditions, with closed eyes. MEG and simultaneous EEG were manually viewed by trained personal using CURRY Scan 7 Neuroimaging Suite.

**Results:** MEG has revealed epileptiform discharges in 57% of the patients. Fifteen percent had focal discharges seen only in MEG. In 75% of these patients, earlier conventional EEG had not been able to localize a focus. Focal discharges were seen in both MEG and in the simultaneous EEG in 42%.

**Conclusion:** MEG detects interictal focal epileptic discharges not captured by conventional EEG. This can lead to a better hypothesis on where to operate.

p185 FINDING A PROPER WAVELET MODEL FOR EARLY DETECTIONS ON EPILEPTIC SEIZURES

**Purpose:** Early detections of possible seizures on Epileptic Patients are expected for better treatments. To increase the their Signal-to-Noise Ratios four Bandpass Filters were applied ranging 0–4 Hz (delta), 4–8 Hz (theta), 8–13 Hz (alpha), and 13–30 Hz (beta).

**Method:** The research was based on some long term (72 h) of scalp recorded, EEG. Signals of 24 males and 16 female ages 3–35 years. A number of Wavelet Transforms were applied to acquire an idea on the best suited specific wavelet with regard to epileptic seizures. For this a mother 6.8 biorthogonal wavelet was employed and the resulting statistical data namely the means, standard deviations, skewnesses, kurtoses, as well as entropies were compared from normal persons and epileptic patients.

**Results:** The results show the representing number of magnitude 28.73 from normal person and 81.87 from epileptic patients and means 0.89, mean standard deviations 126.31, mean skewneses 0.52, mean kurtosises 6.94, mean entropies 1.16 from normal person and means 81.87 from epileptic patients and means 6.94, mean entropies 0.89, mean kurtosises 0.89, mean skewneses 0.89, mean standard deviations 81.87.

**Conclusion:** The method achieves the highest classification rate of 100% for the database developed, therefore possibility for better treatments of epileptic patients is opened, with a simpler and faster procedure.
Abstracts

p187
EEG ANALYSIS IN PRETERM INFANTS WITH ISCHEMIC BRAIN DAMAGE
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EEG is informative and safe method to assessment cerebral functions in premature infants. Formations of typical neonatal EEG patterns in premature infants depend on postmenstrual age and brain damage. There are two main background EEG patterns of premature infants before 34 weeks: trace discontinue and constant activity.

We analyzed 10 EEG of preterm infants 24–33 weeks of gestation, with ischemic brain damage, recorded with 13 electrodes for median duration 60’. EEG was recorded on the neonatal intensive care unit at 1 week after birth. All infants were divided in two groups: first group included 4 premature infants with hypoxic-ischemic brain damage, recorded with 13 electrodes for median duration 60’. EEG was recorded on the neonatal intensive care unit at 1 week after birth. All infants were divided in two groups: first group included 6 premature infants with intraventricular hemorrhage 3–4 stages (medium gestations age was 26 ± 3 weeks, medium Apgar score 2.8/4.2), and second group included 4 premature infants with hypoxic-ischemic encephalopathy – HIE (medium gestations age was 27 ± 5 weeks, medium Apgar score 4.0/5.8).

Results: EEG in all infants with intraventricular hemorrhage showed trace discontinue. In this pattern intervals of depression of activity more 10’ (17–36’) were present in all patient with intraventricular hemorrhage and in only one infant with HIE.

Main EEG rhythm of constant activity was delta 1–3 Hz. Interhemispherical asymmetrical activity more than 50% recognized in 4 infants with intraventricular hemorrhage, and in 3 – with HIE. Asymmetrical burst activity recorded in 5 infants with intraventricular hemorrhage, and in 1 with HIE. Sleep-wake cycle wasn’t detected.

Conclusions: depression of bioelectrical activity within trace discontinue was more sever in infants with intraventricular hemorrhage, pathological interhemispherical asymmetrical activity was recorded in infants of both groups, and asymmetrical burst activity was detected primarily in infants with intraventricular hemorrhage.

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MULTIMODAL NEUROPHYSIOLOGY IN PRESURGICAL EVALUATION OF EPILEPSY AT THE UNIVERSITY HOSPITAL IN LUND, SWEDEN
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Purpose: Presenting neurophysiological tests used for epilepsy surgery evaluations preformed at the Department of Neurophysiology at the University Hospital in Lund/Sweden.

Method:
- Electroencephalography (EEG)
- Extra cranial video-EEG (EvEEG)
- Single-photon emission computed tomography (SPECT)
- Subtraction ictal SPECT co-registered to MRI (SISCOM)
- Invasive intracranial video-EEG (IvEEG)
- Co-registration: localization of intracranial electrodes using CT, co-registered to MRI
- Electrical Brain Stimulation (EBS)

Results: To illustrate the methods, we are using a case of a 16 year old female who has had seizures with feelings of discomfort and fear since age 12. For identifying the epileptogenic focus we preformed EEG, EvEEG, SPECT, SISCOM, IvEEG and EBS.

Routine-EEG was normal, EvEEG showed in 50% of the seizures low voltage rhythmic theta activity over the right hemisphere, otherwise no typical epileptic activity.

At SPECT examination Tc99m-HMPAO was injected, 7 s after clinical seizure onset. SISCOM showed a hotspot located in the right Cingulate gyrus.

MRI was initially interpreted normal, after SISCOM, MRI was re-examined a cortical lesion was found close to the SISCOM hotspot.

Invasive electrodes where placed. Co-registration with MRI showed strip-electrodes over medial interhemispheric fissure and depth electrode in the right medial frontal hotspot.

IvEEG revealed epileptic seizure activity in depth electrodes 5 s before clinical seizure onset, spreading after 10 s to one of the strips. Interictal activity and high frequency discharges were seen in the depth electrode.

EBS, stimulating depth electrodes induce the same aura as the patient experience at spontaneous seizures. Surgery was preformed and a volume including the hotspot was removed. PAD showed focal cortical dysplasia type 1c. The girl has been seizure free since 3 months.

Conclusion: SISCOM and intracranial electrodes co-registered to MRI is an important tool in presurgical epilepsy evaluation.

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FRONTAL RHYTHMIC BETA ACTIVITY IN CHILDREN WITH ASD OR ADHD
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Purpose: Frontal spindle of the sleep period is seen at 11–12 Hz from an infant. We frequently experience the frontal rhythmic beta activity (FRBA) like frontal spindle, but which has high amplitude and high frequency in frontal predominance including frontal pole areas. The major aim of this work was to clarify the FRBA in children with Autism spectrum disorders (ASD), attention-deficit hyperactivity disorder (ADHD) or intellectual disability (ID) and assessment of neurophysiology of ASD and ADHD.

Method: 126 children (92 boys, 34 girls, mean age 13.1 years) with ASD (77), ADHD (19) and/or ID (45) were studied. Conventional electroencephalogram (EEG) recording and assessment of FRBA more than 13 Hz frequency during the sleep stage 2 were performed.

Results: In 36 children (29 boys, 7 girls, mean age 8.6 years) presenting FRBA (28.5%), the EEG was found characteristic FRBA. 25 of them (69.5%) presented ASD, 11 of them (30.5%) ADHD, 21 of them ID. The characteristic of the FRBA was high frequency with a mean average 15 Hz (13–18) and high amplitude with a mean amplitude 63.8 µV (62.5–185). In 30 children presenting FRBA (83.3%), the EEG was found abnormal (paroxysmal of spikes and sharp waves) in the frontal dominant areas.

Conclusion: 28.5% of children with ASD or ADHD exhibited EEG patterns with the FRBA. These children also showed high percentage of abnormal epileptic-like activity in the frontal dominant areas. The assessment of FRBA indicated that the excitability of frontal lobe and lead to shed light on the neurophysiology of ASD and ADHD.
p91
AN APPROACH TO STAGING SLEEP IN POLYSOMNOGRAPHIC STUDIES IN CHILDREN WITH FOCAL EPILEPSY
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Purpose: The American Academy of Sleep Medicine (AASM) Manual is now widely used in clinical practice for scoring sleep in children. However, polysomnographic records from children with epilepsy often contain interictal EEG abnormalities which may obfuscate features of sleep. Additionally, the AASM Manual does not allow for the scoring of epochs containing ictal events other than as “wake” or “sleep.” We aimed to devise an optimised strategy for the scoring of sleep in children with focal epilepsy.

Method: Patients with focal epilepsy who underwent long-term video EEG monitoring with concurrent polysomnography were included. Sleep was scored using the AASM Manual. EEG features that interfere most with scoring were identified and quantified, exploring the effect of using different EEG derivations, as well as assigning epochs to ‘seizure’ time.

Results: A total of 20 studies in 9 patients with focal epilepsy were analysed. EEG features identified included interictal discharges, focal or generalised slowing of ongoing EEG activity, and seizure-related abnormalities (pre-ictal build-up, ictal discharges, and post-ictal slowing). One study contained continuous discharges, 5/20 frequent discharges, 13/20 infrequent discharges and 1 study no discharges. Eleven seizures were recorded across 4/20 studies. Pre-ictal build-up began a median of 1 epoch (range 0–2) before a seizure, while post-ictal changes lasted a median of 6 epochs (range 5–40). Using a longitudinal bipolar montage including the maximally affected channels, and assigning ictal and peri-ictal epochs to “seizure” time made 19/20 studies scorable. Additionally, there was good inter-observer reliability.

Conclusion: The scoring of sleep in children with focal epilepsy – even those with nightly seizures – is facilitated by applying simple modifications to the AASM guidelines.

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HEART RATE VARIABILITY CHANGES IN PATIENTS WITH UNTREATED TEMPORAL LOBE EPILEPSY: A NEW SUGGESTIVE IMPLICATION
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Objective: The aim of our study was to evaluate heart rate variability changes (HRV) in patients with untreated TLE in interictal (INT), pre-ictal (PRE), ictal (ICT) and post-ictal (POST) states of temporal seizures.

Method: Patients affected by untreated TLE were selected according to ILAE criteria. HRV parameters were extracted from single-lead electrocardiography data collected during diagnostic videoEEG recordings. HRV parameters in time and frequency domains were analyzed: low frequency (LF), high frequency (HF), standard deviation of all consecutive normal R wave intervals (SDNN), square root of the mean of the sum of the squares of differences between adjacent normal R wave intervals (RMSSD). Cardiovascular index (CVI), cardiodynamic index (CSI), and approximate entropy (ApEn) were also calculated from Poincaré plots. All data were logarithmically transformed to correct for any skew in the distribution. Statistical analysis was performed by means of repeated measures ANOVA to compare HRV parameters during each condition (INT, PRE, ICT, POST). LSD test was utilized as post-hoc. p-value < 0.05 was considered statistically significant.

Results: We recorded 21 seizures from a total of 14 patients. Frequency domain analysis showed a significant increase of ICT LF vs. PRE/POST and INT and a higher ICT LF/HH ratio vs. INT and PRE. Time domain variables showed a statistically lower ICT RR interval (vs. PRE) and RMSSD (vs. INT) and a higher ICT SDNN and CSI (vs. INT & PRE). In addition ICT ApEn was significantly lower vs. PRE/POST and INT. Conclusion: Our data confirmed a sympathovagal imbalance in TLE with higher sympathetic tone, as showed by higher LF and LF/HH ratio, lower RMSSD and ApEn, and by the increased CSI and SDNN. Since lower vagal and higher sympathetic tone are predictors of morbidity/mortality in cardiovascular samples, our findings may suggest an early involvement of ANS in TLE.

p93
IS HOME VIDEO-TELEMETRY (HVT) SUPERIOR TO INPATIENT VIDEO-TELEMETRY (VT)?
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Purpose: HVT is a new service provided at home to investigate seizure and sleep disorders and has been successfully established at King’s College Hospital as a routine test. Inpatient video-telemetry is not always successful. Habitual seizures were captured only in 8% on VT retesting as shown in an internal audit. Our purpose is to confirm that the diagnostic yield of patients with a repeat HVT is higher than 8%.

Methods: Between August 2010 and October 2013 225 patients underwent VT as a first test and subsequent HVT as a repeat diagnostic test, according to our database. The telemetry reports of these patients were reviewed. A test was defined as successful if the patients’ habitual attacks were captured.

Results: We identified ten patients who had a repeat HVT following unsuccessful inpatient video-telemetry. In 4/10 patients HVT captured their habitual episodes (40%).

Conclusion: Our results suggest that with repeat HVT 40% of the habitual attacks were captured compared to 8% with repeat inpatient VTs. These results suggest that if repeat telemetry is required, HVT is probably the more successful option to capture habitual attacks. Further work is needed to confirm diagnostic accuracy and utility of HVT considering parameters such as age and nature of disease (epileptic vs. non-epileptic attacks).

p94
PROLONGED PERI-ICTAL CLINICAL-EEG ALTERATIONS IN PATIENTS WITH PCDH19 MUTATION
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Purpose: Protocadherin coding gene (PCDH19) is a major gene in female patients with infantile onset epilepsy, associated with variable frequency (LF), high frequency (HF), standard deviation of all consecutive normal R wave intervals (SDNN), square root of the mean of the sum of the squares of differences between adjacent normal R wave intervals (RMSSD). Cardiovascular index (CVI), cardiodynamic index (CSI), and approximate entropy (ApEn) were also calculated from Poincaré plots. All data were logarithmically transformed to correct for any skew in the distribution. Statistical analysis was performed by means of repeated measures ANOVA to compare HRV parameters during each condition (INT, PRE, ICT, POST). LSD test was utilized as post-hoc. p-value < 0.05 was considered statistically significant.

Results: We recorded 21 seizures from a total of 14 patients. Frequency domain analysis showed a significant increase of ICT LF vs. PRE/POST and INT and a higher ICT LF/HH ratio vs. INT and PRE. Time domain variables showed a statistically lower ICT RR interval (vs. PRE) and RMSSD (vs. INT) and a higher ICT SDNN and CSI (vs. INT & PRE). In addition ICT ApEn was significantly lower vs. PRE/POST and INT. Conclusion: Our data confirmed a sympathovagal imbalance in TLE with higher sympathetic tone, as showed by higher LF and LF/HH ratio, lower RMSSD and ApEn, and by the increased CSI and SDNN. Since lower vagal and higher sympathetic tone are predictors of morbidity/mortality in cardiovascular samples, our findings may suggest an early involvement of ANS in TLE.
degree of mental retardation and autistic features with obsessive/hyperactive traits. PCHD19-related epilepsy is characterized by febrile and afebrile cluster of brief seizures with prominent involvement of the fronto-temporal regions; status epilepticus can occasionally occur in about 1/3 patients. We aim to provide further electroclinical insight about the clinical EEG features of the seizures cluster in benign forms of PCDH19-related epilepsy.

Methods: We selected patients with drug resistant PCDH19-related epilepsy, without severe mental retardation or severe psychiatric features. The patients underwent video-EEG-recordings, clinical +/- neuropsychological evaluation at their baseline, during and after the cluster of seizures.

Results: 10 patients (age 3–14 years) has been selected. All of them had mild cognitive impairment, normal EEG at baseline and recurrent clusters of a few brief seizures (1–3 days) associated with variable degrees of cognitive/behavioural alterations persisting for days to weeks after seizures clusters.

Long-lasting peri-ictal video-EEG recordings were obtained in 6/10 patients; 6/6 had prolonged peri/post-ictal EEG slowing (days–weeks) and 3/6 subjects also had multifocal spikes/slow waves, in 1 case associated with multifocal jerks and in 1 case with several subtle morphic motor seizures.

Conclusions: Most PCDH19 patients share peculiar neuropsychological profile and ictal electro-clinical features suggesting both an ictal involvement and a more persistent impairment of the fronto-temporal limbic structures.

In our patients, we documented furthermore the frequent recurrence of more prolonged clinical-EEG alterations, associated to the typical seizures clusters, possibly reflecting a fronto-limbic status-like condition.

Conclusion: Catamenial epilepsy was dominated into polytherapy group where patients with resistant forms of the disease prevalence. It is determined catamenial epilepsy as predictor of disease resistance.

p196
IDIOPATHIC GENERALIZED EPILEPSIES AND SEIZURE CONTROL
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Purpose: Idiopathic generalized epilepsies (IGE) are pharmacoresponsive epilepsies. The aim is to evaluate the seizure control of IGE in adolescent and adult age with AEDs.

Method: 121 patient, 61 males and 60 females, on age 14–67 years with IGE were evaluated clinically, with EEG and brain imaging (MRI) methods. Valproate was used as monotherapy or in combination with either LEV, LTG, CNZ, TPM.

Results: There was no seizure control in 9 patients non-compliant to AEDs. Seizure relapse 1–4 years after AED withdrawal happened in 6 patients, but not in 3 after long period of seizure control with VPA monotherapy and normal EEGs. Seizure relapse happened in 4 patients during VPA dosage reduction, but not in 2 patients after long period of seizure control and normal EEGs. 11 patients misclassified as focal epilepsies were pseudopharmacoresistant with either CBZ, Pb, DHY. Their gradual withdrawal and VPA introduction as well as polytherapy with either LEV, LTG, CNZ, TPM was helpful for better seizure control in such cases. EEG normalization after detection of spike-wave complexes (SWC) and poly SWC was useful biomarker during AEDs titration and reduction considering seizure control prediction.

Conclusion: Efficacious and effective AEDs are needed for chronic treatment of IGE. Certain lifestyle avoiding seizure precipitation factors is also helpful. EEG as well as clinical evaluation is needed during chronic management of IGE for better seizure control and good quality of life.
Results: Initial shockable rhythm was found in 49.4% and cardiac origin was estimated as 69.2%. Favorable outcome (cerebral performance category, CPC 1 and 2) was found in 39.5%, and cardiac origin showed better outcome than non-cardiac (50% vs. 16%, respectively). Favorable cEEG grade is more common in the good prognosis group (p = 0.001), and favorable aEEG is more common in the favorable prognosis group (p = 0.003). Predictive value of good outcome of cEEG and aEEG showed 90% of positive predictive value (PPV) with 95% of specificity and 85% of PPV with 87% of specificity, respectively. Poor outcome by cEEG and aEEG was estimated as 89% PPV with 94% of specificity and 90% of PPV with 87% of specificity, respectively. Status epilepticus (SE) was found in 28.4% and the majority (78.3%) was myoclonic SE. 12.5% of the SE patients had favorable outcome.

Conclusion: aEEG showed good predictive value in predicting both poor and favorable prognosis after TH. SE was detected in one third, but aEEG showed good predictive value in predicting both poor and favorable prognosis after TH. SE was detected in one third, but aEEG showed good predictive value in predicting both poor and favorable prognosis after TH.

Background: Routine EEG has a diagnostic sensitivity of 50%. Sleep deprivation is the most common and effective stimulation method used to increase the yield of seizure diagnosis. Juvenile Myoclonic Epilepsy (JME) and temporal lobe epilepsy (TLE) are fairly dependent on the sleep-wake cycle and sleep deprivation (SD) is one of the most important precipitant factors.

Objective: The purpose of study was to investigate whether sleep-deprived EEG has a higher diagnostic yield than routine EEG.

Method: Consecutive patients aged 10 years or over who were referred to our lab over the last 5 years with clinical suspicion of JME or TLE and who underwent sleep-deprived EEG after an initially normal routine EEG, were included in this study. Normal night sleep was avoided for at least 12 h before EEG recordings. All EEGs were digitally performed.

Results: 302 patients were enrolled in this study during last 5 years. 104 were male, 198 were female. 94 patients (31%) were with question of JME (26 male, 68 Female) and 208 patients (69%) were referred to rule out TLE (78 male and 130 female). Minimum age was 10 years and maximum age was 46 years. 175 patients (58%) out of 302 were normal on routine EEG and 127 (42%) were abnormal. Out of 175 normal EEG 152 (87%) were found abnormal on routine EEG. Among these 152 SDE 55 (36%) patients were diagnosed as JME and 97 (64%) as TLE. In 35 patients various types of normal variants were also noted in addition to the abnormalities.

Conclusion: Sleep-deprived EEG is a significant and powerful tool with a sensitivity approaching 87%. Based on this enhanced sensitivity, patients suspected of JME or TLE should undergo sleep-deprived EEG as the routine initial test to minimize the delay in diagnosis.

p198 PERSISTENT LOCAL BRAIN ACTIVITY DURING POSTICTAL GENERALIZED EEG SUPPRESSION

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Purpose: Postictal generalized EEG suppression (PGES) frequently occurs after generalized convulsive seizures (GCS) and may be involved in the pathophysiology of sudden unexpected death in epilepsy (SUDEP). PGES is usually determined using conventional scalp EEG which is likely to miss cerebral activity in deeper brain structures. Here, we examined intracranial EEG activity after GCS to unravel the pattern and extent of local brain activity during apparent PGES on scalp EEG (s-PGES).

Method: We retrospectively reviewed electroencephalographic data of people with epilepsy who had GCS during presurgical video-EEG monitoring using simultaneous intracranial and scalp EEG (10–20 system) electrodes.

Results: Twenty GCS with s-PGES of 15 patients with an average number of 88 ± 42 intracranial electrode contacts were included. PGES lasted 29 ± 26 s (range 2–82 s). The majority of GCS with s-PGES (18 of 20) displayed persisting or re-emerging local EEG activity during apparent PGES on scalp EEG in about 10 ± 14% (range 0–42%) of all intracranial contacts. Three patterns were identified: Pattern 1 (11 GCS, 6 patients) consisted of continuous interictal activity in circumscribed brain regions. Pattern 2 (5 GCS, 5 patients) displayed suppressed EEG activity at all intracranial contacts in the early phase of s-PGES, but re-emerging local brain activity before s-PGES dissolved. Pattern 3 (2 GCS, 2 patients) showed persistent focal ictal activity.

Conclusion: Our results reveal that during apparently generalized postictal EEG suppression, local brain activity persists or re-emerges in most GCS. The possible role of such localized neuronal activity in SUDEP remains to be studied.

p199 DIAGNOSTIC VALUE OF SLEEP-DEPRIVED EEG OVER ROUTINE EEG IN JUVENILE MYOCLONIC EPILEPSY (JME) AND TEMPORAL LOBE EPILEPSY (TLE)

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Background: Routine EEG has a diagnostic sensitivity of 50%. Sleep deprivation is the most common and effective stimulation method used to increase the yield of seizure diagnosis. Juvenile Myoclonic Epilepsy (JME) and temporal lobe epilepsy (TLE) are fairly dependent on the sleep-wake cycle and sleep deprivation (SD) is one of the most important precipitant factors.

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Method: Consecutive patients aged 10 years or over who were referred to our lab over the last 5 years with clinical suspicion of JME or TLE and who underwent sleep-deprived EEG after an initially normal routine EEG, were included in this study. Normal night sleep was avoided for at least 12 h before EEG recordings. All EEGs were digitally performed.

Results: 302 patients were enrolled in this study during last 5 years. 104 were male, 198 were female. 94 patients (31%) were with question of JME (26 male, 68 Female) and 208 patients (69%) were referred to rule out TLE (78 male and 130 female). Minimum age was 10 years and maximum age was 46 years. 175 patients (58%) out of 302 were normal on routine EEG and 127 (42%) were abnormal. Out of 175 normal EEG 152 (87%) were found abnormal on routine EEG. Among these 152 SDE 55 (36%) patients were diagnosed as JME and 97 (64%) as TLE. In 35 patients various types of normal variants were also noted in addition to the abnormalities.

Conclusion: Sleep-deprived EEG is a significant and powerful tool with a sensitivity approaching 87%. Based on this enhanced sensitivity, patients suspected of JME or TLE should undergo sleep-deprived EEG as the routine initial test to minimize the delay in diagnosis.

p200 INTERICTAL ELECTROENCEPHALOGRAPHY IN PATIENTS WITH EPILEPSY IN NORTHWESTERN NIGERIA

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Purpose: To evaluate interictal EEG pattern in patients with epilepsy in North western Nigeria.

Method: A cross sectional study involving the analysis of EEGs of consecutive patients with clinical diagnosis of epilepsy over a 5-year period at two diagnostic centres in Kano, northwestern Nigeria. Information on socio-demographic and seizure characteristics was obtained. The recordings from patients were obtained using standard methods and interpreted by two of the investigators. The International Federation of Societies for Electroencephalography and Clinical Neurophysiology definition of interictal epileptiform discharges (IEA) was adopted for the study.

Result: Out of 2,219 patients referred for EEG at the two diagnostic centres during the study period, 2,041 (92%) patients had a clinical diagnosis of epilepsy. Their age ranged between 0.04 and 75 years, with a mean age of 22.8 ± 14.9 years. Overall, EEG was abnormal in 1,178 (57.7%), and 919 (45.1%) had an epileptiform pattern. One thousand six hundred and ninety-one patients had interictal epileptiform discharges, while 103 had abnormal discharges only on hyperventilation. Seventeen out of 19 (89.5%) patients with 3 Hz spike and wave complex had activation by hyperventilation. Most common interictal epileptiform activities were focal spike/sharp and wave and generalized spike/sharp and slow waves. More AED naive (678) than those that were on AED (500) had EEG abnormality and the difference was statistically significant, p = 0.0001.
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**Conclusion:** The study showed that the occurrence of interictal EEG abnormality in patients with epilepsy was about 58%. The proportion of interictal epileptiform discharges was 45% in routine first EEG studies. Among those with epileptiform activity, generalized sharp and wave complexes and focal sharp and slow wave complexes were the most common findings.

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*p201 ARTERIAL SPIN LABELING MRI: A STEP FORWARD IN NON-INVASIVE DELINEATION OF FOCAL CORTICAL DYSPLASIA IN CHILDREN*

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– seizure free after surgery). CBF was lower (Kruskal in 4/5 cases, and with histologically proven FCD type IIb in 4/4 cases (all structural MRI abnormalities in every case, with PET hypo-metabolism

**Results:**

underwent epilepsy surgery.

Whether this finding could be generalized to other epileptogenic lesions localize the epileptogenic zone showing hypo-perfusion in FCD.

Interictal ASL is a non-invasive method that may help to

Conclusion:

to the architectural and functional abnormalities associated with FCD. Mostly, morphological studies have been carried out to analyze the pathology of the disease. In this study, a whole transcriptome screening was performed to understand the molecular mechanisms leading to this cortical malformation.

**Method:** Human Gene 1.0 ST arrays (Affymetrix) were used for microarray analysis on dysplastic and non-dysplastic temporal lobe tissue, obtained from children (n = 7; mean age 2; range 1–5 years) and adult patients (n = 7; mean age 19; range 6–36 years) who had undergone surgical treatment due to intractable epilepsy or low grade tumor resection (n = 8; mean age 17; range 1–27 years). Microarray data were validated by real-time PCR, in situ hybridization and immunohistochemistry for genes of interest.

**Results:** The whole transcriptome screening of dysplastic compared to non-dysplastic temporal neocortex revealed that approximately 0.1% of genes are differentially expressed, with the majority being down-regulated in FCD. In particular, genes affecting oligodendrocyte differentiation and myelination were found to be down-regulated in dysplastic temporal lobes of children and adults. These data could be confirmed by real-time PCR. Accordingly, myelin basic protein-expressing cells were drastically reduced in dysplastic cortex.

**Conclusion:** Our transcriptome screening revealed that only a relatively low number of genes (0.1%) are differentially expressed in the dysplastic temporal cortex when analyzed in the chronic stage of the disease. Nevertheless, we found a significantly reduced expression of myelin-associated genes indicating a disturbance of oligodendrocyte differentiation and myelin sheet formation/maintenance in FCD.

Supported by: The Deutsche Forschungsgemeinschaft (DFG FA 775/2-1).

**p202 GENE EXPRESSION PROFILING OF FOCAL CORTICAL DYSPLASIA SHOWS REDUCED EXPRESSION OF MYELIN-ASSOCIATED GENES IN DYSPLASTIC TEMPORAL LOBE**

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**Purpose:** To localize the interictal cerebral perfusion abnormalities associated with focal cortical dysplasia (FCD) in children with Arterial Spin Labeling MRI

**Method:** We performed a retrospective study of 8 children explored with multimodal investigation of FCD during interictal periods. We performed Brain morphologic analysis with a 1.5T MRI following a dedicated protocol for epilepsy. Brain perfusion was quantified with pseudo continuous Arterial Spin Labeling (ASL). Brain metabolism was imaged with 18FDG-PET in 5 patients. Histology was available in 4 children who underwent epilepsy surgery.

**Results:** Localized decrease of cerebral blood flow (CBF) was noted on visual analysis in all patients with ASL. It was co-localized with the structural MRI abnormalities in every case, with PET hypo-metabolism in 4/5 cases, and with histologically proven FCD type IIb in 4/4 cases (all seizure free after surgery). CBF was lower (Kruskal–Wallis test, p = 0.002) in FCD than in normal cortex.

**Conclusion:** Interictal ASL is a non-invasive method that may help to localize the epileptogenic zone showing hypo-perfusion in FCD. Whether this finding could be generalized to other epileptogenic lesions needs to be further studied.

**p203 BRAIN MALFORMATIONS AS A FACTOR OF EPILEPSY DEVELOPMENT IN CHILDREN AT AN EARLY AGE**

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**Purpose:** Improvement of diagnostics and treatment of epilepsy in children with congenital developmental brain malformations at an early age.

**Method:** During the study we have analyzed clinical, MRI, and electro-physiologic findings in brain malformation (lissencephaly, heterotopia, focal cortical dysgenesis and polymicrogyria, dysgenesis of corpus callosum, cerebellum abnormalities) patients with epilepsy. 99 children (60 boys and 39 girls) at the age from 1 month to 16 years old, including children with epilepsy and congenital malformations of brain, with average age of 5.9 ± 1.1 years old were examined within this study. The control group consisted of 25 children at the age from 2 months to 8 years old (9 girls and 16 boys), with average age of 3.3 ± 0.63 years old. All these children had been observed due to epileptic seizures associated with hypoxic-ischemic encephalopathy and completed cerebral atrophy process. The patients of the main group were divided into 6 groups according to congenital malformations of brain they had: I – 20 patients with lissencephaly, II – 17 patients with subcortical and subependymal gray matter heterotopia, III – 10 patients with Arnold-Chiari malformation I–II, IV – 14 patients with Dandy-Walker malformation, V – 18 patients with focal cortical dysgenesis and polymicrogyria, VI – 20 patients with corpus callosum dysgenesis (isolated).

**Results of the Study:** Seizure onset correlates with disease severity. The patients with lissencephaly had seizure onset before they turned 1 year old, whereas the patients with the rest of cerebral abnormalities had seizure onset significantly later, i.e. at the age of 2.56 ± 0.71. The patients with heterotopy and Arnold-Chiari malformation started experiencing seizures at the age of 4.0 ± 1.28, those with Dandy-Walker malformation at 3.76 ± 1.23, and the children from focal cortical dysgenesis and polymicrogyria group at 3.83 ± 0.93 years old. Seizure onset age for the patients with corpus callosum dysgenesis and the control group

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patients was almost the same (average 2.03 ± 0.5 years old). Seizure frequency: frequent (7 and more a week) seizures were diagnosed in 80% of children with lissencephaly, in 53% of children with heterotopia, in 46.2% of children with Arnold-Chiari malformation, in 47.3% of children with Dandy-Walker malformation, in 56% of children with focal cortical dysgenesis and polymicrogyria and in 58.6% of children with corpus callosum dysgenesis. In focal cortical dysgenesis and polymicrogyria patients we found secondary generalized seizures with frequency up to 12 a year significantly less frequently. Neurological status: the patients with lissencephaly, polymicrogyria and Dandy-Walker malformation had significantly more severe neurological deficit in the form of cranial innervation impairments (internuclear ophthalmoplegia, sunsetting), pseudobulbar syndrome, hemi- and tetraparesis, ataxia, 60% of the patients had secondary microcephaly. Neurological deficit severity degree depended on seizure frequency in patients with lissencephaly, heterotopia, Dandy-Walker malformation, focal cortical dysgenesis and polymicrogyria. Burdened perinatal anamn:is: 72.7% of children with generalized lissencephaly, 52.9% of children with heterotopia, 21.4% of children with Dandy-Walker malformation, 18.2% of children with polymicrogyria and 55% of children with corpus callosum dysgenesis were born from premature abnormal labors, against 44% of control group patients.

Conclusion: Lissencephaly and Dandy-Walker malformation patients had the most severe cases of seizure.

p204
CHARACTERIZATION OF DYSLAMINATION AND OF ALTERATIONS IN LAYER-SPECIFIC NEURON-COMPOSITION IN FOCAL CORTICAL DYSPLASIA
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Focal cortical dysplasia (FCD), a cortical malformation arising during prenatal development, is a major cause of pharmaco-resistant focal epilepsy thus frequently becoming object to neurosurgical resection. However, little is known about the histopathologic and molecular phenotypes underlying the cortical dyslamination patterns in human FCD. The structural, molecular and cellular characterization of an impaired cortical composition and a possible coherence between neuron-specific alterations and epileptogenesis of FCD are subject of the current study.

Layer-specific protein expression (Reelin, Calbindin, Calretinin, SMI32, Parvalbumin, TLE4) was studied by immunohistological techniques on paraffin-embedded sections including double immunolabeling in neuropathologically confirmed mild FCD Type 1 and 2a (n = 15), FCD2b (n = 29) and was compared to a control group with (n = 6) or without epilepsy (n = 3 post mortem cases). Neurospecific protein levels were analyzed by quantitative Western blot analysis. Following systematic quantification of neocortical neuron density and neuron-specific protein levels statistical analysis of layer-specific neuronal subpopulations was performed according to age at surgery and brain region.

Even in severe dyslamination of FCD2b with impaired laminar assign-ment particularly of layer 3 and 5 pyramidal cells we found a rudimentary preservation of laminar structure using lamina-specific markers. The quantitative analysis of layer-specific neuronal subpopulations revealed a highly significant, age-related decrease in distinct interneuron subpopulations especially of Parvalbumin-positive interneurons primarily located in layer 4 whereas supragranular interneurons expressing Calbindin and Calretinin were only marginally affected. Furthermore, TLE4-positive projection neurons in layer 6 were increased in numbers.

Our findings suggest that cortical dyslamination is associated with disturbances in cell proliferation or differentiation, but not primarily with a general migration defect. A differential vulnerability of especially deep-layered interneurons and an increase of distinct layer-specific neurons, respectively, results in a profound, age-related alteration of the neocorti-cal neuronal composition in FCD.

p206
CHARACTERISTICS OF EPILEPSY CHILDREN WHO OVERLAP WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD)
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Purpose: To investigate the prevalence of ADHD in children with epilepsy and to determine the difference of characteristics in patients with epilepsy and concomitant ADHD as opposed to the patients without ADHD for better management.

Method: We retrospectively reviewed 184 patients diagnosed as epilepsy and treated with antiepileptic drug in pediatric neurology department of Seoul St. Mary’s hospital from March, 2009 to May, 2012. Their ages ranged from 6 to 18 years. The subject were included in the study those who made a regular visit for more than a year.

Results: 1 Out of 184 patients, 69 patients (37.5%) had both ADHD and epilepsy (male 46: female 23). 2 In epilepsy children with ADHD, male outnumbered female by almost two fold (male 67: female 33) (p = 0.022). 3 In epilepsy children with ADHD, epileptiform discharges on EEG was focused in central regions in 39% of them (p = 0.014). 4 In 56% of patients without ADHD, their seizures remained under the control with single anticonvulsant, as opposed to 36% of patients with both ADHD and epilepsy (p = 0.001).

Conclusion: The incidence of ADHD in epilepsy children was 37.5%, and patients with epilepsy and concomitant ADHD showed a significant difference and poor response to epilepsy treatment, as opposed to patients without ADHD. Therefore, early detection and establishment of countermeasures for ADHD is necessary.

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A 256-DENSE ARRAY EEG SPECTRAL ANALYSIS IN MESIAL SCLEROSIS AND NEOCORTICAL TEMPORAL EPILEPSY PATIENTS: A COMPARISON AMONG DIFFERENT SPIKE DISTRIBUTIONS
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**OVERTREATMENT OF CRYING SPELLS WITH ANTIÉPILEPTIC DRUGS AS A FORM OF MUNCHHAUSEN BY PROXY: THE ALBANIAN EXPERIENCE**

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**Background and Aims:** Overuse and abuse of antiepileptic drugs is a concern for Albanian health policy makers and specialists in general. Our case series describes the medical history of four children (aging 4–7 years, male/females 3:1) who were consulted emergently in the central polyclinic of Tirana (Albania) due to persistent crying spells. Previously to the specialist visit, children were consulted at a primary care facility and antiepileptic treatment was started. The role of the AED treatment, precise character of the (pseudo) seizures and the familiar setting were cautiously scrutinized.

**Methods:** MRI of the head and electroencephalography were registered to all cases, together with a thorough internist visit and medical check-up. Mothers underwent a psychological interview in another centre, and their psychiatric history was documented. Data upon the dosage and length of antiepileptic therapy was collected.

**Results:** No anatomic changes were registered in all cases; electroencephalography confirmed lack of epileptic activity. EEG was eventually registered anew the next month after the initial visit and lack electrical equivalents of seizures justified the AED tapering off. Six months thereafter children were free from pharmacological therapy, and counseling sessions of respective mothers with psychological assistance were under way. Precise reasons for inventing nonexistent ‘dramatic’ crying spells were found within the familial setting and the personality of the mothers. Psychotherapy for a probable Munchhausen by proxy syndrome was started.

**Conclusions:** Abstaining from unnecessary antiepileptic treatment if no electrical proof of seizure activity, when other findings (clinical visit, MRI) are as well within normality, is an advisable and fruitful measure. Psychological assistance to the caring parent (the mother, as a rule) is indispensable.
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ONE-YEAR SEIZURE OUTCOME FOLLOWING KETOGENIC DIET FOR PEDIATRIC REFRACTORY EPILEPSY: A SINGLE CENTER EXPERIENCE FROM SINGAPORE
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Purpose: To review the seizure outcome up to 12 months following initiation of ketogenic diet (KD) or Ketocal milk formula, in children and adolescents with refractory epilepsy.

Method: We reviewed our cohort of pediatric patients who were initiated on KD as a treatment option for their refractory epilepsy, having failed at least 2 standard anti-epileptic medications. Following the use of KD, the seizure outcome was compared to the baseline seizure frequency.

Results: We initiated a total of 21 patients (11 males and 10 females), aged from 1 to 15 years from 2004 to 2012. Three patients failed the initiation, as they could not tolerate the diet. At 1 month, 2 patients stopped KD because it was ineffective; 2 patients stopped due adverse behavioral change and the diagnosis of NMDA receptor encephalitis respectively. At 3 months, 2 patients (9%) were completely seizure-free, and 6 patients (29%) had seizure reduction of more than 50%. At 1 year, a total of three patients (14%) were seizure-free; seven patients (33%) continued on KD, and all had more than 50% seizure reduction.

Conclusion: The success rate of KD in our pediatric population with refractory epilepsy is similar to previous reports worldwide. A small percentage continues to be seizure-free even after 1 year of KD.

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HEALTH-RELATED QUALITY OF LIFE (HRQOL) IN SCHOOL-AGED CHILDREN WITH “ACTIVE” EPILEPSY: A POPULATION-BASED SAMPLE
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Purpose: To identify factors associated with parent reported Health-Related Quality of Life (HRQOL) in school-aged children with “active” epilepsy.

Method: Factors associated with parent reported HRQOL in school-aged children (5–15 years) with active epilepsy (had a seizure in the last year and/or on AEDs) were investigated in the Children with Epilepsy in Sussex Schools (CHESS) study. The study is a population-based study of neurobehavioural comorbidity in childhood epilepsy. Eighty-five (74% of eligible population) parents of school-aged children with “active” epilepsy completed the Quality of Life in Childhood Epilepsy (QOLCE). The children underwent comprehensive neuropsychological assessment and behavioural diagnoses were made with respect to DSM-IV-TR criteria. Linear regression analysis was undertaken to identify factors significantly associated with total QOLCE scores in this population.

Results: Factors independently significantly associated with decreased total QOLCE scores were seizures before 24 months (p = 0.011), cognitive impairment (IQ < 85) (p = 0.006), DSM-IV-TR anxiety (p = 0.005), DSM-IV-TR depression (p = 0.017) and parent reported school attendance difficulty (p = 0.011). These factors were also significantly associated with decreased total QOLCE score when analysis was limited to children with IQ > 50.

Conclusion: The majority of factors associated with parent reported HRQOL in active childhood epilepsy are related to neuropsychological and neuropsychiatric aspects of the condition. The evidence base for the treatment of these difficulties in childhood epilepsy is still limited. There is thus a need to identify efficacious interventions to reduce the negative impact of these difficulties on HRQOL in childhood epilepsy.

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RESEARCH OF CONCENTRATION OF ZINC IN CHILDREN WITH EPILEPSY
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Aim of the study was to evaluate and compare zinc content in children before age 17 with epilepsy and control group. Was observed 104 child with epilepsy and 28 children of control group, 5 months–17 years. Group with epilepsy consist of 56 boys and 48 girls, control group – 14 boys and 14 girls. Zinc content in hairs was measured using atomic-absorption method.

Results: Statistical analyses of zinc content in boys and girls with epilepsy and control group didn’t reveal any dependence from age of children. Confidence interval (p = 0.95) of zinc content in children with epilepsy was 98.98 ± 4.48 μg/g in boys and 98.53 ± 5.08 μg/g in girls, in control group: 149.29 ± 12.54 μg/g in boys and 142.12 ± 14.78 μg/g in girls. Thus, mean content of zinc in boys and girls with epilepsy was less, then in control group. Study reveal significant (p = 0.95) difference in content of zinc in boys and girls with epilepsy and control group and confidence interval of mean values is (−50.31 ± 10.60) μg/g. Significant difference was also revealed in girls with epilepsy and control group – (−43.59 ± 11.94) μg/g. Results of the study of reliability differences in width distribution of zinc values showed that boys with epilepsy and control group didn’t have significant differences, but in girls of control group is more wide, then in girls with epilepsy (p = 0.934).

Conclusions: In girls and boys with epilepsy under age 17 content of zinc didn’t depend on age. Content of zinc in hairs in girls and boys with epilepsy is significantly lower (p = 0.95) then in control group. Distribution of zinc values in girls of control group is significantly more wide (p = 0.934) then in girls with epilepsy.

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RESULTS OF THE RESEARCH OF TRIIODOTHYRONINE HORMONE CONCENTRATION IN BLOOD OF GIRLS WITH DIFFERENT FORMS OF EPILEPSY
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Introduction: Perspective direction of research in epilepsy nowadays is to study its clinical features and treatment in pubertal age. Treatment of epilepsy should considerate variety of changes in organism in that age and of course the influence of antiepileptic drugs on hormonal profile.
Aim of the Study: Is to evaluate concentration of triiodothyronine in blood of girls with different forms of epilepsy.

Materials and Methods: In study was included 46 girls 8–17 years old with different forms of epilepsy, blood concentration of triiodothyronine was determined in all of them. Statistical analysis include Student’s t-test and Fisher’s F-test.

Results: All girls were divided into 4 groups: 9 girls had generalized idiopathic epilepsy (1 group), 11 girls- generalized symptomatic epilepsy (2 group), 15 girls- focal symptomatic temporal epilepsy (3 group), 11 – other forms of focal symptomatic epilepsy (frontal, occipital or other) (group 4).

Confidence interval (p = 0.95) of T3 concentration in group 1 was 2.76 ± 0.23 nm, in group 2 – 2.67 ± 0.26 nm, in group 3 – 2.07 ± 0.44 nm, in group 4 – 2.56 ± 0.22 nm. Thus, the highest content of T3 was in group of girls with generalized symptomatic epilepsy, the lowest – with focal symptomatic temporal epilepsy.

The study of significance of differences (p ≥ 0.90) mean values of T3 in girls with different forms of epilepsy revealed, that significantly higher concentration of T3 is at generalized idiopathic, then at focal symptomatic temporal epilepsy (0.69 ± 0.58 nm), and at generalized symptomatic, then at focal symptomatic temporal epilepsy (0.60 ± 0.54 nm), and at other forms of focal symptomatic epilepsy, then at focal symptomatic temporal epilepsy (0.49 ± 0.44 nm).

Significant differences (p > 0.90) in width of distribution of values of T3 are found in girls with generalized idiopathic and focal symptomatic temporal epilepsy, with generalized symptomatic and focal symptomatic temporal epilepsy, with focal symptomatic temporal epilepsy and other forms of focal symptomatic epilepsy.

Conclusions: Were revealed forms of epilepsy in which concentration of T3 in blood was the highest, significant differences between T3 concentrations in girls with various forms of epilepsy.

p216 CAN EPILEPSY SYNDROME AND ETIOLOGY PREDICT RESPONSE TO KETOGENIC DIET IN CHILDREN?
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Purpose: To determine the impact of syndrome classification and etiology on ketogenic diet response in children with intractable epilepsy.

Method: Children initiated on ketogenic diet (KD) from January 2009 through December 2012 were identified from the KD diet database at Mayo Clinic Rochester. Charts of those with ILAE recognized clinical syndromes were reviewed to determine etiology, as well as seizure frequency (i) prior to KD onset, (ii) 3 months after KD onset and (iii) at final follow-up on KD. Significant response was defined as >50% decrease in seizures.

Results: 54 children were identified (57% male). Electroclinical syndromes were divided into those without moderate to severe intellectual impairment (Doose, childhood absence, myoclonic absence, juvenile myoclonic, and absence with eyelid myoclonia) (24%) and epileptic encephalopathies (West, Lennox-Gastaut, Dravet, Continuous Spike Wave in Slow Wave Sleep, epilepsy of infancy with migrating focal seizures) (76%). Etiologies included unknown (19%), structural (11%), known genetic (31%), structural and genetic (9%), metabolic/immune (9%), and presumed genetic (formerly idiopathic generalized) (22%). Median age of KD initiation was 2.6 years (range 0.4–13.8 years) and treatment duration was 2.0 years (range 0.25–12 years). Those with electroclinical syndromes without moderate to severe intellectual impairment demonstrated a trend towards better ketogenic diet response (p = 0.064, χ²).

However, when only those with presumed genetic etiology (idiopathic generalized epilepsy) were included in this group, there was a significantly increased response rate (p = 0.031, χ², OR 7.9).

Conclusion: Electroclinical syndrome classification combined with etiology can be potentially helpful in predicting ketogenic diet response in children.

p217 SUICIDAL ATTEMPTS IN CHILDREN AND ADOLESCENTS WITH EPILEPSY
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Introduction: The suicidal behavior is a complex social health problem, being one of the first 5–9 entities of general morbidity and the first 2–3 causes of mortality at young ages. A main problem of the pediatric psychiatry is as well the lowering of the age at which the suicidal accident happens.

The objectives of this study is to determine the incidence of suicide attempts in a sample of children and adolescents suffering from epilepsy.

Materials and Methods: In this study were analyzed cases of attempted suicide recorded in the Child and Adolescent Psychiatry Clinic of Iasi in the period 2010–2012.

Results: 31 cases met all the requirements to be included into this study. Most patients in the study were female, 80.64%. The most affected group is the one over 16 years, 45%. Of all patients 87% were being treated with anticonvulsants. Most of attempts, 84%, were trough ingestion of toxic substances and drugs. Only 13% had suicidal ideation, 10% said they wanted to die before the act and most of them went directly to the attempt without preliminary symptomatology, 77% of patients.

With one attempt were 68% patients, fulfilled trough ingestion, 13% with 2 attempts, 10% with 3 attempts and with more than 3 attempts were 10% of patients.

Conclusions: There is a higher occurs of attempts in girls rather than boys, comparing to the accomplished suicide, where the rate is switch. There is a higher rate of using methods with a smaller chance of succeeding than the accomplished suicide, where there are used more violent methods. The phases of the suicidal behaviour show a more often attitude of directly fulfilling the act, rather than with an existing ideation or affirmation before.

p218 PARATHORMONE AND VITAMIN D LEVELS IN POPULATION UNDER 18 YEARS OLD TREATED DURING 3 YEARS WITH VALPROIC ACID
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Purpose: The purpose of the study was to investigate changes in biochemical markers of bone metabolism occurring during long-term monotherapy with valproic acid (VPA).

Method: Our population consisted of 57 children aged 5–17 years suffering from different kinds of epilepsy. They were treated with valproic acid for at least 2 years with a dose of 30–45 mg/kg/day. We took measurements of parathyroid hormone, calcium, phosphorus and vitamin D levels in blood before starting the therapy and after 2–3 years of continued treatment with valproic acid.

Results: Calcium and vitamin D levels were significantly lower in the treated group. Parathormon and phosphorus levels were significantly higher in the treated group.

Conclusion: Long-term valproic acid monotherapy negatively influences bone metabolism.
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CHILDREN’S EPILEPSY AND SLEEP DISORDER BREATHING
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**Purpose:** The weight of sleep-disorder breathing (SDB) on childhood’s epilepsy isn’t well known. We try to evaluate the influence on epilepsy of adenooidectomy or tonsillectomy in children who present a SDB.

**Method:** Among epileptic children followed at Besançon’s hospital in unit Epilepsy, we were interested in those who present manifestations related to SDB like snoring, apnea, behaviour’s problem and drowsiness. We prescribe a nocturnal oximetry at home and we oriented patient to an Otolaryngologist. Then he decided if tonsillectomy or adenoidectomy are indicated. Thereafter we addressed a questionnaire to the parent to ask them about the evolution of epilepsy. The primary criterion is seizure’s number and/or number of treatment (according to the parent). Then we ask if they consider snoring for a child normal or not. Finally we look oximetry’s results.

**Result:** We send questionnaire to 26 patients, 23 have responded. They have 8.7 years on average, 46% girl and 54% boy. 10 patients (41%) have a focal epilepsy vs. 16 (59%) with a generalized epilepsy. 19 patients were operated and among them 10 (52%) improve their epilepsy. 6 decrease seizure’s number, 2 decrease number of treatment and 2 by both way. 11 parents don’t know or consider snoring for children like normal. 3 oximetry are abnormal (all in surgical patients).

**Conclusion:** In child, Epilepsy can improve surgical treatment of SDB. Snoring is considered like normal for parents. The clinical evidence of SDB must be looked for in children’s epilepsy.

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A CHILD WITH KLINEFELTER’S SYNDROME PRESENTING WITH MENTAL RETARDATION AND EPILEPTIC SEIZURES
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**Purpose:** Klinefelter’s Syndrome (KS) is the most frequent sex chromosome abnormality among males and characterized by hypogonadism and abnormalities of physical maturation. Although neurologic impairment in KS has been recognized, mental retardation is not a typical feature of KS and epileptic seizures or abnormal EEG are reported in a few cases. We describe a case of KS presenting with mental retardation and epileptic seizure.

**Case:** A 6-year-old boy was admitted due to complex partial seizure with staring and generalized tonic seizure. He was born at term following an uncomplicated pregnancy and delivery. However, his early development was delayed and chromosomal study at age of 6 months revealed that the patient had a karyotype of 47, XXX. Despite the ongoing cognitive rehabilitation, he showed remarkable neurocognitive disability. Seizures began with febrile illness at 6 year of age. Since that time, his seizures have deteriorated without provoking factors. Brain magnetic resonance images (MRI) revealed moderate degree of bilateral ventriculomegaly. Electroencephalograms (EEG) showed very frequent spike and slow wave discharges from left or right frontal areas occurring synchronously or independently. His seizures have been well controlled with valproic acid until now.

**Conclusion:** We describe a case with KS who presented with remarkable mental retardation and epileptic seizures. Although rare, epilepsy should be considered as neuropsychiatric phenotype in children with KS.

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TOPIRAMATE IN EPILEPTIC SYNDROMES OF CHILDHOOD WITH CONTINUOUS SPIKE-AND-WAVE DURING SLEEP: RETROSPECTIVE STUDY OF 23 CASES
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**Purpose:** Continuous spike-and-wave during sleep (CSWS) is an age-related EEG pattern occurring in childhood, associated with cognitive and/or behavioural impairment. We report our experience with topiramate (TPM), a broad spectrum antiepileptic drug (AED), in this difficult-to-treat condition.

**Method:** We retrospectively reviewed EEG and clinical data of children with epileptic syndromes associated with CSWS followed in our institution and treated with TPM. Sleep EEG was performed 0–3 months before TPM introduction, and then at 3 and 12 months. Introduction of another AED or withdrawal of a potentially aggravating AED during the first 3 months of TPM treatment were exclusion criteria. In addition to Spike Index, severity of EEG abnormalities was rated using an original scale taking also into account spatial extension of epileptiform discharges.

**Results:** 23 patients were included (19 male, 4–14y, 3 symptomatic cases). At 3 months, EEG was improved in 15 and normalized in 4 children (TPM doses: 2–5.5 mg/kg/day). Among these 19 patients, 17 had cognitive or behavioural improvement. At 1 year follow-up, 22 children were still on TPM and EEG improvement persisted in 10. Among 14 children with clinical seizures, 8 were seizure free at 1 year, while seizure frequency decreased in 6 other patients.

**Conclusion:** TPM may reduce EEG abnormalities in epileptic syndromes with CSWS, with clinical improvement in majority of the patients. However, relapse may occur at long term in nearly half of the cases. Otherwise, TPM seems to be particularly useful to decrease seizure frequency in these patients.

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REFLECTION FROM A SMALL CENTER ON THE TOPIC OF CARE IN PRE-SURGICAL INVESTIGATION OF CHILDREN WITH REFRACTORY EPILEPSY
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Lund is a University hospital performing investigations for surgery in epilepsy. The catchment area covers about 1, 7 million people.

We investigate approximately hundred patients annually, of which a fifth will take part in the pediatric surgery program.


The prerequisite for successful results is good planning and cooperation between different disciplines. Pediatric epilepsy nurses and technologists provide good care for the patient. The nurse with high availability follows the investigation and prepares the patient and the family before and during the stay. To achieve optimal recording with simultaneous video testing during seizures, staff will constantly be present. Daily
interactions with the neurophysiologic ward, regarding EEG and semiology will assure a good registration and lead to optimal adjustments in patient’s medication or diurnal rhythm.

We use SISCOM (Subtracted Ictal SPECT Co-registration on MRI) for mapping high-flow areas in non-lesional cases. The localization of a seizure-related hyperperfusion might lead to finding an actual lesion on MRI, or guiding an invasive registration with placement of electrodes. The SISCOM analysis is performed by the technologist and the result is evaluated in consultation with neuroradiologist and neurophysiologist. 1/3 of SISCOM analyses are performed on request from other centers in Sweden.

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**NEUROFIBROMATOSIS TYPE 1 AND EPILEPSY IN CHILDREN AND ADOLESCENTS-ONE CENTER CLINICAL EXPERIENCE**

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**Objectives:** Neurofibromatosis type 1 (NF 1) is an hereditary disorder, associated with mutation in the NF1 tumor suppressor gene. According to the great clinical variability, epilepsy occurs in 3–12%.

**Patients and Methods:** In a period of 10 years (2003–2012), 42 patients with NF type 1, children and adolescents (20 male, 22 female), aged 2–19 years (12.6 mean age) were retrospectively analyzed for epilepsy and EEG characteristics.

**Results:** Epilepsy developed in 8 (19%) of our patients with NF1. Mean age of seizure onset was 9.1 years. They mainly experienced focal seizures (7). Focal motor seizures in one patient and non-convulsive complex partial epileptic status in the other, were the initial epileptic event. One boy with history of early infantile spasms later developed Lennox-Gastaut syndrome. EEGs disclosed bilateral or focal spike-wave abnormalities. Despite of single unprovoked seizure and initial EEG discharges one patient had long-term history of both seizure and antiepileptic therapy freedom. In addition, eight patients with NF 1 without clinical seizures, showed EEG abnormalities. Two of them had frequent episodes of headache. Stable, favorable seizure control for 12–18 months was noted in five (62.5%) patients, including two with complete seizure control. Intractable seizures occurred in a boy with Lennox-Gastaut syndrome. In seven (87.5%) patients with NF 1 and epilepsy MRI showed brain lesions. Mental retardation, mainly mild, was associated with epilepsy in 62.5% cases.

**Conclusion:** Epilepsy and EEG features are not uncommon in patients with NF type 1. Favourable seizure control could be achieved by antiepileptic drugs in majority of patients. Structural brain lesions, identified by neuroimaging were often associated with pharmacoresistant epilepsy.

**Method:** The PERFECT initiative consists of three phases. Phase 1 was analysis of guidelines/policy; Phase 2 surveyed 128 healthcare professionals (HCPs) to ascertain their perception of how PACS are managed in the community. Phase 3 is an ongoing, cross-sectional survey conducted in five EU countries to understand the experience of PACS from the perspective of the children and their parents/guardians. Planned enrollment is 500 children (3–16 years) with epilepsy, currently receiving rescue medication for PACS and with ≥1 episode of PACS in the previous year. Children and parents/guardians will complete different web-based surveys, and information will be compared with utility scores derived from EQ-5D questionnaires, completed by parents/guardians, HCPs and patients, which rate patients’ health-related quality of life (HRQoL). Patient HRQoL will also be assessed by Neuro-QoL.

**Results:** The HCP survey identified gaps in awareness of how PACS are managed in the community, poor communication between HCPs and schools/settings where seizures can occur, and lack of training for caregivers. Approximately 50% believed that, due to insufficient training, caregivers/school staff are often indecisive when a child experiences a seizure.

**Conclusion:** The PERFECT initiative has demonstrated the need for clearer guidance, open communication between stakeholders, training to all caregivers and a greater emphasis on instilling confidence in parents/caregivers. Phase 3 findings will show the impact that PACS has on children and their families.

The study was funded by ViroPharma SPRL.

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**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 1 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.
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BONES AND BRAINS: A PROSPECTIVE CASE–CONTROL STUDY OF SEASONAL VITAMIN D IN CHILDHOOD EPILEPSY
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Purpose: To investigate seasonal differences in serum 25-hydroxy vitamin D (25(OH)D) in Scottish resident children with epilepsy (CWE) on antiepileptic drugs (AEDs) ≥1 year compared to those without epilepsy.

Method: CWE were enrolled through Royal Hospital for Sick Children (RHSC), Edinburgh, epilepsy clinics. Controls were from previously healthy children attending RHSC’s outpatient/emergency departments. At enrolment, volunteers completed standardised questionnaires on bone pain, quality of life, diet, clinical and demographic details, had 25(OH)D, parathyroid hormone, bone profile, liver assays taken. Volunteers were invited for reassessment 6 months post-baseline. If children did not return, additional children were recruited aimed to achieve case:control of 1:1.

25(OH)D levels (nm) were considered: Deficient <25; Insufficient 25–49; Sufficient ≥50. Chi-squared analyses were used to assess intergroup differences.

Results: 25 CWE (median age 11.7 years) enrolled; all had reassessments. 35 controls (median age 6.31 years) enrolled; 6 had summer and winter assessments, 19 winter only, 10 summer only.

In winter, 13 (52%, 95%CI 34–70%) CWE were deficient, 7 (28%, 95%CI 14–48%) insufficient compared to 10 (40%, 95%CI 23–59%) controls who were deficient, 8 (32%, 95%CI 17–52%) insufficient (NS). In summer, 2 (8%, 95%CI 2–25%) CWE were deficient, 11 (44%, 95%CI 27–63%) were insufficient vs. zero (0%, 95%CI 0–20%) controls deficient and 4 (25%, 95%CI 10–50%) insufficient (NS).

All calcium levels were normal. One CWE had elevated alkaline phosphatase.

Conclusion: A high proportion of Scottish children, with and without epilepsy, are generally deficient/insufficient in 25(OH)D in winter.

Most children without epilepsy have sufficient levels over the summertime whereas a substantial proportion of epilepsy children on AEDs continue to have deficient/insufficient 25(OH)D. Deficient/insufficient 25(OH)D can be present even with normal bone profile.

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EPILEPSIA PARTIALIS CONTINUA IN TICK-BORNE RUSSIAN SPRING-SUMMER ENCEPHALITIS
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Purpose: Epilepsia partialis continua (EPC) has numerous possible etiologies. We describe EPC in the tick-borne Russian spring-summer encephalitis (TBRSE) and compare it with Kozhevnikov-Rasmussen syndrome.

Method: We included 10 patients with EPC in TBRSE. The diagnosis was verified by immunology (antibodies against TBRSE virus). The patients were followed 1–7 years.

Results: We studied 10 patients (8 males, age 10–21 years) with MRI and video-EEG. Nine developed EPC after acute TBRSE, and one had a tick bite without clinical symptoms of encephalitis, but with subsequent EPC. All patients came from Urals and Siberia. The mean age at onset was 8.6 years. The interval from onset of TBRSE to the tick bite to seizure onset was 3–10 months. We identified 3 phases of clinical course of EPC in TBRSE: (i) acute (meningoencephalitis/encephalitis); (ii) development of EPC; (iii) chronic EPC. The effect of antiepileptic drugs differed according to seizure types.

Conclusion: EPC caused by TBRSE is relatively frequent in the Eastern part of the Russian Federation but not west of the Urals. Unlike Kozhevnikov-Rasmussen encephalitis, EPC with TBRSE has diffuse atrophic lesion on MRI and does not progress even in the long term. It appears as disabling but not fatal condition with a time course where three phases can be distinguished.

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DOES COEXISTANCE OF CLINICAL RISK FACTORS AND MOLECULAR MARKERS INCREASE A RISK OF DRUG-RESISTANCE IN EPILEPSY?
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Purpose: Epilepsy is one of the widespread neurological conditions. Despite of introducing many new AEDs in 20–30% of patients the control of seizures remains unsuccessful. Early determination of drug resistance may also contribute to an earlier decision to introduce a non-pharmacological therapy, which prevents preserved drug resistance. The aim of the research was to assess whether there is a correlation between a response to pharmacotherapy and clinical data and/or MDR1 and CYP3A5*3 gene polymorphism.

Method: Patients included in the research (boys and girls) were aged from 33 months to 20 years, and suffering from focal epilepsy. The following clinical data was considered: pregnancy and delivery history, family history, development (I/II), physical and neurological examination, occurrence of febrile seizures and/or status epilepticus, age when the seizures began, type of seizures, etiology and response to AEDs. Polymorphism of MDR1 C3435T was detected using the PCR-RFLP method; CC, CT, TT genotype were evaluated. To analyze polymorphism of CYP 3A5*3 variants of isofoms 1.3 and 3.3 were searched.

Results: Most of the assessed clinical data may be considered as risk factors – age of seizure manifestation, family history, development (I/II), abnormality in physical and neurological examination, occurrence of status epilepticus, type of seizures and their polymorphism. The occurrence of individual clinical risk factors, however, is a weak predictor of possibly poor response to adequately implemented pharmacotherapy. Coexistence of at least three of them is required for such prediction. No correlation between the assessed polymorphism MDR1 C3435T and 1.3 and 3.3 CYP3A5* and drug intractability was stated.

Conclusion: Most of analyzed factors can be treated as risk factors. The presence of single risk factors does not predict drug resistance and poor pharmacological response. The coexistence of at least 3 factors can serve as such a predictor.

Abstracts
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p230
ASSOCIATION OF ABCB AND SCN1A GENE POLYMORPHISMS TO LAMOTRIGINE AND CARBAMAZEPINE IN UKRAINIAN PATIENTS WITH EPILEPSY

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Purpose: In spite of variety AED, treatment remains ineffective in 30% of epilepsy patients. Genetic factors can significantly influence the outcome of drug therapy. In the current study, we addressed the question of whether polymorphisms C3435T (rs 1045642) and C1236T (rs 1128503) of the ABCB1 gene which codes for the P-glycoprotein and rs3812718 of SCN1A gene, encoding the alpha subunit of the neuronal sodium channel, influence response to carbamazepine (CBZ) and lamotrigide (LTG) in Ukrainian population.

Method: 206 subjects, 109 males and 97 females, mean age 35.4 ± 12.2y participated in the study. Drug treatment of subjects was with CBZ (n = 147), LTG (n = 59). Drug-resistant epilepsy was defined as uncontrolled seizures over a year despite attempts to treat with three or more different AEDs.

Results: C3435T genotype of ABCB1 was significantly associated with drug resistance. CC carriers exhibited significantly higher resistance to drug response compared to T allele carriers counterparts: CC (n = 76 of 88 patients) vs. CTTT (n = 35,118). This effect was independent of or sex of the patients and remained significant in each of the drug groups. There was no significant association of C1236T genotype with drug response: CC (n = 7,584) vs. CT (n = 990) vs. TT (n = 132). Rs3812718 genotype of SCN1A gene was significantly associated with developing resistance in response to CBZ and LTG. TT carriers exhibited higher prevalence of resistance to antiepileptic treatment: CCCT (12123) vs. TT (808363). There was no apparent interaction between C3435T and rs3812718 polymorphism in determining drug resistance. Combination of C3435T and rs3812718 polymorphisms gave 100% sensitivity and 66% specificity in identifying drug non-responders.

Conclusion: This study demonstrated significant associations in common polymorphisms of the ABCB1 and SCN1A genes with resistance to CBZ and LTG treatment. Polymorphisms appear to demonstrate an additive effect and indicate the future potential for genetic testing of resistance in patients with epilepsy.

p232
TWO SISTERS WITH STRIKINGLY SIMILAR PHOTOSENSITIVITY, BUT DISCORDANT FOR SCN1A-POSITIVE DRAVET SYNDROME

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Purpose: Dravet patients show photosensitivity in 40%, which is higher than in other syndromes. The question therefore arises whether the photosensitivity trait is connected with the SCN1A gene.

Method: Extensive visual stimulation during long-term video-EEGs was performed in the same center.

Results: A therapy resistant, intellectual disabled 15 year old girl (proband) with onset of epilepsy at 3 months was diagnosed with Dravet syndrome de novo. Gly1433Glu SCN1A mutation. At age 2 parents noticed frequent blinking and myoclonic jerks: EEG registrations under multiple AED showed irregular background, epileptiform discharges (ED) over O- T regions, photoparoxysmal responses (PPRs) between 25 and 40 Hz and pattern sensitivity; she also evoked generalised ED by slow eye movements (selfinduction). In later years she had often seizures induced by sunlight, TV etc and blinking induced episodes of trance at school. PPR-range at age 7 was 30–60 Hz. Her older, normal intelligent sister had seizures evoked by a TV-computer game at age 9. SCN1A-analysis was normal. EEG registrations (no AEDs) showed irregular background with spontaneous ED over the O-P region and a PPR range of 25–50 Hz. Like her sister, she repeatedly evoked generalised ED by slow eye movements. At age 13 (LEV 750 mg) she was photosensitive for 20 Hz only, and pattern sensitive. Of both parents (without epilepsy) only father showed irregular background and some isolated occipital sharp and slow waves spontaneously and during IPS.

Conclusion: Striking similarities were found in photosensitivity between the proband with Dravet (SCN1A mutation confirmed) and her sister: sensitivity to relatively high IPS-frequencies, pattern sensitivity and self inducing behavior. They were however very different in terms of seizure frequency, severity and developmental outcome. These observations suggest that expression of photosensitivity in children with SCN1A-related Dravet syndrome might be largely influenced by other genetic factors.
p233

MOLECULAR CHARACTERIZATION OF A FAMILIAL CHROMOSOME 9q22.2-22.32 DELETION IN A PATIENT WITH CORPUS CALLOSUM AGENESIS AND INTRACTABLE EPILEPSY

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Purpose: We reported a new case of mosaic 9q22.2-22.32 deletion by using high resolution array with corpus callosum agenesis, multiple congenital anomalies and early-onset drug-resistant seizures.

Case Report: A two-year old boy who was the first child of nonconsanguineous parents was presented with delayed motor development, hypotonia, microcephaly, intractable seizures and dysmorphic features including micrognathia, small mouth, high arched palate, low-set ears, congenital joint contractures of the hands and feet, inguinal hernias and undescended testes. MRI studies of the brain demonstrated absence of corpus callosum and hypoplasia of the cerebellar vermis. EOG showed bilateral intermittent generalized semi-rhythmic sharp and slow waves. We detected about 4.8-Mb deletion containing 40 RefSeq genes at chromosome 9q22.2-22.32 with high resolution array analysis. The deletion and paternal origin were confirmed by additional qPCR experiments.

Conclusion: We discussed the genotype-phenotype correlation according to the genes in the deleted region and compared with microdeletion syndrome phenotype described at 9q22.3. We reviewed the literature of chromosomal loci and genes responsible for corpus callosum agenesis and cerebellar vermis hypoplasia.

p234

NEXT Generation Sequencing STRATEGIES FOR MENDELIAN EPILEPSY DISORDERS: A HYPOTHESIS-BASED GUIDELINE FOR PATIENT SELECTION

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Next Generation Sequencing (NGS) technologies allow researchers to examine patients who were under-investigated in the past, including small families (e.g. autosomal recessive) and isolated cases. Also, larger families for whom linkage analysis was performed but positional candidate gene screening did not reveal a pathogenic variant can easily be resequenced. High throughput screenings of epilepsy patients have consequently led to the identification of at least 20 new epilepsy-causing genes. Currently, every lab working on a (presumed) genetic disorder is sequenced. High throughput screenings of epilepsy patients have consequently led to the identification of at least 20 new epilepsy-causing genes. Currently, every lab working on a (presumed) genetic disorder is sequenced. High throughput screenings of epilepsy patients have consequently led to the identification of at least 20 new epilepsy-causing genes. Currently, every lab working on a (presumed) genetic disorder is sequenced. High throughput screenings of epilepsy patients have consequently led to the identification of at least 20 new epilepsy-causing genes. Currently, every lab working on a (presumed) genetic disorder is sequenced. High throughput screenings of epilepsy patients have consequently led to the identification of at least 20 new epilepsy-causing genes. Currently, every lab working on a (presumed) genetic disorder is sequenced. High throughput screenings of epilepsy patients have consequently led to the identification of at least 20 new epilepsy-causing genes. Currently, every lab working on a (presumed) genetic disorder is sequenced. High throughput screenings of epilepsy patients have consequently led to the identification of at least 20 new epilepsy-causing genes. Currently, every lab working on a (presumed) genetic disorder is sequenced. High throughput screenings of epilepsy patients have consequently led to the identification of at least 20 new epilepsy-causing genes. Currently, every lab working on a (presumed) genetic disorder is sequenced. High throughput screenings of epilepsy patients have consequently led to the identification of at least 20 new epilepsy-causing genes. Currently, every lab working on a (presumed) genetic disorder is sequenced. High throughput screenings of epilepsy patients have consequently led to the identification of at least 20 new epilepsy-causing genes. Currently, every lab working on a (presumed) genetic disorder is sequenced. High throughput screenings of epilepsy patients have consequently led to the identification of at least 20 new epilepsy-causing genes. Currently, every lab working on a (presumed) genetic disorder is sequenced. High throughput screenings of epilepsy patients have consequently led to the identification of at least 20 new epilepsy-causing genes. Currently, every lab working on a (presumed) genetic disorder is sequenced. High throughput screenings of epilepsy patients have consequently led to the identification of at least 20 new epilepsy-causing genes. Currently, every lab working on a (presumed) genetic disorder is sequenced. High throughput screenings of epilepsy patients have consequently led to the identification of at least 20 new epilepsy-causing genes. Currently, every lab working on a (presumed) genetic disorder is sequenced.

Purpose: Dravet syndrome is a severe epilepsy syndrome characterized by infantile onset of therapy-resistant, fever-sensitive seizures followed by cognitive decline. Mutations in SCN1A explain about 75% of cases with Dravet syndrome: 90% of these mutations arise de novo. To find the missing heritability of Dravet syndrome, we studied a cohort of nine individuals with Dravet syndrome without an SCN1A mutation, including some atypical cases with onset up to 2 years of age.
Method:
1 Whole exome sequencing was performed on genomic DNA of the nine patients and their unaffected parents. Validation of variants and screening of a cohort of 150 probands with EE similar to the CHD2 mutation carriers was performed by Sanger sequencing.
2 To explore the functional relevance of CHD2 haploinsufficiency in an in vivo model system, we knocked down chd2 in zebrafish using targeted morpholino antisense oligomers.

Results:
1 In two individuals we identified a de novo loss-of-function mutation in the CHD2 gene, encoding the chromodomain helicase DNA binding protein 2. A third de novo CHD2 mutation was identified in an epilepsy proband of a second (stage 2) cohort. All three individuals with a CHD2 mutation had intellectual disability and fever-sensitive generalized seizures with prominent myoclonic seizures, starting in the second year of life or later.
2 chd2 knockdown larvae exhibited altered locomotor activity, and the epileptic nature of this seizure-like behaviour was confirmed by field potential recordings that revealed epileptiform discharges as equivalents of seizures in affected persons which were absent in appropriate control larvae.

Conclusion: Our study provides evidence that de novo loss-of-function mutations in CHD2 are a cause of epileptic encephalopathy with generalized seizures.

P236 ADENOSINERGIC SYSTEM IN MESIAL TEMPORAL LOBE EPILEPSY
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Purpose: Adenosine is a ubiquitous homeostatic molecule that acts as an “endogenous neuromodulator”. Adenosine levels are regulated by the enzyme Adenosine kinase (ADK), synthetized by astrocytes. Unbalanced adenosine metabolism has been implicated in pathologcal conditions such as epilepsy. Evidence from experimental studies support a role for ADK overexpression in brain injury associated with astroglisisis, a morphological hallmark of Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis (MTLE-HS). Nevertheless, the role of adenosine in epileptic hippocampus is controversial since adenosine neuromodulation in this region might result from a balance between inhibitory A1 and facilitatory A2A receptors. The aim of this study was to characterize A1R, A2AR and ADK gene expression in MTLE-HS patients.

Method: Expression levels of ADK, A1R and A2AR were quantified by Real-Time PCR in the hippocampus (lesional and peri-lesional cortical area) of 15 MTLE-HS patients submitted to surgery and compared with 10 autopsy controls with no history of neurological disorders. Relative expression values were calculated using the 2−ΔΔCt method. Differences in ACt were evaluated using Student’s t-test.

Result: Hippocampal ADK, A1R and A2A expression was similar in patients and controls. In the temporal adjoining cortex A1R expression was 2.5 fold higher in MTLE-HS patients than in controls although this difference was not statistically significant. No differences were found in the expression of the other 2 genes.

Conclusion: The difference in expression of adenosine A1 receptors may suggest that adjacent cortical region is contributing to disease progression. It should be stressed that this is a global analysis that does not differentiates between neurons and microglia. Also, it has been described that the different hippocampal regions may have differential gene expression. The gene expression analysis in the different hippocampal regions is underway. It will also be important to characterize these factors at both protein and functional levels.

P237 T1174S SCN1A MUTATION IS ASSOCIATED WITH SEIZURE AND MIGRAINE – MAY IT ALSO CHANGE THE EPILEPTIC ENCEPHALOPATHIES’ COURSE?
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Purpose: Mutations in SCN1A are causative for Dravet Syndrome and GFPS+ but were also identified in families with migraine phenotypes, supporting the link between migraine and epilepsy. The purpose of the report is to present the T1174S (p.Trp1174Ser) SCN1A mutation as a cause of the familial migraine phenotypes, but also as a factor potentially changing the epileptic encephalopathies’ phenotypes caused by the mutations in the SCN1A, ARX and PCDH19 genes.

Method: Four families with different types of epileptic encephalopathies; Dravet Syndrome, Epilepsy and Mental Retardation Limited to Females and West Syndrome of atypical course, underwent the clinical/molecular investigations. Mutation analysis of the SCN1A gene was performed for all probands. For SCN1A negative patients the PCDH19 and ARX genes (depending on phenotype), were studied. Appropriate exons, of the appropriate genes were analysed for the probands’ parents/relatives.

Results: The probands diagnosed clinically with DS had mutations in SCN1A gene – p.Arg712* (de novo) and p.Arg1245* (maternal inheritance). In female EFMR patient (referred as not typical DS) mutation in the PCDH19 gene – p.Asp155Tyr (de novo) was identified. The male patient carrying the mutation in the ARX gene – del79nt-IVS4/EX5 (maternal inheritance) was referred twice as having NE/epilepsy of unknown etiology and later as DS-like. For all probands SCN1A additional mutation p.Trp1174Ser was identified (hereditary in all cases). In some of the families we were able to show its cosegregation with migraine phenotype. In the case of inherited p.Arg1245* mutation, the presence of additional mutation on the second SCN1A allele shifted phenotype from epilepsy to epileptic encephalopathy.

Conclusion: The p.Trp1174Ser mutation may give rise to different phenotypes. It induces divergent functional effects – gain and loss of function of Na+,1,1, and probably not only causes the epilepsy/migraine but also influences on the other epilepsy phenotypes.

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P238 FREQUENCY OF DISTRIBUTION OF 3435 T/C POLYMORPHISM OF MDR1 GENE AMONG PATIENTS WITH DRUG-RESISTANT EPILEPSY AND HEALTHY DONORS
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Abstracts
Purpose: Research C3435T polymorphism of MDR1 gene and estimate its association with formation pharmacoresistance in epileptic patients treated with AED.

Method: 59 patients with pharmacoresistance epilepsy and 35 outbred healthy Uzbek people were included in the research. DNA analysis for the gene MDR1 (C3435T) was performed by PCR thermocycler for CG-96-1 «Corbett Research» (Australia).

Results: The analysis of 3435 T/C polymorphism distribution frequency of MDR1 gene among pharmacoresistance epilepsy patients and apparently healthy donors was made. The distribution of the gene alleles frequencies was found to correspond to Hardy-Vainberg’s law of balance (>0.05). The indicators of relative divergence of expected heterozygosity from the observed ones in the patients and the controls made D = -0.11 and D = +0.08, accordingly. The frequency of genotypic variants of the polymorphism in the patients was: CC – 18.6%, CT – 55.9%, TT – in 25.4% of cases. In the control group: CC – 60.0%, CT – 33.3%, TT – in 6.6% of cases.

The obtained results indicate a considerable influence of functionally weakened variants of C3435T polymorphism of MDR1 on the AED efficiency. For example, among patients poorly or not responding to the therapy, the frequency functionally adverse genotype TT was over 4 times reliably higher than in the controls (χ² = 4.5, p = 0.03; OR = 4.8; 95% CI = 1.013, 22.48).

Besides, thanks to the high specificity (SP = 0.81) and medium sensitivity (SE = 0.6), the calculated AUC indicator (0.70) also proves rather high efficiency by the classifier of the marker as an independent gene-candidate for drug-resistance in epilepsy.

Conclusion: The presence of T-allele of C3435T polymorphism of MDR1 increases the risk of drug-resistance development in epileptic patients and is a reliable and predicting criterion of efficiency and validity of anti-epileptic therapy.

p239
TRIO EXOME SEQUENCING IN 31 PATIENTS WITH SCN1A NEGATIVE DRAVET SYNDROME LEADS TO THE DETECTION OF ANOTHER RECESSIVE SCN1B MUTATION AND THE DISCOVERY OF AT LEAST TWO NOVEL EPILEPSY GENES
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Purpose: To unravel the genetics of the 25% of patients with Dravet syndrome without a SCN1A mutation.

Method: Detailed clinical information and DNA of 51 patients with SCN1A negative Dravet syndrome were collected by the EuroEPINOMICS-RES consortium. Whole exome sequencing was performed on 31 patients and their unaffected parents.

Results: 11/31 patients carried a de novo SCN1A mutation, previously missed due to technical or human errors. 5/31 patients carried mutations in a gene known to be implicated in Dravet syndrome (1 de novo PCDH19, 1 de novo GABRA1, 2 de novo CHD2 mutations, 1 homozygous SCN1B mutation). 1 patient carried a de novo mutation in SCN1A, a gene recently described in patients with epileptic encephalopathy. 2/31 patients each carried a de novo mutation in one of two novel ion channel genes. Respectively 3 and 5 additional epilepsy patients with de novo mutations in these 2 genes were then detected in next generation sequencing studies of consortium partners. The phenotype of patients with mutations in these two novel genes showed considerable mutual overlap. Twelve patients carried one or more de novo mutations in non-ion channel genes not previously linked to epilepsy. Screening of these candidate genes in a larger follow up cohort using a targeted gene panel is ongoing.

Conclusion: SCN1A mutations are more frequent in Dravet syndrome than currently estimated. This study detects the third Dravet patient reported so far with a recessive SCN1B mutation. Trio exome sequencing further reveals mutations in known Dravet and epileptic encephalopathy genes, and leads to the discovery of at least two novel epilepsy genes.

p240
THE MTHFR 677C>T POLYMORPHISM AND POSTSTROKE SEIZURES IN POLISH PEDIATRIC PATIENTS
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Purpose: Hyperhomocysteinemia is an established risk factor for vascular disorders in children and adults. Methylenetetrahydrofolate reductase (MTHFR) is an enzyme that catalyses remethylation of homocysteine (HCys) to methionine. The 677C>T polymorphism within MTHFR gene causes increased concentration of HCys. Previously it was observed that elevated level of HCys plays a role in the development of brain atrophy in epileptic patients. We aimed to analyse relationship between presence of polymorphic variant of 677C>T MTHFR polymorphism and post-stroke seizures in Polish paediatric patients with arterial ischemic stroke (AIS).

Method: The study population consisted of 165 children (white Polish Caucasians) recruited in the Department of Neuropediatrics in Katowice and divided into three groups: 10 children with AIS and poststroke seizures, 30 children with AIS but without poststroke seizures and 125 controls. The MTHFR polymorphism was genotyped using PCR-FLP method.

Results: The TACI stroke was the most common stroke subtype, present in 58% of the children with poststroke seizures. The PACI as well as LACI subtypes were found in 17% of the patients with seizures. We observed that frequency of 677T allele was more prevalent, but not significantly, in the group with poststroke seizures (42%) compared to controls (31%, p = 0.455, OR = 1.59 95% CI 0.40–6.19). Carrier-state of T allele is also slightly frequent in the group with poststroke seizures than in children without seizures as well as controls (67%, 61% and 53% respectively).

Conclusion: The MTHFR polymorphism may have some impact on development of poststroke seizures in Polish patients, although studies based on larger group of patients are needed.

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Abstracts

Imaging 1
Monday, 30th June 2014

p241
WHITE MATTER CHOKING SIGN AND ITS VARIANTS: AN IMAGING SIGN FOR DETECTION AND CHARACTERIZATION OF FOCAL CORTICAL DYSPLASIA
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Purpose: To describe two new signs called “White Matter Choking Sign” and “WM Choking extended” useful for diagnosis of FCD.

Materials and Methods: 165 patients in age group of 6-44 years with refractory epilepsy and 30 ae, sex matched controls were included in this study imaged using Both TLE and ETLE (extra temporal lobe epilepsy) protocols on a 3T MRI system (Achieva, Philips Health care, The Netherlands) with a 3D T1, 3D T2, 3D T2 FLAIR for detection of occult dysplasia. The data was viewed and post-processed using a Philips Portal Work station and Advantage Windows (GE health care system) to generate 3D corticographs of normal, abnormal areas and correlated with multimodal imaging and pathology.

Results: Three patterns emerged in our series of histopathologically proved FCD. The FCDs analysed were as follows: 1B (56), IIA (33), IIB (27), III (39). Sudden truncation or choking of sub-cortical white matter with blurring of interface (White Matter Choking sign) has positively correlated with Focal cortical dysplasia in 82%, WM choking sign underlying a cortical laminar architectural abnormality (White Matter choking Extended sign) has positively correlated with type Ib and Type IIA-92%, abnormal Medullary Spike Pattern was seen in Cingulate gyral FCD (n = 4), Para sagittal Cortical Ribbon dysplasia of type IB (n = 7). Type IB and IIA: sensitivity 92%, specificity 81%, Type IIB sensitivity 92%, specificity 70%; specificity of type IIB improved with presence of trans mantel sign (n = 27) to 95%.

Conclusion: White Matter Choking Sign and White Matter Choking Extended sign offer optimal sensitivity and specificity for MRI detection of FCD.

p242
HYPERCONNECTIVITY IN JUVENILE MYOCLONIC EPILEPSY – A NETWORK ANALYSIS
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Purpose: Graph theory is a technique for studying whole brain connectivity and may detect subtle differences between populations without major brain structural anomalies. In this study we used this approach to look for evidence of differences in structural connectivity within subnetworks in patients with juvenile myoclonic epilepsy (JME) and matched controls.

Method: We performed diffusion tensor imaging (DTI) in 35 JME patients and 35 controls. White matter tracts of the whole-brain network were reconstructed using deterministic fiber tractography. The automated anatomical labeling atlas (AAL) was used to identify regions of interest. Two “node” regions were considered to be connected if a fiber bundle was present with endpoints in each. Weighted connectivity matrices were calculated for each individual and used to look for changes in structural connectivity in patients compared to controls. We used a network-based statistic (NBS) approach to localise subnetworks showing significant between-group differences in connectivity.

Results: We identified one significant subnetwork (p < 0.05 FWE corrected) consisting of 8 nodes (encompassing precuneus, parietal cortical, primary motor and subcortical regions and the right hippocampus) and 7 connections. All of the connections exhibited increased values in the patients compared with the controls.

Conclusion: Both functional and structural hyperconnectivity have previously been reported in JME. A network of hyperconnectivity involving precuneus and subcortical regions – key structures in spike wave generation – along with primary motor areas may contribute to myoclonic jerks, and parietal cortex to absence seizures. This abnormal network may also contribute to the cognitive dysfunction seen in JME. We believe this to be the first reported use of DTI and graph theory in patients with JME.

p243
VOLUME INCREASE OF THE AMYGDALA IN ANTIBODY-ASSOCIATED LIMBIC ENCEPHALITIS REVEALED BY VOLUME-BASED MORPHOMETRY
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Purpose: Limbic encephalitis (LE) is an autoimmune mediated disease leading to temporal lobe epilepsy, mnestic deficits, and psychiatric symptoms. A recent study quantifying FLAIR signal intensities of the temporo-mesial structures could show that the amygdala seems to be primarily affected by this disease especially in the acute disease stage. The aim of the present study was to investigate volume changes of the gray matter in antibody-associated LE by voxel-based morphometry (VBM).

Method: The T1-scans of 63 patients suffering from antibody-associated LE were compared with those of 63 age- and gender-matched healthy controls. VBM analysis was performed using FSL-VBM with its default settings. Voxelwise statistical analyses were applied using permutation-based non-parametric testing (5,000 permutations) with TFCE implemented in the FSL randomize tool, correcting for multiple comparisons (p < 0.05, FWE-corrected).

Results: All included patients suffered from newly onset temporal lobe epilepsy with additional mnestic/psychiatric symptoms in most cases. Serum antibodies associated with LE were positive in all included patients (GAD N = 32, VGKC-complex N = 25, onconeural N = 6). Median age at LE onset was 42.4 years, median disease duration at MRI was 1.3 years. VBM analysis showed gray matter volume increase in both amygdalae in the LE group, whereas we found gray matter volume loss in the thalamus, brainstem, and cerebellum in comparison to the controls.

Conclusion: This is the first study investigating gray matter volume changes in LE by VBM. Our results indicate a bilateral volume increase of the amygdala supporting the hypothesis of a predominant amygdalar affection in the early stage of this disease. We did not find significant hippocampal volume abnormalities while the distribution of extratemporal gray matter volume loss is comparable to that of hippocampal sclerosis in previous studies.
VARIATIONS OF CLINICAL COURSE OF REFRACTORY EPILEPSY CONDITIONED BY BRAIN TRACTS CHARACTERISTICS

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Purpose: Diffusion tensor imaging (DTI) studies have reported different white matter alterations in patients with epilepsy. The current study examined patterns of white matter tracts abnormalities and relationships with clinical and neurophysiologic factors in subjects with epilepsy.

Method: DTI data with tractography were obtained in 46 epilepsy patients (36 with pharmacoresistant subjects and 10 in remission stage) and 10 age-matched healthy controls using 1.5-Tesla MR scanner (Philips). Analysis of fractional anisotropy (FA) and mean diffusivity (MD) for anterior and posterior hemispheric quadrants was performed. Correlation analysis for FA and MD with clinical course of disease, neuropsychological state, EEG-mapping and cognitive event potentials was carried out.

Results: Subjects with epilepsy, as compared to healthy controls, demonstrated four patterns of tracts reduce: in frontal lobe, lateral parts of hemisphere mono- or bilaterally, anterior and/or posterior commissure, complex of several tracts changes. Epilepsy subjects have reduced FA, predominately in the epileptogenic cerebral hemisphere (p < 0.05). MD increasing and pattern of tracts reduce in frontal lobe typified for pharmacoresistant course of disease (p < 0.05). Pattern of tracts reduce in lateral parts of hemisphere monolaterally correlated with focal onset of epilepsy, bilaterally – with generalized seizure onset (r = 0.42, p = 0.03). Anterior and/or posterior commissural reducing correlated with prolonged P300 latency (r = 0.39, p = 0.029). Mean FA and MD was positively correlated with Beck and Spilberger-Hanin scales data (r = -0.2, p < 0.001) and P300 latency (r = 0.23, p < 0.001). Epileptic EEG activity presence was correlated with FA reduction (r = 0.7, p = 0.01).

Conclusion: Epilepsy is associated with widespread disturbances in white matter tracts. DTI data can be predictors of clinical course of disease and cognitive disturbances.

LEVETIRACETAM REDUCES ABNORMAL NETWORK ACTIVATIONS IN TEMPORAL LOBE EPILEPSY

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Purpose: To investigate the effect of Levetiracetam (LEV) on cognitive network activations in patients with drug-resistant left and right temporal lobe epilepsy (TLE) using functional MRI.

Method: In a retrospective study, a left-lateralising verbal and a right-lateralising visual-spatial working memory (WM) paradigm were employed to compare fMRI activations in left (n = 53) and right (54) TLE patients treated with (59) or without LEV. In a post-hoc analysis, activation patterns during WM paradigms were correlated with the prescribed daily LEV dose.

Results: We isolated task- and syndrome-specific effects. Patients on LEV showed normalisation of functional network activations in the right temporal lobe in right TLE during the right-lateralising visual-spatial task, and in the left temporal lobe in left TLE during the verbal task. In a post-hoc analysis in LEV-treated patients, a significant dose-dependent effect was demonstrated in right TLE during the visual-spatial WM task: the lower the LEV dose, the greater was the abnormal right hippocampus activation. At a less stringent threshold, a similar dose effect was observed in left TLE during the verbal task: both hippocampi were more abnormally activated in patients with lower doses, but more prominently on the left.

Conclusion: Our findings suggest that LEV is associated with restoration of normal activation patterns.

CHILDREN OF WOMEN WITH EPILEPSY HAVE REDUCED GREY MATTER AND TOTAL BRAIN VOLUME BY VOXEL BASED MORPHOMETRY

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Abstracts

Purpose: Children of women with epilepsy (CWE) have impaired neuropsychological function. There is little data that explores the neuroanatomical basis for this impairment. Our objective was to compare brain volumes (total, grey matter and white matter volumes) of CWE and antenatal exposure to Anti epileptic Drugs (AEDs) with that of children of women without epilepsy (CWO) and no AED exposure.

Method: Fourteen CWE drawn from Kerala Registry of Epilepsy and Pregnancy aged 10.9 ± 0.9 years and 15 age matched CWO were examined by MRI on 1.5 Tesla Machine. A 3D T1 weighted spoiled gradient sequence was acquired for volumetric analysis. The VBM data analysis was done using VBM8 in Statistical Parametric Mapping 8 (SPM 8). Total volumes of grey matter, white matter was calculated in SPM8 using VBM8 tool. Student t-test was done to assess statistical difference between two groups.

Results: The total brain volume of CWE (1,398 ± 169 ml) was significantly lower (p-value < 0.001) than that of CWO (1,519 ± 217 ml). The total grey matter volume of CWE (633 ± 120 ml) was also significantly lower (p-value < 0.001) than that of CWO (765 ± 101 ml). There was no significant difference in white matter volume of CWE (410 ± 56 ml) and CWO (437 ± 79 ml).

Conclusion: The study shows that CWE have significantly reduced grey matter volume and total brain volume compared to CWO. Reduced brain volumes may have association with their poor neuropsychological and cognitive function.

Purpose: To identify the brain networks involved in the different EEG abnormalities in ring chromosome 20 [r(20)] patients. We hypothesize the existence of both distinctive and common brain circuits for the paroxysmal sharp waves (hSW), the seizures and the slow-wave rhythms.

Method: Thirteen [r(20)] patients were studied by means of EEG simultaneously recorded with functional MRI (EEG-fMRI). A group-level analysis was performed for each type of EEG abnormality separately using a fixed-effect model and a conjunction analysis. Finally, a second-level random-effect model was applied considering together the different EEG abnormalities without distinction between hSW, seizures or theta-delta rhythms.

Results: Theta-delta rhythm was recorded in seven patients, seizures in two and hSW in three cases. The slow-wave rhythm was related to BOLD increases in the premotor, sensory-motor, temporo-parietal cortex and decreases in the default mode (DMN) and the dorsal attention networks (DAN). The ictal-related BOLD changes showed an early involvement of the pre-frontal lobe. Finally, a common pattern of BOLD increases in the bilateral perisylvian regions was found across the different EEG abnormalities.

Conclusion: The BOLD increment in the perisylvian network and the decrease of the DMN and DAN could be the expression of the [r(20)] syndrome-related cognitive and behavioral deficits. The observed BOLD patterns are similar to the ones detected in other epileptic encephalopathies suggesting that different epileptic disorders characterized by neurobehavioral regression are associated with dysfunction in similar brain networks.

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POSTOPERATIVE SEIZURE OUTCOME ASSESSED BY NON-INVASIVE METHODS IN 190 PATIENTS

Purpose: Comprehensive presurgical evaluation aims at correctly localizing the epileptogenic focus in order to achieve seizure control. We assessed the prognostic value of MRI, positron emission tomography ((18) FDG-PET),ictal/interictal single-photon emission computed tomography (SPECT) and electric source imaging (ESI) by means of high resolution EEG (ESI-HR), in a group of operated patients.

Method: We included a cohort of 190 operated patients with >12 months follow-up and computed sensitivity, specificity, AUC and odds ratio for each test while comparing it to the postoperative control.

Results: 78% of all patients were seizure-free, 9% were Class II, 10% Class III and 3% were Class IV. All tests were significantly contributing to a favorable postsurgical outcome (p < 0.05), when the abnormal areas was located within the resected lobe. However, MRI and ESI-HR showed the best performance. Among 82 patients who underwent both MRI and ESI-HR, those who had concordant positive results had a probability of favorable outcome of 93.2% (41/44). When both results were negative, this probability was 0% (0/5), and when they disagreed, this probability was 63.6% (21/33). Among the 52 patients who underwent all imaging procedures, only MRI and ESI-HR were significantly associated with a favorable outcome (MRI: OR 5.8, p = 0.016; ESI-HR: OR 6.9, p = 0.011).

Conclusion: This study shows that the combination of MRI with ESI-HR offers the highest predictive information for postsurgical outcome. The chances to be seizure-free are >90% if MRI and ESI-HR agree.
**Visualization of Meyer’s Loop Before Temporal Lobe Resection Using Deterministic and Probabilistic Tractography**


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**Purpose:** Postoperative visual field defects are common after temporal lobe resection for temporal lobe epilepsy. Preoperative diffusion tensor tractography is a promising technique for visualizing Meyer’s loop. There is currently no standardized method for such tractography. The aims of this study were to:

1. Compare results of deterministic (DTG) and probabilistic (PTG) tractography of Meyer’s loop and
2. Validate their anatomical accuracy by relating results to post-operative perimetry.

**Method:** Eight patients with temporal lobe resection for temporal lobe epilepsy were included. Perimetry and diffusion tensor imaging were performed pre- and post-operatively. Two independent operators analyzed the distance between the temporal pole and Meyer’s loop (TP-ML) using DTG and PTG. DTG and PTG were compared to each other and to data from previously published dissection studies. Resection size and TP-ML by DTG and PTG were compared to post-operative perimetry.

**Results:** Median pre-operative TP-ML for the non-operated sides was 42 mm for DTG and 35 mm for PTG. PTG was a closer match to dissection studies. Intra-class correlation coefficient was 0.4 for DTG and 0.7 for PTG. Difference between pre-operative TP-ML by DTG and PTG and resection length could predict perimetry as to visual field defect or not, although it could not predict degree of defect.

**Conclusion:** PTG of Meyer’s loop is superior to DTG in terms of reproducibility and anatomical accuracy. Both DTG and PTG could predict visual field defect; the prediction model used thus only gives a rough estimate of the anatomical accuracy.

**Abstracts**

**Imaging 2**

**Monday, 30th June 2014**

**p251**

**Tumour Localisation and Secondary Generalisation: MRI Lesion Mapping in Oligodendroglioma Patients**

**Wieschmann U, Milinis K, Keller S**


**Purpose:** Some patients with oligodendroglialomas have generalised tonic clonic seizures (GTCS) whereas others have only simple partial seizures (SPS). We used lesion mapping to investigate the effect of tumour localisation on secondary generalisation.

**Method:** Twenty patients with histologically proven oligodendrogliomas, (10 GTCS and 10 SPS) were included. Data were acquired on a 1.5 Tesla MRI System. Quantitative image analysis studies were performed on 3D T1-weighted images. Images were realigned into the same anterior commissure – posterior commissure orientation, lesions were manually delineated using and segmented lesions were saved as a separate file and binarised. Native MRI images were spatially registered to a common stereotaxic space using both affine and non-linear transformations. The non-linear warps used to register images to the standard template were applied to the corresponding segmented binarised lesions, which transformed lesions into standard non-linear space. The voxel-wise topology of lesions common to patients with GTCS was determined by concatenating all spatially normalised lesions into an individual image and determining the number of times a voxel was intersected by a lesion. The result was a single image file that was colour-coded according to the number of times each voxel was lesioned in GTCS patients. This image was superimposed onto MR template images and tractography maps for neuroanatomical reference. The same was repeated for SPS patients.

**Results:** In GTCS the highest lesion load was in the frontal parasagittal region involving cortex connected to the genu of the corpus callosum. In contrast in SPS the largest lesion load was seen more caudally and laterally in orbito frontal and temporal lobes but sparing cortex connected to the genu.

**Conclusion:** Our data suggest that the genu of the corpus callosum is the major pathway for secondary generalisation.

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**Time-Series Analysis of EEG-MREG Facilitates Interpretation of BOLD Responses in Epilepsy**


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**Purpose:** EEG-MfMRI can detect BOLD changes associated with epileptic spikes non-invasively. MREG (Magnetic-Resonance-Encephalography) is fast fMRI sequence that allows whole-brain fMRI with a time resolution of 100 ms. The present study analyzes the time course of the BOLD-response to epileptic spikes using MREG.

**Method:** Patients with frequent inter-ictal spikes underwent EEG-MfMRI. Spikes timings were used in an event-related analysis to generate functional activation maps, with the HRF modeled by a basis set allowing the estimation of the HRF delay (Liao et al., Neuroimage 16:593–606). Timings of BOLD responses were analyzed in regard to the spike focus.

**Results:** 12 patients with 25 different spike-types were analyzed. Positive BOLD: 15 spikes-types showed a first BOLD response ipsilateral, 3 contralateral to the focus and 7 simultaneously bilateral responses. In 11 spike-types the earliest response was in the same lobe as the focus, the largest BOLD response was found 2.3–11.4s (average 6.1s) after the spike. Negative BOLD: Most negative BOLD responses occurred earlier or at the same time than positive BOLD responses (22/25). In 15 spike-types-only distant BOLD responses were observed, all with overlap with the default mode regions (at average 4.9s).

**Conclusion:** Earliest BOLD responses often correspond with the spike focus and time information might facilitate in interpretation of EEG-fMRI in epilepsy. Negative BOLD occurred earlier but are less focal and often overlap with the default mode network. Fast fMRI has been shown to increase sensitivity of EEG-MfMRI in epilepsy, and facilitates time-series analysis to improve the interpretation of results.

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DIFFUSION TENSOR IMAGING ABNORMALITIES OF THE CORPUS CALLOSUM IN MALFORMATIONS OF CORTICAL DEVELOPMENT
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Purpose: Diffusion tensor imaging (DTI) is a magnetic resonance imaging (MRI) technique that can provide insight into white matter (WM) architecture and microstructure. DTI has demonstrated extensive WM changes in patients with several epileptic syndromes [Yogarajah et al. Epilepsia 2008;49(2):189–200], but few studies have focused on patients with malformations of cortical development (MCD). Our aim was to investigate the diffusion properties of the corpus callosum (CC), a major commissural bundle critical in inter-hemispheric connectivity, in a large group of patients with MCD.

Method: Thirty-two MCD patients and 32 age and sex-matched control subjects were prospectively evaluated at 3.0 T. We analyzed the genu, body, and splenium of the CC with deterministic tractography. We further assessed the CC with region of interest (ROI)-based analyses and evaluated different subgroups of MCD (polymicrogyria/schizencephaly, heterotopia, and cortical dysplasia). Diffusion parameters included fractional anisotropy (FA), mean diffusivity (MD), parallel diffusivity and perpendicular diffusivity. Partial correlations between diffusion changes and clinical parameters (epilepsy duration and age at disease onset) were also queried.

Results: Multiple analyses of variance (MANOVA) demonstrated significant reductions of FA, accompanied by increases in MD and perpendicular diffusivity in all segments of the CC in the patients group with both analytical methods, at Bonferroni adjusted p-values <0.017. There were no significant differences within MCD subgroups, and no correlations between clinical parameters of epilepsy and FA.

Conclusion: Our DTI findings of the CC suggest microstructural abnormalities of major WM tracts distant from the lesion in MCD patients.

DV and nonDV were also matched for the presence of hippocampal sclerosis.

p256
SPATIAL RESOLUTION EVALUATION OF DOUBLE-DENSITY FUNCTIONAL NEAR-INFRARED SPECTROSCOPY FOR THE DIAGNOSIS OF FUNCTIONAL CORTEX
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Purpose: Functional near-infrared spectroscopy (fNIRS) is a neuroimaging technology using for functional brain mapping and diagnosis of epilepsy focus by continuous non-invasive monitoring of tissue oxygenation and hemodynamics in the brain. We developed double density fNIRS (DD-fNIRS) that has two times higher spatial resolution and improved instability due to probe setting compared to traditional fNIRS. The purpose of this study is to clarify the spatial accuracy of DD-fNIRS for functional brain mapping.

Method: Five normal volunteers tried to measure the functional cortex of hand motor and sensory area with finger tapping and pin pricking tasks, respectively, by DD-fNIRS. Each data was calculated by averaging method with five trials of tapping and pricking tasks. On the other hand, five patients with brain tumor seated on close to central sulcus had the examination with the same tasks pre- and/or post-operation. The hand motor and sensory area on MRI image measured by DD-fNIRS were checked with the results of anatomical position measured by MEP or SEP during surgical operation of tumor removal.

Results: Hand motor and sensory cortex were clearly activated separately divided with central sulcus by DD-fNIRS. The relative position between tumor and functional cortex such as hand and sensory area measured by DD-fNIRS was matched up precisely with the anatomical position measured by MEP and SEP during surgical operation.

Conclusion: DD-fNIRS may be a new neuroimaging technology for functional brain mapping and diagnosis of epilepsy focus with higher spatial resolution.

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MULTIMODAL FUNCTIONAL IMAGING IN EPILEPSY SURGERY: A POST HOC ANALYSIS
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Objective: Our aim was to compare the localizing value from: the invasively recorded seizure onset zone (SOZ), the irritative zone (IZ) by high frequency oscillations (HFO) and interictal activity defined by extracranially recording of the cortical source (CURRENt-Loreta).

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Methods: 10 patients with lack of concordance between MRI, semiology, and extracranial EEG findings were included: 7 with negative or inconclusive MRI, 2 with extensive lesions, and 1 with hippocampal (Hc) atrophy. All patients had good outcome at 2 year follow up (Engel I-II), 6 with sustained seizure freedom since surgery. Post-op MRI was coregistered with pre-op reconstructions of intracranial electrodes to define extent of resected electrode positions displaying SO or HFO. s-Loreta was correlated to the resection on MRI.

Results: 1 patient was seizure (sz) free from anterior mTL ectomy despite no resection of affected electrodes in posterior Hc
8 patients had partial or complete resection of affected electrodes:
SOZ: 5 patients (2 sz-free) complete resection
3 patients (2 sz-free) partial resection
HFO-Iz: 2 patients (1 sz-free) complete resection
6 patients (3 sz-free) partial resection
9 patients (5 sz-free) were resected in the same lobar region as indicated by s-Loreta.
8 patients (4 sz-free) complete resection
1 patient (1 sz-free) partial resection

Conclusion: There is no obvious relationship between complete vs. incomplete resection of positions showing SO, HFO in invasively evaluated patients with good outcome. Non-invasive source analysis is addressing the regional rather than exact location of the epileptogenic zone.

p258
DIAGNOSIS OF FOCUS SIDE IN INTRACTABLE MESIAL TEMPORAL EPILEPSY BY FNIRS DURING SPONTANEOUS SEIZURE
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Purpose: To localize the epileptic focus is the most important purpose of the presurgical evaluation in patients with medically intractable partial seizure. Functional near-infrared spectroscopy (FNIRS) is a light based neuroimaging technology for continuous and non-invasive measurement of oxygenated hemoglobin (OxyHb), deoxygenated hemoglobin (Deoxy Hb) with high temporal resolution which allows monitoring regional cerebral blood volume (rCBV) changes during long term video-EEG monitoring in epileptic patients as well as in daily living conditions. The present study will attempt to reveal the usefulness of FNIRS simultaneously recorded with EEG to detect the correct focus side of intractable mesial temporal lobe epilepsy (MTLE) in preoperative evaluation.

Method: Sequential FNIRS recording was performed along with long term video-EEG monitoring. Twelve CPS (complex partial seizure) with/without GTS (generalized tonic clonic seizure) attacks of Eight patients suffered from intractable TLE and underwent selective epilepsy surgery after the diagnostic procedure were recorded during FNIRS recording. We used the 22 channel NIRS system (ETG 4000; Hitachi Medical Corporation, Tokyo, Japan), with infrared light with two wave length of 695 and 830 nm. We measured the change in Oxy and Deoxy Hb after on-set of seizure and calculated laterality index of 3 channels in temporal region to compare with the correct epileptogenic side judged by EEG. We also measured the duration of clinical semiology, EEG and FNIRS changes during seizure. We compared each other and correlation with the change of FNIRS.

Results: Laterality index of 11/12 in OxyHb and 9/12 in DeoxyHb showed increase on the correct epileptogenic side. There was a strong positive correlation between increase in OxyHb and DeoxyHb. Duration of EEG and FNIRS changes showed negative correlation with extent of OxyHb increase.

Conclusion: FNIRS is a non-invasive useful tool for determining epileptogenic side of intractable MTLE patient.

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LANGUAGE LOCALIZATION IN PATIENTS WITH TEMPORAL LOBE EPILEPSY (TLE) USING FUNCTIONAL MAGNETIC RESONANCE IMAGING (FMRI)
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Purpose: To implement language paradigms using visual and auditory stimuli, which predominately involve language areas in the temporal lobe of patients with TLE.

Method: We performed language fMRI using 4 tasks in 23 controls (12 females), 12 right TLE (6 females) and 15 left TLE (7 females). The tasks were:
1. Auditory naming (AN) using reversed speech (AR) as the control condition.
2. Picture naming (PN) with counting while viewing scrambled pictures or blurred faces as the control.
3. Semantic fluency and
4. Free fluency involving word generation without the constraint of category membership.
We considered activations in individual subjects at T > 2.5, 10 voxels.

Results: For AN, 91% of left TLE patients activated the left superior temporal gyrus and 73% activated the right middle temporal gyrus, 91% of the right TLE group and 57% of controls activated the left middle temporal gyrus. For AN-minus-AR, 64% of LTLE patients and 44% of controls activated the left middle temporal gyrus.
For PN, 67% of LTLE patients activated the right superior temporal gyrus and 60% activated the left middle temporal gyrus, 58% of RTLE patients activated the left superior temporal gyrus and 26% of controls activated the right superior temporal gyrus.

Conclusion: AN, AN-AR and PN tasks activated the temporal lobe and these paradigms may be more predictive of language deficits after temporal lobe resection than verbal fluency that activates the inferior frontal gyrus.

p260
EMOTION PROCESSING IN PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY AND AMYGDALA LESIONS
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**Purpose:** Functional MRI (fMRI) studies have demonstrated a major role of amygdalae in processing of emotions. In mesial temporal lobe epilepsy (mTLE), amygdalae are often part of an epileptogenic zone. We aimed to test by fMRI how lesional amygdalae are involved in an emotion response.

**Method:** Twenty patients (9 women; median age 36 years, range 21–58) with mTLE due to unilateral lesions in amygdala and 19 healthy controls (10 women, median age 28 years, range 22–53) were tested with fMRI “dynamic fearful faces” paradigm: a short movie with alternating images of landscape and faces expressing fear. Median age at seizure onset was 24 years, range 6–50, median epilepsy duration – 6 years, range 1–34. Seventeen patients (85%) had drug resistant seizures; 18 (90%) were right-handed. All patients underwent at least two high resolution MRI (1.5T) with an interval of at least 6 months for diagnostic purposes.

**Results:** fMRI signal in amygdalae was elicited in 55% of patients and 74% of healthy controls. Bilateral fMRI signal was observed more frequently in healthy controls compared to patients (53% vs. 5%, p = 0.001). The majority of patients had left-sided mTLE (n = 16, 80%). In these patients, fMRI signal was seen equally ipsilateral and contralateral to epilepsy side (each 25%); bilateral activation was rare (6%). In right-sided mTLE patients (n = 4, 20%), only one had fMRI activation ipsilateral to epilepsy side; the rest (n = 3) had no fMRI signal in amygdala.

**Conclusion:** fMRI activation patterns elicited by “dynamic fearful faces” paradigm differ between patients with unilateral mTLE and healthy controls. Integration of epileptogenic lesions of amygdalae into emotion processing might have important implications for possible postsurgical deficits in patients with drug resistant mTLE.

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p262 DISTINGUISHING EPISODIC MEMORY PROCESSES FAMILIARITY AND RECOLLECTION BY USING EXTAOPERATIVE TEMPOROPARIETAL STIMULATION

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**Purpose:** The MTL and lateral temporoparietal regions have a distinct role in two independent episodic memory processes recollection and familiarity. The entorhinal and lateral temporal regions are associated with perceived novelty as an index of familiarity. Hippocampal and posterior parietal regions are linked to recollection. Although compelling, fMRI only provides us with indirect evidence regarding the role of different regions in recollection and familiarity. In a recent rodent study who were excellent at recognizing scents coupled with a food reward, it has been shown that the animals with a lesioned hippocampus were impaired in the recollection-like processes.

**Method:** We recently used this approach in a pilot-study with 31 years old epilepsy surgery patient with an implanted grid electrode covering the left posterior lateral temporal and low parietal cortex. We stimulated the grid-point previously linked to familiarity based on fMRI, and compared performance with and without stimulation. Before stimulation the patient was presented a list of words. Afterwards and during stimulation another list was presented and the patient had to indicate whether the item was “new” or “old”. Furthermore he had to indicate a confidence judgment about the recognition-decision; guess, probably, or definite.

**Results:** Receiver operating characteristic curves (ROCs) showed that there was a robust reduction in the level of familiarity, but intact recollection. This finding is opposite to hippocampal-lesion evidence in rodents (intact familiarity, but reduced recollection). Together, these findings indeed suggest that recollection/familiarity are mediated by different neural substrates and function independently. Yet, thus far, no study has provided direct evidence for the independent contribution of recollection and familiarity to episodic memory.

**Conclusion:** In this pilot-study we found an indication that direct stimulating familiarity regions reduces familiarity, not recollection. Further research with this procedure to test a suggested double dissociation whether stimulating recollection regions reduces recollection, not familiarity.

p263 INTERICTAL EPILEPTIFORM DISCHARGES (IED) AND MEMORY FUNCTION IN TEMPORAL LOBE EPILEPSY

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**Purpose:** Epilepsy is a common neurological disorder in the clinical picture which includes cognitive impairment. Known from the literature that interictal epileptiform activity can affect the development of cognitive impairment in epilepsy. The purpose of this study was to investigate the possible influence of interictal epileptiform activity on some cognitive functions in adult cohort with temporal lobe epilepsy.

**Method:** We studied a group of patients (n = 31) with partial epilepsy with/without secondary generalization. We evaluated the routine record for the presence of IED. Has been used 19 channel EEG device “Neuron-Spectrum” (Russia), for 30 min, with photic stimulation and hyperventilation. In the treatment of patients used monotherapy. Memory function was evaluated by the «Digit span» task and attention function was evaluated by «Simple Reaction Time». For statistical analysis we use nonparametric statistic: U Mann-Whitney.

**Results:** The average age was 32.8 years (95% CI 25.0–34.7), duration of the disease was 16 years (95% CI 9.9–22.0). In the group with IED (n = 13) we observed a decrease in the amount of numbers – 5.23 (95% CI 4.5–6.1), while in the group without IED (n = 18) noted more named digits (mean 7.1 95% CI 4.5–6.1) and this difference was statistically significant (p = 0.001). In the group with IDE reaction time was 339.7 ms (95% CI 325.0–354.4), in group without 357 ms (95% CI 351.2–378.4) and no statistically significant.

**Conclusion:** Interictal epileptiform discharges with temporal lobe epilepsy registered in the routine EEG record are more associated with impaired memory than with attention.

p264 SEMANTIC MEMORY IMPAIRMENT IN TEMPORAL LOBE EPILEPSY OF ANTERIOR-NEOCORTICAL OR HIPPOCAMPAL ORIGIN

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**Purpose:** To determine the relative contribution of the hippocampus and anterior/neocortical temporal cortex to visual naming impairment in patients with epilepsy of temporal lobe origin.

**Method:** We assessed two kinds of patients on a common battery of semantic tasks:

(i) temporal lobe epilepsy patients resulting from hippocampal sclerosis (HS) (n = 18);

(ii) patients with epilepsy associated to an epileptogenic lesion (i.e. encephalocoele) centered at the temporal pole that spared the hippocampus entirely (ATL patients) (n = 19);

(iii) a matched group of healthy controls (n = 20). The battery included measures of visual naming, category fluency, and visual and verbal semantic recognition.

**Results:** ATL patients exhibited a reduced accuracy in the naming task relative to controls; while patients with HS did not differ from controls. 11/19 patients in the ATL group exhibited scores that were just or below 2 SD of the control group mean. Only 2/18 patients in the mTLE group were below the cut-off score, and two more were just or below 1.5 SD of the control group mean. Additionally, both groups of patients demonstrated relatively mild semantic dysfunction. Impaired performance was observed in different types and modalities of semantic tasks.

**Conclusion:** Damage to left temporal lobe—antero- or medially—produced a mild semantic dysfunction that was evident in different types and modalities of semantic tasks. ATL damage plays an important role in the occurrence of difficulties in visual naming, manifesting in certain degree of anomia or in semantically related naming errors, while ruled out the contribution of hippocampus to difficulties in visual naming. Current study aligns with those suggesting that naming impairment in TLE is related with neocortical temporal lobe damage. Our study highlights the importance of considering the functional status of neocortical aspects of the temporal lobe when evaluating semantic memory in patients with HS.

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**IMPLICIT SEQUENTIAL LEARNING IN TLE PATIENTS**

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**Purpose:** Mesial temporal lobe (mTLE) structures play a key role in explicit memory (ExM). Patients with mTLE have impaired ExM function. There is conflicting data on role of the mTLE for implicit memory (ImM). Sequential learning (SL) as a form of ImM is investigated here with the SRTT (Serial Reaction Time Task) in epilepsy patients with (+) without (−) mTLE.

**Method:** Preoperative patients (study 1) with focal epilepsy (TLE + HS, TLE-HS, extraTLE [eTLE]), and postoperative mTLE-patients (study 2) as well as healthy controls were investigated. Clinical variables and data on standardized neuropsychological diagnostics, especially ExM and SRTT were collected.

**Results:** Patients (n = 45) female 57%, mean age 37.4 ± 13.9 (range 18–71) 82% with TLE, 51% preoperative patients were included. Healthy participants (n = 63, female 55%, mean age 37.6 ± SD 1.69 [range 19–68]) scored better than patients in ImM and ExM (both p < 0.001). Both patient groups showed equally intact learning in SRTT (p > 0.1). TLE had impaired ExM compared to eTLE patients (free recall: 8.6 ± 4.2 vs. 11.3 ± 9.9; p = 0.008). Performance on first vs. last sequence-block revealed a significant interaction (p = 0.026) indicating that eTLE (n = 8) achieve higher speed across learning than mTLE (n = 36). This was more prominent in preoperative (p = 0.045) vs. postoperative patients (p > 0.1). Bihemispheric TLE scored lower on ImM (p = 0.008). There was no gender or hemisphere difference in ImM.

**Conclusion:** All patient groups showed a learning effect, however all patients performed worse than healthy controls. Patients with TLE showed better while learning less well than healthy subjects. Patients with eTLE showed better ImM and ExM consolidation than TLE-patients. Data on aetiology should give further insights into the mode of decline of both memory components. Analysis of MRI-data on extension of respective zone will be used to identify necessary structures for ImM and predict postoperative risks.

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**THE PROGNOSTIC SIGNIFICANCE OF COGNITIVE DEFICITS AFTER A FIRST UNPROVOKED SEIZURE: PRELIMINARY RESULTS OF A 3 YEARS FOLLOW-UP**

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**Purpose:** This study was set up to screen for cognitive deficits after a first unprovoked seizure and their relation related to an increased risk of a second seizure after a first unprovoked seizure. Here we present preliminary results.

**Method:** This prospective study was approved by the local ethics board. Patients aged 18–70 years, who had a first unprovoked seizure, were tested using the Verbal-Learning-Memory-Test, a visual learning and memory test and a German version of the Stroop-paradigma. Three years later they were asked by letter, if another seizure had occurred. When patients showed up with a second seizure in our department earlier, their data were included in this preliminary report as well.

**Results:** Follow-up data of 20 patients (12 male, 8 female) aged on the average 48.48 years at the time of their first seizure were available. 15 patients (~75%) had at least one pathological test result. 7 patients (35%) had experienced a second seizure. The time between the first and the second seizure was 7.4 months on the average. A second seizure was significantly associated with a pathological MRI of the brain being suggestive mainly for astrocytomas or glioblastomas (p = 0.043). Until now there was no significant association between neuropsychological test results and a second unprovoked seizure.

**Conclusion:** Our preliminary data show that cognitive deficits are a frequent finding after a first unprovoked seizure. But the occurrence of further seizures seems to depend mainly on the brain pathology shown by MRI.

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**SENSE OF COHERENCE AND MEMORY SKILLS IN A GROUP PATIENTS WITH AND WITHOUT EPILEPSY**

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**Introduction:** In Antonovsky’s theory, the major concept sense of coherence (SOC) is constituted of three core components called comprehensibility, manageability, and meaningfulness. Sense of coherence is a personality characteristic of a person who helps his successful coping with stress, workload, difficulties. So even in chronic diseases such epilepsy.
Purpose: 1 Finding SOC in a small sample of patients with epilepsy and healthy peer group.
2 Detecting differences in the level of memory function between these two groups.
3 Determining whether the level of memory skills and SOC correlate with each other.

Method: The study group consisted of 60 subjects – including 30 patients with epilepsy aged 24–60 y. (median 36). 14 patients with generalized epilepsy, 13 patients with complex partial epilepsy, 3 patients with simple partial seizures. Most frequent etiology: 30.9% perinatal injury, 26.7% cryptogenic, 15.7% trauma, 9.2% cerebral infection. The control group consisted of 30 people who have never had an epileptic seizure or other serious psychological disorder (organic changes in the CNS, respectively cognitive deficits).

The following questionnaires have been used:
1. SOC – life questionnaire orientation – measured sense of coherence (Antonovsky, 1987)
2. Validated learning memory test (Press, 2006)

Results: Antonovsky sense of coherence – epilepsy sufferers: 137.7 points, control group: 111.8 points.

Learning memory test – number of words remembered (6 attempts) epilepsy sufferers 47.7; control group 61.5.

Conclusion: In the group of patients with epilepsy we have confirmed the assumption of lower number of words memorized, compared to control group.

With respect to SOC, epilepsy patients surprisingly achieved higher score compared to the control group. Result suggests that patients with epilepsy have good internal coping resources (sense of coherence) in managing and coping with the disease.

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MEMORY AND FMRI ACTIVATION IN TEMPORAL LOBE EPILEPSY: TOWARDS PREDICTING SURGERY OUTCOME

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Purpose: Surgical treatment in patients with temporal lobe epilepsy (TLE) involves the risk of post-surgical memory decline. Lateralization or even localization of memory networks preoperatively, may minimize postoperative risk. We developed a fMRI face-name memory task and performed a feasibility study. We investigated three aims. First, the task should provoke hippocampal activation. Second, this hippocampal activation should demonstrate memory reallocation in TLE patients. Third, this hippocampal activation should associate with performance on standard pre-surgical memory tests.

Method: 16 epilepsy surgery candidates and 10 control subjects performed the task. They were instructed to memorize combinations of faces and names during MRI scanning. Individual Lateralization Indices (L1), defined as the relative difference in the number of activated voxels in the left and right hippocampus, were calculated. Patients also performed classical neuropsychological memory tests as part of their pre-surgical evaluation.

Results: The fMRI face-name task provoked hippocampal activation in both epilepsy patients and control subjects. Left TLE patients (LI: M = −0.06, SD = 0.35) showed more right over left hippocampal activation (r8 = 2.15, p < 0.05, 1-tailed). The difference in LI between left hippocampal sclerosis patients (M = −0.23, SD = 0.37) and right hippocampal sclerosis patients (M = 0.48, SD = 0.26) was even more prominent (r4 = 2.72, p < 0.05, 1-tailed). There were strong and significant associations between the LI and verbal (r = 0.87, p < 0.05) and non-verbal (r = −0.94, p < 0.05) memory performance. More left over right hippocampal activation corresponds to better verbal memory and more right over left hippocampal activation corresponds to better non-verbal memory.

Conclusion: There are multiple indications that the fMRI face-name task we used may be a valuable tool in the pre-surgical evaluation of epilepsy patients. A final evaluation and validation should include more patients and data on actual post-surgical memory outcome.

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VARIABLES ASSOCIATED WITH READING DISORDER IN ROLANDIC EPILEPSY

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Purpose: Children with Rolandoic Epilepsy (RE) often present with Reading Disorder (RD). In other groups of children with RD these difficulties are often attributable to phonological processing deficits, impairments that have also been observed in the RE population. However, cognitive and behavioural deficits such as language impairments, inattention and hyperactivity and Developmental Coordination Disorder (DCD) have also been described as prevalent among these children and, therefore, considered possible predictors of reading difficulties. This study aims to investigate the risk factors for Reading Disorder in children with RE.

Method: 84 children and young people (47 probands and 37 siblings), aged 4.8–18.1, were firstly assessed with an achievement test to establish whether or not they presented with RD (RD+ = 20; RD− = 64). Neuropsychological tests assessing language ability, phonological and auditory processing, and questionnaires measuring ADHD symptoms and motor coordination were administered to all participants and their parents. A multiple logistic regression analysis was run with the purpose of investigating which factors were statistically associated with the incidence of RD in this population.

Results: After matching for age, number of seizures and exposure to pharmacological therapy as well as controlling for gender, language (Wald = 5.387, p = 0.020), phonological processing (Wald = 4.213, p = 0.040) and ADHD symptoms (Wald = 4.119, p = 0.042) resulted significantly associated with the presence of RD in children with RE.

Conclusion: Poor language abilities, phonological processing deficits and ADHD symptoms can be considered important risk factors for RD in children with RE. Early educational support targeting these aspects of cognitive function is recommended to enhance the academic achievement of these children.

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SEVERITY OF COGNITIVE IMPAIRMENTS IN BENIGN EPILEPSY WITH CENTRO-TEMPORAL SPIKES

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Purpose: To analyze occurrence and severity of cognitive disorders in children with Benign Epilepsy with Centro-Temporal Spikes (BECTS), evaluating their relationship with clinical-EEG characteristics.

Method: We studied 46 patients with BECTS (16 females, 30 males; mean age at the first examination 6.3 ± 2.5 years). The severity was evaluated according to the following aspects: comorbidity of different types of cognitive/emotional/behaviour disorders, the need for rehabilitation, special educational help, scholastic problems with repeated grades.

Results: Cognitive disorders were found in 18 children, either alone or associated (7 language, 15 learning, 4 ADHD, 2 motor coordination, 4 other). Their occurrence was statistically related to early mean age of seizure onset (5.4 ± 1.5 vs. 6.9 ± 2.5; p 0.028), long duration of epilepsy (3.9 ± 1.7 vs. 2.4 ± 1.8; p 0.01), need for AED therapy (45% vs. 0%; p 0.035), left EEG focus (50% vs. 21%; p 0.05), spreading and generalization of the EEG abnormalities (54% vs. 20%; p 0.019). The severity of cognitive disorders was associated with early epilepsy onset (4.9 ± 1.5 vs. 6.7 ± 2.3; p 0.019) and long duration of disease (3.6 ± 1.7 vs. 2.4 ± 1.9; p 0.04).

Conclusion: Cognitive disorders in BECTS were associated with some clinical-EEG features (early age of seizure onset, long duration of active epilepsy with the need for therapy, left EEG focus with spreading and generalization). Some of these variables (early onset and longer duration of disease) were also associated with a more severe clinical expression of cognitive disorders.

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STORY RETELLING IN 14 AND 15-YEAR OLD YOUNGSTERS WITH EPILEPSY COMPARED TO CONTROL CHILDREN MATCHED FOR INITIAL LEARNING SCORE: ACCELERATED LONG TERM FORGETTING

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Purpose: Secondary school youngsters with epilepsy often encounter school difficulties, repeating grade and being set back. Bad marks at exams in spite of good learning efforts are reported. This study evaluated story retention up to 1 week after initial presentation in 14 and 15-year old youngsters with epilepsy and non-referred, matched controls.

Method: Participants were 17 youngsters with epilepsy (10 boys/7 girls, age = 14.8 years, SD = 0.6) and 15 without epilepsy (6 boys/9 girls; age = 14.7 ± 0.6), matched for scores on initial learning on a Dutch translation of the Wechsler Logical Memory Test – Story 1 (p > 0.744). Mean age at epilepsy onset: 8.2 years (4.3). Seizure characteristics: 8 focal (4 LH, 2 RH, 2 bilateral), 6 idiopathic generalized, 3 MRI+, 2 seizure free, 75% on AEDs. FS-IQ on the WISC-III: 95.5 (12.5).

Procedure: The short story, read to the younger once, was retold immediately (IR), after 20–30 min (DR20), and when the younger returned at Day 2 (Day2; Ns = 8 ± 8) or Day 7 (Day7; Ns = 9 ± 9). Two controls provided data for both Day 2 and Day 7.

Analysis: With epilepsy status as independent variable, two repeated measures ANOVAs with “repeated contrasts” were done. IR, DR20, and either Day 2 or Day 7 were the dependent variables.

Results: Forgetting was largest from IR to DR20; thereafter no significant forgetting occurred to Day2 – similar for both samples. From DR20 to Day 7, further forgetting with an interaction effect (p = 0.029, η² = 0.26), suggested accelerated forgetting in epilepsy relative to controls.

Conclusion: In youngsters with epilepsy with average FS-IQ, accelerated forgetting after a week suggests the need for refreshing information, also after normal learning and short term retention.

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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 is the most commonly used test battery to assess different memory functions in impaired patients with brain dysfunctions of different etiologies. This ongoing study investigates the validation of the Dutch version of the Wechsler Memory Scale – Fourth Edition (WMS-IV-NL) in patients with Temporal Lobe Epilepsy (TLE).

Method: So far, 32 patients with TLE (mostly surgical candidates) enrolled the study (17 males, mean age = 43.8, SD = 15.1). Besides neuropsychological assessment including the WMS-IV-NL, patients underwent a thorough interview and extensive medical investigations. Patients with a clearly identified and localised epileptic focus based on video EEG monitoring and MRI were divided into two groups according to the lateralization of the abnormalities (13 left TLE and 16 right TLE). 32 Matched controls were also examined with the WMS-IV-NL.

Results: Results showed significantly poorer memory performance of patients compared to controls (p < 0.05). This is seen on all five indices and most subtests (except for Logical Memory I [p = 0.06] and Spatial Addition [p = 0.16]). Moreover, patients with left or right temporal focus performed equally on all indices and subtests (p > 0.05). Also, within-subject analyses revealed no differences between the Auditory Memory Index and the Visual Memory Index in both patient groups (p > 0.10).

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.

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EVALUATION OF SHORT AND LONG TERM MEMORY IN REFRACTORY EPILEPSY PATIENTS WITH MESIAL TEMPORAL LOBE SCLEROSIS

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Purpose: To analyze and compared short and long term memory in refractory epilepsy patients with mesial temporal lobe sclerosis medically or surgically treated using neuropsychological tests.
Method: We included 21 surgically treated patients, 19 medically treated patients and 19 control patients followed in our institution between 2003 and 2013. Patient and control groups were closely matched for age. We evaluated short and long term memory (verbal and non verbal), working and semantic memory, attention deficit, language, intellectual quotient (IQ), mood and executive functions. We further evaluated if the loss of acquired memory is due to an acquisition, consolidation or recovery deficit.

Results: Studied groups were similar in sex, family history, educational level and dominant hemisphere. Left temporal lobe sclerosis was more common in both groups. Focal seizures were the most common type not only in surgical but also medically treated patients. Numbers of years with epilepsy were similar in both groups although surgically treated patients suffered fewer seizures than medically treated patients. We found differences in controlled and uncontrolled verbal memory between surgical and medically treated patients. In addition, we found significantly different manipulative tests (processing speed). When comparing between the two groups of epileptic patients and controls we found worse performance in acquisition of information in epileptic patients without any loss in memory consolidation or retrieval.

Conclusion: There were no significant differences in many of the variables studied in both groups or between surgically and medically treated patients with mesial temporal lobe sclerosis involving loss of long term memory. Our results suggest that the loss of acquired memory is due to an acquisition deficit rather than consolidation or retrieval of information. These results may help us with presurgical prognosis and implementation of postsurgical therapies and further understand the mechanisms responsible for the cognitive impairment in patients suffering epilepsy.

Purpose: Rolandic Epilepsy (RE) is the most common epilepsy in children and often presents with persistent neuropsychological impairments seemingly unassociated with the time course of seizures or discharges. Nevertheless, these language and literacy impairments remain unconfirmed, given the moderate number of studies, most of which have modest sample sizes and which vary widely in methodology. These studies have yet to be formally reviewed and thus the following meta-analysis seeks to address this issue.

Method: Using meta-analytical techniques we systematically evaluated 24 studies of children with RE, testing for overall effect size and heterogeneity for any of the following measures: single word reading; phonological processing; expressive language; and receptive language.

Results: Mean effect sizes (Cohen’s d) ranged from 0.73 (CI: 0.53–0.93) for single word reading; 0.50 (CI: 0.23–0.78) for phonological processing; 0.71 (CI: 0.35–1.06) for expressive language and 0.62 (CI: 0.18–1.05) for receptive language. While effect sizes for single word reading and phonological processing were shown to be statistically consistent, those for language were heterogeneous.

Conclusion: This meta-analysis provides conclusive evidence for the presence of reading and phonological processing deficits in children with RE as indicated by medium sized mean effect sizes. However, similarly sized mean effect sizes for language impairments may be moderated by age of sample.

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AUDITORY PROCESSING IMPAIRMENTS IN CHILDREN WITH ROLANDIC EPILEPSY COMPARED WITH THEIR EPILEPSY-UNAFFECTED SIBLINGS
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Purpose: Auditory processing deficits have been noted before in children with Rolandic Epilepsy (RE) (Liasis et al, 2006, Boatman et al, 2008, Smith et al, 2012). Furthermore these children may lack the left lateralized functional advantage indicated by a right ear advantage (Bulgheroni et al, 2008) normally seen in the general population. Given these indications, we wanted to examine further auditory processing and auditory ear advantage in children with RE and test for evidence of heritability by comparing with a group of epilepsy-unaffected siblings.

Method: We compared children with RE aged 5–12 years old (n = 35) and a group of age-matched epilepsy-unaffected siblings (n = 20) with population norms on subs tests of the SCAN-C (ref) using one-sample Student’s t-tests. We also calculated ear advantage scores using Competing Word Subtest of the SCAN-C test for auditory processing disorder and compared these with normative data.

Results: 63% of children with RE and 60% in epilepsy-unaffected sibling group had an ear advantage score seen in only 15% of the normal population. Using more stringent cut-off scores (observed in only 5% of the population), we identified auditory processing impairments in 26% of children and in 30% of epilepsy-unaffected siblings.

Conclusion: These findings show that auditory processing impairments in children with RE are frequent, and may be heritable. The results require confirmation by comparison with a larger sample of locally-recruited healthy controls.
tomy by neurosurgery department while remaining 53 patients were followed up with medical treatment.

**Results:** As a result, video-EEG, MRI, PET and NPT showed similar results in terms of lateralization. The operated patients improved in memory and extra-memorial functions in the following controls. Verbal and visual memory tests, WMS mental control tests, attention, face recognize and visiospatial ability tests were sensitive to detect the disorders in relevant brain regions. Significant decrease at seizure frequency was found in the operated patients after surgery.

**Conclusion:** Our findings showed significantly increase life quality in terms of reduced seizure frequency and better cognitive functions.

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**TREND OF SELECTIVE REMINDING PERFORMANCES BEFORE AND AFTER TEMPORAL LOBE EPILEPSY SURGERY**

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**Purpose:** Temporal lobe epilepsy (TLE) is the most common form of intractable focal epilepsies with complex partial seizures. In many patients (48–75%), therapy-resistant TLE is associated with sclerosis of the mesial temporal lobe structures, which play an important role in verbal memory. It has been demonstrated that verbal memory is impaired and long-term delayed recall of visual and verbal information is severely affected. This study was aimed to determine the postoperative trend of verbal memory in left and right TLE patients.

**Method:** 84 (41 right and 43 left) TLE patients and 26 controls performed a neuropsychological battery including Digit Span (Orsini et al., 1987), Short Story (Novelli et al., 1986) and Verbal Selective Reminding (Buschke and Fuld, 1974). The tests were administered before surgery, 6 months and 1 year after surgery.

**Results:** Results showed that, before surgery, left TLE patients were impaired with respect to controls in all the verbal memory tasks (p < 0.05), while right TLE patients were impaired, with respect to controls, only in the Short Story task (p < 0.05). Six months after surgery, the only detected variation was the impairment of the right TLE patients in Digit Span related to controls (p < 0.05). However, the impairment was no more significant after 1 year. Moreover, 1 year after surgery, it was observed that the performance of left TLE patients in Verbal Selective Reminding was improved and the impairment with respect to controls was not statistically significant.

**Conclusion:** Verbal Selective Reminding, although involving memory abilities, also underlies the capacity of creating strategies to remember the couples of words presented in the task. It seems from the results of the analysis that, 1 year after surgery, left TLE patients were probably able to perform the task using different trajectories of performance.

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

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

**Method:** Patients with epileptic seizures attending the Neurology Medical Outpatient clinic LUTH were evaluated for inter-ictal morbidities using a standard pro-forma. The morbidities assessed were headaches, cognitive impairment (mental retardation and self-reported memory impairment), focal neurologic deficits and behavioural abnormalities. Using the 2010 ILAE classification, aetiology of epilepsies was classified into genetic, structural/metabolic or unknown based on the presence of risk factors.

**Results:** Out of the 103 patients assessed, 33 (32%) had inter-ictal morbidities; 30.1% had one morbidity while the remaining 0.9% had two or more. Frequency of morbidity; memory impairment 17 (16.6%), headaches 16 (15.6%), focal neurological deficits 5 (4.9%), mental retardation 4 (3.9%), behavioural problems 1 (1%), 70 (68%) had no inter-ictal morbidities.

**Conclusion:** Although inter-ictal morbidities are common in patients with epilepsy, majority of the patients were normal in between seizures. The occurrence of Inter-ictal morbidities is not related to the aetiology of seizures. Patients with epilepsy should be evaluated for treatable inter-ictal morbidities on routine follow up.

**Others 1**

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**PROFILING OF METHYLOME AND TRANSCRIPTOME IN EXPERIMENTAL TBI IN RATS**

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**Purpose:** Traumatic brain injury (TBI) is estimated to cause 10–20% of all acquired epilepsies. After the initial damage caused to the head, secondary damage develops over time consisting changes which can lead epileptogenesis. Some evidence suggests that DNA methylation controls part of the gene expression alterations found in epileptogenesis.

**Method:** To address a question, TBI was induced with lateral fluid-percussion injury to adult rats (n = 5). Five sham-operated rats served as controls. At 3 months post-TBI rats were anaesthetized, brain was quickly removed and coronal slices were sectioned to sample the hippocampus and cortex for methylene and transcriptome sequencing.

**Results:** In the hippocampus, 2472 genes was up-regulated and 1808 down-regulated as compared to controls (FDR < 0.05). In the cortex, 134 genes was up-regulated and 42 down-regulated, (FDR < 0.05). The expression of 140 same genes was altered significantly in both brain areas. Most common functional terms in among of differential expressing genes were glycoprotein, signal, plasma membrane and ion/ metal/cation binding. After TBI, methylation was changed in the gene body area in 21 genes in the hippocampus and in 45 genes in the cortex (FDR < 0.05).
Conclusion: Our preliminary result demonstrates long-lasting alternations after TBI in DNA methylation and gene expression in the hippocampus and cortex. Some post-TBI alterations in gene expression can be explained by DNA methylation.

Methods: In present study 32 male Wistar rat (200–250 g) were used to investigate repetitive TMS role in epilepsy score. TMS was performed daily for 1 month and animals’ epilepsy was induced by Pentylenetetrazole (PTZ) intraperitoneal injection. Data were an analysis was done and were comparing with control as well as sham group.

Results: Present data based on epilepsy score measurement showed that seizures were significantly disrupted by pre TMS application. Furthermore, interval as well as severity of epileptic attack was significantly decreased.

Conclusion: We conclude that neural electrical activity of brain play important role in epileptic attack. Also there was significant decrease epilepsy score in pre TMS treated rat.

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LACOSAMIDE MONOTHERAPY IN ADULT PARTIAL ONSET SEIZURES
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Purpose: Lacosamide is indicated for the treatment of epilepsy focal-onset seizures in patients aged >16 years.

Methods: A prospective, open-label observational rating of 55 patients in whom lacosamide was added to a basic therapy. Was titrated from a starting dose of 50 mg/day until seizure freedom or until the maximum tolerated dose by weekly increments of 50 mg/day. Follow-up every 2 months.

Results: Of the 55 patients 25 patients were converted to monotherapy with lacosamide for side effects, 19 partial response, 10 for both reasons, and 1 patient for interaction with methadone. Before the introduction of lacosamide patients had experienced an average of 3 treatments, such as carbamazepine, oxcarbazepine, and levetiracetam. During the assignment of lacosamide was performed CROSS TIRATION. Most frequently associated with lacosamide were carbamazepine, followed by levetiracetam, valproic acid, oxcarbazepine, topiramate and phenobarbital. Of the 55 patients 30 had crises monthly, weekly 13, 11 annual 2 day. Following the conversion, 52/55 patients were seizure-free, 2/55 have gone from crisis to crisis, weekly monthly, one patient was stationary. Lacosamide has proved generally well tolerated during the period of observation.

Conclusion: The descriptive analysis of the collected data, shows how lacosamide could represent an efficacious and well tolerated option as conversion to monotherapy in patients that failed a preexisting monotherapy due to inefficacy, adverse effects or both. Those data should be confirmed by controlled trials appropriately designed.

Abstracts

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STIGMA, TREATMENT AND OTHER PERCEPTIONS TOWARDS EPILEPSY IN NORTHWEST INDIA: A MEDICAL-ANTHROPOLOGICAL STUDY
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Purpose: To study the therapies, existence of diverse myths, beliefs, and perceptions regarding epilepsy prevalent in northwest India from anthropological perspective.

Methods: The present study on patients with epilepsy (PWE) in the age range of 15–50 years from northwest India was conducted to assess the perceptions among them with the help of a pre-tested interview schedule.

Results: 72% of PWE were familiar with the disease. 17% believed that children with epilepsy should not be sent to schools. 20% PWE considered epilepsy as a mental illness. 7% considered epilepsy as a form of insanity, but 58.6% believed that they would have objection to getting their sons or daughters marrying a person with epilepsy. 31% believed that it was a hereditary disease. 55% thought that the disease was a hindrance in their happy living. 59% of the married PWE thought that such patients could lead normal life, however 28.5% married PWE believed that they did not enjoy a normal sexual life. 11.8% married PWE revealed that they had no relationship with their spouses and 23.5% had a little relationship. 21% believed that epilepsy affect the education/studies of a patient. All of them believed that allopathic treatment was beneficial for PWE. Only 27.6% of them believed that complementary and alternative medicines (CAM) such as Ayurveda and Homeopathy were beneficial to PWE at some stages of their treatment regimen. 60% of PWE sought CAM therapies before seeking treatment form the tertiary care hospital Postgraduate Institute of Medical Education and Research, Chandigarh, India.

Conclusion: Epilepsy patients showed greater acceptance and faith in allopathic medicine than the CAM in the present study. The disease affected their social and sexual life. The study revealed that PWE needed more family and societal support to allay their fears and to overcome their problems.

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IMPROVEMENT OF SEIZURE SCORE BY REPARATIVE PRETREATMENT BY TRANSCRANIAL MAGNETIC STIMULATION ON RAT MODEL
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Purpose: Epilepsy is the chronic disorder of the nervous system, which influenced the life of many people around. Several types of protocols have been developed in animal models of epilepsy that can reduce or completely suppress it. However, drug treatment listed as an effective way for many patients, but there are numbers of drugs resistance and side effect. Also surgical resection showed serious complications. Recently, numerous electrical stimulation practices have been established for animal models of epilepsy. Transcranial magnetic stimulation (TMS) is a non-invasive brain stimulation technique. TMS have revealed, diagnostic, research, and even therapeutic applications. Repetitive TMS application showed suppressing cortical hyperexcitability in epilepsy models.

Methods: In present study 32 male Wistar rat (200–250 g) were used to investigate repetitive TMS role in epilepsy score. TMS was performed daily for 1 month and animals’ epilepsy was induced by Pentylenetetrazole (PTZ) intraperitoneal injection. Data were an analysis was done and were comparing with control as well as sham group.

Results: Present data based on epilepsy score measurement showed that seizures were significantly disrupted by pre TMS application. Furthermore, interval as well as severity of epileptic attack was significantly decreased.

Conclusion: We conclude that neural electrical activity of brain play important role in epileptic attack. Also there was significant decrease epilepsy score in pre TMS treated rat.

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CARBAMAZEPINE INHIBITORY EFFECTS IN EPILEPSY ASSOCIATED DISORDER IN RAT
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CELLULAR PROTECTION OF TRANSCRANIAL MAGNETIC STIMULATION IN SEIZURES INDUCED RAT
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Purpose: Epilepsy known as a chronic disorder of the nervous system, many people around the world are influence by epilepsy. Several types of protocols have been developed in animal models of epilepsy that can reduce or completely suppress it. However, drug treatment listed as an effective way for many patients, but there are numbers of drugs resistance and side effect. Also surgical resection showed serious complications.

Method: In present study 36 Wistar rats were treated with Carbamazepine before induction of SD to investigate the role of sodium channel responses in SD-induced spatial memory defect and behaviorally and histologically were evaluated.

Results: Our finding demonstrated that sodium channel blockade could significantly prevent SD induced memory impairment and cellular protection.

Conclusion: We conclude that action potential could play a significant role in SD wave generation and/or depolarization wave propagation and there should be effective in related disorders.

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MODIFIED ATKINS DIET MAY REDUCE SERUM CONCENTRATIONS OF ANTI-EPILEPTIC DRUGS IN ADULTS WITH REFRACTORY EPILEPSY – REPORT OF FOUR CASES
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Purpose: Ketogenic diet, an established treatment for children with medical intractable epilepsy, is a low carbohydrate, high fat diet, with up to 90 energy per cent from fat. The modified Atkins diet is a less restrictive variant, also proven to be effective for children. It contains 70–80 energy per cent from fat, and is increasingly offered as a therapy for adults with severe epilepsy. In our adult clinic we have tried the modified Atkins diet as an add-on treatment to antiepileptic drugs (AED). Here we present four cases that complied with the diet and unexpectedly experienced considerable reductions in serum AED concentrations.

Method: AED serum concentrations are routinely assessed in all patients, and were measured before and after 4 weeks on the modifed Atkins diet. The patients used combinations of two or three AEDs, including carbamazepine, clobazam, lamotrigine, nitrazepam, oxcarbazepine, valproate, zonisamide and topiramate. The patients did not change the type or dose of their AEDs during the diet period.

Results: After 12 weeks on the diet, the average serum concentrations in the four patients were reduced by 35% (range 6–46%) compared to prediet values.

Conclusion: Modified Atkins diet as add-on therapy to AEDs in four patients with medically intractable epilepsy led to a considerable decrease in AED serum concentrations. This observation could be of clinical relevance and measurements of AED serum concentrations should be considered when offering this diet to adults with severe epilepsy.

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EFFECTIVENESS OF A 12 H EXTENDED RELEASE FORMULA OF ETHYL-APOVINCAMINIC ACID IN THE CONTROL OF SEIZURES IN PATIENTS WITH REFRACTORY EPILEPSY
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Purpose: To evaluate the efficacy and safety of a 12 h extended release formula of ethyl-apovincaminic acid developed by Psicofarma SA de CV as adjunctive treatment in patients with drug-resistant partial-onset seizures.

Methods: The 12 h-extended-ethyl-apovincaminic-acid release formula was randomized in a double-blind, parallel-group and multicenter clinical trial. Following 3 months of a baseline phase, patients entered a 12-week double-blind treatment period of placebo or ethyl-apovincaminic acid 2 mg/kg/day final dose, in two times per day equally divided doses.
Results: From 490 epileptic patients evaluated in 5 centers, 87 patients (6–60 years old) covering all the inclusion criteria, including the presence of at least 4 crises per month despite the regular use of 1–4 of the anti-epileptic drugs: carbamazepine, valproate, lamotrigine or topiramate, alone or in combinations were selected. These 87 patients when randomized in the placebo (n = 46) or the ethyl-apovincaminic acid (n = 41) groups experienced similar number of seizures per month (8 ± 5.7 and 7 ± 4.2 median ± SEM, respectively). However, after the 12 weeks double blind period, seizures frequency only was reduced in the ethyl-apovincaminic acid group; from 16.3 ± 4.5 mean ± SEM seizures per month to 6.3 ± 1.2 (p = 0.02). Among the ethyl-apovincaminic acid patients one reported polyuria and polydipsia and other a dramatic intense vomiting episode. In the placebo group adverse effects such as blurred vision, vomiting and dizziness were reported.

Conclusion: This study demonstrates that the 12 h extended release formula of ethyl-apovincaminic acid is safe and markedly effective as add-on therapy for controlling or reducing seizure frequency in patients with drug-resistant partial-onset seizures.

Study funding: Research funding for collection, management and analysis of this study, was sponsored by Psicofarma S.A. de C.V., Mexico.

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LOW GLYCEMIC INDEX TREATMENT (LGIT) – HAS IT GOT A PLACE WITHIN FUTURE DIET TREATMENTS?
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Purpose: At the Danish Epilepsy Center LGIT has been offered since March 2013 as a variation of the Ketogenic diet treatments. Positive results from Classic Ketogenic Diet and Modified Atkins Diet inspired us to investigate whether LGIT could prove a supplementary treatment as the LGIT is branded as being more liberal and palatable.

Method: LGIT patients are following the same clinical path way as the MAD treatment involving start of treatment in the out-patient clinic with a 2 h consultation. Blood samples are done prior to treatment start. LGIT is considered less rigid due to a daily allowance up to 60 g of carbohydrates pr. day and no restricted mealtimes.

Number of patients: 9 patients, with an age range from 8 to 18 years, with different epilepsy background, seizure frequency and semiology. All patients had prior to LGIT taken antiepileptic drugs over years.

Results: One patient dropped out after 3 months due to worsened seizure frequency, whereas one patient had 25% reduction on absences seizures and positive cognitive improvement but stopped due to persisting GTCS seizures. Likewise a patient stopped after 3 months due to a poor outcome considered the effort. Another patient converted to MAD (parental choice). The first patient starting is still on LGIT doing well with an initial 25% reduction in infantile spasms and more days between GTCS. 4 patients are still on the diet and 2 more patients have just started indicating the diet is requested from patients.

Conclusion: In spite of the number of initial drop outs we still consider the diet as a relevant treatment. Probably with higher focus on pre-dialog regarding expectations as the diet is often addressed to young cooperating patients, who can feel diet restrictions as a major intervention in everyday. This issue should maybe be more highlighted.
**Purpose:** Determine the concentration and clarify the role of GABA in the occurrence of seizures in children during the first years of life with congenital anomalies of the central nervous system.

**Method:** We determined the concentration of GABA in blood plasma of 16 children with congenital anomalies of the CNS and frequent seizures in the age from 6 months to 3 years (main group) with subsequent comparison to the control group (12 healthy children) (method of liquid chromatography and analytical method).

**Results:** It was determined that the GABA concentration in blood plasma of children with congenital anomalies of the CNS and frequent seizures (main group) lower than the GABA concentration in the blood plasma of the control group of children with absence of seizures [mean values of the concentrations of GABA in blood plasma of children for main and control groups 11.62 ± 1.31 mg/ml and 24.65 ± 0.85] mg/ml, accordingly. The lowest concentration of GABA was determined in blood plasma in a child with hemimegalencephaly and frequent polymorphic attacks (4.68 mg/ml) and in a child with multiple congenital anomalies of the CNS (hemimegalencephaly, lissencephaly and hypoplasia of the corpus callosum) – 7.37 mg/ml.

**Conclusion:** Studies indicates about statistically significant decrease in the concentration of GABA in blood plasma of children with congenital anomalies of the CNS and frequent seizures in comparison with control group in case of absence of seizures. Therefore, it is necessary to use in the treatment of seizures such drugs that increase the concentration of GABA and normalize the balance between inhibitory and excitatory neurotransmitters.

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**EVOLUTION OF BENIGN FOCAL EPILEPTIFORM DISCHARGES IN THE ELECTROENCEPHALOGRAPHY OF THE PREMATURE NEWBORN WITH WHITE MATTER LESIONS**

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**Purpose:** White matter lesions associated with periventricular leucomalacia and intraventricular haemorrhage are serious neurological complications of prematurity. MRI imaging, cranial ultrasound and EEG can be used to predict neurodevelopment in newborn infants with white matter necrosis. Clinical significance of neonatal benign focal epileptiform discharges and positive rolandic sharp waves in the EEG of the premature newborn infants are controversial.

**Method:** Evaluate MRI findings, ultrasonographic studies, EEG findings (background abnormalities, benign focal epileptiform discharges and positive rolandic sharp waves) and neurological examination of premature newborn infants.

**Results:** In a study of premature newborn infants evaluate the use of the electroencephalogram (EEG) and benign focal epileptiform discharges and positive rolandic sharp waves in the diagnosis and prognosis of periventricular leucomalacia.

**Conclusion:** Severely abnormal MRI findings can suggest poor clinical outcome. Identification of possible marker of periventricular leucomalacia (positive rolandic sharp waves and benign focal epileptiform discharges) would facilitate clinical decision regarding neuroprotective therapy and allow early prediction of long term functional outcome.

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**THE EFFECT OF MONOSODIUM GLUTAMATE CONSUMPTION ON OBESITY, NASAL-ANAL LENGTH AND EPILEPTOGENESIS IN RATS**

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**Purpose:** Glutamate is the major excitatory neurotransmitter in the central nervous system (CNS). Monosodium glutamate (MSG), which is known as china salt among people, is a food additive used in order to increase the sense of taste especially in many fast-foods. It is difficult to predict how MSG can create an impact particularly in children who haven’t completed the development of CNS yet. The aim of this study is to investigate the effect of MSG on temporal lobe epilepsy, on weight gain and on the height.

**Method:** In order to investigate the effect of MSG usage on obesity, epileptogenesis and Nasal-Anal Length (NAL) in rats, 20 days old Wiistar albino rats were divided into 2 groups as MSG and NaCl. A bottle of tap water containing MSG (1.0 g/l p.o.) to MSG group and a bottle of tap water containing NaCl (1.0 g/l p.o.) to NaCl group were given. After 25 days of consumption of MSG and NaCl the NAL of rats is measured. A stimulation electrode and a recording electrode to right hippocampus were placed with stereotactic surgery. Then, kindling process was initiated by determining the electrical stimulation threshold values. Rats were decapitated at the end of experiment and their brains were removed for verification of cannulae placements.

**Results:** Female rats in MSG group showed more weight gain (p = 0.03) than the female rats in NaCl group however among male rats there weren’t significant difference in weight gain. There weren’t any significant difference in NAL and electrical stimulation threshold values (p = 0.21) between MSG and NaCl groups. MSG consuming rats needed very significantly (p < 0.01) less number of stimulation to reach to the Stage 3 and Stage 5 of kindling process compared to NaCl group.

**Conclusion:** MSG consumption lead to obesity in females rats, but not effect on NAL and kindling process.

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**SPECIFIC FEATURES OF SURGICAL TREATMENT OF DRUG-RESISTANT POST-TRAUMATIC EPILEPSIES: MECHANISMS OF EPILEPTOGENESIS AND NEUROPHYSIOLOGICAL BIOMARKERS**

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**Purpose:** The purpose of the present research is optimization of surgical treatment of the post-traumatic temporal lobe epilepsy on the basis of neurophysiological criteria of epileptogenesis.

**Material and methods:** The results of electroclinical examination and surgical treatment of 280 patients at the age of 19–51 with resistant post-traumatic temporal lobe epilepsy have been studied. Pursuant to recommendations of the ILAE use was made of electroencephalography monitoring with topographic brain mapping, electrocorticography, stereoelectroencephalography through depth electrodes.

**Results:** On the basis of the critical chronotopology of electrographical trait-markers specific features of the pre-clinical, early and late (extratemporal) epileptogenesis were identified reflecting the clinical and neurophysiological forms of focal and multifocal temporal lobe epilepsy at different stages of the disease depending on the epileptization pathways. The early monotemporal epileptogenesis is character-
ized by specific features of localization and length of the epileptic focus (zone): according to the electrocorticography-electrosubcorti-
ography–stereoelectroencephalography 79% of our patients were found to have combined damage of the temporal lobe neocortex and limbic structures (hippocampus, amygdala). On the basis of the interhemispheric interconnections three clinical neurophysiological forms of the temporal lobe epilepsy were identified reflecting the dynamics of brain epileptization at different stages of the disease: monoton temporal, bitemporal and “intermediate” (monoton temporal with initial formation of the mirror focus). The morphofunctional basis of the extratemporal links of epileptogenesis was made by the integral adaptive brain systems ensuring support of cerebral homeostasis (Papez, Nauta, Livingston- Escobar-Yakovlev cyclic systems).

Conclusion: The system of clinical and neurophysiological diagnostics developed at the Institute and relying on the use of a complex of modern neurophysiological and neurovisualizing technologies aimed at obligatory pre-surgical and intra-surgical specification of localization of the epileptic focus formed the basis of the strictly differentiated approach I determining the strategy, tactic and scope of adequate surgical intervention with account for individual specific features of epileptogenesis in different forms of post-traumatic temporal lobe epilepsy.

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ASTROCYTES PRE-ACTIVATED BY CILIARY NEUROTROPHIC FACTOR SHOW NEUROPROTECTIVE PROPERTIES IN A MOUSE MODEL OF MESIAL TEMPORAL LOBE EPILEPSY
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Purpose: Activation of astrocytes is a hallmark of hippocampal sclerosis in patients with mesial temporal lobe epilepsy. However, the specific role of activated astrocytes in the epileptic brain is discussed controversially.
We have previously shown that activation of astrocytes by a single, defined stimulus enhances their neuroprotective properties. We injected ciliary neurotrophic factor (CNTF) prior to an epileptogen-inducing injection of kainate (KA) and found that epilepsy-related brain damage was ameliorated and epileptiform activity reduced. In the present study we investigated the underlying molecular mechanisms.

Method: Adult C57Bl/6 mice received either a single CNTF injection into the dorsal hippocampus or sequential injections of CNTF and KA (CNTF + KA) followed by real-time qPCR analysis or immunohistochemistry for glial glutamate transporters (GLT1/GLAST), glutamine synthetase (GS), inwardly-rectifying K+ channel (Kir 4.1) or connexin 43 and 30 (Cx43/Cx30) to characterize molecular changes of preactivated astrocytes.

Results: We show that intrahippocampal injection of CNTF induces a marked and sustained activation of astrocytes reflected by up-regulation of mRNAs encoding glial fibrillary acidic protein (GFAP). Moreover, CNTF signaling via phosphorylation and nuclear translocation of STAT3 as part of the JAK/STAT pathway was specifically activated in GFAP-positive astrocytes. Real-time RT-PCR analysis revealed that CNTF-mediated pre-activation of astrocytes followed by KA injection resulted in a significant up-regulation of Cx43 and Cx30 mRNAs indicating enhanced coupling properties of astrocytes via gap junctions. Moreover GLT1/GLAST and GS mRNA expression was significantly enhanced pointing to improved glutamatergic clearance from the synaptic cleft. Furthermore, Kir4.1 mRNA was significantly higher expressed in CNTF + KA-injected animals. Complementary immunocytochemistry revealed that up-regulation of all these mRNAs occurred exclusively in astrocytes.

Conclusion: In summary, our results indicate that activation of astrocytes prior to an excitotoxic injury leads to molecular changes indicative of the observed neuroprotective and anti-epileptic action.

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SLEEP DISORDERS OTHER THAN PARASOMNIAS, AS MIMICS OF EPILEPSY
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Purpose: Next to parasomnias, other disturbances of sleep are thought to be exceptional as mimics of epilepsy. However, in our third line clinic dedicated to epilepsy and sleep disorders, these mimics are regularly encountered and are described here.

Methods: In our clinic long term (>24 h) video-EEGs always contain sensors which make global polysomnography (PSG) possible (respiration and EMG/muscle tone). In case this recording suggests a sleep disorder, a full PSG, (AASM rules) is done in order to get more details. We are aware that our patient group is a selection from the general population which may give bias in the prevalence figures.

Results: In 1650 consecutive patients video-EEG recordings suggested a serious sleep disorder in N = 255 (15%). During the consecutive PSG in 19 of all patients (1.1%) a sleep disorder was found with characteristics similar to the clinical description of the events during the night without any video-EEG prove of epilepsy. The final diagnoses in this group of 19 patients were obstructive or central apneas (O/CSA) in 9, sleep myoclonia in 5 and excessive periodic limb movements in the other 5 patients. In addition to these 19 patients, two patients had a status cataplecticus during day-time as part of not detected narcolepsy. Elsewhere, this was thought to be an epileptic disorder. Therapy for the sleep disorders resulted in substantial improvement.

Conclusion: In 1.2% of our population a sleep disorder other than parasomnia, proved to be a mimic of epilepsy. This finding has major impact on the therapy.

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POSTTRAUMATIC STRESS DISORDER IN PATIENTS WITH PSYCHOGENIC NON-EPILEPTIC SEIZURES AND ITS CLINICAL SIGNIFICANCE
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Purpose: Patients with psychogenic non-epileptic seizures (PNES) have experienced significant psychic traumas, with particularly high number of childhood sexual and physical abuse, in comparison to controls and the general population. Several studies have shown high rates of comorbid posttraumatic stress disorder (PTSD) in these patients, as compared to general population. The aim of this study was to investigate whether the rate of PTSD in our material is in line with the literature data.

Method: The clinical files of patients with PNES have been retrospec-
tively reviewed in the period of 2010–13 (N = 134). The patients have been diagnosed and treated at our clinic by a comprehensive team involving neurologist, neuropsychologist and psychiatrist. We have analysed the data of 55 patients (of 134) who have completed the PTSD-8 self
report screening scale (1) in addition to the neuropsychological evaluation, as a part of the treatment.

Results: History of psychic trauma was seen in 39 of 55 patients who underwent PTSD screening. Some of them had experienced multiple traumatic events over time. 16 patients (29%) had no psychic trauma in the history at all. In comparison to the literature data we found a lower incidence of sexual abuse (16%) in our material. Only 12 of the 39 patients with psychic traumas (31%) fulfilled the diagnostic criteria of PTSD.

Conclusion: Our experience supports using this simple and validated screening instrument in order to diagnose PTSD in patients with PNES. Longer follow-up is needed to evaluate the clinical significance of the method, whether the diagnosis of PTSD could change the treatment strategies in this patient group.


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EPILEPSY IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)
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Purpose: Our primary aim was to determine the prevalence of epilepsy in a large SLE cohort. A secondary objective was to compare the prevalence of epilepsy between SLE patients with and without other neuropsychiatric SLE manifestations (NPSLE).

Method: Our study population consisted of all 441 patients diagnosed with SLE at the Department of Rheumatology at Karolinska University Hospital from 1998 through 2010. SLE patients were screened for suspected epilepsy using the WHO (WHO/MSD/MDB/00.11) screening questionnaire for epilepsy. Medical records for all those screened positive were reviewed by a trained neurologist (LH). When the epilepsy diagnosis was considered uncertain after the chart review, the patients were all examined personally by the same neurologist (LH).

Results: Out of the 441 patients, 15% (n = 66) were dead and 2.7% (n = 12) were lost to follow up. Hence, the questionnaire was sent to 363 patients, 85% (n = 307) of whom responded. Of these, 41% (n = 127) screened positive and were subject to further examination (chart review of all, additional personal examination of 84). Epilepsy was confirmed in 37 patients (29% of those screened positive), resulting in a prevalence of 10.2% among all SLE patients and 12.0% among those responding to the questionnaire. Of the responding 193 SLE patients without other NPSLE manifestations, 15 (7.8%) had epilepsy, compared with 22/114 (19.3%) patients with other NPSLE manifestations.

Conclusion: Epilepsy is common in SLE, more so among patients with other NPSLE manifestations but sometimes the only NPSLE symptom.

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PREVALENCE AND INCIDENCE OF EPILEPSY ASSOCIATED WITH CONVULSIVE SEIZURES IN RURAL BOLIVIA. A GLOBAL CAMPAIGN AGAINST EPILEPSY PROJECT
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Purpose: We carried out a three-stages door-to-door survey to estimate incidence and prevalence of epilepsy associated with convulsive seizures (EACS) in a rural area of Bolivia.

Method: The study was developed in the Cordillera Province, in the southern-eastern part of Bolivia. 114 rural communities with a total population of 18,907 inhabitants were included in the survey. In order to identify subjects with EACS, trained fieldworkers administered a validated single screening question to the head of each household (stage I). A second and more complex questionnaire was face-to-face administered to each positive subject (stage II) that, in case of positive answer, underwent a complete neurological examination performed by neurologists in order to confirm the diagnosis (stage III). Epilepsy was diagnosed according to the definition proposed by ILAE in 1993 and widely accepted definition of EACS was adopted.

Results: On prevalence day (30th June 2010) we identified 136 subjects affected by EACS of whom 124 had active epilepsy. The lifetime prevalence of EACS was 7.2/1,000 (7.6/1,000 age-adjusted to the world standard population) while the prevalence of active EACS was 6.6/1,000 (6.7/1,000 age-adjusted to the world standard population). Both lifetime and active prevalence showed a peak (10.3/1,000) in the 15–24 years and, overall, were higher among women. During the incidence study period (2000–2010), 105 patients living in the study area had the onset of EACS. The crude incidence rate was 55.4/100,000 person-years and 49.5/100,000 age-adjusted to the world standard population. Incidence was slightly but not significantly higher among women (58.9/100,000 vs. 51.9/100,000).

Conclusion: To date only a few studies have been carried out to estimate the incidence of epilepsy in low and middle income countries. Prevalence and incidence of EACS found in our study are close to those reported in literature.

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INCIDENCE AND PREVALENCE OF EPILEPSY AND STATUS EPILEPTICUS IN PATIENTS WITH GLIOMA
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Purpose: Epilepsy means higher comorbidity in patients with glioma. Incidence varies between 30 and 100% and drug resistance between 15% and 58%, mainly in patients with low grade glioma. On the other hand, in high grade glioma cases, the percentage may increase until the end of the disease and present status epilepticus. Our purpose was to determine the incidence, prevalence and characteristics of patients with epilepsy and/or status epilepticus and glioma according to histological subtype presented in our Neurooncology Committee.
Abstracts

Method: We reviewed clinical histories of patients with glioma presented at the Committee between January 2006 and December 2012. Variables evaluated were age, sex, histology, location, side, epilepsy, number and type of AED, drug-resistance criteria, type of surgery, status epilepticus.

Results: Of 102 patients, 74.5% had epilepsy, with 12% of drug-resistance after resection. 29.5% needed more than 2 AEDs to control seizures. LEV was the AED more used. According to histology type, patients with low-grade glioma had higher percentage of epilepsy (96.7%) comparing to high-grade glioma (65.3%), p < 0.05. About status epilepticus, patients with low-grade glioma presented it in 10.3% of the cases and in the high-grade group in 8.3% (p NS).

Conclusion: Epilepsy was a frequent complication in our cohort, mostly in low-grade glioma patients. However, status epilepticus, although less frequent, was equally presented in both low and high-grade glioma patients.

Method: We included children 0–16 years registered with an epilepsy diagnosis (G40) from 2009 through 2012, in the Norwegian Patient Registry Study of Comorbidity in Childhood Epilepsy.

Results: There is increasing focus on comorbidity in childhood epilepsy, but there are limited population-based data on occurrence of comorbid medical conditions. Such data are needed to improve management of children with epilepsy and resource allocation. We estimated prevalence of comorbidities in childhood epilepsy using nationwide registry data.

Method: Our study population was defined as all those with a hospital discharge diagnosis of epilepsy in the Swedish National Patient Registry (SNPR) at some point during 1998–2005. All deaths in this study were identified by cross linkage to the Cause of Death Registry. Cases with confirmed or suspected (uncertain whether death purposely or accidentally inflicted) suicide were selected and their death certificates, medical records, and autopsy reports reviewed.

Results: Of the 78,520 with epilepsy in the study population, 1891 died during the year 2008. Of the 1891 deaths, 21 were due to suicide and 19 were suspected suicide. Taken together suicide and suspected suicide contributed 2.1% of all deaths in the cohort. The median age of suicide/suspected suicide cases was 53 years (range 12–82), 23/40 were female. In none of these cases, epilepsy was mentioned on the death certificate. For 19 of the 40 cases (48%) a psychiatric diagnosis was mentioned in the last hospital discharge recorded in the SNPR or on the death certificate (12 cases having a substance abuse diagnosis, 3 anxiety disorder and 2 depression).

Method: We included children 0–16 years registered with an epilepsy diagnosis (G40) from 2009 through 2012, in the Norwegian Patient Registry Study of Comorbidity in Childhood Epilepsy.

Results: Of 102 patients, 74.5% had epilepsy, with 12% of drug-resistance after resection. 29.5% needed more than 2 AEDs to control seizures. LEV was the AED more used. According to histology type, patients with low-grade glioma had higher percentage of epilepsy (96.7%) comparing to high-grade glioma (65.3%), p < 0.05. About status epilepticus, patients with low-grade glioma presented it in 10.3% of the cases and in the high-grade group in 8.3% (p NS).

Conclusion: Epilepsy was a frequent complication in our cohort, mostly in low-grade glioma patients. However, status epilepticus, although less frequent, was equally presented in both low and high-grade glioma patients.

Method: We included children 0–16 years registered with an epilepsy diagnosis (G40) from 2009 through 2012, in the Norwegian Patient Registry (NPR), an administrative database recording ICD-10 diagnoses assigned by the specialist health services in Norway. Comorbid diagnoses were also extracted from the NPR. Based on preliminary results of our ongoing validation study, we excluded children with only one registered epilepsy diagnosis combined with an EEG recording, to exclude administrative coding.

Results: 5969 individual children (55% boys, mean age 7.6 years) were administered epilepsy diagnosis combined with an EEG recording, to exclude our ongoing validation study, we excluded children with only one registered epilepsy diagnosis combined with an EEG recording, to exclude administrative coding.

Results and conclusion: The frequency of sleep complaints of 225 epileptic patients were 50.2%. These complaints were snoring, nightmares, periodic leg movement disorder, restless legs, bruxism and combination of them. It was observed that 37.3% of the patients (n:84) were on polytherapy and 62.7% of them (n:141) were on monotherapy. PUKI value was above 5.5 in the 5.3% of the patients (n: 12). Epworth sleepiness scale was ≥8 in the 11.1% of the patients (n:25). The sleep properties of the epileptic patients with epilepsy were revealed that female patients have late sleep inertia and older patients were short sleeper. Furthermore, a statistically significant difference was found between the length of sleep inertia and the frequency of seizure (p = 0.053). It was determined that the patients who had daytime sleepiness had also short periods of sleep inertia. It was revealed that the patients who had long periods of sleep inertia had also bad sleeping quality.

Method: Our study population was defined as all those with a hospital discharge diagnosis of epilepsy in the Swedish National Patient Registry (SNPR) at some point during 1998–2005. All deaths in this study were identified by cross linkage to the Cause of Death Registry. Cases with confirmed or suspected (uncertain whether death purposely or accidentally inflicted) suicide were selected and their death certificates, medical records, and autopsy reports reviewed.

Results: Of the 78,520 with epilepsy in the study population, 1891 died during the year 2008. Of the 1891 deaths, 21 were due to suicide and 19 were suspected suicide. Taken together suicide and suspected suicide contributed 2.1% of all deaths in the cohort. The median age of suicide/suspected suicide cases was 53 years (range 12–82), 23/40 were female. In none of these cases, epilepsy was mentioned on the death certificate. For 19 of the 40 cases (48%) a psychiatric diagnosis was mentioned in the last hospital discharge recorded in the SNPR or on the death certificate (12 cases having a substance abuse diagnosis, 3 anxiety disorder and 2 depression).
Conclusion: The proportionate mortality in suicide/suspected suicide was 2.1% and around half of the patients had a psychiatric diagnosis. This is in line with other studies. It is of concern that in none of these cases was epilepsy mentioned on the death certificate.

p303
THE RELATIONSHIP BETWEEN EPILEPSY AND TYPE 1 DIABETES MELLITUS IN ADULTS
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Purpose: Epilepsy and Type 1 Diabetes Mellitus (T1DM) are both very common conditions. In a number of studies in paediatric T1DM patients the incidence of epilepsy is increased and the predominant co-existence was reported with genetic generalised epilepsy (GE). We sought to characterise for the first time an adult population with concomitant epilepsy and T1DM.

Method: Cases were identified by placing a query into a database containing all patients attending for videotelemetry at Queen Square video telemetry unit from 1988 to 2013. This query covered 7371 records and searched for the words “diabetes” and “diabetic”. Retrospective notes review was performed of all patients identified with this query to identify genuine cases of T1DM. Video EEG reports, neuromaging and clinical background were collated.

Results: 9 patients identified with Epilepsy and T1DM. Average age of seizure onset was 16, three had onset in adulthood. All had poorly controlled epilepsy. 3 had abnormal MRIs, two with left hippocampal sclerosis and the third with changes related to their diagnosis of cerebral palsy. 2 patients had abnormal FDG-PET scans, one which was concordant with their MRI showing left hippocampal sclerosis and the patient had a normal MRI. Only 1 patient had GE with 7 (87.7%) patient’s diagnosed with focal epilepsy (4 right temporal and 4 left temporal).

Conclusion: Compared to paediatric studies, focal epilepsy is much more common in our adult cohort, although a selection bias may play a role. Possible aetiologies such as an underlying autoimmune association via anti-glutamic acid decarboxylase antibodies and a metabolic predisposition mediated by hypergylcaemia should be evaluated in future studies. Because recording of co-morbidities in videotelemetry reports was inconsistent, this data cannot serve as an epidemiological comment of the relative frequency of T1DM in epilepsy.

p304
PREVALENCE, TREATMENT AND IMPACT OF SEIZURE CLUSTERS ON QUALITY OF LIFE
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Purpose: To determine the prevalence, treatment, and severity of seizure clusters on quality of life in a tertiary epilepsy center.

Method: This is a prospective observational cohort study to define the prevalence and characteristics of seizure clustering. Patients were categorized according to their reported seizure frequency over the year prior to enrollment into one of the three groups: prior clusters, active epilepsy and seizure free. The prior clusters group included subjects reporting 2 or more seizures within a 24 h period. Patients record seizure frequency using a diary and will be followed for a period of 1 year. Quality of Life questionnaire (QOLIE-31) was scored out of 100 points where higher scores indicated better function and seizure severity questionnaire (SSQ) was measured on a 7-point scale, where higher scores indicated more severity. We presented the pattern of clustering, use of rescue medication whereas 21 (70%) did not. There were no significant difference in the mean total QOLIE-31 score (p = 0.881) and the total SSQ score (p = 0.062) between the prior clusters group (57.2, SD 20.3; 3.95, SD 1.36) and the active epilepsy group (56.5, SD 18.2; 4.15, SD 1.56). The seizure free group (72.5, SD 16.5) had a significantly better mean total QOLIE-31 score compared to the prior clusters (p = 0.01) and the active epilepsy groups (p = 0.003).

Conclusion: Seizure clustering is not uncommon among patients with epilepsy and rescue medications are underutilized for those patients. Quality of life and seizure severity were not significantly different between the prior clusters and active epilepsy groups. Seizure-free patients had a significantly better quality of life compared to the prior clusters and active epilepsy groups.

p305
CLINICAL PROFILE, ETIOLOGY AND TREATMENT OF EPILEPSY PATIENTS IN A TERTIARY HOSPITAL IN RURAL NIGERIA
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Background: Epilepsy is the most common neurological disorders seen in outpatient clinic in developing regions of the world. The prevalence is highest in developing countries. There is limited data regarding clinical profile of epilepsy from rural communities in Nigeria. Current study aims to find etiology, clinical characteristics and treatment of epilepsy in adults presenting in outpatient clinic, in Southern Nigeria.

Methods: We prospectively enrolled patients with diagnosis of epilepsy seen in outpatient clinic between September, 2010 and August, 2013, and applied standardized questionnaire to obtain data on the demographic, clinical profile, investigations and medications at presentation and follow up.

Results: Epilepsy was diagnosed in 119 patients aged (16–95), mean age was 39.7 ± 21.6 years. Male to female ratio was 1.3: 1 and 33% were students. Mean age of onset was 44.28 ± 26.79 years and the highest age group was 30–39 years (25.9%). Mean period of first clinic visit was 7.7 ± 6.4 years and mean frequency of seizures at presentation was 5.8 ± 7.5 per year. Only 2.3% had positive family history. 102(86%) could afford EEG and 23.8% of our patients with indications for neuromaging could afford this. The commonest abnormal EEG finding was non-specific slow waves (65%) and only 10.6% had spikes and sharp waves. The commonest neuromaging finding was old infarcts in patients 40 years and above. 85.2% of the patients were on monotherapy (Carbamazepine CR). Seizure control was achieved in 63%. Forty five patients had poor treatment compliance and 42.9% had poor clinic attendance, which was due to poor financial status.

Conclusion: Epilepsy remains a significant burden in rural areas. Cost of treatments remains a greater challenge in the management of epilepsy in this environment.

p306
THE BURDEN OF CONVULSIVE EPILEPSY IN RURAL SOUTH AFRICA: USING POPULATION-BASED DATA TO CALCULATE DALYS
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Purpose: Epilepsy, one of the most common neurological disorders globally, affects roughly 70 million individuals. There are few studies that estimate the burden of epilepsy in low income countries, in terms of Disability Adjusted Life Years (DALYs), a summary measure of both morbidity and mortality, used most recently in the 2010 global burden of disease study.

Method: Using prevalence, incidence and mortality data on convulsive epilepsy collected within the Agincourt Health and Socio-demographic surveillance site in rural northeastern South Africa between 2008 and 2012, we estimated the DALYs due to convulsive epilepsy, using both prevalence and incidence-based methods for calculating years of life lived with disability (YLD).

Results: Using the prevalence-based method, we found that convulsive epilepsy was responsible for 332.1 (95% CI: 215.9–454.8) DALYs in the Agincourt HDSS. This equated to 4.1 DALYs per 1,000 individuals (95% CI: 2.7–5.7). Seventy-four percent of this was due to morbidity while 26% was due to excess mortality. The overall number of DALYs increased by 10% when using the incidence-based method to calculate YLDs. Sensitivity analysis concluded that using Agincourt life expectancy values resulted in a 24% reduction in DALYs.

Conclusion: This is the first study to report the DALY burden of convulsive epilepsy in South Africa and the findings are similar to figures reported from rural Kenya and those from the 2010 global burden of disease study. Excess mortality is associated with a significant portion of the burden. Using context-specific life expectancy values (rather than those used in the 2010 global burden of disease study) reduced the burden of epilepsy suggesting that a substantial portion of the burden may be due to context rather than epilepsy. Interventions aimed at increasing treatment coverage and improving the quality of life in people with epilepsy would likely lower the burden of convulsive epilepsy in rural South Africa.

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THE EFFECT OF SPINAL CORD STIMULATION ON CHEMICALLY-INDUCED SPIKE-AND-WAVE SEIZURES IN RATS
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Purpose: Spinal cord stimulation (SCS) has been applied for the treatment of chronic pain for decades. Recent studies have shown that SCS may also modulate seizure susceptibility, but it is unclear which stimulation parameters may be most effective in inhibiting seizures. The objective of the present study was to investigate the effect of SCS pulse frequency in regard to suppression of seizures.

Method: Nine Sprague-Dawley rats were included in this study. Sustained spike-and-wave (SW) seizures were induced by continuous pentyl-enetetrazole infusion. SCS was performed using charge balanced pulses with the intensity set just below the motor threshold. The tested pulse frequencies (i.e. 30, 80, 130 and 180 Hz) were applied in four consecutive SCS sessions which were randomly ordered and separated by 5 min intervals without stimulation. Intracortical field potentials were recorded from the right somatosensory hindlimb area. The normalized SW power (SWP) was calculated and used for quantifying the severity of SW activity. The effects of the different SCS frequencies were compared using the Two-Way Repeated Measures ANOVA and Bonferroni-correction.

Results: Compared with sham-stimulation, 30 Hz SCS increased the SWP by 85% (p < 0.05). In contrast, 130 Hz and 180 Hz SCS reduced the SWP by 29% (p < 0.05) and 31% (p < 0.05), respectively. 80 Hz SCS did not induce significant SW changes.

Conclusion: These results suggest that high frequency SCS (130–180 Hz) may be used as a therapy for refractory epilepsy while 30 Hz SCS should be avoided because of its pro-convulsive effect.

p309
UNILATERAL VS. BILATERAL HIPPOCAMPAL DBS IN A RAT MODEL FOR TEMPORAL LOBE EPILEPSY
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Phase 1: Door to door screening using the WHO Neuroscience Research Protocol to detect neurological disorders by health workers.

Phase 2: Individuals with positive screening had complete neurologic examination by neurologists as well as an EEG recording. The questionnaires for survey of epilepsy in tropical countries (Limoges France) and subjective handicap of epilepsy were administered to all PWE.

Results: 2212 individuals from 231 households were screened during the first phase and 33 cases of neurologic diseases were detected. During the second phase, 10 cases were confirmed to be epilepsy by neurologists, thus giving a crude lifetime prevalence of 10/2212 = 4.5/1000 population (CI 95% –2.30, 8.04). The Subjective Handicap of Epilepsy (SHE)- scale score was directly related to level of seizure control.

Conclusions: The prevalence of epilepsy in Ilie South West Nigeria is rather low compared to previous figures from studies in rural Africa.

Keywords: Epilepsy, Prevalence, Community, Subjective Handicap & Treatment
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Hippocampal deep brain stimulation (DBS) is an experimental therapy for patients with refractory temporal lobe epilepsy. Despite the promising results obtained with hippocampal DBS, the optimal stimulation paradigm is still unknown. This study aims at comparing the seizure suppressive effect of unilateral hippocampal DBS with bilateral hippocampal DBS in a rat model for temporal lobe epilepsy. In the post status epilepticus (SE) intraperitoneal kainic acid rat model of epilepsy stimulation and EEG recording electrodes are implanted in the left and right hippocampus. Continuous EEG monitoring was performed for 50 days. During this EEG monitoring period, rats received 10 day periods of unilateral and bilateral Poisson distributed high frequency hippocampal DBS in a cross-over design intervened with washout periods of 10 days. Unilateral and bilateral hippocampal DBS significantly reduced seizure frequency in 36% and 64% of the rats respectively (p < 0.05). After stopping either stimulation modality, seizure frequency returned to baseline levels. The reduction in seizure frequency was significantly higher during bilateral hippocampal DBS compared to unilateral hippocampal DBS. Rats responding to unilateral hippocampal DBS experienced an even higher seizure suppressive effect during bilateral hippocampal DBS. In 18% of all rats bilateral hippocampal DBS yielded complete seizure freedom. These results indicate that bilateral hippocampal stimulation induces a higher responder rate and has a higher seizure suppressive potential than unilateral stimulation in the kainic acid rat model.

p310
VAGUS NERVE STIMULATION IN PATIENTS WITH DEVELOPMENTAL DISABILITIES
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Purpose: The aim of the study was to evaluate the effect and tolerability of vagus nerve stimulation (VNS) in patients with epilepsy and developmental disabilities following at our Epilepsy Clinic.

Method: Thirteen adult mentally retarded patients with medically refractory epilepsy have got implanted VNS between 2006 and 2012. Most of the patients are living in or receiving home-care. Our comprehensive team, including neurologist, epilepsy nurse and caregivers, is responsible for VNS follow-up. The clinical reports and VNS registration data were retrospectively analysed.

Results: Seizure reduction (>50%) was observed in 8 of the 13 patients, and only milder seizures in 2 further cases. The stimulator was removed in 2 cases because of infection caused by self-mutilation related to disability. Two patients died not related to VNS. Side-effects, i.e. hoarseness and cough were tolerable in 5/13 cases. No remarkable side effects were seen in 5/13 patients as far as it could be evaluated without reliable communication. A clear improvement in vigilance has been observed by the care-givers in 3/13 mentally retarded patients within 1–2 years from the implantation.

Conclusion: Our retrospective data shows promising effect and tolerability of VNS also in mentally retarded patients. Although, no serious complications have been seen, careful patient selection for VNS is advised in disabled patients concerning behavioural aspects. Our experience supports that caregivers should actively be involved both in the pre-surgical process and the follow-up in order to increase safety and welfare. Life-quality measurements in large material could support the effort to consider VNS more often in these patients.

p311
LONG LASTING MEMORIES SCRUTINIZED FROM ELECTRICAL BRAIN STIMULATION: A REVIEW AND ANALYSIS OF 80 YEARS OF LITERATURE IN EPILEPTIC PATIENTS
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Purpose: Electrical brain stimulations (EBS) in epileptic patients can sometimes induce reminiscence of memories. Penfield reported large series of such cases in seminal papers and hypothesised from these observations that our memory may be like a “tape-recorder”, basically encoding all events of our life. Is this true? Can EBS reactivate any of our memories, including all details as he hypothesised?

Method: We propose a review of all reminiscences of memories induced by EBS reported in the literature. These reminiscences all had visual and/ or auditory content in order to differentiate them from déjà-vu/déjà-vécu. They were classified according to modern conceptions of memory (“autobiographical episodic memory”, “autobiographical semantics”, “general semantics”, “other”). Locations of EBS were also analysed.

Results: We collected 256 reminiscences in patients across 26 articles and book chapters from 1958 to 2012 (226 reminiscences) and our own database from 2001 to 2013 (30 reminiscences). 13.3% were related to autobiographical episodes, but very few met all criteria of truly detailed episodic memory (3.9%). In contrast, 36.3% referred to autobiographical semantics. Interestingly, 16.4% related to general semantics (i.e. factual knowledge about the world). 34% had other phenomenological characteristics. 91.4% of the reminiscences originated from EBS of the temporal lobes with no clear difference between the right or left hemisphere. A few originated from EBS to diencephalic structures. After-discharges were inconstantly associated with reminiscences.

Conclusion: These results do not support Penfield’s “tape-recorder” hypothesis and rather favour the idea of a progressive semantisation of episodes. Intriguingly, no EBS of the medial parietal or frontal lobes induced reminiscences whereas these regions are often associated with memory networks.

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PATIENTS/CAREGIVERS SATISFACTION FOLLOWING VAGAL NERVE STIMULATION (VNS) FOR DRUG-RESISTANT EPILEPSIES
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Purpose: To evaluate both patients and caregivers satisfaction following VNS for drug-resistant epilepsies.

Method: 80 patients (72 adults and 8 children) underwent VNS from 1995 to 2012. Mean follow up was 56 months. 16 patients were lost to
follow up, one died, five removed VNS for inefficacy. 58 patients were reached by phone.

Patient satisfaction was evaluated with an oral questionnaire, including patient and caregiver Global Impression of Change (GIC), willingness to do VNS all over again or to suggest it to friends, and a Global Quality of Life Change Score (GQLCS, where 0 was no change and 10 was maximum positive change).

Clinical Global Impression of Change (C-GIC) was obtained from seizure diaries, taking into account seizure frequency and severity.

Non-parametric statistical tests were used to compare patients and caregivers responses.

Results: The phone interview was completed in all the 58 cases. It was answered by the patient in 6, by the caregiver in 26 and by both patient and caregiver in 26 cases.

A great improvement was reported by 25% of patients and by 25% of caregivers, slight improvement by 43.8% and 38.5% respectively, no change by 28.1% and 28.9%, slight worsening by 3.1% and 5.8%, and severe worsening by 0% and 1.9%.

75% of patients and 71.1% of caregivers would do VNS all over again.

Median GQLCS was 6 for patients and 5 for caregivers.

Conclusion: Satisfaction rates were not statistically different between patients and caregivers and were in line with C-GIC, based on seizure diary. In our series, 65% of patients were satisfied by VNS and showed some clinical improvement with reduction in frequency and/or intensity of seizures.

Purpose: Deep brain stimulation is a promising approach for epilepsy treatment. Tuberomammillary nucleus (TMN) is involved in EEG-desynchronization during wakefulness and fast sleep. Its electrical activation was proposed to be effective in disruption of synchronized epileptic activity. We investigated whether stimulation of TMN could interrupt epileptic spike-wave discharges (SWDs) in WAG/Rij rats with inherited absence epilepsy and whether such stimulation would affect sleep-wake cycle.

Method: EEG recorded through chronically implanted electrodes and video registration were used to determine SWD occurrence and stages of sleep and wake. After a baseline recording threshold amplitude of stimulation (100 Hz, 1s train) for SWD interruption was determined for each rat (n = 5). Then the rats were stimulated in a closed-loop mode for 3 h. Then the experiment was repeated twice but stimulation was provided in open-loop mode with amplitudes 50% and 70% of threshold.

Results: Closed-loop stimulation successfully interrupted SWDs but their number was increased by 148 ± 54% (p < 0.05). It was accompanied by increase in number of episodes but not total duration of both active and passive wakefulness. Open-loop stimulation with amplitude 50% threshold did not change neither epileptic activity nor amount of sleep and wake, though 70% threshold stimulation reduced SWDs number by 40 ± 9% (p < 0.05), significantly raised the amount of active wakefulness and decreased the amount of both slow-wave and fast sleep.

Conclusion: We showed that high-frequency stimulation of the TMN was able to disrupt absence epileptic activity if applied at the beginning of SWD. However it caused elevation of SWDs amount possibly associated with disturbed sleep-wake cycle because of close relationship between state of vigilance and SWD occurrence. Open-loop subthreshold stimulation of the TMN was ineffective in changing amount of epileptic activity. The observed decrease in SWDs caused by 70% threshold stimulation was apparently secondary to the movement activation of the rats.
Patient 3 (36 year, male, FLE) with SD 20%, 1/1 seizure triggered stimulation 37s after onset. Stimulation occurred in STEX; there were 155 FP/12 h. SD changed to 50%, 11/15 seizures triggered stimulation a median of 17.5s after onset with 85 FP/12 h. In the follow-up, SD changed to 60% as frequent stimulation led to hoarseness.

Conclusion: Variability of heart rates between different patients required different SD settings; this was more critical than intra-patient variability. Based on these data, it appears that a suitable SD setting can be found for each patient that balances sensitivity and specificity.

p316 EFFECTIVENESS OF VAGUS NERVE STIMULATION (VNS) IN SEVERE NONSURGICAL CANDIDATES AND FAILED INTRACRANIAL EPILEPSY SURGERY PATIENTS

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Purpose: To delineate the effectiveness of VNS in highly selective nonsurgical candidates and failed intracranial epilepsy surgery patients.

Method: This prospective longitudinal observational descriptive study included 20 patients with various severe epileptic syndromes. All underwent pre-surgical 24-h video-EEG monitoring to exclude candidacy for epilepsy surgery. Effectiveness regarding seizure frequency reduction, severity of seizure, neuropsychological functions, and safety of the treatment was assessed at 3, 6, 12, 18, and 24 months after VNS stimulation. Cross-sectional and longitudinal analyses were conducted.

Results: The patients included 5 patients with generalized epilepsy; all were Lennox-Gastaut syndrome (LGS). Fifteen patients experienced focal epilepsy. 6 with bitemporal disease, 4 with nonlesional extratemporal lobe epilepsy, 3 with failed surgery, 1 each with double cortex syndrome, ring chromosome 20, and right hippocampal sclerosis with temporal lobe epilepsy, 3 with failed surgery, 1 each with double cortex syndrome, ring chromosome 20, and right hippocampal sclerosis with temporal lobe epilepsy. 3 with failed surgery, 1 each with double cortex syndrome, ring chromosome 20, and right hippocampal sclerosis with temporal lobe epilepsy.

Conclusion: Given high cost of the VNS device and significantly less percentage of achieving seizure freedom as opposed to resective surgery in medically intractable patients, in our center VNS was therefore employed as a last resort of treatment in patients with severe epileptic syndromes. The effectiveness of the VNS therapy in view of reducing seizure frequency in these patients was not favorable as previous reports in other subgroups. This may be due to relatively greater disease severity.

p317 LEAD MALFUNCTION IN VAGUS NERVE STIMULATION: CLINICAL EFFECT, DIAGNOSIS AND OUTCOME AFTER LEAD REVISION

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Purpose: Analyze Vagus nerve stimulator (VNS) revisions, due to suspected lead malfunction and evaluate causes, clinical effect, diagnostic methods and clinical outcome after lead revision.

Method: 514 patients were treated with VNS for medically refractory epilepsy between 1996 and 2013. 36 (7%) had a surgical VNS revision due to suspected lead malfunction. The clinical situation, lead impedance at VNS testing, X-ray investigations, EMG-assisted lead tests and results from intraoperative exploration were retrospectively analyzed.

Results: 25 of the 36 patients (69%) reported clinical worsening, two patients reported side effects, and in nine patients high lead impedance was detected during routine VNS testing. There was no correlation between the different measurements of high impedance and findings during surgery. In all patients the leads were replaced, and in 31 (86%) resulted in clinical improvement. X-ray investigation of 35 patients was positive in only seven (20%). Since 2010 we have used EMG-assisted lead tests in 15 patients in whom we suspected partial or microbreakage; findings consistent with lead breakage were detected in 10 (66%).

Conclusion: Lead breakage is a seldom complication often causing clinical deterioration. An early revision, with the exchange of leads, results in an improved seizure control. High impedance found in VNS-testing is not a trustworthy indicator of a lead breakage as it cannot differentiate between lead breakage, fibrosis, disconnection or other causes of lead malfunction.

We found EMG-assisted lead tests to be more sensitive than X-Ray investigations to diagnose lead malfunction.

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p318 THE IMPORTANCE OF STIMULATION CYCLE IN VAGUS NERVE STIMULATION FOR DRUG-RESISTANT EPILEPSIES

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Purpose: Vagus nerve stimulation (VNS) is a treatment for drug-resistant epileptic patients excluded from ablative surgery. The patient’s stimulation cycle is only marginally reported in the literature. In this work, we investigated how stimulation cycle can affect VNS. Indications about this record are important because it is associated to the duration of generator and frequency of generator change.

Method: We reviewed the clinical records and stimulation parameters of 21 patients (14 M and 7 F) who responded to VNS (we identify patients as “responders” when the decrease of seizure number was at least 50%). Mean follow-up was 80.42 ± 54.01 months. Stimulation cycles used were the following: slow (30” on-5” off), intermediate (30” on-3” off), fast (7” on-20” off). Our protocol is to start with the slow cycle and, if we have not a “response”, to try the fast and then the intermediate cycle. Each cycle is 1 year in duration or less if patient become a responder. We record the stimulation cycle at the latest available follow-up for each patient.

Results: At latest follow-up, 10 cases (47.61%) were using slow cycle and 8 (38.09%) the intermediate one. Only 3 patients (14.28%) were responders with the fast cycle. In the subgroup of patients with a follow-up longer than 3 years (n = 14), 85.71% of them were using slow or intermediate cycles. Our results indicate that in the subgroup of patients responding to VNS the slow and intermediate cycles maintain the benefit of VNS. This data is important in term of duration of generator that directly affects the cost of this therapy.

Conclusion: In managing these patients after VNS implantation, we suggest to start with the slow cycle and, if there is no response, to switch to intermediate one. At that stage the probability for the patient of being a responder with the fast cycle is very low.
Efficacy and Safety of Trigeminal Nerve Stimulation: An Experience in 8 Patients with Drug-Resistant Epilepsy
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Purpose: There is preliminary evidence that external Trigeminal Nerve Stimulation (eTNS) is safe and may be effective in reducing seizures in patients with drug-resistant epilepsy. The aim of this study is to describe the outcome of a series of 8 patients with refractory epilepsy treated with eTNS.

Method: Patients with drug-resistant epilepsy treated with eTNS in our epilepsy unit were retrospectively evaluated. We analyzed reported side effects and efficacy measured as the reduction in seizure frequency and the rate of responders (≥50% reduction in seizure frequency). We compared seizure frequency during the 12-week period before eTNS initiation (pre-eTNS period) with seizure frequency during an early evaluation period (weeks 1–12) and a late evaluation period (weeks 13–24).

Results: Mean age at time of eTNS initiation was 34 (12–53) years. Subjects had a median number of seizures during the 12 week pre-eTNS period of 20.5 (2–1260) per month. Five patients presented symptomatic or cryptogenic epilepsy, two patients had Lennox-Gastaut syndrome and one patient had progressive myoclonic epilepsy. Stimulation was set at 2.8–6.4 mAs during 8–16 h/day at night. During the early evaluation period the responder rate was 25% (2/8 patients), with a mean reduction in seizure frequency of 3.22% [85.71 to 94.84%]. One patient discontinued eTNS due to lack of efficacy after 12 weeks. During the late evaluation period, the responder rate was 75% (3/4 completed patients), with a mean reduction in seizure frequency of 76.63% [42.1–100%]. An improvement in mood and attention was reported by 6/8 (75%) patients. eTNS was easy to implement in all patients. Adverse effects were very mild and included transient headache and skin irritation.

Conclusion: eTNS was an effective and almost side-effect free therapy in our series of highly drug-resistant epilepsy. Efficacy was observed after the first 12 weeks of treatment.

Efficacy and Safety of Trigeminal Nerve Stimulation for Epilepsy: Early Clinical Experience
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Purpose: We report our early clinical experience of eTNS.

Method: We offer patients with drug resistant epilepsy (aged 9+) eTNS and audit outcome (seizure frequencies, quality of life: QOLIE-10/ED-DQOL, mood: BDI, sleep: Pittsburgh and daytime sleepiness: Epworth) at baseline, 4, 12 and 18 weeks. Patients can continue treatment beyond this. A self-adhesive electrode, attached to the eTNS device, is placed on the forehead, stimulating both trigeminal nerves (120 Hz, 30 s on/off). Patients set the current (noticeable and comfortable, <10 mA, aiming >8 h overnight). Results are mean ± SD, paired t-test used for comparison.

Results: Sixteen adult and 7 children started eTNS before October 2013. Two children discontinued use early (headache without seizure improvement). Another developed transient hypopigmentation from the adhesive. Outcome for the 5 remaining is awaited.
p322
**BILATERAL INTRAHYPOthalamic HAMATOMA – INDICATION FOR RESECTIVE SURGERY?**


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**Purpose:** Hypothalamic Hamatomas (HH) are rare developmental malformations consisting of mixed neurons and glial cells, usually unilaterally attached to the tuber cinereum or mammillary bodies. We report about two patients with bilateral HH.

**Method:** A 51 year-old female patient had infantile spasms in the first year of life. Later on she developed mild gelastic seizures, smiling, short laughing), dyscognitive seizures with oral and bilateral manual automatism, visual auras and tonic seizures. Ictal and interictal EEG showed bilateral temporal or posterior temporal epileptiform discharges with right-sided preponderance. The bilateral HH revealed by MRI was bigger on the right side and more anteriorly located and thus hiding the left one. In an 8 year-old boy epilepsy started at age two. The patient developed gelastic and dacrycic seizures with different kinds of auras (epigastic, vegetative, somatosensory) and dyscognitive seizures. Interictal EEG showed spare fronto-median and right frontal sharp-waves. Ictal EEG was not helpful. Bilateral HH symmetrically attached to the mammillary bodies of each side were detected on MRI, again more voluminous on the right side.

Since drug-resistance was proven in each patient we decided to perform endoscopic ablation of the right HH in both cases.

**Results:** The female patient had more than 50% seizure reduction at 2 years of follow-up. She improved in cognitive functions and behaviour. After a post-operative seizure-free period of 2 weeks, seizures recurred in the boy. However, postsurgical observation time is short.

**Conclusion:** To our best knowledge there are no other reports of bilateral HH in the literature. The question arises if the surgical strategy to remove only the more predominant HH is sufficient to improve seizure outcome and if not, as it seems in our patients, which risks might be associated with a bilateral removal.

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p323
**VALPROATE ASSOCIATED COAGULOpathy AND PLATELET DYSFUNCTION: CLINICAL RELEVANCE FOR EPILEPSY SURGEON**

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Association of valproate with coagulation factors deficiency and platelet dysfunction has been known however only few reports of haemorrhagic complications are available. Valproate commonly being the first line antiepileptic drug in pharmaco-resistant epilepsy (PRE), clinical relevance of this association became important for epilepsy surgeons. Paucity of literature on this issue prompted us to share our experience relevant to epilepsy surgery centres.

We studied total of 169 patients with PRE who underwent surgical intervention at tertiary epilepsy care centre. Pre-operative coagulation screen and platelet counts were normal in all patients. Normal bedside bleeding time and clotting time tests were ensured before surgery in all patients. Valproate was content of polytherapy in 54% of patients (Group A), however 46% patients were not on valproate (Group B). Both the groups were comparable in age, sex with mean age of 17.3 ± 10.3 years. Mean duration of surgery in group A and B were 255 and 250 min respectively (p = 0.27). Average blood loss in group A was 395.7 and 387.2 ml in group B (p = 0.6). The percentage of total blood volume lost in group A and group B was 12.7% and 17.7% respectively (p = 0.4).

There were no bleeding associated complications in either of groups which required intervention.

We concluded that valproate intake does not increase incidence of clinically relevant perioperative haemorrhagic complications in patients undergoing epilepsy surgery and have normal pre-operative coagulation screen and platelet counts. We do not recommend discontinuation of valproate before planned epilepsy surgery in patients with normal coagulation and platelet profile.

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p324
**CLUSTER ORGANIZATION OF THE IRRITATIVE ZONE IN NEOcORTICAL EPILEPSY: IMPLICATIONS FOR PATHOPHYSIOLOGY, SURGERY PLANNING AND OUTCOME**

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**Purpose:** The irritative zone is an area of the brain that generates interictal epileptiform discharges (IEDs) and is used together with other results when planning epilepsy surgery. Unfortunately, the irritative zone possesses low diagnostic value due to lack of a specific marker, that would identify IEDs generated within the epileptogenic tissue. To increase the diagnostic yield, we examined functional organization of the irritative zone.

**Method:** Intracranial EEG recordings from 14 patients with refractory neocortical epilepsy were analysed using an algorithm that groups IEDs according to their spatial profile into clusters. Analysis of clusters enabled determination of their properties. The cluster activity defines its percentage contribution to all IEDs in the given recording. The origin represents the contacts where cluster initiates and the active region marks the area of the most common propagation.

**Results:** On average 27.191 ± 26.155 IEDs per patient were analysed. The results demonstrated that in all patients the irritative zone was composed of multiple clusters with an average number of 6.9 ± 3.2 clusters per patient. Comparison of cluster properties with post-surgical outcome revealed that resection of cluster origins with an activity value above 21% was significantly associated with a favourable outcome. Meanwhile, extending the resection to the active regions did not influence the outcome.

**Conclusion:** This study demonstrates the complex organization and multifocal nature of the neocortical irritative zone in epilepsy patients. It can be stratified into functional components, each with distinct pathophysiological and clinical significance. The ability to identify the key components of this network enhances the yield of presurgical investigation and has potential to improve the results of epilepsy surgery.
p325
NEUROPSYCHIATRIC COMORBITIES IN PATIENTS WITH VNS FOR INTRACTABLE EPILEPSY IN A TERTIARY NEUROPSYCHIATRY SERVICE
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Purpose: Vagal Nerve Stimulation (VNS) is a neurosururgical technique used as adjunctive therapy for reducing frequency/severity of seizures in treatment resistant patients.

Previous VNS studies includes limited data on comorbidities such as intellectual disability (Alexopoulos, A. Seizure 2006; 15(7):491–503.) Others have focused on VNS outcomes with certain comorbidities e.g. Tuberous Sclerosis (Major, P et al Epilepsy & Behavior, 2008; 13 (2):357–360.), Lennox-Gastaut (Kostov, K Epilepsy & Behavior 2009; 16(2):321–324.)

There is increased risk of psychiatric comorbidity in epilepsy (Tellez-Zenteno et al Epilepsia 2007;48(12):2336–44) which can affect outcome. There is little data on neuropsychiatric comorbidities of adult VNS patients with intractable epilepsy.

We aimed to evaluate neuropsychiatric comorbidity in VNS patients at the Burden Centre (neuropsychiatric centre at Frenchay Hospital in Bristol, UK).

Method: We assessed a neuropsychiatric consultant caseload by analysing those with VNS as part of service evaluation. We looked at the following:
- Intellectual disability
- Psychiatric comorbidity
- Neurological/neurodevelopmental comorbidities
- Quality of life

Results: Of 79 cases:
- Intellectual disability: Mild (15), Moderate (9), Severe (10), Profound (2), [Total ID = 36]
- Psychiatric comorbidity: Depression (4), Psychosis (6), Depression&Anxiety (2), Anxiety (3) Hyperphagia (1), Conversion disorder (1), Non epileptic attack disorder (3), OCD (1), Dementia (2) [Total = 23]
- Neurological/neurodevelopmental comorbidities: 30 patients identified. Range was heterogeneous including Autism (9), tuberous sclerosis (2), Lennox-Gastaut (5), Prader-Wili (1), West Syndrome (1) [Total = 30]
- Quality of life: Poor (9), Moderate (20), Good (50)

Conclusion: Within the neuropsychiatric population studied, we identified that 46% had an intellectual disability (mostly mild). 29% had a psychiatric comorbidity while 38% had a neurological/neurodevelopmental comorbidity. Most had documented evidence of good quality of life post VNS.

p327
EPILEPSY SURGERY IN THE POSTERIOR PART OF THE BRAIN IN 96 CHILDREN AND ADOLESCENTS WITH SEVERE DRUG RESISTANT EPILEPSIES
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Purpose: To report demographics, etiologies, types of evaluations, types of surgery and post-operative seizure outcome in 96 children and adolescents with severe “posterior” epilepsies.

Method: Retrospective analysis of the medical charts of the epilepsy center data base. Patients with isolated Temporal Lobe resections were excluded. Minimum follow up was 6 months.

Results: Out of 314 children and adolescents operated on during the time period from September 1998 to December 2015 96 (30%) had “posterior” epilepsies. Age at onset of epilepsy was in the 1st year of life in 50% of the patients (in 2/3 of patients with TPO), during adolescence in 2 patients only.

Average age at operation: 8.6 years. Prolonged EEG-Video-Monitoring were carried out in all; invasive recordings (with subdural grids) was done in 16/96.

Types of resections: TPO 42, TO 28, PO 15, Q 7, TP 4. Etiologies: FCD 46, HIE/alegria 21, TU 15, miscell. 14. Overall po-seizure outcome (Engel’s Class.): Class I 59%, Class II 7%, Class III 19%, Class IV 14%, pending 2%. Class I Seizure outcome/etiology: FCD Type II 89%, TU 86%, post HIE/alegria 60%, FCD Type I 49%.

Conclusion: Epilepsy surgery for severe “posterior” epilepsies is a common procedure In children – in comparison to epilepsy surgery in adults in whom TL-and FL-resections prevail. With respect to post-operative seizure outcome results are satisfying including the outcome in challenging subgroups like those with severe epilepsies post HIE or with widespread FCT type I.
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p328  
COGNITIVE IMPAIRMENT IN EPILEPSY: THE EFFECT OF DRUG THERAPY  
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Purpose: A significant subset of epilepsy patients suffer from cognitive impairment. Multiple factors can affect cognition in epilepsy including the etiology of the seizures, seizure type, frequency and duration, hereditary and psychosocial factors, neuropathology and adverse effects of treatment.

Method: The patients were randomized into two groups according to antiepileptic drug (AED) treatment. Monotherapy group (n: 17, mean age 25 ± 10 years old) and polytherapy group (n: 17, mean age 28 ± 12 years old) enrolled to the study. A control group included 20 clinically healthy subjects (mean age 29 ± 5 years old) with no psychiatric or neurological diagnosis. Individuals in both groups were on average of the same education level and gender. Cognitive performance was evaluated using a test battery including Wechsler memory scale.

Results: Abstraction and visual memory impairments were statistically significant in monotherapy group; backward and forward digit span, abstraction and word counting impairments were found significant in polytherapy group when compared to the controls. There were no significant differences of cognitive test scores between two groups.

Conclusion: Various factors may affect cognition in patients with epilepsy. The cognitive impact of AEDs cannot be ignored. Physicians should consider evaluating cognitive function prior to starting or adding an AED.

p329  
ADJUNCTIVE LACOSAMIDE – 5 YEARS’ CLINICAL EXPERIENCE  
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Purpose: In 2008, lacosamide (LCM) was licensed in Europe for the adjunctive treatment of partial-onset seizures. At that time a prospective audit was initiated at the Western Infirmary to assess outcomes with this antiepileptic drug (AED) in everyday clinical practice. Final results are now presented.

Method: A total of 160 patients (74M; 86F, aged 14–74 years [median 42 years]) with uncontrolled partial-onset seizures (median monthly frequency 1; range <1–300) were started on LCM. After 12 weeks on stable AED doses (median 1 AED; range 1–4), LCM was added and the dose titrated as appropriate with a target range of 200–400 mg/day. Review took place every 6–8 weeks until 1 of 4 end-points was reached: seizure freedom for ≥6 months on a given LCM dose; ≥50% (responder) or <50% (marginal benefit) seizure reduction over 6 months compared with baseline on the highest tolerated LCM dose; withdrawal of LCM due to lack of efficacy, side effects, or both.

Results: Of the 160 patients, 35 (21.9%) remained seizure-free for ≥6 months on a stable LCM dose, while 35 (21.9%) had a ≥50% reduction in seizure frequency and 54 (33.7%) reported a marginal benefit. Five patients became seizure-free on LCM monotherapy following withdrawal of their initial treatment. Outcomes were similar for patients taking LCM with traditional sodium blocking agents (n = 56; 43 [76%] continued LCM) compared to those who also received AEDs with other mechanisms (n = 84; 64 [76%] continued LCM). LCM was discontinued in 36 (22.5%) patients because of lack of efficacy (n = 24, 15%) or side effects (n = 12; 7.5%). Commonest side effects leading to withdrawal were nausea and vomiting, dizziness, sedation, headaches, tremor and ataxia.

Conclusion: LCM is a well-tolerated and effective AED for partial-onset seizures with or without secondary generalization, regardless of concomitant treatment. Commonest dose-related side effects were neurotoxic in nature.

p330  
SAFETY AND EFFICACY OF ZONISAMIDE AS FIRST ADD-ON THERAPY TO CARBAMAZAPINE IN INDIAN ADULT PATIENTS DIAGNOSED WITH EPILEPSY: A SUBANALYSIS  
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Purpose: Evaluation of safety & efficacy of zonisamide as first add-on therapy to carbamazepine in Indian adult patients diagnosed with epilepsy.

Method: This is a prospective, open-label, non-comparative, multicentric, observational study in which patients having partial, generalized and combined seizures were treated with zonisamide (100–400 mg) for 24 weeks as first add-on therapy to carbamazepine. Seizure frequency, CGART and PGATT were assessed every 4 weeks. Primary outcome was reduction in seizure frequency and secondary outcomes were responder rate and seizure freedom over 24 weeks. Statistical analysis of change in seizure frequency was performed by Friedman’s test.

Results: 98 patients enrolled were evaluated by intention to treat analysis. After introducing zonisamide as add-on, significant decrease (p < 0.0001) was seen in seizure frequency at each subsequent follow up visit, compared to the baseline, with maximum decrease seen at week 24 (mean change from baseline = −4.06; 95% CI −5.11 to −3.01; % change −92.13). 24 week seizure freedom and responder rate was seen in 60.20% and 95.92% patients respectively. 79.54% patients showed excellent to good response (CGART) and 84.09% showed excellent to good tolerability (PGATT) to zonisamide therapy at week 24. Most common adverse events were weight loss (8/98 patients), loss of appetite and sedation.

Conclusion: Zonisamide is effective first add-on therapy to carbamazepine in treatment of partial, generalized and combined seizures in adults with good tolerability profile. Other positive attributes of zonisamide are minimal pharmacokinetic interactions and better patient compliance due to long half life.
Purpose: To evaluate the tolerability & efficacy of zonisamide as add-on to existing anti-epileptic therapy—an evaluation in Indian adult population.

Method: Zonisamide (100–500 mg) was used as add-on to existing anti-epileptic therapy for 24 weeks in patients having partial, generalized or combined seizures in this prospective, open-label, non-comparative, multicentric, observational study. Every 4 weeks, patients were evaluated by seizure frequency, CGART and PGATT. Primary outcome was reduction in seizure frequency and secondary outcomes were responder rate and seizure freedom over 24 weeks. Friedman’s test was used for statistical analysis.

Results: 75% of the 518 patients were on monotherapy at the time of enrollment. Approximately same number of patients (30%) were on either valproate or carbamazepine or phenytoin. After addition of zonisamide, a progressive and significant decrease (p < 0.0001) was seen in seizure frequency at each subsequent follow up, compared to the baseline, with maximum decrease seen at week 24 (mean change from baseline = −4.29, 95% CI −5.01 to −3.57; change −91.59). 24 week seizure freedom and responder rate was seen in 36.49% and 92.86% patients respectively. 87.56% patients showed excellent to good response (CGART) and 92.43% patients showed excellent to good tolerability (PGATT) at week 24. Most common adverse events were loss of appetite (22/518), weight loss (16/518) and sedation (12/518).

Conclusion: Lacosamide as add-on treatment in patients suffering from uncontrolled focal seizures was generally well tolerated. Patients that had a significant clinical response to this intervention generally reached this status in <6 months. Combination with other sodium channel blocker AED was not critical for safety or efficacy.

p332 COSMETIC ADVERSE EFFECTS OF ANTI EpILEPTIC DRUGS IN ADULTS WITH EPILEPSY

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Purpose: The objective of the study was to compare the relative prevalence of cosmetic adverse effects (CAEs) among both older and newer antiepileptic drugs (AEDs).

Method: As part of the Columbia AED Database Project, we reviewed patient background, medical history, AED use, efficacy, side effects, and dose and medication changes for 1903 adult patients newly started on an AED (age >16). CAEs included in this study were gingival hyperplasia, hair loss, hirsutism, weight gain, and acne. We compared the overall rate of intolerable CAE (i.e. CAEs that led to AED dosage reduction or discontinuation) attributed to a particular AED by patient report.

Results: Overall, CAEs occurred in 110/1903 (5.8%) patients, and led to discontinuation in 70/1903 (3.7%) patients. Female patients (4.7%, 50/1062) were found to have significantly higher number of CAEs compared to male patients (2.4%, 20/841) (OR = 2.03, p < 0.05). Overall, significantly more CAEs were attributed to valproic acid (n = 270, 21.9% incidence, p < 0.001) and pregabalin (n = 143, 9.8% incidence, p < 0.001). Also, valproic acid had the highest rate of intolerability due to CAE compared to other AEDs. Specifically, weight gain was most associated with valproic acid (13.0%, p < 0.001) and pregabalin (8.4%, p < 0.001), hair loss was most commonly seen in patients taking valproic acid (8.9%, p < 0.001), and significantly higher percentage of patients on phenytoin developed gingival hyperplasia (2.5%, p < 0.001) compared to average.

Conclusion: There is significant variability between all AEDs in terms of their CAE profiles. CAEs appear to occur more frequently in patients taking valproic acid than any other AED, particularly with regards to weight gain and hair loss. Our findings may help facilitate the AED selection process.

p334 A SERVICE EVALUATION OF PERAMPANEL IN CORNWALL, UK

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Purpose: Perampanel (PER) was approved in the EU in 2012 as an adjunctive antiepileptic drug (AED) therapy of partial onset seizures with
or without secondary generalisation in patients with epilepsy aged 12 years and over. The aim of the study was to assess the safety and efficacy of PER in routine neurology clinical practice.


Results: We studied 24 patients aged 22–61, on 1–3 concomitant AEDs (majority were Lamotrigine, Sodium Valproate, Zonisamide, Carbamazepine) with simple partial seizures (SPS), complex partial seizures (CPS) and secondary generalised tonic-clonic seizures (GTC). Titration was simplified and flexible at 2 mg increments (range 2–4 weekly to 12 weekly).

A >50% reduction in seizure frequency from baseline was achieved in 89% of patients with secondary generalised tonic clonic seizures, and in 75% with complex partial seizures. Seizure freedom was achieved in 2 patients for >3 months. Retention rate was 75%.

The most common side effects were unsteadiness 25% (6), dizziness 17% (4) and behaviour disturbances 17% (4), and 8% (2) had increasing seizure frequency, resulting in discontinuation of PER in 25% (6). There were no serious adverse events recorded.

Conclusion: This group of refractory patients had previously tried a median of 8 anti-epileptic drugs (range 1–12). Doses of PER varied from 2 to 6 mg daily with 4 mg proving to be particularly well tolerated, the most efficacious with minimal side effects. Reported side effects were similar to clinical trials with unsteadiness and dizziness being most common, but our >50% responder rates were better than reported in those trials.

Evidence suggests that Perampanel is useful in those with refractory epilepsy. This study was supported by an unrestricted educational grant from Eisai Ltd.

p335
A SERVICE EVALUATION OF PERAMPELAND (FYCOMPAN) AT LEEDS GENERAL INFIRARY
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Purpose: Perampanel was approved in the EU in July 2012 as an adjunctive treatment of partial-onset seizures with or without secondarily generalised seizures in patients with epilepsy aged 12 years and older. The aim of the study was to assess the efficacy and tolerability of Perampanel in clinical practice.

Method: Preliminary data from 39 patients are presented. Data was collected prospectively from patients with simple partial (SPS), complex partial (CPS) and secondary generalised tonic clonic seizures (GTC).

Results: A 50% reduction in seizure frequency from baseline was achieved in 50% of patients with generalised tonic clonic seizures, and in 45% with Complex partial seizures. Seizure freedom was achieved in one person for 3 months. Retention rate for Perampanel was 70% (27 out of 39 pts). The most common reasons for discontinuation were side effects 58% (7 pts), side effects and an increase in seizure frequency 25% (3 pts) and seizures unchanged but increased in severity 17% (2 pts). The most common adverse events in the group as a whole were sedation (46%), dizziness (18%), unsteadiness (15%), headache (10%) and anger or aggression (10%).

Conclusion: These were a very refractory group of patients having previously tried a median number of 9 anti-epileptic drugs (range 5–11). The percentage of patients with a >50% responder rate were similar to open label studies. Reported adverse events were also similar to clinical trials with sedation being the most common. The evidence suggests that Perampanel may be a useful add on therapy for those with refractory epilepsy.

p336
USE OF ADJUNCTIVE RUFINAMIDE FOR PATIENTS WITH LENNOX-GASTAUT SYNDROME IN CLINICAL PRACTICE
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Purpose: To investigate the use of rufinamide as adjunctive therapy for patients with Lennox-Gastaut syndrome (LGS) in clinical practice.

Method: A retrospective study was conducted of LGS patients treated with rufinamide in the epilepsy unit of Hôpital Robert Debré. Efficacy was assessed as response to treatment, where response was defined as ≥50% seizure frequency reduction. Dosing and titration strategies (initiation dose; titration duration; maintenance dose) were analysed in patients who responded to treatment.

Results: Ten LGS patients were included in the study (7 male, 3 female); mean [range] age, 10.5 [3.0–16.0] years. All were treated with 1–4 concomitant antiepileptic drugs and all received concomitant valproate therapy (mean dose, 27.2 mg/kg/day). Overall, 9/10 patients responded to rufinamide treatment. Among responders, mean (median; range) rufinamide initiation dose was 2.6 (3.0; 0.8–5.0) mg/kg/day; mean (median; range) duration of rufinamide titration was 12.6 (12.0; 4.0–20.0) weeks; and mean (median; range) rufinamide maintenance dose was 7.9 (7.5; 3.0–17.5) mg/kg/day. During titration, 8/9 responders experienced seizure aggravation, which resolved with down-titration to a lower maintenance dose. Overall, 3/9 responders subsequently discontinued rufinamide treatment, due to increased seizure severity (n = 2) or frequency (n = 1); the rest continued rufinamide treatment. Rufinamide was well tolerated.

Conclusion: In this retrospective study, the majority of LGS patients treated with adjunctive rufinamide responded to treatment. The dose (initiation and maintenance) and titration duration used in clinical practice at this centre were generally lower and slower, respectively, than those recommended in prescribing information. Abstract preparation supported by Eisai.

p337
MUST DIFFERENT MECHANISMS OF ACTION BE CONSIDERED IN THE ANTI-EPILEPTIC POLYTHERAPY?
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Purpose: To analyze the relationship between the number of mechanisms of drug action (MoDA) in antiepileptic polytherapy and clinical outcomes.

Method: Review of 201 polytherapy combinations tested in 100 patients. We analyze the average number of MoDA in terms of three possible clinical outcomes: improvement (lower seizure frequency), no improvement and adverse effects (AE). Ten MoDA were considered:
1. Fast-inactivated sodium channels,
2. Slow–inactivated sodium channels,
3. High voltage-activated calcium channels,
4. Low voltage-activated calcium channel,
5. GABAA receptor,
6. GABA transporter,
7. GABA transaminase,
8. Modulation of SV2A,
9. Multiple actions,
10. Potassium channel.

 doi: 10.1111/epi.12675
Results: Groups 1 and 9 were MoDA more used. Antiepileptic drugs (AEDs) with GABAergic action were more present in the AE group (7.3%) than in the rest (4.9% improvement, no improvement 1.67%). In AE group, the average of MoDA was 2.2, the remainder 2.4 (p = 0.2). In clinical improvement group the number of MoDA was 2.42 compared to 2.31 in the other (p = 0.29).

Conclusion: We found a tendency to a greater number of MoDA in those combinations that are better tolerated and which led to improvement. In our series, AEDs with GABAergic action were more present in AE group.

p338
MULTIPLE ANTI-EPILEPTIC DRUG USE IN CHILDREN WITH EPILEPSY; THE PREVALENCE AND ASSOCIATED FACTORS
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Purpose: In developed countries, 20–40% of children will not respond to their first drug and may require a second line anti-epileptic drug (AED) or even multiple AEDs to achieve seizure control. Multiple AEDs are associated with poorer adherence, more adverse events, drug interactions and higher costs. We set out to determine the proportion of children requiring multiple AEDs, the factors associated with their use and seizure control in a referral neurology clinic in a resource limited setting.

Method: We consecutively enrolled 139 children with epilepsy attending the pediatric neurology clinic at Mulago National Referral Hospital into this cross sectional study between July and December 2013. We obtained the clinical history and performed physical examinations to describe their clinical features, reviewed EEG recordings and measured serum levels of AEDs. We determined the proportion of children on multiple AEDs and examined for factors associated with multiple AED therapy. Variables with a p-value ≤0.2 at bivariate analysis were subjected to logistic regression. A p-value ≤0.05 was considered statistically significant.

Results: The median age was 6 (IQR 4–10 years) and 78/139 (56%) were male. 94/139 (67.6%) of children were on monotherapy, 42/139 (30.2%) on dual therapy and 3/139 (2.2%) on triple therapy. The commonest drug combination was Sodium Valproate-Carbamazepine (71.1%). The only factor associated with multiple therapy was poor seizure control; ≥1 seizure/day on treatment (OR 3.19, p-value 0.056, CI = 0.97–10.49). Only 13/45 (29%) of children on multiple therapy had attained seizure control and 49% had sub-therapeutic drug levels.

Conclusion: In this population, approximately one third of children with epilepsy were being managed with multiple drug therapy. The only factor associated with multiple drug therapy was poor seizure control which persisted in the majority of patients. This merits further study of interventions that may improve seizure control.

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THE EFFECTIVENESS OF USING “GENERICS” IN THE TREATMENT OF EPILEPSY
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The purpose of this work is to analyze effectiveness and rationality of the using “generic”, their interchangeability with original AEDs and also degree evaluation of regression of epilepsy in the Volgograd region.

Method: The statistical analysis and expert evaluation method of therapy was on the basis on database of 238 patients who are diagnosed with symptomatic focal epilepsy.

Observation time from the last change of therapy up to evaluating its effectiveness is from 5 years to the present. Observation period for evaluating the result was not <3 years.

Results: 1. during the research work was revealed:
A. the great majority of the patients (68.2%) receive treatment by one AED so it is a monotherapy.
B. Carbamazepine (fipepsin retard) is dominated in epilepsy of generics (49%).
C. The share of “generics is 68% “ among antiepileptic drugs in the Volgograd region out of which 46% was added to the therapy as a second drug.
2. degree evaluation of regression of epilepsy:
A. Complete stable remission of epilepsy occurs in 41% of cases, regardless of the type appointed AED (original or “generic”).
B. There is remission of seizures – 19%.
C. There is no stable remission of seizures 27%.
D. There is the lack of effect (at the time of studying) 7%.

Conclusion: “Generics” are quite rational for using in the treatment of symptomatic focal epilepsy along with the original drug.

p340
SAFETY AND EFFICACY OF ESLICARBZEPINE ACETATE TREATMENT IN ELDERLY PATIENTS
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Purpose: The use of eslicarbazepine acetate (ESL) in elderly patients (≥65 years) during its clinical development was limited and as such data on this population is scarce. This study evaluated the tolerability and efficacy of oral ESL as adjunctive therapy in patients aged ≥65 years with partial onset seizures (POS).

Method: Phase III, multicentre, open-label, non-controlled study in 72 patients with at least 2 POS and treated with 1–2 AEDs. After an 8-week baseline-period, subjects entered a 26-week maintenance period starting with 400 mg ESL once-daily and adjusted (400–1200 mg) based on individual response. Safety and tolerability was assessed through adverse events (AEs), laboratory-evaluations, vital-signs, 12-lead ECG, physical/ neurological examinations. Efficacy variable was the change from baseline in standardized seizure frequency (SSF).

Results: Overall, 47 (65.3%) subjects experienced 152 treatment-emergent AEs (TEAEs). The most frequent were dizziness (12.5%), somnolence (9.7%), fatigue, convulsion and hyponatraemia (8.3%, each). The incidence of TEAEs was 43.1%, 29.2% and 4.2% for 400, 800 and 1200 mg ESL, respectively. Three subjects died due to cardiac failure, glioblastoma multiforme and ischaemic stroke (relationship unlikely/not related). Overall, 18 (25.0%) subjects discontinued prematurely due to TEAEs. The incidence of clinically significant findings was low for vital signs, ECG, physical and neurological examinations. ESL decreased SSF from 2.9 seizures (at baseline) to 1.2 during the maintenance period. Median relative change in SSF was −54.1%.

Conclusion: This study demonstrated that once daily doses of ESL (400–1200 mg) as adjunctive therapy in elderly subjects with POS did not raise major safety concerns and was efficacious.

Study supported by Bial – Portela & Cª, S.A.
p341 SAFETY OF ESLICARBAZEPINE ACETATE AFTER 4 YEARS OF POST-MARKETING EXPERIENCE IN EUROPE

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Purpose: The European Commission granted on April 21st 2009 a marketing authorization valid throughout the European Union for eslicarbazepine acetate (ESL) as adjunctive therapy in adults with partial-onset seizures, with or without secondary generalization. This study evaluated the safety profile of ESL after 4-years of marketing experience in 18 European countries.

Method: From October 1st 2009 (first launch of ESL in the market) until 21st October 2013, safety data was pooled and analysed from post-marketing sources, including spontaneous, health authority, literature reports, and non-interventional studies. All adverse drug reactions (ADRs) were coded using MedDRA version 16.0, and assessed for seriousness and listedness. Cumulative results were compared with the approved Reference Safety Information.

Results: The estimated patient exposure was 434,468.3 patients-months. 367 serious and 509 non-serious ADRs from spontaneous, competent authorities and literature reports, and 15 serious ADRs from post-marketing non-interventional studies were reported. Most commonly ADRs were listed and reported in the SORs nervous system disorders (188); metabolism and nutrition disorders (150), general disorders and administration site conditions (129) and skin and subcutaneous tissue disorders (80). The most frequent reported terms were hyponatraemia (114), no adverse event (66), convulsion (48), off-label use (32), dizziness (29), fatigue (25), blood sodium decreased (21), vertigo (18) and rash (17).

Conclusion: ESL cumulative safety data during the 4-year marketing experience was in accordance with cumulative experience from clinical trial data, and no new safety issues were identified. Based on the available information, the risk-benefit profile of the product remains unchanged and favourable.

Study supported by Bial – Portela & Cª, S.A.

p342 PREFERRED FLAVOUR OF ESLICARBAZEPINE ACETATE ORAL SUSPENSION TO PAEDIATRIC EPILEPTIC SUBJECTS

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Purpose: To optimize the compliance with drug administration in paediatric population, it is important that the taste of the medicinal product is well accepted by children. This study investigated subject preference of 3 flavours of the ESL oral suspension as assessed using a visual analogue scale (VAS).

Method: Phase II, multinational, double-blind, randomised study to determine the taste preferences of 3 different-flavoured (tutti-frutti, grape or banana) samples of the ESL oral suspension in children 5–8 years of age. Thirty-eight (38) subjects were enrolled to have at least 30 completing VAS assessments for the 3 tastings. Taste score was analysed using a 1-way analysis of variance. The proportion of subjects was compared using 95% confidence intervals (CIs).

Results: Mean VAS score for tutti-frutti was higher (7.1) than for grape (5.8) or banana (5.8), although the difference was not statistically significant. Tutti-frutti was also more frequently considered by the children to be the preferred flavour (39.5%) compared to grape (31.6%) or banana (28.9%) and tutti-frutti was less frequently considered to be the worst flavour (18.4%) compared to grape (44.7%) or banana (36.8%). None of these differences was statistically significant. In one subject two serious adverse events were reported, occurring within 24 h of the taste test: acute laryngitis (severe) and acute respiratory insufficiency (moderate).

Conclusion: Tutti-frutti had a higher VAS score than the other 2 tested flavours and was more frequently considered to be the preferred flavour, although differences were not statistically significant.

Study supported by Bial – Portela & Cª, S.A.

p343 SEIZURE RESPONSE TO PERAMPANEL IN A SEVERE REFRACTORY GROUP OF EPILEPSY PATIENTS

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Purpose: Using our epilepsy electronic patient record (EPR), we collected seizure response data on all patients initiated on perampanel.

Method: The EPR was interrogated to identify all patients initiated on perampanel. A total of 28 patients had been commenced on Perampanel over a 1 year period. Patients who had been on the medication for <3 months were excluded. Data was collected on each patient’s epilepsy syndrome, age, gender, number of concomitant AEDs, number of previous AEDs, previous surgical interventions, dose titration, experienced side effects, and seizure outcomes.

Results: Twenty patient responses were analysed. Eight patients were excluded; 6 were <3 months on perampanel, at the time of data collection. Two others were excluded after a period of Video EEG monitoring demonstrated that the burden of their seizures were non-epileptic events. The age profile was a median of 31.3 years (Range 28–63). The gender ratio was evenly spread with Female: Male; 11:9. All patients had severe refractory epilepsy having previously failed a median of 10 AEDs (Range 5–17).

None of the 20 patients followed up became seizure free. Seven (35%) experienced a seizure improvement >50%; a further 6 (30%) experienced a positive but unsustained response, with 7 (35%) experiencing no response to perampanel therapy. Eleven (55%) patients reported side effects; most commonly fatigue (7 of the 11 patients). However, this group of patients were all on polytherapy, with 15 (75%) on >3 AEDs and only 5 (25%) on <3 AEDs. Mood and behavioural alteration was reported in 6 of the 11 patients with side effects, 2 patients reported dizziness.

Conclusion: Thirteen (65%) of this severe refractory epilepsy patient group demonstrated some seizure improvement. The retention rate between 6 and 12 months was 10 (50%) patients, with 7 (35%) patients reporting clear seizure improvement.

p344 LONG-TERM NON-INTERVENTIONAL STUDY OF LACOSAMIDE SAFETY AS ADD-ON THERAPY IN PATIENTS WITH EPILEPSY AND UNCONTROLLED PARTIAL-ONSET SEIZURES

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Purpose: To determine the preference of 3 different-flavoured (tutti-frutti, grape or banana) samples of the ESL oral suspension in children 5–8 years of age. Thirty-eight (38) subjects were enrolled to have at least 30 completing VAS assessments for the 3 tastings. Taste score was analysed using a 1-way analysis of variance. The proportion of subjects was compared using 95% confidence intervals (CIs).

Results: Mean VAS score for tutti-frutti was higher (7.1) than for grape (5.8) or banana (5.8), although the difference was not statistically significant. Tutti-frutti was also more frequently considered by the children to be the preferred flavour (39.5%) compared to grape (31.6%) or banana (28.9%) and tutti-frutti was less frequently considered to be the worst flavour (18.4%) compared to grape (44.7%) or banana (36.8%). None of these differences was statistically significant. In one subject two serious adverse events were reported, occurring within 24 h of the taste test: acute laryngitis (severe) and acute respiratory insufficiency (moderate).

Conclusion: Tutti-frutti had a higher VAS score than the other 2 tested flavours and was more frequently considered to be the preferred flavour, although differences were not statistically significant.

Study supported by Bial – Portela & Cª, S.A.
LACOSAMIDE ADDED TO A MONOTHERAPY IN EPILEPSY PATIENTS WITH PARTIAL-ONSET SEIZURES: FINAL ANALYSIS OF THE VITOBA STUDY

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Purpose: This prospective non-interventional study (Clinical trials.gov: NCT01098162) evaluated seizure control and tolerability of lacosamide in adults with partial-onset seizures receiving one concomitant antiepileptic drug (AED).

Method: This 6-month observational study was conducted in clinical practice in Germany. Outcome variables included seizure freedom and reduction in seizure frequency at last study visit (6 months) compared with 3-month retrospective baseline, as well as treatment-emergent adverse events (TEAEs).

Results: Of 573 patients enrolled, 571 were evaluable for safety, 520 for seizure control (FAS), and 499 were treated with in-label doses at any time (mFAS). Baseline median seizure frequency was 2.3 (FAS) and 2.0 (mFAS) per 28 days; 37.7% (FAS) and 38.1% (mFAS) were treated with only one lifetime AED. During the final 3 months of the study, 44.3% (FAS, n = 515)/45.5% (mFAS, n = 494) were seizure free; 71.8%/72.5% of patients showed a ≥50% reduction and 62.5%/63.8% a ≥75% reduction in seizure frequency. In the mFAS, ≥50% responder rates and seizure-freedom rates were numerically higher in patients aged ≥65 years (81.1% and 56.7%, n = 90) compared with patients aged <65 years (70.5% and 43.1%, n = 404), and in patients receiving lacosamide after the first monotherapy (50% responders 82.1%, seizure free 60.5%, n = 190) compared with patients who had received more than one previous AED (66.4% and 36.2%, n = 304). The most common TEAEs judged by physicians to be related to lacosamide were fatigue (10.3%, n = 59) and dizziness (8.8%, n = 50). 81.3% of the patients completed the study; 10.6% of patients discontinued due to a TEAE.

Conclusion: These results indicate that lacosamide improved seizure control and was generally well tolerated when used as adjunctive treatment to a monotherapy in routine clinical practice.

Supported by UCB Pharma
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A CASE OF MYCOSIS FUNGOIDES LIKE LESIONS DEVELOPING AFTER LEVETIRACETAM THERAPY

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**Purpose:** Levetiracetam (LEV) is a new antiepileptic drug effective in patients with partial onset seizures in adults and children, idiopathic or symptomatic generalized seizures. LEV-related side effects were observed at a rate of 17.2–51.3%, and usually occur in the first 5 months of treatment. Central nervous system side effects are the most common side effects but usually mild, other common side effects are irritability, drowsiness, and dizziness. Antiepileptic drug-induced skin reactions, most commonly PHT, CBZ, OXC, FB, LTG, ZNS and is seen depending on pyrimidine, VPA, TPM, GBP, TGB and connected LEV is rarely reported.

**Method:** 30 year old male patient consulted twice with JTKN in 10 months once asleep. During the wakefulness and sleep EEG of the patient, left frontal theta and sharp wave activity was observed. After neurological examination, routine blood tests and MRI of the patient which were normal, LEV 500 mg/day was started. After about 3 months LEV initiation the abdominal region at the sides of the body pale pinkish macular erythematous with uncertain margins were seen. In the skin puch biopsy, mild perivascular mononuclear inflammatory cells in the dermis infiltration were detected.

**Results:** We concluded that similar mycosis fungoides drug reaction was the cause. The patient discontinued by reducing drug LEV and another medication with capable rare skin reaction, VA, was started.

**Conclusion:** Although antiepileptic drug-induced skin reactions including maculapapular rash is very rare, cases like Steve Johnson syndrome or toxic epidermal necrosis have been reported. MF-like skin reactions, PHT, CBZ, OXC have been previously reported in literature. However, there is no case associated with levetiracetam. We think that using LEV with a different mechanism of action that causes skin reaction like MF, could be the first parameter in literature.

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PERAMAPANEL AS ADD-ON TREATMENT IN PATIENTS WITH DRUG-RESISTANT FOCAL EPILEPSY: THE CLINICAL EXPERIENCE OF THE DANISH EPILEPSY CENTER

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**Purpose:** Perampanel (PER) is an active AMPA receptors antagonist that has been approved in Denmark for adjunctive treatment of partial-onset seizures. We report our clinical experience in a group of epilepsy patients who started PER at the Danish Epilepsy Center.

**Method:** PER was introduced as add-on treatment in 22 patients (mean age: 32 years; age range: 20–64 years) with drug-resistant focal epilepsy. Pre-existing treatment consisted of 1–3 AEDs. Four patients had also VNS. Mean epilepsy duration was 17 years (range: 2–54). Most common etiologies were: low-grade brain tumor (5 patients), cortical dysplasia (3), mesial temporal sclerosis (2). In 7 patients etiology was unknown. Simple partial seizures were reported in 8 patients, complex partial seizures in 17 patients; secondary generalized seizures occurred in 16 patients.

**Results:** PER daily dose was: 4 mg (9 patients), 6 mg (6), 8 mg (6); 1 patient took 2 mg. Two mg increments were performed every 2–4 weeks. Mean follow-up was 8 months (range 3–13 months). Efficacy on seizure frequency was: seizure freedom: 2 patients; >50% seizure reduction: 3 patients; <50% seizure reduction: 5 patients; interruption of treatment: 12 patients (7 due to side effects; 5 because of complete lack of efficacy). Response to PER was not related to etiology. Common side effects were: fatigue (8 patients), aggressiveness (5), dizziness (4). Nine patients did not report side effects.

**Conclusion:** In our highly refractory epilepsy patients PER significantly improved seizure frequency in about one fourth (23%) of cases (2 patients achieved seizure freedom). Intolerable side effects led to PER discontinuation in about one third (32%) of patients, all with high doses of concomitant AEDs, suggesting that PER tolerability profile has to be further investigated in a clinical setting. Nonetheless, our findings in a difficult-to-treat patient population indicate that PER is a promising new AED.

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EFFICACY AND TOLERABILITY OF LAMOTRIGIN IN NEWLY DIAGNOSED EPILEPSY

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**Purpose:** Evaluation of Lamotrigine monotherapy outcome in epilepsy outpatients and comparison of adverse effects, in patients with newly-diagnosed epilepsy.

**Method:** 212 outpatients at the Clinic of Neurology, Clinical Centre Nis, were included in the study, during the period from 01.01.2011 to 31.12.2013. In open-label, non randomized, add-on trial over a period of 3 years, we analysed efficacy and tolerability of lamotrigin monotherapy in total of 212 untreated patients (117 male) with a recent diagnosis of epilepsy (61 idiopathic generalized epilepsy, 126 localisation-related epilepsy, 25 unclassified epilepsy). The follow-up period was minimum 6 months. Efficacy was classified as:

1. remission without adverse effects;
2. remission with adverse effects;
3. >50% seizure reduction;
4. <50% seizure reduction;
5. seizure worsening.

We analysed age at onset, manifestations and frequency of seizures, before and after treatment, tolerability and adverse effects. Seizure frequency was compared before and after treatment. Drug titration period was 3 months of drug involvement, and monitoring of therapeutic effects and side effects in the next 6 months.

**Results:** A total of 212 patients (median age 48.15 years, range 18–84) evaluable at this analysis. The median doses of lamotrigine was 250 mg daily. Remission without adverse effects was obtained in 89 patients (41.98%); remission with adverse effects in 38 patients (17.92%); seizure reduction of >50% in 61 patients (28.77%); seizure reduction of <50% in 18 patients (8.49%) and seizure worsening in 6 patients (2.83%). The tolerability of lamotrigine was generally good. The most frequent adverse effects were imbalance/dizziness (12.45%), headaches (7.86%), trembling (4.57%), epigastric discomfort (6.69%), rash (4.27%). Therapy was withdrawn in 5 (2.36%) patients.

**Conclusion:** Our study suggests high efficacy and good tolerability of lamotrigine in patients with newly-diagnosed epilepsy as a monotherapy.
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p350 ASSESSING LONG-TERM EFFECTS OF ESLICARBIAZEPINE ON LIVER VALUES AND LIPID METABOLISM PROFILE
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Purpose: Efficacy, safety and tolerability of eslicarbazepine has been assessed by phase II and III clinical trials. Post authorisation studies suggest no effects on lipid metabolism profile, even when being well documented with carbamazepine. The objective of our study is to assess long term effects of eslicarbazepine on liver and lipid metabolism profiles in a group of patients attended in our center since eslicarbazepine was marketed.

Method: Retrospective cohort study of patients attended and treated with eslicarbazepine at our epilepsy center between 2009 and 2013. Laboratory values were assessed previously and after treatment with eslicarbazepine.

Results: We included 108 patients in the analysis. HDL, LDL, VLDL, TGC, GGT, GOT and AST did not changed significantly after 3 years of treatment in our survey. Medium follow up was 2 years.

Conclusion: No statistically significant changes were documented with eslicarbazepine acetate in lipid and liver profiles after long term treatment with eslicarbazepine. Eslicarbazepine is a safe drug in relation to liver and lipid profile metabolism.

p351 LONG-TERM EXPERIENCE WITH LACOSAMIDE IN PEDIATRIC EPILEPSY PATIENTS – A RETROSPECTIVE EUROPEAN MULTICENTRE REPORT
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Purpose: There is still limited data concerning long-term efficacy and safety of Lacosamide (LCM) in pediatric patients.

Method: Pooled data from retrospective chart reviews performed by four pediatric epilepsy centers in middle Europe were analyzed. Screened were all patients <16 years with drug resistant focal epilepsies and treated with oral add-on LCM for >12 months. Outcome (compared to baseline = the year prior to treatment initiation) was assessed at an annual basis and at time of last observation. Response was defined as>50% reduction in seizure frequency for a minimum period of 3 months at last follow-up.

Results: 64 patients were identified, 41 (29 boys; mean age 10.9 years) were analyzed. The median duration of epilepsy before LCM was 3.8 years (4.4 months–15.8 years). The median baseline seizure frequency was 58 (24–684). The mean LCM treatment duration was 18 months (13–46 months). The mean LCM dose was 11.5 mg/kg/day (1.7–10.5 mg/kg/day). Patients were receiving a median of two concomitant antiepileptic drugs (range 1–3). There were 39% responders (>50% seizure reduction) at 12 months and 28% at last assessment. 100% seizure control was seen in 10% at 12 months and in 8% at last assessment. Seizure aggravation was seen in 2 patients (later diagnosed as primary generalized epilepsy and Dravet syndrome). Side effects (mostly mild) were reported by 35% of patients, the most frequent being drowsiness (21%) and irritability (12.5%). There were no significant laboratory anomalies in liver function, renal function, or hematology.

Conclusion: Our data suggest LCM long-term treatment in pediatric patients with difficult to treat focal epilepsies to be safe at doses up to 10 mg/kg/day without any major side effects. As severe seizure aggravation was seen in patients with generalized epilepsies, LCM should be used with extreme caution when syndrome diagnosis is unclear.

p352 EUROPEAN NON-INTERVENTIONAL REGISTRY STUDY OF ANTIETEPILEPTIC DRUG USE IN PATIENTS WITH LENNOX-GASTAUT SYNDROME: INTERIM ANALYSIS
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Purpose: Interim analysis of an ongoing European registry study, designed to capture long-term data (≥21 months) on >100 Lennox-Gastaut syndrome (LGS) patients initiating rufinamide as add-on therapy and up to 125 LGS patients receiving other antiepileptic drugs (AEDs).

Method: The registry is enrolling LGS patients (age ≥4 years) requiring modification to any AED treatment, including initiation of rufinamide. Its primary objective is to evaluate long-term safety. Effects of treatment on seizure control is also being assessed.

Results: As of October 2013, 97 patients were enrolled, of whom 60 (40 male/20 female) initiated rufinamide (“rufinamide” group) and 37 (20 male/17 female) were initially allocated other AEDs (“other AEDs” group). At baseline, mean (standard deviation [SD]) age was 15.8 (9.6) and 15.4 (11.6) years in the rufinamide and other AEDs groups, respectively; mean (SD) time since LGS diagnosis was 5.3 (8.0) and 4.7 (6.0) years, and mean (SD) number of prior AEDs was 5.6 (3.6) and 7.1 (5.6), respectively. Median (range) follow-up duration was 25.2 (1–55) and 29.0 (3–56) months, respectively. At Month 12, the proportion of patients with improvement in all seizures (“minimally”, “much”, or “very much improved”) was 18/35 (51.4%) and 9/25 (36.0%) for rufinamide and other AEDs, respectively. AED-related adverse events have been reported for 31.7% (rufinamide) and 27.0% (other AEDs) patients, and have led to discontinuation of 5.0% and 2.7% patients, respectively. No unexpected safety findings have emerged to date.

Conclusion: The registry is providing useful information on LGS and its management.

Supported by Eisai

p353 EVALUATION OF ANTIETEPILEPTIC DRUG USE IN THE PREGNANT PATIENTS WITH EPILEPSY IN A UNIVERSITY HOSPITAL IN ISTANBUL
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Purpose: Antiepileptic drug (AED) use of patients with epilepsy during pregnancy is critical for the risk of pregnancy lost, major congenital malformations or intrauterine growth retardation. US Food and Drug Administration pregnancy risk factors of the AEDs are “C” or “D”; considered to have possible teratogenic effects on the fetus. This study aimed to evaluate the patients with epilepsy on AED therapy who were consulted by pharmacology outpatient clinic of a university hospital.

Method: Patients with epilepsy on monotherapy or polytherapy with AEDs (n = 35) consulted during or prior to pregnancy were included. Demographic characteristics and drug information of the patients were recorded on the consultation day. Follow-up of pregnancies were realized by several phone calls according to the expected delivery dates. Changes in the therapy, delivery outcomes of the pregnancies and neonatal health information were questioned.

Results: Lamotrigine (34%), carbamazepine (31%) and valproic acid (26%) were the most common AEDs found in the therapeutic regimens of patients with epilepsy on monotherapy (66%) or polytherapy (34%). Twenty-three percentage of patients were consulted for pregnancy planning, 77% were pregnant. Among the pregnant patients 48% resulted with delivery, 11% had medical termination and 7% spontaneous abortion, 77% were pregnant. Among the pregnant patients 48% resulted with delivery, 11% had medical termination and 7% spontaneous abortion.

Conclusion: In conclusion consultation prior to pregnancy is important for pregnancy outcomes exposed to AEDs.

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LACOSAMIDE MONOTHERAPY IN PATIENTS WITH EPILEPSY PREVIOUSLY TREATED WITH A COMBINATION THERAPY: INTERIM RESULTS OF AN OBSERVATIONAL STUDY
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Purpose: To evaluate the long-term efficacy and tolerability of lacosamide (LCM) monotherapy in Alzheimer’s disease patients with AED-resistant partial epilepsy who had completed a previous add-on treatment phase.

Method: This was a prospective study, comprised of a randomized, parallel-group, 6-month phase, followed by a continuation phase for a further 6 months. LCM mean dose was 300 mg/day. The primary efficacy was assessed measuring the change in 28-day seizure rate from baseline to the study end at 12 months. Secondary efficacy was based on responder rate, i.e., percent of patients with at least 50% seizure frequency reduction.

Results: 15 out of 67 patients (age range 62–80 years) withdrew from the study: LCM group (4 subjects dropped for multiple failed appointments, 3 for non-compliance); control group (4 subjects dropped for non-compliance, 4 for adverse events). 52 patients completed the study. After 6 months’ treatment the first group was switched to LCM monotherapy, the second group continued on a bitherapy.LEV, LTG, OXC were the most frequent concomitant AEDs. All analyses were based on the number of patients who completed 1 year of observation. During the 1-year treatment, efficacy results were higher in the LCM group than in the other one.

Under LCM add-on therapy, 14 pts (41.17%) became seizure free, 10 pts (29.41%) experienced a reduction in seizure frequency of 50–90%. No significant changes in seizure-control was observed in 10 pts (29.41%). Patients remained seizure-free even after switching to LCM monotherapy. Control group: 5 pts (15.15%) became seizure free, 12 pts (36.36%) had a 50–90% reduction, 16 (48.48) no significant reduction. 2 pts (6.06%) had increased seizures. Dizziness was the most common adverse event in LCM group, sedation in control group.

Conclusion: These results show the long-term efficacy and tolerability of LCM as combination therapy or as monotherapy with no increased seizures.

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PERSISTENT HICCUPS WORSENED BY TOPIRAMATE
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Purpose: The association of hiccups and antiepileptic drugs (methsuximide, phenytoin) is uncommon. We describe a patient with epilepsy with persistent hiccups during treatment with topiramate (TPM).

Method: Description of a clinical case.

Results: The patient is a man now 59 years old, suffering from drug-refractory cryptogenic epilepsy, with onset (first generalized convulsive seizure) at age 20, characterized by clusters of absences associated with oral automatisms (probably already present) and occasional convulsions. The patient, always treated with polypharmacy (barbiturates, phenytoin, sulthiame) began to show after a few years of therapy, sedation, and, by the age of 40 years, hiccups, first sporadic, then continuous for periods of weeks. Interpreted as psychogenic, the hiccup was treated on several occasions with various neuroleptics, without success. When, at age 55, was added TPM at a dose of 200 mg/day, still associated with PB and PHT, hiccups became continuous; but attempts to discontinue the drug caused a seizures worsening. Only later (at age 57) with replacement of TPM with valproate (2000 mg daily) first reappeared periods of interruption of the symptom, and finally, its cessation, stable after 2 years of follow-up.

Conclusion: The refractory hiccups can occasionally be induced by antiepileptic drugs; particularly, in the reported case, it was worse by TPM, out of which other paroxysmal side effects (cough, restless legs syndrome) were reported.

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LACOSAMIDE AS TREATMENT OF FOCAL SYMPTOMATIC EPILEPSY IN A PATIENT WITH LIVER ALCOHOLIC CIRRHOSIS
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Purpose: Selecting an appropriate AED for patients affected by liver failure who have new-onset epileptic seizures can be challenging because first-line agents may contribute to worsening encephalopathy and result in hepatotoxicity.

Case report: We describe the case of a 64-year-old man affected by severe liver disease (Child C) due to alcoholic cirrhosis. The patient showed a focal seizure with secondarily generalization characterized by ascending parasthesias followed by hyposthesia and jerks on the right limbs. Brain MRI showed an intracerebral haemorrhage in left parieto-occipital regions. After the neurosurgery procedure, seizures reappeared and were initially managed with levetiracetam (up to 3000 mg per day). After 1 month the patient showed focal seizures with secondarily generalization under a stable treatment with levetiracetam (3000 mg per day), therefore he received phenobarbital (50 mg per day) as add-on treatment. The
Patient became stuporous and mental status fluctuated. In addition break-through seizures later developed. EEG showed generalised polymorphic slowing, diffuse triphasic sharp wave and left temporo-parietal spikes. Phenobarbital was immediately stopped and a single oral loading dose of lacosamide (200 mg), followed approximately 12 h later by a 100 mg twice daily up to 200 mg twice a day maintenance dose was started. By the third day of lacosamide therapy, the patient became more responsive. One-week later EEG showed sporadic interictal sharp waves in temporoparieto-occipital regions and normal background activity. After 6 months the patient was still seizure free at follow up. The patient was added in the liver transplant waiting list but he died within 6 months of follow up.

Conclusion: Lacosamide was chosen for its favourable pharmacokinetic properties as an alternative to other AEDs. Lacosamide may offer some advantages in the treatment of epilepsy in patients with liver failure; however, further prospective evaluation of its efficacy and safety in this clinical setting is needed.

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CONCOMITANT USE OF ESLICARBZEPINE ACETATE (ZEBINIX) WITH CARBAMAZEPINE IN EVERYDAY CLINICAL PRACTICE USING A RETROSPECTIVE MULTICENTRE AUDIT

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Purpose: We report on the concomitant use of eslicarbazepine acetate with carbamazepine in routine clinical practice.

Method: A retrospective multicentre audit of outcomes following treatment with eslicarbazepine acetate for localisation-related epilepsy across 7 UK sites (2009–2013). 201 patients with median values for age 42.5 (17–83) years; duration of epilepsy 16.5 (0–65) years; 2 (0–4) concomitant AEDs; 12 month (2 days–53 months) duration of treatment and 0–12 (64% ≥) previous AED exposures. Eslicarbazepine acetate dosage ranged from 600 to 1600 mg/day. Carbamazepine dosage ranged from 400 mg to 1000 mg/day. Baseline seizure types comprised secondarily generalised tonic-clonic seizures (78.2%), complex partial seizures (74.3%) and simple partial seizures (23.8%).

Results: 105 patients (52%) experienced ≥50% seizure frequency reduction. Treatment emergent adverse events (TEAEs) were reported in 87/201 (43%). The concomitant use of carbamazepine was a predictor of TEAEs. Of the 31 subjects taking both carbamazepine and eslicarbazepine acetate, the most common TEAEs were disturbance in attention/concentration 19.4% (n = 6); fatigue 19.4% (n = 6) diplopia 16.1% (n = 5); dizziness 16.1% (n = 5) abnormal coordination 9.7% (n = 3). Aside from abnormal coordination, TEAEs were higher than predicted based on the summary of product characteristics (SPC) for eslicarbazepine acetate (Zebinix).

Conclusion: In the routine clinical use of concomitant carbamazepine and eslicarbazepine acetate (Zebinix), consideration should be given to reducing the baseline dose of carbamazepine prior to adding in eslicarbazepine acetate (Zebinix) with a slow titration regime for eslicarbazepine acetate (Zebinix) to maximise tolerability.
because of bad taste or spilling of the drug when placed into the mouth. 10/13 patients (76.9%) would use it again.

Buccal midazolam is a useful and convenient treatment for seizure clusters in adults. It is efficacious to stop the seizures, well tolerated and easy to use.

p359
EXPERIENCE WITH BUCCAL MIDAZOLAM FOR SEIZURE CLUSTERS IN ADULTS
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A high number of patients with drug resistant epilepsy experience seizure clusters which need early treatment to avoid progression to status epilepticus. In Spain, only rectal diazepam, very inconvenient for adults, has been available to treat these clusters at home. Recently, buccal midazolam has been approved in the pediatric population. Here we report our experience with this formulation in adult patients.

We performed a retrospective analysis of 21 patients who had been prescribed buccal midazolam in two tertiary hospitals in Barcelona. Their demographic and clinical features were as follows: mean age 33.38 years (12–57), focal epilepsy (19 patients, 90%), generalized symptomatic epilepsy (2 patients, 10%). Most patients had weekly seizures (57%), with 38% having seizure clusters every month, 15% every week and 10% every day. Mean number of antiepileptic drugs was 2.8. Eight patients had vagal nerve stimulator implanted and one had deep brain stimulators.

Of the 21 patients who had prescribed buccal midazolam (10 mg), 13 had already used the drug. 6/13 reported immediate efficacy to stop seizures, 5 reported efficacy between 5 and 30 min after use, in 2 patients efficacy could not be assessed (postictal use in one patient, difficult administration in another one). Seizures recurred only in 2 patients. As adverse effects most patients reported somnolence and one patient experienced paradoxical insomnia although seizures were controlled. Compared with other drugs previously used (mainly rectal diazepam), 8/13 patients prefer buccal midazolam because of efficacy and easy use, 2 patients report need of additional dose, and 3 patients prefer other options because of bad taste or spilling of the drug when placed into the mouth. 10/13 patients (76.9%) would use it again.

Buccal midazolam is a useful and convenient treatment for seizure clusters in adults. It is efficacious to stop the seizures, well tolerated and easy to use.

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MTOR SIGNALING PATHWAY AND CELL PROLIFERATION ARE ALTERED DURING THE DEVELOPMENT OF ABSENCE EPILEPSY IN A GENETIC ANIMAL MODEL
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Purpose: Several studies have demonstrated the involvement of mTOR pathway in epilepsy and the process of epileptogenesis1,2. The hyperactivation of this pathway in the brain is observable in the initial phase after an epileptogenic insult and, its inhibition by rapamycin prevents the development of spontaneous seizures2,3. We have recently demonstrated that inhibition of mTOR permanently reduces the number and duration of absence seizures in WAG/Rij rats, a animal model of absence epilepsy; furthermore, it was observed that mTOR phosphorylation was significantly increased in the cortex of 6 month-old WAG/Rij rats but not other brain areas4. However, it was not clear whether this hyperphosphorylation was a cause or a consequence of the absence seizure.

Method: To clarify the role of mTOR in epileptogenesis in WAG/Rij rats, we analyzed immunohistochemically:
1. the brain expression levels of total mTOR and its phosphorylated form in young (before seizures) and adult WAG/Rij rats, compared with age-matched Wistar rats;
2. the proliferation of hippocampal neuronal stem/progenitor cells assessed by BrdU analysis at different ages in both strains.

Results: We found that WAG/Rij rats have higher levels of total mTOR expression in several brain areas than control Wistar rats; furthermore, phospho-mTOR staining is higher in young WAG/Rij rats in comparison to control and adult WAG/Rij rats. Finally, the age-related decline in hippocampal neuronal progenitor cell proliferation rate was significantly slower in WAG/Rij rats, indicating a change in proliferation characteristics.

Conclusion: Our results support a role for persistent mTOR activation and consequent change in hippocampal progenitor cell proliferation during the epileptogenic process leading to the development of absence seizures in WAG/Rij rats.

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THE MECHANISM OF ACTION OF ANTI-EPILEPTICS ON GAMMA OSCILLATIONS – DERIVATION OF AN ANALYTICAL EQUATION FROM DYNAMIC CLAMP EXPERIMENTS
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Purpose: Since 1963 drugs of benzodiazepine type have been the drug of choice for status epilepticus. While their molecular action on GABA receptors is relatively well understood, less is known about their dynamic action on neuronal excitability and spiking patterns. We have studied this by analyzing the effect of benzodiazepines (BDZ) on neocortical interneurons. These neurons are interconnected by GABAergic synapses and by electrical synapses. Networks of fast-spiking interneurons have been demonstrated to be responsible for gamma oscillations (30–80 Hz) in vivo. The main effect of BDZ is to enhance the action of GABA, resulting in sedative, anxiolytic, anticonvulsant, muscle relaxant and amnesic effects.

Method: Sagittal slices of somatosensory cortex were prepared from postnatal day 13–19 Wistar rats. Whole-cell recordings were made from 10 nonpyramidal neurons in cortical layers 2/3, 4, and 5. The ability of the interneuron to synchronize to the synaptic input of a virtual cell was tested. The GABAergic synapses allowed entrainment to lower frequencies.

Results: We introduced a compound GABA/electrical synapse in the interneurons using the dynamic clamp technique. We constructed phase response curves (PRC) showing the change in the cycle period of the oscillation induced by the synaptic event as a function of the phase at which it was delivered. The negative slope of the phase delay in the PRC was found to be proportional to the induced GABA conductance. Using these phase response curve results and synchronization theory, we derived an analytical expression for the lower frequency limit of the gamma band as a function of the BDZ concentration and conductance properties of the neuron.

Conclusion: We conclude that BDZ probably have their effect by changing the synchronization properties of neocortical interneurons. An
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in-depth understanding of how pharmacological agents modulates the rhythm of the brain is of great clinical importance.

**p362**
THE IMPACT OF THE ANTIEPILEPTIC DRUGS LAMOTRIGINE, TOPIMARATE AND LACOSAMIDE ON GLIAL PROPERTIES IN AN IN VITRO CO-CULTURE MODEL OF INFLAMMATION

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**Purpose:** Glial cells are the immune cells of the central nervous system (CNS). They directly interact with neurons, termed also as neuronal-glial network. Astrocytes build a functional syncytium via gap-junction by connexin43 (Cx43), which could have implications in seizures pathogenesis as well. Antiepileptic drugs (AEDs) reduce seizures, mostly on acting on neuronal function; however, little is known about AEDs' effect on surrounding glial cells. Therefore, we investigated the effect of AEDs (lamotrigine (LMT), topimarate (TPM) and lacosamide (LAC)) on glial viability, microglia morphology and Cx43 expression in a physiological and inflammatory modified in-vitro astroglia/microglia co-culture model.

**Method:** Primary astrocytes were prepared from brains of postnatal (P0–P2) Wistar rats and were co-cultured with microglia 5% (M5) (physiological condition) or 30% (M30) (mimicked inflammatory condition). Co-cultures were treated with AEDs for 24 h with different concentrations (5–50 µg/ml). Viability and proliferation was measured using the MTT assay. The microglial morphology was assessed by immunocytochemical staining and astroglial Cx43 expression was detected by western blotting.

**Results:** LMT and TPM reduced glial viability in a dose-dependent manner in M5 and M30 co-cultures. Furthermore, TPM decreased and LAC increased the number of activated microglia in M30 co-cultures. In addition, LMT increased the Cx43 expression in M30 co-cultures. In contrast, none of AEDs changed microglial phenotypes and Cx43 expression in M5 co-cultures.

**Conclusion:** Inflammation in the CNS is accompanied by disturbance of glial cell functions. Our results showed differential regulation of microglia by AEDs. As inflammatory process in the CNS might be an underlying cause for epileptic disorders, we suggest considering and investigating the role of AEDs on glia activity in vivo and further in human to benefit from AEDs therapy.

**p363**
THE ANTIEPILEPTIC AND NEUROPROTECTIVE EFFECTS OF PERIODIC FASTING ON PENTYLENETETRAZOL-INDUCED SEIZURES IN RATS

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**Purpose:** Periodic fasting (PF) was suggested to display antiepileptic and neuroprotective effects, which is in stark contrast to severe fasting or starvation. However, these beneficial effects seem to depend on the type and duration of the used feeding protocol. There are discrepancies concerning both antiepileptic and neuroprotective effects of a PF-diet. This study was designed to evaluate the antiepileptic and neuroprotective effects of different PF protocols on in adult rats.

**Method:** generalized seizures were caused by repetitive injection of pentyleneetetrazol (PTZ) for a period of 4 weeks every other day. While control animals had free access to food and water, animals on a PF-diet were on intermittent fasting for 24 h every 48 h for 4-weeks before (T1), after (T2), or both before and after (T3) the injection of PTZ. Behavioural studies were Recurrent carried out after PTZ-injections and histological investigations were performed after the experiments were completed.

**Results:** Seizure assessment showed that the severity of seizures was significantly decreased in groups T1 and T3 when compared to control rats. Dark neuron densities in hippocampal CA1 and CA3 areas were decreased in PF groups, but never in the temporal cortex. The PF-diet also decreased the number of TUNEL-positive neurons in the hippocampus in both areas and all PF-diet protocols. We observed a correlation between an increase in the density of dark neurons and a decrease in the volume of normal neurons in all PF groups in the CA1 hippocampal area.

**Conclusion:** These results support the idea that a PF-diet has anticonvulsive and neuroprotective effects on epileptic rats but underlines that different PF-diet protocols can have varying effects. Anticonvulsive effects were strongest when the PF-diet started before the onset of excitotoxic injuries, the number of dark neurons was decreased and apoptosis was prevented by all PF-diet protocols investigated in this work.

**p364**
A COMPARATIVE STUDY OF PERFORANT PATHWAY STIMULATION IN C57BL/6 MICE AND SPRAGUE-DAWLEY RATS

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**Purpose:** Perforant pathway stimulation (PPS) in rats is a long-standing and well-established method of modeling temporal lobe epilepsy. The possibility of using genetically altered mouse resources enables many possibilities to gain novel insight into the mechanisms underlying epilepto- and icto-genesis, which could lead to novel treatments. In this in vivo study, we evaluated the electrophysiological network response to PPS and examined the neurodegeneration at several time points following various durations of PPS in mice and compared our findings to those from previous studies in the rat.

**Method:** Prolonged bilateral electrical stimulation of the perforant pathway in urethane-anesthetized C57BL/6 mice. Continuous video monitoring for behavioral seizures.

**Results:** In mice, as in Sprague-Dawley rats, PPS evokes epileptiform discharges in dentate granule cells and irreversibly damages hippocampal neurons. PPS lasting 24 h induced acute degeneration of hilar mossy cells and peptide-containing interneurons, and later spontaneous seizures. Interestingly, we found that as little as 2 h of PPS in mice causes hilar neurodegeneration, which was nearly completely restricted to mossy cells. This is unlike the rat, where the shortest duration of PPS that indices hilar neurodegeneration is ca. 12 h. A further difference is that neurodegeneration in mice is always detectable with Fluoro-Jade B immediately after the conclusion of PPS, whereas neurodegeneration in rats is often first visible after 18–24 h.

**Conclusion:** In summary, these results demonstrate that neurons are more vulnerable to PPS in (anesthetized) mice, which may be due to weaker intracelluar “defense” mechanisms, e.g. calcium binding proteins, or may involve neuronal death pathways that differ from identically stimulated rats. Further experiments are required to elucidate the underlying mechanisms.
p365
THE EFFECT OF CARBAMAZEPINE ON NEURONAL DAMAGE IN PENTYLENTETRAZOL MODEL OF EPILEPSY
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Purpose: Epilepsy, a disorder characterized by recurrent seizures, is the most common disorder in the nervous system. Studies showed that carbamazepine has anti-epileptic effects. However, there is no evidence regarding its neuroprotective effects. In this study the effects of carbamazepine was evaluated on Pentylenetetrazol model of epilepsy in the brain of rats.

Method: Animals were age- and weight-matched and divided into five groups of six rats each:
1. intact groups: without any manipulation,
2. control group: After PTZ injection (30 mg/kg) behavioural study (the convulsive behaviour was observed for 30 min, and resultant seizure were scored.). After that, histological evaluation executed.
3. Sham group: instead of PTZ just the vehicle (PBS and glycerol) were injected then behavioural study and histological process were fulfilled.
4. Experimental group A: At first Carbamazepine was injected (10 mg/kg), after 30 min PTZ was injected, then behavioural and histological effects were evaluated.
5. Experimental group B: At first Carbamazepine was injected (40 mg/kg), after 30 min PTZ was injected, then behavioural and histological effects were evaluated.

Results: The effect of Carbamazepine on the density of dark neurons in rat hippocampus (CA1 and CA3) areas and the temporal cortex after induction of seizure by PTZ injection between groups showed there are significant decrease in the density of dark neurons in the experimental groups compare to control and sham groups.

Conclusion: The results showed that carbamazepine acts as a neuroprotective substance in the nerves system after seizure attacks.

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HESPERIDIN POTENTIATES THE NEUROPROTECTIVE EFFECTS OF DIAZEPAM AND GABAPENTIN AGAINST PENTYLENTETRAZOLE (PTZ) INDUCED CONVULSIONS IN MICE: POSSIBLE BEHAVIORAL, BIOCHEMICAL AND MITOCHONDRIAL ALTERATIONS
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Purpose: Epilepsy is a chronic neurological disorder with complex pathophysiology. Several evidences suggest role of oxidative stress and mitochondrial dysfunction in pathophysiology of epilepsy. Hesperidin acts as a powerful anti-oxidant agent against superoxide, singlet oxygen and hydroxyl radicals. Thus, present study has been undertaken to evaluate the possible neuroprotective mechanism of hesperidin against pentylenetetrazole (PTZ) induced convulsions in mice.

Method: Sixty male laca mice (20–25 g) were randomly divided into 10 treatment groups (n = 6). Seven days pre-treatment of hesperidin (100, 200 mg/kg, p.o.) was carried out before PTZ (80 mg/kg, i.p.) challenge, whereas diazepam (0.2, 0.5 mg/kg) and gabapentin (10, 20 mg/kg) were administered intraperitoneally 30 min before PTZ administration i.e. on 7th day. Following PTZ challenge, severity of convulsions (onset of jerks, myoclonic seizures, extensor phase and death), brain anti-oxidant enzyme levels and mitochondrial complex enzymes activities were estimated.

Results: Single intraperitoneal PTZ (80 mg/kg) challenge demonstrated severe convulsions, oxidative damage (raised lipid peroxidation, nitrite concentration as well as depleted reduced glutathione, SOD and catalase levels), and depletion of mitochondrial enzyme complex (I, II, IV) activities. Hesperidin (200 mg/kg), diazepam (0.5 mg/kg) and gabapentin (20 mg/kg) pre-treatments attenuated PTZ induced behavioural, biochemical and mitochondrial alterations. However, administration of hesperidin (100 mg/kg) in combination with diazepam (0.2 mg/kg) or gabapentin (10 mg/kg) potentiated their neuro-protective effect which was significant as compared to their effects per se in PTZ treated animals.

Conclusion: Hesperidin possesses potent anticonvulsant activity which might be mediated via modulation of GABA/benzodiazepine receptor action.
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REGULATION OF BRAIN P450 CYTOCHROME
EXPRESSION IN A MOUSE MODEL OF SEIZURES

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Purpose: Recent evidence has indicated the expression of P450 metabolic enzymes in the human drug resistant epileptic brain. However, whether seizures or exposure to anti-epileptic drugs determine P450 expression remains unclear. Moreover the role of the constitutive androstane receptor (CAR) and pregnane X receptor (PXR), key P450 nuclear transcription factors, has never been evaluated in the brain.

Method: Seizures were induced by intraperitoneal injection of kainic acid in mice to evaluate the effect of acute seizures on CYP2E1, CYP3A4 and CYP2C expression. The effect of anti-epileptic drugs was evaluated in vivo and in vitro using organotypic hippocampal cultures. PXR and CAR knockout (KO) mice were used to evaluate the brain levels of CYP3A4 and CYP2C. The latter enzymes are controlled by PXR/CAR in the liver. The expression of MDR1 was also evaluated.

Results: Acute seizures induced CYP2E1 expression in the CA3 region and dentate gyrus. CYP2E1 co-localized with NEUN and GFAP. CYP3A4 and CYP2C expression was observed in neurons and vessel and was not significantly changed after seizures. Interestingly, treatment with phenobarbital induced CYP3A4 expression at the cerebrovasculature in vivo. We also analyzed the levels of metabolic enzymes in CAR and PXR KO mice. In the absence of seizures, basal brain levels of CYP3A4, CYP2C and MDR1 were significantly reduced in the CAR KO mice. Histological brain evaluation showed that lack of PXR or CAR was associated with neuronal dispersion in the CA2 hippocampal region and discontinuous CD31 endothelial staining in the parietal cortex.

Conclusion: These results constitute the first attempt to identify the factors regulating P450 in the epileptic brain. In the brain, P450 enzymes may share mechanisms of transcription similar to those described for peripheral organs of metabolism. Further studies are ongoing to fully elucidate the pathophysiological determinants of CYPs brain expression.

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LOSS OF M-CURRENTS DURING STATUS
EPILEPTICUS

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Purpose: To characterize the impact of status epilepticus on M currents recorded from hippocampal Dentate granule cells (DGCs) and CA3 pyramidal neurons. To study M current modulation of synaptic transmission in the hippocampus.

Method: Status epilepticus was induced by Lithium/Pilocarpine. M currents and excitatory post synaptic currents were recorded using patch clamp electrophysiology.

Results: M-currents could be recorded from DGCs and CA3 pyramidal neurons, action potential independent release at Mossy fiber terminal-CA3 synapse was modulated by M-currents. Furthermore, prolonged hippocampal seizures reduced M-current amplitude and density on DGCs and CA3 pyramidal neurons and eliminated M-current modulation of synaptic transmission at Mossy Fiber-CA3 synapse and Schaffer collateral CA1 pyramidal neuron synapse.

Conclusion: Loss of M currents may contribute to the self-reinforcing nature of status epilepticus.

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THE EFFECT OF STATUS EPILEPTICUS ON
HIPPOCAMPAL EPILEPTIC AFTER DISCHARGES IN IMMATURE RATS

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Purpose: Pilocarpine status epilepticus (SE) elicited in immature rats results in only moderate morphological damage in limbic structures. Therefore we decided to study possible functional consequences.

Method: Experiments were performed in male Wistar rats on P12, P15, P18, P25 and P32. Experimental rats on P11 were injected with LiCl (3 mmol/kg i.p.) 24 h prior to injection of pilocarpine (40 mg/kg i.p.). A single dose of paraldehyde (0.07 ml/kg for P12 rats) was injected intraperitoneally 1.5 h after the onset of SE. Control animals in both age groups were treated with equal doses of LiCl and paraldehyde, but the pilocarpine solution was replaced with saline. Experimental groups consisted from 8 to 12 animals. Electrodes were implanted stereotaxically under isoflurane anesthesia into right dorsal hippocampus, left dorsal hippocampus and left sensorimotor cortex. One hour after surgery threshold intensity for elicitation of hippocampal afterdischarges (ADs) was estimated. Biphasic 1-ms pulses were applied for 2 s at 60-Hz frequency. Stimulation series were applied six times with 20-min intervals. EEG activity and behavior were recorded and saved on a hard disc. Duration of the afterdischarges was evaluated off-line with One Way ANOVA. Subsequent pairwise comparison was realized with Holm-Sidak test. p < 0.05 was taken as statistically significant.

Results: First stimulation always induced an AD accompanied by epileptiform automatisms. Repeated stimulation frequently failed in P15 control rats but not in P15 rats after SE. In older groups 20 min interstimulation interval was long enough to elicit the hippocampal ADs. The duration of hippocampal ADs was significantly shortened after first two stimulations in P15 rats after SE. P18, P25 and P32 rats after SE had a high incidence of recurrent hippocampal ADs after each stimulation.

Conclusion: Consequences of LiCl-pilocarpine SE in immature rats studied by means of hippocampal ADs may indicate an increased excitability of this structure.

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SEIZURE DETERMINANTS IN THE ISOLATED
GUINEA PIG BRAIN PREPARATION (FORUM SESSION
“INTEGRATED MODELS FOR THE STUDY OF
SEIZURE MECHANISMS”)

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Purpose: To reconstruct the patterns of generation and propagation of epileptiform activity and to analyze the putative role of blood brain bar-
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Results: Acute seizures similar to those observed in focal epilepsy models/humans can be established in this preparation. Arterial application of bicuculline induces focal epileptiform activity in the limbic area characterized by fast activity followed by ictal discharges. Such fast activity correlates with interneurons firing and IPSPs in principal neurons and it is associated with a slow rise in [K+]o. Ictal activity relays with the expression of endothelial adhesion molecules and the release of IL-1β from astrocytes, reflecting cerebral inflammation. A rapid increase in [K+]o, and extravasation of intravascular FITC-albumin are observed, suggesting BBB impairment. IL-1β receptor antagonist Anakinra (10 μM) treatment counteracts epileptiform discharge and reduces BBB damage, confirming a correlation between cerebral inflammation, BBB impairment and seizure generation. The involvement of interneurons in the early phase demonstrates that inhibitory networks may have pro-epileptic implications. In the same areas, systemic application of kainic acid induces synchronous oscillation in beta-frequency range, associated with a slow [K+]o rise leading to ictal-activity. Seizure generation seems to be related to astrocyte activation, since application of P2X7R antagonist A-438079 (100 μM) prevents synchronization of neuronal oscillation, associated with a lower efflux of [K+]o, and eventually with a counteraction of ictal-activity.

Conclusion: In two models of seizure, induced by alteration of either excitatory or inhibitory networks, the use of the in vitro isolated brain allows precise reconstruction of the mechanisms underneath ictal events.

This abstract is presented for the FORUM SESSION “Integrated models for the study of seizure mechanisms”.

p372 MOTOR COMPENSATION OF HEMISPHERIC LESIONS

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Purpose: It has been hypothesized that motor compensation of hemispheric lesions is mediated by the reinforcement of contralesional uncrossed fibers of the pyramidal tract (PTc), but also of the bilaterally organized cortico-rubro-spinal system. While the importance of so-called alternate motor fibers (aMF), which most likely comprise the cortico-rubro-spinal system, has been demonstrated in motor recovery after stroke, no white matter correlate of motor compensation in patients after hemispherectomy has been observed up to now. In the current study, we used Diffusion Tensor Imaging (DTI) to examine PTc and aMF in patients after hemispherectomy. We hypothesized that, if PTc or aMF mediated motor compensation, DTI-derived indicators of structural integrity such as fractional anisotropy (FA) would allow for the detection of corresponding plastic remodeling.

Methods: 20 patients after functional hemispherectomy and 10 healthy and matched controls underwent DTI at 3 T. Patient’s motor impairment of the upper extremity was assessed with a common motor function tests. Using probabilistic tractography, we reconstructed PTc and aMF separately.

Results: Voxel-wise analyses within delineated tracts revealed significantly lower FA values in patients as compared to controls along PTc. Comparably higher FA values were solely found within aMF. Further, more, voxel-wise analyses yielded significant motor function FA correlations along PTc. The inverse motor function FA relation was observed only within aMF and particularly in the vicinity of the contralesional red nucleus.

Conclusions: The motor function FA correlation along PTc is most likely indicative of degenerative processes, whereas motor function FA correlations within aMF possibly represent the result of preceding plastic remodeling. aMF may, thus, be thought to compensate the motor deficit caused by hemispherectomy. A retrospective study aiming to identify clinical markers of successful motor compensation mediated by aMF is ongoing and will be presented at the meeting.

p373 AUTOIMMUNE EPILEPSY: THE ROLE OF ANTIBODIES

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Epilepsy is a relatively common neurological disorder but its etiology cannot be identified in many cases. There is increasing evidence that autoimmune mechanisms might have a role in some patients. Autoantibodies were found in childhood epilepsy syndromes such as Rasmussen’s encephalitis and Landau-Kleffner syndrome and positive response to immunomodulative therapy was distinguished in some others like Lennox-Gastaut syndrome and infantile spasms. Also it is demonstrated that presence of antibodies like anti-Ganglioside M1 antibodies, anticardiolipin antibodies, lupus anticoagulant and anti-Glutamic acid decarboxylase antibodies, in autoimmune diseases has close relationship with seizure onset. Increased incidence of autoantibodies without systemic manifestation of autoimmune diseases is also demonstrated in isolated epileptic patients with unknown etiology. Moreover epilepsy and following antiepileptic therapy can alter immune responses and so it is difficult to determine which autoantibodies arise as a consequence and which are causative. Due to high possibility of coexistence of autoantibodies, more investigation is necessary to find out other potential autoantibodies which are targeting nervous system and triggering epilepsy.

p374 ANTIPEEPLETIC DRUG BINDING TO POTASSIUM CHANNELS: ROLE OF AROMATIC RESIDUES

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Purpose: Antiepileptic, local anesthetic and antiarrhythmic drugs acting on Nav and hERG channels have been assumed to bind to aromatic residues in the internal vestibule; to F1764 and Y1771 in Nav (Ragsdale et al., 1996) and to Y652 and F656 in hERG (Mitcheson et al., 2000). Despite a lack of such residues in Kv channels, some local anesthetics (e.g. bupivacaine) bind to Kv channels with a considerable affinity. To explore the role of aromatic residues for local anesthetic binding we investigated the effect of phenytoine, bupivacaine and quinidine on Shaker channels mutated to residues corresponding to the most C-terminal of the two aromatic residues in the S6 segment of the Nav and the hERG channels, (V473Y and P474F respectively).

Method: The channels were expressed in Xenopus oocytes and the currents measured with the two-electrode voltage clamp technique.

Results: The results suggest that aromatic residues do not increase the binding affinity of phenytoine, bupivacaine or quinidine to Kv channels. Rather, the affinity decreases.
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**Conclusion:** Aromatic residues seem not to be necessary for high-affinity antiepileptic, local anaesthetic and antiarrhythmic binding to voltage-gated ion channels. The specific role of aromatic residues in Nav and hERG channels seems thus related to specific structural constraints in these channels, not seen in the Shaker channel.

**Method:** Retrospective review of 50 partial seizures, with or without impairment of consciousness, without secondarily generalization, including recordings of good quality of the ECG and the oxygen saturation during seizures. We measured the ANI, based on the variability of RR intervals in high frequencies, which is an index reflecting the parasympathetic tone. We compared seizures with oxygen desaturation inferior to 90% to seizures without desaturation, over a period of 20 min centered at the beginning of the seizure.

**Results:** At the beginning of seizures, ANI dropped significantly, with no significant difference between the 2 groups of patients. However, ANI was significantly lower at the end of the seizure, and up to 5 min after the end of seizures with desaturation (p < 0.01), even though the period of desaturation was completed. Our results are in favor of a more prolonged impairment of autonomic nervous system (ANS) during seizures with 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.

**Purpose:** To search for the new anticonvulsants that could be devoid of the usual disadvantages, that is so called “biotic”, is still to be an actual and unsettled problem of the modern neuropharmacology.

**Method:** In our study we observed: 1. Molecular geometry and quantum chemistry of the barbiturates and benzodiazepines pharmacophores, main GABA conformers (linear, cyclic, scoop), glycine and β-alanine in the approximation of molecular mechanics with the use of the MM2 force field; 2. Influence intraventrical injection of GABA, glycine and β-alanine and their intraperitonal injection on the cerebral neurophysiological activity in white rats (taking of EEG and performing computer analyses cerebral cortex bioelectric activity by determine of extend of inhibition of spectral density) 3. Anticonvulsant activity different one-valence salts aforementioned inhibitor amino acids using strychnine, picrotoxin, pentylentetrazol and maximal electro seizure models.

**Results:** 1. Molecular geometry derivatives of barbiturates, benzodiazepines, glycine and cyclic β-alanine-conformer by its molecular geometry in largest remind cyclic GABA-conformer. 2. Introducing in same dosage (intraventrical injection), powerful and prolong inhibition of the brain cortex bioelectrical activity are place in the the next order: glycine>β-alanine>GABA. 3. Introducing in same dosage (intraperitonal injection) only their Li salts show inhibition of the brain cortex bioelectrical activity, but not their K, Na salts. 4. It was founded good anticonvulsant activity Li salt of glycine and less β-alanine and GABA on the main convulsive models (pentylentetrazol and maximal electro seizure) 5. Probably, Li salt of glycine has possibility passing through HEB using channel with strong inside field (11-th Eisenman’s row).

**Conclusion:** 1. Apparently, GABA-cyclic conformer, β-alanine and glycine are natural endogen agonists GABA-a-benzodiazepines receptor’s complex in CNS, in that time barbiturates and benzodiazepines are their artificial agonists. 2. Li salts of glycine, β-alanine and GABA have possibility passing through HEB using channel with strong inside field (11-th Eisenman’s row).

**Purpose:** To compare the changes in parasympathetic tone during and after partial seizures, according to the presence or absence of 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.

**Method:** Retrospектив review of 50 partial seizures, with or without impairment of consciousness, without secondarily generalization, including recordings of good quality of the ECG and the oxygen saturation during seizures. We measured the ANI, based on the variability of RR intervals in high frequencies, which is an index reflecting the parasympathetic tone. We compared seizures with oxygen desaturation inferior to 90% to seizures without desaturation, over a period of 20 min centered at the beginning of the seizure.

**Results:** At the beginning of seizures, ANI dropped significantly, with no significant difference between the 2 groups of patients. However, ANI was significantly lower at the end of the seizure, and up to 5 min after the end of seizures with desaturation (p < 0.01), even though the period of desaturation was completed. Our results are in favor of a more prolonged impairment of autonomic nervous system (ANS) during seizures with 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.

**Purpose:** Cortical representation of the motor functions was shown to be altered in epilepsy. The motors maps expansion was observed in electrically kindled rats (the epilepsy model) suggesting that under conditions of chronic epileptogenesis reorganization of both neuronal network and synaptic transmission occurs. Chemical kindling used in our study provides conditions under which both brain hemispheres and subcortical neurons undergo convulsive influences not equal to the conditions in electrically kindled model. The aim of work was to investigate the cortical localization of the neurons responsible for both forelimbs proximal and distal muscular jerks in conditions of picrotoxin-induced kindling and postkindling model.

**Method:** Adult Long-Evance rats were kindled by picrotoxin injections and the postkindling period was estimated according to Shandra A. et al. (1996). Rat’s V layer of the neocortex motor zone microelectrostimulation was performed according to Rousche P. et al. (2003). The animals were randomized into the control, kindled and postkindled groups.

**Results:** In kindled rats cortical motor zone responsible for forelimbs both proximal and distal muscular jerks was increased by 220–230% compared to a control group (p < 0.01). The total cortex area in kindled rats in which microelectrical stimulations resulted in forelimbs motor activity was 2.2 times greater compared to the same control index (p < 0.01). In the third group, changes of the motor area size in postkindling period were similar to those observed in kindled rats.

**Conclusions:** The data obtained indicate a significant expansion of neocortex motor zones responsible for the kindled rats forelimb muscles contractions. In postkindling period no differences in the forelimbs motor cortical representation were seen. These results allow to conclude that brain chronic epileptogenesis mechanisms involve certain cortical neurons reorganization into the principally new network with the new synaptic connections between different groups of the neurons.

**Conclusion:** Disturbances of parasympathetic system in seizures with oxygen desaturation are related to changes in parasympathetic tone. 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.
p378 EFFECTS OF IL-1β SIGNALING ON SYNAPTIC PROTEINS AND STRUCTURAL INTEGRATION OF NEWBORN NEURONS IN THE ADULT MOUSE BRAIN

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Purpose: Neurogenesis is a constantly ongoing process in the adult brain and takes place in the hippocampus and lateral ventricles. The newly born neurons connect with the surrounding network of neurons and form integrated functional neurons. There are a number of different pathways and processes that regulate neurogenesis and synaptogenesis, including epileptic seizures, and a plethora of proteins and components vital for the establishment of functional synapses. Interleukin-1 (IL-1) is thought to be one of the key factors in these processes, affecting spine size, synaptic transmission and signal strength. In the present study, our objective is to investigate how IL-1 signaling affects the expression of synaptic proteins, such as neuroligin-2 (NL-2), neurexin-1 (NL-1), N-cadherin, PSD-95 and gephyrin on newly born neurons in the hippocampus and what consequences this may bring in terms of synaptogenesis and structural integration into the surrounding environment.

Method: We utilized a mouse model lacking the interleukin-1 receptor gene, IL-1R1 knockout (KO) mice, and a wildtype (WT) group. Newborn neurons were visualized with retroviral vector expressing green fluorescent protein. Synaptic protein expression was evaluated with immunohistochemistry and high-resolution confocal microscopy.

Results: Gross morphology of 6 weeks old neurons and spine density on their apical dendritic tree did not differ between IL-1R1 KO and WT groups. However, a trend towards an increase in immature spines with a filopodia morphology was evident. Total number and size of NL-2 clusters on the new neurons did not differ between groups.

Conclusion: The results implicate that IL-1 signaling could be important for the development of excitatory synapses on spines, while it may not be crucial for NL-2 depending adhesion in inhibitory synapses.

p379 EFFECTS OF KINDLING STIMULATIONS ON PARVALBUMIN IMMUNOREACTIVITY IN SUBSTANTIA NIGRA PARS RETICULATA OF GAERS AND WISTAR RATS

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Purpose: One of the mechanisms that control epileptic seizures involves the neural network in the substantia nigra pars reticulata (SNR). Two functionally discrete regions, SNRanterior and posterior were demonstrated to mediate distinct effects on epileptic seizures. Genetic Absence Epilepsy Rats from Strasbourg (GAERS) show a resistance to secondary kindling, suggesting that the SNRposterior is an important site underlying this resistance. In this study, the immunoreactivity of parvalbumin (PV) positive GABAergic neurons in the SNRposterior was compared between GAERS and Wistar animals following kindling stimulations.

Method: Electrically stimulated or sham-operated adult male GAERS and Wistar rats were used in the experiment. Following the sixth electrical stimulation of basolateral amygdala, rats were transcardially perfused with neutral buffered formalin solution and brains were removed. The sagittal sections were treated with mouse anti-PV antibody and were analyzed with a computer based programme.

Results: There was no difference in the basal PV immunoreactivity of the SNRposterior or SNRanterior between sham operated GAERS and Wistar rats. Slightly increased PV immunoreactivity in SNRposterior was detected both in stimulated GAERS and Wistar rats than those in sham operated groups.

Conclusion: Densitometric analysis of PV positive GABAergic neurons in both SNRanterior and posterior did not reveal significant differences between sham operated GAERS and Wistar rats. Increased PV immunoreactivity in the SNR posterior of stimulated groups indicates importance of the SNR posterior in modulating epileptic seizures.

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p380 USING THE STIGMA SCALE OF EPILEPSY (SSE) TO ASSESS EFFECTIVENESS OF AN EPILEPSY IN-SERVICE PROGRAMME FOR EDUCATORS

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Purpose: Addressing stigma towards epilepsy in educational settings is a key step in ensuring an improvement of the quality of life of young persons with epilepsy. The aim of this study was to assess the effectiveness of training courses in reducing the perceived stigma by a group of educators, by using the stigma scale of epilepsy (SSE).

Method: Educators who attended an in-service 3 day course on epilepsy were asked to fill in the SSE, at the beginning of the course and at the end. The SSE scale used contained questions about the individual perception of epilepsy. Participants were asked to check the most appropriate class of answers for each item.

Results: A total of 60 educators attended the course. Their mean age was 34.7 ± 12 years and their teaching experience ranged from one to eighteen years (mean ± SD 8.4 ± 9.4 years). Forty six had no experience with children with epilepsy, while twelve had children with epilepsy in the classroom. All the participants completed the questionnaires on both occasions. The overall mean scores of the SSE at the beginning of the course were 31.86 (SD = 12.51; max = 50.00; min = 11.11) while following the course, it was reduced to 27.86 (SD = 10.99; max = 44.00; min = 9.72), (p < 0.05). At the beginning of the course, the items which were perceived as beginning the most common difficulties people with epilepsy have in their daily lives are emotions and prejudice, while at the end of the course, these were school and work.

Conclusion: The SSE can be a useful instrument in validating and improving such training courses. This type of analysis could provide a useful tool for tailoring the education of educators working in this field of epilepsy. It will also help to focus appropriate population-based studies and educational campaigns on epilepsy in schools and universities.

p381 EPILEPSY AND ANTI-EPILEPTIC DRUGS TREATMENT IN ELDERLY

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Abstracts

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**Purpose:** Is to present cases with epilepsy treated at the Neurology Clinic of the University Clinical Center of Kosovo in Pristina for the years 2012–2013 according to age, gender, location, type of epilepsy, etiological factor and therapy ordinated.

**Method:** The data were extracted from hospital records of patients with epilepsy treated in the Neurology Clinic for the 2 years period. We analysed cases over the age of 60. Data processing was done with the statistical package Instat 3. The X2 – test was used to test data.

**Results:** From the 78 cases included in the survey, the highest percentage with 25.6% was in the age group from 60 to 64 years old, 23.1% were 65 to 69 years, 25.6% were 70 to 74 years, while 75 to 79 years 15.4% and 80 or more years were 10.3%. Analysed according to the gender patients male patients were in 52.6% of the cases but without significant difference (p > 0.05). Analysed according to the settlement, 51.3% were from the city, without significant difference (p > 0.05). With partial epilepsy were 57.7% of the cases while 42.3% with generalized epilepsy. Main etiological factors were Stroke in 31.0% of the cases, hypertension in 29.4%, diabetes mellitus in 10.3%, Insufficienza vasorum in 5.6%, cerebral tumors in 4.0%. Tegretol was used in 67.9% of cases as main therapy, Phenobarbiton in 24.4% and Valproat in 2.6%.

**Conclusion:** Epilepsy in elderly is common clinical problem, mostly partial epilepsy. The goal of management should be the maintenance of seizures control without medication side effects and the maintenance of normal life style. Working towards in increasing the awareness of population is needed too.

p382 LACOSAMIDE AS ADD-ON TREATMENT IN EPILEPTIC ELDER PATIENTS

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**Purpose:** The third most common neurological disorder in old patients is epilepsy, and, as the population ages the syndrome has become a substantial public health problem, reaching in USA the average of 1.5% of those >65 year old. Epilepsy in senior can be present since early life or have the onset in the contest of an acute medical or neurological illness and in non-acute settings, perhaps including the aging process itself. Treatment efficacy without side effects is an important goal especially in elder patients and the failure of a variety of AEDs to adequate control seizures in these patients underscores the fact that we need additional drugs with improved efficacy and safety. Lacosamide is a new AED effective as adjunctive therapy for partial onset seizures that acts selectively enhancing slow inactivation of sodium channels, and in this report we focus on its efficacy as “add-on” to refractory treatments in elderly.

**Method:** In 20 elder patients with partial epilepsy mainly secondary to stroke and tumour that had no seizures complete control with first line AEDs treatment, we administered Lacosamide reaching the maximal dosage of 200 mg twice a day. In some of these patients the above dosage was reached slowly while in some patients, due to clinical conditions, we preferred the 200 mg oral “bolus”.

**Results:** All the patients, when Lacosamide was added to the first AED, improved their clinical situation, reducing seizures in frequency or severity. No serious side effects have also been reported. In 4 patients after 3–4 months following an early improvement the clinical manifestation returned as before.

**Conclusion:** Our data indicate that Lacosamide is an effective adjunctive tool for the treatment of elder patient with resistant partial-onset seizures that can be associated to the first line AEDs treatment with no substantial side effects.

p383 REDUCED GREY MATTER VOLUME AND PROLONGED ARTERIAL ARRIVAL TIME IN AN MRI STUDY OF OCCULT CEREBROVASCULAR DISEASE IN LATE ONSET EPILEPSY

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**Purpose:** 1/3 of all diagnoses of epilepsy are made in patients over 60 (Tallis et al, Age and Aging, 1991; 20: 442–448) and this diagnosis is often termed late onset epilepsy (LOE). When no clear underlying aetiology is found occult cerebrovascular disease (CVD) is often implicated.

The aim of this study was to investigate the association between LOE and structural and functional cerebrovascular markers using magnetic resonance imaging (MRI).

**Method:** MRI scans were performed using a 3T Philips whole-body scanner. The imaging protocol included a T1 weighted image - GM volume; FLAIR sequence – WML lesions and MRI-ASL for CBF and tA. A non-rebreathing circuit was used in conjunction with a gas mixture (21% O2 and 79% CO2), to induce hypercapnia in subjects during scanning.

Baseline CBF and tA values were extracted from the whole brain region during the initial 5 min breathing room air. The vasodilator stimulus of hypercapnia enabled calculation of cerebrovascular Reactivity (CVR) as a% change in CBF or tA divided by the% change in ETCO2.

**Results:** 15 HC and 14 patients with LOE participated in the study. Patients with LOE had significantly lower GM volume than HC (mean [SD]: 0.34 [0.04] vs. 0.38 [0.01], p = 0.02) and a trend towards a higher WML volume than HC (mean [SD] 1416.5 [1498.6] vs. 514.2 [480.9]).

Baseline CBF did not significantly differ between the two groups but baseline tA was found to be significantly longer in patients with LOE than HC (mean [SD] 1538.9 [128.5] vs. 1363.1 [166.6], p < 0.01). Measures of CVR both in CBF (p = 0.85) and tA (p = 0.51) were found not to differ significantly between the two groups.

**Conclusion:** Differences in structural and functional cerebrovascular markers lend support to the concept that occult CVD may be important in epileptogenesis.

p384 CORRELATIONS BETWEEN EEG AND CT SCAN IN VASCULAR EPILEPSY

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**Purpose:** The purpose of the study is to evaluate whether there are systematic correlations between the type of epilepsy, EEG changes,
and cerebral imagery features in elderly patients with vascular epilepsy.

Method: In the study were included 160 patients with epilepsy considered as being of vascular origin. Inclusion criteria were: age of 60 years or more, epilepsy onset after at least one stroke attack, time interval between the stroke and the first epileptic manifestations: 1 month to 1 year. The stroke type was either ischemic or hemorrhagic. Exclusion criteria were: epilepsy onset before stroke, history of traumatic brain injury or brain surgery (regardless of indication). We performed clinical neurological examination, computerized EEG with hyperventilation and photic stimulation, and brain CT scan. However, since 51 of our patients (32%) did not show any seizure activation with the afore-mentioned procedures, they were further tested with sleep deprivation. We had 15 ictal and 145 interictal EEG recordings. Seventy-five patients underwent 2 CT scans each, one early (within the first 24 h after the stroke), and a second one at the first epileptic manifestation. The other 85 patients had only the latter CT scan examination.

Results: We found (i) focal EEG changes corresponding to localized CT scan alterations in 25% of our patients; (ii) focal EEG changes associated with multiple CT scan lesions in 45% of patients; (iii) no EEG changes in 30% of our patients.

Conclusion: Since the majority of our patients with successful activation of seizures did show uncorrelated, multiple vascular lesions on the CT image, we conclude that there is no consistent correlation between EEG modifications and CT scan imagery in vascular epilepsy patients.

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CLINICAL CHARACTERISTICS OF MESIAL TEMPORAL LOBE EPILEPSY WITH AMYGDALA ENLARGEMENT: ASSOCIATION WITH LATE-ONSET TEMPORAL LOBE EPILEPSY?
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Purpose: An increasing number of recent reports have described amygdala enlargement (AE) in patients with mesial temporal lobe epilepsy (mTLE) and no hippocampal sclerosis (HS). However, compared with mTLE with HS, the clinical characteristics of mTLE with AE are not well established. We attempted to clarify these characteristics in the present study.

Method: Between May 2010 and December 2013, 23 patients who were diagnosed with temporal lobe epilepsy based on epileptiform waves on EEG and found to have AE (ipsilateral to the epileptogenic focus) on MRI by both visual and statistical evaluations at our center were studied. The clinical course, imaging findings, physiological tests and neuropsychological evaluations were summarized.

Results: Among 23 patients (12 men and 11 women), the epileptogenic focus and AE were on the left in 9, on the right in 13, and bilateral in 1. A history of febrile convulsion was found in only 2 patients. The ages of epilepsy onset varied widely (mean ± standard deviation; 46.9 ± 21.9 years), ranging from 15 to 76 years. Over one-half of the patients (12 patients) had onset at 50 years or above. Response to antiepileptic drugs (AED) was also diverse; but over one-half of the patients (13 patients) achieved freedom from seizure. Especially, 8 of 12 patients with onset at 50 years or above became seizure-free. Even among those with onset at 50 years or above, among 3 patients suspected of tumor on 18F-methionine PET, 2 had poor response to AED.

Conclusion: Compared to mTLE with HS, the clinical characteristics of mTLE with AE may include a lower association with febrile convulsion, later onset, and better response to AED (especially in those without suspected tumor). Especially, non-tumorous cases with onset after middle ages may represent a homogeneous syndrome.

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SYMPTOMATIC EPILEPSY IN THE ELDERLY
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Purpose: The aim of this study was to evaluate the clinical, and anatomo-morfolological characteristics of elderly patients with symptomatic epilepsy.

Methods: We retrospectively reviewed the clinical records of 200 patients (105 males and 95 females) aged 65 years or older at the time of study.

Results: Epilepsies were classified as generalized in 33 patients (16.5%), partial in 125 (62.5%), complex partial seizures(CPS) in 36 (18%) and tonic-clonic status epilepticus (SE) in 6 (3%). Symptomatic partial epilepsy (SPE) began at all ages (65–81 years), patients had no family history of epilepsy and half of them had a past history of cerebrovascular disease. MRI detection of the symptomatic epilepsy were brain tumors, posttraumatic sequels, post vascular sequels, and neurodegenerative diseases.

Conclusions: The neuroimaging methods are the option for diagnostic in elderly patients with symptomatic epilepsy. Cerebrovascular disease is the most common cause of seizures in the elderly, and complex partial seizures (CPS) are the most common seizure type in this age group. Precise localization of the seizure focus can be appropriate surgical candidates and a favorable prognosis is expected with curative surgical procedures.
carbamazepine but this was later changed to valproate due to worsening of bradycardia with prolonged pauses on 24 h ECG recording. During this period, there was marked deterioration in his level of function, with less engagement in rehabilitation. He was treated with antidepressants, L-thyroxin and a permanent pacemaker was inserted. General condition improved and he was discharged to a rehab facility. Post discharge he continued to have episodes of unresponsiveness and increased weakness on the right side. He died of pneumonia 6 months after his initial stroke.

Conclusion: Differentiating seizures from syncope can be difficult in the elderly. Although pre-existing bradycardia makes cardiac syncope more likely, normal blood pressure during episodes, prolonged confusion after the episode and persistence of symptoms after insertion of pacemaker favours seizures. Detailed assessment and prolonged monitoring may be needed to reach a diagnosis in this age group.

Purpose: To determine hormonal abnormalities among women with epilepsy, who were long-term treated with antiepileptic drugs.

Methods: 62 women with epilepsy of reproductive age (mean age 25.7 ± 6.6 years) were enrolled in the study. Group I included 14 WWE using valproate; group II consisted of 16 WWE taking carbamazepine; group III included 21 WWE using new AEDs (oxcarbazepine, lamotrigine, levetiracetam, topiramate); group IV – 11 WWE taking polytherapy. All women were investigated: sex hormones – luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin (PRL), estradiol (E), progesterone (P), testosterone (T). Concentrations of LH and FSH were assumed to be a marker of retrospective hypothalamic-pituitary axis dysfunction or to side effects of antiepileptic drugs (AEDs) (Luef G. & Rauchenzauner M., 2009; Verrotti A. et al., 2011). Postictal elevations in serum concentrations of prolactin were assumed to be a marker of retrospective evidence of epileptic seizure (Bauer et al., 1996).

Results: Hyperprolactinemia was revealed among 23% of women using valproate (786.3 mIU/l); among 15% of WWE taking carbamazepine (786.3 mIU/l); among 25% of WWE using new AEDs (802.9 mIU/l); among 27% of WWE taking polytherapy (905.8 mIU/l). Clinical manifestations of hyperprolactinemia associated with menstrual disorders (oligomenorrhea) in 6% of WWE. The level of prolactin was significantly higher in women with idiopathic generalized epilepsy in the first phase menstrual cycle (515.1 mIU/l) than in symptomatic focal epilepsy (343.2 mIU/l) (p = 0.016).

Conclusion: Hyperprolactinemia was revealed in about 1/4 of WWE, who were long-term treated with antiepileptic drugs, but serum concentrations of PRL were not more than 1,000 mIU/l and were evaluated that functional hyperprolactinemia in women with epilepsy taking AEDs, and specific treatment was not needed.

Purpose: The teratogenic potential and neurodevelopmental effects of antiepileptic drugs (AEDs) are documented in some studies. We evaluated the pregnancy complications and perinatal outcomes in our patients with juvenile myoclonic epilepsy (JME).

Method: Between 1998 and 2008 we enrolled 21 women with JME (25 pregnancies, mean age 26.4, ranged 22–34 years). Prospective, observational, one-center study of pregnancy complications, adverse perinatal and neurodevelopmental outcomes were carried-out. AEDs used during pregnancy were: valproate-VPA, 750–1,500 mg/day (6), lamotrigine-LTG, 150–300 mg/day (8) in monotherapy and in VPA+LTG combination (5), topiramate-TPM, 200–400 mg/day (2) and levetiracetam-LEV, 1,500–2,500 mg/day (4). Preconceptional folic acid of 4–5 mg was used. No alcohol abuse was noted. IQs of children (at age of 5) and parents were measured.

Results: 22 children (13 male, 9 female) were born to women with JME. No major congenital malformations were found. Unilateral sensory-neural deafness was diagnosed in one child (exposed to LTG+VPA in utero). Three cases of miscarriage (8–10 gw) were noted during exposure to VPA, VPA+LTG or TPM. One case of premature birth occurred. Cesarean delivery was performed in two patients. No case of late pregnancy bleeding was noted. Small for gestational age in one and Apgar score of <7 in two babies are noted. Daily dose of VPA for >1,000 mg seems to be associated with lower IQv (93.2) of children at age of 5. No similar influence of LTG used during pregnancy was noted.

Conclusion: No both major congenital malformations and severe perinatal complications were found in children born to women with JME. Infants exposed to VPA >1,000 mg in utero had lower IQv scores at age of 5.

Purpose: To study the interaction of migraine paroxysms and epileptic seizures.

Materials and methods: We observed 52 women with symptomatic epilepsy associated with migraine. The age of the patients was from 25 to 45 years. All the patients were examined in clinical conditions by using clinical-neurologic investigations. Supplementary methods of investigations such as electroencephalography, magnetic resonance imaging, cardiology were also used.

Results: We detected that migraine paroxysms and epileptic seizures were not connected during the time and existed concurrently in 28 patients. Migraine paroxysms induced epileptic seizures in 10 cases. Epileptic seizures provoked the development of migraine paroxysms in 13 patients. The interaction of the development of migraine and epilepsy was observed in the patients in consequence of brain injuries which can provoke the development of these diseases.

Conclusion: The progress of epilepsy and migraine and their interaction are directly associated with the influence of female sexual hormones in women; the preventive effect of antiepileptics in the treatment of migraine, in our opinion, can be determined by modulation of biochemical phenomenon of aura or by influence on the activity of the nociceptive system. Therefore, antiepileptics can be baseline medicines in the treatment of migraine, which is associated with epilepsy.
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CHANGES IN LEVETIRACETAM PLASMA CONCENTRATIONS DURING PREGNANCY AND ITS AFFECTION ON SEIZURE FREQUENCY
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Purpose: Levetiracetam (LEV) is associated with a low risk of malformations in nursed infants. However, LEV pharmacokinetics during pregnancy is still not well known.

Our aim was to investigate pregnancy-induced changes in LEV plasma concentration-to-dose ratio (LEV C/D-ratio), and to evaluate if such changes were related to seizure deterioration.

Method: 19 pregnancies in 17 women with epilepsy on LEV monotherapy were studied retrospectively. Statistical analysis (Friedman’s test with post-hoc analysis by Wilcoxon signed-rank test, Bonferroni correction and Mann–Whitney U-test) were performed to test for statistically significant changes in C/D-ratio means.

Results: The mean LEV C/D-ratio in first, second and third trimesters respectively were significantly lower than at baseline (Z = 2.900, p = 0.004; Z = 3.180, p = 0.001; Z = 3.180, p = 0.001). The average decline was 55% compared to baseline. Seizure deterioration was seen in 35% (6 of 17 completed pregnancies). There was no significant difference in mean drop in patient with and without seizure deterioration. LEV dosage was increased in all cases with a median of highest pregnancy dose being 200% of dose at conception. A significant increase in mean LEV C/D-ratio was seen within the first 4 weeks postpartum compared to the mean rate in the third trimester (Z = 2.521, p = 0.012).

Conclusion: This study confirms that pregnancy clearly enhance LEV elimination, but with considerable inter-individual variability. No clear association between declining dose-corrected plasma levels and seizure deterioration has been seen. Larger prospective studies are needed to understand the true extent of pregnancy-induced alterations and their clinical importance.

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CAPTURING WOMEN’S NARRATIVES OF EPILEPSY, PREGNANCY AND POSTNATAL CARE: A QUALITATIVE STUDY
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Purpose: As part of the EMPiRE (Anti-Epileptic drug Monitoring in PREGnancy) Randomised Controlled Trial, the authors carried out a qualitative study of women’s experiences of pregnancy whilst living with epilepsy. The purpose of this research was to explore women’s narratives of pregnancy and postnatal care while managing their condition.

Method: Semi-focused interviews were conducted with 32 women. Participants were interviewed twice: once upon recruitment into the trial and once 6 weeks after giving birth. Interviews were analysed using a narrative analysis.

Results: The authors present findings based on the initial and follow-up interviews. We will contextualise women’s diverse experiences of pregnancy and epilepsy, highlighting the varied histories women have with their condition, the additional health and fertility concerns faced by some, and how socio-cultural factors may influence their experiences. We will examine how women negotiate their drug regimens as they “weigh up” the risks and benefits of having a baby whilst managing epilepsy. Women’s labour and postnatal experiences will be explored, as well as their reflections on their pregnancies after having their babies. Finally, we will compare the experiences of stigma by women with more “severe” and frequent seizures with those women who have more “mild” and controlled seizures.

Conclusion: This research begins to address the dearth of qualitative research on women’s experiences of pregnancy, postnatal care and epilepsy. There may be a tension between the professional’s focus on drug adherence and the patient’s experience of doubt, as she must live with the consequences. Women’s varied positions on the spectrum of seizure types must be more fully recognised as this informs how they understand and manage their condition.

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RISK OF BIAS AND CLINICAL HETEROGENEITY IN ANTIEPILEPTIC DRUG TERATOLOGY STUDIES
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Purpose: Teratology of antiepileptic drugs (AEDs) has been investigated in non-randomised observational studies, as it is unethical to randomise pregnant women to treatment alternative to investigate harms. Observational studies are subject to a number of biases and a Cochrane systematic review was conducted to examine methods used in neurodevelopmental teratological studies.

Methods: Assessed studies comprised of prospective cohort or registry studies including women with epilepsy and a control or comparator group. A tool created by the Cochrane Non-Randomised Study Methods Group and further developed by the Cochrane Epilepsy Group was employed to assess risk of bias in non-randomised studies. Using a five-point Likert scale two independent reviewers rated studies in terms of:

1 Selection bias.
2 Missing data.
3 Selective reporting.
4 Confounding variables.
5 Any other bias in line with pre-determined parameters.

Clinical heterogeneous factors were also examined.

Results: Included studies comprised of 18 prospective cohort studies and 7 prospective registry studies. Ratings of high or unclear levels of bias were prominent in domains of controlling for confounding variables (76%), selective reporting (48%), and other biases (64%) across included studies. Bias in the form of missing data and blinding were marginally improved (40% and 28% respectively). Factors of clinical heterogeneity were large including failure to analyse drugs separately, different outcome measurements, age of children at assessment, study design and type of control group.

Conclusion: Risk of bias and clinical heterogeneity across neurodevelopmental studies limits evidence synthesis therefore obstructs evidence based prescribing for women in their childbearing years. Increased research activity and more rigorous methodologies are required.
Abstracts

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TEENAGE PREGNANCIES IN WOMEN WITH EPILEPSY CLINICALLY VALIDATED DATA FROM THE OPPLAND PERINATAL REGISTRY
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Purpose: Teenage pregnancies are often considered to be risk events. Very few studies have assessed the frequency of child births among teenagers with epilepsy. Hence, we set out to assess the proportion of women with epilepsy having teenage pregnancies in Oppland County, Norway and compare to the expected.

Method: Information on all pregnant women who gave birth in Oppland County was prospectively registered in the local database. The pregnancy and birth registry of Oppland (OPR). This contains 40,000 births, of which 0.6% are by mothers with epilepsy. Among the 25,203 primary cases (first birth registered in OPR), 153 were women with epilepsy. All diagnoses of epilepsy were validated by a neurologist (AHF). Possible group differences in categorical and continuous variables were tested using the \( \chi^2 \) test and \( t \)-test respectively. Odds ratios (ORs) were estimated with the use of multiple logistic regression analysis, controlling for substance abuse and psychiatric co-morbidity.

Results: Amongst primary cases there were 7.8% (n = 12) teenage births by women with epilepsy compared to 4% (n = 1004) without epilepsy (p < 0.004). Having epilepsy was an independent predictor in multivariate logistic regression analysis for teenage births with an OR of 2.04 (p = 0.016). The frequency of contraceptives (pills or intrauterine devices) was lower among teenagers with epilepsy (22%) than those without epilepsy (31%) (p = 0.348).

Conclusion: Having epilepsy was an independent predictor of teenage pregnancy. Whether this might be a consequence of less use of safe contraceptives or other risk taking behaviors often associated with epilepsy, remains unclear. The demand for vigilance towards young women with epilepsy is underlined by the medical and psychosocial burden often associated with teenage pregnancy.

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FERTILITY RATE AMONG WOMEN WITH EPILEPSY
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Purpose: To study the patterns of fertility among women with epilepsy compared to middle rates in Russia and world

Method: 155 women with epilepsy at the age of 16–45 years. were included in the prospective observation uncontrolled one-center research of side effects of antiepileptic drugs (AEDs) on reproductive health (RH). Three groups were allocated: 1 g – AEDs monotherapy, 2 g – polytherapy, 3 g – without AEDs. Medical and social determinants of health included assessment of reproductive health, family functioning assessment by accounting fertility rate, marital status and number of children. STATISTICA for Windows system (version 5.5) was used.

Results: 1 gram consisted of 70 patients (45%), 2 g – 65 (42%), 3 g – 20 (13%). Average age of the surveyed women was 25 years. Patients in optimal reproductive age (20–30 years) – 62% prevailed. Statistically significant differences in clinical characteristics between groups weren’t detected. 47% of women were married. Percent of women planning pregnancies was 45%. 53% of women had RH disturbances, 40% – due to side effects of AEDs. AEDs polytherapy enlarged the frequency of disturbances of RH (p < 0.001). 31% of women had children (with no differences between groups). Only 18% of children were born before mother’s disease. 35 women had one medication and 5 taken polytherapy during pregnancy. Fertility rate among surveyed women with epilepsy was 0.3. It is 1, 4 for Russia. Fertility rate for simple replacements of generations should be 2, 15. Optimal rate is 4, 0.

Conclusion: Fertility rate among women with epilepsy was lower than optimal due to medical and social reasons. Disturbances of reproductive health are frequent side effects of antiepileptic drugs. It is necessary to monitor reproductive health during antiepileptic drugs treatment.

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ANTIEPILEPTIC DRUG THERAPY DURING PREGNANCY AND OBSTETRIC OUTCOMES IN MOSCOW REGION: COMPARING OF 1998 AND 2013 YEARS
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Purpose: To analyze types of epilepsy, antiepileptic drug therapy and pregnancy outcomes in women with epilepsy (WWE) in 1998 (1-st group) and after 15 years – in 2013 year (2-nd group).

Method: 49 pregnant WWE in 1998 and 113 in 2013 years were analyzed. Focal epilepsy was observed in 54 women (56.2%) and 76 (67.1%) of WWE. The pregnancy was terminated in 86 women (87.1%) and 89 (79.5%) of WWE. The pregnancy was terminated in 86 women (87.1%) and 89 (79.5%) of WWE. Medical-social characteristics including median age, duration of disease, number of young women (before 18 years) were similar in both groups.

Results: AED treatment included (1-st and 2-nd groups): no therapy 3 (6.1%) and 12 (10.6%); monotherapy 33 (67.3%) and 83 (75.5%); bi-therapy 11 (22.4%) and 17 (15.0%); poly-therapy 2 (4.1%) and 1 (0.9%). Monotherapy included: Carbamazepine 17 (51.5%) and 31 (37.3%); Valproate 7 (21.2%) and 19 (22.9%); Barbiturates 3 (9.1%) and 5 (6.0%); other drugs 6 (18.2%) and 28 (33.8%). Levetiracetam in 2013 was the 3-rd most popular drug in monotherapy 13 (15.7%), Remission took place in 29 (59.2%) and 78 (69.0%) of WWE. The pregnancy was terminated by vaginal delivery in 32 women (65.3%) and 72 (63.7%); Cesarian section in 13 cases (26.5%) and 38 (33.6%); operative vaginal delivery in 1 (2.0%) and 0 in 2013; late termination of pregnancy 3 cases (6.1%) and 3 cases (2.7%) accordingly.

Conclusion: The number of pregnant WWE in 15 years increased more than twice. The percentage of remission and monotherapy increased 10%. Vaginal delivery performed in 65%. Levetiracetam was the most popular among new drugs in 2013.
THE EFFECTS OF ANTIEPILEPTIC DRUGS ON TRANSPORTER EXPRESSION IN HUMAN PLACENTA
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Purpose: In utero exposure to antiepileptic drugs (AEDs) has been associated with fetal loss, intrauterine growth restriction, major congenital malformations and impaired postnatal cognitive and behavioral development. Up to date, most mechanistic studies on AED teratogenicity have investigated their direct effects on the fetus or their impact on the concentrations of hormones and nutrients in maternal plasma. The aim of this study was to better understand the effects of AEDs on the placenta. We investigated AEDs-induced regulation of the drug efflux transporters, P-glycoprotein (P-gp) and the breast cancer resistance protein (BCRP).

Method: Placental tissue of gestational age 7–10 weeks was collected from elective abortions. Villous explant cultures were incubated with VPA (0.25–1.0 mM), CBZ (0.03–0.06 mM), or the vehicle, for 5 days. Transporter protein expression was evaluated using Western blot analysis.

Results: At 0.25 and 0.5 mM, VPA significantly (p < 0.05) reduced the expression of placental BCRP. A trend towards reduced P-gp and BCRP expression was observed following incubation of placental villi with CBZ, although the number of placentae collected so far was too small for statistical analysis.

Conclusion: Our initial results suggest that AEDs may affect the expression of placental transporters that protect the fetus against xenobiotics. Further studies are now being conducted with larger numbers of placentae and additional AEDs in order to better understand the potential effects of these compounds on placental function. If validated, these results may point at novel mechanisms through which AEDs affect fetal development.

DEVELOPMENT OF METHODOLOGY FOR IMAGING THE EFFECTS OF ANTIEPILEPTIC DRUGS ON THE PLACENTAL BARRIER IN VIVO
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Purpose: The placenta plays a significant role in the transfer of nutrients to the fetus and excretion of waste products and xenobiotics from the fetus back to maternal plasma. The transfer of these compounds across the placenta is performed by passive diffusion and by placental transporters. The goal of this project was to develop a near-infrared (NIR) imaging methodology for studying the effects of antiepileptic drugs on the placental barrier.

Method: The study was conducted in mice on gestational day 17.5 (late-gestation), following 4 days treatment with 200 mg/kg valproic acid (VPA) or the vehicle. Indocyanine green (ICG) (8 mg/kg, i.v.), which is a substrate of several placental transporters and normally does not cross the placenta, was used as the NIR probe.

Results: Treatment with VPA did not significantly enhance the emission of ICG in maternal blood and in the fetus. However, placental ICG emission increased 1.8-fold (p < 0.01) compared to that of controls. VPA also significantly (p < 0.05) decreased hepatic ICG distribution and the liver:forelimb AUC ratio.

Conclusion: ICG accumulation with the placenta suggests an effect of VPA on placental permeability, possibly through modulation of placental transporters activity. The results emphasize the role of the placenta as a protective barrier for the fetus. Although the transplacental transfer of ICG was not affected by VPA, the effects of xenobiotic accumulation on placental tissue itself require further investigation.

PREVALENCE OF ANTIEPILEPTIC DRUGS EXPOSURE IN PREGNANT WOMEN IN THE EMILIA ROMAGNA REGION (ITALY): RESULTS FROM THE ESPEA (EMILIA ROMAGNA STUDY ON PREGNANCY AND EXPOSURE TO ANTIEPILEPTIC DRUGS)
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Results: 26, 5% of patients achieved medically induced remission (n = 9), 2 patients (5.8%) continue to suffer from generalized convulsive seizures. 67.7% of patients complain to myclonias, although only 17.6% of patients observe that their myclonias has frequent induced nature. The majority of female patients received drugs based on valproic acid (58, 8%). Side effects were mostly caused by valproates – 70% of patients, the most frequent of them were hair loss (30%) and weight gain (25%). Patients with JME had average values of hormones within normal limits, but if compared with a healthy group (n = 7) a difference in most values by 1.5–2 times was observed. 40% of women had progesterone level decrease at the second phase of their menstrual period. Double increase of lutening hormone level was indicated in 8 patients (22.9%).

Conclusion: Thus, patients with JME have hormonal sphere deviations, which may act as a predisposing factor to gynecological disorders. In the nearest future we plan to continue patient recruitment. The research data need further thorough examination, detection of dependence from the taken medication and seizure character observation.

Purpose: To assess the prevalence of Anti-Epileptic Drugs (AEDs) exposure in pregnant women with or without epilepsy in the Emilia Romagna Region (RER), Northern Italy.

Method: This is part of a larger retrospective population-based study, whose primary aims also included describing AEDs prescription patterns in pregnant women with regard to the indication (epilepsy or other diseases) and assessing the risk of major congenital malformations following AEDs exposure during pregnancy in the RER (4 million inhabitants). Data were obtained from official regional registries: Certificate of Delivery Assistance; Hospital Discharge Card; reimbursed prescription databases. We identified all the deliveries and the hospitalized abortions occurred between January 2009 and December 2011. AEDs exposure during pregnancy was evaluated considering delivery date and gestational age for deliveries, and, for abortions, wherein gestational age was unknown, considering the 3 months preceding the event. The following active substances were considered: Phenytoin, Ethosuximide, Clonazepam, Carbamazepine, Oxcarbazepine, Rufinamide, Valproic acid, Vigabatrin, Tiagabine, Lamotrigine, Felbamate, Topiramate, Gabapentin, Levetiracetam, Zonisamide, Pregabalin, Lacosamide.

Results: We identified 145,243 pregnancies: 111,284 deliveries (113,117 newborns) and 33,959 abortions. Six hundred and eleven (0.42%, 95% CI: 0.39–0.46%) were exposed to AEDs: 537 to one, 74 to 2 or more AEDs. The most used substances were Carbamazepine (23% of all exposed pregnancies), Valproate/Valpromide (21%), Lamotrigine (17%). Three hundred and fifty-three newborns (0.31%, 95% CI: 0.28–0.35%) were exposed to AEDs during the first trimester.

Conclusion: The prevalence of AEDs exposure in pregnant women in the RER was 0.42%. There were two main limits: Clobazam is not reimbursable, therefore it is not recorded in the considered databases, and approximately one half of the abortions was not detectable, since not hospitalized or not recorded. Therefore our result could be slightly underestimated.

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ANTIEPILEPTIC DRUG USAGE AND THE EFFECTS OF THEM ON THE FOETUS IN EPILEPTIC PREGNANT WOMAN
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Objectives: In this study, we discussed antiepileptic drug usage in epileptic pregnant women and the effects on their fetus.

Methods: Fifty six epileptic pregnant women who were followed in our epilepsy outpatient clinic between January 2012 and January 2014 were included. Demographic data, medical history, seizure type, antiepileptic drug usage, and malformations were evaluated.

Results: The mean age of patients was 26.85 (18–37) years. 3 patients have a history of consanguinity, 4 patients have a family history of epilepsy, 8 patients have a history of febrile convulsion. The seizures began between 3 years and 30 years of age. The first epileptic attack was occurred during the pregnancy in 7 patients. The main seizure type was generalized tonic-clonic (80%). The most commonly chosen antiepileptic drugs were lamotrigine (42%) and carbamazepine (35%). Eleven patients (%21) were using polytherapy during pregnancy. In this period, 45 patients gave birth. Three pregnancies were ended with spontaneous abortion in the first trimester and ectopic pregnancy was present in two patients. One pregnancy was terminated because of cardiac defect, one baby died because of HELLP syndrome. One patient is still pregnant. One kidney anomaly was observed in one born baby. Any major malformation had been seen.

Conclusion: Pregnancy in epileptic women must be planned and regular visiting to the clinics can provide successful pregnancies and healthy offspring.

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FREQUENCY AND CLINICAL PROFILE OF CATAMENIAL EPILEPSY AMONGS WOMEN WITH EPILEPSY ATTENDING A TERTIARY CARE HOSPITAL IN ENUGU, SOUTH EAST NIGERIA
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Purpose: Seizure exacerbation at different phases of the menstrual cycle of some women with epilepsy (WWE) has been well characterized and described as catamenial epilepsy (CE). Catamenial epilepsy has been well studied in developed countries however, paucity of data exists in most developing nations including Nigeria. This study aims to assess the frequency, clinical and sociodemographic correlates of menstrual related epilepsy in women attending the adult neurology clinic of University of Nigeria Teaching Hospital (UNTH) Enugu, southeast Nigeria and to compare with observations in other regions.

Method: We did a chart review of case notes of all female patients with epilepsy who presented to the neurology clinic of our hospital between January 1st, 2009 to December 31st, 2010. A total of 102 female patients were identified out of which 62 had documentation of the presence or absence of menstrual related seizures and were included in the study. Sociodemographic and clinical data were documented and the frequency of catamenial seizure defined as perimenstrual or periolumination seizure exacerbation was determined. Data was analysed using Epi Info 7.

Results: 16.13% (n = 10) of the study population had catamenial epilepsy, all of the perimenstrual type. The mean age of those with catamenial epilepsy was 29.30 ± 7.79 vs. 33.71 ± 11.80 for those without catamenial epilepsy. Those with catamenial epilepsy are more likely to be single with higher seizure frequency, longer duration of seizure, less seizure remission, have partial type of seizure and use polytherapy. None of these clinical and sociodemographic correlates achieved statistical significance between those with and without catamenial epilepsy.

Conclusion: About one in six women with epilepsy in south east Nigeria have catamenial epilepsy. Identifying female patients who have catamenial epilepsy through encouraging WWE to keep seizure frequency-menstrual cycle diary will help better management of such seizures.
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INTRACRANIAL EEG INVESTIGATIONS OF FOCAL CORTICAL DYSPLASIAS: ADDED VALUE OF DEPTH ELECTRODES IN COMBINATION WITH SUBDURAL GRIDS TO LOCALISE THE SEIZURE ONSET ZONE
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Purpose: Focal neocortical dysplasias (FCD) are common pathological substrates found in patients with neocortical epilepsy. Due to the three-dimensional extent of the lesion and the potential location of the dysplastic area in the deep cortices of the brain, identification of the seizure onset zone (SOZ) and of the resection margins with subdural electrodes only can be challenging. We investigated the added value of combining subdural grid coverage and supplemental depth electrodes in the presurgical evaluation of adult patients with suspected FCD.

Method: We retrospectively analysed 11 cases with a suspected area of FCD on imaging, implanted with grids and depth electrodes to cover deeper structures as part of their presurgical assessment. Our analysis included electrode contacts of visually determined maximum ictal onset. Our series comprised 6 females, 5 males (Mean [SD] age 36 ± 10 years) implanted with a total of 78 ± 17.5 electrode contacts: 66.2 ± 17.6 grid, 8.9 ± 6.8 strip and 13.4 ± 6.6 depth electrode contacts.

Results: Histopathology confirmed FCD type IIb in 7 of 8 resected cases. Of these, 85.7% of patients achieved Engel Class I outcome postsurgically at 1.87 ± 0.64 years follow-up. Depth electrodes yielded the maximum seizure onset zone in 6 cases: in 5 the SOZ was in the frontal lobe maximal at the area of cortical thickening or within the FCD and in one case in the depth of the superior frontal sulcus. Depth electrodes additionally helped to separate the dysplastic cortex involved in epileptogenicity from the hand/foot motor area in one patient.

Conclusion: The use of added depth electrodes provides valuable information to fully delineate the SOZ particularly in cases where the FCD is located in deep frontal areas which are difficult to access with additional grids or strip electrodes.

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ABNORMAL FUNCTIONAL BRAIN NETWORK IN EPILEPSY PATIENTS WITH FOCAL CORTICAL DYSPLASIA
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Purpose: Despite of recent interest of network approaches derived from graph theory on epilepsy, resting state network analysis of focal cortical dysplasia (FCD) brain compared with control brain has not been adequately investigated. Here we investigated the difference in the resting state functional network between epilepsy patients with focal cortical dysplasia (FCD) and healthy subjects by using whole-brain magnetoencephalography.

Method: We retrospectively analyzed MEG signals from 35 epilepsy patients with FCD and 23 healthy controls. A global mutual information (MIglob) as a measure of strength of functional connectivity, and the global efficiency (Eglob) as a measure of efficiency of functional network were calculated for theta (4–7 Hz), alpha (8–12 Hz), beta (13–30 Hz), and gamma (31–45 Hz) bands to compare global network differences between FCD patients and controls groups.

Results: FCD brains at the resting state had stronger functional connectivity (MIglob) in the beta (p = 0.000) and gamma bands (p = 0.007), and also showed higher efficiency of functional network (Eglob) in the beta (p = 0.001) and gamma bands (p = 0.003) than controls. For the type of FCD, functional connectivity of FCD type I (MIglob, p = 0.004; Eglob, p = 0.012) and type II (p = 0.016; Eglob, p = 0.006) in the beta band were higher than that of normal controls. In the gamma band, the values of FCD type II were higher than those of normal controls (MIglob, p = 0.001; Eglob, p = 0.000) and FCD type I (MIglob, p = 0.038; Eglob, p = 0.031).

Conclusion: We revealed that FCD brains had increased functional connectivity in the beta and gamma bands at the resting state compared with those in healthy controls. Resting state network differences could be used even when there is no prominent interictal spike activity, and would enhance our understanding of epileptogenesis of FCD.

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MISLEADING AGE RELATED FOCAL SPIKE-WAVES IN CHILDHOOD EPILEPSY SURGERY CANDIDATES
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Purpose: “Benign” Epilepsy of Childhood with Centro-Temporal Spikes (BECTS) is the most common form of “idiopathic Focal Epilepsies” (IFE) (ILAE 1989). The occurrence of “benign” EEG patterns in structural epilepsies (ILAE 2010) during pre-surgical evaluation could be misleading. Our purpose is to evaluate how a detailed analysis of inter-ictal EEG abnormalities help to distinguish in epilepsy surgery candidates: focal self limited EEG trait “genetically determined and from interictal EEG abnormalities related to “structural” etiologies.

Method: Among 674 children with focal epilepsy candidates to a presurgical evaluation, we report 9 patients (1.4%) who presented with the association of these two types of interictal EEG abnormalities:. Demographic characteristics, Ictal and inter ictal EEG patterns, neuroimaging were analyzed. Post-operative electroclinical follow up is also studied.

Results: Regarding etiology, 3 patients showed a cortical developmental malformation (MCD), 3 had DNET, 1 patient had hippocampal sclerosis, 1 had vascular malformation and 1 had Tuberosclerosis. Mean age at epilepsy onset ranged from 6 months to 12 years. All patients who benefited from surgery (5/9) were postoperatively in Class I. Detailed analysis of EEG shows clear differences between the two types of interictal abnormalities (morphology, topography and modality of activation during sleep). “Age related and self limited” nature of EEG abnormalities was confirmed by their disappearance at adolescence (3 patients).

Conclusion: In a serie of pediatric epilepsy surgery candidates, we demonstrated the rare association of interictal EEG abnormalities related to...
"genetically determined, self limited" and "structural" etiologies. Detailed and accurate neurophysiological analysis helps to discriminate the two EEG traits. The co-existence of a these two EEG patterns does not preclude favorable outcome.

**p047**
ASYMMETRIC SEIZURE-RELATED MODULATION OF ATRIOVENTRICULAR CONDUCTION IN PEOPLE WITH BILATERAL MESIAL TEMPORAL LOBE EPILEPSY

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**Purpose:** Previous clinical studies provided conflicting data on asymmetric cerebral control of cardiac function, which may partially be caused by different study designs and high inter-individual variability. Such an asymmetric representation could be important in epilepsy, as a proportion of seizures are associated with bradyarrhythmias including atrioventricular (AV) conduction block. Here, we investigated whether seizure-related changes in AV conduction depend on the side of seizure-activity in mesial temporal lobe epilepsy (mTLE).

**Method:** To account for inter-individual variability, EEG and ECG data were reviewed from people with pharmacoresistant mTLE undergoing pre-surgical video-EEG telemetry with seizures from both hippocampi as assessed by hippocampal depths electrodes. RR and PR intervals were determined at different timepoints using a one-lead ECG. PR intervals were plotted vs. the corresponding heart rate (HR) and submitted to linear regression. The resulting slope was considered as a measure of peri-ictal modulation of AV conduction. Data are given as mean ± SD.

**Results:** Fifty-six seizures of 14 patients (5 men, 34.7 ± 9.8 years) were included in this study (2 seizures per side and patient). There were no significant differences of absolute PR intervals and HR before and during unilateral ictal activity between left- and right-sided hippocampal seizures (pooled data: preictal PR intervals 146 ± 22 ms; ictal PR intervals 140 ± 25 ms; preictal HR 84 ± 14 bpm; ictal HR 105 ± 19 bpm). The peri-ictal modulation of AV conduction, however, appeared greater with left-sided seizures, as the slope of the PR/HR correlations was significantly steeper with seizures originating in the left hippocampus (p < 0.0001; left –0.37 ± 0.11 ms/bpm, right –0.22 ± 0.16 ms/bpm).

**Conclusion:** Our preliminary data suggest that peri-ictal modulation of AV conduction depends on the side of seizure-activity, supporting the notion of asymmetric cerebral control of cardiac function. The clinical relevance of this subtle finding is unclear, but may indicate a side-dependent susceptibility to seizure-related AV node dysfunction in mTLE.

**p048**
FREQUENCY AND CLINICAL CORRELATES OF FRONTAL INTERMITTENT RHYTHMIC DELTA ACTIVITY IN THE ADULT NEUROLOGICAL INTENSIVE CARE UNIT

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**Purpose:** Frontal intermittent rhythmic delta activity (FIRDA) is characterized by transient rhythmic delta waves localized mainly over frontal orolar regions. It has been associated with various structural lesions, degenerative disorders and metabolic disturbances. The prevalence is very low (<1–6%) in outpatient clinics, but little information exists about its’ frequency in intensive care units (ICU). Therefore we sought to identify the frequency of FIRDA in our adult neuro-ICU, together with accompanying clinical characteristics.

**Method:** We retrospectively reviewed the video-EEG reports of all patients who were monitored in our adult neuro-ICU from 2009 to 2013. Patients who had at least one EEG with FIRDA were identified. Clinical, imaging and laboratory data were collected from patient charts.

**Results:** Among 139 patients 26 (18.7%; 13M; age 23–82) fulfilled the above criteria. Final diagnoses were: 16 ischemic stroke, 3 hemorrhagic stroke, 3 non-convulsive status epilepticus, 2 encephalitis, 1 reversible leukoencephalopathy syndrome, 1 venous infarct. Eleven patients had anemia, 8 patients had a metabolic disturbance (4 hepatic and 2 renal dysfunction, 4 hyperglycemia, 1 hypotension; 3 patients had multiple metabolic abnormalities). Glasgow coma scale score at EEG onset was <8 in seven patients. Duration of EEG recordings ranged between 1.5 and 198 (mean 28.4, median 22) h. Additional epileptic discharges were detected in 8 and triphasic waves in 3 patients. Nine patients had >1 EEG evaluations, and FIRDA was a consistent finding in only one of them.

**Conclusion:** The prevalence of FIRDA is much higher in the neuro-ICU. The majority of patients have structural brain lesions and metabolic disturbances are common. However the fact that FIRDA rarely recurred in control EEGs suggests that multiple etiologic factors may play a role in the generation of this EEG pattern in critically ill patients.

**p049**
THE SENSITIVITY OF SHORT SLEEP EEG IN NEW ONSET EPILEPSIES

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**Purpose:** Routine EEG may be normal by up to 50% after the first unprovoked epileptic seizure. Recurrence rate of epileptic seizures after the initial unprovoked seizure is not high enough to justify early treatment in many of the patients. Therefore it is crucial to identify the recurrence risk of first seizure. Sleep EEG may be helpful in this setting. Aim of this study is to evaluate the sensitivity of short, daytime sleep EEG in new onset epilepsies.

**Method:** All patients who had unprovoked epileptic seizures (number and duration not restricted) and not yet treated with antiepileptic drugs were recruited to this study. All of the patients had a routine EEG. If routine EEG revealed epileptiform activities, no further test was applied. In the case of normal routine EEG, each patient had sleep EEG. Before the sleep EEG recording day, each patient had a sleep deprivation (half of total sleep). The tests were realized daytime and patients were left to sleep for 2 h. 10–20 electrode montage system was used in Nihon Kohden EEG device.

**Results:** Starting from 2010, 241 patients were recruited to the study, prospectively. Mean age of the patients were 28.40 (11–83) and 109 patients were male. Seventy seven patients had abnormal routine EEG, so they were not included in the sleep EEG study. Twenty three patients could not sleep. Twelve patients did not join to the study. The results were analyzed for the rest 129 patients. Fifty four patients had epileptiform activities during sleep EEG.

**Conclusion:** It seems that short sleep EEG may increase the sensitivity in new onset unprovoked seizures.
p410 AUTOMATIC ANALYSIS AND TRENDING OF LONG-TERM SCALP EEG USING NEUROTREPND

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Purpose: A computational method called NeuroTrend to automatically assess long-term scalp EEGs during recording was developed. The EEG is scanned for rhythmic activity (0.7–13.5 Hz), rhythmic spike-wave (SW) patterns, and periodic patterns. The results are displayed graphically on a large time scale up to 100 h. The ability of NeuroTrend to support EEG evaluation in epilepsy monitoring units (EMUs) is shown by assessing the detection results of seizure epochs.

Method: Unselected long-term scalp EEGs from 99 adult patients including seizures recorded at several EMUs were included in a comparative study. The duration of the recordings was between 12 h and 166 h adding up to 8,170 h in total. The start of the seizures were marked by clinical EEG experts and compared to the automatically detected patterns of NeuroTrend. If a rhythmic or SW pattern with at least 6 discharges was found by NeuroTrend in a range of 1 min before and 3 min after the seizure marker it was considered as true positive detection.

Results: The average seizure detection sensitivity per patient was 81% with a 95% confidence interval of 74–87% when using rhythmic and SW patterns for detection. For 72 patients (71%) all seizures were detected correctly. The detection sensitivity did not rise significantly when periodic patterns for detection. For 72 patients (71%) all seizures were detected correctly. The detection sensitivity did not rise significantly when periodic patterns for detection.

Conclusion: NeuroTrend is a software tool for the analysis of long-term EEG recordings. The reduction of the EEG to clinically relevant information allows a graphical representation of up to 100 h of data on a single screen. This representation significantly reduces the time for data analysis in EMUs and reveals trends in the neurological state of the patient. It was shown in this study that it can be used for highly reliable detection of epileptic seizures amongst other applications.

p412 INCREASED VARIABILITY IN BACKGROUND SENSORIMOTOR NEURAL ACTIVITY IN BECTS

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Purpose: Benign Epilepsy with Centro-Temporal Spikes (BECTS) is a common childhood epilepsy characterised by sensorimotor seizures affecting mouth and face and high amplitude centro-temporal spikes. We hypothesised that background activity would differ between patients and controls in the sensorimotor network but not elsewhere, and that differences would dominate in the beta band due to its prominent role in motor processing.

Method: 17 Patients with BECTS and 12 age-matched typically developing controls underwent MEG, MRI, and psychobehavioural tests. During MEG, participants performed a 3-min resting state session. We used a novel ICA MEG analysis method (Brookes et al. PNAS, 2011) to assess sensorimotor and visual resting state network activity by calculating areas of high temporal correlation in oscillatory activity. We also assessed variability of oscillatory time-frequency activity in individual motor cortex, localised using a left and right finger abduction task.

Results: In the sensorimotor network, patients had a greater standard deviation of component amplitude than controls, suggesting greater variability of activity, whereas there was no difference in the visual network. Network values did not correlate with age. The coefficient of variation (standard deviation/mean) in peak frequency was greater for patients than controls in the beta band (13–30 Hz) only, which showed a trend for a negative correlation with age in both patients and controls. In addition, patients had a greater coefficient of variation in power for activity >50 Hz. Although the latter may reflect a jaw or neck muscle artefact, the limitation on higher frequencies cannot explain the greater frequency variability in the beta band.

Conclusion: We found greater sensorimotor beta band variability in background MEG activity in BECTS, compared to controls, but no difference in visual cortex activity. These findings may point towards a “disorganised” functional sensorimotor network in patients.

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COULD EEG FEATURES PREDICT THE STATUS EPILEPTICUS OUTCOME?
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Purpose: SE is a neurological emergency that requires immediate diagnosis and care. We aim to describe electrical and clinical features in a series of patients with SE and the response to antiepileptic drugs (AEDs).

Method: From a total of 92 SE patients admitted to our hospital from September 2010 to April 2012, we selected retrospectively 54 with EEG recording at the moment of the suspected diagnosis. We collected different variables including type of SE, semiology, etiology, EEG pattern, distribution of abnormalities and response to treatment, considering as refractory the requirement of more than 2 AEDs.

Results: Most of the cases were symptomatic SE, 28 with lesional findings: 46.4% acute and 53.6% remotes, half of them related to cerebrovascular disease. Anoxic encephalopathy was the second most frequent etiology. Approximately 70% of all patients presented a focal SE with contralateral hemispheric electrical repercussion in 36.8%.

The most frequent SE type was non convulsive SE (68.5%). Convulsive SE (31.5%) were related to less response to AEDs (p = 0.011) and higher mortality rate (p = 0.044).

A single ictal EEG activity was observed in 32 patients, being the wax and wane pattern the most frequent and the less refractory to treatment (p = 0.01).

The rest 22 patients showed a mixed ictal EEG activity, where periodic pattern stood out as main finding; both associated whit longer remission (p = 0.006 and 0.011 respectively) and major mortality rate (p = 0.003 and 0.001).

Preservation of alpha rhythms (33.3%) was related to a lower mortality rate (p = 0.001).

Conclusion: We found that complex EEG patterns were related to worse prognosis. The EEG is an important tool in order to characterize the SE and might help to predict the outcome and also to optimize the management of the treatment in these patients.

INTERICIAL EEG IN EILEPTIC CHILDREN
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Purpose: The modern antiepileptic Drugs-AED can imitate normalization of clinical futures in epileptic children and change the typical epileptiform pattern of EEG. For this reason the correct evaluation of EEG in interictal period gain a special significance for adequate treatment strategy. Was an elaborate criterion for investigation of interictal EEG patterns using computer EEG approach to study the correlation between clinical and neurophysiological outcomes. The aim of this study was to investigate alteration of different EEG characteristics in epilepsy contingent during the treatment.

Method: Following quantitative characteristics of EEG were analyzed: absolute values of the power spectra; EEG-topography- spatial distribution of frequency ranges. 87 epilepsy patients aged 3–9 years were examined.

Results: Quantitative Spectral analysis of interictal EEG reveals that most powerful are the oscillations of 3–8 Hz with prevalent amplitude 60–120 µV. The essential value has morphology of the theta-waves and its distribution. The presence of rhythmic monomorph high amplitude theta-waves of tempo-parietal localization in interictal EEG of children is a negative finding despite of normalization clinical status and allows to expect renewing of seizures after canceling of AED.

Conclusion: The value of EEG date as predicting seizure exacerbation in children with new onset epilepsy is important. Careful follow-up EEG, including repeated EEG recordings and date analysis will be usefully to identify changes predictive of seizures aggravation after initiation of treatment.

DIFFERENTIATION OF EEG PATTERNS IN PATIENTS WITH NONCONVULSIVE STATUS EPILEPTICUS FROM EEG PATTERNS IN PATIENTS WITH TRIPHASIC WAVE USING WAVELET ANALYSIS
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**Purpose:** Distinguishing nonconvulsive status epilepticus (NCSE) from trichiphasic wave (TW) with metabolic encephalopathy is sometimes difficult because NCSE and TW are indistinguishable by clinical symptoms and can produce very similar electroencephalographic (EEG) patterns. We asked whether differences in frequency-domain characteristics of the sharp or spike component of the NCSE generalized sharp wave or TW by wavelet analysis may be helpful in differentiating between these conditions.

**Method:** We retrospectively analyzed EEG data from 25 patients presenting with decreased level of consciousness (12 in NCSE; 13 in TW). We performed wavelet time-frequency decomposition of 10 min of EEG data containing generalized spike/sharp and slow wave or TW activity. For each patient, we obtained the mean log spectral bandpower (15–30 Hz) containing spike/sharp components of the generalized sharp wave or negative sharp components (referred as “fast components, FC”). For comparison, we obtained bandpower containing slow wave portions of generalized sharp wave or trichiphasic wave (referred as “slow component, SC”).

**Results:** Mean 15–30 Hz relative log band power ($B_{FC} - B_{SC}$) was 5.88 ± 2.13 dB for NCSE and 2.01 ± 0.95 dB for TW ($p < 0.01$). The corresponding 15–30 Hz ratio of log band power ($B_{FC}/B_{SC}$) was 1.101 ± 0.035 for NCSE group and 1.036 ± 0.018 for TW ($p < 0.01$).

**Conclusion:** This study suggests wavelet analysis of high-frequency (15–30 Hz) band power may be useful for distinguishing generalized equivocal EEG patterns that can be seen in either NCSE or TW, but which are otherwise very difficult to differentiate with visual analysis.

**On average, the proposed method could detect the presence of epileptic events with high sensitivity of 91% (49 out of 54) and a very low false detection rate of 0.02/h (16 false alarms in 780 h).**

**Conclusion:** By using ratio of two specific spectral power bands, one can build more robust algorithms than using simple spectral powers. The proposed method uses Power Spectral Density (PSD) of iEEG signal, which is very low computational cost. These make the method ideal for clinical application and to be implemented in portable low-power budget devices for real-time monitoring of epileptic patients.

**p418 STATNET EEG A FAST AND RELIABLE OPTION IN PATIENTS SUSPECTED FOR NCSE**

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**Purpose:** The conventional method of EEG lead application is 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 personnel after minimal training. The objective is to compare the setup time and time delay from EEG request to start of EEG acquisition between the StatNet and routine EEG test and assess the quality of the recordings and the ability to detect abnormal findings.

**Method:** Between September and November of 2013, 16 patients suspected for non-convulsive status epilepticus from ER or ICU were included. Minimally trained epilepsy fellow applied StatNet electrodes to record EEGs. Trained technicians applied routine EEGs in the same group of patients. We compared the time from EEG request to start of EEG acquisition and the setup time between both tests, as well as the duration of artifact and ability to detect abnormal findings. The nonparametric Mann–Whitney two sample T-test was used for comparisons and Kappa score was used to assess the inter-observer reliability.

**Results:** Mean age of patients was 60.4 ± 17.4 years. The inter-observer agreement for detection of abnormal findings was 0.83 for StatNet EEG and 0.74 for routine EEG. The delay from the time of EEG requisition to the start of EEG acquisition in the StatNet test was significantly shorter at 23 ± 11.4 than the conventional EEG, which was 249 ± 343 (p = 0.0001). The setup time was also significantly shorter in the StatNet test, 9.10 ± 2.55 compared to the conventional EEG, 17.51 ± 3.27, (p = 0.0001). Finally, there was no difference in the percentage of artifact during the recording between StatNet and routine EEG respectively (42% vs. 39%, p = 0.89).

**Conclusion:** This study demonstrates that StatNet EEG is valid and reduces the delay to a Stat EEG compared to a conventional EEG, without significant compromise of study quality.

**p417 A ROBUST LOW COMPLEXITY ALGORITHM FOR REAL-TIME EPILEPTIC SEIZURE DETECTION**

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**Purpose:** This paper presents a very low complexity and yet robust method for automated seizure detection using a single intracranial electroencephalogram (iEEG) recording.

**Method:** The ratio of spectral power between 10 and 15 Hz and 0.5–3 Hz frequency bands is used as a measure to detect the epileptic seizures. A threshold is subsequently applied on the measure. Alarm is generated when the measure passes the threshold.

The method was applied on long-term continuous iEEG recordings of 5 patients with refractory partial epilepsy from European Database on Epilepsy, EPILEPSIAE [Klatt J et al. Epilepsia 2012;53(9):1669–1676]. Recordings were obtained with sampling rate of 1KHz at the epilepsy unit of the University Hospital of Freiburg, Germany. The recording length is 780 h containing 54 epileptic seizures.

**Results:** The epileptic seizures were characterized by highly synchronous neuronal activities starting in specific frequency range(s), which decrease as seizures proceed. The frequency of synchrony occurred usually in a single narrow band of iEEG signals, e.g. 13 ± 2 Hz, while recurring similar as both higher and lower order harmonics. The spectral power of low frequency Delta waves (0.5–3 Hz) also reduced by initiating the seizure. Thus the proposed relative spectral power feature highlighted these changes, and reduced the number of false detections.

**On average, the proposed method could detect the presence of epileptic events with high sensitivity of 91% (49 out of 54) and a very low false detection rate of 0.02/h (16 false alarms in 780 h).**

**Conclusion:** By using ratio of two specific spectral power bands, one can build more robust algorithms than using simple spectral powers. The proposed method uses Power Spectral Density (PSD) of iEEG signal, which is very low computational cost. These make the method ideal for clinical application and to be implemented in portable low-power budget devices for real-time monitoring of epileptic patients.

**p419 THE LONGITUDINAL STUDY OF FOCAL EEG FINDING IN TEMPORAL LOBE EPILEPSY: IS IT AGE-DEPENDENT?**

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**Purpose:** To estimate possible influence of aging and epilepsy duration on interictal EEG changes in patients with temporal lobe epilepsy (TLE).
Method: We retrospectively analyzed interictal EEG finding from the medical records at the time of epilepsy onset and during presurgical evaluation in 65 patients (29 men and 36 women; age ranged 18–61 years; mean 37.46 ± 11.29; 39.90 ± 10.79 males, 37.11 ± 11.82 females; p = 0.783) with medically intractable temporal lobe epilepsy (TLE). In all patients the diagnosis of pharmacoresistant TLE was established and all were referred for resective surgery. In all patients interictal EEG findings at the epilepsy onset and during presurgical evaluation were classified as: (i) normal; (ii) nonspecific; (iii) bilateral; (iv) focal; (v) nondetermined. As the change of interictal EEG we considered the different type of dominant finding at the early stages of the disease comparing to the present finding.

Results: In the same cohort, we found 42% patients with focal EEG finding at the epilepsy onset and 88% during presurgical evaluation. We did not find the change of interictal EEG finding in terms of the patient age (p = 0.336), earlier onset (p = 0.286) and epilepsy duration (p = 0.812).

The difference was not presented neither in terms of patient sex, focus lateralization, presence of hippocampal sclerosis and history of febrile seizures.

Conclusion: We found no influence of age at epilepsy onset or seizure duration on interictal EEG finding in patients with TLE. However, better temporal and spatial resolutions during presurgical evaluation were of essential importance for the detection of focal EEG changes.

Conclusion: As already stressed by Schmitt et al, EDB is a specific pattern suggesting NMDAR encephalitis. It appeared sometimes lately during the course of the disease, and can be preceded by precocious signs, like bA and RDA, that should be looked for carefully.

p420 EEG CHRONOLOGICAL CHANGES DURING THE COURSE OF ANTI-NMDA RECEPTORS ENCEPHALITIS: A FOUR CASES STUDY

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Purpose: A specific EEG pattern in Anti-NMDAR encephalitis, the extreme delta-brush (EDB) activity, has been recently described (Schmitt et al. 2013). We sought to analyze retrospectively EEG recordings in 4 patients suffering from Anti-NMDAR Encephalitis, emphasizing on the chronological modifications during the course of the disease.

Method: We visually reviewed the clinical and sequential EEG data (range: 4–45) performed during the acute and recovery phase of the disease. We specifically looked for rhythmic delta frequency activity (RDA), diffuse excess beta frequency activity (bA), and extreme delta brush (EDB) pattern for 3 different periods of time: 1) before 2) during the 10 days period following immunomodulating therapy, and 3) more than 2 months after the beginning of the disease.

Results: All patients were female, aged 16–28 years, with neuropsychiatric symptoms and seizures as common clinical features. Diagnoses were confirmed biologically. On the EEGs, EDB was observed in 3 patients. It appeared at the first registering for 1 patient (day 6 from clinical onset) but only on the second (day 6) or fourth record (day 9) for the others. This pattern can be observed only intermittently (patient 1), and was frequently preceded by other pathological patterns: RDA (3 patients / 4) and bA (4 patients / 4), which seems to mix together secondarily to form the EDB pattern. RDA can be focal or generalized. After 2 months, EEG shows persistent EDB and/or RDA for the three patients.

Conclusion: Anti-epileptic drug (AED) resistance occurs in 30% of epilepsy patients, and is not specific to particular AEDs or syndromes. Transcranial magnetic stimulation (TMS) measures cortical excitability in vivo. Previous work shows cortical excitability is higher in AED-resistant patients compared to treatment-responders, after chronic treatment (Badawy et al, Int J Neural Syst. 2013). The cortical silent period (CSP) was not assessed in this previous work. CSP reflects cortical inhibitory mechanisms; motor evoked potential (MEP) amplitude reflects global cortical excitability. Furthermore, the ratio of CSP/MEP ratio has been shown to reduce between-subjects variability, (Orth et al, Clin Neurophys, 115, 1076–82). We hypothesised that CSP/MEP would differ between well controlled and poorly controlled patients with epilepsy on chronic AED treatment.

Method: We studied 21 patients with well (<4 seizures/year) and 21 with poorly controlled epilepsy (>20 seizures/year). Using Magstim 200 with EMG activity measured from first dorsal interosseous muscle, resting (RMT) and active motor threshold (AMT) were obtained prior to CSP measurements. An automated method was used to measure CSP duration.

Results: Patients with well controlled epilepsy had significantly lower AMT and RMT in the left hemisphere (LH) (AMT p = 0.008, RMT p = 0.003) and right hemisphere (RH) (AMT p = 0.035, RMT p = 0.044). Patients with well controlled epilepsy also had significantly increased MEP amplitude (p = 0.003) and significantly reduced CSP/MEP ratio (p = 0.006) in LH.

Conclusion: According to these data, cortical excitability is higher in well-controlled patients as indicated by increased MEP amplitude and a lower CSP/MEP ratio. This could be due to medication effects or an underlying biological difference between AED responders and non-responders. Future work should examine whether MEP amplitude or CSP/MEP ratio prospectively predict AED response.
litis (RE) was considered based on her clinical presentation. PET scan with FDG indicated diffuse hyper metabolism on the left and hypometabolism on the right. She underwent a lumbar puncture that was unremarkable and her infectious work up was negative. CSF oligoclonal bands were negative as well and CSF electrophoresis was within normal limits. Serum NMDA receptor antibody was positive. Brain biopsy was not performed and her oncological workup was negative.

**Results:** Her seizures were well controlled on a combination of Trileptal and Keppra and her hemiparesis and language regression have been reversed to a large degree with monthly IVIG infusions. Her repeat contrast brain MRI showed no atrophy and her repeat serum NMDA receptor antibody was negative. Her clinical presentation strongly suggested RE but she did not fulfill either part A or B of the diagnosis criteria for this disease. The diagnosis of RE rests on clinical, electrophysiological (EEG) and morphological studies (MRI, histopathology). In most chronic patients differential diagnoses are few.

**Conclusions:** There are a limited number of case reports of Rasmussen’s-like Encephalitis with NMDA receptor antibody positivity. Thus, the clinical significance of this association is yet to be determined. This case emphasizes the particular challenges in the early recognition of Rasmussen’s Encephalitis, before progressive hemiatrophy and progressive loss of neurological functions are evident. Early diagnosis is desirable as immunosuppressive therapy may be most effective at this time and may improve the end point of the disease.

**Abstracts**

**P423 TEMPORAL LOBE EPILEPSY SURGERY IN CHILDREN – ELECTROCLINICAL PROFILES AND OUTCOMES ACCORDING TO ETIOLOGY**

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**Purpose:** To analyse the electro-clinical semiology, neuropsychology and surgical outcomes in children with temporal lobe epilepsy surgery (TLS).

**Methods:** Fifty TLS children (median age 10 years) were studied, including patients with different etiologies: mesial temporal sclerosis (MTS-12), focal cortical dysplasia (FCD-12), tuberous sclerosis (TS-6) and low-grade tumours (LGT-20). Analysis was based on findings from comprehensive multimodal assessment, performed pre-surgically and 1 and 3 years after surgery.

**Results:** Early-onset epileptic spasms linked to focal discharges and generalized epileptiform activity were observed in children with TS (100%), FCD (42%) and LGT (15%). Focal spikes and typical temporal lobe seizures were mostly observed in children with MTS (92%) and in children with LGT with an epilepsy onset beyond 3 years of age (60%). FCD manifests mainly with epileptic spasms and/or focal seizures before 3 years of age (67%). “Hypomotor” and “hypermotor” seizures were also observed. Low cognitive level varied in relation to etiology: TS-100%, type I FCD-71%, type II FCD-25%, MTS-33%, LGT-10%. Psychopathology was noted in 32%, half of them behavioural disorders. Posturgically, favourable seizure outcome was not significantly different among the etiological groups. One and 3 years after surgery, 86% and 88% respectively, were in Engel classes I and II. The mean duration of postoperative follow-up was 6 years. Poor seizure outcome was associated with residual pathology outside the temporal lobe resection. Memory or language improvements were observed in 38% and 14% patients respectively. IQ decline was noted only in two patients.

**Conclusion:** Electro-clinical and neuropsychological features in children with TLS vary in relation to etiology, topography of the lesion, age at seizure onset, and age at evaluation. A favourable postsurgical outcome in respect to seizure control and neuropsychological functioning is obtained in most patients.

**P424 CLINICAL CHARACTERISTICS OF CHILDREN WHO DEVELOP LATE ONSET EPILEPTIC SPASMS: A SINGLE CENTER 3-YEAR REVIEW FROM SINGAPORE**

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**Purpose:** To review the clinical characteristics of children who develop epileptic spasms during the course of their refractory epilepsy.

**Method:** We reviewed our cohort of pediatric patients, who were confirmed to have epileptic spasms captured during their video-EEG recordings, in a 3-year period from 2011 to 2013 inclusive. Epileptic spasms are described as paroxysmal motor movements involving sudden flexion or extension predominantly of axial and/or proximal limb muscles, outside the age of infantile spasms. The characteristic EEG pattern consists of a generalized slow wave transient followed by fast rhythm or brief polyspikes of low amplitude and diffused attenuation described as electrodecremental response. We obtained clinical information regarding prior presentation with infantile spasms, the developmental ability, and the response to anti-epileptic drug (AED) treatment.

**Results:** We have 10 patients with late onset epileptic spasms recorded, with the characteristic EEG patterns. Most of the patients had 2–5 spasms captured in the routine video-EEG study. Half the patients were diagnosed with West syndrome (infantile spasms with hysparrhymia) at least 2 years prior to the onset of epileptic spasms. Eight patients have severe global developmental delay, one has mild mental retardation, and one patient has neuroregression. The genetic causes identified included lissencephaly, tuberous sclerosis, Pallister Killian syndrome, and late infantile neuronal ceroid lipofuscinosis (NCL); acquired causes included intracerebral hemorrhage and enterovirus encephalitis. The child with NCL was conservatively managed with only 1 AED. All the remaining 9 patients failed at least 2 AEDs. Only 1 patient responded favorably with ketogenic diet.

**Conclusion:** Late onset epileptic spasms are associated with children who already have developmental delay. In our series, half of the children who developed epileptic spasms in childhood had prior West syndrome. The response to treatment remains poor despite the use of newer anti-epileptic drugs.

**P425 GENETIC EPILEPSIES WITH FEBRILE SEIZURES PLUS – SPECTRUM OF PHENOTYPES IN PATIENTS WITH SCN1A-RELATED SEIZURES IN POLISH POPULATION**


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**Purpose:** The aim of this research was diagnosis and clinical description of epileptic syndromes caused by SCN1A mutations.

**Method:** 203 patients with epilepsy and/or febrile seizures with suspected SCN1A mutation, based on inclusion and exclusion criteria were included in the screening process.
Results: Mutations were detected in 57 (28%) cases. Majority of patients (50 cases–87.5%) suffered from Dravet syndrome, 8.8% (5 cases) were diagnosed as GEFS+ 3% as vaccines encephalopathy and Panayotopoulos syndrome (1 case per each respectively). Mutations were not detected in children with isolated febrile seizures, family febrile seizures nor in patients with myoclonic – atatic epilepsy, Rasmussen syndrome nor Lennox-Gastaut syndrome.

Conclusion: The frequency of SCN1A mutation in children with suspected Dravet syndrome or GEFS+ in Poland is similar to other countries. SCN1A mutations were also found in Panayotopoulos syndrome, which is very rare. Phenotype spectrum of SCN1A-related disorders is diverse but confirmation of presence of SCN1A gene mutation is essential for correct diagnosis, treatment and genetic counselling, and on the other hand, clinical and EEG data as well familial history is very important to perform appropriate molecular testing.

p427
OUT-OF-HOSPITAL MANAGEMENT OF CHILDREN WITH PROLONGED, ACUTE, CONVULSIVE SEIZURES IN SWEDEN
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Purpose: The Practices in Emergency and Rescue medication For Epilepsy managed with Community administered Therapy (PERFECT) initiative was set up to gain a better understanding of how prolonged, acute, convulsive seizures (PACS) are managed outside the hospital in Europe. This paper presents findings for Sweden.

Method: A review of existing clinical and non-clinical guidance governing the management of PACS and the administration of rescue medication was conducted, as was a survey of 12 neurologists or paediatric neurolologists, 3 paediatricians and 5 epilepsy nurse specialists to gauge their perceptions of the care received by children who present with PACS outside of hospital.

Results: Existing guidelines, be they national, regional or local, offer few explicit recommendations for out-of-hospital settings. According to Socialstyrelsen’s guidelines on the management of medicines at school, the treating physician is responsible for drawing up an individualised care plan, together with the school head, for all children with a history of PACS. Epilepsy specialist nurses play a critical role in ensuring that such plans get implemented, and act as a critical link between clinical and community settings. Regions where specialist nurses are not present may find it more difficult to ensure that children receive appropriate management throughout the chain of care.

Conclusion: Findings suggest that gaps remain in the management of PACS outside of hospital. National guidelines that span both in- and out-of-hospital settings, greater investment in epilepsy specialist nurses and systematic training of all relevant caregivers on the appropriate management of PACS in children are needed.

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p428
MEDICAL REDUCTION OF ROLANDIC SPIKES AND SPEECH DISORDERS REDUCTION. IS IT EQUAL?
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Purpose: To examine the correlation between the medicinal reduction of Rolandic spikes and speech disorders in children.

Method: The study included 29 patients aged 2–13 years (mean age 6 years 8 months) with dynamic observation from 2 to 5 years. In all patients were identified specific EEG epileptiform abnormalities in the form of Rolandic spikes with different lateralization. After medical reduction of these disorders children were observed for 2–5 years. Patients were divided into 3 groups depending on the age of the first ictus (group 1 – under 3 years, the group 2 – from 3 to 7 years and a group 3 – after 7 years old). All children received antiepileptic therapy with Sultiamine in age dosage, additional drug therapy was not performed. All children received speech therapy.

Results: The most severe speech disorder detected in children with Rolandic spikes localization in centro-temporal region. During follow up for 5 years was observed repeated change of lateralization in all children with a certain regularity. It was found that the reduction of speech disorders are not in direct correlation to the AED induced Rolandic spikes reduction.
p430
WEST SYNDROME: CLINICAL- ELECTROENCEPHALOGRAPHY CORRELATION
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Purpose: To analyze etiology, clinical and EEG features the most common form of infantile Epileptic Encephalopathy – West syndrome.

Method: In the outpatient Department of the pediatric medical University from 2009 to 2014 examined 575 patients aged from 1 month to 18 years with paroxysmal disorders. West syndrome diagnosed in 32 cases (5.6%). All patients underwent clinical and laboratory, the electroencephalographic study (videoEEG), of molecular-genetic and neuroimaging.

Results: The disease has debuted the first year of life in all patients (debut 4 ± 1.2 months). Slight predominance of males (17: 15). Etiological factors were malformations in 10 children (focal cortical dysplasia, lissencephaly, agenesis of the corpus callosum), congenital neurological and skin disorder (tuberous sclerosis – 4, encephalotrigeminal angioma-tois Sturge-Weber syndrome-1), genetic syndromes (Aicardi syndrome), chromosome abnormalities (Down syndrome in one patient). Perinatal factors - hypoxic-ischemic and hemorrhagic brain damage – caused development of the disease in 11 patients (34%). Postnatal factors have 2 children were transferred meningoencephalitis and development of the secondary ischemia-hemorrhagic infarction have a child in the postoperative period. Idiopathic option West syndrome diagnosed in 2 cases. 31 children disease debuted with the development of infantile spasms, in one case observed transformation Ohtahara syndrome. Prior to the debut neurological deficit was observed in 24 children. All the patients of the main ictal manifestations were infantile spasms, usually mixed (flexion-extension). Hypsarrhythmia was an obligate interictal pattern. A classic option is indicated by 21 patients, 11 – modified version of hypersrhythmia (asymmetric, hypsarrhythmia with episodes of voltage attenuation with pattern »flash-suppressions, hypersynchrony). All patients were treated with a combination of the anticonvulsants and hormonal drugs. Remission for 6 months was observed in one patient, in other cases a transformation West syndrome in partial or multifocal resistance epilepsy or Lennox-Gastaut syndrome.

Conclusion: West syndrome is polietiologic disease with characteristic clinical and electrophysiological manifestations and poor outcome.

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A CHILD WITH ICTAL VOCALIZATIONS AND GENERALIZED EPILEPSY
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Purpose: To report a patient with unusual ictal vocalizations observed in the context of generalized epilepsy.

Method: Case report and review of the literature.

Results: We report the case of a child aged 13 years with juvenile-onset generalized epilepsy who presented with ictal “ovine vocalizations” (resembling bleating of the sheep). The ictal electroencephalogram (EEG) revealed a clear correlate of vocalisations with time-locked generalized spikes and polyspike discharges and the 3T cerebral magnetic resonance imaging (MRI) ruled out any focal lesion. The boy is currently seizure free under treatment with valproic acid, after 8 months of follow-up.

Conclusion: Ictal vocalizations in the form of articulate speech and nonspeech sound productions have been described in focal epilepsies, with seizures mainly originating from the frontal and temporal lobe. To our knowledge, this phenomenon has not been described in generalized epilepsies. Our observation suggests that ictal non-speech vocalizations may be observed not only in focal, but also in generalized epilepsies; the exact underlying mechanism of this ictal phenomenon needs to be further delineated.

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NEURODEVELOPMENT IN PRESCHOOL CHILDREN OF FIFE AND LOTHIAN EPILEPSY STUDY: NEUROPROFILES – A POPULATION-BASED STUDY
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Purpose: There is limited population-based data on neurobehavioural comorbidities in early-onset epilepsy (EOE) (onset < age 5 years). Early identification increases the likelihood of optimum medical, social and educational management. NEUROPROFILES, an ongoing 2 years, population-based, case-control study aims to identify the spectrum of neurobehavioural comorbidities, their risk factors, and to explore neuroimaging and eye-tracker biomarkers.

Method: Since May 1, 2013 all Fife and Lothian resident preschool children with newly diagnosed EOE are being enrolled using active multi-source capture-recapture surveillance and offered detailed age-appropriate neuropsychological assessment including Bayley Scales of Infant and Toddler Development-III, Wechsler Preschool and Primary Scales of Intelligence-III, NEPSY-II, Conners Early Childhood, Social Resonance Scale-2, Adaptive Behaviour Assessment, and Behaviour Rating Inventory of Executive Function-Preschool. Matched controls are being recruited through public advertisement. Eye-tracking and brain MRI correlates are being examined.

Results: 18 children with EOE (incidence 68/100,000/year) have been identified (13M:5F; mean age 28 months, range 2-56). Fifteen EOE (83%, 95% CI 66–100) and 16 controls (7M:9F; mean age 33 months, range 4-58) have been assessed. Preliminary analyses indicate some evidence toward a greater proportion of EOE children with cognitive ability scores < 1SD below the mean vs. controls (p = 0.07). They also exhibit poorer language development (p = 0.01) and motor development (p = 0.02), poorer adaptive behaviour (p = 0.005), social communication (p = 0.005), social functioning (p = 0.02), and more externalising behaviour (p = 0.001).

Conclusion: NEUROPROFILES is the first UK prospective population-based study to focus on neurobehavioural comorbidities in children with EOE. Preliminary data suggest impaired neurodevelopment is detectable early in EOE, particularly in social and behavioural domains. Our final data may provide the basis for development of guidelines for determining individual psychosocial and educational needs of affected children.

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THE CHARACTERISTICS OF EPILEPTIC CHILDREN HOSPITALIZED IN EPILEPSY CENTER FOR CHILDREN IN POLAND
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Purpose: The aim of the study was to describe the epileptic population of children hospitalized in The Department of Developmental Neurology, Poznan University of Medical Sciences, Poland.

Method: Between 2011 and 2013 years 2903 patients were hospitalized in the Department of Developmental Neurology. Age of children hospitalized was 1–18 years of age. Girls accounted for 46% of the study group.

Results: The most common cause of hospitalization were epilepsy (27%), tension headaches (9.5%) and migraine (6%), developmental delay (8.6%), Attention Deficit Hyperactivity Disorder (5%), narcolepsy (4%), syncope (4%), autism (4%), sleep disorders (3%), mixed disorders of conduct and emotions (5%), school problems (3%) and others less frequently observed. The most common form of epilepsy observed was focal epilepsy (70%). The antiepileptic drugs used to treat were: VPA (68%), LEV (24%), CBZ (18%), LTG (10%), TPM (8%), CLB (7%), OXC (7%), VGB (5%) and others. Incorrect EEG records were detected (68%), LEV (24%), CBZ (18%), LTG (10%), TPM (8%), CLB (7%), OXC (7%), VGB (5%) and others. Incorrect EEG records were detected in significant part of epileptic patients (82%). Abnormal in magnetic resonance imaging (MRI) of head were observed in the most of patients with epilepsy (56%). Among the most common MRI abnormalities cortical atrophies (47%), arachnoid cysts (10%), cortical abnormality and microgyria and pachygyria were observed in MRI.

Conclusion: The most common cause of hospitalization in the Department was epilepsy. In the study group the focal seizures were most frequently observed. The drug most commonly used to treat epilepsy was VPA. The cortical atrophies was observed most often.

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EPILEPSY IN A COHORT OF CHILDREN WITH TUBEROUS SCLEROSIS COMPLEX
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Epilepsy is one of the most common medical problems in tuberous sclerosis complex (TSC) leading to search for medical help.

Purpose: To analyze the characteristics and the course of epilepsy in our cohort of patients with TSC.

Method: Retrospective analysis of medical records of all TSC cases registered within 1982–2012 at the Kaunas Clinics.

Results: The diagnosis of TSC was confirmed in 44 children aged 2 weeks–16 years (median 2 years at diagnosis). Epilepsy was diagnosed in 41 (93%), in 52% of cases it started within the first year of life as infantile spasms (IS) (34%) or focal seizures (FS) (39%), mainly. Epilepsy was refractory in 86% of cases, 18% experienced epileptic status. Cognitive development was abnormal in 30 (73% of total group), all had epilepsy. IS as initial seizure type were related to subsequent refractory seizures (p = 0.014). Early onset of epilepsy was associated with the number of antiepileptic drugs used (p = 0.03) and cognitive deficits (p = 0.011). Vigabatrin (VGB) (available since year 2000) was used in 17 (41% of epilepsy cases). 5 patients treated with VGB for IS became seizure-free for 1 year or more, 4 had temporary/partial benefits and 2 patients with FS became seizure-free, 5 had temporary/partial benefits. Relatively preserved cognitive functioning was in 3/7 patients with FS and in 2/8 patients with IS.

Conclusion: Early seizure onset was related to drug-resistant epilepsy and cognitive disorder regardless the types of medications used. VGB was more effective for the control of IS than FS, but better spasm control did not always determine better cognitive outcomes, though our small group did not allow to make reliable comparisons.

p436
NOCTURNAL PARTIAL SEIZURES WITH AFFECTIVE SYMPTOMATOLOGY: 10 YEARS FOLLOW-UP
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Purpose: Nocturnal paroxysmal events with affective symptomatology may have various etiologies. Epileptic seizures with affective semiology consisting of brief and sudden panic symptoms associated with interictal spike-waves complexes in temporal regions.

Our purpose is to better evaluate diagnosis and prognosis of patients with nocturnal partial seizures and affective symptomatology.

Method: We describe two patients of 12 and 14 years old with paroxysmal nocturnal events in differential diagnosis with pavor nocturnus, anxiety disorders, gastroesophageal reflux disease. Intercritical and critical Video-EEG and neuroimaging were performed.

Results: In both patients epilepsy started in preschool age with stereotyped episodes characterized by sudden awakening, terrifying expression, myoclonus palpebral uni / bilateral and, in one case, autonomic symptoms. Serial video-EEG showed seizures starting from temporal regions. The neuroimaging showed no significant alterations. After 10 years follow-up, all the patients showed an evolution almost insensitive to drug therapy with spontaneous improvement.

Conclusion: Differential diagnosis in nocturnal paroxysmal events is often hard to reach. In our patients, diagnosis was made by serial EEG recordings and critical Video-EEG. The stereotypical and overlapping characteristics of seizures and the lack of sensitivity to therapy appear to be suggestive of an age-related electro-clinical entity with unknown etiology and spontaneous benign course, as already suggested in the literature.

p437
CLINICAL AND NEUROLOGIC OUTCOMES OF GEFS+ AT CHEONGJU IN SOUTH KOREA
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Purpose: Febrile convulsion is the most frequently diagnosed convulsive condition in infancy or childhood, with an incidence of about 2–15%. In this study, we checked clinical feature and neurologic assessment of GEFS+ (Generalized Epilepsy with Febrile Seizure Plus).

Method: This study retrospectively examined clinical feature and neurologic assessment of GEFS+. We studied 24 GEFS+ children of Chungbuk National University hospital from January 2012 to December 2012. We formed them into two groups by age of first seizure; Group A (<6 years) and Group B (≥6 years). We analyzed the clinical features, EEG findings and the neurologic outcomes of the subjects.

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Results: The mean age of GEFS+ was 5.6 years. 11 subjects had their initial febrile seizures under 6 years of age while 13 subjects after 6 years of age. 5 Subjects had family history of seizure. The types of convulsions were mainly generalized. Eight (33.3%) showed abnormal finding on EEG and eight (33.3%) were treated with anti-epileptic drug. The group with the initial seizures occurred under 6 years of age had more family of seizures, more developmental delay and was treated by antiepileptic drug.

Conclusion: This study showed clinical feature and neurologic assessment of GEFS+.

p438
THE INDIVIDUAL TOLERABILITY OF THE VALPROIC ACID IN CHILDREN SUFFERING FROM EPILEPSY WITH CYTOCHROME P450 POLYMORPHISMS AND MITOCHONDRIAL DISORDERS
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Purpose: Valproic acid (VPA) is a widely-used antiepileptic drug with good efficacy, safety and pharmacoeconomic profile with not frequent adverse drug reaction. The present study investigated the effect of cytochrome P450 polymorphisms and GSTM1, GSTT1, NAT2 genetic polymorphisms on the side effects in children received the VA.

Methods: Patients with different forms of epilepsy, seizures frequency, illness duration aged from 6 months to 16 years have been studied. 33 patients had side effects: neurological toxicity, hepatotoxicity, muscle fatigue, thrombocytopenia. DNA samples analysis was performed with method of oligonucleotide biochips hybridization (BIOCHIP Ltd, Russia).

Results: In children with epilepsy with adverse drug reactions the genetic polymorphisms were found: heterozygous on CYP1A1 in 5 patients (15.1%), heterozygous CYP2C9 (C430T) – 9 (27.2%), heterozygous A1075C-3 (9%) totally on CYP2C9-12 (36.3%), CYP2C19 (G598A)-9 hetero and 1 homozygous (30%), CYP2D6 (G1934A)-hetero 11, homo 2 (39.4%), CYP2D6 (DelA2637)-6 (18.2%) – totally on CYP2D6-19 (57.6%). The homozygous deletion GSTM1 in 21 patients (63.6%), GSTT1 in 4 patients (12.12%), NAT2 hetero/homo 27 patients (81.8%). Two and more polymorphisms on cytochromeP450 and GSTM, GSTT1, NAT2 had 93.9% of patients. The VPA concentration were significantly correlated with side effects in children with epilepsy with adverse drug reactions the genetic polymorphisms in CYP2C9, CYP2D6, in genes of the second phase of biotransformation (GSTM1, GSTT1, NAT2). In these patients the mitochondrial diseases (MD) were confirmed by molecular analysis of mtDNA by sequence.

Conclusions: In our investigation the main role in adverse drug reactions in VPA treatment plays the genetic polymorphisms in CYP2C9, CYP2D6, in genes of the second phase of biotransformation (GSTM1 and NAT2) with two and more of genetic polymorphism in one patient. Adverse effect of VPA in children with MD didn’t determine by CYP450 polymorphisms, but because of mitochondrial metabolism of VPA.

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2-YEAR EEG FOLLOW-UP OF 24 CHILDREN WITH FREQUENT INTERICTAL EPILEPTIFORM DISCHARGES (IEDS) IN THE SPECTRUM OF BENIGN FOCAL CHILDHOOD EPILEPSIES: CORRELATION OF IED CHANGES WITH CHANGES IN MEDICATION AND SEIZURE FREQUENCY
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Purpose: We prospectively determined the 2-year time-course of the IED frequency in children with benign focal epilepsies (BFE) and/or typical IED. IED changes were correlated to changes in seizure frequency and AEDs (anti-epileptic drugs).

Method: 24 children were observed with a repeated 24-h ambulatory EEG at 6 months and 2 years. 30 10-s EEG pages in waking and 30 pages in sleep were categorized as: [No IEDs], [10–20% IEDs], [20–40% IEDs], [40%–80% IEDs], [80–100% IEDs] on the page (I s containing IED(s) = 10%). “EEG remission” (EEG-R) was defined as stable decrease/disappearance of IEDs compared to baseline concluded from both EEGs.

Results: At baseline 3 patients had no observed seizures, 4 were seizure free ≥2 years, 17 had ≥1 seizures last year. 13 patients used AEDs. 12 patients were identified with EEG-R after 2 years. A higher age of seizure onset (mean 5.0 vs. 7.3 years, R = 0.51 p = 0.01) was the only baseline feature correlated with EEG-R. EEG-R could not be predicted from EEG changes at 6 months compared to baseline. EEG-R was significantly correlated with seizure freedom in the last 6 months of the 2-year follow-up period, being observed in 12/12 patients with EEG-R and in 5/12 patients without EEG-R (R = 0.51 p = 0.01). EEG-R was not correlated with AED changes. Seizure reduction was not correlated with AED changes.

Conclusion: We confirm the self-limiting time-course in this disease concerning IED frequency and seizure frequency, which we observed in 50% of the patients in 2 years, and especially in patients with seizure onset at older age. We found no relationship of this benign course with AED changes.

Our results therefore encourage the restraint in treating these patients with AEDs. If patients with on-going frequent IEDs and cognitive failure can benefit from treatment, is still a question to be answered.

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ENDOSCOPIC DISCONNECTION OF HYPOTHALAMIC HAMARTOMA IN CHILDREN WITH DRUG RESISTANT EPILEPSY: TECHNIQUE AND RESULTS REGARDING A POPULATION OF 94 PATIENTS
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Purpose: Hypothalamic hamartomas (HH) may induce drug resistant epilepsy (DRE) requiring surgical treatment. Disconnective procedures have been shown to be safe and as effective as removal of the lesion. We report on a large surgical series of 94 pediatric patients from our institution, with emphasis on the surgical technique and seizure outcome.
Method: Ninety-four patients with HH and DRE operated on between 1998 and 2013 were retrospectively reviewed. Hamartoma disconnection was performed using either monopolar coagulation, thulium laser or ultrasonic dissection through a Robot-guided transventricular endoscopic route. Few patients were operated through an open pterional approach. Results in terms of safety and outcome of epilepsy were analyzed.

Results: Mean age at surgery in all patients was 11.6 years. Mean age at seizure onset was 30.5 months; 68% of the patients experienced gelastic or dacrycyst seizures as first seizure type. Mental retardation was present in 59%. According to Delalande’s classification, 4.3% of the patients had a hamartoma of type I, 58.5% of type II, 25.5% of type III, and 11.7% of type IV. Endoscopic transventricular disconnection was performed in 96% of the patients: in a single procedure in 53% and in more than one procedures (2–5) in 47%. With a mean follow up of 5.8 years, 74% of all patients and 83% of patients with type II hamartoma had an excellent seizure outcome (Engel 1 or 2). Eighteen patients presented postoperative complications which consisted in recent memory deficit (4), hemiparesis (2), hormonal dysfunction (10), third nerve palsy (3) and hydrocephalus (5). With a mean follow up of 5.8 years, 74% of all patients and 83% of patients with type II hamartoma had an excellent seizure outcome (Engel 1 or 2). Eighteen patients presented postoperative complications which consisted in recent memory deficit (4), hemiparesis (2), hormonal dysfunction (10), third nerve palsy (3) and hydrocephalus (5).

Conclusion: Transventricular endoscopic HH disconnection is well tolerated, with an acceptable morbidity, and can easily be repeated in case of large lesions or seizure persistence. Overall seizure outcome is excellent, particularly for type II hamartomas.

Epilepticus (AEIMSE): Report of four cases

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Purpose: Some acute encephalopathies, which combine specific age of occurrence, fever as an apparent triggering factor, and development of status epilepticus, are now defined as “acute encephalopathies with inflammation-mediated status epilepticus” (AEIMSE).

Method: We describe onset, follow-up and outcome of four cases observed at our hospital, from 2009 to 2013. Intercritical EEG, neuroimaging, neuropsychological assessment and immunohistochemical analysis were performed.

Results: All patients were female with mean age of 6 years at onset (range 3 years 6 months–10 years). All were previously healthy children and presented, after a few days from a febrile episode, recurrence of fever associated with focal and generalized seizures which rapidly evolved in acute encephalopathy with status epilepticus. Examination for investigate viral and autoantibodies causes resulted negative. In two patients, MRI showed hypersignal in T2/Flair or TR/FLAIR, mainly in hippocampal regions. In the other two patients MRI were negative. AE treatment was performed using either monopolar coagulation, thulium laser or ultrasonic dissection through a Robot-guided transventricular endoscopic route. Few patients were operated through an open pterional approach. Results in terms of safety and outcome of epilepsy were analyzed.

Conclusion: All our patients presented a biphasic clinical course, as seen in another case series. Knowledge of the etiology, pathologic mechanisms, or efficient treatment of this disastrous encephalopathy is still limited. Early control of seizure activity is likely to be the key to reduce relevant sequelae, but epilepsy outcome can be unpredictable.

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COULD VAGUS NERVE STIMULATION SERVE AS FIRST LINE OF TREATMENT FOR EPILEPSY IN RETT SYNDROME?

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Purpose: Rett Syndrome (RTT) is an X-linked neurodevelopmental disorder characterized by deceleration of head growth, loss of spoken language, and of purposeful hand skills, gait abnormalities and stereotypic hand movements. Epilepsy affects 50–90% patients. We present the clinical evolution of 2 patients suffering from RTT and epilepsy treated with Vagus Nerve Stimulator (VNS).

Method: Case 1: A 5 year old girl with RTT early seizure variant – with a clinical picture highly suggestive of CDKL5 mutation and also epileptic seizures which had infantile spasms aspect, and after 1 year of age Lennox-Gastaut syndrome (atonic and tonic seizures, atypical absences), almost 60 seizures daily. The seizures were resistant to all antiepileptic drugs, corticosteroids and ketogenic diet. Her EEG had hypsarrhythmia which persisted in time. She had motor and cognitive developmental delay. At the age of 4 years and 6 months, she was implanted with VNS. Good seizure control was obtained, her cognition improved and she began to walk independently.

Case 2: A 6 year old girl suffering from RTT early seizure variant, with epilepsy from the neonatal period, initially as myoclonic seizures and then infantile spasms, which were resistant to antiepileptic drugs. After being implanted with VNS at 5 years of age, good seizure control was obtained with motor progress and interpersonal contact improvement despite persisting EEG abnormalities.

Results: VNS had a good effect on both epileptic seizures and global development in patients with RTT.

Conclusion: Considering the evolution under treatment, the authors raised the idea of using VNS as a first line of treatment for epilepsy in RTT. Larger prospective studies are necessary to confirm this hypothesis.

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COULDEPILEPSY IN 16P11.2 MICRODELETION: DESCRIPTION OF EPILEPTIC PHENOTYPE IN 5 CHILDREN

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Purpose: To describe the epileptic phenotype in 5 children with de novo 16p11.2 microdeletion.

Method: We reviewed a case series focused on epilepsy features, non-epileptic paroxysmal events, and extraneurological symptoms. Genetic analysis included array CGH in patients and their parents and the functional analysis of genes involved in microdeletion.

Results: Epilepsy started within the second year of life in all cases. The onset of epilepsy was marked by apparently generalized seizures, followed by focal seizures; one patient presented with an epileptic encephalopathy characterized by drug resistant spasms. Non epileptic paroxysmal events were associated in two cases in the form of paroxysmal kinesigenic dyskinesia and motor stereotypes. The 16p11.2 microdeletion included the following genes with a potential role in epileptogenesis: QPRT (quinolinate phosphoribosyltransferase), DOC2A
Abstracts

EPILEPSY IN CHILDREN WITH RARE GENETIC DISORDERS
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Purpose: To present cases of children with rare genetic diseases accompanied with epileptic seizures.

Method: Files of 8 children (4 male, 4 female) with rare genetic disorders are evaluated. Results from genetic testing, clinical symptomatology, comorbid conditions, investigations (EEG and brain MRI) and therapies are presented.

Results: Genetic examinations are performed in children with Angelman Syndrome, Rett Syndrome, Turner Syndrome, Wolf-Hirschhorn Syndrome, Sotos Syndrome, Cornelia de Lange Syndrome, X-linked adrenoleukodystrophy and tuberous sclerosis. The diagnosis of these conditions was confirmed via genetic testing. Epileptic seizures are registered in patients with Angelman Syndrome, Rett Syndrome, Wolf-Hirschhorn Syndrome, Turner Syndrome, tuberous sclerosis, Cornelia de Lange Syndrome, whereas epileptic EEG forms were found in the rest of the conditions, however without clinical correlation. Generalized changes on the EEG are found in children with Angelman Syndrome, Rett Syndrome, Cornelia de Lange Syndrome, Wolf-Hirschhorn Syndrome, and tuberous sclerosis; while focal changes appear in patients with X-linked adrenoleukodystrophy, Turner Syndrome and Sotos Syndrome. Evident changes in the brain MRI are found in 5 children: agenesis corpus callosum, demyelinating changes, reduction of gray matter volume, and dilatation of lateral ventricles. Nearly all children suffer from delayed speech, psychomotor, psychosocial and mental development and almost all children have dysmorphic stigmata. Concerning the treatment of seizures, the following antiepileptic drugs were used: Valproates, Levetiracetam, Carbamazepine and Lamotrigine. It should be noted that the child with X-linked adrenoleukodystrophy died at the age of 10.

Conclusion: Taking into consideration the fact that all children present from light to severe developmental abnormalities which affect physical and intellectual development, antenatal diagnosis is necessary in risky pregnancies and in families with children with genetic disorders. Maximal efforts need to be put into efficiently reducing epileptic seizures, but equally for treatment of delayed speech, psychomotor and psychosocial development.

OUTCOME OF INFANTILE SPASMS WITH ACTH TREATMENT IN HOLOPROSENCEPHALY PATIENTS-CASE REPORTS
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Purpose: Holoprosencephaly is a complex brain malformation characterized by failure of complete separation of the forebrain into two distinct cerebral hemispheres and into a distinct telencephalon and diencephalon and is typically associated with midline facial anomalies. Approximately half of the children with holoprosencephaly have seizures including infantile spasms. The aim of our material is to present two clinical cases from our own experience with holoprosencephaly and infantile spasms with good outcome after ACTH treatment.

Method: Both cases had holoprosencephaly revealed by brain imaging and infantile spasms with onset at the age of around 6 months, associated with hypsharhythmia pattern on EEG. As Vigabatrin is not available in our country the first choice of treatment was Topiramate with doses gone up to 10 mg/kg/day but no response was achieved in either of them. The second step was initiation of adrenocorticotropic hormone with seizure control shortly after initiation. We use short cures of ACTH administration over a 4 weeks period.

Results: Seizure control was obtained shortly after initiation of ACTH treatment and cessation of seizures is now longer than 10 months for both patients.

Conclusion: Even if ACTH efficacy has been demonstrated in infantile spasms the exact mechanism of action remains unclear. The cessation of infantile spasms under ACTH treatment in the two clinical cases with this type of structural brain malformation comes to emphasize once more onto the superior therapeutic efficacy and the complex mechanism of action of ACTH treatment.

DRUG-RESISTANT EPILEPSY AND EPILEPTIC SYNDROMES IN CHILDREN
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Objective: To study the etiological, clinical features and structural changes in the brain at early age children with drug-resistant epilepsy.

Materials and methods: We studied 59 children (boys – 36, girls – 23) with drug-resistant epilepsy.

Results: Epileptic syndromes in study group presented as epileptic encephalopathies in 30 patients – 50.8% (Otahara syndrome – 1, severe myoclonic epilepsy in infancy – 2, malignant migrating partial seizures in infancy – 1, West syndrome – 20, Lennox-Gastaut syndrome – 6); symptomatic generalized epilepsy in 21 patients – 35.6%; symptomatic focal epilepsy in 8 patients – 13.6%).

Results of MRI/CT study: Cortical atrophy was presented in 25 (42.4%) patients with outcome of hypoxic-ischaemic encephalopathies, congenital viral meningoencephalitis, natal intracranial haemorrhage. Malformations of cortical development in combination with other brain abnormalities were found in 18 (30.5%) patients and included schizencephaly/hydrocephalus, schizencephaly/pachygyria, hemimegalencephaly/asymmetric hydrocephalus, lissencephaly, pachygyria/agenesis of the corpus callosum/hydrocephalus, laminar heterotopia, polymicrogyria, congenital porencephaly. In 3 patients with tuberous sclerosis were detected cortical tubers, in 5 patients with outcome of herpes encephalitis - secondary porencephaly, in 2 patients with temporal lobe epilepsy - mesial sclerosis, in 1 patient - recurrent frontal lobe astrocytoma, in 1 child with Leigh disease - symmetrical areas of low density in the basal ganglia and brainstem. In 7 cases (11, 9%) structural changes in the brain have not been identified.

Conclusion: Pre-, peri- and postnatal brain injury was probably the commonest cause for 42.4% of cases. Brain congenital anomalies were found in one-third of cases. Severe hypoxic-ischemic encephalopathy, intrauterine viral infection, congenital malformations of cortical development of the brain led to the development of drug-resistant epilepsy and epileptic syndromes. The absence of structural changes in 7 cases requires an
p451
EFFECT OF MODIFICATIONS OF THE NATIONAL VACCINATION PROGRAM ON SEIZURE RISK FOLLOWING PERTUSSIS VACCINATION IN DRAVET SYNDROME PATIENTS IN THE NETHERLANDS

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Purpose: In Dravet syndrome (DS), an epileptic encephalopathy caused by SCN1A-mutations, first seizures are reported following pertussis vaccination in 7–57% of cases. We studied the effect of modifications in the Dutch vaccination program on the risk of first and subsequent seizures following vaccinations in DS-patients.

Method: We retrieved data from hospital, child-health-clinic, and the vaccination register for all DS-patients with pathogenic SCN1A-mutations, below the age of 19, after parental consent. Seizures within 24 h after vaccination were considered “vaccination-associated”. Modifications studied were (i) the advancement of start of the schedule from 3 to 2 months of age in 1999 (“wP3” vs. “wP2”) and (ii) the transition from whole-cell to the less reactogenic acellular pertussis vaccine in 2005 (“aP2”). Differences were tested using non-parametric, Chi-square or Fisher’s test and multivariate logistic regression.

Results: In 16 of 77 DS-children (21%) the first reported seizure was vaccination-associated. For wP3 this was 29% (6 of 21), for wP2 19% (5 of 26) and for aP2 12% (3 of 24) (p = 0.4) with similar median ages (3.7, 4.0, 4.3 months, resp., p = 0.9). The median age at first non-vaccination-associated seizure was similar between groups with and without vaccination-associated seizure onset (5.5 resp., 6.1 months, p = 0.449). 92% of DS-children received all 4 infant-vaccinations, but 24% without pertussis component. The risk of reported subsequent seizures following vaccination in infancy was significantly lower for aP and non-pertussis vaccines (p < 0.001), bilateral independent interictal epileptiform discharges during wakefulness (p < 0.007) and sleep (p < 0.001); less lateralized and localized ictal EEG discharges (p < 0.001), staring (p < 0.001), oro-alimentary automatisms (p = 0.008), and head deviation (p = 0.03); more frequent bilateral hand dystonia (p < 0.01), and bilateral abnormal brain MRI (p < 0.001).

Conclusion: Our data suggest the existence of a well recognizable BTLE phenotype that can be differentiated non-invasively from UTLE. In BTLE the epilepsy onset occurs later in life and hippocampal sclerosis is significantly less frequent than in UTLE. The bilateral involvement of temporal lobes rarely produces head deviation and oro-alimentary automatisms, whereas bilateral hand dystonia, bilateral ictal/interictal EEG, and normal MRI or bilateral MRI abnormalities are significantly more expressed in BTLE.

The recognition of a peculiar BTLE phenotype may have important prognostic and treatment implications.

p453
Efficacy of the ketogenic diet in Dravet syndrome vs. other therapies- when to start with?

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Purpose: To evaluate the efficacy and tolerability of the ketogenic diet (KD) in patients with Dravet Syndrome (DS) and to determine its place in the context of other treatment regimen.

Method: This retrospective chart review included all children with genetically confirmed DS treated at our center since 1999. Data collected included type of mutation, age at treatment initiation and treatment lag, overall seizure frequency and frequency of different seizure types, especially prolonged seizures and status epilepticus. Efficacy and safety of the KD were evaluated comparing documented side effects and seizure count 3 months prior to treatment (baseline) with that at 3, 6, 12 months and last follow-up after initiation of the KD. Response was defined as >50% reduction in seizure frequency. In addition, the efficacy of the KD at 3 months was compared with that of various antiepileptic drug (AED) regimens and the vagus nerve stimulation (VNS).

Results: Responder rates of the KD were equally effective than the currently propagated gold standard Stiripentol + Valproate + Clobazam and

p452
BITEMPORAL EPILEPSY: A SPECIFIC PHENOTYPE IN THE TEMPORAL LOBE EPILEPSY SPECTRUM?

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Purpose: Besides the classical “mesio-temporal” epilepsy syndrome, a spectrum of different unilateral temporal lobe epilepsy (UTLE) subtypes has been recognized by SEEG. A bilateral form of TLE (BTLE) has been hypothesized, but a specific phenotype has not been described.

Our study aims to identify the electro-clinical and neuroimaging features of BTLE. The final aim is differentiating BTLE from UTLE, based on the hypothesis that BTLE may be characterized by a specific phenotype.

Method: Among the patients submitted to presurgical evaluation at the three participating epilepsy centers, we identified 48 BTLE subjects with video-EEG recorded seizures showing a significant bilateral TL involvement.

We collected the electro-clinical and neuroimaging data of all of these patients. The study population was then statistically compared to an historical group of 38 UTLE patients surgically treated and seizure free since then (follow up >1 year).

Results: BTLE patients showed significant differences compared to UTLE: older age at epilepsy onset (p = 0.009); less positive family history for epilepsy (p = 0.02); more frequently normal brain MRI (p < 0.001); bilateral independent interictal epileptiform discharges during wakefulness (p < 0.007) and sleep (p < 0.001); less lateralized and localized ictal EEG discharges (p < 0.001), staring (p < 0.001), oro-alimentary automatisms (p = 0.008), and head deviation (p = 0.03); more frequent bilateral hand dystonia (p < 0.01), and bilateral abnormal brain MRI (p < 0.001).

Conclusion: We suggest the existence of a well recognizable BTLE phenotype that can be differentiated non-invasively from UTLE. In BTLE the epilepsy onset occurs later in life and hippocampal sclerosis is significantly less frequent than in UTLE. The bilateral involvement of temporal lobes rarely produces head deviation and oro-alimentary automatisms, whereas bilateral hand dystonia, bilateral ictal/interictal EEG, and normal MRI or bilateral MRI abnormalities are significantly more expressed in BTLE.

The recognition of a peculiar BTLE phenotype may have important prognostic and treatment implications.
Abstracts

Bromides (responder rates 70%:89% and 70%:78%), showing no statistical difference to Valproate monotherapy (70%:48%), Topiramate (70%:35%), VNS (70%:37%), but being significantly superior to Levetiractant (70%: 30%) (p = 0.007). No status epilepticus occurred while patients were on the diet, and the frequencies of prolonged generalized and myoclonic seizures were reduced as compared to pretreatment baseline. No severe side effects requiring termination of the KD were observed. Although the effect of the KD was independent of age at initiation, it had to be withdrawn due to incompliance more frequently in solid food-fed older children as compared to infants and young children treated with the liquid ketogenic formula.

Conclusion: According to our results the KD should be strongly considered early for infants with DS shortly after disease onset.

p454
INCREASED FREQUENCY OF PRE-EXISTING SEIZURES DUE TO VOLTAGE-GATED POTASSIUM CHANNELS (VGKC) – COMPLEX-ASSOCIATED LGI1 AUTOANTIBODIES ENCEPHALITIS

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35 year old female patient was admitted on 27.03.2013 with spells of tingling feeling on the nose and forehead region, strange taste and smell sensations and bright colourful images with deja vu feeling. She had experienced approximately 100 attacks, lasting 20–60 s per day since 26.02.2013. After the attack she felt tired, complained of memory problems, clumsiness in the right hand and paranoid thoughts. Patient had had similar tingling feeling with duration of 3–4 s 1–2 times per month for years. She also had depressive episodes with self-injuring during the last 10 years. Also, she had experienced attacks induced by emotional stress (diagnosed by psychiatrist as non-epileptic breath-holding spells) up to 3 years of age.

The patient’s father was of brazilian origin and she had previously been diagnosed with sickle cell anemia. Clinical evaluation: no focal neurological signs, paranoid thoughts but no cognitive deficits in extensive neuropsychological testing. EEG demonstrated focal epileptic activity in the right temporal region. MRI of brain was completely normal. Routine clinical workup was unremarkable.

Serum LGI1 antibodies were positive (LGI1 IgG positive 1:32). Patient was diagnosed with autoimmune encephalitis with voltage-gated potassium channel (VGKC) – complex-associated LGI1 autoantibodies. She was treated with methylprednisolone pulse therapy 1 g × 5 iv. After the treatment all her symptoms resolved and her repeated EEG was normal.

p455
NMDA RECEPTOR ENCEPHALITIS PRESENTING AS PARTIAL STATUS EPILEPTICS: CASE REPORT AND DISCUSSION

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Objective: Challenging differential diagnosis.

Background: Anti-NMDA receptor encephalitis develops in 5 distinct phases:

1 The Prodrom.
2 The Psychotic phase.
3 The Non-responsive phase.
4 Hyper-kinetic phase.
5 Gradual recovery.

Case report: We describe the case of a 17 years old right handed female with a complex partial seizure 2 weeks prior followed by psychiatric manifestations such as personality changes, anxiety and psychotic symptoms. She had fluctuating short term memory, linguistic and developmental regression, echopraxia and autonomic instabilities. Later she progressed to mutism.

Her EEG showed numerous focal electrographic seizures arising from the left temporal hemisphere and continuous slowing in the left temporal and central regions consistent with partial status epilepticus. Her non-consent head CT was unremarkable while her contrast brain MRI revealed increased T2 signal within the cortical left temporal and parietal region. NMDA receptor encephalitis was high on our differential and her status epilepticus was considered autoimmune in origin. Her seizures were eventually controlled after multiple AED’s including Keppra, Dilantin, Valproic Acid and Solumedrol. She underwent a lumbar puncture that was unremarkable and her infectious work up was negative. Her CSF NMDA receptor antibody returned positive 10 days later while the paraneoplastic panel was negative. Her oncological work up was unremarkable and no tumor was found on a whole body PET scan and abdominal/vaginal ultrasound. Her symptoms have been reversed after 5 curses of plasmapheresis followed by IVIG. Her repeated MRI was improved and her EEG was normal. She had mild behavioral and cognitive dysfunctions but she was discharge home with outpatient rehabilitation.

Conclusions: This case emphasizes the particular challenges of early recognition of organic origin of neuropsychiatric disorders before progressive loss of neurological functions is evident. Early diagnosis is desirable as immunosuppressive therapy may be most effective at this time and may improve the end point of the disease.

Genetics 2
Tuesday, 1st July 2014

p456
THE POLYMORPHISMS WITHIN FIBRINOGEN ALPHA AND BETA GENES AND POSTSTROKE SEIZURES IN POLISH PEDIATRIC PATIENTS

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Purpose: Previously, number of data showed that genetic risk factors are related to paediatric ischemic stroke. The variations in the fibrinogen beta (FGB) gene (e.g. 455G>A polymorphism) gene) as well as some environmental factors affect plasma fibrinogen level and elevated level of fibrinogen is known factor for cerebrovascular diseases. On the other hand, Thr312Ala polymorphism in fibrinogen alpha (FGA) gene may affect fibrin clot structure which is important in the pathogenesis of ischemic stroke. A history of acute brain ischemia is burdened with consequences such as motor impairment (hemiparesis observed most commonly), speech impairment and intellectual regression. Particularly noteworthy is the problem of epilepsy occurring after ischemic stroke in children.

The objective of the present study was to find association between 455G>A polymorphism in FGB gene and Thr312Ala polymorphism in FGA gene and poststroke seizures in paediatric patients.

Method: The study population consisted of 149 children (white Polish Caucasians) recruited in the Department of Neuropediatrics in Katowice and divided into three groups: 10 children with poststroke seizures, 30
patients with AIS but without seizures and 109 controls. The FGA and FGB polymorphisms were genotyped with PCR-RFLP method.

**Results:** We observed that frequencies of genotypes and alleles of FGB polymorphism were similar in all analyzed groups. Whereas, prevalence of carriers of FGA A allele was higher in the group with poststroke seizures compared to controls (80% vs. 37%, \( p = 0.007, \text{OR} = 6.90\) 95% CI 1.26–49.68). We also observed that 312A allele of Thr312Ala polymorphism was more common in patients with seizures after stroke than in patients without seizures as well as in controls (50% vs. 28% (\( p = 0.07, \text{OR} = 2.53\) [0.79–8.14]) and 20% (\( p = 0.002, \text{OR} = 4.07\) [1.45–11.42]), respectively).

**Conclusion:** The FGA polymorphism may be related to poststroke seizures in Polish children, although further studies are needed. Funded: NN-6-296/06.

**p457 IDENTIFICATION OF VARIANTS IN MICRONRNA GENES INVOLVED IN EPILEPTIC ENCEPHALOPATHIES**

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**Purpose:** Emerging evidence indicates that microRNAs are involved in the pathomechanism of epilepsy. However, a mutation analysis of microRNAs has never been performed for the epileptic encephalopathies (EE). We anticipate that variants in brain-expressed microRNAs that alter the expression of their target genes can lead to the severe phenotype (EE). We anticipate that variants in brain-expressed microRNAs that alter the expression of their target genes can lead to the severe phenotype (EE). We therefore conclude that a seizure reduction of >50% following dietary treatment is not a suitable criterion for identifying patients with GLUT1-DS, as these patients generally achieve complete seizure freedom shortly after diet initiation.

**Method:** Two “Multiplex Amplification of Specific Targets for Rese- quencing” (MASTR) assays were made using the Multiplexer software (Multiplicom N.V.). The first one contains brain-expressed human microRNAs. For the second assay, microRNAs were selected based on

- 1 An in literature described link between the microRNA and epilepsy.
- 2 Described expression in human brain tissue during early stages of development.
- 3 Validated microRNA-target interactions between microRNAs and epilepsy genes.
- 4 In-house CNV data.

Both MASTR assays will be used for screening of a cohort of 500 EE patients, but can also be used for screening of milder forms of epilepsy.

**Results:** To investigate the importance of microRNAs in EE, we will screen microRNAs and genes involved in the biogenesis of microRNAs, using two MASTR assays. The first one contains 289 microRNAs. The second one consists of 178 microRNAs and the exons of 6 genes involved in microRNA biogenesis (AG02, DICER1, DGCR8, DROSHA, TARBP2, XPO5).

**Conclusion:** We will screen microRNAs and microRNA biogenesis genes using a novel approach, to detect variants that might be causal for EE.
suspected metabolic disorder, was found to have a heterozygous de novo mutation in STXBP1. A boy of Middle Eastern background, born to consanguineous parents, with progressive myoclonic epilepsy was found to be homozygous for a frameshift deletion in KCND7. In two sibships and one trio, no likely genetic cause was found in the exome data.

**Conclusion:** Exome sequencing as a technology allows better molecular diagnostics of selected patients. The findings can be unexpected and difficult to predict on a clinical basis. As of today, exome sequencing is a very good method to find the genetic cause of diseases if the inheritance is recessive, de novo dominant or there are good candidate genes based on the phenotype.

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### p460

**SCN2A MUTATIONS: EXPANDING THE PHENOTYPE TO AUTISM, LATE-ONSET SEIZURES AND ACUTE ENCEPHALITIS WITH REFRACTORY, REPEATED PARTIAL SEIZURES**

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**Purpose:** To report 2 patients with SCN2A mutations and previously unreported phenotype.

**Method:** Case descriptions and review of the literature.

**Results:** Patient 1: Normal pregnancy and birth, slight motor delay. At 1 year, appearance of abnormal eye contact, language and fine motor skills difficulties. A CGH-array revealed a 2q24.3 (A_14_P138733 > A_14_P138637)x1 deletion, encompassing the proximal half of SCN2A. The boy presented with generalized tonic-clonic seizures at 7 years, followed by tonic-clonic, myoclonic and behavioral arrest seizures. At 13 years, he presented with an acute exacerbation of seizures in the context of a febrile respiratory infection. These were observed repeatedly at a high frequency, and were refractory to multiple therapeutic approaches administered. An extensive diagnostic work-up did not reveal any specific finding. After a 1-month stay in the intensive care unit, he regained his previous seizure frequency and neurological state.

Patient 2: Normal pregnancy and birth. The patient presented at the age of 2 years with speech delay and autistic features. Between the age of 3 and 5 years, several fever-associated seizures occurred. At the age of 6 years he presented with four clusters of generalized tonic-clonic seizures. Valproic acid allowed optimal seizure control, and was tapered 6 years later, without seizure recurrence. At 15 years, he still is unable to speak and shows severe autistic features. Whole exome-sequencing revealed a de novo c.1508dupA; p. Asn503Lysfs*19 SCN2A mutation.

**Conclusion:** The clinical spectrum associated with SCN2A mutations includes autism and early-onset epilepsies. Rare patients without seizures have also been reported. Our 2 patients presented with autistic features, developmental delay and late-onset epilepsy. One of them also presented a transient event resembling acute encephalitis with refractory, repetitive partial seizures (AERPPS). This presentation further expands the spectrum of manifestations associated with SCN2A mutations. We also suggest that SCN2A mutations may represent a specific risk factor for acute encephalopathies.

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### p461

**RARE COPY NUMBER VARIATION IS COMMON IN ROLANDIC EPILEPSY AND DISRUPTS KNOWN EPILEPSY GENES**

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**Purpose:** Rolandic Epilepsy (RE) is a common developmental epilepsy with a complex genetic background, only partially understood. RE is characterized by focal sensorimotor seizures during sleep, as well as cognitive, reading, language and attention problems. Rare copy number variation (CNV) is important in the pathophysiology of other epilepsies and neurodevelopmental conditions. In this study we sought to investigate the contribution of CNV to the RE phenotype.

**Method:** Five groups of patients with typical RE were included in this study: U.K.: 41, Argentina: 6, Sardinia: 62, U.S.A.: 52, Kerala India: 34. SNP genotypes from genomic DNA were analysed with Illumina OmniExpress arrays. CNVs were called using PennCNV whilst incorporating QC correction. Cut-offs for CNV calling: >15 SNPs and >20 Kb in size. CNVs were further validated by >90% overlap with QuantSNP CNVs. Enrichment of Gene Ontology (GO) categories was tested using INRICH and WebGestalt. CNVs were defined as rare if they showed >90% overlap with the Database of Genomic Variants or for Kerala cases, not present in a Kerala control.

**Results:** 117 Rare CNVs were seen in 86/195 cases. 61 individuals had one rare CNV, twenty had two, and five had three. Average CNV length 208Kb, with five over 1 Mb. Only one patient carried a “hotspot” CNV; a 1.2 Mb deletion at 16p13.11. Several CNVs disrupt genes reported to cause epilepsy or other neurodevelopmental disorders, including ARHGAP32, ARHGEF15, CACNA2D1, CTNNA3, GRIN2A, GRID2, NRG3 and NRXN1. GOCategory analysis showed enrichment of cellular metal ion homeostatis, chemokine activity, ionotrophic glutamate receptor activity and presynaptic membrane.

**Conclusion:** A heterogeneous mixture of rare CNV is common in patients with RE across ancestral backgrounds. Some of these CNVs are likely involved in the pathogenesis of the disorder due to disruption of known epilepsy/neurodevelopment genes. This structural heterogeneity may contribute to the phenotypic diversity and comorbidities common in RE.

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### p462

**CHD2 MUTATIONS PRODUCE AN EARLY CHILDHOOD ENCEPHALOPATHY WITH PROMINENT PHOTOSENSITIVE SEIZURES**

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**Purpose:** CHD2 mutations are associated with photosensitive seizures and an early childhood encephalopathy. Here we report three patients with CHD2 mutations presenting with an early childhood encephalopathy along with photosensitive seizures and additional neurodevelopmental delay and learning difficulties.

**Method:** Whole exome sequencing was performed on three probands with photosensitive seizures and an early encephalopathy. Mutations in CHD2 were confirmed by Sanger sequencing. Whole-exome sequencing of the parents was performed to confirm the de novo nature of the mutations.

**Results:** Whole exome sequencing revealed a de novo c.3460G>T mutation in CHD2, resulting in a p.Glu1154Stop truncating mutation. Sanger sequencing confirmed this mutation in the probands, and it was absent in the parents, confirming the de novo nature of the mutation.

**Conclusion:** CHD2 mutations are associated with an early childhood encephalopathy along with photosensitive seizures and additional neurodevelopmental delay and learning difficulties. This study extends the clinical spectrum associated with CHD2 mutations and highlights the importance of whole-exome sequencing in the diagnosis of early childhood encephalopathies.


**P463**

**GENOME WIDE ASSOCIATION STUDY FOR CUTANEOUS ADVERSE REACTION OF LAMOTRIGINE**

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**Purpose:** Cutaneous adverse reaction is well known adverse drug reaction of lamotrigine (LTG). Genetic markers have been found well for carbamazepine but not for LTG. We evaluated the gene related with cutaneous adverse reaction of lamotrigine with genome wide association study.

**Method:** Thirty-three Korean epilepsy patients with skin rash derived by LTG was genotyped with Affymetrix 500k sNP array and age matched 12 healthy Korean population cohort which had genotyped with Affymetrix 5.0 sNP array was parceled out by Korean NIH.

**Results:** Among selected markers, rs13287547 from GWA analysis and rs12668095, rs17149848, rs79007183 from imputation analysis were significant (p-values of 0.027, 0.009, 0.024, and 0.025 at the allelic analysis, respectively). rs13277547 and rs12668095 are located at intergenic places near C9orf92/BNC2 and TNS3 genes, and rs17149848 and rs79007283 are located at intronic regions within GRM8 and CRAMP1L genes, respectively.

**Conclusion:** This study can be the foundation of discovering clinical biomarkers of LTG induced cutaneous adverse reaction, and further researches are needed for discovering how these intergenic markers can influence on the function of near genes in many populations.

**P464**

**LG11 EXPRESSION IN GLOBLASTOMA MULTIFORME WITH AND WITHOUT EPILEPSY**

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**Purpose:** LG11, the leucine-rich, glioma-inactivated 1 gene, was first identified as a putative suppressor gene in glioblastoma multiforme (GBM) and subsequently found altered by point mutations in autosomal dominant lateral temporal epilepsy, a rare form of idiopathic focal epilepsy. Although the function of this gene is largely unknown, LG11 disruptions can be partly responsible for two such different conditions such as GBM and epilepsy. We hypothesized that the expression of LG11 in GBM could be influenced by the coexistence of epilepsy.

**Method:** We studied the expression of LG11 in tumor specimens of 23 patients with GBM, 10 of them showing epilepsy and 13 displaying other clinical features. The expression of LG11 was assessed at mRNA and protein levels by qPCR and immunoblot, and compared in the two subgroups.

**Results:** The two groups did not differ in terms of age of onset (58 vs. 60) and tumor localization (fronto-temporal in most cases). Real time qPCR analysis revealed variable LG11 expression in tumor tissues of both subgroups with or without epilepsy and no overall significant difference between them. Western blot analysis detected LG11 signals in 4 out of 7 tumor samples of patients with epilepsy (57%), whereas only 3 out of 13 samples of patients without epilepsy (23%) expressed detectable amount of LG11.

**Conclusion:** These data suggest that LG11 expression in GBM tumor tissues varies widely but shows that can be higher in patients with epilepsy compared to the group without seizures. The significance of this finding needs confirmation in future studies.

**P465**

**SEROTONIN RECEPTORS IN MESIAL TEMPORAL LOBE EPILEPSY**

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**Purpose:** Serotonin (5-hydroxytryptamine – 5-HT) is a neurotransmitter and neuromodulator fundamental in neurodevelopment and brain plasticity. Functions of 5-HT are mediated by different receptors distributed through the Central Nervous System (CNS). Deregulation of serotonergic pathway was implicated in the pathogenesis of epilepsy. 5-HT receptors (HTR1A) could have an anti-convulsant effect. HTR1A expression may be modulated by the polymorphism rs6295. A study in brain tissue from Mesial Temporal Lobe Epilepsy with hippocampal sclerosis (MTLE-HS) patients showed that serotonin type 2a receptor (HTR2A) is down regulated. HTR2A function may be influenced by the rs6314 polymorphism that recently was associated with an early onset of TLE. The aim of this study was to analyse the association between rs6295 and rs6314 polymorphisms and the development of MTLE-HS in a Portuguese population.

**Methods:** A cohort of 122 MTLE-HS patients (67F, 59M, mean age = 44 ± 11 years, age of onset = 13 ± 9 years; 112 patients with drug refractory epilepsy) was compared with a cohort of 270 healthy individuals (HI). Genotyping was performed by Real Time PCR using Taqman methodology.

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doi: 10.1111/epi.12675
Results: The frequency of rs6295CC genotype was higher in MTLE-HS patients when compared to controls (34.9% vs. 24.5%, p = 0.031 OR = 1.64 [1.04 – 2.60]). The rs6314 genotype frequencies were similar between patients and controls. No association was found between these polymorphisms and MTLE-HS clinical features (age of onset and PS antecedents).

Conclusion: This study indicates that rs6295CC genotype may be a risk factor for MTLE-HS development, which is different from previous studies (Stefuli J, et al., 2010). The rs6295CC genotype is associated with a higher HTR1A gene expression. This may unbalance serotonin homeostasis lowering the threshold for seizure development. The study of other 5-HT receptors and transporters is underway. Supported by A BICE Tecnifar Grant 2012.

Imaging 3 Tuesday, 1st July 2014

p466 A SINGLE-VOXEL SPECTROSCOPY STUDY OF HIPPOCAMPAL METABOLIC DYSFUNCTION IN PATIENTS WITH JUVENILE MYOCLONIC EPILEPSY, FRONTAL LOBE EPILEPSY AND PSYCHOGENIC NONEPILEPTIC SEIZURES
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Purpose: Proton magnetic resonance spectroscopy (MRS) studies have shown neuronal dysfunction with differing patterns of abnormality in various types of epilepsy pathogenesis. Our aim was to identify metabolic differences in the hippocampi of patients with juvenile myoclonic epilepsy (JME), frontal lobe epilepsy (FLE), and psychogenic nonepileptic seizure (PNES) compared to normal healthy subjects by using single-voxel MRS.

Method: The study included 18 patients with JME, 38 with FLE, and 15 with PNES. The control group consisted of 24 age-matched healthy volunteers (mean age: JME: 22.3; FLE: 23.7; PNES: 25.0; controls: 25.8). All patients and controls underwent normal neurological examinations and magnetic resonance imaging. Quantitative single-voxel MRS was conducted at 1.5 Tesla with a sequence of TR/TE = 1,323/136 ms with a voxel size of 30 x 15 x 15 mm in both hippocampi. LC-Model was used to estimate the absolute concentrations of N-acetyl-aspartate (NAA), choline (Cho), creatine (Cr), and the ratio of NAA to Cho + Cr (NAA ratio).

Results: Significant reductions in NAA and the NAA ratio were observed in the left hippocampus in the JME group compared to controls (NAA: 8.22 vs. 8.89, p < 0.05; NAA ratio: 0.92 vs. 1.03, p < 0.01). Furthermore, significant reductions in NAA were found in both hippocampi in the FLE group compared to controls (right: 7.79 vs. 8.28, p < 0.05; left: 8.14 vs. 8.89, p < 0.01). The bilateral hippocampal NAA ratios were not reduced significantly in the FLE patients. In PNES patients, NAA and the NAA ratio in both hippocampi were not significantly lower than in the controls.

Conclusion: These data support the hypothesis that JME and FLE involve neuronal dysfunction within the temporal lobe as well as the frontal lobe. However, neuronal dysfunction in PNES might demonstrate normal hippocampal metabolism and differ from epileptic pathogenesis.

p467 LATERALIZATION OF HIPPOCAMPAL ACTIVATION FOR SURGICAL GUIDANCE IN REFRACTORY PEDIATRIC EPILEPSY
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Purpose: Memory impairments are a common comorbidity in children with epilepsy; however, few studies have used functional magnetic resonance imaging (fMRI) to assess these memory difficulties. We developed a paired association learning fMRI task to directly probe verbal and visual memory and elicit hippocampal activation (HA) on an individual basis for use in presurgical mapping.

Method: Fifteen children with focal epilepsy (ages 8–16; mean = 13.2; 8 female) participated in an EPI BOLD 3T block design paired association learning task with word pair stimuli (verbal memory; n = 15) and abstract designs (visual memory; n = 14). Image normalization and segmentation was done using subjects’ high-resolution T1 images with the VBM8 Toolbox in SPM8, then applying those parameters to EPI images. We calculated a laterality index (LI) for the hippocampal region of interest (Anatomical Atlas Library in Wake Forest PickAtlas) using the LI Toolbox bootstrap method.

Results: On an individual basis, 80% demonstrated HA during learning and recall for the verbal task, while 86% had HA during learning and 71% during recall for visual memory (p = 0.05, uncorrected). Categorical LI distribution was primarily left lateralized for both verbal (Learning: 10 L, 3 B, 1 R; Recall 8 L, 4 B, 2 R) and visual memory (Learning: 6 L, 4 B, 3 R; Recall 9 L, 1 B, 3 R). There was a trend for a positive correlation between Verbal Memory Learning HA LI and CMS Verbal Delayed Composite (r = 0.10; r = 0.554, p = 0.097).

Conclusion: Results demonstrated that the verbal and visual learning paradigms elicit reliable HA on an individual basis at lenient thresholds. This activation was left lateralized for both verbal and visual memory and left-lateralized HA during verbal memory related to better verbal memory performance (trend). Our results show that it is feasible to use these memory paradigms as a probe of HA in children with focal epilepsy.

p468 ICTAL SUBTRACTION SPECT PLOT ANALYSIS BY STATISTICAL PARAMETRIC MAPPING (ISAS) ON REFRACTORY STRUCTURAL EPILEPSY
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Purpose: The ISAS analysis is an implementation of the ictal subtraction SPECT (interictal SPECT subtracted from ictal SPECT) that normalises each patient’s difference image with a database of healthy subjects, thereby reducing the individual variability. This study presents applicability of the ISAS in a group of consecutive patients with refractory focal seizures.

Method: 26 patients undergoing presurgical evaluation at our department were additionally investigated with subtraction SPECT. The tra-
cer (Tc-99 m-HMPAO) was always injected within the first min after clinical or electrical seizure onset. Interictal SPECT was performed after at least 24 h without generalised seizures. The analysis followed a previously described methodology (McNally et al, Epilepsia 2002; 43: 68–74).

Results: Patients were classified as having a temporal lobe (TLE, n = 9), extratemporal (eTLE, n = 15) or in 2 cases multifocal epilepsy. 1 TLE patient and 3 exTLE patients had a structural lesion in MRI. Post-processing revealed a lesion in 3 additional patients (1 TLE).

ISAS showed a clear, single hyperperfusion cluster in 18 patients (9 exTLE), being inconclusive in the rest, even after repeated scans in 2 patients. There was a concordance between ISAS and the MRI findings in 7 cases (6 exTLE). In 2 patients a lesion could be identified post-hoc after carefully inspection of the functionally active region.

Up to now 2 TLE patients have resected (Engel IA and IIA), and 4 with exTLE have been studied with depth electrodes, which supported a resection in all cases. Two from those patients are awaiting a resection, one of them has rejected the procedure and the last one turned seizure after invasive evaluation. Surgery was discarded on one exTLE patient due to the postoperative risk of hemianopia.

Conclusion: ISAS is an effective tool in the presurgical evaluation of epilepsy, with better concordance with MRI in exTLE.

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EARLY RADIOLOGICAL SIGNS OF PIAL ANGIOMA IN STURGE-WEBER SYNDROME
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Purpose: To determine early signs of pial angioma on MRI in infants with Sturge-Weber syndrome (SWS).

Background: 35% newborns with facial capillary malformation in ophthalmic area will have SWS with pial angioma, high risk of seizures and cognitive impairment.

Method: Infants with facial plan angioma involving ophthalmic area and first MRI at the age of 6 months or younger were included in the study. The 2nd MRI was done from 7 months on. The MRI protocol included 1.5 T MRI, 5 mm slices. T1 and T2-weighted axial, sagittal brain imaging, axial and coronal T1 SE with fat saturation and gadolinium iv. as a gold standard.

Results: Among 25 patients, 15 (60%) had SWS type I. First neurological exam was normal in 20 patients; 5 infants had either hemi-neglect (3) or hemianopsia (2); none had hemiparesis. The 1st MRI showed pial angioma in 11 infants; 15/25 had a hyposignal of white matter (WM) on T2 sequence. Hypersignal of WM on T1 was present in 12/25 patients. Five patients had no angioma visible on the 1-st MRI (2 patients without gadolinium), but hyposignal of WM on T2 (3 cases) and hypersignal of WM on T1 (1 case) was noted. The 2nd MRI with Gadolinium, from the age 8 months on, confirmed pial angioma in all 5 cases. Ten children had no signs of pial angioma on 2nd MRI. Sensitivity for T2 hyposignal of WM on 1 st MRI was 87% and specificity 80% and for T1 hypersignal 67% and 80%, respectively.

Conclusion: Hyposignal of WM on T2 and hypersignal of WM on T1 sequence represent an early sign even when pial angioma is not yet seen. Recognizing pial angioma during clinically silent period enables clinician to establish a better follow up and to consider preventive anti-convulsive treatment.

p470
NEURONAL NETWORKS RELATED TO THE OFFSET OF ABSENCE SEIZURES: AN EEG-FMRI STUDY
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Purpose: Several studies investigated hemodynamic changes related to the onset of generalized spike and wave discharges (GSWD), revealing the presence of a diffuse neuronal network involved in GSWD generation in patients with Idiopathic Generalized Epilepsy (IGE). In the present EEG-fMRI study we analyzed instead the neural correlates of GSWD termination studying BOLD changes at discharges offset in patients with IGE.

Method: 18 patients (6 male; mean age 25 years) with IGE underwent EEG-fMRI co-registration at our center. Analysis was conducted with SPM8 software. Regressors included in the analysis were 1) offset and duration of GSWD 2) offset of GSWD.

Results: On average, 17 events in each patient were recorded. Group analysis of GSWD onset confirmed prior results showing BOLD increments in the thalamus bilaterally and BOLD decrements in precuneus/posterior cingulate cortex. Direct comparison offset vs. onset showed an increment of BOLD signal in the prefrontal regions bilaterally and in the primary visual cortex. The comparison offset vs. onset revealed increment of BOLD signal in precuneus/posterior cingulate cortex and decrement in the dorsolateral prefrontal cortices.

Conclusion: FMRI results documented different cortical involvements at GSWD onset and offset. In particular, at GSWD onset, activation of frontal cortices was evident. Conversely, the neural network at GSWD termination involved a relative increase of BOLD signal in the precuneus/posterior cingulate region. Precuneal/posterior cingulate neuronal activity might participate actively to the GSWD termination or it might reflect the recovery of the neural activity in cortical region that are “suspended” during GSWD. Moreover, at GSWD offset, we observed BOLD decrements in the dorsolateral prefrontal regions: it could represent a reduction in neuronal activity in those regions that were active during GSWD, or, conversely, it might be the hemodynamic correlation of an “active” inhibition of frontal cortex which is necessary to interrupt GSWD.

p471
EEG TIME-VARYING EFFECTIVE CONNECTIVITY IN LEFT AND RIGHT TEMPORAL LOBE EPILEPSY
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Purpose: We aimed to analyze the dynamic behavior of epileptic networks through the study of the effective connectivity at a whole-brain scale during interictal spikes in temporal lobe epilepsy patients (TLE) using high-resolution EEG signals. We aimed to understand the connectivity pattern differences in right vs. left TLE (RTLE vs. LTLE).

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Method: Sixteen patients, 8 with RTLE and 8 with LTLE, were selected for the study. We assessed the connectivity changes of cortical networks during interictal spikes compared to baseline periods at high-temporal resolution, using high-density EEG recordings. The source activity was obtained for 92 regions of interest using an individual head model and a distributed linear inverse solution. A multivariate, time-varying and frequency-resolved Granger causality analysis was applied to the source signal of all ROIs. A non-parametric statistical test was carried out to assess the difference in outflow, in each ROI, between interictal spikes vs. baseline.

Results: In both groups, the key driving structures were located in the medial temporal pole, and their driving towards other regions was higher at the time of the spike. In LTLE the keys drivers were only ipsilateral while in RTLE the key drivers were both ipsilateral and contralateral. Moreover, in RTLE we observed a transcallosal driving pattern from the ipsilateral to the contralateral regions that was not seen in LTLE. The localization of the main drivers, for all the patients, was concordant with the epileptogenic zone estimated invasively.

Conclusion: The used approach was able to identify the major contributors to interictal epileptic activity in both RTLE and LTLE, concordant with invasive electro-clinical findings. Furthermore, a different connectivity pattern was observed in RTLE and LTLE, suggesting that they are not simply symmetrical entities. This enhanced characterization of the epileptic networks increases our understanding of these conditions and could have clinical implications for epilepsy surgery.

\textbf{p472}

\textbf{SIMULTANEOUS EEG-FMRI: POSTERIOR SLOW-WAVES COMPARED WITH OCCIPITAL ALPHA IN CHILDHOOD ABSENCE EPILEPSY}

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Purpose: Occipital alpha (8–10 Hz) is recorded in scalp EEG during resting-state-eyes-closed and it is associated with specific BOLD changes. Slowing of occipital alpha is seen in neurological conditions including epilepsy and it is a marker in clinical EEG. It has been shown that (i) thalamic lesions are related with alpha suppression and disorganization; (ii) increased BOLD in thalami is correlated with alpha; (iii) thalamus plays also a role in CAE. Here we investigated a patient with CAE showing typical alpha rhythms alternating with posterior-slow-waves (2.7 Hz) to identify the generators of abnormal posterior EEG slowing in CAE.

We used simultaneous EEG-fMRI to investigate patterns of BOLD activation associated with posterior-slow-waves and its relationship with BOLD activation associated with alpha.

Methods: A 10 year diagnosed with CAE underwent simultaneous-EEG-fMRI.

64-channel-MRI-compatible system (Brain Products) was used to record EEG. MRI was performed using 1.5T Siemens scanner. T1-volume and two-EPI sessions (TR = 2160 ms, TE = 30 ms, 30 slices, 300 volumes, 3 x 3 x 3 mm) of 10 min were acquired. During the first session, the subject viewed a movie. During the second session, the subject rested with eyes closed. 11 runs of posterior-slow-waves (2.7 Hz) were recorded, alternating with typical alpha oscillation (8.6 Hz).

After EEG standard artefact corrections, slow waves were marked in O1, O2, P7, P8, Oz and entered into a GLM using SPM8. T-maps were calculated.

Results: Runs of posterior-slow-waves were positively correlated with the middle-frontal cortex, bilateral-frontal pole, right supramarginal gyrus, and bilateral-inferior-temporal lobe (p < 0.001 uncorrected).

Conclusion: EEG-fMRI revealed a brain network included posterior regions and medial frontal cortex, a region found abnormal in other IGE syndromes such as JME which correlated with posterior slow-waves. This suggests a relationship between the generators of posterior slow-waves and other aspects of structural and functional brain abnormality in IGE. Further data is needed to confirm these findings.

\textbf{p473}

\textbf{VERBAL AND VISUAL MEMORY FUNCTION IN TEMPORAL LOBE EPILEPSY: RESULTS OF A BLOCKED VS. EVENT-RELATED ANALYSIS}

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Purpose: There is evidence for a functional dissociation between the anterior and posterior left and right medial temporal lobe (MTL) mediating verbal and visual memory encoding. This study aimed to use functional MRI (fMRI) and compare block and event-related designs for evaluation of material specific memory in temporal lobe epilepsy (TLE).

Methods: We scanned 65 patients with unilateral TLE due to hippocampal sclerosis (37 left) and 20 healthy controls on a 3T GE-MRI scanner. All subjects performed an fMRI memory paradigm which examined the encoding of words, pictures and faces. Two ways of analysis, a blocked and event-related analysis (ERA), were performed on the same data set.

Results: ERA revealed significantly less activation in the left anterior MTL in left TLE and significantly less right anterior MTL activation in right TLE compared to controls. Blocked analysis showed a similar laterализation pattern in posterior MTL regions.

ERA showed that greater left than right anterior MTL activation on encoding words correlated with better verbal memory on standard neuropsychological tests in left TLE; in right TLE, greater right than left anterior MTL activation on encoding faces correlated with better visual memory. Relatively greater ipsilateral than contralateral posterior MTL activation predicted better verbal memory outcome in left and better visual memory outcome in right TLE following surgery.

The blocked analysis did not reveal any significant correlations in anterior or posterior MTL regions with out of scanner memory performance.

Conclusions: ERA allows detection of activations arising specifically during successful encoding. Our results suggest that subsequent memory effects are effectively mediated by anterior MTL structures. Preoperative reorganization of memory to posterior MTL regions was associated with better postoperative memory outcome, while more posterior activity as detected with a blocked analysis was related to deficiencies of block designs caused by additional cognitive processes other than memory encoding.

\textbf{p474}

\textbf{DURATION OF TEMPORAL LOBE EPILEPSY IN CHILDREN IS ASSOCIATED WITH LOSS OF HIPPOCAMPAL TISSUE AND MEMORY DYSFUNCTION}

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Purpose: There is evidence for a functional dissociation between the anterior and posterior left and right medial temporal lobe (MTL) mediating verbal and visual memory encoding. This study aimed to use functional MRI (fMRI) and compare block and event-related designs for evaluation of material specific memory in temporal lobe epilepsy (TLE).

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We present two cases of TSC patients with a severe refractory partial complex epilepsy beginning at early infancy. Both showed unique neuro-radiological features of the suspected epileptogenic tuber that includes an enhancing component typical for SEGAs and usually not seen in tubers.

The first patient had an excision of the epileptogenic tuber at the age of 22 months and after the operation became seizure free but with severe mental retardation, autism and severe behavioral problems. The second patient was operated at the age of 9 months and is now seizure free with normal development. Both patients had a rare pathological finding consistent with SEGAs tissue within the tuber.

We describe a new type of lesion in TS patients “Tuber SEGAs” with special neuroradiological and pathologic features and with significant clinical implications.

Early surgical work up is critical for good neurological and developmental outcome and possible due to its special features. If the surgical work up is inconclusive m-TOR inhibitor treatment should be strongly considered for epilepsy because of the SEGAs component.

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TUBER-SEGAs: THE IMPORTANCE OF EARLY DIAGNOSIS OF A NEW NEUROLOGIC FINDING ON BRAIN MRI OF TS PATIENTS
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Tuberous Sclerosis is an autosomal dominant genetic disorder with frequent and significant neurologic involvement. The main neuroanatomic features of TSC include cortical tubers, subependymal nodules and subependymal giant cell tumors (SEGAs). The neurologic symptoms of TSC include epilepsy, cognitive impairment, autism spectrum disorders and mental health issues.

Epilepsy is highly correlated with cortical and subcortical tubers which consist of abnormally migrating neurons, while SEGAs are typically located intraventricularly, adjacent to the foramina of Monro and are with no epileptogenic effect.
p477 PROTON SPECTROSCOPY (1H-MRS), IN PATIENTS WITH NOCTURNAL FRONTAL LOBE EPILEPSY (NFLE)

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Purpose: To identify structural alterations and/or metabolic disorders in patients with Nocturnal Frontal Lobe Epilepsy (NFLE) using advanced techniques of Magnetic Resonance (MR).

Method: We enrolled a series of NFLE patients attending our Epilepsy and Sleep Centers. NFLE diagnosis was confirmed by videopolysomnographic recording of at least one major episode (hypermotor or asymmetric bilateral tonic/dystonic seizure) or at least two minor stereotyped episodes (paroxysmal arousals). Semiology, seizure frequency and therapy were assessed for all patients. For each patient, one sex- and age-matched (±5 years) control subject was recruited. All subjects were studied using advanced MR techniques such as proton spectroscopy (1H-MRS). In particular, 1H-MRS was performed on two regions of interest: the thalamus and the anterior cingulated gyrus.

Results: Nineteen patients (7M; mean age 34 years, range 19-50) and 14 controls (6M; mean age 30 years, range 19-40) were included. At enrollment five patients were seizure free. In the remaining seizure frequency ranged from early (6 pts) to multiple episodes per night (8 pts). MR did not disclose gross abnormalities in any patient. The ratio N-Acetyl-Aspartate/Creatine concentration ([NAA]/[Cr]) was significantly reduced in the anterior cingulated gyrus in patients compared with controls (p = 0.021). In thalamus no differences were found in the [NAA]/[Cr] between patients and controls.

Conclusion: Our preliminary data on 1H-MRS in NFLE patients showed hypometabolism of cingulated cortex that correlates with high seizure frequency, confirming its role in pathophysiology of NFLE.

p478 MICROSTRUCTURAL CONNECTIVITY AND GREY MATTER STUDY IN BITEMPORAL LOBE EPILEPSY

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1 Epilepsy Unit, Neurology Department, L’Hospital de Llobregat, University Hospital of Bellvitge, Spain, 2 Bellvitge Biomedical Research Institute - IDIBELL, Cognition and Brain Plasticity Group, L’Hospital de Llobregat, Spain, 3 Department of Basic Psychology, L’Hospital de Llobregat, University of Barcelona, Spain, 4 Neurology Department, L’Hospital de Llobregat, University Hospital of Bellvitge, Spain, 5 Diagnostic Imaging Center, Hospital Clinic, Barcelona, Spain, 6 Catalan Institution for Research and Advanced Studies, Barcelona, Spain

Purpose: Pathology in patients with temporal lobe epilepsy (TLE) involves grey-matter (GM) and also white matter (WM) abnormalities in a wide corticosubcortical network. However, the impact of neuronal loss in TLE on specific WM fiber pathways and associated functional systems remains unclear, as well as seizure propagation pathways. We aimed to analyze GM and WM inter and intrahemispheric changes in hippocampal sclerosis (TLE+BHS) patients.

Method: Seven TLE+BHS patients (all confirmed by video-EEG recording and MRI) were compared to a control sample of 15 participants (matched for handedness, age and years of education). Two different techniques of MRI post-processing analysis were used: a) morphometric analysis of the T1-weighted images using Voxel Based Morphometry (VBM); b) DTI image analysis using FSL’s Tract Based Spatial Statistics (TBSS) to compare FA values.

Results: The VBM study showed WM reduction bilaterally at the hippocampal commissure, fornix and also at the parahippocampal gyrus (left > right). There was also a significant reduction of GM that affected the hippocampus (left > right), left thalamus and left parahippocampal area. The TBSS results showed many limbic pathways with significant decreased FA (bilateral fornix, internal capsule, cingulum, uncinate fasciculus and the anterior commissure). Also corpus callosum, showed reduced FA values. In summary, results obtained evidenced a reduced FA or volume in commissural pathways (the corpus callosum, anterior commissure and hippocampal commissure) when compared TLE+BHS patients to a matched healthy control group.

Conclusion: The current results, of a particular patient TLE subgroup -with bilateral hippocampal damage- where interhemispheric connectivity plays an essential role, support that commissural pathways may have a role in inter-hemispheric seizure propagation. Interestingly, our analysis also showed a more significant pattern of reduced connectivity and neuronal loss on the left hemisphere, although the bilaterality of the sample, which supports the idea that the left side is more susceptible to the extrahippocampal damage.

p479 REFLEX TRAITS IN IDIOPATHIC GENERALIZED EPILEPSIES: AN EEG-FMRI STUDY

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Purpose: The presence of reflex traits in idiopathic generalized epilepsies (IGE) is largely known. In this study we identified the hemodynamic maps of generalized spike-and-wave discharges (GSWD) recorded in IGE patients with reflex traits respect with the one detected in IGEs without reflex features. We aim to reveal differences that might be linked with the presence of reflex traits 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 GSWD were selected. Based on the electro-clinic data, the population recruited was divided into Group (1): IGE with reflex traits and Group (2): IGE without reflex traits. We considered as reflex traits the followings: photosensitivity, eye closure sensitivity and sensitivity to praxis. Within each IGE 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 GSWD in the reflex traits group compared with the not-reflex group.
Conclusion: Our results showed that the GSWD recorded in patients with reflex traits involve distinctive cortical networks (motor cortex). This finding might explain the different clinical features (myoclonus) observed in these patients.

p480
MORPHOMETRIC MRI ANALYSIS ENHANCES VISUALIZATION OF CORTICAL TUBERS IN TUBEROUS SCLEROSIS
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Purpose: Focal cortical dysplasias (FCD) type IIb and cortical tubers in tuberous sclerosis complex (TSC) are histopathologically similar and are both epileptogenic lesions frequently causing pharmaco-resistant focal epilepsy. Conventional visual MRI analysis combined with morphometric analysis of T1- and T2-weighted MRI volume data sets was shown to be of higher diagnostic sensitivity in detecting and delineating FCD than visual analysis of conventional MRI alone. Here, we investigated whether morphometric MRI analysis is of equal benefit for visualizing tubers in patients with TSC.

Method: Morphometric analysis was applied to T1- and partly also T2-weighted 1.5T or 3T MRI volume data sets of 14 TSC patients using a fully automated MATLAB script (i.e. MAP07) commonly used for FCD detection. Morphometric feature maps (i.e. “junction image”, “extension image” and “thickness image”) highlighting blurring of the grey-white matter junction, abnormal gyration and abnormal cortical thickening, respectively, were created. The visualization of tubers in the morphometric maps was compared with that in the conventional MR sequences (i.e. T1- and T2 images and coregistered FLAIR images, when available).

Results: In all patients, morphometric analysis visualized all tubers detected in the normal MRI, and additionally highlighted extra tubers which were not detected by visual analysis of the conventional MR sequences. When 3T MRIs and T2 volume data sets were available for postprocessing, the number of additionally detected tubers was even more numerous. These formerly overlooked tubers were usually smaller than the tubers already found in the conventional MRI.

Conclusion: Morphometric analysis of MRIs in TSC can highlight subtle tubers which are likely to be overlooked by in conventional MR sequences alone. Additionally detected tubers are of potential importance for the presurgical evaluation in pharmaco-resistant focal epilepsy.

p481
SURGICAL OUTCOMES OF PATIENTS WITH MAGNETIC RESONANCE (MRI)-NEGATIVE AND POSITRON EMISSION TOMOGRAPHY (PET/CT) POSITIVE TEMPORAL LOBE EPILEPSY
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Purpose: The aim of this study was to assess the usefulness of routine fluoro-2-deoxyglucose PET/CT (FDG-PET) in presurgical evaluation patients with non-lesional temporal lobe epilepsy.

Method: 16 patients with refractory temporal lobe epilepsy (7 women, age 30 ± 8 year) without structural MRI (1.5 Tesla) evidence of temporal lesions underwent interictal FDG-PET examination. All of them had non-invasive video-EEG with recorded seizures and Wada test with bilateral of memory testing (Milner test). Tailored anterior temporal lobe resection was done, from October, 2008, to march, 2012. Postoperative outcome was measured (Engel classification). Mean outcome follow up after surgery was 3.3 ± 0.9 year.

Results: The FDG-PET area of hypometabolism was observed predominantly in one temporal lobe in 14 of 16 patients. The FDG-PET findings corresponded with EEG ictal onset zone in 14 patients, and 10 of them had also identical memory deficiency lateralization.

In group of 10 patients with congruent video-EEG, FDG-PET and memory deficiency, 5 patients were completely seizure free since surgery (Class 1A), 2 patients were free of disabling seizures (Class 1B) and almost seizures free was 1 patient (Class 2B). Without improvement after surgery were 2 patients (class 3).

Only congruence of FDG-PET with ictal onset zone was seen in group of 4 patients - 1 of them was seizures free (Class 1A), 2 patients were almost seizure free (Class 2B), and one had no improvement (Class 4). In 2 of 16 patients FDG-PET hypometabolism was similar in both temporal lobes. The first was without improvement after surgery (Class 4). The second one only with correlation of seizures site of onset with Milner test had excellent outcome (Class 1A).

Conclusion: In our study, the predictive value good seizures outcome after temporal lobe epilepsy surgery in cases without MRI signs of temporal lobe lesion was congruence of FDG-PET with video EEG recorded seizures, and memory deficiency lateralization.

p482
WHITE MATTER TRACT CHANGES WITH AGE IN TEMPORAL LOBE EPILEPSY WITH UNILATERAL HIPPOCAMPAL SCLEROSIS
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Purpose: While white matter (WM) changes have been demonstrated in normal aging, whether patients with temporal lobe epilepsy (TLE) follow a similar trajectory is unknown. We investigated age-related changes of diffusion tensor imaging (DTI) parameters in 10 WM tracts in TLE with unilateral hippocampal sclerosis (HS).

Method: DTI (32 directions) was acquired at 3T from 111 controls (75 females, 25.7–80.1 years) and 171 patients (107female, 22.6–74.2 years) with TLE and unilateral HS (94 left HS). Ten tracts [3 parts of the corpus callosum (CC), CST, IFO, ILF, anterior and posterior cingulum, uncinate and fornix] were delineated by semi-automatic deterministic tractography (ExploreDTI) to yield fractional anisotropy (FA). In addition to group comparisons with General Linear Model, the average of left/right tracts FA were regressed linearly vs. age.

Results: The FA of all tracts was reduced in patients over the full age range. The regression of FA × age for all tracts from patients were significant (p-value max 0.039). For controls, the FA × age regression was not significant for CST (p = 0.07), uncinate (p = 0.23) and posterior cingu- lum (p = 0.54). The trajectories were parallel for CC, anterior cingu- lum, IFO and ILF for TLE and controls. A steeper trajectory for TLE was observed for the fornix, CST, uncinate and posterior cingulum.

Abstracts
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Conclusion: TLE with HS is associated with widespread WM abnormalities. Different age related trajectories suggest that some tracts (CC, anterior cingulum, IFO, ILF) are abnormal from the early stages of disease but follow a similar trajectory to controls, while other tracts (fornix, CST, uncinate and posterior cingulum) demonstrate a more rapid aging effect.

Methods: We performed DTI in 38 children with DD (68.4% boys) and 39 healthy children (48.7% boys) aged 6–12 years. Tractography bilateral clusters of AF were detected manually from MRI data; ventral streams, i.e., IFOF, UF and ILF were identified using regions of interest. DTI parameters such as fractional anisotropy (FA), volumes, count of fibres were correlated with the severity (n = 13 mild, n = 18 moderate, n = 7 severe) and type (i.e. n = 11 receptive, n = 27 expressive) of the speech impairment. Statistical analysis was performed using ANOVA.

Results: In children with DD, lower volumes of the right AF (p < 0.001), right and left IFOF (p = 0.001, p < 0.001), right and left uncinate fascicle (p < 0.001, p < 0.001) and right and left ILF (p < 0.001, p < 0.001) were found compared to controls. Further, lower fractional anisotropy of left AF (p = 0.005), right IFOF (p < 0.001) and left UF (p = 0.049) was found children with DD compared to controls. DTI parameters did not correlate with the severity of type of the DD.

Conclusions: Developmental dysphasia is associated with insufficient left arcuate fascicle and also ventral tracts, indicating significance of ventral streams during language development. Their identification in patients with epilepsy surgery might help to preserve their specific language skills. DTI parameters in healthy and DD children will be compared to language connectomes of patients with epileptogenic lesion in language regions.

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p485
COGNITIVE OUTCOME 2 YEARS AFTER FRONTAL LOBE EPILEPSY SURGERY
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Purpose: To investigate cognitive outcome after frontal lobe resections (FLR) for epilepsy, the second most common surgical treatment for drug resistant epilepsy, in a single centre series.

Method: Neuropsychological examinations were performed prior to and 2 years after surgery in 30 consecutive patients who underwent FLR (15 in the speech-dominant hemisphere). Cognitive outcome was evaluated with particular consideration to the side (dominant/non-dominant) and site of surgery (lateral, mesial, orbital, premotor/SMA) and seizure outcome. Cognitive domains assessed were speed, language, memory, attention, executive functions and global intelligence. Twenty-five healthy controls were assessed at corresponding time points.

Results: At baseline the patient group performed below controls in variables depending on speed, aspects of executive functions and global as well as verbal intelligence. Two years after surgery a significant change was obtained only for one variable. The FLR group had less improvement than the controls on the test “Figure assembly” (p = 0.028) that measures visual analysis. However, at the individual level only two patients had a reliable decline in this test (using reliable change indices [RCIs]) while a reliable decline was rather common for the test “Comprehension” (observed in 56% of the patients), that measures abstract reasoning ability concerning social conventions. This latter decline was seen especially in the lateral (71% of the patients) and premotor/SMA (57% of the patients) resection groups whereas the finding was not prominent in the...
mesial and orbital resection groups (25% of the patients). Seizure outcome and side of surgery did not influence these results.

**Conclusion:** The main finding was cognitive stability 2 years after FLR although a reliable decline in a test measuring abstract reasoning ability was rather common at the individual level, mainly in the lateral and premotor/SMA resection groups.

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### Abstracts

**p486**

**PREDICTORS OF NEUROPSYCHOLOGICAL DYSFUNCTION IN CHILDREN WITH INTRACTABLE EPILEPSY DUE TO TUBEROUS SCLEROSIS**

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**Purpose:** The following risk factors of mental deficits have been reported in large series of pediatric patients with tuberous sclerosis (TSC): Number of cortical tubers, TSC2 mutation, early seizure onset, intractable seizures and infantile spasms. We focused on analyzing predictors of neuropsychological dysfunction in children selected for excisional epilepsy surgery, invariably presenting with drug-resistant seizures.

**Method:** Comprehensive clinical, neurological, neuropsychological, EEG, MRI and surgical data of 21 children with TSC who underwent resective epilepsy surgery at Miami Children’s Hospital were analyzed. Individual variables were related to the presence of mental retardation in patients.

**Results:** Patient with mental retardation had significantly earlier seizure onset (p = 0.003), higher incidence of infantile spasms (p = 0.018) and early psychomotor development delay (p = 0.037) in their personal history. Slow background EEG activity was more frequently present in mentally-challenged subjects (p = 0.008). Other variables (such as type and frequency of seizures, type of epileptiform EEG activity and other characteristics of epilepsy, age at time of surgery or extend of the resection) showed no differences between patients with and without mental retardation.

**Conclusions:** In surgically-treated subjects with intractable epilepsy caused by TSC, early onset of epilepsy, incidence of infantile spasms and slow background EEG activity were found the most important risk factor for developmental delay. On the other hand, number of cortical tubers, duration of epilepsy and the extend of surgeries were not significantly associated with cognitive development. Psychomotor development was typically delayed from birth in the group of subjects with mental retardation that might suggest the congenital nature of developmental problems in the TSC.

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**p487**

**EMOTION RECOGNITION AND FAUX-PAS IDENTIFICATION IN TEMPORAL LOBE EPILEPSY PATIENTS: CORRELATION OF PERFORMANCE WITH AMYGDALAR AND HIPPOCAMPAL VOLUMES**

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**Purpose:** Emotion recognition from facial expression and identification of social faux-pas depend on intact temporal lobe structures. There is extensive evidence that patients with temporal lobe epilepsy (TLE) are frequently impaired in these functions. The aim of our study was to assess the correlation between emotion recognition, faux-pas identification, and amygdalar and hippocampal volumes in TLE patients.

**Method:** An experimental Emotion Recognition Test (ERT) adapted from Ekman and Friesen and short version of Faux Pas Test (FPT) were used to evaluate emotion recognition and social cognition in a group of patients with unilateral, refractory TLE (6 with right-sided and 8 with left-sided). Based on high-resolution MRI (T1-weighted images, 1.5 mm slice thickness, perpendicular to AC-PC line) amygdala and hippocampal volumetry was manually performed. Volumes were measured in coronal sections by InsightSnap software and normalized to intracranial volume.

**Results:** Almost 36% of TLE patients scored abnormal in ERT and 50% in FPT irrespective of the epilepsy lateralization. The volume of amygdala and hippocampus did not correlate with the performance in the ERT nor the FPT. There was a trend in correlation between the low score in ERT and the volume of ipsilateral amygdala (Pearson correlation test, r = -0.44; p = 0.11). On the other hand, the patient with most prominent bilateral atrophy showed no functional impairment.

**Conclusion:** In our small cohort of TLE patients the volume of amygdala or hippocampus did not predict the performance on ERT or FPT which allow us to hypothesize that rather functional network changes may be responsible for the impairment.

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**p488**

**ATTENTION DEFICIT IN PATIENTS WITH TEMPORAL LOBE EPILEPSY: CLINICAL, NEUROPHYSIOLOGICAL AND NEUROIMAGING CHARACTERISTICS**

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**Purpose:** Neurobehavioral features in epilepsy – cognitive impairment first of all, do not arise only due to effects of recurrent seizures, medications and adverse social reactions to illness. Lately, there is a growing pool of evidence that clinical course and topography, pato-anatomy and neurophysiology of epileptogenic areas are involved.

**Method:** Our group consists of 57 out-patients with TLE, 18–65 years of age, both sexes and various education levels. For this work we considered attention index, visual and verbal attention span - using Wechsler intelligence and memory scale, as well as TMT (A and B) test.

**Results:** We documented AD in 36/57 patients (63%). Years of life, sex and education level, as well as duration of illness and seizure frequency were similar in two groups. There were more focal epileptic discharge in EEG in group with AD – 18/36 (50%) than in group without AD – 8/21 (38%). There was more pathological findings in MRI (mostly postrumatic or tumorous) in AD group – 20/36 (55%) than in the other one – 8/
Conclusion: Patients with TLE have significant AD, which is in correlation with pathological EEG and MRI findings. Future clinical studies will provide new data about cognitive functioning of patients with TLE - how the attention problems and other cognitive impairment develop over time.

Conclusion: The results suggest that the diagnosis of IDD might be independent of mood and anxiety disorders although the patients with IDD are more likely to have mood or anxiety disorders.

Conclusion: Psychotic substance use is a major problem among people living with epilepsy. Determining the magnitude of this problem will assistance to identify need for substance abuse treatment among people living with epilepsy.

Conclusion: Psychoactive substance abuse is a major problem among people living with epilepsy. Determining the magnitude of this problem will help develop appropriate strategies for intervention. It is of utmost importance to identify need for substance abuse treatment among people living with epilepsy.

Conclusion: Based on symptom-level analyses, children with epilepsy experience the same depressive and anxiety symptoms as children with JIA and healthy children. However, there might be different clusters of symptoms specific to children with epilepsy, which might have clinical implications.

Conclusion: The prevalence rates of IDD and any mood and anxiety disorders were 15.1%, 29.3%, and 21.1%, respectively, 60% of patients with IDD had any mood or anxiety disorders. Concerning ANOVA of IDD total score and severity, the both main effects of IDD and any mood and anxiety disorders were significant, while the interaction was not significant.

Conclusion: The results suggest that the diagnosis of IDD might be independent of mood and anxiety disorders although the patients with IDD are more likely to have mood or anxiety disorders.
Method: Two hundred and two caregivers of children with seizure disorder were administered socio-demographic questionnaires at the child and adolescent outpatient clinic between October 2011 and March 2012. The Structured Clinical Interview for DSM – IV axis I Diagnosis (SCID) was used for diagnosis of Generalized Anxiety Disorder and Major Depression.

Results: One hundred and forty six (72%) of the caregivers were females, with mothers of patients accounting for 66% of respondents. The prevalence of generalized anxiety among the respondents was 12%, while that of major depressive disorder was 50.5%. The socio-demographic characteristics of carers associated with psychiatric morbidity included older age range ($\chi^2 = 18.67$, $p = 0.001$), being employed ($\chi^2 = 10.41$, $p = 0.015$), longer duration of care ($\chi^2 = 18.07$, $p = 0.001$) and being patients’ mother ($\chi^2 = 10.17$, $p = 0.032$).

Conclusion: Depression and anxiety are common among caregivers of children with seizure disorders. Caregivers’ socio-demographic characteristics and patients’ clinical variables are associated with prevalence of anxiety and depression. These findings suggest the need to adopt a holistic approach to the detection of these disorders and developing adequate intervention for these caregivers.

Others 3 Tuesday, 1st July 2014

p495 PECULIAR PSYCHOGENIC NONEPILEPTIC SEIZURES (PNES) CHARACTERISTICS IN PATIENTS WITH BORDERLINE INTELLECTUAL FUNCTIONING OR MENTAL RETARDATION Chiesa V1, Savini M1, Vignoli A2, Turner K1, Oggioni G1, La Briola F1, Zambrelli E1, Canevini MP2

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Purpose: Psychogenic nonepileptic seizures (PNES) are a relatively common disorder, often misdiagnosed as epilepsy. Especially when epileptic seizures coexist, the diagnosis might be difficult. The gold standard for PNES diagnosis is video-EEG recording of a typical attack. PNES are referred to be common in patients with low IQ. The aim of our study is to clarify PNES semiology and characteristics in this population.

Method: We analyzed demographic and clinical characteristics of 25 patients with mental retardation or borderline intellectual functioning (BIF), with a certain diagnosis of PNES, recorded by Video-EEG. Then we examined all recorded episodes, according to clinical classification of PNES recently proposed by Hubsch et al.

Results: Similar to general population, we found a clear female prevalence (85%) in patients with mental retardation or BIF; onset of PNES occurred meanly at the age of 29, and the mean delay in diagnosis was nearly 2 years. An higher proportion (84%) of patients with coexistent epilepsy was found in our group respect to available literature data for general PNES population. PNES occurred spontaneously during video-EEG recording in 60% of patients; in remaining 40%, PNES were induced by suggestion techniques, which showed a sensitivity of 100% in our patients. A clear psychiatric comorbidity was present in 60% of patients; almost 50% was treated with psychiatric drugs (neuroleptics, antidepressants and benzodiazepines), whereas 80% of patients assumed AED.

No differences in PNES semiology were found.

Conclusions: Despite PNES semiology in our sample not differs from general population, we found some peculiar clinical aspects in patients with BIF or mental retardation, such as more frequent epilepsy comorbidity, and major susceptibility to induction techniques.

p496 PROVOCATION OF NON EPILEPTIC SEIZURES BY SUGGESTION IN CHILDREN AND ADOLESCENTS POPULATION Starczewska M1, Steinborn B1

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Purpose: To evaluate the method of saline provocation during video EEG recording in patient with non-epileptic events.

Method: This was retrospective study conducted at the Department of Developmental Neurology in Poznan. We evaluated 400 patients, aged 9–18 years, of both sexes who underwent video EEG monitoring between 1 January 2006 to 31 December 2009. All studies were reviewed and reported by board certified neurophysiologists. We studied consecutive patients with suspicion of epilepsy diagnosis using saline provocation during video EEG recording, suggesting that this could produce a typical seizures.

Results: PNES occurred more frequently in girls. We observed: headache, dizziness, tremors, malaise, numbness, fainting, immobility, lack of contact, nausea, limb weakness, limb shaking, irritability, limb...
stiffening and eye deviation. No changes in bioelectrical activity were notice during this symptoms.

**Conclusion:** This study suggest that PNES are frequent in developmenta l age. Saline provocation is a sensitive method of identification of PNES.

### p497 INCIDENCE OF OXYGEN DESATURATION IN PSYCHOGIC NON-EPILEPTIC SEIZURES

**Teasdale E**, **Derry C**, **Brotherstone R**, **Duncan S**


**Purpose:** Hypoxemia occurs in over 30% of epileptic seizures. It is widely assumed not to occur in psychogenic non-epileptic seizures (PNES).

**Method:** We reviewed all inpatient video-EEG monitoring studies from May 2005 to June 2008, identifying 281 events from 74 patients. 203 events from 45 patients were epileptic attacks and 78 events from 29 patients were PNES. 2 patients had both PNES and epileptic seizures. We reviewed oxygen saturations in all events, using the accepted threshold of below 92% to define desaturation. We excluded from analysis all events in which desaturation appeared artifactual.

**Results:** Oxygen saturation data was available in 225 (80%) of the 281 events (166 epileptic, 59 PNES). In the PNES group, after exclusion of 3 events due to artefact, desaturation was seen in 14 (25%) events. In the epilepsy group, oxygen desaturation was observed in 64 (39%) events, 9 (30%) of patients with PNES demonstrated oxygen desaturation in at least one attack compared with 26 (57%) of subjects with epilepsy. Two patients with PNES and oxygen desaturation had events from sleep, with clinical episodes apparently arising from sleep-related desaturations from undiagnosed obstructive sleep apnea (OSA). Overall oxygen desaturation in PNES was observed in 25% of attacks, compared with 38.5% of true epileptic seizures. This difference was not statistically significant ($\chi^2 = 3.376, p = 0.66$).

**Conclusion:** Hypoxemia is widely recognized in epileptic seizures. Oxygen desaturation is sometimes used as an objective clinical marker to distinguish epileptic seizures from PNES. Our findings indicate oxygen desaturation can occur in a significant proportion of patients with PNES. Mechanisms underlying desaturation are unclear. Breath holding (possibly after a period of hyperventilation) is a plausible explanation for some attacks. Some sleep-related PNES may be directly related to apnoea episodes in individuals with OSA. Caution should be used when interpreting oxygen desaturation as evidence of an epileptic basis to seizures.

### p498 LONG TERM FOLLOW-UP (10 YEARS) OF LIMBIC ENCEPHALITIS ASSOCIATED WITH VGKC-COMPlex LGII ANTIBODIES

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**Purpose:** A new distinctive seizure semiology referred to as “facio-brachial dystonic seizures” (FBDS) has been identified as closely related with high levels of voltage-gated potassium channels complex antibodies (VGKC-comp-Abs), in particular the leucine-rich-glioma-inactivated-1 (LGI1) subtype. We report a clinical case with 10 year clinical and laboratory follow-up, that was not yet described in the literature.

**Method:** A 77 years patient was diagnosed at the age of 67 (2004) with limbic encephalitis (LE) with disease onset in 2003. In the following 10 years he presented two clinical relapses (2007, 2013) of LE associated with FBDS. He was treated each time with high doses of steroids (1 g Methylprednisolon for 4 days) and anti-epileptic drugs (Phenyoin, Carb-amazepin, Levetiracetam, Zonisamide, Valproic Acid, Pregabalain). Since the last relapse (6.30.13) we added an immunosuppressive therapy with Azathioprine.

**Results:** VGKC-Abs in the CSF were always negative. VGKC-Abs serum levels progressively decreased until normal values after immunosuppressive therapy with Azathioprine. Serum and CSF LGI1 were persistently positive over 10 years.

**Conclusion:** FBDS, that are typical manifestations preceding VGKC-comp-Abs non-paraneoplastic LE, can also relapse over the long term. In line with previous reports we observed that FBDS are responsive to steroids treatment but not to anti-epileptic drugs. Serum and CSF LGI1 was the only persistent positive marker through the years despite the immunosuppressive treatment.
Introduction: The paroxysmal nonepileptic events (PNES) of childhood are a group of disorders, syndromes and phenomena that mimic true epileptic seizures. The differential diagnosis of PNES is very broad spanning a wide variety of physiologic, organic and behavioral conditions.

Objective: To assess the etiology of childhood PNES in different age groups.

Methods: Retrospective study included 59 patients (20 boys and 39 girls) aged 1 month to 18 years diagnosed with PNES. The follow-up period was 1.5 years. The etiology of nonepileptic events was assessed and compared afterwards according to age.

Results: The most frequent cause of PNES was syncope (30.5%), followed by psychogenic non-epileptic seizures (18.6%). 11.9% had apparent life-threatening events (ALTE) as an underlying cause, 8.5% hypoglycemia, 6.8% some kind of intoxication and 3.4% migraine headaches, whereas 20.3% of cases of PNES were due to other causes. We noticed more frequent occurrence of ALTE in infancy (5.57 ± 6.29 months) and syncope (155.16 ± 36.13 months) and psychogenic non-epileptic seizures (168.64 ± 52.07 months) in adolescence.

Conclusion: Our results suggest that organic disturbances were the most frequent causes of PNES in younger children, while autonomic dysfunction disorders and psychogenic non-epileptic seizures were predominated in older children.

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p502 REPEATED MILD BRAIN TRAUMA AND EPILEPSY
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Purpose: Mild traumatic brain injury or concussion is caused by a jolt that shakes a brain back and forth inside a skull. The main symptom of post-concussive syndrome is persistent headache for 1–2 weeks, lasting up to months after the injury. Repeated concussions can lead to long-term memory loss, psychiatric disorders, brain damage and even epilepsy.

Method: Retrospective data analysis of patients with neurologic symptoms playing different sports treated at our Neuropediatric Unit from January 1th 2011 to 30th April 2012 was done. Neurologic symptoms among young athletes were the cause of hospitalization among 6.4% of children with neurological diagnosis.

Results: 54 children were admitted to our Department after or related to repeated mild brain injury while playing sports. Mean age was 12.5 years (range 9–18). Admittance was urgent in 26 children and in 28 a hospitalization was indicated after an outpatient visit and exam. The reason for hospital evaluation was headache in 37 and among them 8 had headache accompanied by dizziness, 1 by visual symptoms an 1 by pre-syncope attack. Three children had syncope or seizures. Two children had TIA, tingling or psychomotor problems. Other children had dizziness, peripheral nerve palsy, tremor or anizocoria. Children with epilepsy following repeated mild brain trauma were successfully treated.

Conclusion: Although a concussion is considered a mild brain injury, it can leave lasting damage if rest is not long enough to let a brain fully heal afterward. When repeated it can lead to serious neurological problems including epilepsy. If a child or adolescent has had a number of concussions, chronic encephalopathy can occur. A doctor must advise the child to avoid the activities that may put them at risk for future head injuries and to discontinue contact or other sports.

p504 NON-ADHERENCE TO AEDS IS A MAJOR CAUSE OF ACUTE HOSPITALIZATION IN PATIENTS WITH EPILEPSY
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Purpose: Epileptic seizures can be provoked by several factors. Better understanding of these factors may improve a patient’s sense of control and could reduce seizures. In daily practice, recognition of seizure precipitants relies heavily on clinical or video-EEG evidence which can be difficult to obtain. Studies of seizure provocation are largely based on selected, hospital-based patient populations which may lead to biased occurrence estimates. Self-reported seizure precipitants are rarely studied, yet necessary to understand experiences of patients and improve epilepsy management.

Method: We performed a cross-sectional community-based study of 248 epilepsy patients, selected by pharmacy records of AED use. Self-reported seizure precipitants and potential associated characteristics were assessed using questionnaires.

Results: Almost half of all patients (47%) reported one or more seizure precipitants of which stress, sleep deprivation and flickering lights were the most common. In this community-based setting, light-provoked seizures were especially frequent compared to the literature. Idiopathic Generalized Epilepsy (IGE), a lower age at seizure onset and having aura or prodromes were found important independent prognostic factors associated with provoked seizures.

Conclusion: IGE and a younger age at seizure onset have been linked to provoked seizures in earlier reports. The finding of auras or prodromes as an prognostic factor was unexpected though case reports have described provoked seizures in patients having auras. Assessment of these factors may facilitate early recognition of seizure precipitants in daily clinical practice. This is important to optimize epilepsy management for a large group of patients with epilepsy as provoked seizures are expected to occur frequently.
Abstracts

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Purpose: Poor adherence to antiepileptic drugs (AED) persists as a major obstacle to an optimal treatment of epilepsy. We aimed to assess the clinical relevance of this problem by means of therapeutic drug concentration monitoring (TDM), and to investigate the clinical characteristics of patients prone to AED non-adherence.

Method: Unselected, consecutive patients with epilepsy acutely admitted to hospital for seizures (n = 255) were included. Non-adherence was defined as having serum concentration/dose ratio at admission of less than 75% of the actual patient’s own control value (probable non-adherence: 50–75% and definite: <50%).

Results: A large proportion of patients (38%) was non-adherent to AED treatment (definitely 23% and probably 15%). Non-adherence was more common in generalized compared to focal seizures (p = 0.026) and in those <30 years compared to older patients (p = 0.0017).

Conclusion: AED non-adherence is a common cause of seizure breakthrough in patients with epilepsy, particularly in adolescents and young adults. Prompt measurements of AED serum concentrations should be available as part of the emergency care for patients acutely hospitalized for seizures to permit this issue to be thoroughly addressed prior to discharge.

Special Reflex Features in Two Epileptic Patients with Phenylketonuria

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Purpose: Phenylketonuria (PKU) is the most common form of amino-acid metabolism disorders. 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 two cases with PKU having reflex-induced seizures.

Method: Adult epileptic patients with PKU were evaluated retrospectively and two patients showing reflex epilepsy features were investigated regarding to seizure type, provoking factors, electroencephalographic and imaging findings.

Results: Case 1: 32-year-old male patient with a history of PKU, had experienced his first seizures at 3.5 years old. He had TV and light induced reflex seizures showing self-induction behavior such as adhering to the TV, hand waving toward the sun. Twitching in front of flashing or reflecting lights were observed and generalized convulsions were added in the course.

Case 2: 18-year-old female patient diagnosed with PKU since 1.5 years old had experienced her first seizures at the age of 15. Seizures were characterized by frequent nystagmoid eye movement periods persisting for 5–6 h. She had secondary generalized convulsions with head version to the left and jerks on the left arm. The seizures were triggered by bright, colored flash and tram lights. The seizures were triggered by hot water and sudden voices, as well. Both patients were motor and mentally retarded. Cranial imagings revealed no specific abnormality. EEG’s showed mild and diffuse slowing and right frontal hypersynchrony in the first patient. Seizures were continuing despite multiple antiepileptic drug combinations.

Conclusion: Although some clinical and electrophysiological features have been described, photosensitivity and reflex features have never been reported in epileptic patients with PKU. Evaluating photosensitivity and other reflex features can contribute to the management of these patients and understanding of epilepsies associated with metabolic diseases.

p506 Post-Stroke Epilepsy in the Third Level Hospital in Marrakech, Morocco

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Purpose: The post stroke epilepsy defined by the occurrence of at least two unprovoked seizures usually in late stroke suits, is reported in 3–5% of stroke survivors and is responsible for at least one third of epilepsy after age 60. Frequency among young adults is less precise.

The goal of this study is to describe the clinical, paraclinical and evolutive features of patients having suffered a post-stroke epilepsy in our context.

Method: Authors report a retrospective study from January 2000 to December 2009. This study collected 110 post-stroke cases. Our depart- ment is a third level structure which covers much of southern Morocco. All patients benefited from brain imaging, EEG, ECG, echocardiography, Doppler cervical arteries and infectious, hematologic and immunological assessments.

Results: Out of 110 cases diagnosed for stroke in young patients, 13 developed a post-stroke epilepsy with a mean age of 36.4 years. Epilepsy was partial type in 81.1% of cases. In most cases it was reaching the cerebral ischemia affecting Sylvian artery in 55% of cases. The etiology remained unknown in 53.7% of patients. With antiepileptic treatment, remission of seizures was total in 97% of patients, was used in bitherapy or polytherapy in the remaining 3%.

Conclusion: The post-stroke epilepsy is the most common causes of epilepsy in the elderly “patients over 60 years old”, whereas in younger patients, few data are available, especially regarding the frequency. Among the risk factors for this entity in young adults in the aftermath of stroke: The younger age, intracerebral hemorrhage and extended stroke. There are currently no guidelines concerning the therapeutic treatment of epilepsy in particular post-stroke towards indications.

Epileptic Asystole: A Clue to the Interpretation of Syncope-Like Attacks in Adults

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Purpose: Ictal asystole is an increasingly diagnosed pattern of temporal lobe seizures, mostly because of a widespread use of long-term video-EEG monitoring. Although usually linked with an increased risk of SUDEP, its significance remains controversial. Here we report 4 new cases showing ictal asystole.

doi: 10.1111/epi.12675
Method: These patients (3 M, 1 F, aged 50–74 years) underwent video-EEG monitoring because of problems of differential diagnosis with paroxysmal non-epileptic events (3 cases). They also performed interictal EEGs, brain MRI and full cardiological evaluation.

Results: These patients had a history (ranging from few days to several years) of syncpe-like episodes (3) and nocturnal paroxysmal events (1) preceded by abdominal rising sensation (2) and olfactory hallucination (1). We recorded a number of seizures from each patient except one who had only one seizure captured during his first video-EEG performed in the emergency room. The seizures showed initial left focal ictal temporal discharge followed by EEG flattening and tonic activity. In one case the seizure had a right temporal onset and a left temporal end. Ictal asystole lasted for 6–25 s and was accompanied by loss of consciousness, pallor/ sweating and mild myoclonic jerks. Three of 4 patients had PM implantation and reported disappearance of ictal consciousness impairment.

Conclusion: Retrospectively, in our series, ictal asystole could be suspected on the basis of syncpe-like episodes preceded by mesial temporal auras. These cases raise problems of differential diagnosis and require expert neurological and cardiological evaluation.

Purpose: To clarify the relationship between headaches (HAs) and somatic/psychiatric comorbidity in patients with epilepsy depending on the effectiveness of treatment (remission over 1 year or drug-resistant).

Method: Among 404 patients with different etiological forms of epilepsy and disease duration more than 5 years, 168 patients were found (using targeted questionnaire) to have primary and secondary HAs. The types of HAs and time of their occurrence in relation to the seizure onset were evaluated. Additionally somatic and psychopathological examination of patients was conducted to identify somatic and psychiatric comorbidity.

Results: Among 168 patients with HAs there were 70 (41.7%) persons in remission and 98 (58.3%) persons were drug-resistant. Among 71 patients (42.3%) HAs were primary with predominance of tension-type HAs, in 97 (57.7%) they were either secondary or unclassified. HAs in patients in remission were accompanied by memory (r = 0.10, p < 0.05) and sleep disorders (r = 0.13, p < 0.01), more frequently encountered in patients with coronary heart disease (r = 0.18, p < 0.01), cerebrovascular disorders (r = 0.20, p < 0.01) and psychiatric disorders (r = 0.31, p < 0.01). In drug-resistant patients suffering from HAs, somatic comorbidity often was observed (r = −0.15, p < 0.01), especially diseases of liver and biliary tract (r = 0.19, p < 0.01) as well as psychiatric comorbidities were present (r = −0.17, p < 0.01): depression (r = 0.23, p < 0.01), memory disorders (r = 0.14, p < 0.01), hypochondria (r = 0.19, p < 0.01), apathy (r = 0.15, p < 0.01), dysphorias (r = 0.21, p < 0.01). Drug-resistant patients without HAs often had psychiatric comorbidity (r = −0.14, p < 0.01), but they did not have observable connection with somatic diseases.

Conclusion: To reduce HAs in patients with drug-resistant epilepsy treatment of psychiatric comorbidity is primarily required, in patients who are in remission – somatic pathology should be treated in the first place.

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AN ALTERNATIVE TO COLLODION
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Purpose: Improve Electrode Application for Long-Term EEG/Video Monitoring without using Collodion.

Method: Prepare the skin as usual. Cut gauze into one inch by one inch squares. Fill a 10 mm electrode cup with a conductive paste (Ten20® conductive paste or Elifex®), just enough to fill the cup. Squeeze a bit of cream (EC2® genuine Grass electrode cream), on a piece of gauze to hold the electrode down for about 10 s which dries up fast. This method does not actually “mix” conductors, since there is almost no contact between the two. One conductor is inside the electrode cup and the other one is on the outside and not serving any conducting function. The electrode impedance should be less than 5,000 Ohms and balanced. After the impedances are found to be satisfactory apply a piece of 3M™ Micropore® Micropore Hypo-Allergenic Surgical Tape over the electrodes on forehead and the temples, e.g., F7, Fp1, Fp2, F8, T1 and T2. Now you are ready to wrap the head. Two 4 inch self-adhering, conforming bandages are used. Tape the head wrap for security and then place a net over the electrodes in remission and 98 (58.3%) persons were drug-resistant. Among 71 patients (42.3%) HAs were primary with predominance of tension-type HAs, in 97 (57.7%) they were either secondary or unclassified. HAs in patients in remission were accompanied by memory (r = 0.10, p < 0.05) and sleep disorders (r = 0.13, p < 0.01), more frequently encountered in patients with coronary heart disease (r = 0.18, p < 0.01), cerebrovascular disorders (r = 0.20, p < 0.01) and psychiatric disorders (r = 0.31, p < 0.01). In drug-resistant patients suffering from HAs, somatic comorbidity often was observed (r = −0.15, p < 0.01), especially diseases of liver and biliary tract (r = 0.19, p < 0.01) as well as psychiatric comorbidities were present (r = −0.17, p < 0.01): depression (r = 0.23, p < 0.01), memory disorders (r = 0.14, p < 0.01), hypochondria (r = 0.19, p < 0.01), apathy (r = 0.15, p < 0.01), dysphorias (r = 0.21, p < 0.01). Drug-resistant patients without HAs often had psychiatric comorbidity (r = −0.14, p < 0.01), but they did not have observable connection with somatic diseases.

Conclusion: To reduce HAs in patients with drug-resistant epilepsy treatment of psychiatric comorbidity is primarily required, in patients who are in remission – somatic pathology should be treated in the first place.

Purpose: To reduce HAs in patients with drug-resistant epilepsy treatment of psychiatric comorbidity is primarily required, in patients who are in remission – somatic pathology should be treated in the first place.

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BECTS INCIDENCE IN WALES – UNREPORTED OR OVERESTIMATED?
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Purpose: Benign Epilepsy with Centrotemporal spikes (BECTS) is reported to be one of the most common childhood epilepsy syndromes. We noted through a separate research study a slower than predicted recruitment from our local population and wished to evaluate further the incidence of BECTS in Wales.

Method: We used the Welsh Paediatric Surveillance Unit – established for anonymised ascertainment of specific conditions in Wales, to identify incident cases of BECTS, over a 2 year 9 month period (1/3/2010 to 31/12/2012). A case ascertainment questionnaire was then sent to the notifying reporting clinician to collect demographic and clinical information.

Results: There were 34 confirmed cases of BECTS – giving a calculated incidence of 2.7 cases per 100,000 children (aged 1–14 years) – from 91 notifications. Thirty-three were excluded; 15 (16%) were duplicates, 5 (6%) were diagnosed outside the study period, and 13 (14%) did not have BECTS after review of clinical information. No information was returned for 24 notifications. Two cases were documented to have combined speech & coordination difficulties, while one case each had a speech or coordination problems identified. Seventeen (50%) cases did not have
neuroimaging. There was a marked regional variability in incidence figures.

The incidence of BECTS in our study was much lower than reported in the literature (10.7 to 21 per 100,000) even if corrected for our incomplete data. Only four children (11.7%) were reported to have problems with speech or coordination, which again is much lower than the 30% to 56% in literature.

Conclusion: Low reporting rates may reflect either a failure to recognize the syndromic presentation, the effect national clinical guidelines that do not recommend EEGs after first clinical seizure in children or a poor response rate to our study. It may also be that previous reports overestimate the true incidence of BECTS.

p511
THE EFFECT OF A ‘DIRECT BENEFIT TO THE PATIENT’ ON THE INCLUSION RATE IN TWO, EPIDEMIOLOGICALLY NEARLY IDENTICAL, STUDIES IN PATIENTS AFFECTED BY BOTH EPILEPSY AND INTELLECTUAL DISABILITY
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Purpose: The number of patients with epilepsy in combination with intellectual disabilities (ID) is substantial and for this, the inclusion of these patients for epilepsy research is essential. However, recruitment of patients with ID is, for ethical and legal issues, often complicated. In addition, it is usually not the patient but the legal guardian who has to give consent for the study. Still, little is known about the factors that determine the inclusion rate in studies with patients affected by both epilepsy and ID. In this study, we investigated the influence of a ‘potential direct benefit to the subject’ on the inclusion in two epidemiologically identical studies as we considered that this might be essential to consent.

Method: The study compared two cross sectional studies of institutionalised subjects with both epilepsy and ID. Both studies were implemented in the same way, in the same population. The difference with respect to recruitment was that in one study there was a potential benefit to the subject (osteoporosis prevention) whereas in the other study (genetic risk factors on available blood samples) there was not.

Results: Of the 260 subjects in the ‘direct benefit’ study, 207 subjects (80%) could be included, 30 (11%) refused and 23 (9%) did not respond. In the ‘no benefit’ study with 266 subjects, 79 (30%) were included, 66 (25%) refused en 121 (45%) did not respond.

Conclusion: The presence of a potential benefit to the subject is important with respect to the recruitment rate in studies that involve patients with both epilepsy and ID. As epilepsy in ID is highly prevalent, and vice versa, knowledge that might improve the inclusion rate is important to prevent the exclusion of a group of patients who are so important for the study of epilepsy.

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EPILEPSY AND AUTISM IN SIBLINGS
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Purpose: Epilepsy and autism spectrum disorder (ASD) often occur together in the same individual, but the recurrence risk in siblings of the two disorders has not previously been studied.

Method: This was a population-based cohort study in Denmark of all children born in Denmark between January 1, 1980, and December 31, 2004. Children were identified and followed up to December 31, 2010. We calculated the adjusted hazard ratio (aHR) for epilepsy and ASD among siblings having an older sibling with epilepsy and ASD, and compared this to siblings where the older sibling did not have these disorders.

Results: The aHR of epilepsy in younger siblings of older siblings with ASD was 1.26 (95% CI 0.82–1.94) when compared to the risk of epilepsy in younger siblings of older siblings without ASD. The aHR of ASD in younger siblings of older siblings with epilepsy was 1.37 (95% CI 1.05–1.78) when compared to the risk of ASD in younger siblings of older siblings without epilepsy.

Conclusion: We found limited evidence that epilepsy and ASD share the same familial risk factors.

p513
LONG TERM RISK OF EPILEPSY AFTER COMPLEX FEBRILE SEIZURE: A CHILEAN MULTICENTRIC STUDY
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Purpose: Evaluate the risk factors associated to epilepsy and refractory epilepsy subsequet to complex febrile seizure (CFSs) in long term follows up.

Method: Prospective observational multicenter national epilepsy Chilean study, conducted between January 2011–September 2013. Children with first CFSs, were included, between 1 month to 15 years. Defined: repeated febrile seizures in 24 h or as longer than 10 min. Clinical epidemiological and follow up were collected. Children with first Symptomatic and simple febrile seizure were excluded.

Results: 28 patients with complex febrile seizure before 5 years of age. Of these children, 9 (32.1%) had subsequent afebrile seizure. The cumulative probability of epilepsy was 10.3% at 24 months. 8/9 patients had abnormal control EEG, significantly associated with subsequent afebrile seizure, (p-value< 0.001). 2/13 neuroimaging with abnormal MRI developed epilepsy.

Conclusion: The occurrence of complex febrile seizures do not represent a risk for future epilepsy in our study, but the abnormal EEG, maybe represent a underlying epilepsy, and is important to consider the family history, to detect promptly epilepsy GEFS+ or Dravet syndrome.

p514
NEUROCYSTICERCOSIS: A CASE REPORT
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Purpose: The World Health Organisation [WHO] estimates that the world’s 50 million with epilepsy is due to neurocysticercosis. The objective of this case report is to show that neurocysticercosis is a treatable cause of epilepsy.
Method: The subject is a 48 year old woman who presented with subcortical nodules on the face, recurrent headache and epileptic seizures. The headache was primarily frontal and the subcortical nodules were non-tender. These symptoms started 6 months prior to presentation at our health facility. There is no family history of epilepsy. The seizures were not relieved by phenobarbitone. Physical examination was non-revealing. FBC, FBS, CSF, HIV and MRI of the brain and eyes were ordered. CSF serology was not done because lumbar puncture was declined.

Results: Hb 14.8 g/dl, FBS 5.4 mmol/l, WBC 6.6 and HIV- negative. MRI, numerous round points with T1 hypointense. T2 hyperintense- dot-form cortex seen in all cerebral slices. Cerebral sulci and gyri are normal. Lateral third and fourth ventricles and cistern are not dilated. The midline structures are not shifted. The brain stem, cerebellum and pituitary glands are normal. Praziquantel 1500 mg bd (50 mg/kg) was given for 6 weeks together with prednisolone. Treatment was given according to the Consensus guidelines on treatment of neurocysticercosis. Repeat MRI after 6 weeks of treatment is normal and the patient is seizure free.

Conclusion: Epilepsy due to neurocysticercosis is amenable to treatment. High dose praziquantel is well tolerated and is effective in treating neurocysticercosis.

p515 OUTCOME OF CHILDREN WITH EPILEPTIC VERTIGO
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Purpose: Epileptic vertigo is relatively rare form of epilepsy, making 6% of all causes of vertigo. The aim of this paper is to show the outcome of our patients with epileptic vertigo due to motor and cognitive functions as well as according to seizure control. We present three children with vertigo as the main symptom of epilepsy.

Patients: Three of our patients with epilepsy were presented with repeated paroxysmal vertigo. All of them had normal results of otorhinolaryngological and ophthalmologic examinations. They all had focal and paroxysmal electroencephalographic discharges, with localized spikes and/or generalized spike wave complexes, with normal magnetic resonance of the brain. They started with anticonvulsant therapy (oxcarbazepine or valproic acid) and became seizure free during the therapy. The first patient was taking oxcarbazepine for two and a half years, and after the medication discontinuing, she is seizure free for a year and a half. Other two patients were treated with valproic acid, and also didn’t have any similar seizures after the therapy initiation. All of them had their EEG normalized. Their cognitive development is average. They didn’t have any impairment in motor functions during the course of disease or after.

Conclusion: Outcome of our patients with epileptic paroxysmal vertigo is excellent. They all have their electroencephalogram normalized, they are seizure free on and after anticonvulsant therapy, without motor impairments and with normal cognitive development.

p516 NON-TRAUMATIC COMPRESSION FRACTURES FOLLOWING A CLUSTER OF GTCS – IN AN OSTEOPOROTIC YOUNG ADULT MALE
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Introduction: Vertebral thoracic non traumatic compression fractures following GTCS are rare; suggesting a previous bone fragility and presents with back pain or can by less asymptomatic.

Case report: A 38 years old male, construction worker, father of 3 children was admitted for strong re acute interscapular pain following two GTCS occurred at early morning witnessed by his wife. Since 2005 he referred bilateral radicular C, L pain with moderate osteoporosis established at bone density rate. MRI established herniated C4-C5, and L5-S1 discs. On admission he presented prolonged post-ictal confusion, not recalling the episodes of LOC and unable to mobilize. On objective examination he showed muscles tenderness from D5–D10 with inferior paraparesis but no spincters impaired.

Thoracic MRI confirmed a compressive fractures of D6 and slighter of D7. The bone scintigraphy revealed trackers fixation highlighted in T6, T7, at (3, 8, 12, 15) ribs and humeral degenerative changes all evoking benign fractures. EEG distinguished anterior bilateral IEDs whilst head CT, MRI was normal thus VPA was introduced not taken regularly.

Other routine laboratory tests besides a mild hyperfibrinogenemia, slight increased ALP, hypercholesterolemia, mild hepatosteatosis resulted at normal parameters. Total Calcium level at serum were measured at norm, phosphor level slightly decreased, hyper trocalcitonina but no sign of thyroid malignancy at doppler imaging. Free serum calcium level, urinary calcium dosage, and PTH resulted normal as well. A recent bone density reconfirmed the moderate osteoporosis at higher risk fractures already occurred. Diabetes mellitus and hypercorticism as unusual causes of osteoporosis and no long-term usage of glucocorticoid drugs were not reported. The pain was conservatively managed with NSAID, analgesic, bed rest and toraco-lumbar brace mobilization whilst for his seizures Valproat was reintroduced.

Conclusion: Vertebral thoracic fractures with no trauma could be associated with seizures in a young male with previous bone fragility stated.
Epilepsy. Worse outcome in terms of seizure control and intellectual disability was associated with earlier onset (particularly in the first month of life) and the presence of a recognizable cause of the disease.

p518
SEIZURE ONSET ZONE VS. RESECTION AREA: TOWARDS A QEEG-BASED SURGERY OUTCOME PROGNOSIS?
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Purpose: Accurate prognosis of surgery outcome is essential for epilepsy patients and physicians. Despite favorable outcome in the majority of patients, non-responders remain an issue. We investigate the prognostic value of three quantitative EEG (qEEG) analysis methods.

Method: We retrospectively analyzed 20 peri-ictal segments of intracranial EEG (iEEG) from 10 patients. 6 patients had excellent surgery outcome (Engel I) and 4 had unfavorable outcome (Engel IV). The channel-wise contribution to three qEEG measures was evaluated: absolute signal slope (ASS, Schindler et al., Clin. Neurophysiol. 2001;112:1006–1017), non-random cross-correlation (NRC) and significantly non-linear interrelation (NLI, Rummel et al., Phys. Rev. E 2011;83:066215). The visually defined seizure onset zone (SOZ) and the neuroradiologically confirmed resection area (RA) were compared.

Results: The overlap between SOZ and RA was not different between outcome groups (Jaccard index, U-test p > 0.3). In each group one patient had several seizure types (chi2-test p < 0.7). The following significant differences (U-tests p < 0.05, FDR corrected) were obtained: In the Engel I group the RA contributed stronger to all qEEG measures than the SOZ. In contrast, no differences were obtained for Engel IV (p > 0.1). Group I differed from IV by larger pre-ictal and ictal ASS in the RA and larger post-ictal ASS and NLI in the SOZ. The contribution of RA and SOZ to NLI was larger than for ASS. The SOZ contributed stronger to NLI than to NRC.

Conclusion: The overlap between SOZ and RA did not correlate with epilepsy surgery outcome. In contrast, significant differences between the groups were detected for the qEEG measures ASS and NLI in SOZ and RA. If these results generalize to larger patient groups, qEEG-based comparison of visual SOZ and putative RA could potentially be used for outcome prognosis.

p519
OUTCOME OF VIDEO EEG MONITORING IN A TERTIARY CARE EPILEPSY CENTER
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Purpose: Video-EEG (VEEG) monitoring is a diagnostic tool that is used to help confirm the diagnosis of epilepsy, characterize seizure type, and localize epileptic foci. To investigate this within our population, we analyzed VEEG outcomes in consecutive adult patients referred to our metropolitan tertiary care epilepsy center.

Method: The outcome of 100 consecutive adult elective VEEG admissions at Long Island Jewish Hospital from July 2011 to January 2012 was reviewed. The questions to be answered by the admission were documented in the clinic note prior to admission. Our analysis included: 1. What was the question to be answered by VEEG? 2. Was the question answered by VEEG monitoring? 3. When was the question not answered, why? 4. Did the outcome of monitoring alter medical or surgical management?

Results: The admission question was answered in 77 patients (see table for admission question). Of the 23 patients whom the question remained unanswered, 14 did not have events, 4 did not wish to continue monitoring, and 4 had events suspicious for simple partial seizures or auras without EEG correlate. In 1 patient, the reason the question was not answered was unclear (see chart). In the patients whom the admission question was answered, 43 had medications adjusted upon discharge: 11 had medications solely increased, 2 patients had medications solely decreased, 11 had a new medication added, 8 had one medication stopped and 16 patients had multiple medication adjustments.

Conclusion: We demonstrated in our population that VEEG is a useful tool to aid in seizure localization, diagnosis and characterization since the question of admission was answered in the majority of patients (77%). Medications were altered upon discharge in approximately 2/3 of patients whom the question was answered. Fifteen percent of total admissions proceeded with epilepsy surgical evaluation and 5% underwent craniotomy for epilepsy surgery.

Status Epilepticus 1
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100 CASES IN THE TREATMENT OF STATUS EPILEPTICUS WITH INTRAVENTRICAL LEVETIRACETAM
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Purpose: We assessed the efficacy of LEV IV in the treatment of various types of status epilepticus (SE).

Method: LEV IV was administered at dosages of 1,000, 2,000 or 3,000 mg either as an infusion (1,000 mg in 100 ml NaCl 0.9%, 15 min) or fractionated (500 mg in 20 ml NaCl 0.9%, 1–2 min). Termination of SE was the effectiveness criterion. Tolerability was assessed by evaluating treatment-related adverse events (AEs).

Results: Since its launch in 2006, we have used LEV IV to treat 100 patients with various types of SE. In general, LEV was administered as second-line therapy, after benzodiazepines. Overall, LEV terminated SE in 58% of patients. LEV was more effective in terminating simple partial SE (22/28, 78.6%) than complex partial (28/48, 58.3%) SE and nonconvulsive SE (8/15, 53.3%). For the treatment of (secondary) generalised tonic-clonic SE, LEV was not sufficient at a dosage up to 3,000 mg (0/9, 0%), and the supposed faster effect of fractionated application was without benefit in these cases. Serious AEs were not reported. Prolonged somnolence (especially in elderly patients) was reported, but it was difficult to determine whether this was caused by LEV, benzodiazepines and/or post-seizure twilight state.

Conclusion: LEV IV is an alternative in the treatment of partial (simple and complex partial) SE.

p521
A CASE REPORT OF NEW ONSET REFRACTORY STATUS EPILEPTICUS (NORSE) IN QATAR
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Purpose: To characterize a patient with new-onset refractory status epilepticus (NORSE syndrome).

Method: This is a case report of NORSE seen at Hamad Medical Corporation in Qatar, previously healthy 45-year-old right-handed man presented with episode of abnormal behavior and agitation on the background of 3-days history of fever, malaise.

Results: The next day after admission patient developed status of generalized tonic-clonic seizures. He was intubated for airway protection, started on Midazolam followed by Propofol IV infusion and placed on continuous EEG monitoring. The seizure originated from the left anterior temporal region progressing into generalized rhythmic sharp wave activity. He continued to have breakthrough seizures, despite multiple anti-convulsant medications, including high doses of Levetiracetam, Valproic acid, Topiramate, Phenytoin. An exhaustive search for infectious, autoimmune including MNDa encephalitis and potassium channel encephalitis and paraneoplastic causes of refractory seizures did not yield any specific etiology. He was treated with one empiric course of intravenous immunoglobulin for presumed autoimmune encephalitis. After over one and half months of refractory seizures patient has stabilized. At the onset of status epilepticus, the MRI showed bilateral temporal increased T2 and FLAIR signal intensity. Subsequent MRI studies performed at 1 month later demonstrated progressive hippocampal atrophy and mild decrease in T2 signal intensity.

Conclusion: Based on our patient and those described in the literature, we characterize the NORSE syndrome. Increased recognition of this clinical entity is needed to help delineate the underlying etiology of this unique severe illness.

p522
FOCAL FRONTAL LOBE STATUS EPILEPTICUS CAUSING PATHOLOGICAL CHANGES OF LAMINAR NECROSIS INVOLVING CORTICAL LAYER 5
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Purpose: Prolonged Status epilepticus may cause select neuronal necrosis in experimental animal models of SE but is not proven in humans. We describe a case of prolonged SE with pathological changes of laminar necrosis, acute ischemic changes and small vessel proliferation particularly in cortical layer 5 demonstrated on brain biopsy.

Method: Case report. A 72 year old male prisoner was admitted to University Hospital in a confusional state which was present at least 2 weeks prior to admission. An EEG obtained on Day 2 showed frontal lobe seizures consistent with non convulsive SE. Multiple doses of lorazepam with high doses of valproic acid, phenytoin and levetiracetam failed to control seizures. Patient had a brain biopsy since tumor and encephalitis were considered likely etiologies and the patient did not respond to conventional AED treatment.

Results: A frontal brain biopsy showed striking laminar small vessel proliferation in cortical layer 5 with loss of neurons in layer 5 and scattered neurons with acute ischemic changes. There was no evidence of malignancy, infection or cortical dysplasia. An Initial MRI showed anteriomedial frontal lobe edema and leptomenigeal enhancement which improved on a subsequent study. CSF was normal.

Conclusion: The issue whether focal SE in a hemodynamically stable well oxygenated patient can cause irreversible brain damage is controversial. In our patient focal SE was the likely cause of both the reversible MRI changes and irreversible brain pathological findings. Laminar necrosis has many causes and we suspect that the laminar necrosis confined to cortical layer 5 with hypoxic neuronal changes and vascular proliferation were related to prolonged (>2 weeks) status epilepticus. Possible mechanisms including excitotoxic neuronal injury vs. anoxia will be discussed. This case supports more aggressive treatment of focal SE to prevent permanent neuronal death.

p523
CLINICAL CORRELATES AND PROGNOSTIC IMPLICATIONS OF PERIODIC LATERALIZED EPILEPTIFORM DISCHARGES IN PATIENTS WITH STATUS EPILEPTICUS IN ACUTE PHASE OF STROKE
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Purpose: Periodic lateralized epileptiform discharges (PLEDs) are uncommon electroencephalographic (EEG) findings usually occurring in acute structural brain lesions such as stroke.

Objective: To analyze the clinical and EEG findings of acute stroke patients with a history of status epilepticus in which EEG disclosed periodic epileptiform discharges.

Method: We studied prospectively the occurrence of seizures within 14 days after acute stroke in 1,456 consecutive patients admitted to our hospital. Those with clinical and electroencephalographic SE were identified and analyzed. The EEG patterns, clinical findings, and prognosis in the SE patients with PLEDs were studied.

Results: Within the group of 146 patients (10%) with post-stroke seizures, thirty-eight patients (26%) presented with SE. Partial motor seizures with or without secondary generalization were the most frequently encountered type of SE. EEG disclosed PLEDs in 19 patients aged 56–90 years. PLEDs were observed in 13, and bilateral independent PLEDs (BIPLEDs) in 6 patients. The main etiology found in the group of patients with PLEDs was acute hemispheric stroke (n=16; 84%), and lobar haemorrhage (n=3; 16%). The mortality rate in patients presented with SE and PLEDs pattern was 36%, as 7 of 39 patients died during their hospitalization. The patients presenting with BIPLEDs early in the course of SE had a significantly higher mortality compared to those with PLEDs (50% vs. 30% in those with no PLEDs; p = 0.03).

Conclusion: PLEDs are common in the patients presented with SE in the acute phase of stroke. Patients with BIPLEDs had significantly higher mortality compared to those with PLEDs patterns.

p524
NATIONAL DATA OF STATUS EPILEPTICUS IN THAILAND
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Purpose: Status epilepticus (SE) is a major neurological emergency with high mortality. The national database of SE in Thailand and developing countries is limited in terms of incidence and treatment outcomes. Therefore, we studied national data of SE in Thailand.

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Abstracts

**Method:** We retrospectively explored national data in Thailand for reimbursement of all adult patients (over 18 years old) admitted SE patient in the fiscal year 2004–2012. SE patients were diagnosed and searched based on ICD 10 (G41) from the national database of Universal Health Coverage Insurance System

**Results:** We found 12,367 SE patients. The average age was 48.14 years (18–104 years) and 8,119 patients were males (65.7%). Discharge status of most SE patients was improved (9,231 cases, 74.6%), while 2,033 patients (16.4%) did not improve and 1,045 patients (8.4%) died. The most common co-morbid diseases were hypertension (1,790 patients, 14.5%) and DM (1,064 patients, 8.6%) and the most common complications were cardiac dysfunction in 1,201 patients (9.7%), Cardiopulmonary resuscitation was done in 266 patients (2.2%), and mechanical ventilator used in 3,990 patients (32.3%).

**Conclusion:** SE is high mortality and need ventilator. Pneumonia is most common complication.

**p525**
PREHOSPITAL TREATMENT AND OUTCOME OF CONVULSIVE STATUS EPILEPTICUS (CSE) IN CHILDREN
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**Purpose:** Aim of the study was to evaluate the role of prehospital treatment on outcome of CSE among children of post neonatal age.

**Method:** Prospective, hospital-based study was performed in Tbilisi, Georgia. Patients aged from 1 month to 18 years with CSE, admitted to the emergency department of M. Iashvili Children’s Central Hospital from March 2007 to March 2012 were included. Outcome was assessed at discharge, neurological deterioration or no consequence.

At admission all patients were evaluated by pediatrician and pediatric neurologist and on 30th day after admission by pediatric neurologist.

**Results:** The data was analyzed according age, sex, etiology, seizure duration, type of seizure, recent CSE, existence of neurological abnormality before CSE and their influence on morbidity and mortality. We evaluated effect of pre hospital treatment on outcome. From 48 admissions 4 patients have not received ambulance service. The mean time of ambulance arrival to the emergency department after onset of CSE was 25 min, range from 15–45 min. 13 (27%) patients needed artificial ventilation.

We identified a statistically significant increase of incidence of artifical ventilation (p < 0.001) in patients receiving more than one dose of BZD in pre-hospital setting. In case of appropriate pre-hospital treatment (using one dose of BZD), seizure duration ranged from 30–70 min (median 40, 65 min). In case of “inappropriate” (using more than one dose BZD) treatment seizures lasted from 30–180 (median time 65.8 min).

Statistically significant association was detected between pre-hospital treatment adequacy, and mechanical ventilation, patients with adequate pre-hospital treatment were less frequently ventilated (p < 0.05) and had shorter duration of status:

**Conclusion:** Non Standardized pre hospital treatment of pediatric CSE in Tbilisi had statistically significant negative influence on outcome of CSE in children.

**p526**
INCIDENCE OF PERI-ICTAL DIFFUSION MRI CHANGES AND THEIR ROLE IN ADULT PATIENTS WITH STATUS EPILEPTICUS
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**Purpose:** Role of MRI in the status epilepticus (SE) is unclear. Various peri-ictal changes on diffusion-weighted image (DWI) have been reported in the small number of patients. We investigated the incidence of various peri-ictal changes on DWI in the SE and their clinical significance.

**Method:** 185 adult patients with acute status epilepticus between March 2011 and October 2013 were included. The type and etiology of SE were analyzed with details of clinical, laboratory, EEG, CT, and MRI data. All patients received DWI and follow-up MRI. Remote and local Peri-ictal changes were classified as previously described with some modification (AJCole).

**Results:** 27% of the patients had established epilepsy, and acute symptomatic causes were found in the 67% of the study patients. Peri-ictal changes were found in the 39% of the patients. The most common finding was the focal cortical cytotoxic lesions, which were found in the 31% of patients. The hippocampal peri-ictal changes were found in 14.4% of the patients, and 18% of them were bilateral in location. Ipsilateral diencephalic lesions were found in 6.5% of the patients, and PRES-like lesion was found in 2.7%. No cerebellar diachisis was found. Remote peri-ictal changes were less than the local changes (9.2% vs. 41.2%). The incidence of peri-ictal changes among various SE types was similar: generalized convulsive SE was 35.6%, epilepsy partialis continua was 30%, and 33.3% in the non-convulsive SE. Permanent changes were found in 16.8% of the patients. Modified Rankin scale was not different (53.1% vs. 51.7%) according to the presence of peri-ictal lesion, but mortality rate was lower in patients with peri-ictal change (6.25% vs. 11.7%).

**Conclusion:** Peri-ictal changes were common, found in 39% of the SE patients. Local changes were more common than remote changes and the incidence was not different among various SE types.

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SURGERY FOR MESIAL TEMPORAL LOBE EPILEPSY DUE TO HIPPOCAMPAL SCLEROSIS: 4 YEARS EXPERIENCE FROM EPILEPSY CENTER ZAGREB, CROATIA
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**Purpose:** We present short term results of MTLE patients operated on due to hippocampal sclerosis.

**Method:** 29 patients were operated on from November 2009 until April 2013. There were 12 female and 17 male, with the mean age of 36.1 years and mean epilepsy duration of 22 years. Standardized preoperative epilepsy evaluation was performed including detailed clinical history taking, continuous videoEEG monitoring, high resolution 1.5 T or 3T magnetic resonance (MR), neuropsychological examination, interictal PET/CT scanning and visual field examination.

Selective amygdalohippocampectomy via subtemporal approach was performed in 26 patients (10 right-sided, 16 left-sided) and in three
patients a right-sided standard temporal lobectomy with AH was performed. Follow-up ranged from 8 months to 51 months. Patients were classified according to the ILAE and Engel classification.

Results: 6 out of 29 patients were followed for more than 4 years, 9 patients for more than 3 years, 8 patients for more than 2 years and 6 patients for more than 1 year. Out of 23 patients with more than a 2 years follow up, 19 patients (82%) are completely seizure and aura free (ILAE = 1a; Engel = 1A). Two patients are ILAE = 2; Engel = IC. Two patients are ILAE = 3; Engel = IIA.

Conclusion: We presented results from Zagreb Epilepsy center surgical programme. In the majority of patients selective AH was performed using subtemporal approach. Complications occurred in only one patient with only transient morbidity. Despite the short term follow-up we feel encouraged with the surgical and seizure outcome and find it comparable with other published series.

p528
INTROOPERATIVE 1.5T MR IMAGING AND FUNCTIONAL NEURONAVIGATION IN RESECTIVE EPILEPSY SURGERY: EXPENSIVE HYPE OR FUTURE TECHNOLOGY? CONCLUSIONS FROM 10 YEARS’ EXPERIENCE IN 400 PATIENTS
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Purpose: Intraoperative MR imaging and functional neuronavigation in resective epilepsy surgery may contribute to precise identification and save resection of epileptogenic tissue. Thus, seizure outcome may improve and complications decrease. Exploring this hypothesis, a retrospective analysis of patients operated on using multimodal intraoperative imaging was performed.

Methods: Four hundred patients (185 female, 215 male, mean age 36.7 years, from 5 to 69 years) suffering from medically refractory epilepsy (range, 5–69 years) were treated with standard mesial temporal lobe surgery. Most patients presented with temporal lobe epilepsy (MTLE). Although 13 showed GS only, other types of seizures (non-GS) included complex partial seizure (n = 58), generalized tonic-clonic seizure (n = 46), and tonic seizure (n = 36). Mean age at onset was 1.8 years (range, 0–11 years) for GS and 5.5 years (range, 0–21 years) for non-GS. Mean age at surgery was 13.6 years (range, 1–50 years). Ninety-nine patients presented with gelastic seizure (GS). Although 13 showed GS only, other types of seizures (non-GS) included complex partial seizure (n = 58), generalized tonic-clonic seizure (n = 46), and tonic seizure (n = 36). Mean age at onset was 1.8 years (range, 0–11 years) for GS and 5.5 years (range, 0–21 years) for non-GS. Mean maximum diameter of HH was 17.9 mm (range, 5–80 mm). Coronal magnetic resonance imaging classified intra-hypothalamic type (n = 26), mixed-type (n = 65; with bilateral attachment in 28), and parahypothalamic type (n = 9) according to Kameyama’s classification. Comorbidities were precocious puberty (n = 35), behavioral disorder (n = 47), and mental retardation (n = 51). Twenty-seven patients underwent treatment before our SRT. No permanent morbidities accompanied a total of 133 SRTs, including multi-staged surgeries. In 82 patients with follow-up for >1 year, GS and non-GS ceased after all SRT in 70 (85%) and 67 cases (82%), respectively. All behavioral and intellectual problems were improved.

Conclusion: SRT represents the best treatment for HH with minimum risk.

p530
COMBINED FOCUSED ULTRASOUND AND GAMMA KNIFE TREATMENT OF MESIAL TEMPORAL LOBE EPILEPSY: COMPUTER SIMULATION STUDY
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Purpose: ExAblate Neuro, an MRI guided Focused Ultrasound Surgery (MRgFUS) system, causes thermal coagulation of well defined focal brain targets with minimal edema but is difficult for use in the vicinity of bone. Leksell Gamma Knife (LGK) can be applied close to bone, but can cause significant edema. We evaluated the feasibility of a combined MRgFUS and LGK treatment for mesial temporal lobe epilepsy (MTLE).

Method: A simulated data was created with the ablation target defined as anterior hippocampus, parahippocampal gyrus and efferent amygdala. We simulated multi session MRgFUS target ablation taking into account the tissue’s acoustic properties, skull beam aberration and safety constraints. Simulated LGK irradiation (24-Gy 50% isodose) was performed on the remaining target, which couldn’t be ablated by MRgFUS. The
resulting edema severity was estimated using edema scale (ES) (Fisher RS et al. In: Engel Jr et al. Epilepsy a comprehensive textbook. Lippincott Williams and Wilkins, 2008:1415–1430), and compared between whole target LGK irradiation and the combined treatment.

**Results:** The defined target volume was 12.99 cm³. MRgFUS could ablate 8.06 cm³ (62.05%). The remaining 4.93 cm³ was simulated irradiated by LGK. Estimated edema severity following LGK ablation of the whole target was 3.6 ES, compared to 0.2 ES following the combined treatment, 18 times improvement.

**Conclusion:** Using MRgFUS prior to treatment with LGK for MTLE, allows relatively large volume ablation with reduced edema; can be performed in multi sessions; can be used for functional mapping and reduces the ionizing radiation needed, thus making such an approach promising for clinical use.

**p531 VISUAL FIELD DEFECTS AND PERMISSION TO DRIVE IN ADULTS AFTER TEMPORAL LOBE RESECTION FOR EPILEPSY**

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**Purpose:** The ability to drive is an important goal for many patients who consider epilepsy surgery. Visual field defects (VFDs) after temporal lobe resection (TLR) for epilepsy are not uncommon, but the proportion of patients in whom the VFDs preclude driving is less often described. This study aims to relate VFDs to seizure outcome and permission to drive after TLR in a Swedish cohort.

**Method:** For all adults who had a TLR for epilepsy in the Gothenburg Epilepsy Surgery Series 1990–2012 neuro-ophthalmological reports and seizure outcome data were retrieved from the patient files. Visual field assessments including Goldmann perimetry are routinely performed preoperatively and 3 months after TLR. The neuro-ophthalmological assessments on VFDs and driving were related to seizure outcome.

**Results:** 114 TLR were performed 1990–2012. For 98 patients, complete pre- and postoperative neuro-ophthalmological assessments could be retrieved. 11 patients with preoperative VFDs (mostly due to previous vigabatin use) were excluded. Of the remaining 87 patients, 45 (52%) had no VFD, 25 had a partial homonymous quadrantopia (29%), 15 (17%) had a complete homonymous quadrantopia, and two (2%) had a homonymous hemianopia postoperatively. In 15/87 patients (17%), the postoperative VFD was judged to preclude driving.

**Conclusion:** Major VFDs are rare after temporal lobe surgery for epilepsy. However, even minor VFDs may preclude driving in seizure-free patients. This is an important factor to consider in preoperative patient counseling.

**p532 PLACE OF STEREOTROHO ENCEPHALOGRAPHY AFTER A FIRST FAILED EPILEPSY SURGERY**

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**Purpose:** Epilepsy surgery failed in 30–40% of patient with drug resistant partial epilepsy. The selection of patients who could benefit from a second surgery is an important step to improve the management of these patients (Surges et al 2013). Our purpose is to study the role of Stereoelectro-encephalography (SEEG) approaches after a first failed epilepsy surgery.

**Method:** From SEEG database (300 SEEG), 12 patients have been investigated by depth electrodes after an initial failure of epilepsy surgery. Demographic data, etiology of epilepsy, results of preoperative evaluation, results of SEEG, surgery option and outcome were determined.

**Results:** Cortical dysplasia were identified in 6 patients, hippocampal sclerosis in 1 patients, ganglioglioma in 2 patients, astrocytoma in 1 patient, perinatal stroke in 1 patients, cryptogenic case in 1 patient. SEEG identified 9 patients with temporal epilepsy (lateral 1, mesial 3, lateral-mesial 1, bilateral in 1, temporal plus 3), 2 patients with frontal lobe epilepsy, and 2 patients with parietal lobe epilepsy. SEEG led to an explanation of surgery failure demonstrating a bilateral EZ (2 cases), an epileptogenic zone larger that the initial surgery (7 cases) or a multifocality (3 cases). Five patients with focal EZ were operated leading to a good post-surgical outcome (3 class IA and 2 class IIA).

**Conclusion:** The SEEG play a key role in selection of patients who may benefit a second epilepsy surgery after a first surgical failure. Good surgical outcome can be expected when a focal EZ is eventually identified.

**p533 LESION FOCUSSED STEREOTACTIC THERMO-COAGULATION INSTEAD OF OPEN RESECTION: A NEW WAY IN EPILEPSY SURGERY?**

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**Purpose:** In epilepsy surgery it is still debated how small surgical interventions can be without compromising the success of surgery. In particular in patients with epileptogenic lesions recognized by magnetic resonance imaging (MRI) it is unresolved whether resection or destruction of the lesion suffices to eliminate the epileptogenic zone. We present a minimal invasive epilepsy surgery approach which can contribute to solving this question.

**Method:** Two patients with pharmaco-resistant epilepsy due to focal cortical dysplasia type IIb according to 3 Tesla MRI were treated with lesion-guided stereotactic high-frequency thermo-coagulation. In both patients pathognomonic epileptic discharges were recorded from the lesion via the stimulation device prior to coagulation. In one patient the suspected proximity of the pyramidal tract and the lesion was proven by eliciting motor evoked potentials from the depth of the lesion.

**Results:** In both patients seizure activity (several per day or week, respectively) ceased following coagulation focussed to the lesion (at time of submission for 11 and 5 months). Neither patient suffers from postoperative neurological deficits.

**Conclusion:** Cessing of seizure activity after destruction of lesions as recognizable in 3 Tesla MRI implies that in small bottom-of-sulcus dysplasias the epileptogenic lesion may be identical with the epileptogenic zone. Focussed lesion destruction could be a further development of the concept of individually tailored epilepsy surgery. Yet, our results require replication by future studies. The applied technique is suited for high precision surgery close to eloquent brain structures.
p534  
**PEDIATRIC EPILEPSY SURGERY TECHNIQUES GENERAL ISSUES: INTER-CENTER WORLDWIDE VARIABILITY**  
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**Purpose:** A web-based questionnaire was sent to several centers with a wide geographical representation in order to understand the present practice status around the world.  

**Method:** A web-based survey comprising 14 questions was filled up by 52 centers representing all continents. Questions investigated the number of procedures / year, the type of procedures carried out, operating room approaches as for hair shaving, use of steroids, mannitol, valproate and antibiotics, and technical issues related to flaps opening and closing. The peroperative and postoperative use of imaging was also investigated. The materials / drugs used for anesthesia, skin prep, hemostasis and dural replacement were evaluated.  

**Results:** The mean number of procedures per year was 48. All centers performed resective and disconnective procedures. 96% of the centers carried out lesionectomy, 88% VNS, 51% multiple subpial transaction, 17% laser ablation, 13% thermocoagulation, and 9% DBS. 36.5% of the centers performed craniotomy before surgery. 48% of the surgeons shaved the hair, 40% used steroids, 21% used mannitol, 98% used prophylactic antibiotics. 46% of the centers gave intravenous AEDs during surgery. 88% of the surgeons used high-speed drills for craniotomy, 67% closed the skin with resorbable stitches, while 85% used non-resorbable material for bone flap closure. 44% used a subgaleal drain. 55% of the centers performed ECoG. 34% of the centers performed an immediately post-operative CT scan; MRI was more often performed later than 3 months. 63% used iodine-based fluids for skin prep, 59% used surgical for hemostasis, and 59% of the kids were anesthetized with propofol. 26% of the surgeons used autologous grafts for dural replacement; 13% of them never perform dural replacement.  

**Conclusion:** There was wide variability throughout most of the items investigated. There were no clear geographic or country specific differences. Many of these issues would need adequate RCTs to be further investigated.  

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**SURGICAL STRATEGIES OF FLE WITH CORTICAL DYSPLASIA IN TERMS OF EXTENT OF RESECTION**  
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**Purpose:** With advance of new structural and functional neuroimaging techniques, the opportunities and indications for surgical intervention of cortical dysplasias are rapidly expanding. Therefore, cortical dysplasia became the most frequent (33%) etiology of Pediatric Epilepsy Surgery via ILAE 2004 Outcome Survey, and third major substrate (13%) in Adult Epilepsy Surgery Patients as well. For these reason, many articles relating cortical dysplasia were already published retrospectively regarding usually clinical, pathological characteristics and surgical outcomes, but few regarding extent of resection.  

**Method:** Our protocol, the tailored resection for minimalism by intraoperative tailoring for determination of the extent of resection as well as surgical outcomes, out of total 726 epilepsy surgery series for 15 years since our Epilepsy Surgery Program became the most frequent (33%) etiology of Pediatric Epilepsy Surgery via ILAE 2004 Outcome Survey, and third major substrate (13%) in Adult Epilepsy Surgery Patients as well. For these reason, many articles relating cortical dysplasia were already published retrospectively regarding usually clinical, pathological characteristics and surgical outcomes, but few regarding extent of resection.  

**Results:** Eleven patients with frontal lobe epilepsy from sixty-seven patients with histopathologically proven as cortical dysplasia (TLE:48, FLE:11, PLE:5, OLE:3) were selected for this topic and reviewed the surgical strategies with respect to intraoperative tailoring for determination of the extent of resection as well as surgical outcomes, out of total 726 epilepsy surgery series for 15 years since our Epilepsy Surgery Program were commenced in 1992. Severe Type II cortical dysplasias in histological findings present more often with extratemporal, and more intractable seizures.  

**Conclusion:** The strategies of epilepsy surgery, such as FCD lesionectomy alone or how much do we resect as adjacent corticectomy, and how do we decide the extent of resection will be presented greater detail along with the practical aspect of surgical treatment for intractable epilepsy with cortical dysplasias.
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PATIENT EXPERIENCES OF EPILEPSY SURGERY – A LONGITUDINAL QUALITATIVE STUDY
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Purpose: To explore patients’ subjective hopes, fears and experiences before and after epilepsy surgery.

Method: As part of a national prospective longitudinal study of HRQOL at baseline, 2 years, and at long-term follow-up after epilepsy surgery, open-ended questions supplemented surveys. Of the 96 patients who answered surveys, 87 answered open-ended questions at baseline, 91 at 2 years and 63 > 10 years after surgery. The answers to the open-ended questions were analysed by qualitative content analysis. The text was sorted into meaning units: each meaning unit was related to same content and context and labelled with codes. The codes were abstracted into 12 subcategories and after a process of reflection and discussion they were abstracted to four categories.

Results: Before surgery, the category Anxiety of the unknown illuminated fear of the operation, continued seizures, and complications. The category A belief of a “normal” life illuminated hopes for seizure- and medication reduction, a richer social life and self-confidence. After surgery, the category Increased independence illuminated symptom reduction, relief from worries and fears, and a new life. The category Changes to the worse illuminated a few patients’ experiences of psychological and physical complications.

Conclusion: The majority of patients considered that they had a better life with increased independence and less fear after epilepsy surgery while a minority had negative experiences, some even if they were seizure-free. These results emphasize the need of information and support, pre- and postoperatively, to increase the possibility to find coping strategies in the new life situation after epilepsy surgery.

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EPILEPSY SURGERY IN CHILDREN WITH CONTINUOUS SPIKE AND WAVES DURING SLOW SLEEP
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Purpose: To investigate the postoperative developmental course of language abilities in children after epilepsy surgery due to heavy-to-treat epilepsy and continuous spike and waves during slow sleep (CSWSS).

Method: We included all patients of our Pediatric Epilepsy Surgery Program who fulfilled following inclusion criteria: (i) regular follow-up visits including developmental data and a postoperative follow-up of at least 2 years and (ii) CSWSS or a pathological sleep pattern (PSP – no proper sleep architecture and an increase of spikes but not fulfilling the criteria of CSWSS) before surgery. Developmental quotients (DQ) before surgery and at the last follow-up visit (two or more years postoperative) were calculated. Associations between the postoperative DQ (pDQ) and postoperative sleep pattern (2 years postoperative) or the postoperative seizure outcome (2 years after surgery) were analysed. For statistical analysis, nonparametric Wilcoxon and Chi-square tests were applied.

Results: 24 children (15 female) were included and their median follow-up duration after surgery was 4.0 years. Analyzing the complete group we found a significant increase of the pDQ (p = 0.04). Seventeen/24 children (70.8%) had a normal sleep pattern after surgery (CSWSS: 9/12 – 75.0%, PSP: 8/12 – 66.7%). Focusing on normal postoperative sleep pattern vs. pathological sleep pattern we did not find a significant increase of the pDQ (p = 0.08). But by analyzing the subgroup with CSWSS we found a significant increase of the pDQ (p = 0.01). Nineteen/24 children (79.1%) were seizure-free at the last visit (CSWSS: 11/12 patients [91.6%], PSP 8/12 patients [66.7%]). By analyzing the complete group we found a significant increase of the pDQ (p = 0.02).

Conclusion: Postoperative seizure freedom and the extinction of the preoperative pathological sleep pattern were predictive for good postoperative developmental outcome. Children with typical CSWSS seemed to show a better postoperative development of the language abilities than children with other disturbances of the sleep pattern.

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DO ANTIIEPILEPTIC DRUG CHANGES AFFECT COGNITIVE OUTCOME AFTER EPILEPSY SURGERY?

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Purpose: In regard to the cognitive consequences of epilepsy surgery, the question of whether antiepileptic drug (AED) changes affect cognitive surgical outcome has not yet been addressed in detail.

Method: Patients who underwent temporal (TLE, n = 87) or extratemporal (E-TLE, n = 29) lobe epilepsy surgery were evaluated in regard to executive functions (EpiTrack), memory (combined verbal/figural VLMT/DCS-R), and depression (BDI) before and 1 year after surgery.

Results: At baseline executive functions were impaired in 60% of the patients (E-TLE > TLE), total memory in 54% (no difference TLE E-TLE), 49% had mood problems (BDI > 10). Seizure free rates were 63% for TLE and 69% for E-TLE. Postoperatively, gains (22%) in executive functions (TLE = E-TLE) were greater than losses (15%), and memory losses (21%) were greater than gains (10%) (TLE > E-TLE). Mood improved in 32% and worsened in 11% of the patients. Number of drugs was reduced after surgery. Withdrawn drugs were mostly carbamazepine, oxcarbazepine, zonisamide, clonazepam, added drugs were mainly lamotrigine or levetiracetam. Regression analyses indicated better baseline, reduced drug load, and total seizure control as predictors of improved executive functions, temporal lobe surgery determined memory decline, and percent seizure reduction positively modulated mood.

Conclusion: The present data suggest that improvements of executive functions after epilepsy surgery are in part due to AED changes. Reduction of total drug load but also change from risky AED to cognitively neutral or positive drugs need to be controlled when discussing cognitive effects of surgery and seizure control.

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INSULAR SURGICAL RESECTION IN NON TUMORAL, PHARMACORESISTANT EPILEPTIC PATIENTS: REPORT ON 6 CASES EXPLORED BY SEEG

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Introduction: The role of the insular lobe in intractable epilepsy has long been neglected. Stereo – electroencephalography (SEEG) provides the opportunity to explore the insular cortex, in order to identify the epileptogenic zone involving the insular cortex and to better understand its involvement in brain functions. However insular resection is rarely performed because of the significant risks of neurological complications related to the surgical removal of this area.

Objective: This pilot study was undertaken to assess the effectiveness and safety of insular surgical removal on seizure control based on anatomo-electroclinical correlations provided by SEEG.

Patients and methods: 6 right handed patients (3 males, 3 females) with drug-resistant epilepsy, underwent comprehensive presurgical evaluation. Based on video-EEG recordings, they all underwent SEEG evaluation with bilateral (n = 4), or unilateral right (n = 2) insular depth electrodes placement. Preoperative MRI was normal in 4 cases, 1 patient had right insular focal cortical dysplasia, 1 patient had a right Rolandic opercular postoperative scar (cavernous angioma). All patients underwent right insular corticectomy by subpial, trans opercular approach.

Results: Intracerebral recordings confirmed “pure” right insular epileptogenic zone in all patients. After surgery, 5 of 6 patients were seizure-free (Engel I) with a mean follow up of 28.2 months (9–65), and the latter had a significant reduction in seizure frequency (Engel IIIa). Histological findings revealed a focal cortical dysplasia in 5 cases, and one case of gliosis scar. All patients had minor transient neurological deficit (facial paresis, dystartria).

Conclusion: SEEG allowed high reliable anatomo-electroclinical correlations, leading to insular epilepsy diagnosis. Insular corticectomy cured 5 out of 6 patients without permanent neurological deficit. These results suggest that the SEEG should be performed more systematically when insular epilepsy is suspected even if preoperative MRI is normal, and corticectomy should legitimately be part of the therapeutic armamentarium for curative purposes.

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SURGICAL TREATMENT OF EPILEPSY IN PATIENTS WITH TUBEROUS SCLEROSIS

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Purpose: Surgical treatment of epilepsy patients with tuberous sclerosis complex (TSC) is a challenge due to multiple brain lesions and multifocal epileptic activity in EEG. We report the data regarding the strategy of preoperative evaluation of pediatric patients with TSC and the outcome after surgical treatment.

Method: Eleven children (median age – 4 years, range: 1–13 years) with TSC-associated epilepsy underwent surgery. In 1 patient resection was avoided in order to prevent neurological deficit. In all patients preoperative evaluation included MRI as well as analysis of seizure semiology and interictal/ictal video-EEG. MEG was performed in 4 patients with discordant video-EEG data and clinical semiology, in order to define the “dominant epileptogenic” tuber. Three patients underwent invasive EEG because of discordant data obtained noninvasively (1 case) or because of close proximity of the epileptogenic lesion to eloquent cortex (2 cases). Seven patients underwent focal resection: disconnection was used in 3 patients (posterior quadrantectomy – in 2 cases, and anterior frontal sub-total hemispherectomy – in 1 case).

Results: Seven patients exhibited lateralized focal seizure semiology and in all of them semiology coincided with the dominant focus of regional interictal epileptiform activity. Ictal EEG demonstrated fewer focal changes; regional ictal onset was noted in 4 out of 7 patients. Ictal MEG was advantageous in localizing seizure onset-zone (SOZ) in 3 patients whose seizure semiology and EEG-data were uncertain. Invasive EEG allowed to localize SOZ and to map eloquent cortex in all 3 cases. Median duration of the follow-up period was 13 months (3 months–4 years). Eight patients were seizure-free. Presence of variable seizure semiology was associated with less favorable outcome; the Engel Class 2A and 3A outcome was achieved in the remaining 2 cases.

Conclusion: In carefully selected cases surgery is an effective way of treating epilepsy patients with TSC.
EVIDENCE-BASED RECOMMENDATIONS FOR THE ASSESSMENT OF EPILEPSY SURGERY IN A DEVELOPING COUNTRY

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Purpose: The presurgical evaluation and surgical treatment of the epilepsies is absolutely dependent on the availability of well-trained epileptologists and epilepsy neurosurgeons. This group of professionals are those that establish the essential technologies in relation to each patient.

Method: Since 1984 we began to developed the surgical program according French school, this group of patients were studied in base to semiology clinic, interictal EEG, TAC and acute implantation of depth electrodes for delineation of epileptic zone (EZ). Since 1995 there was a drastic modification in the protocol diagnostic, “Step 1” included video-EEG monitoring, MRI (1.5 T), neuropsychological and psychiatric evaluation. If we arrive to define EZ it is follow by surgical treatment. “Step 2” add SEEG and/or grid subdural electrodes.

Results: Between 1984–1995 underwent surgery 33 patients, and between 1996–2013, 215 subjects. The average duration of epilepsy before referral was 24 years. Invasive studies since 1996 were performed on 20% patients. The mean duration of follow-up post-surgical was approximately 15 years. Surgical outcomes was stable over time, in temporal lobectomy 88% patients were class I (Engel) and in extratemporal surgery 70% patients were class I.

Conclusion: These patients need to be identified early in life before the psychosocial consequences of prolonged disability prevent useful rehabilitation. Our results were similar to those obtained in reference centers from developed countries. Most of the patients reported, were evaluated with the technology available in the 1990s, may be thought as the minimum requirement and it is accessible in the majority centers of the Third World.

INSULAR AND INSULO-OPERCULAR EPILEPSY IN CHILDHOOD: PRESURGICAL STEREODEE EGG EXPLORATION AND SURGICAL OUTCOME

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Electric and clinical correlations in insular epilepsy are well-known in the adult population but poorly described in the children’s one. Insular surgical techniques are being refined and early surgery often improves the cognitive outcome, thus a better knowledge of the correlations should allow an earlier surgery.

Among 136 children with cortical resection at the Rothschild Foundation between 2009 and 2013, 15 among them were operated on the insular cortex after stereoelectroencephalographic (sEEG) exploration showing that the epileptogenic onset zone belongs to the insular cortex.

Mean epilepsy onset occurred at 17 months, with subtle focal seizures and infantile spasms and 3 among them had previous status epilepticus. Then, vegetative symptoms and asymmetric motor seizures became obvious. MRI of 10 patients showed focal insular abnormalities. The FDG-PET scan showed focal hypometabolism in one case, large or multifocal hypometabolism in 11 cases. Only 3 children had normal cognitive development. Scalp EEG showed focal interictal abnormalities in one patient, multifocal in 9 of them, involving the frontal lobe in 10 patients, the central or temporal cortex in 10 others. The ictal onset was never focal, but bilateral or including at least two lobes. sEEG analysis confirmed that the insular cortex was part of the ictal onset zone and the epileptogenic zone involved insula plus frontal or central cortices. Electrical stimulation reproduces the spontaneous seizures in 3 patients. A cortical focal dysplasia was found in 11 patients. Twelve patients were Engel 1 with cognitive improvement but 2 had permanent motor deficit.

The insufficient description of the subjective symptoms made the diagnosis of insular epilepsy difficult during their early childhood. Multifocal frontal interictal EEG spikes were suggestive of insular onset and SEEG, a reliable presurgical method in this population, confirmed the hypothesis. A tailored resection based on a sEEG can lead to an excellent outcome.

FEASIBILITY OF USING AN ONLINE TOOL TO ASSESS APPROPRIATENESS FOR AN EPILEPSY SURGERY EVALUATION

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Purpose: Epilepsy surgery continues to be underutilized. To aid in the referral of patients for an epilepsy surgical evaluation, we recently developed a tool (www.epilepsycases.com) that can be used to determine the appropriateness of referral. Our objectives were to examine the applicability of applying this tool in a clinical setting and to determine if appro-
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LONG-TERM FOLLOW-UP AFTER HEMISPHEROTOMY FROM THE PATIENTS’ PERSPECTIVE
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Purpose: To report long-term seizure outcome and parents’/patients’ perception of outcome after hemispherectomy.

Method: Data from the Swedish National Epilepsy Surgery Register on the 29 patients undergoing hemispherotomy 1995–2010 who had a 5- or 10-year follow-up were analysed. Age at operation was 0.3–20.6 years, median 4.1 years. The families were contacted and so far 21 accepted to be interviewed. Aetiology was acquired in one and developmental in the remaining 17. Eight had a 5-year and 13 a 10-year follow-up. The age of the patients at the interview was 7–37 years: 11 were ≤16 years, 10 were ≥19 years. Two of the adults could be interviewed themselves. The parents answered the ELDQOL questionnaire, and open questions on fulfillment of expectations and satisfaction with the operation.

Results: 8/21 (38%) were seizure-free at the long-term follow-up. Three with seizure freedom at 2-year follow-up had later seizure relapse. All had learning disabilities of varying degree. The two adults were both seizure-free and scored high on satisfaction. Thirteen parents were very satisfied with surgery, two were very dissatisfied. All who were satisfied also stated that their expectations had been fulfilled to some degree, also parents whose children still had seizures. Sixteen assessed their children’s health to be good/very good, and 15 assessed their quality of life to be good/very good.

Conclusion: In this series the long-term seizure freedom rate was quite low, possibly due to the high percentage of developmental aetiology (81%). Still, parents reported a high level of satisfaction with surgery, with surprisingly small differences between parents with seizure-free children and the parents of children with seizures. The parent-reported health and quality of life scores were high. Even when seizure freedom is not obtained, the parents find the operation to have been worthwhile at long-term follow-up.

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FACTORS INFLUENCING WILLINGNESS TO PARTICIPATE IN CLINICAL TRIALS AMONG PATIENTS WITH EPILEPSY
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Rationale: Clinical trials (CT) are essential for the development of new effective treatments in medicine. We aimed to assess factors which motivate patients with epilepsy (PWE) to participate in CT and the concerns they have. Knowledge of this factors may improve the recruitment and quality of future trials.

Methods: A questionnaire was sent to a random sample (N = 2,000) of the members of the Finnish Epilepsy Association who had epilepsy and who were 18 years or older. The survey was completed by 325 subjects. The survey included statements which the respondents assessed using a Likert scale from 1 (strongly disagree) to 5 (strongly agree).

Results: Most of the respondents (70%) thought that PWE should be asked to participate in clinical trials. Altogether 82% of the PWE wanted to have all available information about the CT and the new drug before giving the consent. Also, approximately half of the PWE would only agree to participate if their own physician conducted the CT. Additionally, 45% of the PWE would participate in CT in order to receive improved care of their epilepsy and 60% would participate to receive the best treatment available. Half of the respondents would only participate in CT wherein at least one of the trial treatments had been previously shown to be effective. Only 28% of the PWE would participate in placebo-controlled CT and 10% would participate in CT that included a risk of severe adverse effects.

Conclusion: Possible personal health benefits are a strong motivating factor for willingness to participate in a CT. The use of placebo in the CT or the risk of severe side-effects significantly decreases the willingness to enter into a CT. During the recruitment, special attention should be paid on the information given about the trial and its methodology.
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COMPARISON OF ARTIFICIAL NEURAL NETWORK AND REGRESSION ANALYSIS FOR PREDICTION OF INITIAL LAMOTRIGINE MONOTHERAPY EFFICACY IN ADULT PATIENTS WITH NEWLY DIAGNOSED LOCALIZATION RELATED EPILEPSIES

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Purpose: To develop and compare the logistic regression (LR) and artificial neural network (ANN) models for prediction of initial lamotrigine (LTG) monotherapy efficacy in adult patients with newly diagnosed localization related epilepsies.

Method: Prospective longitudinal study included consecutive series of adult patients with newly diagnosed localization – related epilepsy started of LTG monotherapy. LR analysis using backward procedure was performed with treatment failure as the outcome variable. We evaluated both calibration and discrimination of the models. Internal validation of the models was performed with bootstrapping techniques. ANN model was developed using the same input and output variables as LR model. We evaluated calibration and discrimination characteristics of the models as well as pre and post test probabilities of the outcome. Comparison was performed on whole dataset as well as independent test set.

Results: A total of 159 patients on LTG monotherapy have been included in final analysis. Among them 78 (49.06%) patients had persistent seizures. Finally fitted multivariate model included: (i) age at therapy start, (ii) presence of complex partial seizures, (iii) etiology of epilepsy and (iv) interaction of age and epilepsy etiology. In the independent test set, rate of correctly classified outcome was 75% for the LR model and 93.8% for the ANN model. After positive LR model prediction probability of outcome was 78.26% while it was 93.33% after ANN prediction. There are significant differences for c-statistics (LR 0.855 vs. ANN 0.992, p = 0.03).

Conclusion: Results suggest better potentials of ANN model than LR model for predictions of initial LTG monotherapy efficacy. Further studies of the strengths and limitations of this method are needed with larger prospective samples and external validation, before an ANN can be reliably applied in a clinical setting. If validated, our models can serve as additional tool for patient counseling and clinical decisions.

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ANTIEPILEPTIC DRUGS AND COGNITIVE FUNCTIONS IN CHILDREN WITH SYMPTOMATIC AND CRYPTOGENIC FORMS OF EPILEPSY

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Purpose: Comparison of the safety and influence of antiepileptic drugs phenobarbital, topiramate and lamotrigine on cognitive functions and behavior in children with symptomatic and cryptogenic focal forms of epilepsy.

Methods: We observed 96 patients aged from 1 month to 17 years old with focal forms of epilepsy and divided them into 3 groups according to using antiepileptic drugs: 1 group – 31 patients were treated by topiramate in doses from 56 up to 500 mg/day, from 2.8 up to 17 mg/kg/day (on the average 6.6 mg/kg/day), 2 group – 31 patients – received therapy by lamotrigine in doses from 25 up to 250 mg/day, from 0.5 up to 6 mg/kg/day (on the average 3.6 mg/kg/day), 3 group – 34 patients – received therapy by phenobarbital in doses from 12 up to 300 mg/day, from 1.5 up to 12 mg/kg/day (on the average 6.4 mg/kg/day). All drugs were used in monotherapy or in combine therapy with other antiepileptic medication. Period of observation were from 6 month till 4 years 6 month.

Results: Behavior problems (agression, dysphoria, excitability, hysterical reactions) were noted in 7 (21%) of patient, treated by phenobarbital and in 2 (6%) of patient, treated by topiram and lamotrigine, after full clinical remission Landolt syndrome were registered. Negative effect of phenobarbital on memory, attention, and school learning were observed in 12 (36%) of patient after treatment of phenobarbital more than 2 years. And in opposite. 11 (35%) of children, treated by topiramate and 65% has shown significant improvement in they cognitive functions.

Conclusion: This study has shown topiramate and lamotrigine is not only high effective, but safe new antiepileptic drugs for treatment focal forms of epilepsy and safe cognitive functions in children.

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RETROSPECTIVE EVALUATION OF ANTIEPILEPTIC DRUGS AND KETOGENIC DIET IN 40 PATIENTS WITH CDKL5 MUTATIONS: LOW LONG-TERM EFFICACY

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**LACOSAMIDE IN MESIAL TEMPORAL LOBE EPILEPSY (MTLE) WITH HIPPOCAMPAL SCLEROSIS (HS)**

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**Purpose:** Traditional belief was that MTLE accompanied by HS was synonymous to drug-resistant epilepsy. In the last few years, however, the identification of MRI features of HS in patients with familial and sporadic MTLE who displayed a good seizure control with a single antiepileptic drug (AED) most commonly carbamazepine or oxcarbazepine at low dosage. We describe 13 patients with MTLE with HS and their efficacy to de novo treatment of lacosamide (LAC).

**Method:** We observed the records of 13 patients with MTLE and HS according to ILAE classification. All patients performed presurgical video-eeg-monitoring (alternatively awake and sleep deprived EEG recordings) and MRI of the brain using a 3T scanner with specific protocol for epilepsy purposes. Patients received LAC as monotherapy directly or with other antiepileptic drugs. Seizure frequency, adverse effects were recorded and follow-up was conducted for 3 to 24 months (median 12 months).

**Results:** A familiar history of febrile convulsions or epilepsy was observed in three of the patients. Three of the patients had a personal history of simple febrile convolution. The mean age at seizure onset was 20.4 ± 17.0 years, the mean duration of epilepsy was 23.4 ± 17.0 years. The mean dose of LAC was 358.3 mg ± 66.0 (1 pt. 200 mg/die, 3 pt. 300 mg and 8 pt. 400 mg). In total, 6 patients (46.2%) achieved seizure freedom, whereas 4 patients showed a ≥ 50% reduction (30.8%) of seizure frequency.

**Conclusion:** Our results may suggest that LAC at doses of 200 to 400 mg/day reduces seizure frequency in MTLE. LAC might be particularly effective in patients with MTLE with HS.

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**EFFICACY AND SAFETY OF LACOSAMIDE IN ADD-ON IN CHILDREN AND YOUNG ADULTS WITH PHARMACORESISTANT EPILEPSY**

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Lacosamide (LCM) is a new antiepileptic drug that enhances the slow inactivation of voltage-gated sodium channels.

**Purpose:** Prove the efficacy and safety of LCM in children and young adult with pharmacoresistant epilepsy.

**Method:** Multicentric, prospective, uncontrolled, observational, open label therapeutic trial. Population: 110 patients (54 ♂ 56 ♀). Age: 59 pts <16 years and 51 pts >16 years. Follow-up: 3 to 12 months. Dose: 4–10 mg/kg/die in children and 200–400 mg/die in young adults. Epilepsy type: focal symptomatic (62 pts), focal presumed-symptomatic (19 pts), focal with CSWS (7 pts), Lennox-Gastaut-like (11 pts), Lennox-Gastaut (3 pts), Dravet Syndrome (1 pts), indeterminate (7 pts). Etiology: malformations (33 pts), presumed symptomatic (31 pts), genetic (17 pts). Side effects were usually mild and include: restlessness, aggressiveness, dizziness, dyspepsia, drowsiness, insomnia, headache, vomit, and diplopia.

**Conclusion:** LCM is a good add-on therapy in patients with refractory epilepsy. In particular it is more effective in focal epilepsy and in young patients. Our data suggest that there are no differences if LCM is used with SCB+ or SCB-.

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Abstracts

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Eleven patients (35.5%) discontinued LCM: Ten (32.3%) within the first trimester and one (3.2%) after the first year of treatment. Reasons for discontinuation were lack of efficacy (9.7%), adverse drug reactions (ADRs) (22.6%) or both (3.2%).

Twenty-eight patients (90.3%) experienced ADRs. More frequently reported were dizziness (48%), ataxia (13%), aggression (10%), headaches (10%), psychosis (10%), confusion (10%) and postural tremor (10%).

Main ADRs leading to LCM discontinuation were dizziness, headache, diplopia, ataxia and psychosis.

Conclusion: Lacosamide was effective in our selection of highly pharmacoresistant cases. 39% of our patients responded in the addition of Lacosamide achieving seizure reduction of ≥50% for a period of 2 years, whilst 6.5% became seizure free.

64.5% of patients continued treatment for the whole study period. Withdrawals occurred more often because of CNS related ADRs than because of LCM ineffectiveness and were confined within the first trimester of treatment. Further studies might examine whether slower LCM titration and closer patient monitoring could influence favorably LCM retention rates in our population.

p554
LONG-TERM EFFICACY OF ZONISAMIDE VS. CARBAMAZEPINE MONOTHERAPY FOR TREATMENT OF ADULTS WITH NEWLY DIAGNOSED PARTIAL EPILEPSY: ANALYSIS BY BASELINE SEIZURE TYPES
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Purpose: To assess the long-term efficacy of once-daily zonisamide vs. twice-daily controlled-release carbamazepine monootherapy in adults with newly diagnosed partial epilepsy, by baseline seizure types.

Method: Patients completing a Phase III non-inferiority trial, comparing monotherapy with zonisamide (200–500 mg/day) vs. carbamazepine (400–1,200 mg/day) for treating partial seizures, entered a long-term, double-blind extension study (zonisamide, N = 137; carbamazepine, N = 158). Efficacy (≥24-month seizure freedom and retention) was analysed by baseline seizure types (intent-to-treat populations).

Results: Overall ≥24-month seizure freedom rates were 32.3% for zonisamide vs. 35.2% for carbamazepine. For patients with a history of simple partial, complex partial, secondarily generalised tonic-clonic and generalised tonic-clonic seizures, ≥24-month seizure freedom rates for zonisamide vs. carbamazepine were 27.3% [15/55] vs. 26.2% [16/61], 31.4% [32/102] vs. 34.3% [34/99], 24.3% [37/152] vs. 34.9% [52/149] and 45.7% [16/35] vs. 38.2% [13/34], respectively. Overall retention rates for zonisamide vs. carbamazepine were generally similar at all time-points (27.7% [38/137] vs. 27.8% [44/158] at 18 months). For patients with secondarily generalised tonic-clonic seizures, retention rates were generally lower with zonisamide vs. carbamazepine (18.9% [4/74] vs. 30.3% [27/89] at 18 months), whereas for those with generalised tonic-clonic seizures, they were higher with zonisamide vs. carbamazepine (33.3% [7/21] vs. 18.2% [4/22] at 18 months). For simple/complex partial seizures, retention rates were generally similar between treatments.

Conclusion: Zonisamide and carbamazepine monotherapies demonstrated favourable long-term efficacy in adults with newly diagnosed partial epilepsy. Any differences between treatment groups may reflect low patient numbers in seizure type subgroups.

Supported by Eisai

p555
AN OVERALL AND DOSE-RESPONSE META-ANALYSIS OF EFFICACY OF NEWER GENERATION ANTIEPILEPTIC DRUGS IN THE TREATMENT OF SECONDARILY GENERALIZED TONIC-CLONIC SEIZURES
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Purpose: To perform an overall and a dose-response meta-analysis of randomized controlled trials on the efficacy of newer antiepileptic drugs (AEDs) in the treatment of secondarily generalized tonic-clonic seizures (SGTCS).

Method: Comprehensive literature searches (Medline, Embase and European Medicine Agency website) for randomized controlled trials of new AEDs in pharmacoresistant partial epilepsy were performed. A random effects meta-analysis of data from all the selected randomized controlled trials was developed to evaluate the efficacy of newer AEDs at approved doses against SGTCS in patients aged 12 years and older. The outcome measure considered was the responder rate (percentage of patients with at least 50% seizure frequency reduction). As second aim a dose-response meta-analysis was conducted for all the AEDs for which responder rates data against SGTCS at different doses in more than one study were available (perampanel, retigabine and topiramate only).

Results: 11 records of 15 randomized controlled trials were included. 9 AEDs were evaluated. The total risk ratio of all newer AEDs included in the overall meta-analysis (50% responder rates in SGTCS compared to placebo) was 1.49 (95% CI 1.29–1.72, p < 0.0001). The dose response meta-analysis suggested that the optimal doses for perampanel, retigabine and topiramate were 8,900 and 400 mg/day respectively with a risk ratio of 1.60 (95% CI 1.28–2.01) for perampanel, 1.90 (95% CI = 1.14–3.17) for retigabine and 2.30 (95% CI = 1.34–3.97) for topiramate.

Conclusion: Efficacy data on SGTCS are seldom reported in published articles. To our knowledge this is the first meta-analysis confirming that newer AEDs included were effective as adjunctive treatment against SGTCS compared to placebo. We also found the most effective dose for perampanel (8 mg/day), retigabine (900 mg/day) and topiramate (400 mg/day).

p556
ZONISAMIDE AND RETINAL VASCULITIS – A CAUSAL RELATIONSHIP?
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Purpose: Zonisamide is classified as sulfonamide, a novel drug whose structure is not related to other anticonvulsivants, and with a very wide action mechanism. It decreases cellular excitability threshold by complementary mechanisms of action, acting at sodium and calcium channels, as well as GABA and glutamate system, having a stabilizing effect on the neuronal membrane and reducing hypersynchronisation phenomena. Was approved in 2005 in Europe for the treatment of partial seizures with current level of evidence A in monotherapy. Occulsive retinal vasculitis is an inflammatory disease of retinal vessels, charac-
terized by microinfarcts, hemorrhages and edema, with significant visual impairment.

**Methods:** We describe a case of male patient of 43, with complex partial seizures since age 12, who developed a picture of bilateral occlusive retinal vasculitis after introduction of zonisamide.

In adulthood he went under various therapeutic regimens. Was controlled with oxcarbazepine 600 mg tid which was replaced by zonisamide 150 mg id in September 2012. Two months after the introduction of the drug, began complaint about visual impairment. He was attended by ophthalmology, coming to a diagnosis of bilateral occlusive retinal vasculitis. At that time he was medicated with alprazolam, trazodone and zonisamide 150 mg id. Due to coincidence with the introduction of zonisamide, and because cases of systemic vasculitis associated with this molecule are described, we decided for the immediate suspension of the drug, and switch to esicarbamazine.

**Results:** The case was reported to Infarmed. The patient went through immunomodulatory treatment with cyclosporin A, prednisolone, and anti VEGF and laser photocoagulation. Six months after discontinuation of zonisamide, retinal lesions regressed frankly, restoring eyesight for 8/10.

**Conclusion:** Retinal vasculitis is a serious adverse effect potencially associated with zonisamide. If, prospectively or retrospectively, others cases of retinal vasculitis be reported in patients taking zonisamide, a causal relationship is likely to be established.

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**p557**

**EFFECTS OF ADJUNCTIVE ZONISAMIDE TREATMENT ON WEIGHT AND BODY MASS INDEX IN PAEDIATRIC PATIENTS WITH PARTIAL EPILEPSY**

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**Purpose:** To assess the effects of adjunctive zonisamide treatment on weight and body mass index (BMI) in children with partial epilepsy.

**Method:** Effects on weight and BMI of adjunctive zonisamide treatment (target dose 8 mg/kg/day) in children with partial epilepsy were assessed using data from a Phase III, multicentre, randomised, double-blind, placebo-controlled trial and its long-term, open-label extension study. Changes in weight were correlated with skeletal development (hand X-rays) and sexual maturation (Tanner stage transition) using scatterplot analyses.

**Results:** Overall, 179 patients received zonisamide. Decrease in weight ≥5% was reported for 64/179 (35.8%) patients. Of these, 30/64 (46.9%) were overweight/obese at study entry, compared with 15/64 (23.4%) at study end. 33/64 (48.4%) had normal weight at study entry, compared with 22/64 (65.6%) at study end. Three patients were overweight at start of treatment and four more became overweight by study end. Overall, 152/179 (84.9%) zonisamide-treated patients either did not lose weight on treatment or did not change BMI category on treatment. Scatterplot analyses of bone age and delay in maturation vs. weight change revealed no consistent pattern of delay in bone maturation in patients with weight loss. Similarly, analysis of Tanner transition times vs. weight change indicated no trends towards increasing transition time with weight change.

**Conclusion:** The incidence of weight loss in paediatric patients treated with zonisamide appeared to be most common in those with high baseline BMI values. Furthermore, weight loss did not appear to be associated with any consistent effects on growth and development. Supported by Eisai.

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**IMPACT OF ADJUNCTIVE PERAMPanEL ON BEHAVIOUR IN ADOLESCENTS WITH REFRACTORY PARTIAL-ONSET SEIZURES**

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**Purpose:** Explore the impact of adjunctive perampanel on behaviour in adolescents with refractory partial-onset seizures, supplementing previously reported primary cognition outcomes (Meador et al., AAN 2014).

**Method:** Adolescents (N = 133; 12–17 years old) were randomised to placebo or perampanel (target dose 8–12 mg/day) for 19 weeks. Safety endpoints included mean change (±SD) from baseline in child behaviour checklist (CBCL) total competence and total problem score (study not powered to detect differences). Treatment-emergent adverse events (TEAEs) related to hostility or aggression were identified using narrow and broad standard medical query terms.

**Results:** Median perampanel maintenance dose was 10 mg/day. Change from baseline was not notably different between perampanel and placebo groups for CBCL total competence score (0.0 ± 3.5 vs. +0.2 ± 3.5; p = 0.619 [unadjusted]; higher score indicates better competence), or competence subscales. The change from baseline was not notably different between perampanel and placebo for CBCL total problem score (−2.4 ± 16.5 vs. −4.8 ± 15.3; p = 0.174 [unadjusted]; increase implies worsening), or problem subscales such as aggressive behaviour. TEAEs related to hostility or aggression occurred in 2 (4.2%) placebo patients (1 aggression, 1 irritability) and 15 (17.6%) perampanel patients (7 aggression, 6 irritability, 1 laceration, 2 anger). The only psychobehavioural serious TEAE was aggression (perampanel n = 2, placebo n = 0); both cases recovered without perampanel dose adjustment.

**Conclusions:** Although adverse events suggestive of behavioural change were higher with perampanel vs. placebo, assessment of behaviour with the validated CBCL tool showed no notable impact on behavioural competence or behavioural problems.

**Acknowledgements:** Study sponsor: Eisai Inc. Medical writing support: Choice Healthcare Solutions, funded by Eisai Ltd.

**p559**

**DO LEVETIRACETAM (LEV) AND BRIVARACETAM (BRV) DIFFER IN THEIR EFFECT ON THE PHOTO-PAROXYSMAL EEG RESPONSE (PPR) IN EPILEPSY PATIENTS?: RESULTS OF A RETROSPECTIVE, DATA MINING STUDY**

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**Purpose:** LEV, and LEV-analogue, BRV, have similar chemical structures; yet, their pharmaco-dynamic profiles differ. BRV has a 10x-higher affinity to the SV2A-binding site, plus unique actions: BRV is active in both animal seizure models of maximal electroshock and pentyleneetrazol, with an effect on Na+ channels & NMDA receptors (Matagne, 2008; Schulze-Bonhage, 2011). Uncontrolled observations show that some patients with less than an optimal response to LEV respond to BRV (Van
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Paesschen, 2013). Potential for differences between LEV and BRV need to be explored.

Method: We retrospectively compared data on epilepsy patients with a reproducible PPR from two Phase IIa studies with single-oral doses 250–1,000 mg LEV and 10–80 mg BRV (Kastelein-Nolst Trenité et al., 1996 & 2007) in the standardized photosensitivity model for: a. #&% of patients showing either a complete abolition, reduction or no change (insufficient change, i.e., SPR <3); b. time of onset and duration of PPR effect, including variability observations (no PPR measurements were performed at 0.5 h for LEV); c. the relationship of these pharmacodynamic changes to their respective plasma-concentrations.

Results: After BRV intake, more patients showed complete abolition and diminished PPR vs. LEV. BRV 80 mg appears to be equally suppressive to 750 mg LEV. Time to onset of LEV PPR effect = 1 h post-dose on Day 1 and the effect duration was ≥ 6 h. For BRV, onset time for PPR = 0.5 h post-dose on Day 1, but PPR duration variability was observed (1–32 h). Rising LEV and BRV plasma concentrations did appear to visually correlate with greater PPR effect.

Conclusion: This combined data suggests BRV has a potentially earlier, greater pharmacodynamic PPR suppressive effect vs. LEV at the single doses studied. A direct "head-to-head" comparison of BRV vs. LEV in the Photosensitivity Model is warranted. (UCB Pharma sponsored this investigator-initiated-study).

p560
EFFECTIVE OF ADJUNCTIVE LACOSAMIDE (≤400 MG/ DAY) IN COMPLEX PARTIAL AND SECONDARY GENERALIZED SEIZURES IN ADULTS WITH FOCAL EPILEPSY: POOLED ANALYSIS OF THREE OPEN-LABEL EXTENSION TRIALS

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Purpose: To evaluate the long-term efficacy of adjunctive lacosamide (≤400 mg/day) in controlling complex partial seizures (CPS) and secondary generalized seizures (sGS) in patients ≥16 years with focal epilepsy.

Method: Data pooled from three open-label extension (OLE) trials (up to 8 years) of adjunctive lacosamide (100–800 mg/day) in adults with partial-onset seizures. Responder rates (≥50%) and freedom from sGS and combined CPS and sGS were evaluated from the OLE studies for patients exposed to ≤400 mg/day lacosamide (primary, double-blind and OLE trials) who reported sGS, and CPS or sGS, respectively (baseline, primary trial).

Results: Of 363 patients exposed to lacosamide ≤400 mg/day (mean epilepsy duration 24 years; 72% tried ≥4 lifetime AEDs; 84% on 2–3 concomitant AEDs), 150 reported sGS (median 2.5 seizures/28 days) and 342 reported CPS or sGS (median 7.6 seizures/28 days). In the yearly completer cohorts between 47.4% (1-year; 45/95), 58.3% (3-year; 35/60), and 50.0% (5-year; 13/26) of patients were free of sGS for ≥12 months, and between 25.5% (1-year; 56/220), 33.3% (3-year; 48/144), and 37.5% (5-year; 21/56) of patients were free of CPS and sGS for ≥12 months. The ≥50% responder rates were 64.2% (1-year; 61/95), 75.0% (3-year; 45/60), and 73.1% (5-year; 19/26) for sGS and 62.7% (1-year; 138/220), 70.8% (3-year; 102/144), and 71.4% (5-year; 40/56) for CPS and sGS combined.

Conclusion: Long-term adjunctive lacosamide treatment (≤400 mg/day) resulted in a clinically relevant reduction in CPS and sGS frequencies in adults with difficult-to-treat focal epilepsy.

Supported by: UCB Pharma

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TOLERABILITY OF LACOSAMIDE CONVERSION TO MONOTHERAPY: A HISTORICAL-CONTROLLED MULTICENTER, DOUBLE-BLIND, RANDOMIZED TRIAL

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Purpose: To evaluate the tolerability of conversion to lacosamide monotherapy in patients with partial-onset seizures.

Methods: Patients (16–70 years) on a stable regimen of 1–2 antiepileptic drugs were randomized 3:1 to lacosamide 400 or 300 mg/day (Clinicaltrials.gov: NCT00520741). Doses were titrated from 200 mg/day to the randomized dose in 100 mg/day weekly increments. Maintenance Phase included a 6-week background AED Withdrawal Phase and 10-week lacosamide Monotherapy Phase.

Results: 425 patients received lacosamide (300 mg/day n = 106, 400 mg/day n = 319); 271 (63.8%) completed the Monotherapy Phase. Treatment-emergent adverse events (TEAEs) experienced by ≥10% of patients during the treatment period were dizziness (24.0%), headache (14.4%), nausea (13.4%), convulsion (11.5%), somnolence (10.4%), and fatigue (10.1%). These were most common during the Titration Phase, except TEAEs coded to "convulsion." Respective incidences during Titration, AED Withdrawal, and Monotherapy Phase were 17.4%, 5.8%, and 4.7% for dizziness; 7.8%, 4.7%, and 5.6% for headache; 9.2%, 2.9%, and 2.9% for nausea; 1.4%, 6.5%, and 6.2% for convulsion; 8.2%, 2.9%, and 0.6% for somnolence; and 7.8%, 1.8%, and 1.8% for fatigue. 10.4% of patients experienced TEAEs considered to be severe. Overall, 72 patients (16.9%) discontinued at any time during the study because of AEs. 22 (5.2%) discontinued during Titration, 49 (11.5%) during Maintenance (40 of whom also met predefined seizure-related study exit criteria) and one during the Transition Period. 17 patients reported serious AEs during the treatment period, convulsion was the only TEAE reported by more than one patient (n = 5). Three patients died (due to polytrauma [n = 1] and sudden unexplained death in epilepsy [n = 2]; none considered lacosamide related).

Conclusion: Lacosamide monotherapy was generally well tolerated with a safety profile similar to that seen in adjunctive lacosamide trials. The most frequently reported TEAEs had a higher incidence during Titration vs. Monotherapy Phase.

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PERAMPANEL IN THE TREATMENT OF EPILEPSY: A MULTICENTRE EVALUATION

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Purpose: To evaluate outcome following treatment with perampanel in chronic partial epilepsy.

Method: A multicentre prospective observational study to evaluate long term outcome in adult patients aged 16 or over treated with perampanel has been initiated. Data relating to monthly seizure counts, global assessments, adverse events and drug doses have been recorded.

Supported by: UCB Pharma
**Results:** A total of 44 cases, mean age of 40 years, 38 with symptomatic partial and 6 with symptomatic generalised epilepsy have been identified so far. Twenty three had cognitive or neurological deficits. Mean duration of treatment was 25 years. An average of six previous drugs was used. All started on two mg/day with titration of two mg every 2–4 weeks. The mean retention on perampanel was 4 months. The maximum dose was 10 mg. Among 31 patients, five had a 50%+ improvement in seizure control and six less than 50%. No patient became seizure free. Ten discontinued medication, one due to increased seizures, two due side-effects and seven due to side-effects and lack of efficiency. The commonest side effects were sedation (7) and mood disorders (4).

**Conclusion:** In patients with highly refractory epilepsy who have tried multiple previous medications, initial experience is that perampanel may be a useful adjuvant treatment. Tiredness and sedation were the commonest side effects. Further recruitment and follow up continues and will allow assessment of prolonged seizure remissions and use in sub groups such as those with learning disability.

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**p563**

**CLINICAL EXPERIENCE WITH PERAMPANEL IN A REGIONAL EPILEPSY CLINIC**

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**Purpose:** Perampanel is a novel antiepileptic drug that inhibits the AMPA class of glutamate receptors. It has been available in the UK since September 2012. Data from post marketing studies can complement those from regulatory trials, and help inform the use of newer drugs. We undertook a retrospective analysis of efficacy and tolerability of perampanel in 30 patients with refractory epilepsy attending a regional epilepsy service in the UK

**Method:** Demographic and clinical data of patients with refractory epilepsy prescribed perampanel were collected by review of records. Efficacy, as measured by responder rate (>50% reduction in seizure frequency), retention and adverse effects were analysed.

**Results:** 30 patients were prescribed perampanel, 16 (53%) female. Median age was 30.5 years (range 19–80). 26 (87%) had focal epilepsy, 3 (10%) had generalised epilepsy and 1 patient had unclassified epilepsy. 26 patients had simple and complex partial seizures, 15 had generalised tonic clonic seizures, 3 had myoclonic jerks and 1 patient each had absence and atonic seizures. Median dose of perampanel was 8 mg (range 2–12 mg). 19/30 patients continued perampanel until the end of follow up (retention rate 63.3%). Of these 5 (26%) patients were classed as responders (>50% reduction). 3 (15%) had >50% improvement in seizure frequency, and 11 (58%) had no change or deterioration of seizure frequency. 11 withdrew, 9 (82%) due to adverse effects, and 2 (18%) due to lack of efficacy. Dizziness (n = 8), sedation (n = 7), unsteadiness (n = 5), behavioural disturbance (n = 6) confusion / mental slowing (n = 4), and depersonalisation / abnormal thoughts (n = 3) were the most commonly reported side effects.

**Conclusion:** Perampanel appears to be effective and well tolerated in real life clinical practice. Responder and retention rates mirror regulatory studies. Neurocognitive and behavioural adverse effects appear the most common reason for treatment withdrawal in our centre.

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**p564**

**CLINICAL TRIAL FEASIBILITY AND UK PRACTICE SURVEY OF ROLANDIC EPILEPSY AND PANAYIOTOPOULOS SYNDROME**

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**Purpose:** The evidence base for management of childhood epilepsy is poor, especially for specific epilepsy syndromes such as rolandic epilepsy (RE) and Panayiotopoulos syndrome (PS), for which there is considerable international variation in practice. The aim of this study is therefore to describe current practice and gauge opinions about RCT designs for RE and PS.

**Method:** We conducted an online professional survey of 590 UK paediatricians treating epilepsy. Thirty two questions covered annual caseload; investigation and management practice; factors influencing treatment; antiepileptic drug preferences; and hypothetical trial design preferences.

**Results:** There was a total of 132 respondents out of 590 individuals (22%), of which 81% were general, community or neurodisability paediatricians, and 95% at consultant seniority. We estimated annually 751 new RE cases and 233 new PS cases by summatung individual reported caseloads. EEG is requested at least half the time in approximately 70% of cases; MRI brain is requested at least half the time in 40–65% cases; and neuropsychological evaluation in 7–8%. Forty percent of cases were not treated. Carbamazepine would be the preferred older drug and levetiracetam the preferred newer drug in a hypothetical trial. Both active and placebo designs were considered acceptable.

**Conclusion:** Management practices among respondents are broadly in line with national guidance. A large proportion of patients remains untreated. There is a large sampling frame of new onset RE and PS cases to construct a randomized controlled trial. Clinicians seem amenable to both placebo and head-to-head RCTs to address questions of antiepileptic effectiveness and cognitive/behavioural outcomes.

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**LACOSAMIDE FOR UNCONTROLLED PRIMARY GENERALIZED TONIC-CLONIC SEIZURES: AN OPEN-LABEL PILOT STUDY WITH 59-WEEK EXTENSION**

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**Purpose:** To assess safety and seizure frequency during adjunctive lacosamide treatment of patients (16–65 years) with idiopathic generalized epilepsy (IGE) and uncontrolled primary generalized tonic-clonic seizures (PGTCS).

**Method:** A multicenter, open-label pilot study (SP0961 [NCT0118949]) comprised 12-week Historical Baseline, 4-week Prospective Baseline, 3-week Titration (adjunctive lacosamide titrated [by 100 mg/day/week] from 100 mg/day to 400 mg/day), and 6-week Maintenance. Patients completing SP0961 could enter long-term extension (SP0962 [NCT0118962]) at dose received at end of SP0961, followed by flexible-dose treatment period (100–800 mg/day with optional add-on AEDs) of up to 59 weeks. Primary variables were: change in absence seizure-days/28 days or myoclonic seizure-days/28 days from Prospective Baseline to Maintenance (SP0961); incidence of treatment-emergent adverse events (TEAEs) and withdrawals due to TEAEs (SP0962).

**Results:** Of 49 patients enrolled, 40 (82%) completed SP0961; 5 discontinued due to AEs and 4 withdrew consent. 39 enrolled in SP0962; 29
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(74%) completed and 2 withdrew due to TEAEs. Small mean±SD decreases in number of absence seizure-days/28 days were recorded from Prospective Baseline to Maintenance in SP0961 (−0.37 ± 4.80) and during Treatment Period in SP0962 (−2.38 ± 5.54). Changes in myoclonic seizure-days were: −2.19 ± 5.80 for SP0961 and −2.78 ± 6.43 for SP0962. Median%changes in PGTCs frequency/28 days using 16-week Combined (Historical+Prospective) Baseline were −100% to Maintenance in SP0961 and −72.3% during Treatment Period in SP0962. During SP0962, 25 patients were PGTCS-free for 6-months, 14 were PGTCS-free for 1-year. TEAEs (incidence ≥15%) in SP0961 were: dizziness (39%), nausea (27%), headache (16%), somnolence (16%); SP0962: dizziness (26%), upper-respiratory tract infection (26%), headache (18%), tremor (15%).

Conclusion: Adjunctive lacosamide treatment did not systematically worsen absence or myoclonic seizures in patients with IGE. A minority of patients showed an increase in absence seizure-days which was not clearly treatment-related. PGTCs frequency was reduced in both studies. Safety profile after ≥12-months adjunctive lacosamide in patients with uncontrolled PGTCs was similar to that known for POS, except for study-specific seizure-related AEs.

Supported by: UCB Pharma

p566 EFFECTS ON QUALITY OF LIFE OF LACOSAMIDE AS FIRST AND LATER ADJUNCTIVE TREATMENT FOR UNCONTROLLED PARTIAL-ONSET SEIZURES: A MULTICENTER OPEN-LABEL TRIAL

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Purpose: To evaluate the effects of lacosamide on quality of life (QOL) in earlier and later line adjunctive treatment in patients with partial-onset seizures (POS).

Method: This open-label trial (Clinicaltrials.gov: NCT00955357) enrolled patients with uncontrolled seizures (≥3 POS during 3 months prior to study entry but ≤40 POS/28 days), despite adequate prior treatment. Patients started at 100 mg/day and were titrated to 400 mg/day lacosamide with weekly dose increases of 100 mg/day. Group 1 included patients initiating lacosamide as first adjunctive therapy to a first monotherapy at ≥24 months since diagnosis; Group 2 included patients initiating lacosamide as later add-on to ≥1–3 concomitant AEDs, after ≥2 previous AEDs, at ≥5 years since diagnosis. The primary efficacy variable was proportion of patients achieving seizure freedom for the first 12 weeks of the 24-week Maintenance Phase.

Results: Of 456 patients who received lacosamide, 444 had at least one post-baseline seizure assessment and were included in the Full Analysis Set (FAS); mean [SD] age 39.2 [13.4] years, 50% female; 91 patients were in Group 1 and 353 in Group 2. Overall, mean change from baseline in QOLIE-31-P total score was 2.7 (SD 15.28, n = 414). Corresponding change in QOLIE-31-P total score for Group 1 was 4.6 (SD 16.24, n = 82) and for Group 2 was 2.3 (SD 14.89, n = 332). Improvements were seen for all QOLIE-31-P subscales except Medication Effects (−1.1 [SD 33.23] for Group 1 and −2.4 [SD 30.28] for Group 2). The subscale with the greatest change from baseline was Seizure Worry (6.0, SD 23.78); 11.3 (26.31) in Group 1 and 4.7 (22.98) in Group 2. Mean change from baseline in QOLIE-31-P total score for patients who completed the 24-week Maintenance Phase (n = 304) was 5.3 (SD 15.02) and improvement in Medication Effects was 3.1 (SD 28.87).
Abstracts

p568 PRAGMATIC LONG-TERM OPEN-LABEL STUDY ON THE EFFECTIVENESS OF LACOSAMIDE AS ADD-ON THERAPY IN REFRACTORY PARTIAL EPILEPTIC PATIENTS
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Purpose: To evaluate efficacy and tolerability of lacosamide as long-term add-on treatment in patients with refractory partial epilepsy (RPE).

Method: Pragmatic, open-label, multicentre, prospective study. Study population: PE patients no responders to at least two adequate antiepileptic drugs (AEDs).

After 3 months with stable therapy lacosamide was administered up to a minimum dosage of 200 mg/die; further increases in relation to clinical decision. Efficacy analysis was based on the comparison of baseline and follow-up monthly seizure frequency; multivariate analysis was used to evaluate in risk factors. Tolerability was assessed reporting adverse events.

Results: 65 patients (30 M; mean age 41 years; 28 Cryptogenic PE, 37 Symptomatic PE); mean duration of epilepsy: 23 years; mean number of previous AEDs: 6.9 (range: 2–15). Mean follow up: 13.3 months (range: 0–24); mean lacosamide dosage: 396 mg/die (range: 100–500).

58 patients entered efficacy analysis. No statistical differences (>0.001) were found in the comparison of median monthly seizure frequency after lacosamide: 7 (12%) patients were responders (>50% seizure reduction). After multivariate analysis (N-way ANOVA) no clinical (neurological and psychic examination, etiology, length of disease, number of previous AEDs, other concomitant Na-channel blocking AEDs, EEG lateralization) and demographic (sex) factors were found to modify drug response. 12 (18%) dropped-out for adverse events, mainly dizziness, mostly if lacosamide was associated to Na-blockers.

Conclusion: Our preliminary data show a good efficacy and tolerability of lacosamide in relation to the refractoriness of the epilepsy of study population and to the high number of AEDs associated.

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p569 BRIVARACETAM BIOAVAILABILITY/ BIOEQUIVALENCE COMPARISON BETWEEN 10, 50, 75 AND 100 MG TABLETS AND 100 MG INTRAVENOUS BOLUS IN HEALTHY VOLUNTEERS
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Purpose: To determine the bioequivalence of three brivaracetam (BRV) oral tablet formulations (10 mg, 75 mg and 100 mg) vs. BRV 50 mg oral tablet and to compare the bioavailability of BRV 100 mg intravenous (iv) bolus vs. BRV 50 mg and 100 mg oral tablets, in healthy volunteers.

Method: This Phase I, randomised, open-label, crossover study comprised five treatment periods, separated by a one-week wash-out. All participants received single doses of BRV (10 mg, 50 mg, 75 mg and 100 mg oral tablets and 100 mg iv bolus injection), according to a 5-way Latin square crossover design, under fasting conditions. Pharmacokinetic parameters, dose-normalised to 50 mg (Cmax, AUC(0-5a) and AUC(0-t)), were analysed by ANOVA.

Results: Twenty-five participants (age: 20–54 years; 13 male) were randomised. The 90% confidence intervals (CIs) around the Cmax, AUC(0-5a) and AUC(0-t) ratios for BRV 10 mg, 75 mg and 100 mg tablets vs. BRV 50 mg tablet were entirely contained within the standard bioequivalence limits (0.80–1.25). For BRV 100 mg iv bolus, bioequivalence vs. BRV 50 mg and 100 mg oral tablets was met for AUC(0-inf) and AUC(0-t) (90% CIs: 0.95–1.01), but iv Cmax was partly outside the limits (90% CIs: 1.19–1.39).

Conclusion: Based on dose-normalised pharmacokinetic parameters, BRV 10 mg, 75 mg and 100 mg oral tablets were bioequivalent with BRV 50 mg. BRV 100 mg iv bolus injection had similar bioavailability to BRV 50 mg and 100 mg oral tablets.

UCB-sponsored

p570 CLINICAL EXPERIENCE WITH THERAPEUTIC DRUG MONITORING OF ESLICARBzapine ACETATE IN NORWAY
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Purpose: To investigate the implementation of therapeutic drug monitoring for eslicarbazepine acetate in clinical practice with focus on pharmacokinetic variability, pharmacokinetic interactions, tolerability and efficacy. This forms the basis to evaluate its suggested reference range (50–140 mmol/l).

Method: Retrospective data from therapeutic drug monitoring services from main laboratories in Norway during 2012–2013 was included. Eslicarbazepine acetate is analysed as oxcarbazepine where the racemic monohydroxy-derivative is measured. Supplementary clinical data were evaluated where possible and handled anonymously. Drug fasting samples at assumed steady state were used.

Results: So far, 88 patients have been included. Based on the preliminary data from 2012, samples from 57 patients were analysed at the National Center for Epilepsy. The mean daily dose and serum concentrations were 1,038 mg (range 400–1,200 mg) and 53 mmol/l (range 23–97), respectively, where 44% were below the reference range. From 34 patients supplementary clinical data was evaluated (19/15 women/men, average age 34). Twenty-eight patients used 1–2 other AEDs, 8 used monotherapy. The 15 patients that switched from oxcarbazepine or carbamazepine showed no significant changes in serum sodium levels. No other main alterations in tolerability were observed. A beneficial efficacy was obtained in 23 patients, 3 had an uncertain effect, while the drug was withdrawn in 8 patients.

Conclusion: The pharmacokinetic variability of eslicarbazepine acetate is extensive. Therapeutic drug monitoring is implemented to evaluate the balance between efficacy and tolerability in the individual patient.
P571

PATIENTS’ VS. PRESCRIBERS’ VIEW OF ANTIPILEPTIC MEDICATION

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Purpose: Recognition and evaluation of current treatment as well as adverse effects are important factors for a successful treatment with antiepileptic drugs (AEDs). The purpose of this study was to investigate the patients’ vs. the prescribers’ view of the current medication with AEDs in patients with epilepsy, and to evaluate the patients’ perception of adverse effects.

Method: Retrospective data from a questionnaire answered by 175 patients and their physicians at the National Center for Epilepsy, Norway, were used. Both filled in previous and current AED medication and dosage, and the patients registered adverse effects in the Adverse Event Profile. All data were anonymized. The study had approval from the Regional Ethics Committee.

Results: Questionnaires from 174/175 patients and their physicians were analysed.

- The patients’ mean age was 43 years (21–83 years), 85 women/89 men. Age at epilepsy onset was 18 years (0.5–65 years). 165 patients (95%) had an epilepsy diagnosis. 2/3 of the patients used AED polytherapy (patients: 0–3 physicians: 0–4).

- The number of previously used AEDs was 0–11. The most commonly used AEDs were lamotrigine (n = 63), valproate (n = 50), levetiracetam (n = 43), carbamazepine (n = 34) and oxcarbazepine (n = 27). A total of 18 AEDs were registered. When patients and their physician registered current AEDs and dosages there was a discrepancy regarding dosage in 67 cases in 45 patients (26%) and current medication in 22 patients (13%), respectively. 150 patients (86%) reported one or more adverse effects. 118 (68%) experienced one or more adverse effects always/often, while only 9 patients reported no adverse effects.

Conclusions: In about 25% of the cases the patients and prescribers did not agree upon the actual AED medication. It is important to listen to patients’ perception of adverse effects. Improved information and communication about clinical use of AEDs may contribute to improved treatment of patients with epilepsy.

P572

LENOX-GASTAUT SYNDROME AND VAGUS NERVE SIMULATOR: CASE REPORT OF 5 YEAR FOLLOW UP

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Purpose: The Lennox-Gastaut Syndrome (LGS) is a severe childhood epileptic encephalopathy characterized by multiple types of intractable seizures, cognitive and behavioral abnormalities and specific electroencephalographic features. Most patients are refractory even with polytherapy, so alternative treatment is indicated. Callosotomy was the only option in these cases, but recently the vagus nerve stimulator (VNS) has become a less invasive option. This is a case report of a patient with LGS, which despite antiepileptic drugs had daily seizures, who underwent VNS, with significant reduction of seizures. We discuss the nonpharmacological treatment of LGS, comparing the callosotomy with VNS.

Method: Case report.

Results: Male, 19 years, developed epileptic seizures at 10 months of age. Began with uncontrolled seizures, with severe electroencephalographic abnormalities (figure 1 and 2), developmental delay and subsequent diagnosis of LGS. Despite the use of different antiepileptics drugs, there were several daily seizures. Thus surgical treatment was indicated and VNS was chosen. At the first 3 months was observed reduction of seizures about 20% and mental performance improvement. 1 year after, this decrease was 30% and significant intellectual development and psychomotor progress were noticed. About 4 years after VNS treatment, the seizures severity decreased and there were a reduction of 40% in those frequency.

Conclusion: The VNS is a less invasive alternative for the treatment of farmaco-resistance epilepsy, with efficacy in seizure control and improved psychomotor development similar to callosotomy.

P573

FIRST CLINICAL EXPERIENCES WITH PERAMPanel IN VIENNA

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Purpose: Perampanel (PER), an oral selective antagonist of a-aminono-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors, was licensed in 2012 as add-on therapy for patients with focal seizures with or without secondary generalization.

We intend to report our experiences on the efficacy and safety of perampanel in a clinical setting without the highly standardized circumstances of a phase III study.

Methods: We evaluated 38 consecutive medically refractory epilepsy patients at our tertiary epilepsy center, who were started on an add-on therapy with perampanel between November 2012 and June 2013. Follow up time was 3 months. A mean baseline monthly seizure rate based on the 3 months before start of perampanel was compared with the mean seizure rate based on 3 months after start of perampanel. Patients with sufficient language skills and IQ completed the “EpiTrack” at baseline and after 3 months, a screening tool to assess cognitive side effects of antiepileptic drugs.

Results: 3 Patients were lost to follow up. Of the remaining 35 patients 11 patients (31.4%) discontinued PER, which makes a retention rate of 68.6%. Of the 11 patients, in 3 individuals (27.3%) therapy was discontinued because of lack of efficiency, while in the remaining 72.7% PER was stopped because of side effects, namely irritability in 4 patients, suicidal ideation in 1 patient, vertigo and gait disorder in 5 patients. Among the 35 patients, 2 patients became seizure free (5.7%). Of the 24 patients who stayed on PER, 23 patients could reliably report seizure rate. 11 individuals (47.8%) had a reduction in seizure frequency of at least 50%. PER doses ranged from 4–8 mg (mean 5.43). 18 patients completed both Epi-Tracks. In 15 patients (83.3%) the comparison of EpiTrack raw scores revealed no change.

Conclusion: In most patients PER did not affect cognition. 5.7% of patients became seizure free. The retention rate was 68.6%.
p574  
**A NEW MEPS/HPLC-DAD ASSAY FOR THERAPEUTIC DRUG MONITORING OF PHENOBARBITAL, PHENYTOIN, CARBAMAZEPINE, LAMOTRIGINE, OCARBAZEPINE, AND THEIR ACTIVE METABOLITES CARBAMAZEPINE-10,11-EPOXIDE AND LICARBAZEPINE IN HUMAN PLASMA**

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**Purpose:** Development and validation of a high-performance liquid chromatography method with diode-array detection (HPLC-DAD) for the simultaneously quantification of phenobarbital, phenytoin, carbamazepine, lamotrigine, oxcarbazepine, and their active metabolites carbamazepine-10,11-epoxide and licarbazepine in human plasma using a novel sample preparation procedure based on microextraction by packed sorbent (MEPS).

**Method:** Aliquots of human plasma samples were pre-treated with acetonitrile and after some intermediate steps were submitted to MEPS procedure. Chromatographic separation of the analytes and ketoprofen, used as internal standard (IS), was achieved within 14 min on a LiChroCART Purospher 100–5 4.0 × 250 mm column using water-methanol-triethylamine (73.2:26.5:0.3, v/v/v) adjusted to pH 6.5 with ortho-phosphoric acid 85% (94%) and acetonitrile (6%) pumped at 0.1 ml/min. The analytes and IS were detected at 215, 237 or 280 nm.

**Results:** The method was validated according to the international guidelines showing to be accurate (bias < ± 14.81%), precise (coefficient variation <9.72%), selective and linear (r² > 0.9946) over the concentration ranges 0.1–15 µg/ml for carbamazepine; 0.1–5 µg/ml for carbamazepine-10,11-epoxide and oxcarbazepine; 0.4–40 µg/ml for licarbazepine; 0.1–20 µg/ml for lamotrigine; 0.2–40 µg/ml for phenobarbital and 0.3–30 µg/ml for phenytoin; The absolute recovery of the analytes ranged from 57.80% to 98.13% and they showed to be stable over all the conditions studied.

**Conclusion:** This new bioanalytical assay was successfully applied to real plasma samples from polymedicated epileptic patients, being a suitable, efficient and cost-effective tool for routine therapeutic drug monitoring of patients taking phenobarbital, phenytoin, carbamazepine, lamotrigine and/or oxcarbazepine.

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p575  
**THERAPEUTIC DRUG MONITORING OF ANTICONVULSANTS IN CLINICAL PRACTICE IN RUSSIA**

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**Purpose:** To study and analyze the frequency of achievement the therapeutic concentrations (TC) of CBZ and VPA in epilepsy patients in clinical practice in Russia.

Method: In 614 epilepsy patients (mean age 35.5 ± 0.5; range 18–80 years) was studied therapeutic drug monitoring of VPA (n = 295) and CBZ (n = 314) in different drug forms. We use the range of TC (Cmin, Cmax) for VPA 50–150 mg/l, for CBZ 4–12 mg/l.

**Results:** The frequency of achievement TC on VPA was 66.4% in average dose – 1325.1 ± 29.6 mg/day (range 600–3,000 mg/day) with no difference between prolong and immediate release drug forms. The frequency of sub-TC VPA was 16.3% and over-TC – 1% (n = 3). In patients with over-TC were treated with prolong drug forms in mean dose 1,800 mg/day, Cmax 164.2 ± 2.4 mg/l; the toxic concentration for CNS (175 mg/l) was not achieved in any cases. In VPA doses <500 mg/day there was no patients with TC, in 1,001–1,500 mg/day TC have 75% patients, in doses 1,501–2,000 mg/day – 97% patients, in >2,000 mg/day – 86% patients and there was high risk of overdose (4%). The frequency of TC on CBZ was 78.6%, the average daily dose was 922.2 ± 23.0 mg/day (range 200–2,000 mg/day) with no difference between prolong and immediate release drug forms. The frequency of sub-TC CBZ was 6.3% and over-TC – 1.25% (n = 4). In patients with over-TC mean dose 1,250 mg/day, Cmin 13.5 ± 0.2 mg/l, Cmax 15.1 ± 0.7 mg/l. In initial doses <600 mg/day 64.3% patients have TC, in doses >600 mg/day – 87%. In daily doses 600–1,200 mg and >1,200 mg 1.3% and 4.1% patients have over-TC by both Cmin and Cmax, only by Cmax – 8.8% and 18.4%, respectively.

**Conclusion:** The frequency of TC on VPA and CBZ is high with rare cases of over-TC, but there was problem of paradox low concentrations in single cases. CBZ have less predictable concentrations in range therapeutic doses than VPA.
p577
EFFECT OF DOSING INTERVALS ON THE PHARMACOKINETIC PROFILE OF USL255, ONCE-DAILY EXTENDED-RELEASE TOPIRAMATE
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Purpose: Understand the pharmacokinetic effects associated with various dosing scenarios of once-daily, extended-release topiramate (USL255) and immediate-release topiramate (TPM-IR).

Method: Single-dose data were used to simulate steady-state pharmacokinetic profiles of twice-daily TPM-IR and USL255. The pharmacokinetic effect of a missed dose was simulated for both topiramate formulations. Additionally, administration of a USL255 dose 6, 12, 18, and 24 h (double dose) later than scheduled was evaluated. Mean-predicted topiramate concentrations for all dosing scenarios were compared to steady-state levels. Simulated minimum (Cmin) and maximum plasma concentrations (Cmax) were evaluated for 96 h.

Results: The impact of a missed dose on Cmin was slightly greater for USL255 compared with TPM-IR, but levels returned to within 10% of steady-state levels within 4 days and 2.5 days, respectively. After delayed administration of USL255, mean-predicted plasma concentrations decreased incrementally as the time delay increased; however, topiramate plasma concentrations were above Cmin steady-state levels within 4–8 h after administration of the delayed dose. For each of the delayed-dose scenarios (6–24 h late), plasma concentrations were generally highest 2 days after the scheduled dose; Cmax values were between 2.1–11.8% higher than steady-state and Cmin values increased from 2.6–10.2%.

Conclusion: Compared with TPM-IR, a missed USL255 dose increased the time to return to steady-state plasma concentrations. However, if a missed dose was taken up to 24 h after scheduled administration, USL255 displayed a fast return to steady-state without markedly increasing Cmax levels. These data provide valuable information that may help clinicians instruct patients on topiramate dosing.

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p578
NON-CONVULSIVE STATUS EPILEPTICUS TRIGGERED BY EMERGENCY CONTRACEPTION (LEVONORGESTREL) IN PATIENT WITH EPILEPSY AND LAMOTRIGINE THERAPY
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Purpose: Lamotrigine and oral hormonal contraception has both mutual interaction reducing each other plasmatic levels, resulting in reduced efficiency of both medicines. In our awareness there was not yet described a Non-Convulsive Status Epilepticus induced by emergency contraception in epilepsy and Lamotrigine therapy.

Method: We report a clinical case of a 28-year old woman diagnosed with new-onset epilepsy who developed a Non-Convulsive Status Epilepticus being under Lamotrigine therapy (150 mg/die) and use of Emergency Contraception-Levonorgestrel-based compound (1.5 mg).

Results: The patient was diagnosed with epilepsy with tonic-clonic generalized seizures of unknown (normal brain MK) origin, in the context of sleep deprivation and alcohol consumption at the age 26 year-old. EEG was showing few brief paroxysms of polyspike-slow wave with maximal bifrontal expression. The therapy was initiated with Lamotrigine at the dosage of 150 mg/day. After 6 months of the Lamotrigine therapy and good compliance, the patient after intake of emergent contraceptive pill (Levonorgestrel) had a recurrence of tonic-clonic generalized seizure, which evolved in confusion, psychomotor agitation and later during that day into spatial-temporal disorientation. EEG showed a continuous epileptic activity (spike-slow wave with maximum expression on frontal-temporal regions bilaterally). The epileptic activity reduced significantly after Clonazepam 1 mg per os confirmed by 24 h video EEG. The plasmatic level of Lamotrigine was below the therapeutic range (2.7 mg/dl). The patient was dismissed with slight increase of Lamotrigine dosage (200 mg/day) and good 9 month follow-up.

Conclusion: We hypothesized that the patient developed a Non-Convulsive Status Epilepticus triggered by administration of emergency contraception (Levonorgestrel) 1.5 mg that reduced the serum level of Lamotrigine. In this report we want to bring attention to possible interaction with immediate effect of emergent oral contraception in epileptic female patients with Lamotrigine therapy.

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p579
AMELIORATION OF NEURAL IMPAIRMENT BY MK-801 IN HIPPOCAMPAL CA3 AREA OF CORTICAL SPREADING DEPRESSION INDUCED RATS
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Purpose: The cortical spreading depression phenomenon is restricted to the brain and seems to be involved in both neuronal and glial cell populations. Glutamate release in extracellular space is the major event in SD phenomenon, which caused cellular depolarization. Inhibition of glutamate receptor has been proposed to play an active role in CSD preconditioning. Hippocampal cell damage is mostly result by CSD. Hippocampus roles in various brain activities have been clearly described; in our previous study we have presented that repetitive CSD may associated with neuronal injury in the hippocampal neurons.

Method: In the present study 36 juvenile Wistar rats were used to investigate roles of NMDA receptor antagonist on repetitive CSD induction in CA3 of hippocampus. Four consecutive CSD were induced during 4 weeks and histopathological study in CA3 hippocampus region was revealed. We have also investigated NMDA receptor (MK-801) inhibitory roles of CSD on cellular death include apoptosis and cell shrinkage.

Results: Our findings have suggested the same idea that repetitive CSD could significantly enhanced neural cell death in CA3 hippocampal region. However pretreatment with MK-801 could significantly decrease mean number of apoptotic cells in CSD induced animals.

Conclusion: It has been concluded that NMDA receptors blockages could prevent CSD wave induced cellular damage.

p580
BETA ADRENERGIC BLOCKADE REVERSES INCREASED CARDIAC EXCITABILITY IN A MODEL OF ACQUIRED EPILEPSY
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Purpose: Sudden unexpected death in epilepsy (SUDEP) accounts for as high as 30% of epilepsy-related deaths. Sudden cardiac death from fatal arrhythmias has been proposed as a potential SUDEP mechanism based on the importance of arrhythmia in SUDEP. It has been reported that beta-blockers have been used for many years as treatment for arrhythmias and SUDEP. The hypothesis of this study is that beta-blockers can reverse increased cardiac excitability in a model of acquired epilepsy.
on the observation that epileptic individuals exhibit resting tachycardia and prolonged QTc. However, whether these changes predispose to stimulation-induced ventricular tachycardia (VT) and whether β blocker, the therapy for VT prevention in long QT syndrome, is effective remain unknown.

Methods: We induced status epilepticus (SE) in rats by pilocarpine (300 mg/kg, i.p.). Serial EKGs were obtained at various time points following SE. Atenolol (10 mg/kg, i.p. bid) or normal saline (NS) were given for 2 d prior to electrophysiological (EP) studies. In vivo EP studies were performed between 7 and 14 mo following SE on the following groups: (i) sham + NS, (ii) sham + atenolol, (iii) epileptic + NS, (iv) epileptic + atenolol. Programmed electrical stimulation (PES) was used to induce VT. An animal was considered to be more susceptible to stimulation-induced arrhythmias if 2 out of 3 trials resulted in VT. Continuous variables were analyzed using Student t-test or 2-way ANOVA. Categorical variables were analyzed using Chi square test. The results are expressed in mean±SEM.

Results: Compared with the age-matched sham rats, epileptic rats began to exhibit elevated HR (271.5 ± 4.4 vs 254.6 ± 3.7 bpm, n = 20–21/group, p < 0.01) and prolonged QTc (314 ± 7 vs 264 ± 10 ms, n = 20–21/group, p < 0.01) at 2 mo following SE, coinciding with the appearance of recurrent seizures. These differences persisted chronically (n = 17–18/group, p < 0.05). Atenolol decreased HR (12.9 ± 2%, n = 6, p < 0.01) and shortened QTc (12.7 ± 1.6%, n = 6, p < 0.01) in the epileptic rats. PES induced VT in 31% sham + NS, 0% sham + atenolol, 65% epileptic + NS and 22% epileptic + atenolol (n = 4–17, p < 0.05).

Conclusions: Cardiac changes are associated with increased stimulation-induced VT suggesting that sudden cardiac death from arrhythmias may contribute to SUDEP. QTc shortening and decreased VT incidence with β blocker in this model suggests a potential therapy in epileptic individuals with prolonged QTc.

Funding: NIH/NINDS; Epilepsy Foundation; CURE

p581
NS-PTEN KO MOUSE MODEL OF CORTICAL DYSPLASIA WITH EPILEPSY IS ASSOCIATED WITH HIPPOCAMPAL MICRO- AND ASTROGLIOSIS
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Purpose: Cortical dysplasia (CD) is characterized by malformation of the cortex and epilepsy. At the molecular level, CD is associated with hyperactivation of the mammalian target of rapamycin (mTOR) pathway and with inflammation and gliosis (micro- and astrogliosis). While aberrant mTOR signaling and neuroinflammation are associated with recurrent seizures, the link with epilepsy is unclear. In this study, we evaluated neuroinflammation in a mouse model of CD characterized by epileptogenesis and constitutively active mTOR pathway due to a neuronal subset-specific knockout of the PTEN gene (NS-PTEN KO).

Methods: We used western blotting and immunohistochemistry to examine the protein levels and distribution of markers of microglia (IBA1, CD11b), astrocytes (GFAP), neurons (NeuN), and mTOR pathway activation (phosphorylated ribosomal S6 protein) (p-S6) in the hippocampi of adult NS-PTEN KO and WT mice.

Results: We found that the staining for IBA1, CD11b, GFAP and p-S6 appeared stronger in hippocampi from KO compared WT mice. In KOs, IBA1- and CD11b-stained microglia appeared amoeboid and hypertrophied compared to WTs. As expected, intense p-S6 staining was evident in cells lacking PTEN within the granule cell layer dentate gyrus of the KOs. p-S6 staining co-localized with NeuN in both WT and KO groups and with scattered CD11b positive cells.

Conclusion: Our findings suggest increased activation of micro- and astrogliosis in the hippocampus of NS-PTEN KO mice, and hyperactivation of the mTOR pathway in reactive microglia, suggesting a role for mTOR hyperactivity in the inflammatory process associated with CD. Future studies will evaluate if immunomodulating therapies can induce epileptic individuals exhibit resting tachycardia and prolonged QTc.

Funding: NIH/NINDS; Epilepsy Foundation

p582
INCREASED ACTIVITY OF HYDROGEN PEROXIDE- REMOVING ENZYMES IN HIPPOCAMPAL MICROGLIA OF PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY DUE TO HIPPOCAMPAL SCLEROSIS
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Purpose: Hippocampal sclerosis (HS) is characterized by lower neuron counts compensated by gliosis. This shift in cellular content could significantly affect redox milieu, since astrocytes show considerably higher basal activity of hydrogen peroxide-removing enzymes – catalase (CAT) and glutathione peroxidase (GPx) compared to neurons. This study compared CAT and GPx activity in hippocampi of epileptic (HS) and non-epileptic humans.

Method: Using biochemical assays and Western blot (Wb), we examined activity and level of CAT and GPx in hippocampi of 9 drug-resistant patients with mesial temporal lobe (TL) epilepsy due to HS that underwent TL resection and amygdalohippocampectomy (age 38.0 ± 6.1 years) and 10 hippocampi obtained by autopsy from 6 neurologically intact controls (37.2 ± 7.6 years).

Results: CAT activity in HS was 4 times higher (mean ± SD: 162.3 ± 96.4 U/mg of proteins) compared to controls (42.1 ± 16.9 U/mg of proteins; p < 0.001), while the activity of GPx was twofold higher (HS: 149.4 ± 31.6; controls: 75.1 ± 26.4 U/mg of proteins; p < 0.001). These findings were confirmed by Wb.

Conclusion: Our results match previous findings in neocortex of drug-resistant epilepsy patients and hippocampus of chronic epilepsy animal models. Despite the believe that drastic increase of CAT and GPx activity corresponds to oxidative stress, we suppose that final issue is not high, but opposite, very low (subphysiological) level of hydrogen peroxide. This could obstruct normal redox signaling, which is involved in the regulation of numerous cellular functions, one of them being the activity of specific ion channels.
Abstracts

p583
METALLOME OF SCLEROTIC HIPPOCAMPUS IN PATIENTS WITH DRUG-RESISTANT MESIAL TEMPORAL LOBE EPILEPSY
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Purpose: Altered hippocampal metalome is strongly implicated in the pathology of mesial temporal lobe epilepsy with hippocampal sclerosis (mTLE-HS). We aimed to determine sodium, potassium, calcium, magnesium, iron, copper, manganese, and zinc concentration in epileptic human hippocampi.

Method: Hippocampi of 24 drug-resistant mTLE-HS patients (age: 35.6 ± 9.4 years) that underwent anterior temporal lobe resection and amygdalohippocampectomy surgery, and 17 hippocampi obtained by autopsy from 13 controls (age: 40.5 ± 12.9 years) were analyzed using inductively coupled plasma optical emission spectrometry.

Results: Epileptic hippocampi showed significantly lower concentrations (μg/g of tissue) of copper (HS: 2.34 ± 0.12; control (C): 3.57 ± 0.33; p < 0.001), manganese (HS: 0.205 ± 0.030; C: 0.409 ± 0.064; p = 0.004), and potassium (HS: 2001 ± 59; C: 2322 ± 61; p < 0.001), and increased sodium level (HS: 1131 ± 22; C: 1040 ± 25; p = 0.010). Zinc concentration was slightly higher in HS (13.97 ± 1.51 μg/g) compared to controls (10.97 ± 1.03 μg/g), whereas iron, calcium, and magnesium levels did not differ.

Conclusion: Our results provide a relevant prerequisite for understanding the potential involvement of different metals in the pathology of HS, emphasizing general deregulation of metalome, copper and manganese deficiency, and the absence of iron accumulation.

p584
RETINAL NERVE FIBER LAYER THICKNESS: A POSSIBLE BIOMARKER OF DRUG RESISTANCE IN EPILEPSY
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Purpose: Epilepsy has been associated with cerebral white matter tract abnormalities. Retinal nerve fiber layer thickness is related to the axonal anterior visual pathway and is considered a marker of overall white matter “integrity”. Retinal nerve fiber layer thickness was previously assessed in a cohort of people with epilepsy and a history of vigabatrin exposure, showing significant thinning compared to healthy controls. We hypothesised that retinal nerve fiber layer changes would occur in people with chronic epilepsy, independently of previous vigabatrin treatment, related to clinical characteristics of epilepsy.

Method: Three hundred subjects with chronic epilepsy and 90 healthy controls were included. People with previous exposure to vigabatrin or known ocular disease were excluded from the analysis. Retinal nerve fiber layer imaging was performed using spectral-domain Optical Coherence Tomography.

Results: People with epilepsy had significantly lower average retinal nerve fiber layer thickness and lower thickness of each of the 90 quadrants than healthy controls (p < 0.001, Wilcoxon rank-sum test). In a multivariate logistic regression model, drug resistance was the only significant predictor of abnormal retinal nerve fiber layer thinning (OR 2.09, CI 95% 1.09–4.01, p = 0.031). Duration of epilepsy and the presence of intellectual disability also showed a significant relationship with retinal nerve fiber layer thinning in a multivariate linear regression model (coefficients: -0.16, p = 0.004 and -4.0, p = 0.044, respectively).

Conclusion: This suggests that drug-resistant epilepsy is associated with thinning of the retinal nerve fiber layer. As this is easily assessed by optical coherence tomography, retinal nerve fiber layer thickness is a candidate biomarker of drug resistance and, by extension, of epilepsy severity. Longitudinal studies are now needed. The underlying mechanisms are unknown and may be diverse.

p585
ACONITUM COCHLEARE WOROSCHIN-OIL ATTENUATES THE MOLECULAR MARKERS OF EPILEPTOGENESIS IN PENTYLENETETRAZOLE INDUCED KINDLED MICE WITH SAFE TOXICITY PROFILE
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Purpose: Epilepsy is a chronic neurological disorder, characterized by recurrent seizures occurring as a result of synchronized discharges of neurons in brain. As 33% of patients develop resistance against therapy while others are not without side effects, therefore, need for better and safer drugs is crucial. Neurutrophic factors and Oxidative stress are emerging as mechanisms that may play an important role in the etiology of seizure-induced neuronal death. In the present study, Aconitum cochleare Woroschin-oil (ACR-oil) was tested for its ability (i) to suppress the convulsive and lethal effects of Pentylenetetrazole (PTZ) in kindled mice, (ii) to attenuate the PTZ-induced oxidative injury in the brain tissue and (iii) to modulate the gene expression BDNF and its receptor Trk-B when given as a pretreatment prior to each PTZ injection during kindling acquisition. Diazepam and valproic acid, major antiepileptic drugs, were also tested for comparison.

Methods: Once acute screening was done, all groups except for control group were kindled by injections of PTZ with an interval of 48 h (n = 12). In the 18th injection, all groups were sacrificed and the brain samples were collected and used for determination of oxidative stress parameters and targeted gene expressions by PCR.

Results: Our results suggest that ACR-oil treatment (100 mg/kg, 200 mg/kg) significantly inhibit, both acute and chronic PTZ induced seizures (p < 0.05). Toxicity studies demonstrate that the test oil is devoid of major toxic effects on suggested doses. Our test oil not only produced antiepileptic effect but also diminished the PTZ induced oxidative stress (p < 0.05, p < 0.001).
**Conclusions:** Based on our results, we conclude that ACR-oil might be acting as an antiepileptogenic lead formulation by controlling the cellular expression of the factors that contribute in the development of epileptogenic plasticity in the CNS. Further studies are needed to elucidate its mechanism of action.

**Results:** Thirty-one of the identified proteins were up-regulated in epileptic rat, among them dihydrophosphinidinase, V-type proton ATPase and alpha-synuclein. Seven proteins were down-regulated, i.e. fructose-bisphosphate aldolase, phospholipase A2, ATP-binding cassette, malate dehydrogenase and guanine nucleotide-binding protein. Two proteins were expressed only in the control group: L-lactate dehydrogenase, and phosphatidylyethanolamine-binding protein. In the free SE group were identified twenty-five differentially expressed proteins compared with epileptic and control animals, between them dihydrophosphinidinase was up-regulated and V-type proton ATPase was down-regulated. Statin and creatine kinase B were expressed only in the SE free group.

**Conclusion:** Some proteins expressed in the hippocampus of rats presenting SRS were also detected in patients with TLE. Increased expression of dihydrophosphinidinase-related protein 2 is related to schizophrenia. Animals SE free also exhibit alterations in protein expression.

**Purpose:** The expression of pro-inflammatory cytokines IL-1β and TNF-α in the hippocampus of rats was examined by RT-PCR or Western blot after the administration of one or seven doses of: vinpocetine, carbamazepine or valproic acid. Next the effect of the anti-seizure drugs was investigated on the rise in pro-inflammatory cytokines expression induced by LPS inoculation in vivo. To validate our methods the changes induced by the pro-convulsive agents: 4-aminopyridine, pentylentetrazole and pilocarpine were tested. Finally, the effect of the anti-seizure drugs on seizures and on the concomitant rise in pro-inflammatory cytokines induced by 4-aminopyridine was explored.

**Methods:** The expression of the pro-inflammatory cytokines IL-1β and TNF-α in the hippocampus of rats was examined by RT-PCR or Western blot after the administration of one or seven doses of: vinpocetine, carbamazepine or valproic acid. Next the effect of the anti-seizure drugs was investigated on the rise in pro-inflammatory cytokines expression induced by LPS inoculation in vivo. To validate our methods the changes induced by the pro-convulsive agents: 4-aminopyridine, pentylentetrazole and pilocarpine were tested. Finally, the effect of the anti-seizure drugs on seizures and on the concomitant rise in pro-inflammatory cytokines induced by 4-aminopyridine was explored.

**Results:** A single or repeated dose of vinpocetine reduced the expression of IL-1β and TNF-α from basal conditions. A single carbamazepine dose reduced the expression of IL-1β, but only repeated carbamazepine doses reduced also TNF-α expression. The LPS-induced increase in both cytokines was reduced by vinpocetine and carbamazepine. In contrast, valproic acid, which failed to reduce IL-1β and TNF-α expression in basal conditions also failed to prevent the rise in both cytokines induced by LPS. Tonic-clonic seizures induced either by 4-aminopyridine, pentylentetrazole or pilocarpine increased IL-1β and TNF-α expression markedly. Although 4-aminopyridine-induced changes were reduced by single doses of all the tested anti-seizure drugs, valproic acid was less effective.

**Conclusion:** Among the anti-seizure drugs, vinpocetine and carbamazepine, which mechanism of action involves a decrease in ion channels permeability, also reduce cerebral inflammation.
seizure-induced neuron death and microglia activation in the hippocampus compared to vehicle treated group.

**Conclusion:** These results suggest that citicoline may not have neuroprotective effects after pilocarpine-induced seizure. The present study suggests that clinical application of citicoline after seizure needs careful considerations.

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**p589**

**MEMORY IMPAIRMENT CAUSED BY SPREADING DEPRESSION MODULATED BY INJECTION OF NIFEDIPINE**

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**Purpose:** Spreading depression known by transient loss of spontaneous and evoked neuronal activity and changes in ionic, metabolic and hemodynamic characteristics of the brain. Many studies have focused on the role of Ca2+ channels in spreading depression, however this role is not completely clear yet. On the other hand it has proven that impairment of memory is one of the main effects of spreading depression. In our study we aimed at determining the role of Ca2+ channel-blockers on repetitive spreading depression in terms of its effect on memory.

**Method:** Wistar rat (60–80 g) randomly chosen in 4 groups and Nifedipine 1 mg/kg were administrated weekly after 3 mol/L KCl injection for induction of repetitive SD in rat for 4 week. The groups were evaluated by T-maze memory test and SD group were compared with control groups.

**Results:** T-maze test data demonstrated that in repetitive spreading depression group memory was impaired during the weeks. In group which Nifedipine have been administrated memory improvement has been significantly observed.

**Conclusion:** Our study showed that administration of Nifedipine as a Ca2+ channel-blockers could significantly reduce the level of memory impairments, which naturally followed by repetitive spreading depression.

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**CHRONIC FOCAL DELIVERY OF VIGABATRIN INTO THE SUBTHALAMIC NUCLEUS IS ANTICONVULSANT IN THE PENTYLENETETRAZOLE SEIZURE THRESHOLD TEST IN RATS**

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**Purpose:** Focal delivery of antiepileptic drugs directly into brain regions involved in seizure modulation is a promising strategy to overcome pharmacoresistant epilepsy. This study investigates, if chronic microinjection of vigabatrin, an irreversible inhibitor of the GABA-degrading enzyme GABA-aminotransferase (GABA-T), into the subthalamic nucleus (STN) of rats leads to long-lasting anticonvulsant effects.

**Method:** Chronic microinfusion of 10 μg vigabatrin per day over a period of 3 weeks bilaterally into the STN was conducted using implantable microinfusion pumps. The anticonvulsant efficacy was assessed weekly in the pentylenetetrazole (PTZ) seizure threshold test. Finally, neurochemistry was performed in post mortem tissue.

**Results:** Preliminary data show a significant increase in PTZ seizure thresholds up to 2 weeks, in individual rats even up to 3 weeks. The activity of the GABA-synthesizing enzyme glutamic acid decarboxylase (GAD) was reduced in the STN after three weeks of chronic microinfusion. GABA was increased due to complete GABA-T inhibition.

**Conclusion:** Chronic microinfusion of vigabatrin into the STN in rats exerts clear anticonvulsant effects up to 3 weeks in the PTZ test. The loss of anticonvulsant efficacy after 3 weeks in most rats could be the consequence of a tolerance development due to feedback GAD inhibition in response to the high GABA levels. We currently investigate, if chronic microinfusion of 5 μg VGB per day into the STN exerts anticonvulsant effects without inducing GAD inhibition.

**Acknowledgments:** Vigabatrin was provided free of charge by Sanofi-Aventis Deutschland GmbH. The study is supported by a grant (FOR 1103 / GE1103/7-2) from the German Research Foundation (Bonn, Germany). L. Gey is supported by the Konrad-Adenauer-Stiftung e.V.

**p591**

**ELECTROGRAPHIC AND BEHAVIORAL CHARACTERIZATION OF EP-80317 ANTICONVULSANT EFFECTS IN PILOCARPINE-TREATED RATS**

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**Purpose:** In a previous study based on behavioral analysis, we demonstrated that EP-80317, a growth hormone secretagogues-receptor 1a ligand, displays anticonvulsant properties in animal models of status epilepticus (SE). In this study we characterize EP-80317 activity by video-electrocorticography (ECoG).

**Method:** We recorded video-ECoG from 20 pilocarpine-treated rats. Before pilocarpine administration, rats received either EP-80317 or saline. Behaviors associated with electrographic events were graded according to a modified Racine’s scale.

**Results:** As assessed by video-ECoG, SE was developed in 100% of saline-pretreated pilocarpine rats and in only 50% of EP-80317-pretreated rats (p < 0.05). Although number of induced-seizures was similar in both groups (saline: 3.25 ± 1.1; EP-80317: 2.35 ± 0.98; Mean±SEM), we observed a different rate of convulsive vs. non-convulsive seizures (saline: 95.4% convulsive, 4.6% non-convulsive; EP-80317: 47.7% convulsive, 55.3% non-convulsive). To evaluate whether these results were dependent on a moderate activity of EP-80317 or, instead, on full response to EP-80317 in some rats and failure response in others, we subdivided the EP-80317 group in two distinct populations: rats that experienced SE (EP-80317/SE) and rats that did not (EP-80317/non-SE). Interestingly, we observed that the rate of convulsive seizures was 75% in EP-80317/SE (similarly to saline-pretreated group) and only 15% in EP-80317/non-SE. We analyzed the behavioral and ECoG temporal development of pilocarpine-induced events. We found that saline-pretreated pilocarpine rats showed a worsening in behavior and seizure duration, and a progression of power spectrum of stage 5 seizures. Similar progression was observed in EP-80317/SE rats, but not in EP-80317/non-SE rats, where differences in behavior and electrographic activity were not evident when comparing the last with first pilocarpine-induced seizure.
Conclusion: These findings further demonstrate that EP-80317 has anti-convulsant properties in the pilocarpine model of SE, and suggest the presence in the rat population of full responders and non-responders.

p592
THE EFFECT OF RAPAMYCIN (SIROLIMUS) ON PENICILLIN-INDUCED EPILEPTIFORM ACTIVITY IN RATS
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Purpose: Aim of this study is to investigate acute effects of mTOR inhibitor rapamycin, which has antimicrobial, antineoplastic and anti-inflammatory effects, on experimental penicillin-induced epilepsy model in rats.

Method: In this study 40 adult male Wistar rats were used and these rats were divided into 5 groups as control, vehicle (dimethylsulfoxide), and the doses of 0.1 mg/kg, 0.4 mg/kg and 0.8 mg/kg groups of rapamycin. All of the substances were administered intraperitoneally except penicillin. After rats were anesthetized with administration of the 1.25 g/kg dose of urethane intraperitoneally, the left part of the cortex was opened and the electrodes were placed on somatomotor area. Electrocorticogram recordings were performed by Powerlab System. After 2 h from rapamycin application, epileptiform activity was induced by penicillin which was applied intracortically. The time to onset of first spike wave latency, spike-wave frequency and spike-wave amplitude of epileptiform activity were calculated by LabChart software, and obtained data were analyzed statistically.

Results: Any epileptiform activity was not observed before penicillin administration in all groups. In rapamycin groups, the doses of 0.4 mg/kg and 0.8 mg/kg reduced significantly both frequency and amplitude of epileptiform activity according to control and DMSO groups. According to latency there was no statistically significant difference between the groups.

Conclusion: Spike-wave frequency and amplitude of epileptiform activity are reduced by administration of rapamycin in the rats, however latency is not affected. These findings indicate that rapamycin may be a potential antiepileptogenic drug in future.

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THE EFFECT OF THYMOCQUINONE ON PENICILLIN-INDUCED EPILEPTIFORM ACTIVITY IN RATS
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Purpose: Thymoquinone (TQ) is derived from Nigella sativa which is a traditional medical plant and used as a food additive. Aim of this study is to investigate acute effects of thymoquinone, which has been shown anti-convulsant, antiepileptic, antioxidant and neuroprotective effects, on experimental penicillin-induced epilepsy model in rats.

Method: In this study 56 adult male Wistar rats were used, and these rats were divided into 7 groups as sham, control (saline), thymoquinone (non-induced with penicillin), vehicle (dimethylsulfoxide, DMSO), and the doses of 10 mg/kg, 50 mg/kg and 100 mg/kg of thymoquinone. All of the substances were administered intraperitoneally except penicillin. After rats were anesthetized with administration of the 1.25 g/kg dose of urethane intraperitoneally, the left part of the cortex was opened and the electrodes were placed on somatomotor area. At the 30th min of thymoquinone application, epileptiform activity was induced by intracortical (ic) administration of penicillin (500 IU, 2.5 μl). Obtained electrocorticographic (ECoG) data from recordings were analyzed by software. The first spike latency, spike-wave frequency, and spike-wave amplitude of epileptiform activity were analyzed statistically.

Results: There were no epileptiform activity in sham and thymoquinone (non-induced with penicillin) groups. Thymoquinone at the doses of 10 mg/kg, 50 mg/kg and 100 mg/kg significantly increased the latency time to onset of first spike wave and decreased the frequency vs. control and DMSO groups. However, comparing spike-wave amplitude of epileptiform activity there were no significant difference between the groups after 20th min from penicillin administration.

Conclusion: The results of the present study show that administration of thymoquinone has antiepileptic effect in penicillin induced model of epilepsy in rats and it may be a potential antiepileptogenic drug in future.

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INDIRECT ACTIVATION OF THE ENDOCANNABINOID SYSTEM: 2- ARACHIDONYLGLYCEROL MEDIATES CANNABINOID-DEPENDENT EFFECTS IN A MOUSE MODEL OF TEMPORAL LOBE EPILEPSY
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Purpose: The endocannabinoid (eCB) system serves a key function in regulating neuronal activity. Thus, the eCB system can be considered a putative target for central nervous system diseases including epilepsies. In this study we investigate if inhibition of the 2-arachidonoylglycerol synthesizing enzyme, monoacylglycerol lipase (MAGL), has an impact on epileptogenesis and ictogenesis in the kindling model of temporal lobe epilepsy.

Method: Male NMRI-mice were stimulated electrically once daily via an implanted depth electrode and received injections of the MAGL-inhibitor (n = 12, 8 mg/kg, i.p) or vehicle (DMSO:Cremophor EL:saline in a ratio of 1:1:18; n = 12) 60 min prior to each kindling stimulation to determine whether treatment exerted any enduring effects (Mann-Whitney U test, student’s t-test, two-way ANOVA for repeated measurements).

In addition, we aimed to affirm that the observations are cannabinoid type 1 receptor (CB1R) mediated by using MAGL-inhibitor treated conditional CB1R knockout mice (CamK-CB1 KO) along with littermate controls (CamK-CB1 WT, work in progress).

To evaluate an anticonvulsive potential of the MAGL-inhibitor, fully-kindled male NMRI-mice (n = 10) received vehicle or the MAGL-inhibitor (4 mg/kg, 8 mg/kg, 16 mg/kg) every second day and the seizure threshold was analyzed.

Results: The MAGL-inhibitor retards the development of generalized seizures (p = 0.0066) and decreases seizure (p < 0.0001) and after-discharge duration (p < 0.001). Furthermore, seizure thresholds in treated mice are higher in non-kindled mice (p = 0.0325), whereas seizure thresholds after kindling acquisition proved to be comparable in both groups (p = 0.8939).

In fully-kindled mice the duration of behavioral (p = 0.0549) and electrographic seizure activity (p = 0.0962) was slightly decreased in response to 4 mg/kg MAGL-inhibitor.
Conclusion: The data demonstrate that indirect CB1R agonism can interfere with the development of a hyperexcitable network in the amygdala kindling model, but has only minor effects in fully-kindled mice. Future studies in chronic epilepsy models are necessary to confirm whether the data indicate a preventive potential of CB1R agonism.

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SYNERGISTIC INTERACTION OF SOME SELECTED COMBINATIONS AMONG THREE ANTIEPILEPTIC DRUGS IN THE MOUSE MAXIMAL ELECTROSHOCK-INDUCED SEIZURE MODEL – A TYPE I ISOBIOGRAPHIC ANALYSIS
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Purpose: To isobio graphically characterize types of interactions for 4 selected three-drug combinations of various antiepileptic drugs (oxcarbazepine + topiramate + phenobarbital, oxcarbazepine + topiramate + pregabalin, oxcarbazepine + phenobarbital + pregabalin and phenobarbital + topiramate + pregabalin) in the maximal electroshock-induced seizure (MES) test in mice.

Method: Tonic hindlimb extension (seizure activity) was evoked in albino Swiss mice by a current (25 mA, 50V, 50 Hz, 0,2s stimulus duration) delivered via auricular electrodes. Type I isobio graphic analysis for the studied antiepileptic drugs (administered intraperitoneally for a fixed drug dose ratio of 1:1:1) was used. Potential concurrent adverse-effect profiles of interactions of three-drug combinations of antiepileptic drugs were evaluated in the chimney (motor performance), passive avoidance (long-term memory), and grip-strength (muscular strength) tests.

Results: The three-drug combinations of oxcarbazepine + topiramate + phenobarbital, oxcarbazepine + topiramate + pregabalin, oxcarbazepine + phenobarbital + pregabalin and phenobarbital + topiramate + pregabalin (at the fixed-ratio of 1:1:1) exerted synergistic interaction with respect to their anticonvulsant activity in the mouse MES model. None of the studied three-drug combinations was associated with any concurrent adverse effects with regards to motor coordination, long-term memory or muscular strength.

Conclusion: Synergistic anticonvulsant activity of the examined three-drug combinations (oxcarbazepine + topiramate + phenobarbital, oxcarbazepine + topiramate + pregabalin, oxcarbazepine + pregabalin and phenobarbital + topiramate + pregabalin) in the mouse MES model, could offer patients with drug resistant epilepsy some favorable triple therapy regimens, if the results from this study would be extrapolated into clinical settings.

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NEUROPLASTICITY AND NEUROGENESIS IN EPILEPSY – IS IT POSSIBLE?
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Proliferation of the central and peripheral neural systems cells, support of the existing neurons and stimulation of growth and differentiation of new neurons and synapses is conducted by neurotrophic factors, including brain-derived neurotrophic factor (BDNF). The rL-2 is a very important regulatory cytokine, which is produced by the brain cells and supports growth of embryonic septum and hippocampal neurons.

Purpose: To study the influence of the rIL-2–medicament (Roncoleukin) – cytokine drug of Interleukin’s series containing recombinant human Interleukin-2 (rIL-2), which is a structural and functional analog of the endogenous IL-2, – on the immune response and clinical characteristics of patients with epilepsy (PE).

We studied plasma levels of cytokines IL-1β, IL-2, soluble IL-2 receptor (sIL-2R), IL-6 and BDNF in 51 patients with epilepsy (PE) before and after the treatment with Roncoleukin. It was injected subcutaneously in a solution of 1 ml at 1.0 mg (1,000,000 ME rIL-2), daily, 3 in total. The effectiveness of the therapy was estimated by the frequency dynamics of the epileptic seizures and EEG.

Results: Initial immune status of PE was characterized with the imbalance of pro- and anti-inflammatory cytokines in plasma: increase in concentration of cytokines IL-1β, IL-2, IL-6, and decrease in sIL-2R.

Revealed decrease of rIL-2 in PE understood as a functional deficit and indication for treatment with exogenous rIL-2. Production of BDNF significantly increased (4,448 and 7,023 pg/l (p < 0.01, respectively), by more than 4 times decreased the concentration of pro-inflammatory cytokine IL-8 after Roncoleukin treatment of PE. Changes of these immunological parameters correlated with clinical improvement of PE: reduction of seizure frequency and positive EEG changes.

Thus Roncoleukin treatment modulated the inflammatory process and increased plasma level of BDNF in PE. It is may indicate the possibility of positive neurogenesis and neuroplasticity and open new opportunities of epilepsy treatment.

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EXPOSURE OF THE IMMATURE BRAIN TO BENZODIAZEPINES LEADS TO COGNITIVE IMPAIRMENT AND DECREASED NEUROGENESIS LATER IN THE LIFE
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Purpose: To assess whether early benzodiazepine exposure affects cognitive abilities and neurogenesis later in life.

Method: Clonazepam (CZP) was administered from postnatal day (P) 7 until P11 in doses 0.5 or 1.0 mg/kg/day i.p. At P12–P23 animals were exposed to homing test. To assess short- and long-term memory juvenile animals (P12–P32) were submitted to the passive-avoidance paradigm, at intervals 0, 2 and 24 h. Habituation within- and between-sessions was assessed in adult animals (P70) in the open field (OF) in four 10-min sessions. Distance moved and time spent in central zone were compared between the 1st and 4th session. Spatial memory was tested in the Morris water maze. Additional groups of animals were used to assess neurogenesis at age of 3 months.

Results: Changes of learning and emotional responsiveness were observed in homing test in P12 and P23 rats. Early CZP exposure did not impair habituation, but CZP animals spent more time in central zone of OF. In the Morris water maze both control and CZP animals were able to learn the task, but animals with high dose of CZP spent more time swimming. No impairment was found in the passive avoidance test. However animals exposed to CZP showed a shorter latency to enter the dark compartment in the first session. Early exposure to CZP reduced number of DCX+ neurons by 24.2% and hippocampal volume by 8%.

Conclusion: Short term exposure to CZP during early postnatal development affected behavioral responsiveness related to motivation and learning of juvenile rats. In the adulthood, animals exposed to CZP exhibited
impaired non-associative learning and acquisition of the MWM task. Cognitive impairment was associated with decline of neurogenesis and hippocampal atrophy in the adult brain.

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EFFECT OF ZINC PRETREATMENT PER SE AND WITH ANTI-EPILEPTIC DRUGS (AEDS) IN EXPERIMENTAL SEIZURE MODELS
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Purpose: The possibility of altering zinc levels is emerging as a new target for treatment of many neurological disorders including epilepsy. Zinc is a component of health supplements and its presence can cause an interaction in epileptic patients. Therefore, role of zinc in seizure models and with antiepileptic drugs sodium valproate (SV) and phenytoin (PHT) was studied using experimental models of seizures in rats.

Method: Male wistar rats, 150–250 g were administered zinc 2, 20 and 200 mg/Kg orally for fourteen days. Sixty minutes after the last dose Pentyleneetrazole (PTZ, 60 mg/Kg i.p.), or Maximal electroshock (MES – 150 mA, 0.2 s duration) challenge was given. In other groups SV (150/300 mg/Kg, i.p.) or PHT (40 mg/kg i.p.) was administered 30 min before PTZ and after 30 min of zinc administration and seizure responses noted, rats sacrificed and brain and serum samples collected for estimation of, Malondialdehyde (MDA) and reduced glutathione (GSH) and zinc levels.

Results: Zinc pretreatment at all doses had no effect on MES seizures. In PTZ seizures, with the lowest dose used ie. 2 mg/kg, a protective effect against PTZ – induced seizures was observed. It also altered other parameters studied ie. MDA and GSH and brain and serum levels of zinc. On combining with sodium valproate, the protection offered by the 100% anticonvulsant dose of SV (300 mg/kg) in PTZ seizures was not affected by zinc pretreatment. The combination of protective dose of zinc ie. 2 mg/kg with subanticonvulsant dose of SV (150 mg/kg) offered only a modest advantage over either drug alone. Combination of phenytoin with zinc had no effect on any of the parameter tested.

Conclusion: Zinc supplementation may offer advantage in epilepsy patients and does not alter seizure control in patients on SV or PHT. However, the neurotoxic potential needs to be further evaluated.

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A COMPARISON OF TREATMENT AND EMERGENCY CARE USE FOR PROLONGED SEIZURES IN CHILDREN OCCURRING IN THE COMMUNITY IN ITALY: A MODEL BASED ANALYSIS
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Purpose: Buccolam, a special pre-filled syringe of midazolam formulated for easier oromucosal administration (OMM), is indicated in prolonged, acute, convulsive seizures (PACS) in pediatric patients. Trials confirmed that OMM is at least as effective as existing treatments. Current care in Italy for community PACS is rectal diazepam (RD), but carers are often reluctant to use it due to social acceptability issues. Aim of the study was to establish whether the use of OMM could affect community treatment of PACS.

Method: A “repeated decision tree” was designed to capture the “patient flow” of previously diagnosed epileptic patients with a community seizure. The tree had the following key nodes:
- Whether parents/carers administer treatment
- When treatment is attempted, whether administration is successful
- Whether the seizure is >10mins and/or repeats
- Whether an ambulance is called
- Whether the patient is admitted as an inpatient after being in the ER

Results: These patients experience on average ~7 seizures/year. An ambulance is called in 49% of cases (patients treated with OMM) or in 67% (RD) of cases. The carer cannot (or chooses not to) administer the treatment in 30% (OMM) or 39% (RD) of cases, the attempted administration is not successful in 15% (OMM) to 49% (RD) of cases.

Conclusion: The model showed that a greater carer willingness and success administering Buccolam compared to RD leads to a significant reduction in the number of emergency ambulance calls/ER visits, with a corresponding reduced impact on the QoL of patients/families and on the total cost/burden of the disease.

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THE USE OF JUST CHECKING (JC) MOTION PASSIVE INFRA RED (PIR) SENSORS AS ASSISTIVE TECHNOLOGY TO SCREEN FOR NOCTURNAL SEIZURES (NS) IN PATIENTS WITH SEVERE INTELLECTUAL DISABILITY (ID) WHO WERE UNABLE TO GIVE INFORMED CONSENT OR AT RISK OF BECOMING BEHAVIOURALLY DISTRESSED WHEN ATTEMPTS WERE MADE TO HAVE OVERNIGHT EEGS
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Purpose: JC provides 24 hr online charts showing patient activity and staff intervention. JC is assistive technology without breach of privacy. JC was used to screen for movements suggestive of NS in people with ID and treatment resistant daytime epilepsy of over 15 year duration who could not provide reliable history due to communication and cognitive difficulties, while considering the issues of infringement of privacy and informed consent.

Method: JC consists of PIR sensors that are triggered by movement to generate activity charts accessible through a password protected website. JC is easy to install, with sensors being placed on walls, beds or door frames and a control box. The box sends the data collected via mobile phone network to the website. The activity charts can be viewed in real time giving a clear picture of individual routines.

Results: 5 patients were studied for 3 months:
Case 1: Immediate action taken as it was apparent that one member of staff was failing to carry out regular observations on an individual during the night as per careplan post seizure.
Case 2: Referral for overnight EEG to investigate unexplained night time movement unknown previously.
Cases 3 & 4: Showed evidence that during the night that the 2 individuals required no support at night thus changing the waking staff to a sleep in leading to considerable cost saving.

Case 5: Showed staff checks on an autistic patient had a disturbing effect on his sleep making him vulnerable to seizures next day leading to 75% improvement in seizures on changes being made.

**Conclusion:** NS are high risk factor for SUDEP and often undetected. The results enabled greater understanding of individual needs, treatment changes, carer monitoring and risk reduction. It gave insight to individual routines, level of independence and suspect NS which patients were unable to articulate themselves.

**p601**
**EPILEPTIC SEIZURES WORKUP IN THE EMERGENCY DEPARTMENT- A RETROSPECTIVE DATA ANALYSIS**

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**Purpose:** The main purpose was to analyse routine workup for patients with seizure in the emergency department (ED).

**Method:** Data analysis was performed on 228 patients with seizure who were examined in the ED at the University Hospital Dubrava from Jul 1 2012 to Jul 1 2013.

**Results:** 173 patients presented with generalized seizure and 55 with partial seizure. 102 patients had first epileptic seizure in life. 75% patients underwent computed tomography (CT) and only 21.3% had pathological finding. Patients up to 40 years presenting with first seizure had generalized seizures and no pathological CT findings. 25.7% patients older than 40 years presenting with first seizure had partial seizure (100% of them had pathological CT finding) and 74.4% had generalized seizure (37% of them had pathological CT finding). In group of patients older than 40 years with previously diagnosed epilepsy 8.8% had pathological CT finding, but only 2.5% of them had a new pathology (p = 0.0041). 213 patients were examined in the ED after the seizure had ceased and 57.6% of them received preventive parenteral antiepileptic therapy (AET). There was no difference in the outcome (seizure recurrence in 24 h) in comparison with patients who were not given preventive AET (p = 0.3337).

**Conclusion:** There is no indication for CT scan in all patients with seizure on changes being made, or if their seizure frequency was greater.

**Conclusion:** A patient’s subjective account of their memory loss does correlate with their score on an objective assessment tool. The greater the number of anti-epileptic medications a patient was taking, the greater the severity of memory impairment. Furthermore, patients taking Carbamazepine scored lower objectively. Larger numbers are required to support this trend further, so that patients at increased risk of these side effects can be warned accordingly.

**p602**
**MEMORY & EPILEPSY: WHAT FACTORS DETERMINE THE SEVERITY OF MEMORY DECLINE IN EPILEPTIC PATIENTS?**

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**Purpose:** To assess rates of memory loss in epileptic patients, and identify potential trends.

**Method:** A cross-sectional study involving 47 patients aged 16–68, known to have epilepsy. While attending out-patient epilepsy clinics in two district general hospitals, subjects completed 2 memory assessments: one objective (TYM), one subjective (ABNAS).

**Results:** The data showed statistically significant correlation between the TYM and the ABNAS scores. Lower TYM scores were seen if patients were on multiple drug therapy, or if their seizure frequency was greater.

**Conclusion:** A website aimed for adolescents with epilepsy to increase and spread knowledge about epilepsy and how to cope with social human problems when having epilepsy. A second aim was to develop a tool for professionals to use in educating the patient about epilepsy.

**Method:** A focus group of seven young people with epilepsy was used to define the need for information about living with epilepsy and defining the requirements for the design of the website.

Teenagers were interviewed about how they deal with their diagnosis, everyday life, social factors and friendship.

**Results:** The results from the focus group discussions were used to develop a website compatible with smartphones, tablets and computers using responsive design principles. Information about epilepsy, epileptic syndromes, and antiepileptic drugs was written and reviewed by health care professionals and adjusted for the target group.

Life stories from adolescents with epilepsy were anonymized and recorded to audio files at the website and illustrated with pictures unfamiliar to the responder. A communication agency was involved in making the design of the website.

**Conclusion:** A website aimed for adolescents with comprehensive information about epilepsy that also can be used by healthcare professionals for patient education.

The website is supported by the Swedish Epilepsy Society, the Swedish Society for Neuropediatricians and Föreningen Margarethahemmet.
including direct patient contact, mailing campaigns, and social media advertising. Patients registered through an online study website and completed informed consent and validation queries before entering the study. Participants initially completed two validated surveys representing the primary study outcomes: the Epilepsy Self-Management Scale (ESMS) and the Epilepsy Self-Efficacy Scale (ESES), two measures of patient self-knowledge used extensively in epilepsy clinical trials. Upon completion, participants were directed to the PatientsLikeMe platform and engaged at their own discretion. After six weeks, study members were asked to complete the surveys again. An incentive was offered upon study completion.

**Results:** A total of 249 Veterans with epilepsy consented, validated, and joined the online platform. The mean age was 50.2 years, 80.7% were male, and 75.1% were non-Hispanic white, consistent with U.S. Veteran demographics. 92 participants (36.9%) completed the second survey set at the conclusion of the study. Using paired t-test and Wilcoxon sign-rank methods, both the ESMS (p = 0.01) and ESES (p = 0.03) total scores demonstrated statistically significant improvements at the end of six weeks participation. Additionally, the ESMS information management subscale displayed significant improvement (p-value < 0.001).

**Conclusion:** This first-time, pragmatic study of an online health management platform demonstrates statistically significant improvements in established epilepsy metrics of patient self-management and self-efficacy. This work demonstrates the potential impact of digital health solutions in epilepsy and serves as a foundation for further research.

**p605**

**WHAT DO “THEY” KNOW ABOUT EPILEPSY?**

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**Purpose:** Epilepsy is one of the poorly understood diseases among public. We purposed to investigate the knowledge of disease among people with epilepsy.

**Method:** A questionnaire was developed and consisted of items about demographics and general knowledge. For the measurement of knowledge, correct answers were scored as 1 and the wrong ones as 0, leading to a total score between 0–25.

**Results:** Of the 330 patients with epilepsy, the mean score of knowledge was 15.97 ± 3.80 (range: 4–24). There were high correlation between the groups of education level (r=0.305) and household income (r=0.240) with respect to knowledge score (p < 0.01) 0.305% of patients thought that “epilepsy is a mental illness.” 19.1% believed that the disease is related to mental retardation, and 20.6% did not know if it is true or not. 27.6% stated seizures can be triggered by a fearfull situation. 11.5% of patients did not know if marriage is forbidden or not for people with epilepsy. 4.2% believed that it is forbidden to give birth child for people with epilepsy, and 10.8% did not know if it is forbidden or not. 44.2% did not know if they should take antiepileptic medication or not during pregnancy. We also showed the wrong beliefs about management of seizures; putting a spoon into mouth or smelling onion during a seizure.

**Conclusion:** We showed that even people with epilepsy do not know well about their illness. We should study more to overcome the wrong beliefs leading prejudice, stigmatization and inaccurate treatment of epilepsy.

**p606**

**PARENTING STRESS DOES NOT NORMALIZE AFTER CHILDHOOD EPILEPSY SURGERY**

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**Purpose:** To investigate stress in parents before and after epilepsy surgery of their child and to know whether surgery outcome made a difference.

**Method:** A prospective study. Parents of 31 consecutively included patients completed the Parenting Stress Index shortly before and two years after surgery. At similar time intervals, control data were obtained from parents of 31 healthy, sex- and age-matched control children. Intelligence of the children was measured at both time points.

**Results:** Before surgery mean standard stress scores were higher in parents of patients than of controls (multivariate analysis, F = 5.05, p < 0.001). Two years after surgery stress had decreased in parents of patients (F = 3.54, p = 0.007), notably on subscales that already before surgery reflected much stress: 2/7 parent-related subscales (“Role Restriction,” “Spouse”) and 1/6 child-related subscales (“Distractibility/Hyperactivity”). Still, at follow-up parents of patients expressed significantly more stress than control parents (F = 2.92, p = 0.003), mainly because their stress remained high not only on “Role Restriction” but also on 5/6 child-related subscales. Furthermore, the lower the child’s intelligence, the more stress parents expressed, stress decreased more in parents of patients with low intelligence and in parents of patients who became seizure-free (n = 21) than in parents of patients with seizure recurrence (n = 10).

**Conclusion:** Parenting stress decreases but does not normalize after epilepsy surgery. In order to prevent undue parenting stress, psycho-education should render parents aware of frequently occurring epilepsy-related stress inducers and their change after surgery.

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**p607**

**THE RELATIONS AMONG STIGMA, OVERPROTECTION, DISCLOSURE AND CONCERNS RELATED WITH EPILEPSY**

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**Purpose:** To determine the relations among stigma, overprotection, disclosure and concerns related with epilepsy.

**Method:** One hundred and forty six adult individuals with epilepsy were participated into the study. The participants filled the questionnaire individually during their outpatient visit or via Epilepsy’s Association’s webpage.

**Results:** The participants’ mean age was 31.15 ± 10.91, and mean duration of epilepsy was 11.92 ± 8.76. 57.5% of the sample was female with...
an 10.72 ± 3.21 average year of education. In the study we used previ-
ously developed epilepsy stigma, overprotection in epilepsy and con-
cerns caused by epilepsy and epilepsy knowledge scales. The results showed a high correlation between stigma and concerns related social life ($r = 0.75$, $p < 0.01$), concerns related with future ($r = 0.55$, $p < 0.01$), concerns related with marriage and having children ($r = 0.44$, $p < 0.01$), overprotection by family ($r = 0.43$, $p < 0.01$) and disclosure of epilepsy ($r = 0.61$, $p < 0.01$). Gender did not revealed any significant differences in none of the variables, but in the level of epilepsy knowledge ($r = 3.15$, $p = 0.01$) which was higher in females. Number of seizures created sig-
nificant differences in concerns related with future life ($F (3,125) = 3.57$, $p < 0.01$), concerns related with marriage and having children ($F (3,125) = 3.01$, $p < 0.05$) and overprotection ($F (3,125) = 2.97$, $p < 0.001$).

Conclusion: The results indicate that stigma should be addressed with some other variables such as overprotection and disclosure in order to get a more clear picture about the social restrictions imposed by felt stigma.

p608
UNEXPECTED READING EPILEPSY MISDIAGNOSED AS CRYPTOGENIC FOCAL EPILEPSY
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Purpose and methods: Reading epilepsy (RE) is a rare form of epilepsy considered as a “generalized epilepsy with a specific mode of activation”. The seizure hallmark consists of perioral myoclonia (POM) elicited by reading and a generalized tonic-clonic seizure (GTC) is almost invariably unavoidable if reading is not stopped. Here we report two adult patients with RE misdiagnosed for years as cryptogenic focal epilepsy.

Results: Both patients had a history of 3–4 apparently spontaneous GTCs in their twenties during sleep and/or wakefulness. One patient had a history of febrile convulsions in childhood and a personality disorder diagnosed at age 20. History, EEG studies (including a previous 5-day video-EEG monitoring in one patient) and MRI were all uninformative. Both patients were diagnosed as “cryptogenic focal epilepsy” but refused antiepileptic drug treatment. A video-EEG monitoring showed occa-
sional left fronto-central interictal epileptiform activity during sleep or on awakening. During neuropsychological testing, reading induced an increase of left or bilateral fronto-central spikes. POM became evident in both patients while reading aloud. When re-interrogated one patient rec-
ognized random facial-cranial jerks when reading aloud for the last 1–
2 years.

Conclusion: Some patients with RE may be unaware of POM and are prone to be misdiagnosed as focal cryptogenic epilepsy. A correct syn-
dromic diagnosis has relevant diagnostic and therapeutic practical implica-
tions (avoids further unnecessary etiologic studies and helps select the most appropriate antiepileptic drug). Neuropsychological testing during EEG monitoring may be specially useful in patients with cryptogenic epi-
lepsies as the history and/or routine EEG studies may not be enough to reach a diagnosis of reflex epilepsy.

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PERFORMANCE OF A MULTIDISCIPLINARY SPECIALIST SERVICE FOR ADULT PATIENTS WITH EPILEPSY AND INTELLECTUAL DISABILITY
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Purpose: Patients have difficulty finding the appropriate care service when they suffer from both epilepsy and ID (Intellectual Disability). Epi-
lepsy-centre Kempenhaeghe started a specialised clinic in 2008 for adult patients with refractory epilepsy and ID. Care was provided by a mul-
tidisciplinary team including a neurologist, a doctor specialised in persons with ID and a psychologist. The performance of the clinic was evaluated by studying the patients who were referred in 2011 and 2012.

Method: Data were accessed retrospectively through the electronic patient records of all 2011–2012 patients, including referral questions, demographic variables and outcome of the diagnostic workup.

Results: 47 patients were included, mostly referred by a neurologist (31) or by an ID-specialist (10).

The main questions concerned treatment issues (53%), diagnostic issues (49%) and behavioural problems (28%).

Laboratory tests were performed in the majority (83%), while 55% underwent seizure-detection, 26% an MRI and 19% an EEG. Genetic evaluation was done in 21%.

Medication was adjusted in 91% of the patients with treatment issues and in 77% of those with behavioural problems. In the latter group, the psychologist offered advice in 69% on day-structure, approach, living environment or activities.

Epilepsy was excluded in 6 of the 7 patients where the initial diagnosis was doubted.

Behavioural nor motor symptoms could be attributed to the epilepsy in 21 patients, where initially the primary carer had suspected a link.

After the diagnostic workup, 75% could be referred back to their spe-
cialist, while 21% remained in care of the Epilepsy centre and a minority was referred to another specialist, e.g. a geneticist or a rehabilitation spe-
cialist.

Conclusion: A multidisciplinary setup in an epilepsy centre contributes to the solutions that meet health care demands of patients with Epilepsy and ID.

p610
IMPACT OF FEATURE FILM “EK NAYA DIN” – FIGHT AGAINST EPILEPSY ON NORTH INDIAN STATES
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Purpose: People’s education in North Indian state through shows of “Ek Naya Din” – a feature film for fight against epilepsy.

Method: The present study is a questionnaire based study, which was conducted in wide mass base, with 22,334 subjects observing 500 shows of “Ek Naya Din” – a feature film for fight against epilepsy. Out of these, 2,000 subjects were given a descriptive proforma with part A and part B, which were to be opened and filled before the start of the film (part A) and after watching the film (part B). The work was supervised by a Neu-
rologists and 9 trained volunteers.
Results: 81 percent of subjects felt that they became aware about various psychosocial aspects of epilepsy, after watching 63 min of film. 1,433 subjects, out of 2,000 subjects knew about the importance of medical help, if someone had epilepsy in the family. Subject appreciated the role of a good parental care and friend’s help in the need of hour, in the life of an epileptic.

Conclusion: “Feature film “Ek Naya Din” – fight against epilepsy is an excellent media tool in North India, for epilepsy education.

p611
SOCIODEMOGRAPHIC DISPARITIES IN ADMINISTRATION OF ANTIEPILEPTIC DRUGS TO ADULTS IN GERMANY
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Purpose: Large epidemiological databases allow studying medical care in different subgroups of the population in the presence of common guidelines. This study aimed for such analyses regarding utilization of antiepileptic drugs (AED) for epilepsy in Germany.

Method: Data source was the Disease Analyzer® database that is representative for the German population and assembles anonymous demographic and medical (diagnoses, prescriptions) data obtained from the practice computer system of general practitioners and specialists throughout Germany. 43,712 adult patients with epilepsy diagnosis (ICD10: G40.X) seen in 2010–2012 by 346 neurologists were retrospectively analysed according to sociodemographic characteristics, comorbidity and AED treatment. Multivariate logistic regression was applied to calculate adjusted odds ratios (OR) with 95% confidence intervals (CI).

Results: Women received largely lamotrigine (OR 0.68; CI 0.65–0.72; p < 0.001). Men were treated preferably with carbamazepine (OR 1.29; CI 1.23–1.35; p < 0.001). Patients covered with statutory health insurance (SHI) were treated more often with valproate (OR 0.84; CI 0.76–0.93; p < 0.001) and showed a higher rate of obesity (SHI: 3.1%; private health insurance (PHI): 1.6%; p < 0.001) while PHI was associated with administration of levetiracetam (OR 1.27; CI 1.16–1.4; p < 0.001). Carbamazepine (OR 0.80; CI 0.76–0.85; p < 0.001) and primidone (OR 81; CI 0.72–92; p < 0.001) were frequently administered in urban areas. Living in an urban community raised the likelihood to be treated with levetiracetam (OR 1.25; CI 1.17–1.28; p < 0.001).

Conclusion: In spite of common guidelines, AED treatment differed significantly among adults with epilepsy in Germany. Beside gender, type of health insurance and place of residence determined AED administration.

p613
PERCEPTION OF EPILEPSY AMONG NIGERIAN SCHOOL CHILDREN
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Purpose: It is estimated that 80% of people suffering from epilepsy around the world, reside in developing world such as Africa and it remains a stigmatized condition. Reducing the stigma of epilepsy is paramount to reducing its impact and so improving quality of life. Unfortunately, there have been no studies conducted to explore the perception of epilepsy among Nigerian children. We therefore carried out a survey on the knowledge and attitude of epilepsy among primary school students aged 9–12 years.

Method: We used a questionnaire to determine if the children knew what epilepsy is, and if they did not know, what did they think epilepsy is. Fifty children (35 boys and 15 girls) with mean age 11 years; from a sixth grade of a primary school in northeast Nigeria completed the questionnaire individually at the same time in the classroom. All of them were from a sixth grade class of a public elementary school in Yola, northeast Nigeria. This school was chosen because it is typical of the public schools in this city. The students were, on average, from lower-middle socioeconomic status families and attended school for 5 h each day. We chose the sixth grade because it comprises the eldest children capable of expressing themselves adequately in writing and reflecting social perceptions. The process took about 15 min.

Results: Only 5 (10%) children said they knew what epilepsy is; which 3 perceived as a disease of evil spirit and 2 thought as disease which is contagious and without a cure. Seventy percent would not like to associate with a peer with epilepsy.

Conclusion: The perception about epilepsy was poor with antecedent negative consequences. There is a need for educational programs in elementary schools which must be adapted to the specific cultural nuances of the localities.

p614
PARENTAL DISTRESS AND PERCEIVED SOCIAL SUPPORT IN PARENTS OF CHILDREN WITH IDIOPATHIC EPILEPSY
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Purpose: To analyze parental distress and perceived social support in parents of children with idiopathic epilepsy.

Method: We studied 24 parents (14 F, 10 M; mean age 44 ± 4.5 years) of 17 children (11 F, 6 M; mean age 9.2 ± 2.9 years) with idiopathic epilepsy (14 focal, 3 generalized). The following measures were analyzed: 1. Parental Stress Index-Short Form (PSI-SF); 2. Multidimensional Scale of Perceived Social Support (MSPSS), to assess social support; 3. Inventory of Pediatric Epilepsy Scale (IPES), to assess parental perception of the psychosocial impact of epilepsy on the family. Scores were statistically compared with data of the Italian validation sample.

Results: Parents of children with epilepsy reported higher scores of general parental distress (t = 3.53, df = 23, p < 0.05). With respect to the perceived social support, they did not differ from the Italian validation sample (friends: r = 0.14, p > 0.05; family: r = −0.24, p > 0.05; other: r = 0.87, p < 0.05). The correlation between PSI and IPES was strongly significant (r = 0.67, p = 0.001) while the correlations among PSI vs MSPSS, and IPES vs MSPSS were not significant.

Conclusion: Parents of children suffering from idiopathic epilepsy show high index of general parental distress. Perception of social support seems to be not influential on parental distress and on the perception of impact of the epilepsy. Data support a significant correlation between parental distress and perception of the psychosocial impact of epilepsy on the family system.
p615 HOW DOES THE LABEL “EPILEPTIC” INFLUENCE ATTITUDES TOWARDS EPILEPSY?
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Purpose: Persons suffering from epilepsy are still often called „epileptics” by laymen but also by some medical professionals. The purpose of our research was to find out whether
1 calling a person with epilepsy (PwE) an „epileptic” negatively influences attitudes towards them, and if so,
2 whether this influence is more pronounced in certain types of social interactions.

Method: Two randomly assigned groups of college-preparatory high school students were asked about their attitudes towards PwE via anonymous questionnaires that included demographic data, a modified version of the Bogardus social distance scale and questions on knowledge about epilepsy. Two versions of the questionnaire were identical except for the term „PwE” in first group (group A) being replaced with the term „epileptic” in the second one (group B). Mann-Whitney test was used to compare attitude scores between groups.

Results: There were 425 subjects in total, 208 in group A and 217 in group B. Total score for negative attitudes was higher in group B (p = 0.007). Subjects in group B expressed more negative attitudes when asked about sharing a room with a PwE (p = 0.005) and marriage with a PwE, either concerning someone close to them (p = 0.024) or themselves (p = 0.033). Females and subjects having better knowledge on epilepsy had a higher total score for negative attitudes in group B (p = 0.01 and p = 0.003, respectively), while in their counterparts attitudes were the same no matter what term had been used.

Conclusion: The term „epileptic” can lead to more negative attitudes toward a PwE. This seems to be especially true for more intimate life domains (cohabitation or marriage with PwE), while in more impersonal domains (such as communicating and working with PwE), semantic difference was not found. Certain subgroups such as females and persons with better knowledge on epilepsy might be particularly sensitive to this difference.

p617 INTERICTAL EPILEPTIC ACTIVITY AND ITS IMPACT ON DRIVING ABILITY
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Purpose: Epilepsy patients have a higher risk of traffic accidents due to seizures while driving. Interictal epileptic activity (IEA) cannot be seen by an observer and is not realized by patients but can lead to transient cognitive impairment. Its impact on driving is unclear and has rarely been investigated [1, 2, 3]. We aimed at determining the unknown latencies of digital devices in a realistic driving simulator and preliminary recordings of reaction times (RT) during IEA.

Method: Patients drove in a realistic driving simulator (Foerst) combined with simultaneous EEG registration (Trackit). Stop signs were triggered during IEA or baseline EEG. Their appearance on the screen was detected with a RGB-color sensor, and used to calculate the effective RT (eRT) to foot pedal brake signal detection. A microcontroller and single-board computer running Linux performed EEG signal processing and recording from Trackit, RT measurement, and display.

Results: EEG processing with IEA detection and stop sign trigger output by the Linux computer required 15 ms. The median latency between this trigger output and appearance of the stop sign on the screen of the driving simulator was 234.4 ms. The variance of this delay was large with a non-Gaussian distribution (range 190–611 ms). eRTs of six healthy controls and one epilepsy patient were recorded. Average eRTs of controls were 871.4 ± 20.2 ms. eRTs of the patient were 846.7 ± 123.9 ms (n = 38) during baseline EEG and were prolonged by 113 ms (p = 0.004) to 960.4 ± 126.1 ms during generalized IEA (n = 16).

Conclusion: Digital device cascades show long and unpredictable latencies between triggering and display. The measurement of the time when the on-screen stop signal becomes visible to the subject is a prerequisite to record eRTs in a realistic driving simulator. Preliminary eRTs are slowed during generalized IEA.

p618 INCIDENCE, HOSPITALIZATION COSTS AND RISK FACTORS OF EPILEPSY-RELATED INJURIES AND ACCIDENTS
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Purpose: The objective of this study was to provide incidence estimates, determine hospitalization costs and define risk factors for epilepsy-related injuries and accidents.

Method: Adult outpatients with epilepsy from general practitioners, neurologists and an epilepsy center were enrolled for a three months observation period. Data on socioeconomic status, course of epilepsy as well as quality of life measurements were recorded using validated patient questionnaires. Costs of inpatient treatment due to injuries and accidents were derived from billing data in a population-based hospital cohort.

Results: We enrolled 276 outpatients and searched for potential risk factors in this cohort. Overall, 50 patients (18.1%) suffered from epilepsy-related injuries and accidents in a three months period. Lacerations (n = 28; 10.1%), abrasions and bruises (n = 17; 6.2%), fractures (n = 8; 2.9%), burns (n = 2) and one car accident were reported. Epilepsy-related injuries and accidents were related to an active epilepsy, occurrence of generalized tonic-clonic seizures, drug-refractory course as well as reported ictal falls and ictal loss of consciousness in the medical history.

In the hospital cohort nine of the 96 inpatients (9.3%) presented with seizure-related fractures and other lacerations requiring admission. Seizure-related injuries resulted in mean hospitalisation costs of €3,399 ± 1,464 (range 1,364–5,468) per patient per admission. Seven patients presented with fractures of the scull, vertebra, maxilla, mandible, zygomotic bone and limbs; two patients had lacerations requiring hospital admission. This resulted in 8.8% of the total inpatient costs due to epilepsy.

Conclusion: Epilepsy-related injuries and accidents are responsible for a substantial proportion of hospital costs associated with epilepsy. Injuries and accidents are frequently reported, reinforcing the necessity to further evaluate the burden and optimise the treatment of epilepsy.
p619

**DRIVING AMONG EPILEPSY PATIENTS IN WEST CHINA**

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**Purpose:** To survey the driving status of PWE in West China and to explore the socio-demographic and clinical factors associated with driving.

**Methods:** Between October 2012 and October 2013, all adult patients who came to our epilepsy clinic in the West China Hospital were invited to participate. Logistic regression was used to detect the patient factors associated with driving.

**Results:** A total of 657 patients completed this study. We found that 128 (19.5%) of these patients had driven recently (during the past year); among them, 80 (62.5%) experienced at least one seizure in the previous year. A logistic regression suggested that being male, being younger than 50 years old, married, having a higher personal income, experiencing no seizure while awake and taking fewer antiepileptic drugs were independently associated with recent driving.

**Conclusion:** This study showed that a considerable proportion of patients continue driving despite uncontrolled seizures. More detailed and operational driving restrictions may be needed for patients in China in order to strike a better balance between patients’ quality of life and public safety.

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p620

**FEASIBILITY OF WHOLE BODY VIBRATION TRAINING IN PEOPLE WITH EPILEPSY, OSTEOPENIA AND AN INTELLECTUAL DISABILITY**

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**Purpose:** To investigate the feasibility of whole body vibration therapy (WBV) in a high-risk population as an additional, non-pharmacological, approach to bone health.

**Method:** A prospective feasibility study. 20 patients, with refractory epilepsy and an intellectual disability were included. WBV training sessions were performed thrice weekly, for a period of 12 months. Training load increased gradually according to an individual program. At 6 and 12 months a semi-structured interview was conducted. Additional assessments at fixed times (T = 0, 3, 6, 9 and 12 months) included a DXA-scan, Quantitative Ultrasonography (QUS) and serum biomarkers CTx and PINP.

**Results:** There were no drop-outs during the 12 month period. Compliance reached an average of 91% attendance. No serious adverse effects were reported. Interviews largely demonstrated satisfaction with the training program. 10 patients (50%) reached the target, ending in 3 × 3 min of vibration with a frequency of 40 Hz, 3 times a week. All 20 patients were able to endure the frequency of 40 Hz (100%). A significant increase of BMD or improvement in bone metabolism could not be demonstrated in this study, possibly due to the short follow-up period.

**Conclusion:** WBV is a feasible non-pharmacological approach to bone health in this population.

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p621

**TRANSIENT GLOBAL AMNESIA: HIGH DENSITY EEG RECORDING OF ACUTE PHASE AND RECOVERY**

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**Purpose:** Transient Global Amnesia (TGA) is a completely reversible condition characterized by an antero-retrograde amnesia with acute onset and remission within a few hours. An hippocampal dysfunction have been hypothesized so far, based on brain MRI findings of reversible unilateral or bilateral restricted diffusion. Ischaemic, epileptic or metabolic underlying mechanisms have never been fully demonstrated. Aim of the study: to map throughout High Density EEG focal modifications of background activity during TGA and after recovery.

**Methods:** Hereby we describe 2 TGA cases with a negative brain CT scan. EEG has been recorded, by means of 256 channels high density (HD-EEG) system (EGI, Oregon), during the acute phase and once the symptoms had completely recovered. The signal was post-processed and the analysis was made on 64 channels out of 256. We performed spectral analysis and compared both hemispheres both in acute and recovery conditions.

**Results:** In both patients our results show an asymmetry between hemispheres in acute phase, with an amplitude increased of theta band in one temporal region, which disappeared in the recovery phase.

**Conclusion:** HD-EEG may provide insights on the localization of neuronal network dysfunction in these patients.

p622

**DISTINCTIVE INTERICTAL AND Ictal VIDEO-EEG FEATURES OF EPILEPSY IN SCN8A ENCEPHALOPATHY**

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**Purpose:** SCN8A mutations have been recently associated with early infantile epileptic encephalopathy with a broad phenotypic spectrum. We aim to further delineate the clinical-EEG features of SCN8A-related epilepsy.
Method: We studied 9 SCN8A positive patients, age range: 8 months–16 years. They underwent clinical and neurophysiologic investigations including prolonged video-polygraphic recordings during wakefulness and sleep.

Results: Anamnestically, epilepsy onset occurred at a mean age of 5 months with polymorphic, drug resistant seizures, cognitive deterioration and pyramidal/extra-pyramidal signs ± loss of eye contact (6/9pt). Non-convulsive status epilepticus occurred in 5/9 and SUDEP in 2/9 patients. Interictal EEG at epilepsy onset was normal in 5/9 patients; during the follow up in all cases occurred progressive background deterioration and focal/multifocal spike-and-waves abnormalities, predominant in the temporo-occipital regions and/or generalized spike waves. Nocturnal sleep EEG (3/9 patients) was normally structured. Ictal video-EEG recordings were obtained in 4/9 patients (follow-up 10–25 months); all seizure types have been documented. Patients had both focal and generalized seizures (FS,GS), the latter consisting of GTCS, pseudo-absences, spasms and myoclonus. FS were usually prolonged (3–5 min), with prominent hypomotor and vegetative semiology, evolving to asymmetric tonic/tonic-clonic manifestations ± secondary generalization. Ictal EEG showed diffuse EEG desynchronization (GS) or post-temproal seizure onset (FS), slow spreading and migration of the ictal discharge (2/4 patients) from one hemisphere to the contralateral during the same seizure.

Conclusions: Despite the description of a heterogeneous epileptic phenotype associated to SCN8A encephalopathy, our patients exhibit a distinctive ictal and interictal EEG pattern, suggesting an epileptogenic dysfunction in the temporo-occipital regions, also confirmed from the recurrence of cortical visual impairment. We also speculate that the presence of ictal vegetative symptoms and the long seizures duration with frequent secondary generalization could represent risk factors for SUDEP. Awareness of this distinctive phenotype will likely enhance recognition of this disorder.

p623 AUDITORY STEADY-STATE RESPONSES ARE ABSENT IN DRAVET SYNDROME AND PRESENT IN OTHER EPILEPTIC SYNDROMES

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Purpose: Around 70–80% of patients with Dravet Syndrome have mutations in the SCN1A gene, which encodes the alpha subunit of the type I voltage gated sodium channel. This channel has a key role in the generation of gamma oscillations that are related with cognition. Cortical gamma oscillations can be studied by means of steady-state responses. The purpose of this work was to study the steady state responses in Dravet syndrome and check the specificity of the potential changes.

Method: 9 epileptic patients with Dravet Syndrome and 10 patients with other epilepsies of similar ages were studied. Auditory steady-state responses were evaluated using a tone modulated in amplitude by a sinusoid whose frequency increases linearly in frequency (‘chirp’) from 1 to 120 Hz. Time-frequency transforms were used for the analysis of the evoked responses.

Results: No auditory steady-state responses were found in patients with Dravet Syndrome within the studied range. Patients with other epilepsies, as described in normal subjects, showed two maximal amplitude of the responses around 40 Hz and in the 80–120 Hz range.

Conclusion: Steady-state responses are absent (or at least severely impaired) in patients with Dravet syndrome, suggesting a global impairment in the mechanisms involved in cortical oscillatory activity generation in these patients. This finding could not be explained exclusively by the presence of epilepsy or the antiepileptic drugs intake, pointing to the important role of the channelopathy itself.

p624 INTRACRANIAL EEG SEIZURE-ONSET PATTERNS CORRELATE WITH INTERICTAL HFOS IN PATIENTS WITH REFRACTORY EPILEPSY

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Purpose: A variety of EEG patterns occur at the beginning of seizures. High-frequency oscillations (HFOS) are good indicators of seizure onset (SO) areas. It remains unclear, however, whether interictal HFOS differ in brain areas generating seizures with different morphologies. We investigated if different intracranial EEG SO patterns display diverse interictal HF0 rates.

Method: We analysed intracranial EEG SO patterns from 38 consecutive patients with lesional drug-resistant focal epilepsy. SO patterns were classified as: low-voltage fast activity (LVFA), sharp activity at ≤13 Hz, periodic spikes, burst of polyspikes, and burst-suppression. HF0 (ripples and fast ripples (FR)) were visually marked during 5 min of recording during slow wave sleep (500 Hz filter and 2000 Hz sampling). The Kruskal Wallis test was used to assess HF0 rates across SO patterns, with Bonferroni correction for multiple comparisons.

Results: In total, 211 channels were selected: 82 with LVFA; 46 with sharp activity at ≤13 Hz; 21 with periodic spikes; and 47 with burst of polyspikes. 15 could not be classified. Ripple rates differed significantly across SO patterns (median ripple rates – LVFA: 6.3, sharp activity at ≤13 Hz: 0.7, periodic spikes: 3.8, burst of polyspikes: 4.4; p < 0.01). In addition, significant differences were found for the fast ripple rates in SO patterns (median FR rates – LVFA: 0.2, sharp activity at ≤13 Hz: 0, periodic spikes: 1.2, burst of polyspikes: 1.2; p < 0.05).

Conclusion: Distinct SO patterns display different rates of interictal HF0s. Compared to other patterns, sharp activity at ≤13 Hz was associated with a lower HFO rate. This suggests that the region displaying this ictal morphology is, indeed, a region of spread, and not an area of seizure onset. Different ictal-onset morphologies may result from distinct mechanisms underlying seizure generation. Therefore, another explanation would be that the mechanisms that generate this type of EEG morphology do not generate HF0s.

p625 EEG COHERENCY IN CHILDREN WITH AUTISM

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Purpose: We tried to identify pattern of altered functional brain connectivity in children with autism. Previous magnetic resonance imaging and EEG coherence studies indicated existence of altered regional brain connectivity, and there are promising studies of EEG coherence as possible diagnostic instrument for ASD.

Method: We compared EEG coherence of 18 children with autism spectrum disorder (ASD) without epilepsy or epileptic discharges in EEG, with normal controls matched by age and gender. We recorded standard 24-channel EEG in awake and alert state. Two to six minutes of artifact-free EEG was exported to ASCII format for coherence analysis in Matworks Matlab software. We used autocorrelation to determine stationary epochs and then coherence values for all possible pairs of electrodes for
16 two Hz wide frequency bands were calculated. For coherence calculation we used Welch’s averaged periodogram and time-varying Partial Directed Coherence and compared results.

**Results:** Principal components analysis identified 38 factors that explained about half of the variance and gave pattern of regional brain connectivity. We found stable pattern of decrease of both short and long-distance coherences for the ASD-group when compared to the controls.

**Conclusion:** EEG coherence is promising tool for identification of altered brain connectivity pattern in children with ASD.

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**p626**

**WHITE BLOOD CELL COUNT IN PATIENTS WITH EPILEPTIC SEIZURES**

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**Purpose:** The role of inflammation in epileptic seizures has been widely studied and received increased attention during the last years. The aim of the current study is to examine basic inflammatory markers such as White Blood Cells (WBC) in patients after epileptic seizures and after non-epileptic episodes of loss of consciousness.

**Method:** The sample consists of 78 participants divided into two groups:

1. Group A consists of 56 patients (33 males, 23 females, median age 46 years, IQR 33–53.5 years) with a diagnosis of epileptic seizures or epilepsy who were hospitalized in the Third Department of Neurology of the Aristotle University of Thessaloniki, “G. Papanikolou” Hospital, in 2013. The diagnosis of all patients was further supported by epileptic discharges observed in routine EEG recordings.
2. Group B consists of 22 patients (9 males, 13 females, median age 28 years, IQR 20–52 years) with episodes of loss of consciousness of mostly vasovagal or syncopal origin. Resting EEGs were performed in all patients and the findings were normal. The two groups were not age- or gender-matched (p > 0.05).

**Results:** No difference was observed in the WBC count between the two groups (p > 0.05; Group A: median WBC 7.16, IQR 5.72–9.69; Group B: median WBC 7.10, IQR 6.30–9.67). However, patients with generalized seizures had higher WBC count than patients with partial seizures (p < 0.05).

**Conclusion:** According to the results of the current study, WBC count in patients after generalized seizures is elevated compared to patients that experienced partial seizures, a finding that agrees with that observed in previously published studies. No difference was observed in the WBC count in patients with epilepsy and those with loss of consciousness. However, a limitation of the study is that the two groups were not gender- or age-matched.

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**p627**

**THE ROLE OF EEG IN EPISODES OF LOSS OF CONSCIOUSNESS: ONE OR MORE RECORDINGS?**

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**Purpose:** To investigate the role of one or more EEG’s, performed in our laboratory during last year, in patients with episodes of loss of consciousness (LOC). There is much concern about the “over-reading” phenomenon leading many times to a false diagnosis. This is more crucial in patients with LOC and with no definite or known history of epilepsy due to the influence of the EEG findings on further investigation and treatment.

**Method:** In 2013, 1139 EEG studies were performed in the laboratory of 3rd Department of Neurology of Aristotle University of Thessaloniki. 133 patients (58 males, 75 females, mean age 46.17) with 170 EEG’s met the criteria as having an episode of loss of consciousness. All EEG’s were blindly reviewed by two readers. We also analyzed the inter-rater variability by calculating kappa value and reported the waveforms usually misinterpreted.

**Results:** The kappa coefficient was 0.82 which is almost perfect. 67 patients (37.4%) had an abnormal EEG. The diagnosis of epilepsy was confirmed in 22 patients (16.5%). More than one EEG study was performed in 40 patients (18 males, 22 females, mean age 42.2, SD ±18.73 years). In the group of patients with >1 EEG performed, 12.5% had some clinical or further investigational effect and in 5% the diagnosis of epilepsy was confirmed. It is of interest that the remaining 7.5% had a misinterpreted EEG (wicket spikes, fluctuation of background activity) which falsely led to a diagnosis of epilepsy.

**Conclusion:** In patients referred for LOC episodes EEG is a tool that can help to establish the diagnosis of epilepsy or even to guide in performing further investigations. Though first EEG was abnormal in 37.4% and placed the diagnosis of epilepsy in 16.5% of the patients additional EEG’s did not show the same effect.

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**p628**

**NON-CONVULSIVE STATUS EPILEPTICUS IN PATIENTS WITH POST COMA UNCONSCIOUSNESS AT SEVERE CRANIOCEREBRAL INJURY**

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**Purpose:** Was determination of frequency of development of the non-convulsive status epilepticus in patients with severe craniocerebral injury in case of development of post coma unconsciousness.

**Method:** There were 86 patients under observation (age 22–46 years) with severe craniocerebral injury. Inclusion criteria were:

1. acute period of coma,
2. restoration of spontaneous breathing,
3. non-consciousness (productive contact, reality awareness),
4. no convulsive syndrome, myoclonus,
5. no epilepsy in past medical history (before the injury).

EEG monitoring was carried out for 2–4 h every day up to the outcome.

**Results:** A criterion for determination of non-convulsive status epilepti-cus was a presence of epileptic activity with index not less than 30%. A feature of epileptic activity was localization in the frontal-central parts without any generalization. Epileptic patterns were registered in 18 patients (21%). Such patients were prescribed antiepileptic drugs which were administered up to the moment of reduction of epileptic phenomenon. Duration of the antiepileptic therapy has made 10–16 days. Restoration of clear consciousness has occurred in 16 cases, in 2 cases permanent vegetative condition has developed. Individual qspike – slow wave} complexes and outbreaks of “sharp” waves were registered in 52 patients (60%). However the index of such epileptic activity was below 10–15%. Antiepileptic therapy was not carried out in such patients. Restoration of
Cortical activity in tinnitus patients clearly differed from normal. Changes in cortical activity may both elicit and suppress tinnitus. When coexistent with hearing loss, tinnitus may be the result of neuronal hyperactivity provoked by reduced peripheral input. This hyperexcitability is suspected to be located in the parts of auditory cortex that represent intact hearing frequencies. Sound stimuli are believed to modulate centrally generated sensation, leading to tinnitus inhibition. The goal of the study was to observe spontaneous cortical activity and cortical activity modulated by tinnitus-matched sound in tinnitus patients compared with healthy subjects with no otoneurological symptoms.

**Design:** Data were prospectively collected from 50 tinnitus patients (24 women, 26 men; mean age 42.5 years, range 20–63) and 25 healthy subjects (12 women, 13 men; mean age 40.4 years, range 18–61). Cortical activity was recorded in all subjects with the eyes closed, open, during photostimulation, hyperventilation, and photostimulation using 19-channel quantitative electroencephalography (EEG). Sound applied to the tinnitus patients was individually matched (frequency and intensity) with ability (based on patient report) to mask the tinnitus. Maximal and mean amplitude of the delta, theta, alpha, and beta waves, and type and amount of the pathologic EEG patterns were noted during each recording (i.e., stimulation). Differences in cortical localization and the influence of sound stimuli on spontaneous cortical activity were evaluated between groups.

**Results:** The tinnitus group exhibited decreased delta activity and increased alpha and beta activity. These changes were predominantly located in the bilateral temporal cortex and frontal lobes. Hyperventilation increased the intensity of the differences. Tinnitus patients had more sharp-slow waves and increased slow wave amplitude. Sound stimuli modified the EEG recording; the delta and beta wave amplitudes increased whereas alpha-1 wave amplitude decreased. Photostimulation only slightly affected the temporal region.

**Conclusions:** Cortical activity in tinnitus patients clearly differed from that in healthy subjects, i.e., tinnitus is not a “phantom” sign. Changes in cortical activity included decreased delta wave amplitudes and increased alpha-1, beta-1, and beta-2 wave amplitudes, and pathologic patterns. Cortical activity modifications occurred predominantly in the temporal region. Photostimulation affected spontaneous cortical activity only in tinnitus patients, and although the applied sound was individually matched, the pathologic changes were only slightly improved.

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**p631**
**PERCEIVED STIGMA OF PATIENTS WITH REFRACTORY EPILEPSY AND INTELLECTUAL DISABILITY**

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**Background:** The limited research of perceived stigma and its determinants in patients with epilepsy and intellectual disability motivated our study in this area.

**Purpose:** We aimed to assess perceived stigma and its determining factors in Bulgarian patients with refractory epilepsy and intellectual disability.

**Methods:** We conducted a study based on questionnaires designed for people with intellectual disability (stigma scale, Glasgow Depression Scale, Glasgow Anxiety Scale) and a purposeful interview on clinical and social factors of 64 patients with refractory epilepsy and intellectual disability.
Results: We found perceived stigma in 89.28% of cases which was mild in 32.14%, moderate in 32.14%, and severe in 25% of study participants. Perceived stigma was associated with depression ($\chi^2 = 12.57, p = 0.006$) and anxiety ($\chi^2 = 7.01, p = 0.03$). Depression proved to be the only significant predictor of perceived stigma on multivariate regression analysis ($F = 13.44, p = 0.001$).

Conclusion: We have affirmed very frequent perceived stigmatization in Bulgarian patients with refractory epilepsy and intellectual disability and its correlation with concomitant depression and anxiety.

p632
Efficacy of Add-on Lacosamide in Refractory Epilepsy Patients with Learning Disabilities
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Purpose: The efficacy and safety of lacosamide (LCM) has been shown in previous studies in patients with refractory partial-onset epilepsy. Our aim was to evaluate the efficacy and tolerability of this drug in refractory patients with learning disabilities (LD).

Methods: This retrospective study included all patients with LD and refractory epilepsy treated with add-on LCM at our Epilepsy Clinic in the period of 2009–2013.

Results: Eighteen patients, 15 male and 3 female were included in the study with the mean age of 38 (26–59) years. Fourteen patients were diagnosed with focal epilepsy and four with Lennox-Gastaut syndrome. Their seizure frequency was an average of 13 (1–30) per month. Fifteen patients (83%) were taking two or more AEDs (1–4) and 4 patients had also nervus vagus stimulator. All of them had tried in average 5.2 AEDs (2–14) before LCM was added. The dose of LCM was increased with 50 mg per week until the target dose of 200–300 mg was reached. Further dose adjustment was made in order to achieve an optimal seizure control. Over 50% of seizure reduction was seen in 44% of patients during the follow-up (10–48 months). Eight patients discontinued the drug, because of lack of efficacy and/or adverse effects. The most frequently reported side effects were dizziness, tiredness and aggressiveness. Two patients died but none of them was suspected to be related to the drug.

Conclusion: Lacosamide appears to be an effective and safe AED when used as adjunctive therapy also in patients with LD. Slower upitation than suggested should be considered to reduce the risk of side-effects.

p633
The Modified Atkins Diet in Patients with Refractory Epilepsy and Severe Intellectual Disability – Design of a Randomized Controlled Trial
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Rationale: A high proportion of patients with intellectual disability (ID) and epilepsy have recurrent seizures despite multiple trials of anti-epileptic drugs. The last decade, studies have been published evaluating the effect of the Modified Atkins Diet (MAD) – a less restricted form of the ketogenic diet – on seizure frequency in children and adults with pharmacoresistant epilepsy. These studies have shown high tolerability and efficacy of the MAD on seizure control. However, trials including adult patients with ID are lacking.

Purpose: We aim to establish efficacy, safety and feasibility of the MAD in adult patients with ID and pharmacoresistant epilepsy.

Method: We have designed a prospective open-label randomized controlled trial in institutionalized adult epilepsy patients with severe ID. Inclusion criteria include seizure frequency of at least two seizures per month, substantial interference with quality of life and failure of at least two antiepileptic drugs. Patients will be randomized to receive the MAD or no dietary intervention for a period of 4 months. Medication will be continued during the trial-period. Responder is defined by having > 50% reduction in seizure frequency. We expect to have 45% responders in the intervention group, compared to 11.5% in the control group. A sample size of 27 patients per group was estimated to enable a difference that was significant at 5%, with a power of 80%. Primary outcome parameter is the number of responders 4 months after randomization, compared between the two groups. Secondary outcome parameters are: (i) retention rate, (ii) effect on daily functioning as expressed by the Habilitative Improvement Scale (HIS), (iii) feasibility in this population and setting, (iv) adverse events attributable to the MAD and (v) predictive factors of a positive response to the MAD.

Results: Ethics approval was obtained on October 29th, 2013. In January 2014 we included the first participants.

p634
The Effect of Selective Serotonin Reuptake Inhibitors on the Frequency of Epileptic Seizures in Young People with Severe Epilepsy
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Purpose: Pre-clinical studies suggest possible benefits of selective serotonin reuptake inhibitors (SSRIs) as antiepileptic agents. Currently there is limited evidence to prove its efficacy as an antiepileptic and there are few studies looking at the effect of SSRIs exclusively on epileptic seizures. The aim of the current study is to demonstrate the effect of SSRIs on total seizure frequency.

Method: This study was conducted at a residential centre for young people with complex epilepsy and associated co-morbidities. Young people with epilepsy who were prescribed SSRI for mood disorders and/or obsessive rituals were selected for the study. Total seizure frequencies were collected for each patient for a six month period prior to and after starting SSRIs.

Results: Thirteen patients (nine males, four females; age range 11–27 years) were included in the study. Six patients had generalised epilepsy and seven had focal epilepsy. 6/13 (46.1%) of the patients showed reduction in their total seizures after starting treatment with 4/13 (30.7%) showing more than 50% total seizure reduction and the antiepileptic was altered in one of these patients. The seizures worsened in 5/13 (38.4%) and the remaining 2/13 (15.3%) showed no difference in their seizure pattern. 7/13 (53.8%) of the population had abnormal brain imaging. 4 of these patients had worsening of their seizures after starting SSRI treatment.
However there was no overall difference in response between the focal and generalised epilepsies.

**Conclusion:** SSRIs are not contraindicated in young people with severe epilepsy.

Particular care may be needed in patients with structural abnormalities.

**p635**

**DOWN’S SYNDROME AND EPILEPSY – AN RETROSPECTIVE AUDIT**

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**Purpose:** The goal of this audit was to describe a cohort of Down’s syndrome patients attending a single epilepsy unit.

**Method:** The audit included 34 patients; information was collected retrospectively using clinical notes and letters from general practitioners.

**Results:** We identified 34 cases (16M [47.1%]; 18M [52.9%]; age range 16–64 (median 48 years; SD 13.31); 12 patients (35.3%) were alive, 13 (38.2%) had died and relevant information was unavailable for 9 (26.5%) cases. In our cohort 18 (52.9%) patients suffered from dementia, 12 (35.3%) were cognitively intact and information was unavailable in 4 (11.8%) cases. Generalized epilepsy was diagnosed in 16 (55.9%) patients, while 6 (17.6%) suffered from focal and in 9 (29.5%) cases there were not enough information available for syndromic classification. Myoclonic seizures were present in 18 (52.9%) of 34 patients. After excluding 4 cases without documented cognitive status, statistically significant association (Chi = 13.032; df = 1; p = 0.001) between myoclonic seizures and dementia was observed. There were no statistically significant differences (U [df] = 73.00; Z = -1.484; p = 0.138) in the age of the onset of epilepsy between groups of patients with (median 49.5 years; SD = 10.89) and without dementia (median 42.5 years; SD = 17.20). Significant difference were observed (U [df] = 63.50; Z = -2.781; p = 0.005) in the age of the onset of epilepsy between groups of patients with (median 35.0 years; SD = 17.39) and without myoclonic seizures (median 50.0 years; SD = 6.48). In patients without myoclonic seizures (n = 14), 12 month remission was observed in 2 patients, no remission in 6 and data were unavailable in six cases. In patients with myoclonic seizures (n = 18), no patient had a documented remission and in four cases relevant data were absent.

**Conclusion:** Our audit demonstrated an association of myoclonic seizures with dementia in patients with Down’s syndrome. The presence of the myoclonic appeared to be associated with unsatisfactory treatment outcomes.

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**ARE REPETITIVE FEBRILE SEIZURES COMORBID WITH LEARNING DISABILITIES OR BEHAVIOUR DISORDERS?**

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**Purpose:** To analyze cognitive and behaviour functioning of a series of children suffering from febrile recurrent seizures.

**Method:** Twenty five children from 4 to 7 years old suffering from recurrent febrile seizures (at least three episodes) with normal IQ and non

other neurological deficits were tested to quantify cognitive function in the domain of visual and verbal memory, attention, inhibitory control, cognitive flexibility and verbal fluency and behaviour disorders. For cognitive evaluation Illinois Test of Psycholinguistic Aptitudes (ITPA), Intelligence Test for pre-school children of David Wechsler (WPPSI), Children’s Embedded Figures Test (CEFT), STROOP Test and Repeated Target Symbols Test were used. For behaviour DSM-IV teacher evaluation criteria questionnaire and IPE (Inventory of Problems at School), Miranda 1993 were used.

**Results:** The cognitive domains that showed high prevalence of disturbances were verbal memory (37.5%), alertness (37.5%), selective attention, (45.8%) and cognitive flexibility (47.82%). The behaviour domains that showed higher prevalence were attention, (33.4%), hyperactivity, (20.8%), learning disabilities 59% and behaviour problems (29.1%). Conners criteria were fulfilled in 20.8% of children.

**Conclusion:** There may be a subgroup of children suffering from febrile seizures that could be at risk of learning disabilities and behaviour problems. Is mandatory to identify this children and give them accurate psychopedagogic support.

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**FEATURES OF SYMPTOMATIC MESIAL TEMPORAL LOBE EPILEPSY RELATED TO THE AGE OF ITS MANIFESTATION**

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**Purpose:** To reveal some features of focal temporal lobe epilepsy (TLE), depending on the age of the seizures’ onset. We observed 78 patients and divided them into 3 groups. The representatives of the 1st group (n = 43) had first seizures at the age from 12 to 35 years, 2nd (n = 18) at 35–55 years, 3rd (n = 17) at 55–73 years. The main etiological factor of patients from the 1st group is hippocampal sclerosis (79.1%), often in combination with the effects of perinatal brain damage (65.1%) and febrile seizures in anamnesis (55.3%). Patients from the 2nd group mainly have traumatic etiology of epilepsy (44.4%) and sequelae of anoxia with brain edema (22.2%). In the 3rd group vascular and traumatic etiologies were the most common.

**Materials and Methods:** In first group temporal lobe epilepsy in 69.6% of cases started with complex focal seizures and in 31.4% – with secondarily generalized tonic-clonic seizures. Characteristic and prognostically unfavorable feature is the increase in seizures’ polymorphism (3–4 kinds of attacks) in 2.7 ± 0.7 years from their onset in 67.5% of patients. In the 2nd group complex focal seizures with dialetic (38.8%) and autonomic (61.2%) symptoms dominated, usually without distinct polymorphism. In the 3rd group non-convulsive paroxysms in type of “temporal syncopation” predominated (47.1%).

**Results and Discussion:** Ordinary EEG results in all groups were uninformative. EEG video monitoring of sleeping revealed epileptiform activity in approximately the same number of observations in the 1st and 2nd groups (65.1% and 61.1%) and less frequently (52.9%) – the 3rd group. In the treatment of representatives from the 1st group most frequently (52.2%) was observed a drug-resistant course. Three patients from the group 1 had distinct therapeutic effect using an additional method of treatment (setting of the vagus nerve stimulator) and 2 patients had such effect after radical surgery – sided temporal lobectomy. In the 2nd group 44.4% of patients achieved complete remission, reduction in frequency of seizures >50% was observed in 38.9% of patients. Therapy of representatives from the 3rd group was the most successful: complete remission of seizures in 88.2%.

**Conclusions:** Thus the age, when the first seizures began, reflected on the further development of epilepsy, on the tactics and results of treatment.
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ROAD TO A CURE FOR DRAVET SYNDROME
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Purpose: When it comes to research and drug discovery, rare diseases face a number of unique challenges, including limited understanding of the disease, few interested researchers, lack of validated animal models, and an unclear business case for companies to invest in developing treatments. This is the case of Dravet syndrome, a genetic disease characterized by a drug refractory epilepsy accompanied by other central and motor disorders for which there is no effective treatment. In such a challenging medical environment, patient groups are the main drivers for innovation. The Dravet Syndrome Foundation (DSF) was created in 2011 by a group of parents determined to play an active role in identifying a cure for Dravet.

Method: The initial objective was twofold: to provide free high quality genetic testing to all suspected Dravet cases worldwide and to identify a cure in 5 years. Such an ambitious objective required a strategic roadmap and extensive collaboration following an open access collaborative model.

Results: The poster highlights the key areas under this roadmap as well as our progresses so far. Beginning by our success in providing free genetic testing to hundreds of patients worldwide, we will illustrate how our mission of removing barriers to research on Dravet syndrome has the potential to fast track the development of effective treatments and perhaps a cure in a way that would have been impossible without the involvement of patient groups.

Conclusion: We hope the strategic model that we have developed will help other patient organizations build their own roads towards a cure.

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REFRACTORY TEMPORAL LOBE EPILEPSY WITH ANTI-CASPR-2 ANTIBODIES
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Purpose: Apart from being a causal factor in autoimmune encephalitis, antineuronal antibodies occur in patients with epilepsy. In temporal lobe epilepsy (TLE), anti-GAD and anti-VGKC antibodies are occasionally observed. According to literature, anti-VGKC antibodies observed in TLE fail to show contactin-associated protein 2 (caspr2) reactivity. Here, we report three patients with anti-caspr2 antibodies and TLE.

Method: Indirect fluorescence kits with HEK293 transfected cells (Euromimmun AG) were used for antibody detection. From 243 patients tested for antibodies against membrane antigens during 2 years, four (1.6%) had anti-caspr2 antibodies — three presented with TLE.

Results: All three patients were males. First (S-K, age 66) had late-onset TLE with bilateral mediatemporal T2/FLAIR signal increase on MRI. He was seizure free on medication. Antibodies were tested because of short-term memory problems. Other two cases included refractory left-TLE (R-N, age 41, TLE onset age 20) and right-TLE (S-M, age 55, TLE onset age 26). On MRI, both had ipsilateral hippocampal sclerosis with contralateral mediatemporal T2/FLAIR signal increase. Neuropsychologically, both showed bifrontal and parietal dysfunction in addition to left temporal (R-N) and bitemporal (S-M) impairment. TLE in R-N was unsuccessfully treated with left amygdalo-hippocampal stereotactic electrocogulation. Both latter patients had additional antibodies (R-N: anti-Hu, anti-AMPA1; S-M: anti-Ma2). Oncoscreening failed to demonstrate tumours. Corticosteroid treatment was unsuccessful in R-N and S-M. Subjective improvement of memory was noted by S-K (follow-up exam is scheduled).

Conclusion: Anti-caspr2 antibodies are associated with (refractory) TLE. Clinical picture includes male sex, older age, bitemporal involvement and neuropsychological deficit.

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TWO SIBLINGS WITH AN IDENTICAL CDKL5 MUTATION: GENOTYPE AND PHENOTYPE EVALUATION
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Introduction: We present two sisters with an identical de novo CDKL5 mutation, (c. 283-3_290 deletion), but different phenotype. CDKL5 syndrome is a rare severe genetic encephalopathy, characterized by a psychomotor delay, hypotonia and seizures, starting the first months of life. Clinical presentation and advanced genetic evaluations will be discussed.

Case Report: From the age of 8 weeks, the eldest girl experienced daily infantile spasms and tonic seizures. The EEG was apparently normal, but developed into that of a severe epileptic encephalopathy. She became seizure free for half a year. Since then, daily intractable seizures have remitted and various anti-epileptic drugs, including ketogenic diet, have been used. From birth, she was hypotonic and experienced a severe developmental delay. In between the two girls, a healthy brother was born. During the third pregnancy, both parents (neither being a carrier of the CDKL5 mutation) refused genetic prenatal testing. Umbilical cord blood evaluation confirmed the same CDKL5 mutation in their second daughter. At the age of 6 weeks, she had a normal neurological examination and EEG, despite one non convulsive epileptic discharge. Anti-epileptic drug treatment was not started. As expected, at 10 weeks of age, tonic clonic seizures appeared, followed by daily infantile spasms and tonic seizures. They have been drug resistant, despite anti-epileptic drugs. Corresponding with this, her previously normal EEG developed into an Ohtahara pattern, and with increasing age into hypsarrhythmia. The clinical and EEG presentation of the second girl is more severe and a regression was present.

Conclusion: Despite the fact that both girls have the same CDKL5 mutation, they show phenotype differences. Germline mosaicism, in which case the recurrence risk may theoretically increase to 100% for girls, is suspected and evaluated. These sisters are the first siblings reported with an identical CDKL5 mutation. Prenatal testing is strongly recommended in such cases.

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LENNON–GAUSTAUT SYNDROME IN ADULT PATIENTS
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Purpose: To study the long-term clinical and electroencephalographic outcome of Lennox – Gastaut syndrome (LGS) from the childhood till adulthood.

Abstracts
Method: We used the definition of the LGS by the International League against Epilepsy. The evolution of different seizure types and electroencephalographic (EEG) findings, as well as cognitive and behavioral outcome is assessed.

Results: The sample consisted of 26 patients (9 female, 17 male) followed-up during average period of 19.8 years. Age at diagnosis was 3.6 (2–6) years; age at the end of follow-up was 34.4 years (18–42). We made 1–10 (EEG) examinations per year, an average of 24.6 per patient. At baseline all patients (n = 26) were in fully developed stage of illness. At the end of follow-up 5 patients (19.2%) were still in fully developed stage of syndrome with frequent tonic, atomic, myoclonic seizures, rare atypical absences with or without generalized tonic-clonic seizures. Bilateral slow spike wave complexes during wakefulness and generalized paroxysms of spikes during sleep were registered. In 17 patients (65.4%) frequency of seizures was reduced, and predominant tonic and focal seizures. In this group slow spike wave complexes was registered in 5, focal spike wave complexes and multiple independent spike complexes in 6, short-term rapid paroxysms during sleep without clinical correlates in seven patients. Complete remission of attacks (≥ 3 years) is achieved in 4 (15.4%) patients with slow basic EEG activity of low amplitude and short-term and irregular discharges during wakefulness and sleep. A moderate to severe cognitive impairment and behavioral disorders: hyperactivity, aggressiveness and autistic tendencies were observed in all patients, and psychosclerosis developed in three of them.

Conclusion: Large epileptiform EEG changes are concomitant with high frequency and severity of seizures, while the poor and slow EEG activity with rare or absent epileptiform changes were associated with severe sequelae of LGS.

p642 INVESTIGATION OF INTERICTAL CARDIAC RHYTHM ABNORMALITIES, HEART RATE VARIABILITY AND RELATED FACTORS IN UNTREATED PATIENTS WITH IDIOPATHIC GENERALIZED EPILEPSY

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Epilepsy is a disease known to occur with autonomous phenomena. Earlier studies indicate decreased cardiac rhythm abnormality and heart rate variability during ictal and interictal periods among epilepsy.

Purpose: To compare cardiac rhythm abnormalities and heart rate variability (HRV) during interictal period between idiopathic generalized epilepsy (IGE) patients and healthy control group. Members of patient group had no antiepileptic drug use before or did not use antiepileptic drugs for at least six months.

Method: Fifteen IGE patients, and 26 healthy individuals included in the study. To eliminate heart disease, Transhitoracic Echocardiography (TTE) and 24-hour rhythm Holter monitoring was performed on the patients and the control group.

Results: The results have revealed normal cardiac rhythms and heart rate range within both patient and control groups. 25% supraventricular premature beat, 33.3% ventricular premature beat rate was observed among patient group, while no rhythm abnormalities were viewed. In the analysis of time-dependent parameters of HRV, SDNN, SDANN, SDNN index values and frequency-dependent parameters total power, LF and VLF values, no difference was detected between the patient group and control group. No indicative results were found between HRV’s association with epilepsy duration and seizure frequency.

Conclusion: Earlier studies indicate decreased cardiac rhythm abnormality and HRV during ictal and interictal periods among epilepsy patients. The decrease in frequency dependent parameters regarding HRV analysis, might be associated with the decrease in parasympathetic tone, which also might be the indicator of SUDEP’s (sudden unexpected death in epilepsy) underlying mechanism. However, in our study, HRV parameters of untreated patients with idiopathic generalized epilepsy were not significantly different from the control group. In the next phase of our study, after 12 months from the initiation of drug therapy, HRV of patient group will be compared with control group and the effects of antiepileptic drugs on HRV will be investigated.

p643 LAFOARA DISEASE SIMILAR TO JUVENILE MYOCLOニック EPILEPSY

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Purpose: Lafora disease (LF) is a type of progressive myoclonic epilepsy with poor prognosis, but different from the Juvenile myoclonic epilepsy (JME). We presented here a LF case similar to JME.

Case Report: A 17-years-old girl was admitted to our clinic because of myoclonic jerks since 3 years and recently emerged generalized tonic clonic seizures. She was taking Na-valproate, 1,000 mg/day. Before admittance to our clinic, zonisamid and carbamezapine were added to her therapy by another medical center, because of the increased myoclonic jerks. These medicines were discontinued in our clinic because of their side effects, instead, levetiracetam was started. However, this was switched to lamotrigine, again to avoid the side effects of levetiracetam. In doing this, the frequency of her jerks decreased and generalized tonic clonic seizures disappeared. Consequently, she was diagnosed as JME. In spite of controlling her jerks and seizures with Na-valproate of 2 × 500 mg and lamotrigine of 2 × 100 mg, she complained poor concentration, forgetfulness and difficulty in understanding of spoken words. Because her EEG had increasingly slow background activity we investigated her for progressive myoclonic syndrome. Her parents were first degree relative; her cousin and uncle had epilepsy. Her laboratory findings and brain MRI were normal. In skin biopsy we found PAS-positive Lafora bodies. Her follow up nearly 4 years yielded good control of jerks, except slowly progressive cognitive impairment.

Conclusions:
1 LF disease may be similar to JME at the beginning, fallow up EEG and cognitive status being helpful for the diagnosis of progressive myoclonic epilepsies;
2 Lamotrigine may be an alternative therapeutic agent in cases of LF disease with jerks as an adjunctive therapy.

p644 EYELID MYOCLONIA WITH ABSENCES: A RETROSPECTIVE FOLLOW-UP STUDY OF CLINICAL AND ELECTROPHYSIOLOGICAL CHARACTERISTICS

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Purpose: Eyelid myoclonia with absences (EMA) is a distinct syndrome of Idiopathic Generalized Epilepsies (IGE) characterized by...
eojlidan myoclonia, with or without absence, eye closure induced seizures, EEG paroxysms or both and photosensitivity. This is a longitudinal study of video EEG and clinical follow up characteristics of patients with EMA.

**Method:** We studied the clinical and EEG features of 16 consecutive patients with EMA; all sequential video EEG were reviewed and analyzed.

**Results:** Eleven females and 5 males, with mean onset at 7 years, were followed up from 1 to 19 years (average 7 years). Three (18.75%) had family history of IGE, all had at least one generalized tonic clonic seizure (GTCS), 7 (43.75%) had absence status and half admitted to, or had EEG evidence of, self induction at some stage. Fourteen patients had pyknoleptica EMA at onset. Fifteen patients had generalized discharges, mainly driven from the posterior regions (75%) on eye closure, while 9 had also posterior focal spikes. Sleep, awakening and hyperventilation activated focal and generalized discharges in most. All were treated with valproic acid (VPA) at some stage; 12 are still on, of whom 5 also on clonazepam. Levetiracetam (LEV) or lamotrigine; 3 patients are on LEV and one off antiepileptic medication. Four patients (25%) are seizure-free; all on treatment. The rest have improved with occasional situation-related GTCS and infrequent episodes of EMA. Six patients are not photosensitive.

**Conclusion:** EMA is one of the most pharmaco-resistant syndromes of IGE with well-recognizable generalized, but also focal, electrophysiological characteristics that reveal a special role of the occipital lobes.

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**AETIOLOGY OF EPILEPSY IN IRELAND (SERIES OF PATIENTS IN A TERTIARY CENTRE)**

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**Introduction:** The aetiology of epilepsy is an important decisive factor in the treatment and prognosis of patients with epilepsy. Epilepsy is a heterogeneous disorder, the symptoms of which are preventable and controllable to some extent. Significant inter- and intra-country differences in incidence and prevalence exist because multiple etiological factors are implicated.

**Purpose:** To describe the distribution of syndromes, aetiology of epilepsy in our cohort of patients.

**Method:** We conducted a cross-sectional descriptive study of patients with epilepsy who were treated in our epilepsy department. The Epilepsy Patient Record (a national electronic system specially designed for epilepsy patient) was interrogated and data were collected regarding syndrome and aetiology.

**Results:** We had a total of 1,827 patients with an underlying known or suspected aetiology for epilepsy: 423 patients had post traumatic brain injury, 23%. 299 patients there was a genetic implication for their epilepsy, 16%. 252 patients there was a positive history of perinatal injury 13.7%. 229 patients had mesial temporal sclerosis 12.5%. 181 patients had brain tumour 9.7%. 82 patients had a vascular malformation 4.4%. 68 patients had a stroke 3.7%. 57 had Cortical Developmental Malformation 3.1%. 50 patients had encephalitis 2.7%. 43 patients had hydrocephalus 2.3%. 24 patients had Chromosomal Abnormality 1.3%. 19 patients had Neurocutaneous Syndrome 1.01%. 3 patients had Neurodegenerative Disease 0.16%.

**Conclusion:** In our cohort of 2,206 patients 1,410, (63.9%) had a diagnosis of localisation related epilepsy. 521 patients were diagnosed with generalised epilepsy (23.6%), 112 with non epileptic seizure (5%) and no specific diagnosis was given in 142 patients (6.4%).

**References**


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**CLINICAL FEATURES AND EVOLUTION OF EPILEPSY IN HEMICONVULSION-HEMIPLEGIA-EPILEPSY (HHE) SYNDROME**

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**Purpose:** Hemiconvulsion-Hemiplegia-Epilepsy (HHE) syndrome is an uncommon epileptic disorder characterized by the occurrence of prolonged hemiclonic seizures followed by development of hemiplegia, typically in the course of a febrile illness before the age of 4 years. Following a variable interval, subsequent epilepsy develops. We describe the clinical features and evolution of epilepsy in a population of patients with HHE syndrome.

**Method:** 15 patients (F:M = 5:10; mean age 45 years; age range: 29–66 years) with HHE followed at our centre were investigated. Over the years all of them underwent repeated clinical examinations, EEG, MR scanning. Mean follow-up at our center was 15.8 years (range 2–50 years).

**Results:** Etiology was: prolonged febrile convulsions (7 patients), status epilepticus (2 patients), head trauma (3 patients); unknown (3 patients). Mean age of onset of epilepsy was 3.8 years (range: 9 months to 11 years). Hemiparesis was on the right side in 10 patients, left side in 5 patients. In all patients MR scanning showed hemispheric atrophy of variable degree contralateral to the hemiparetic side. All patients suffered from simple (mainly motor) (SPS) or complex partial seizures (CPS), with possible secondary generalization (SGTC). At the time of our observation seizure frequency was 2–3 CPS per year (1 patient), 1SPS/CPS per month (3 patients), 2–5 SPS/CPS per month (4 patients); weekly or daily seizures (2 patients); unknown (1 patient). Seizure disappearance was observed in 4 patients (age range: 29–66 anni), whose epilepsy duration ranged from 10 to 54 years (median: 24 years). All patients were treated with 1–4 AEDs.

**Conclusion:** In our patients with HHE syndrome, epilepsy was mild (≤1 seizure/month) in 4 (26%) patients or disappeared in other 4 (26%), suggesting that the long-term evolution of the epileptic disorder in HHE can have a favourable course.

**References**

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**Purpose:** Reflex seizures are reliable triggered by some identifiable factors like music, eating, reading, thinking, light, hot water, startle, somatosensory or proprioceptive stimuli. “Hot water epilepsy” which is induced by contact with hot water is the most known reflex seizures trigger by
heat. There is no enough knowledge about triggering by cold stimulus for epilepsy.

**Method:** 26 years old male patient was admitted with epilepsy after inducing feeling cold during cold weather. His routine laboratory tests and cranial MR were completely normal. He has different types EEG chances, focal or generalized.

**Results:** The seizures were avoided to a large extent by avoiding cold weather. He had a good response to the neurological treatment (lamotrigine 200 mg/day and carbamazepine 1,200 mg/day).

**Conclusion:** The induction of epileptic seizures by cold weather hasn’t been reported before. Its physiopathology is unknown but similar with hot water epilepsy genetic factors that determine an alteration in cranial thermoregulation may be involved and this needs further investigations.

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**p648 PSYCHIATRIC DISTURBANCE IN CHILDREN WITH EPILEPSY**

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This presentation is based on the December 2013 report of the ILAE Child Neuropsychiatry Taskforce. Epidemiological studies indicate that psychiatric disturbance is present in about 30–50% of children with epilepsy. ADHD occurs in around 30% of children with epilepsy. Standard ADHD medication is effective in around 70% of children with both epilepsy and ADHD; it does not appear to be associated with any increase in seizures. A high proportion of children with epilepsy also have autism spectrum disorder, around 20%. A recent survey found anxiety in about 17% and depression in about 8% of children with current epilepsy. Psychosis in children with epilepsy is very rare but it is much more common in teenagers. It can be postictal, interictal or drug induced. Epilepsy syndromes associated with behavioural/psychiatric disturbance include West syndrome, Dravet syndrome, Lennox-Gastaut syndrome and juvenile myoclonic epilepsy. Subtle behavioural manifestations of epilepsy can result from frequent absence seizures, frequent localised epileptiform discharges, transitory cognitive impairment, transient epileptic amnesia and electrical status epilepticus of slow wave sleep. Recognition and prompt treatment is of major importance. Behavioural adverse effects can be associated with phenobarbital, valproate, gabapentin, topiramate, levetiracetam and zonisamide. Epilepsy surgery can result in psychiatric improvement or deterioration in individual children but there is little overall group effect. Treatment with psychotropic medication, including methylphenidate, dexamfetamine, atomoxetine, clonidine, selective serotonin reuptake inhibitors or low-dose risperidone can be beneficial and is unlikely to precipitate seizures. The key to the successful management of psychiatric disturbance in children with epilepsy is meticulous assessment to determine the cause, allowing rational management to be implemented.

**p649 PRIMARY SYSTEMIC CARNITINE DEFICIENCY CAUSING INFANTILE ONSET SEIZURES**

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**Purpose:** To describe the case of an 11 month old girl, one of 5 children to consanguineous parents, who presented with Infantile onset seizures with hemi-convulsion and a background of familial low carnitine and acyl carnitine in parents and siblings.

**Method:** We describe a girl born at full term via Caesarean section and breast fed for two months with no concerns. Three days after her first immunisations (65 days old) she awoke from sleep screaming and collapsed with asystole. She was revived but developed generalized tonic clonic seizures requiring Phenyoitin, Phenobarbitone and Midazolam infusion until finally controlled. Her Carnitine levels were low so she was started on oral Carnitine. An echocardiogram suggested possible cardiomypathy and septal hypertrophy. When tried to wean her anti-convulsants she developed eyelid flickering and eye rolling episodes with right hemiconvulsive movements of her arm with or without involving of the right leg, whereas the left arm was kept flexed. She continued to have clonic seizures involving the upper more than the lower limbs and accompanied with generalised 2.5 -3 hertz spike and wave activity lasting up to 9 seconds. She is currently on Carnitine, Clobazam and Ethusuximide.

**Results:** A brain MRI showed paucity of the white matter with a degree of delay in myelination, but otherwise unremarkable. Toxic or metabolic disorder was suggested. Resting EEG was not suggestive of any particular underlying syndromic diagnosis. However there were interictal epileptiform discharges most evident in light sleep and suggestive of symptomatic generalised seizures. Routine muscle histopathology showed patchy increase in lipid more prominent in slow fibres, supporting a diagnosis of carnitine transporter deficiency. Further metabolic and neurologic tests were inconclusive. EMG was normal. Complete genetics were awaited. She also has global developmental delay and hypotonia.

**Conclusion:** Working diagnosis primary systemic carnitine deficiency and symptomatic generalised seizures.

**p650 ABSENCE SEIZURES IN A PATIENT WITH CELIAC DISEASE (CD)**

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**Purpose:** To describe a 17 year old female with well controlled CD on a gluten free diet since the age of 13 that presented with an episode of loss of consciousness (LOC). Seizures are very rare in patients with CD. The majority are focal with or without secondary generalization. Neurological complications are reported to be at about 8%. Epilepsy accounts 1.6% while headache or peripheral neuropathy at about 55%.

**Methods:** A 17 year old female presented after an episode of LOC. She was confused for about 10 minutes and finally had a brief fall with no clear signs of tonic-clonic movements. After that she was still confused and this resolved after half an hour. She could not recall the event afterwards. Her parents reported brief inattention episodes since the diagnosis of CD.

**Results:** Her clinical examination, blood samples and CT scan were all normal. We performed a routine and a sleep deprived EEG which did not reveal any abnormal activity. Brain MRI findings were unremarkable.
We planned a prolonged video EEG which showed 3 Hz spike and slow wave activity. She also had multiple episodes of behavioral arrest and staring when this activity lasted more than 3–4 s. A diagnosis of typical absence was made. She wa started on Levetiracetam with improvement.

**Conclusion:** This is a rare case of epilepsy in a patient with celiac disease. Review published studies underline that epilepsy is very rare and mostly of symptomatic or cryptogenic origin. There is one published case with typical absence. However, epilepsy was diagnosed since the age of three and CD at the age of 25. Our patient had a clear 3 Hz spike wave activity and also typical events during video EEG. Patient’s presenting event probably was an absence status epilepticus.

### p651
**IDENTIFICATION OF OSTEOPOROSIS AMONGST PEOPLE WITH INTELLECTUAL DISABILITIES (ID) BEING TREATED WITH ANTIEPILEPTIC DRUGS (AEDS)**

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**Purpose:** People with ID being treated for epilepsy with AEDs should be assessed for osteoporosis. We examined if there is a validated screening tool for this population and if the common clinical risk factors associated with osteoporosis are considered?

**Method:** Two main screening tools, FRAX and Q Fracture are used in primary care in the UK to assess risk of osteoporosis. Concurrent ID, epilepsy and AED treatment give a high clinical index of suspicion of osteoporosis risk. We used these tools to risk score 20 outpatients with ID, epilepsy and AED treatment where there was a clinical suspicion of osteoporosis risk. A DEXA scan for each patient is being requested to check if either screening tool has been sensitive enough to identify those individuals the DEXA scan demonstrates to be at risk.

**Results:** Of the 20 patients screened 18 scored within the “low risk band” on both screening tools. Of the two people identified as higher risk: one was 75 years old, the other had a previous fracture both heavily weighted factors in existing tools. However amongst 18 “lower risk” scoring individuals one person had a DEXA scan indicating osteoporosis and six had factors potentially increasing their risk of osteoporosis not included or appropriately weighted in current tools (two had BMI less than 18.5 and four were non-weight bearing). We plan to complete DEXA scans for all 17 and present the findings.

**Conclusion:** Osteoporosis is an important and treatable co-morbidity in those with ID taking AEDs. There is a lack of a suitable tool to screen this population. Key pervasive clinical factors such as non-weight bearing, poor mobility, poor nutrition and syndrome diagnosis have not been considered. This is an important under-evaluated area as it carries a risk of mortality, morbidity and huge financial implications in treatment.

### p653
**NITRAZEPAM AS FIRST LINE TREATMENT IN WEST SYNDROME**

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**Purpose:** To report our experience of using Nitrazepam as first line treatment in West Syndrome. A previous report from our centre highlighted the beneficial role of Nitrazepam as the first line treatment for infants with West Syndrome.

**Method:** Data was collected on all infants diagnosed to have West syndrome from our clinical and neurophysiological database from 2009 to 2013. The data included clinical presentation, EEG findings, treatment, response to treatment and aetiological diagnosis.

**Results:** Seventeen infants were diagnosed over 4 years (7 boys). Median age at diagnosis was 6 months. The onset of spasms before the diagnosis ranged from 1 day to 4 months. Seven were Idiopathic and 8 Symptomatic. Sixteen infants were treated with Nitrazepam as first choice and 6 (37.5%) of them had complete resolution of spasms and normalisation of EEG without any other treatment. Infants who had an incomplete response to Nitrazepam were given ACTH with good response. Two were refractory to medical therapy. In the Idiopathic group (570%) out of 7 responded to Nitrazepam alone and 2 required ACTH treatment. The symptomatic group included 2 infants with Down’s syndrome who made full recovery on Nitrazepam alone. Nitrazepam was tolerated well without any significant side effects. The median dose of Nitrazepam was 0.6 mg/kg/day and the median clinical response time was 9 days (1–17 days). Pooled with earlier data, over 14 years our centre has treated 16 out of 61 (26%) infants with Nitrazepam alone (52% Idiopathic and 12% Symptomatic). The adverse events were significantly low in those treated with Nitrazepam alone.

**Conclusion:** Nitrazepam is an effective and safe first line treatment in Idiopathic West Syndrome. Infants with Down’s syndrome responded well to Nitrazepam. A trial of Nitrazepam should be considered as the first line in all cases while awaiting results of investigations.
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EPILEPTIC ENCEPHALOPATHIES: COMORBIDITY OR A CAUSE OF AUTISTIC SPECTRUM DISORDERS IN EARLY CHILDHOOD
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Purpose: The reasons of autistic spectrum disorders (ASD) prevalence increasing and pathophysiological causes that lie in background of these conditions remain a subject of debates. The purpose of this study was to explore connection between epileptic encephalopathies (EE) and ASD.

Method: 20 early age children (middle age of 2.2 ± 1.2 years) with ASD became object of research. Complex examination includes the analysis of clinical-neurophysiological data, results of video-EEG monitoring, brain MRI, measurement of blood plasma levels of gamma-aminobutyric acid (GABA) was conducted.

Results: Signs of epileptiform activity in the routine EEG were registered in 17 children (85%). Among them 9 had focal epileptiform discharges, 5 – high amplitude bilaterally synchronous slow waves. In 3 cases ESES were diagnosed. Clinical seizures were observed in 12 from 20 patients (60%) and 40% of children were seizure free. 9 from 12 patients with seizures had a history of cognitive an language skills regression that appeared after the seizure debut. Brain MRI identified structural abnormalities in 60% of patients, among them atrophic changes in hemispheres or temporal lobe, arachnoidal cysts, corpus callosum hypoplasia.

There were determined the concentration of GABA in blood plasma of 9 children with ASD and seizures (main group) with subsequent comparison to the control group (12 healthy children). It was determined that the GABA concentration in main group lower than the GABA concentration in the blood plasma of the control group of children (16.85 ± 1.19 and 24.65 ± 0.85 mg/ml accordingly).

Conclusion: Traditionally epileptic seizures are considered to be comorbid condition to ASD. But our observations indicate that epileptic encephalopathies could lead to ASD development by themselves in many cases. They appear often on background of structural brain (according to brain MRI findings) and metabolic abnormalities (low GABA blood level) and characterized clinically by drug-resistant epileptic seizures or persistent epileptiform activity.

Method: Twenty-three patients with ESES followed at the Danish Epilepsy Center between 2002 and 2013 were enrolled. Inclusion criteria were:
1) normal neurodevelopmental baseline,
2) no perinatal injuries,
3) normal brain MRI,
4) appearance of cognitive/behavioural deterioration ± epileptic seizures;
5) spike wave index (SWI) during sleep ≥50%.
All patients underwent at least 1 (mean: 6.2; range: 1–12) 24-h video-EEG recording. All patients received at least 1 (mean: 3; range: 1–10) neuropsychological examination. Follow-up range: 11 months to 11 years 3 months.

Results: Thirteen subjects were male, 10 were female. Family history was positive for epilepsy in 8 subjects. Mean age at ESES diagnosis was 6 years (range: 2 years 11 months to 10 years 2 months). Range of ESES duration was 5 months to 6 years 11 months. Most common clinical symptoms at the time of ESES diagnosis were seizures, behavioural changes, concentration/attention problems ± hyperactivity, loss of school/school skills, language difficulties, memory problems. Age range of epilepsy onset was 2–8 years. Ten patients had atypical BECTS, 5 had Landau Kleffner syndrome. Three subjects never suffered from seizures. Maximum SWI during all-night NREM sleep ranged from 50% to 98%.

Epileptic abnormalities in sleep during ESES were focal in 6 children, multifocal in 7, hemispheric in 7, diffuse in 3. At last follow-up 6 patients still presented ESES, whereas ESES remission was observed in 17 cases: cognitive functions and behaviour recovered in 14 patients, whereas 3 did not show any improvement. Of these 17 patients, 10 received corticosteroid therapy.

Conclusion: Our findings show that ESES in idiopathic cases, despite the heterogeneity of clinical and EEG features, can bear a favourable outcome in most of the cases.

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ENCEPHALOPATHY RELATED TO STATUS EPILEPTICUS DURING SLOW SLEEP (ESES): ELECTROCLINICAL FEATURES AND EVOLUTION IN A COHORT OF IDIOPATHIC CASES
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Purpose: To investigate the electroclinical features and the evolution of Encephalopathy related to Status Epilepticus during slow Sleep (ESES) in a cohort of idiopathic cases.

Method: The anatomical sources of epileptic magnetoencephalography (MEG) spikes were retrospectively analysed of 60 patients with ESES and epileptic encephalopathy, or who were suspected to develop encephalopathy. MEG was collected during a nap or light thioental anaesthetia. Networks of epileptic spikes were modelled with equivalent current dipoles, and the dipole locations were displayed on the subjects’ magnetic resonance (MR) images.

Results: Three main generator areas were found:
1) perisylvian,
2) sensori-motor, and
3) fronto-parietal.
Half of the patients had bilateral perisylvian spike sources associated with the Landau-Kleffner syndrome or with dysarthria and verbal dyspraxia. Four of these patients had unilateral or bilateral perisylvian polymicrogyria, while 26 patients had no specific etiology. Fifteen (25%) patients had multiple focal spikes along the sensori-motor strip. These patients had typically been referred for delayed speech, problematic behaviour, clumsiness, or changed hand dominance. Typical Rolandic seizures developed during follow-up. Nine patients had either focal frontal (2) or parietal (7) focus with secondary spread to bilateral fronto-parietal networks. These patients had anatomical lesions like perisylvian cysts,
perinatal hemispheric infarction, thalamic lesions, hypoxia-ischemic encephalopathy etc. Finally, six patients with the most severe developmental delays, had combinations of two or three of the main epileptic generator areas.

**Conclusion:** MEG provides a relatively easy method to identify ESES patients with serious developmental threat (e.g. Landau Kleffner syndrome) as well as those, whose ESES appears to be an intensive form of benign rolandic epilepsy.

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**Antiepileptic Treatment in Dravet Syndrome: An Additional Complexity for the Families**

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**Purpose:** The aim of this study is to explore the complexity of antiepileptics (AEDs) polytherapy in patients with Dravet syndrome (DS) with a special interest in “management” of the families concerning preparation and administration.

**Method:** We proposed auto-administered semi-close on-line questionnaire to families of patients with DS in December 2013 on the website of DS alliance, France. Questions addressed different aspects of patients’ medication: medicines preparations (time and modalities), daily doses, knowledge of side effects. Parents were also questioned about the risk of errors, the difficulty of preparation and administration by them or other care givers, and how they manage drugs administrations in special situations.

**Results:** 90 families answered the questionnaire. Patients were aged from 0.84 years to 17.60 years (mean 8.06). 86% of children had at least 3 AEDs: clobazam (92%), valproate (89%), stiripentol (80%) and topiramate (47%). KD was used in 21% but 4% had the diet at the time of the questionnaire. 38% had other medicines mainly for sleep (50%) and behavioral (35%) disorders. Mothers (96%), fathers (58%) and grandparents (51%) prepared the drugs and administered it respectively in 96%, 61% and 57% of patients. 8%, estimated major AEDs manipulations (crushing, diluting, dividing, ...) and 31% estimated a major risk of error. 75% agreed on the facility of preparation and administration but they were unhappy with the texture and flavor of medicines. 13% of parents didn’t know the side effect of administered medicines. 66% of parents call their specialist for side effects and their GP for drug interactions.

**Conclusion:** This study raises the difficulties in families with children with DS having polytherapy. Parents estimated a high risk of error and problems with texture and flavors. These results emphasize the need for further development of children friendly formula and for families education in chronic diseases.

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**Incidence of Neonatal Seizures: A Prospective Study**

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**Materials and Methods:** Prospective study, collecting all infants born alive at HPMI, between January 1, and December 31, 2010. Inclusion criteria: non-epileptic events in the neonatal period. The aim of our study is to analyze the incidence, clinical characteristics and etiology of neonatal seizures (NS) at Hospital Publico Materno Infantil de Salta (HPMI).

**Results:** The overall incidence of NS was 4.57 per 1,000 live births in the HPMI (378/8,092), 3.84 per 1,000 live births for term neonates (26/6,766), 8.29 per 1,000 live births for premature infants (11/1,326). The incidence was higher among infants weighing less than 1,200 g (49/690, 1,000 live births). The most frequent etiology was intrapartum hypoxic-ischemic encephalopathy (HIE) 27.20% followed by neonatal encephalopathy (NE) 21.80%. Focal clonias were the most frequent type of seizures. The incidence of NS was highest during the first two days of life. Seizures are the most frequent clinical manifestation of neurological disorder in the neonatal period. The aim of our study is to analyze the incidence, clinical characteristics and etiology of neonatal seizures (NS) at Hospital Publico Materno Infantil de Salta (HPMI).

**Discussion:** Clinical seizures occurring within the first 28 days of life for full term infants and 40 completed weeks for preterm infants. Exclusion criteria: non-epileptic events in the neonatal period.

**Results:** The overall incidence of NS was 4.57 per 1,000 live births in the HPMI (378/8,092), 3.84 per 1,000 live births for term neonates (26/6,766), 8.29 per 1,000 live births for premature infants (11/1,326). The incidence was higher among infants weighing less than 1,200 g (49/690, 1,000 live births). The most frequent etiology was intrapartum hypoxic-ischemic encephalopathy (HIE) 27.20% followed by neonatal encephalopathy (NE) 21.80%. Focal clonias were the most frequent type of seizures. The incidence of NS was highest during the first two days of life. The neonatal death rate among infants with NS was 24.32%. It was higher in preterm infants.

**Conclusions:** The incidence of NS is high in infants born alive at HPMI and it is more frequent in premature neonates. EHI and NE were the most...
frequent causes of NS and focal clonias were the most frequent type of seizures. The mortality rate in neonatal infants is high and it is higher among babies with very-low birth weight.

Results: The mean age to admit initially is 8 ± 9 days (from 1 days to 21 days). The male is 5 and female is 5. The myoclonic seizures is 5, tonic seizure is 3, apnea is 1 and subtle seizure is 1. The etiology of neonatal seizure is that hypocalcemia is 5, intracranial hemorrage is 1 and hypoxic ischemic encephalopathy is 1. The Brain sono, antiepileptic drug, doses of drug. We studied 10 neonate treated neonatal seizure who visited our hospital since January 2011 to December 2013.

Conclusion: We studied treatment of neonatal seizure: A systemic review. Phenobarbital is effective and tolerable in neonatal seizure in Chungbuk Korea. The further study is necessary about other antiepileptic drug.

Method: We retrospectively studied the type of epilepsy, etiology, EEG, brain sono, antiepileptic drug, doses of drug. We studied 10 neonate treated neonatal seizure who visited our hospital since January 2011 to December 2013.

Results: The mean age to admit initially is 8 ± 9 days (from 1 days to 21 days). The male is 5 and female is 5. The myoclonic seizures is 5, tonic seizure is 3, apnea is 1 and subtle seizure is 1. The etiology of neonatal seizure is that hypocalcemia is 5, intracranial hemorrhage is 1 and hypoxic ischemic encephalopathy is 1. The Brain sono is that germinal matrix hemorrhage with IVH is 1 and diffuse echogenicity periventricular white matter of lateral ventricle is 1. Abnormal EEG is 70%. The treatment is that phenobarbital is 7. The mean maintenance dose is 5 ± 4 mg/kg/day The mean duration of therapy is 1 ± 2 months, and the duration of therapy ranged from 1 to 3 months. 90.0% of patients became seizure free.

Conclusion: We studied treatment of neonatal seizure: A systemic review. Phenobarbital is effective and tolerable in neonatal seizure in Chungbuk Korea. The further study is necessary about other antiepileptic drug.

Results: All affected members in this family carried a novel KCNQ2 mutation c.63-66delGGTG(p.K21fsX40), causing a framework shift and early chain termination.

Conclusion: This family supports the recent observation that KCNQ2 mutation should not be considered always as benign and genetic counseling in these families cannot guarantee a definite benign course. In summary, our family shows phenotypic variability in the same KCNQ2 mutation and this has implications for diagnosis, prognosis and genetic counseling. It is suggested that other modifier genes and environmental factors are involved in this heterogeneity.

Method: We report a novel mutation in a KCNQ2 exon, cause de novo mutations in KCNQ2 have been found in 10% of neonatal Epileptic Encephalopathies (EE). We describe anti-epileptic drug (AED) treatment during the acute neonatal on-set phase and ongoing intractable seizures in patients with KCNQ2 encephalopathy.

Results: Seizure on-set was between 1 and 5 days of age (median 2 days) with status epilepticus (SE) and EEG pattern of burst suppression in 3 patients and multifocal epileptiform abnormalities in 4. Seizures consisted of asymmetric tonic posturing often followed by focal clonic jerking and were accompanied by apnea. All patients failed to respond to several AEDs. Administration of IV Phenytoin (PHT) during SE in the neonatal period produced complete and persistent seizure control with the disappearance of the burst suppression pattern in 2/7 patients. Both patients were then changed to Carbamazepine (CBZ) for ongoing treatment. Four patients had recurrent and intractable seizures up to age 3, 7, 12 and 13 months when oral CBZ was added and all achieved seizure freedom. The remaining patient was seizure-free on PHT from 14 months to 3.5 years when PHT reduction caused SE complicated by hepatic and renal failure and pancreatitis. Patients remained seizure-free during a mean follow-up of 32 months. All patients had severe developmental delay with axial hypotonia.

Conclusions: In our 7 patients with KCNQ2 encephalopathy, administration of IV PHT during SE or oral CBZ was rapidly and persistently effective. CBZ and PHT are sodium channel blockers and their effects on ion channel homeostasis may impact on the role of neuronal potassium channels. Their beneficial effect in KCNQ2 encephalopathy may inform the pathophysiological understanding of this disorder.
p664 BUMETANIDE AND HEARING LOSS: RESULTS OF A PHASE I/II DOSE FINDING AND FEASIBILITY TRIAL OF BUMETANIDE FOR SECOND LINE TREATMENT OF NEONATAL SEIZURES (NEMO)

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Purpose: Bumetanide is a widely used loop diuretic in neonatal population and is considered to have a favourable safety profile. Preclinical data have suggested it may be an effective treatment for neonatal seizures. We aimed to assess the safety and optimal dose of bumetanide.

Method: Using bivariate Bayesian design we performed an open label study to evaluate the dose-efficacy and dose-toxicity relationship of bumetanide. Full term babies with hypoxic ischaemic encephalopathy and seizures not responding to phenobarbital were allocated via bivariate continual reassessment method to one of 4 dose levels (0.5–0.3 mg/kg). Adverse events and seizure burden were assessed continuously. Pharmacokinetic data were evaluated by population approach.

Results: Fourteen out of 30 screened babies were included. Nine neonates completed treatment, 3 were withdrawn for clinical reasons and 1 due to an adverse reaction (moderate dehydration). All but 1 baby also received aminglycsoides. No short term, dose-limiting toxicity was observed but 3/14 babies were found to have hearing loss on later auditory testing (delayed toxicity). EEG analysis showed that 5/14 babies had reduction in seizure burden after the initial dose (efficacy as per protocol). Including delayed toxicities, the posterior estimated dose-response relationships indicate that all doses are estimated to be toxic. Subsequent data analysis showed that seizure control was sustained in only 2/14 babies. There was no significant relationship between bumetanide exposure, HIE grade and aminoglycoside co-medication and hearing loss. The trial was terminated prematurely.

Conclusion: Although bumetanide demonstrated good short-term tolerability, we found a much higher incidence of hearing loss compared to the literature or our own historical data. This may be explained by accumulation of risk factors (hypoxia, aminoglycoside, loop diuretic) in an increased susceptibility to drug-induced hearing loss in the immature brain. Due to adverse benefit-risk ratio, further efficacy trials using bumetanide at this dose regimen cannot be recommended.

p665 ROLES OF LIMBIC-HYPOTHALAMIC-PITUITARY-ADRENAL (LHPA) AXIS ACTIVITY AND GAMMA-AMINOBUTYRIC ACID TYPE A RECEPTOR (GABAAR)-MEDIATED EXCITATION IN PROPOFOL-INDUCED ELECTROENCEPHALOGRAPHIC SEIZURES IN NEONATAL RATS

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Purpose: Human and animal studies suggest that neonatal anesthesia may have long-term consequences for brain development. Neither the full scope of developmental abnormalities nor their underlying mechanisms are well understood. We have previously shown that sevoflurane, a general anesthetic agent that enhances GABAAR activity, administered to neonatal rats, causes an increase in seizure levels of corticoids, electroencephalographic seizures, and abnormal behavior later in life. To test the hypothesis that altered LHPA activity and GABAAR-mediated excitation are involved in mediation of neonatal-anesthesia caused electroencephalographic seizures, the effects of propofol and etomidate – aesthetics with similar GABAAR-mediated mechanisms of action but differential effects on adrenal synthesis of corticoids, were studied in postnatal days (P) 4–6 and P17–P22 Sprague Dawley rats.

Method: Anesthesia was induced with 40 or 8 mg/kg and maintained with 20 or 4 mg/kg/60 minutes of propofol or etomidate intraperitoneally, respectively. Electroencephalographic activity was recorded for 1 hr before and 1 hr after administration of propofol or etomidate.

Results: Anesthesia with propofol was associated with continuous spikes and seizure-like electroencephalogram patterns in P4–P6 rats, but not in P17–P22 rats. Etomidate was weaker at inducing seizure-like activity (F(1,16) = 4.579, p < 0.05). Propofol-induced seizure-like activity was either depressed or eliminated by RU 28318, RU486, or bumetanide, blockers of the mineralocorticoid receptors, glucocorticoid receptors and Na+-K+-2Cl- co-transporter, respectively. Propofol, but not etomidate, increased serum levels of corticosterone in animals that underwent experimental manipulations similar to those used to study electroencephalographic activity (F(2,15) = 17.237, p < 0.001). Etomidate induced electroencephalographic seizures in neonatal rats pretreated with exogenous corticosterone (F(2,15) = 4.975, p < 0.05).

Conclusion: Our results suggest that an increase in corticoid levels along with GABAAR-mediated excitation is required for propofol-induced electroencephalographic seizures in neonatal rats.
Abstracts

Chondroplasia dysfunction using genome analysis in patients with MTLE-hippocampal sclerosis (HS).

Method: 44 patients with MTLE and 86 matching healthy controls were included in this study. The patients were divided into four groups according to their clinical presentations as the following: Group 1 consists of patients with intractable epilepsy who refused operation; Group 2 of operated seizure-free patients; Group 3 of operated patients with seizures; and Group 4 unoperated seizure-free patients with or without antiepileptic drugs. Blood samples were used to isolate DNA. Parallel tagged sequencing was employed to allow pyrosequencing of 130 samples. Complete mtDNA is amplified in two overlapping fragments (11 and 9 kb). The PCR amplicons were pooled in equimolar ratios. Titanium kits are used to produce shotgun library according to the manufacturer protocol.

Results: The average coverage in total was 130 ± 30 and 337 bp fragment length was received from all samples. The mean mtDNA heteroplasmy in patients was 26.35 ± 12.3 and in controls 25.03 ± 9.34. Three mutations had prominently high significance in patient samples. The most significantly associated variation was located in the ATP-8 gene (8,502 A>T, Asn46Ile) whereas the other two were in the same gene in different subunits, ND4 (11,994 C>T, Thr412Ile) and ND5 (13,231 A>C, Lys299Gln).

Conclusion: We have observed that four mutations were significantly related to the presence of epilepsy. These mutations were found at 8,502, 11,914, 11,994, and 13,231 bp of mtDNA, which resulted in amino acid change at the MT-ATP-8, MT-ND4 and MT-ND5 genes. It also provides information about how to protect mitochondria as a means of effective prevention against seizures, seizure-induced brain damages and intractable epilepsy.

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NO EVIDENCE FOR A ROLE OF CYSTATIN B GENE IN JUVENILE MYOCLONIC EPILEPSY

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Purpose: Juvenile myoclonic epilepsy (JME) is a common form of idiopathic generalized epilepsy (IGE) that has a relevant genetic contribution, but so far genes related to JME families remain largely unknown. JME shares electro-features with Unverricht-Lundborg disease (EPM1) that is a form of the progressive myoclonic epilepsy characterized by myoclonus, epilepsy and progressive neurologic deterioration. EPM1 is caused by mutations in the gene that codes for cystatin B, an inhibitor of cysteine protease. EPM1 results from defective function of cystatin B, a cysteine protease inhibitor, as a consequence of mutations in CSTB. The diagnosis can be confirmed by identifying the common dodecamer repeat expansion mutation or other disease-causing mutations in CSTB. We already excluded a role of the dodecamer repeat expansion in patients with JME. In the present study, we enlarged the study group and investigated if the so-called minor EPM1 mutations might account for a proportion of the genetic susceptibility to JME.

Method: Forth-five patients (32 women; mean age: 22.2 ± 6.8; mean age at onset: 15.4 ± 2.8) with JME were enrolled. Twenty-four had a positive family for JME or IGE. DNA was extracted by standard methods. The molecular diagnosis was carried out to identify the common dodecamer repeat expansion mutation or other disease-causing mutations in CSTB. All subjects provided written informed consent, as required by ethics committees in each epilepsy centre of all the participating investigators.

Results: The molecular analysis did not depict dodecamer repeat expansions or other disease-causing mutations in CSTB in all 44 patients with JME.

Conclusion: Our study did not support a role for cystatin B gene in patients with JME.

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SODIUM CHANNEL MUTATIONS AND GENERALIZED EPILEPSY WITH FEBRILE SEIZURES PLUS

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Purpose: This work aims to present two cases of generalized epilepsy with febrile seizures plus (GEFS plus) with genetic mutations not yet described in the literature.

Method: Clinical case description.

Results: Case 1: Female, 16 years old, with an inaugural episode of febrile seizures at 4 months of age, after diphtheria-tetanus-pertussis vaccination. Febrile seizures continued up to 5 years of age, then she had several seizures with no fever and others triggered by physical exercise. She had no relevant personal history or obvious familial history of epilepsy. Neurological examination was normal with no cognitive impairment. The routine electroencephalogram (EEG) reveal right, sometimes bilateral parieto-occipital paroxysmal activity and the MRI showed left peririgional white matter T2-weighted hyperintensity. Testing the possibility of GEFS plus syndrome, the genetic investigation confirmed a SCN1A gene mutation, in exon 13, which results in a premature STOP codon, resulting in a non functional, truncated protein, consistent with GEFS plus type 2. Case 2: Female, 13 years old, with an inaugural episode of febrile seizures at 2 months of age. She had febrile seizures up to age 6. She was asymptomatic until age 12, when she evolved with 3 dialeptic seizures, without fever, two of them followed by tonic-clonic movements. There is a familial history of consanguinity and maternal lineage febrile seizures. Neurological examination was normal and EEG and MRI studies were unremarkable. Genetic studies revealed a mutation in SCN9A gene which results in substitution of a serine for arginine at position 1,181 making the diagnosis of GEFS plus type 7 more likely.

Conclusion: There are hundreds of sodium channel mutations linked to epilepsy, almost all in the SCN1A gene. Mutations in SCN9A gene have been associated with other neurological diseases and rarely with epilepsy. Thus, we find on these cases relevant scientific knowledge.

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METHYLATION PATTERNS IN HUMAN FRONTAL LOBE EPILEPSY OF UNKNOWN ORIGIN

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Purpose: Epigenetic mechanisms play a role in the pathophysiology of epilepsy. Pathogenic mutations in epigenetic regulators are associated with the development of Rett Syndrome whilst abnormal methylation profiles are associated with temporal lobe epilepsy (e.g. Reelin hypermethylation and increased expression of DNA methyltransferases). The aim of this study was to determine the genome-wide methylation profile of the frontal lobe tissue in patients affected by frontal lobe epilepsy of unknown origin.
**Methods:** Frontal lobe tissue specimens were collected from patients undergoing surgery for frontal lobe epilepsy on the basis of intracranial EEG recordings; the brain MRI and the pathology report were “non diagnostic”. DNA was extracted from FFPE blocks from the area under the incidental electrode (cases) and compared to DNA extracted from FFPE blocks from the surrounding area (controls). Bisulphite converted DNA samples were analysed on the Illumina HumanMethylation450K array. Data analysis was performed using the “ChAMP” package, implemented in “R” software. T-test and Wilcoxon test were used for pair analysis as appropriate.

**Results:** Significant variability in methylation was identified in three genes previously associated with epilepsy: *CHRNA2* (TSS200/TS1500), *CNTN2* (all regions), *POMT2* (body). All were hypermethylated in cases compared to controls (*CHRNA2*: Average beta value cases 0.4441988, Average beta value controls 0.5197810, Wilcoxon p value: 0.03499; *CNTN2*: Average beta value cases 0.4851552, Average beta value controls 0.4413986; Wilcoxon p value: 0.02202; *POMT2*: Average beta value cases 0.5184051, Average beta value controls 0.4599721, Wilcoxon p value: 0.03499).

**Conclusions:** Hypermethylation of epilepsy related genes might be implicated in frontal lobe epilepsy in patients with microscopically and macroscopically normal histopathology.

**p670**

**THE GENETICS OF STATUS EPILEPTICUS – A REVIEW OF THE KNOWN CAUSATIVE GENES**

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Status epilepticus, like all of epilepsy, is multifactorial in its causations. Genetic factors play an important role in many patients. The genetics are complex and rarely is a single gene the sole or even overwhelming cause. There are epigenetic and epistatic factors and also, with changing gene expression over time, the important influence of time and development. In this study, we set out to identify, by a systematic review of the literature and genetic databases, those genes which are known to result in epilepsy which typically takes the form of status epilepticus. We have divided our findings according to the age of onset of the epilepsy. We have compared this to the known genes that result in epilepsy but not typically status. The purpose is to see whether a consideration of the genes that result in status throw any light on the molecular processes which differentiate status from epilepsy.

**Method:** We developed a standardized case record form (CRF) capturing all relevant clinical data with an emphasis on antiepileptic drug (AED) history. Concomitantly we developed an electronic CRF and patient database. We generated definitions for pharmacogenomic phenotypes including: remission with the first well-tolerated AED; failure of first AED due to lack of efficacy or adverse drug reactions; broad AED resistance; late response to specific AEDs and adverse drug reactions. To test cross-centre phenotyping consistency, medical records of one patient from each of 10 centres were anonymized, with redaction of all potential clues to identity. They were subsequently phenotyped by trained clinicians from seven centres, using the definitions and electronic CRF. Over 500 different phenotype items were collected per patient. Inter-rater agreement was assessed for nine key phenotype items and for AED outcome classification according to the phenotype definitions.

**Results:** Mean inter-rater agreement per phenotype item was 71%. Mean inter-rater agreement for AED outcome classification was 82%. Overall agreement for all phenotype items and AED outcomes combined across all cases was 74%. Most of the disagreement could be explained by differences in interpretation between raters, with lower agreement for more subjective phenotypes (e.g. number of appropriate and adequate AED trials and number of failed AED trials).

**Conclusion:** Very good agreement was reached on patient classification, such that differences in classification are not expected to affect analysis. The results highlight potential pitfalls in cross-centre phenotyping, directing further training and emphasising the importance of a standardized CRF and detailed definitions. These issues need evaluation and should be taken into account when performing and interpreting multi-centre studies that involve large-scale phenotyping.

**p671**

**INTER-RATER RELIABILITY OF MULTICENTRE PHENOTYPING FOR GENOMIC ASSOCIATION STUDIES IN EPILEPSY**

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**Purpose:** Homogenous phenotyping and patient classification are essential requirements for the validity of large-scale genomic association studies. We report the results of a cross-centre phenotyping validation test undertaken across the EpiPGX consortium.

**Method:** Differences in gene expression levels were compared in patients with new-onset absence epilepsy in three independent cohorts (10 case/control pairs per cohort). Analysis of gene expression levels was performed using blood lymphocytes obtained from patients with absence epilepsy and controls. In cohort 1 we performed a genome wide transcriptional analysis using Affymetrix HGU 133 2.0+ microarrays. Statistical analysis generated a list of differentially expressed genes. In cohorts 2 and 3, the 75 most significant genes from the analysis of cohort 1 and 21 additional candidate genes were followed up using quantitative real time PCR (qRT-PCR).

**Results:** Overall, 30 patients and 30 controls were investigated. We found suggestive evidence for differential expression of several genes
including B2M, CLCN2, HSP90B1, KLF13, RAD21, RANBP9, RCN2, TES, and TRIM8, which are consistently up-regulated in patients.

**Conclusion:** In summary, various new potentially disease relevant genes and processes have been identified. The role of CLCN2 and RCN2 as candidate genes for absence epilepsies is further supported by gene expression studies. These findings may provide a novel insight into the molecular mechanisms of absence epilepsies, possibly hinting at new pathophysiological pathways.

**p673**

**WHOLE EXOME SEQUENCING OF PATIENTS WITH TUBEROUS SCLEROSIS WITHOUT A PREVIOUSLY IDENTIFIED MUTATION**

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**Purpose:** Tuberous sclerosis complex (TSC) is an autosomal dominant disorder, characterized by hamartomas in multiple organ systems. Mutations in two genes, TSC1 and TSC2, are found in 85–90% of patients. The proteins encoded by these genes are involved in negative regulation of the mTOR pathway, which is known to be involved in tumor cell proliferation and cortical development. However, quite consistently, no mutations in any of the two known genes are found in 10–15% of patients with a clinical diagnosis of TSC. This might be due to technical limitations in current diagnostic methods or the existence of other causative genes that have yet to be identified. The aim of this study was to identify the cause of TSC in patients with unknown etiology.

**Method:** Whole exome sequencing was performed in nine patients with a clinical TSC in whom traditional Sanger sequencing and MLPA analysis of TSC1 or TSC2 had failed to reveal any mutations. The exome was enriched by using the Agilent SureSelectXT Human All Exon Capture kit (~51 Mb, V4). Sequencing was performed with 100 bp PE reads on an Illumina HiSeq2000, yielding an average coverage of 100x.

**Results:** We identified four pathogenic mutations in four different patients, two in TSC1 and two in TSC2 (three indels and one splice site mutation).

**Conclusion:** Four out of nine patients had mutations in the TSC genes. Technical aspects explain why these had not previously been revealed by diagnostic testing. No pathogenic mutations were found in other genes in the mTOR pathway, and hence five patients are still without an identified genetic etiology. This could be because we are not able to detect low grade somatic mosaicism or because locus lies in a non-coding region. The possibility of a third, hitherto unidentified TSC-gene seems less likely.

**p674**

**INTRODUCTION OF GENE PANELS IN DNA DIAGNOSTICS FOR EPILEPSY**

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**Purpose:** Epilepsy is characterized by clinical and genetic heterogeneity. To date more than 100 genes are associated with epilepsy. Until recently, molecular diagnostic testing of patients consisted of serial Sanger sequencing of individual genes, consuming considerable time and expenses. We present the implementation and first results of next generation (NGS) or massive parallel sequencing (MPGS) of gene panels for epilepsy in DNA-diagnostic testing.

**Method:** 126 epilepsy associated genes were selected for a range of epileptic phenotypes. Genomic DNA was enriched for these 126 genes using a custom AgilentSure SelectXT kit. Sequence analysis of exons and flanking intronic sequences was performed using a SOLiD™-5500XL system. This method covers at least 94% of bases with >99% sensitivity. Within respective panels >99% coverage per gene is obtained through supplementary Sanger sequencing. Mutation analysis and interpretation was performed using Cartagenia Bench Lab NGS.

**Results:** Ten epileptic phenotypes were defined, associated with 2–50 individual genes. When clinical manifestations did not allow allocation to a specific phenotype, all 126 genes were analyzed. To date, 43 patients were screened for mutations in these 126 genes. In 17 patients at least one probable causative variant was found. In total 22 variants were reported, three of which were definitely underlying the clinical phenotype. The 19 remaining variants were either reported as pathogenic but associated with a recessively inheriting disease (1) or as variants of uncertain clinical significance (VUS) (18). These VUS will be followed up by carrier testing of the parents and/or segregation analysis in family members.

**Conclusion:** NGS based DNA diagnostics shows to be a reliable method to detect mutations in a large number of genes in a single experiment. Currently only few patients are tested, the diagnostic value of this method in a heterogeneous disease such as epilepsy will be evaluated in the near future.
Results: We have identified three heterozygous missense mutations in KCNT1: p.Arg928Cys in a family with ADNFLE, learning disability and psychiatric comorbidities, p.Arg398Gln in a family with focal epilepsy, multifocal epilepsy with learning difficulties and MMFSI, and p.Gly228Ser in a sporadic patient with MMFSI. The p.Arg928Cys variant was found in 5 family members with ADNFLE. Learning disabilities, memory deficit and psychiatric problems, including depression, suicide attempt, anxiety and ADHD were seen in 4/5 family members. In addition to the epilepsy and other neurological phenotypes, one member has been reported to have cardiac arrhythmia and another had SUDEP. The p.Arg398Gln variant has been previously reported in an ADNFLE family and was seen here in a family with focal epilepsy, multifocal epilepsy and MMFSI.

Conclusion: This study extends the range of phenotypes associated with KCNT1 mutations. Each patient reported thus far with a KCNT1 mutation exhibit seizures. The severity of the observed co-morbidities range from moderate to severe incapacitation. We report here that the same KCNT1 mutation, p.Arg398Gln, is associated with both ADNFLE and MMFSI, rendering genotype-phenotype correlations difficult. Furthermore, we report on two individuals with ADNFLE and cardiac problems or SUDEP.

p676
IDENTIFICATION OF PRESUMED DISEASE-CAUSING GENETIC VARIATIONS BY A NGS SCREENING PANEL TARGETING 31 CHILDHOOD EPILEPSY-RELATED GENES

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 31 known epilepsy genes was developed for next generation sequencing using the Ion Torrent PGM platform. Potentially causative variants were evaluated by literature and database searches and submitted to bioinformatic prediction algorithms. Potentially causative variants were evaluated by literature and database searches and submitted to bioinformatic prediction algorithms. Whenever possible, identification of a variant, familial segregation analysis was performed whenever possible.

Results: We identified a presumed disease-causing variant in 7 of 29 patients. The aberrations included two de novo STXBP1 variations (c.794 + 5G>A and c.1437-6_1488delinsAT) and two de novo CDKL5 variations (c.577G>C and c.2152 + 1G>T) all found in patients with either unclassified EE or West syndrome. Furthermore, we identified an inherited KCNT1 (c.2782C>T) variation in a family with ADNFLE, and two de novo SCN1A variations; one in a previously reported SCN1A negative Dravet patient (c.625dupC), and one in a patient with GEFS+ (c.4786C>T).

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 presumed disease-causing genetic variation in 25% of the analyzed patients.

Genetics 4
Wednesday, 2nd July 2014
p677
TWO NOVEL AND THREE KNOWN EPM2A AND NHLRC1 (EPM2B) GENE VARIANTS LEADING TO LAFORA DISEASE IN TURKISH PATIENTS
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Purpose: Lafora Disease (LD) is a type of autosomal recessive progressive myoclonus epilepsy that is associated with NHLRC1 and EPM2A genes. Therefore, genetic studies have an important role in the differential diagnosis of LD. In this study, we aimed to determine the genetic defects in Turkish LD patients that had first been diagnosed upon clinical and electrophysiological evaluation.

Method: All coding sequences and exon-intron boundaries of EPM2A and NHLRC1 genes were screened for mutations via Sanger sequencing in 12 unrelated LD cases after obtaining their informed consent. Upon identification of a variant, familial segregation analysis was performed whenever possible.

Results: Genetic analyses revealed 2 novel homozygous missense variants in 2 unrelated cases in genes NHLRC1 and EPM2A, respectively. Additionally, 3 previously reported homozygous clinical variants were detected in 4 unrelated cases (NHLRC1: c.436G>A; Asp146Asn, EPM2A: c.259A>G; p.Lys87Glu and c.721C>T; p.Arg241X). We noticed a relatively slow clinical progression in patients with NHLRC1 mutation. Interestingly we observed that similar baseline EEG abnormalities were continuing on EEG follow ups after years, without severe and worsening impairment of background activity. Half of the patients showed photosensitivity, four of them were sensitive to lower stimulation frequencies.

Conclusion: In this study, we identified 5 variants in genes NHLRC1 and EPM2A in 6 unrelated LD cases. No clinically associated variants in the remaining 6 cases were detected in these genes. We speculate that variants in control regions of NHLRC1 and EPM2A or more likely other currently unidentified genes may be responsible for the disease status in these patients. Therefore, we propose to carry out further studies including linkage and/or exome sequencing analyses.

p678
A NEW THERAPEUTIC FORMULA OF INFANTILE SPASMS IN DOWN SYNDROME?
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Purpose: Down syndrome (DS) is the most common genetic condition characterized by a supplementary 21 chromosome usually from the
mother side. Association with epilepsy was described in 1.4–17% of children with DS, most frequent infantile spasms. Our aim is to find a therapeutic clue for this type of seizures.

**Method:** Medical records of children admitted for Down syndrome with infantile spasms were retrospectively analyzed in a period of 5 years (2009–2013). The clinical data (onset, types of seizures, clinical and mental examination, treatment, evolution) and laboratory tests (EEG and cerebral MRI) were analyzed and compared to published studies in order to find a specific trait useful for future prognosis.

**Results:** 39 patients were diagnosed with DS, 10 children associated epilepsy, from which 6 had infantile spasms (50% boys and 50% girls). The spasms appeared symmetrically, in clusters, predominantly on awakening, with hypsarhythmia on EEG. Their imaging studies (cranial sonography or cerebral MRI) were normal. The seizures were controlled with ACTH, vigabatrine or topiramate. 33% were treated only with ACTH for 6 weeks. All patients had a good evolution, without infantile spasms and improvement of global evolution, but 83% with a certain degree of mental retardation. One patient had myoclonic absences at 6 years of age of which were controlled by levetiracetam.

**Conclusion:** Considering the results of our study and also the published data regarding the evolution of infantile spasms in DS, which is a treatable form of epilepsy, the authors proposed this type of epilepsy to be treated only with ACTH for 6 weeks. In order to confirm this hypothesis, larger prospective studies are necessary.

**p679 EPILEPTIC ENCEPHALOPATHY WITH CONTINUOUS SPIKES AND WAVES DURING SLOW SLEEP IN GURRIERI SYNDROME**

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**Purpose:** Gurrieri syndrome is a rare syndrome characterized by epilepsy, moderate to severe mental retardation, constitutional particularities and specific skeletal abnormalities (iliac crest with aspect of "rabbit ears"). Until now, only 7 cases have been published, with probable autosomal recessive traits but the affected gene has not been found yet. The epileptic trait was as focal resistant seizures, but no case with epileptic encephalopathy with continuous spikes and waves during slow sleep (CSWS) was described. Our aim is to present a case of Gurrieri syndrome with epilepsy which evolved to CSWS and its evolution under specific treatment.

**Method and Results:** Vlad is a 12 year old adopted boy (unknown family history) diagnosed with Gurrieri syndrome at 8 years of age, who showed dysmorphic features (large hands and feet, typical iliac crest abnormalities), moderate mental retardation and epilepsy. Seizures started at the age of 14 months, as focal motor seizures on the right hemisphere which were temporally controlled by antiepileptic drugs. After 5 years, seizures reappeared at awakening, as focal aspects same as initially but in clusters and also correlated with appearance of hyperkinetic behaviour. Cerebral MRI was normal. Sleep EEG showed a generalized spike and wave pattern, asymmetrically, more than 85% of non-REM sleep (NREM), compatible with the diagnosis of CSWS. Valproic acid was tried, topiramate, levetiracetam, lamotrigine, but when ACTH was added to valproic acid and EEG and cognition improved and the number of seizures was reduced.

**Conclusion:** Authors have presented the first case of CSWS as part of Gurrieri syndrome which showed a good outcome after steroid treatment.

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patients each carried a de novo mutation in one of two novel epilepsy genes. Respectively, additional epilepsy patients with de novo mutations in these 2 genes were then detected in next generation sequencing studies of consortium partners. Eleven patients carried one or more de novo mutations in genes not previously linked to epilepsy, however several of these genes have previously been associated with intellectual disability or autism. Screening of these interesting candidate genes in a larger follow up cohort using a targeted gene panel is ongoing.

Conclusion: Trio exome sequencing of MAE patients reveal that MAE is a very heterogeneous disorder with only ten percent of the patients having mutations in known epilepsy genes. GLUT1 mutations seem to be less frequent than previously suspected. In addition we detected several interesting candidate genes and this study leads to the discovery of at least two novel epilepsy genes.

p682
NO ASSOCIATION BETWEEN C3435T POLYMORPHISM IN MDR1 GENE AND ANTI-EPILEPTIC DRUG RESISTANCE IN PUERTO RICAN CHILDREN WITH EPILEPSY
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Purpose: The Multidrug Resistance 1 gene (MDR1) encodes for the major transmembrane efflux transporter P-glycoprotein. Mutations within this gene have been proposed among the causes for anti-epileptic drug (AED) resistance. The goal of our study was to examine the hypothesis of association between AED resistance and the C3435T polymorphism on the MDR1 gene among Puerto Rican children with epilepsy.

Method: DNA was extracted from oral mucosa epithelial cells obtained from 90 pediatric patients with epilepsy (age range: 1–19 years). Of those patients, 51 were classified as responders (controls) and 39 as non-responders based on their AED response. Genotype was determined using a real-time PCR assay.

Results: Genotype frequency among non-responders (18CC, 10CT, 11TT) was not significantly different from that expected based on the genotype frequency for controls (22CC, 22CT, 7TT) (χ² = 4.093, df = 2, p = 0.13). Allelic frequencies (Non-responders: 59% C, 41% T vs. Controls: 65% C, 35% T) were also not significantly different between non-responders and controls (χ² = 0.764, df = 1, p = 0.38) and were in hardy-weinberg equilibrium with the observed genotype frequencies.

Conclusion: In conclusion, we found no evidence of association between the C3435T polymorphism in the MDR1 gene and AED resistance among Puerto Rican children with epilepsy.

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p683
CLINICAL FEATURES OF FOUR EGYPTIAN FAMILIES WITH FAMILIAL FOCAL EPILEPSY WITH VARIABLE FOCI (FFEVF)
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Purpose: FFEVF is an autosomal dominant partial epilepsy characterized by occurrence of epileptic arising from different cortical areas in different family members. We describe 4 small Egyptian families that would fit this diagnosis.

Method: Patients were recruited from outpatient clinics of Ain Shams University hospitals. Patients with autosomal dominant partial epilepsy, with different focus in different family members were identified. Affected family members were invited for clinical examination. EEG and imaging studies were reviewed.

Results: Four small families were identified that met the criteria of FFEVF. This included 11 patients with epilepsy (7 males, 4 females). The age of onset ranged from 9 months to 37 years. Patients suffered from complex partial seizures, with or without secondary generalized seizures. Patients showed marked variation in localization of seizure onset, seizure frequency and response to antiepileptic medications. Most patients had normal brain imaging, but mesial temporal sclerosis was shown in one patients. Neurological examination was normal in all patients. One patient had cognitive abnormalities, and one patient had history of a psychotropic episode and substance misuse.

Conclusion: FFEVF is rare, with about 10 families described in literature since it was first identified in by Schaefer and co-workers in 1998. Recently, it was shown to be caused by mutations in DEPDC5 gene. The true prevalence of the condition is not known, and it might be under reported. Identification of more families, from different parts of the world, would help improve our understanding of this rare condition.

p685
DO CHD2 GENE MUTATIONS DETERMINE MYOCLONO-ASTATIC EPILEPSY?
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Introduction: Mutation in the CHD2 gene, encoding chromodomain 2 binding protein 1, have been reported in epileptic encephalopathies with variable phenotypes including Dravet-like epilepsy and Lennox-Gastaut syndrome.

Case Report: We report a girl who presented myoclonic astatic epilepsy (MAE) and carrying a de novo missense mutation (c.1861C>T/p.R621W) in CHD2 identified by exome sequencing. The patient has no familiar/personal antecedent. Psychomotor development was apparently normal during the first 2 years and till the onset of epilepsy. Generalized tonic-clonic seizures started at the age of 2.3 years and at 3 she presented tonic seizures during sleep and myoclono-astatic seizures during wakefulness. Ictal EEG showed generalised polyspikes followed by EEG flattening with superimposed fast rhythms clinically corresponding to a
myoclonic-astatic seizure. Global developmental slowing, mainly affecting language and communication skills, was evident since the onset of seizures and the child showed hyperkinetic behaviour. Brain MRIs showed a mild cerebellar hypotrophy. At last observation (17 years) she had weekly seizures despite polytherapy with VPA, CZP and LTG, and severe intellectual disability.

Conclusions: This observation widens the clinical spectrum linked to CHD2 mutations to MAE. The detailed analysis of the patients reported in literature suggested that some of these patients should also be ascribed to MAE as defined by the ILAE classification and we suggest that patients with MAE with unfavourable outcome should be tested for CHD2.

Imaging 5
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p686
MRI FINDINGS IN REFRACTORY EPILEPSY
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Purpose: To study MRI in patients with refractory epilepsy in an area endemic for neurocysticercosis (NCC).

Method: Forty (26 M, 14F) consecutive patients with definite diagnosis of refractory epilepsy formed the study material. Detailed clinical, electro-physiological & Neuro imaging studies were used to confirm the diagnosis. Detailed MRI evaluation on an epilepsy protocol with 1.5 Tesla device (Siemens, Germany) was performed. It included Axial T1, T2, FLAIR, DWI, Sagittal T3, Oblique Coronal T2, FLAIR, T1, FLAIR, Volume 3 DMPGR, SWI, & T2 relaxometry.

Results: Majority (82.5%) of the patients were in the age range of 11–30 years with 47.5% having refractoriness beyond five years. Partial seizures were the commonest with 19 having an aura, 28 had automatism & 20 had post ictal phenomenon. EEG was normal in 15 patients while 17 had focal abnormalities. CT scans of the head revealed NCC in 3 & encephalomalacia in one. MRI was normal in 7 patients (17%) MTS (Mesial Temporal Sclerosis) was the commonest abnormality (13 Patients) followed by NCC in 6 patients.

Conclusions: Despite the endemicity of NCC, MTS remains the commonest cause of refractoriness.

p687
COMPARISON OF LANGUAGE FMRI DURING TWO TESTS OF ASSOCIATION AND LANGUAGE IN TEMPORAL LOBE EPILEPSY PATIENTS
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Purpose: Temporal lobe resection for temporal lobe epilepsy (TLE) can cause verbal decline. Functional MRI (fMRI) to visualize critical language areas would be useful to predict decline and tailor the resection. We sought to improve pre-operative language fMRI, using the pyramids and palm trees test (PPT)- a semantic association task- which is known to activate lateral temporal regions.

Method: Six patients (age 28 [18–39]; 1 male, 1 left handed) with left TLE (duration 18 ± 11 years; heterogeneous etiology) underwent two fMRIs: the clinical scan consisting of a silent verb-generation task, compared to looking at meaningless characters (contrast VG) and the PPT, compared to a size-judgment task (contrast PPT). The threshold was set to voxel level Puncor < 0.001, cluster level Pcorr < 0.05.

Results: The VG showed bilateral inferior frontal lobe activations in all. Left lateral temporal activation was seen in half, whereas bilateral temporal activations was seen in the rest. The PPT showed left inferior frontal activation in 67%, the rest showed bilateral inferior frontal activations. Left temporal lobe activation was seen in half of the patients, 33% had bilateral activation and one patient had no suprathreshold activations. When regions that activated more in PPT than VG were analyzed, there was left sided activation centered on the superior and middle posterior temporal gyrus in all but one. The reverse contrast showed no lateral temporal lobe activations.

Conclusion: To use fMRI for predicting decline after surgery, one should be able to localize regions necessary for language processing at the individual level. One region that was clearly different comparing the PPT and VG paradigm was the activation of the posterior temporal gyrus. We postulate that language fMRI using PPT might be better to predict cognitive decline after TLE surgery than fMRI using the verb-to-noun paradigm.
Conclusion: Multimodal imaging adds complementary information on preferred seizure onset zone in this equivocal case with widespread epileptogenic lesions/dual pathology. Parietal generators should be considered in patients that present with a typical clinical MTLE syndrome and dual pathology.

p689 CANNABINOID RECEPTOR TYPE 1 AVAILABILITY AND SPONTANEOUS TEMPORAL LOBE SEIZURES

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Purpose: Activation of the cannabinoid receptor type 1 (CB1) has been associated with both anti- and pro-convulsant effects. A post-ictal increase in the availability of CB1 receptors was recently demonstrated in vivo in humans with TLE and hippocampal sclerosis (HS) (Goffin K et al. Brain 2011;134:1033–1040). We hypothesised that participants with mesial and neocortical TLE, relative to healthy controls, would demonstrate increased CB1 receptor availability, assessed with a novel PET radioligand, [11C]MePPEP (Terry GE et al. NeuroImage 2009;48:362–370).

Method: Eight participants with refractory TLE (five females; median age range 42/30–60 years) and 20 healthy controls (eight females; median age range 29/20–66 years) were scanned on two separate days after an intravenous bolus injection of ~370 MBq of [11C]MePPEP. Parametric volume-of-distribution images (V1) were created using spectral analysis. V1 was compared on a voxel-by-voxel basis by ANCOVA using Statistical Parametric Mapping (SPM8).

Results: At the group level, CB1 availability in TLE was higher in the ipsilateral temporal lobe in postictal scans than in controls (p < 0.005 uncorrected), as hypothesised. Focal increases were seen in the mesial and occipital lobes. CB1 availability was negatively correlated with time since last seizure (p < 0.05). However, in individual patients, focal increases were inconsistent in the epileptogenic temporal lobe.

Conclusion: At the group level, CB1 availability in TLE was higher in the ipsilateral temporal lobe in postictal scans than in controls (p < 0.005 uncorrected), as hypothesised. Focal increases were seen in the mesial and occipital lobes. CB1 availability was negatively correlated with time since last seizure (p < 0.05). However, in individual patients, focal increases were inconsistent in the epileptogenic temporal lobe.

p690 TRANSIENT LESION IN THE SPLENIUM OF THE CORPUS CALLOSUM AND A SUDDEN ANTI-EPILEPTIC DRUGS WITHDRAWAL DURING VIDEO-EEG TELEMETY

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Purpose: Transient focal lesions in the splenium of corpus callosum (SCC) has been described in patients with epilepsy during video-EEG telemetry (V-EEG-T) and was attributed to a rapid reduction in the dose of antiepileptic drugs (AEDs). The aim of this study was to determine the incidence of focal lesions of SCC and its correlation with the rapid withdrawal of AEDs in patients after V-EEG-T.

Method: In the period between 01.06.2010 and 31.12.2013, V-EEG-T (duration: 5–15 days) was performed in 564 patients. In 497/564 (88.4%) patients MRI according to temporal protocol was performed within 7 days after the V-EEG-T and region of SCC was examined in order to detect focal lesions.

Results: In 18/497 (3.6%) patients (males: 9, age range: 18–60, median: 37 years) we found asymptomatic focal zone (T2 and FLAIR hyperintense) in the central part of the SCC. V-EEG-T demonstrated that 15 patients had epilepsy (primary generalized 2 and focal 13), 2 psychogenic non-epileptic seizures and 1 hypocamcal tetany. Patients were treated with AEDs: carbamazepine+lamotrigine: 5; carbamazepine+other drug: 4; lamotrigine: 4; lamotrigine+valproate: 4; lamotrigine+levetiracetam: 1 patient. AED doses were ≥1 defined daily dose. In all patients AEDs were withdrawn suddenly during 1–3 days and reintroduced after 4–10 days in 15 patients with epilepsy. Seizures were recorded in 12/18 patients: 5 had focal and GTC. 1 GTC and absence, 5 focal, 1 myoclonic and 6 patients had no seizures. In 6 patients the MRI was repeated. In 1 patient focal lesion in the SCC was present after 30, but not after 80 days of the V-EEG-T. In another 5 patients a focal lesion was no longer present after 237 to 1,726 days following V-EEG-T.

Conclusion: The only common feature in all 18 patients with focal lesion in the SCC is the sudden withdrawal of carbamazepine and/or lamotrigine.

p691 ATYPICAL LANGUAGE NETWORKS IN EPILEPSY: THE INTERACTION WITH THE EPILEPTIC NETWORK

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Purpose: Atypical language network location and/or lateralization have been reported in a relevant proportion of patients with epilepsy. The presence of structural lesion, early age of epilepsy onset and epilepsy severity has been associated with atypical language; however the underlying mechanisms of this phenomenon are still unknown. In this study we used fMRI to map both the epileptic network and the language network, to investigate the effect of interictal epileptiform discharges (IED) on language activation.

Method: An eight year old left handed girl with left frontal lobe epilepsy secondary to a perinatal left middle cerebral artery stroke underwent simultaneous EEG-fMRI and language fMRI. Maps of the epileptogenic network related to the IED and language maps for verb generation, picture naming and picture describing were generated using statistic parametric mapping.

Results: EEG-fMRI analysis showed bilateral frontal cortical areas and basal ganglia involvement during the generation and spread of IED. In particular, it revealed involvement of language relevant areas: bilateral inferior and middle frontal gyri (right > left). Crucially, these regions were not significantly activated during language fMRI. Instead, language activation in the structurally-intact (right) hemisphere was located more posteriorly and superiorly.
Abstracts

Conclusion: Lack of activation in the right-sided homologue of Broca’s area may be explained by suppression or displacement of activity by the epileptic network. Interaction between epileptic and cognitive networks provides insight into the atypical organization of language in patients with epilepsy.

Purpose: Surgical intervention for intractable epilepsy often involves resection of tissue in close proximity to eloquent cortex. The long-term effects on cognition, in particular language, are not well-documented in paediatric populations. In addition, many children with left hemisphere focal epilepsy show atypical language localisation and lateralisation. The current study evaluates changes in language lateralisation after resective surgery and whether this correlates with changes in verbal abilities.

Method: This preliminary report investigated 20 children who underwent investigations for surgical treatment of medication-resistant epilepsy, including functional MRI (fMRI) during a covert verb-generation task to determine hemispheric language lateralisation. Fifteen subsequently underwent surgery, whilst 5 did not. Seven healthy sibling controls were also recruited. Patients were reassessed 6 years after presurgical baseline assessment. All subjects underwent the same language fMRI protocol as used at baseline. Lateralisation indices were calculated for Broca’s region and the temporal lobes. All subjects underwent neuropsychological testing of verbal and non-verbal intelligence (Wechsler Intelligence Scale-IV). Verbal IQ scores increased in the surgical group from pre-operative baseline to follow-up (p = 0.042), and decreased in the non-surgical group (p = 0.014). Baseline and follow-up lateralisation indices showed significant positive correlations (Broca’s area: r = 0.813, p < 0.001, temporal lobes: r = 0.697, p < 0.001) indicating relative stability over time. Pre-operative lateralisation was not related to post-operative verbal function, but at follow-up greater left-sided temporal lobe lateralisation was correlated with better verbal scores (r = 0.39, p = 0.045).

Conclusion: Our findings suggest that surgical intervention for epilepsy does not cause large changes in language lateralisation. Overall better verbal intelligence is associated with a more typical language lateralisation. Our preliminary results suggest improved verbal function in surgical compared to non-surgical patients, which is not driven by major changes in language lateralisation.

Purpose: Metals are intrinsic to the architecture and function of the brain. Disruptions and changes to the levels of biometals have also been linked to epilepsy. However, little is known about the role of metals across scales, types of epilepsy, brain locations, and co-localization. Here we report on ongoing studies from the first application of synchrotron imaging to post-surgical human epilepsy tissue.

Methods: Cortical (n = 17) and hippocampal (n = 7) tissue samples resected during epilepsy surgery were examined using synchrotron x-ray fluorescence imaging (SXRF) at the Stanford Synchrotron Radiation Lightsource. Using two beamlines with resolutions down to the micron, we were able to visualize metal distributions and examine colocalization of elements (e.g., iron, copper, zinc) at scales ranging from layers to vessels and cells.

Results: Cortical layers were distinguishable in both focal cortical tissue and cortical tissue distal to a hippocampal focus (removed via a minimally invasive procedure in order to attain access to the hippocampus). Layers and tracks were also highly visible in multiple metal windows in the hippocampus. The most striking metal distributions were seen at lesion sites, with iron concentrations being a particularly pronounced marker of sclerotic areas. Most interestingly, cortical tissue in a subset of patients showed elevated levels of copper.

Conclusions: This study illustrates the vast information regarding metal distribution and co-localization that is now accessible with postsurgical SXRF imaging. Specifically, mapping the atomic composition of brain tissue in epilepsy opens new avenues for non-invasive patient-specific tests. In particular, identifying changes in metals could offer new ways of understanding symptomology, biomarkers, and mechanisms that could in turn suggest novel metal-based therapies (e.g., dietary, chelation) aimed at addressing metal imbalance, deficiency or overload.

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Purpose: To investigate the contribution of Diffusion Tensor Imaging (DTI) and Diffusion Tensor Tractography (DTT) in identifying abnormalities in MRI negative patients with cryptogenic extratemporal focal epilepsies.

Method: 14 patients with cryptogenic extratemporal focal epilepsy were investigated. DTI data was acquired on a GE Sigma HDx 3T Scanner, using an acquisition scheme with 64 diffusion weighted directions, a b-value of 1,000 m²/s, 2.4 mm slice thickness and 2 mm in-plane resolution. Fractional anisotropy (FA) maps were investigated for focal changes and asymmetries. Streamline DTT of the whole brain was used and the number of reconstructed streamlines in homolog anatomical areas were compared. Asymmetries of more than 10% for FA maps and more than 20% for the streamline count were rated as significant.

Results: Asymmetries in the number of reconstructed streamlines were found in nine of the 14 patients (64%). In eight of them, these changes were consistent with the clinically suspected seizure onset zone, based on video-EEG-monitoring and nuclear medicine data, however, in two patients DTT indicated more widespread, hemispheric changes, beyond the seizure onset zone. FA maps showed asymmetries beyond 10% in only one patient. In two patients, the seizure onset zone was confirmed in the area of DTT abnormalities by intracranial electrodes, the other patients are still awaiting invasive evaluation, including the one with discrepant DTT findings.

Conclusion: Lack of activation in the right-sided homologue of Broca’s area may be explained by suppression or displacement of activity by the epileptic network. Interaction between epileptic and cognitive networks provides insight into the atypical organization of language in patients with epilepsy.
Conclusion: These preliminary data show the potential role of DTT and DTT as complementary lateralizing and localizing imaging modality in cryptogenic extramisiotemporal epilepsy. We hypothesize, the observed changes reflect migration disorders, where heterotopic neurons disrupt the microstructural order of white matter underlying the seizure onset zone. DTT appears to be more sensitive than FA maps, and this method may be less sensitive in patients with small circumscribed focal pathologies.

p695
AN FMRI RESPONSE TO FACIAL EMOTIONAL EXPRESSIONS IN BENIGN CHILDHOOD EPILEPSY WITH CENTRO-TEMPORAL SPIKES
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Purpose: Only limited knowledge is available regarding social cognitive skills in benign childhood epilepsy with centro-temporal spikes (BCECTS), a condition associated with educational underachievement that might partly result from suboptimal social function.

Method: We studied 16 patients with BCECTS (aged 6‒13 years) and 14 age and sex matched controls (aged 6‒16 years) using event-related functional magnetic resonance imaging (fMRI) with an emotional discrimination task consisting in viewing happy, fearful, scrambled and neutral faces. Subjects had to label faces expressing happiness (first session) or fear (second session) by pressing a button on a response pad.

Results: Neuroimaging results in healthy controls showed bilateral activations within a widespread network including frontal, temporal and occipital brain regions. The patient group activated different parts of this network, mostly in the left hemisphere. Whole-brain analysis demonstrated that BCECTS participants (group level) had enhanced activation in the right superior temporal gyrus, anterior and posterior cingulate gyri and anterior insular cortex while viewing fearful faces than by non-emotional facial expressions during the happy face detection task. There was also a significant increase in reaction time in patients who made more errors in the detection of happy and neutral faces.

Conclusion: Patients failed to suppress active viewing of fearful faces during detection of faces expressing happiness. They also tended to misclassify happy and neutral emotional faces as stimuli of negative valence. Our preliminary findings demonstrate impairment in social cognition in BCECTS.

p696
READING, LISTENING AND MEMORY-RELATED BOLD SIGNAL RESPONSE IN CHILDREN WITH EARLY-STAGE TEMPORAL LOBE EPILEPSY OF UNKNOWN CAUSE – AN FMRI STUDY
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Purpose: The changes in functional brain organization associated with paediatric epilepsy are largely unknown. Since children with epilepsy are at risk of developing learning difficulties even before or shortly after the onset of epilepsy, we assessed the functional organization of memory and language in paediatric patients with temporal lobe epilepsy (TLE) at an early stage in epilepsy.

Methods: Functional magnetic resonance imaging was used to measure the blood oxygenation level-dependent (BOLD) response to four cognitive tasks requiring reading, story listening, memory encoding and retrieval in a population-based group of children with TLE of unknown cause (n = 21) and of normal intelligence and a healthy age and gender-matched control group (n = 21).

Results: The BOLD response differed significantly between the two groups in the story listening task requiring auditory comprehension and verbal memory. Activation was found to be significantly stronger in the TLE patients relative to the controls, and in particular among the patients with abnormal electroencephalograms (EEGs). Significant differences were found in the right hemispheric temporal structures, thalamus and basal ganglia. In the patients with abnormal EEGs, significantly increased activation was found bilaterally in the temporal structures, basal ganglia and thalamus relative to those with normal EEGs. In the patients with normal interictal EEGs the significant BOLD signal differences were found to be increased deactivation relative to those with abnormal EEGs or the controls. All the significant differences were located outside the temporal structures.

Conclusions: Our results suggest that TLE entails a widespread disruption of brain networks. This needs to be taken into consideration when evaluating learning abilities in patients with TLE. Deactivation may be a sign of neuronal inhibition implying that not only activation but also deactivation may have a role in functional brain organization, and both should be imaged when conducting fMRI studies. The thalamus seems to play an active role in TLE.

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A CASE OF BODY DYSMORPHIC DISORDER AFTER EPILEPSY SURGERY AND CHILDBIRTH
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Purpose: Body dysmorphic disorder (BDD) is characterized by preoccupation with misperceived defects of appearance or excessive concern about slight physical anomalies. We report a patient with BDD after epilepsy surgery and childbirth.

Method: A 35-year-old right-handed woman had complex partial seizures that caused loss of consciousness. She underwent left temporal lobectomy at the age of 30 and subsequently remained seizure free. Her WAIS-R also improved from 76 before to 85 after surgery. At age 34, immediately after childbirth, she began to feel that the swelling of her both superior eyelid seemed to threaten other people. She failed to solve
the problem even after twice seeking cosmetic surgery. She was referred to our psychiatric department by her neurosurgeon. We followed her by prescribing paroxetine and cognitive-behavioral intervention.

**Results:** BDD is a relatively common psychiatric disorder (0.7–1.1%), but our patient had some atypical characteristic compared with the previously reported demographic data: (i) sudden onset, (ii) late onset at the age of 32 years (mean age at onset is generally 16.4 years [SD = 7.0]), and (iii) issue of excessive concern limited to one body part (eyelid) (generally, the mean number of body areas is 5–7). We considered that the atypical onset of BDD in our patient was related to improvement of her postoperative cognitive function and to the psychological stress of the life event (childbirth).

**Conclusion:** Postoperative cognitive improvement and improvement in a patient’s activities of daily life might induce de novo psychiatric symptoms.

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**p699**

**PSYCHIATRIC COMORBIDITY AND SEIZURE CONTROL IN PATIENTS WITH TUBEROUS SCLEROSIS COMPLEX**

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**Purpose:** Psychiatric disorders are common in tuberous sclerosis complex (TSC) and affect 25–50% patients. Dysregulation of the signaling through the mTOR pathway is suggested as underlying mechanism. Psychiatric comorbidity and seizure control in TSC patients was investigated.

**Method:** Clinical records of 43 patients (19 male, 24 female, mean age: 17.1 ± 9.3) with TSC were retrospectively reviewed. Epilepsy developed in 90.6% TSC children. Early focal seizures and/or infantile spasms (IS) occurred in 23 patients. Early treatment (within a week after IS were detected) with vigabatrin or ACTH for IS was started in 13 children. 15/39 TSC patients achieved seizure freedom.

**Results:** Behavioral and anxiety disorders were most prevalent: autism spectrum disorders (ASD - 34.8%), ADHD (41.8%) and mood disorders (23.3%). Five patients developed psychosis. Mental retardation was noted in 72.1%. Deficits in social functioning before the age of 5 appeared in 11/15 ASD patients. Severe MR (IQ < 35), language deficit or autistic features were observed in 7/10 children with larger delay of treatment compared with 4/13 with early IS therapy. In 9/15 children with ASD, long-term complete/favorable seizure control was found. No severe intractable epilepsy was found in remaining patients. None of patients with psychosis was seizure free. Antipsychotics, antidepressants and anticonvulsants with mood-stabilizing properties improved target symptoms, such as aggressiveness, obsessions, compulsive behaviour, and hyperactivity in >50% of TSC patients. Suppression of paroxysmal EEG abnormalities showed indirect benefits on behavioral problems.

**Conclusion:** Psychiatric disorders are common in patients with TSC. There are no uniform relations between seizure control and psychiatric disorder. Differently from psychotic TSC patients, these with ASD achieved long-term favorable seizure control. Early IS treatment was associated with better cognitive outcome.

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**p699**

**VALIDATION OF THE GENERALIZED ANXIETY DISORDER-7 IN PEOPLE WITH EPILEPSY: A MEPSY STUDY**

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**Purpose:** The Generalized Anxiety Disorder-7 (GAD-7) is a valuable instrument to screen anxiety for primary care patients. However, it has not been validated in people with epilepsy (PWE). Therefore, we validated the GAD-7 and examined the differential effect of GAD-7 from adverse effects of antiepileptic drugs (AEDs) on the detection of anxiety in Korean PWE.

**Method:** Eligible patients who visited outpatients clinics in 4 tertiary and 1 secondary care hospitals underwent several instruments including the Mini International Neuropsychiatric Interview-Plus Version 5.0.0 (MINI-Plus 5.0.0), the Korean version of the Neurological Disorders Depression Inventory for Epilepsy (K-NDDI-E), the Korean version of the Liverpool Adverse Event Profile (K-LAEP), and the Quality of Life in Epilepsy-10 (QOLIE-10).

**Results:** Two hundreds forty-three patients were enrolled in the study and 51 patients (21.0%) had GAD by MINI-Plus 5.0.0. Cronbach’s α coefficient for the GAD-7 was 0.924. At a cut off score of 6, the GAD-7 had a sensitivity of 92.2%, a specificity of 89.1%, a positive predictive value of 69.1%, and a negative predictive value of 97.7%. The GAD-7 score was well correlated with the K-NDDI-E score, the K-LAEP score, and the QOLIE-10 overall and subscale scores. The impact of adverse effects of AEDs on the GAD-7 was less than that on the K-NDDI-E.

**Conclusion:** The GAD-7 is a reliable and valid screening tool to detect GAD in PWE.

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**p700**

**THE ANTIDEPRESSANT SERTRALINE DIMINISH THE EXPRESSION OF IL-1β AND TNF-α MRNA INDUCED BY SEIZURES IN THE HIPPOCAMPUS**

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**Purpose:** Recently we found that the antidepressant sertraline was an effective inhibitor of hippocampal presynaptic Na+ channels permeability in vitro and of tonic-clonic seizures in the animal in vivo. Several studies indicate that pro-inflammatory cytokines in the central nervous system are increased by both, epilepsy and depression, and the inhibition of Na+ channels has been shown to decrease pro-inflammatory cytokines in microglia, the possibility that sertraline could overcome the rise in the pro-inflammatory cytokines expression induced by seizures was investigated here.

**Methods:** The effect of sertraline, administered once or for seven consecutive days at a low dose (0.75 mg/kg) on IL-1β and TNF-α mRNA expression in the hippocampus was determined by RT-PCR. The effect of sertraline (at doses in the range from 0.75 to 25 mg/kg) on the rise in IL-1β and TNF-α mRNA expression accompanying generalized tonic-clonic seizures induced by the convulsive agents, 4-aminopyridine (4-AP) or pentylenetetrazole (PTZ), and on the increase in IL-1β and TNF-α mRNA expression induced by lipopolysaccharide (LPS) also was investigated.

**Results:** Under basal conditions, a single injection of sertraline at a low dose (0.75 mg/kg) is already able to reduce IL-1β mRNA expression in the hippocampus, and after repeated doses also TNF-α. Tonic-clonic sei-
The increase in IL-1β and TNF-α induced by 4-AP were insensitive to a single 0.75 mg/kg sertraline dose, but were completely abolished by the administration of 0.75 mg/kg sertraline for one week. The increase in IL-1β and TNF-α mRNA expression accompanying seizures induced by PTZ was also sertraline sensitive, as was the increase in pro-inflammatory cytokines expression induced by the inoculation of 100 mg/kg LPS.

**Conclusion:** On the basis of present results we conclude that the reduction of 100 mg/kg LPS.

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**EEG, brain CT / MRI, Wechsler Intelligence Scale for Preschool Period and Wechsler Intelligence Scale for Children and Behavior Problem Index.**

**Results:** 34 children had IQ > 70, and 49 children had IQ < 70. All children with mental retardation had symptomatic/cryptogenic epilepsy. Behavioral difficulties were present in a majority of cases: hyperactivity (54.21%), difficulties in socialization (81.92%), immaturity (67.46%), aggressiveness (56.62%), hostility and oppositional behavior (78.31%). Between children with epilepsy and behavioral difficulties and/or mental retardation 52 showed marked interictal epileptiform discharges at EEEG and 43 showed the onset of epilepsy in infancy.

**Conclusion:** Children with epilepsy often associate mental retardation and behavioral difficulties. These problems are more frequent in children with symptomatic/cryptogenic epilepsy where the seizures are not completely controlled by antiepileptic medication, the age of onset of epilepsy is smaller and EEG display interictal epileptiform discharges. These results show that it is important an accurate analysis and follow up of the neuropsychological competences at children with epilepsy.
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PSYCHIATRIC DISORDERS IN PATIENTS WITH EPILEPSY
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Purpose: The aim of the study is to find the prevalence of four major psychiatric disorders in outpatients with epilepsy and to determine if there is any kind of correlation between psychiatric disorders and seizures types.

Method: We included in our study 410 patients presented at our outpatient Epilepsy Center, Service of Neurology, University Hospital Center “Mother Theresa” from January to October 2013.

Results: We found 48 patients (11.7%) with anxiety disorders not considering specific subtypes of them. Anxiety disorders were more frequent in cases with altered or loss of consciousness such as in temporal focal and generalized tonic-clonic seizures. Psychoses affect 10 patients (2.43%) particularly in cases with aura or altered consciousness of temporal lobe but frontal lobe epilepsy is also common. Depression disorders, not specifically divided, were found in 20 patients (4.9%) which correlates with the duration of the disease, intractable seizures, and polytherapy. Two patients (0.49%) had suicidal attempts without causing death. Mental retardation was found in 16 patients (3.9%) especially in patients with seizures beginning since infancy. The overall prevalence of four major psychiatric disorders in our group of patients with epilepsy was found to be nearly 23.4% (96 patients).

Conclusion: The main psychiatric disorders were found to correlate with duration of the disease, alteration or loss of consciousness, intractability of seizures and polytherapy treatment.

p705
SUBSTANCE USE DISORDERS AND PSYCHOTIC DISORDERS IN EPILEPSY: A POPULATION-BASED REGISTRY STUDY
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Purpose: Epilepsy affects a large number of people worldwide. Psychiatric comorbidities may add to the burden of the disease. We studied the five-year prevalence of substance use disorders and psychotic disorders among people with epilepsy from a population-based perspective using registry data.

Method: The Norwegian Patient Register is nationwide and contains diagnostic codes according to ICD-10 as assigned by Norwegian specialist health services (hospitals and outpatient clinics). Our research file contained diagnostic information for individuals born 1930–1994 registered with a diagnosis of epilepsy (ICD-10 code G40.x) at least once during 2008 – 2012. We compared the proportion registered with diagnoses related to substance use disorders or psychotic disorders in this population to similar figures in the general Norwegian population.

Results: Being registered with a diagnosis of alcohol use disorder was 4.42 (95% CI 4.22–4.62) times more frequent among people with epilepsy than in the general population, while a drug use disorder diagnosis was 3.86 times more frequent (95% CI 3.67–4.06). Similar figures for all psychoses combined, schizophrenia spectrum disorders and bipolar disorders were 2.96 (95% CI: 2.80–3.12), 2.94 (95% CI: 2.71–3.19), and 2.29 (95% CI: 2.10–2.49), respectively.

Conclusion: Diagnoses of substance use disorders and psychotic disorders were more frequent in people with epilepsy than in the general population. Psychiatric comorbidity requires particular attention both in the diagnostic work-up and in the management of epilepsy.
nia, a key symptom of major depression, in the kainic acid rat model for temporal lobe epilepsy (TLE).

**Method:** Anhedonia was assessed in kainic acid (KA) and saline (SAL) injected rats using the saccharin preference test (SPT). To exclude differences in taste perception, the quinine aversion test (QAT) was performed. Both groups were randomly subdivided in a VNS and a SHAM group, yielding 4 experimental arms: KA-VNS (n = 7), KA-SHAM (n = 7), SAL-VNS (n = 7) and SAL-SHAM (n = 8). Both VNS groups received 2 weeks of VNS, while the SHAM groups were not stimulated. Thereafter, the SPT and QAT were repeated.

**Results:** In the SPT, the KA groups showed a significantly lower saccharin preference compared to the SAL groups (results are expressed as median and IQR): 19.4% (60.0%), 10.3% (7.0%), 97.5% (5.0%) and 97.2% (4.0%) for the KA-SHAM, KA-VNS, SAL-SHAM and SAL-VNS group respectively (p < 0.05). No differences in aversion towards quinine were found: 6.3% (4.0%), 8.0% (18.2%), 6.7% (8.4%) and 7.7% (18.6%), (p > 0.05), showing that taste perception was not compromised after KA-induced status epilepticus. Two weeks of VNS significantly increased the saccharine preference in the KA-VNS group: 10.3% (7.0%) before treatment vs. 71.1% (81.0%) after treatment (p < 0.05), while it had no effect on quinine aversion. No effects of VNS or SHAM were found in the other groups.

**Conclusion:** VNS reduced anhedonia in the KA model for TLE, indicating that VNS could likewise diminish depressive symptoms in patients suffering from TLE and comorbid depression.

**p708**

**PECULIAR PROPERTIES OF ELECTROENCEPHALOGRAPHIC CHANGES IN CHILDREN WITH AUTISM SPECTRUM DISORDER AND SPEECH DISTURBANCES**

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**Purpose:** To assess electroencephalographic (EEG) changes in children with autism spectrum disorder and speech disturbances.

**Method:** Pre-school children with autism spectrum disorders and speech disorders (n = 56) were included in the first group. The control group consisted of children (same age) with mild delayed speech development without organic brain damage (n = 42). Boys dominated in both groups (79% and 74%, respectively). Long-term EEG-monitoring including night or daytime sleep was performed in all 98 patients. Investigations were carried out according to standard procedures using the international system of electrode placement "10-20". Children with diagnosed "epilepsy" were excluded from the study. We calculated Risk Ratio (RR) and 95% confidence intervals with Review Manager 5.2 for comparisons of frequency of occurrence of epileptiform discharges in children with autism spectrum disorder and control group.

**Results:** EEG abnormalities (regional and generalised epileptiform activity) were found in 11/56 children (19.6%) in the study group and 1/42 (2.4%) in the control group; RR = 8.25 [95% confidence interval: 1.11–61.43]; p = 0.04. 27% of children in the first group had regional epileptiform activity in the left or right temporal-occipital areas. 27% had typical Rolandic spikes, other patients had epileptiform discharges in different regions.

**Conclusion:** Electroencephalogram of children with autism spectrum disorders is often associated with epileptiform EEG changes (especially in the centromesiofrontal [Rolandic] and temporal-occipital areas).

**Conflicts of Interest:** None.

**p709**

**SLEEP DISORDERS IN PATIENTS WITH DRUGRESISTANT FOCAL EPILEPSIES**

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**Purpose:** Sleep disorders are one of the most common comorbidities in epilepsy patients. Nonetheless, they are poorly described in the literature and not related with its potential impact on the quality of life. The aim of our work is to analyse the prevalence and category of sleep disorders in a population of focal pharmacoresistant epilepsies.

**Method:** We prospectively evaluated a consecutive group of patients admitted to our Epilepsy Monitoring Unit using PSQI, ESS and Qolie-10 tests during the first day of evaluation and before AEDs were reduced and seizures facilitated.

**Results:** 166 patients were analyzed. From the whole group, 103/166 (62%) showed a score indicative of “bad sleep quality” on PSQI. In the ESS, 41/137 patients (29%) scored for increased daily somnolence. Lower QOLIE scores were significantly correlated with daily somnolence. Anxiety and depression measured by STAI and BDI correlated with lower sleep quality on PSQI. We did not found any significantly statistically difference between subcategories of focal epilepsies.

**Conclusion:** The prevalence of sleep disorders in patients with refractory epilepsy is high. Daily somnolence seems to be directly related with quality of life. Possibly, there exist a narrow connection between sleep disorders and psychiatric symptoms. No differences between epilepsy forms were found.

**p710**

**DO EPILEPTIFORM ABNORMALITIES ON EEG AT ADHD ASSESSMENT INFLUENCE ON THE USE OF METHYLPHENIDATE, ANTIEPILEPTIC DRUGS AND EPILEPTIC SEIZURE OCCURRENCE DURING TWO YEARS FOLLOW-UP?**

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**Purpose:** The purpose of this retrospective study was to investigate whether epileptiform abnormalities (EA) recorded on EEG at the attention-deficit/hyperactivity disorder (ADHD) assessment in children without previous epilepsy influence on the use of methylphenidate (MPH), antiepileptic drugs (AED) and epileptic seizure occurrence during two years follow-up.

**Method:** Subjects were 517 ADHD children (82.4% male), aged between 5 and 14 years, mean 9.5 ± 2.6, who were diagnosed between January 2000 and December 2005 who performed at least one standard EEG at ADHD assessment. EA were found in 27 cases although they had no previous epilepsy (EA group). These 27 cases were matched on age and gender and compared with 27 cases without EA (non-EA group). Measure outcomes were: the use of AED, the use of MPH and epileptic seizure occurrence during two years follow-up.

**Results:** At baseline of the 27 cases from EA group, 10 (37%) were on AED. 24 of 27 children were treated with MPH, and initial positive response to MPH was achieved in 20/24 (83.3%). In the non-EA group,
25 of 27 cases were treated with MPH, and 22/25 (88%) had documented positive effect of MPH treatment. At one and two years follow-up, 20/24 (83.3%) and 19/24 (79.2%) cases from EA-group used MPH compared to 22/25 (88%) and 18/25 (72%) cases from non-EA group. AEDs at one year follow-up were used in 10 patients, and at two years follow-up in 2 cases from EA group. Nobody from non-EA group was treated with AED. In addition, epileptic seizure occurrence was not recorded in any case during the study.

Conclusion: The EA occurrence at ADHD assessment in children without previous epilepsy was not associated with diminished use of MPH or with epileptic seizure occurrence, but it was related to temporary use of AED.

p711 DEPRESSION AND ANXIETY IN A GROUP OF SEVENTY PATIENTS WITH EPILEPSY
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Purpose: The aim of this study was to investigate the interaction between psychiatric co morbidities (depression and anxiety) and epilepsy in outpatient Clinic for epilepsy in Clinical Centre of Montenegro.

Method: Patients with a diagnosis of epilepsy according to the ILAE criteria were consecutively enrolled in a study during six months. Total number of included patients was seventy- forty patients with partial and thirty patients with idiopathic generalized seizures. They were administered two tests – Hamilton Depression Scale (HAM-D) and Hamilton Anxiety Scale (HAM-A) for the evaluation of depression and anxiety.

Results: Prevalence of depression in our sample was 24.2% whereas anxiety was present in less than 10%. Patients with partial seizures, especially patients with temporal lobe epilepsy, were more depressed contrary to the patients with idiopathic generalized seizures who were more anxious. Depression was associated with unemployment, marital status and number of seizures (p < 0.05). Anxiety was associated with the higher number of seizures and number of medications (polytherapy) (p < 0.05). Both depression and anxiety were not associated with education or gender.

Conclusion: Psychiatric problems among patients with epilepsy are common and often overlooked and thus integrated psychiatric and neurological care is needed in order to achieve good quality of life in these patients.

p712 MISDIAGNOSIS OF EPILEPTIC SEIZURES AS PSYCHOGENIC – A RARE PROBLEM
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Purpose: Compared to the misdiagnosis of psychogenic seizures as epileptic little is known about the reverse problem: epilepsy being misdiagnosed as psychogenic fits. The purpose of this study was to evaluate this in a population of in-patients who were referred to our centre for the first time.

Method: In this retrospective study files of 138 in-patients were analyzed with regard to an epilepsy misdiagnosed as psychogenic seizures in the past. Reasons for diagnostic errors were evaluated.

Results: 138 patients (median age 42 years [range: 20–76]) were scanned. 7 (5%) of them (median age 29 years [range: 24–65]) had been misdiagnosed with psychogenic seizures prior to admission. Duration of symptoms before revised diagnosis was 1–7 years (median 3 years). Most patients showed dyscognitive seizures, one patient predominant hypomotor and tonic seizures (up to 150 per day), one tonic seizures plus psychogenic seizures. Interictal EEG was normal in 3 patients (all with normal MRI). Ictal EEG was normal in one patient (with lesion in gyrus cinguli and tonic seizures). In this patient a co-existence of epileptic and non-epileptic seizures was found.

Conclusion: Misdiagnosis of epileptic seizures as psychogenic is rare. Risk factors have to be discussed on the base of the individual cases.

p713 EPILEPSY AS PSYCHOLOGICAL PROBLEM
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Purpose: It is known that chronic illness such as epilepsy, are connected with psychological problems. The aim of study was to determine level of depression and correlation of depression with frequency of epileptic seizures at patients with epilepsy.

Method: First group included 100 patients (50 males and 50 females), with generalised tonic-clonic seizures; second group included 100 patients (50 males and 50 females), with simple focal seizures. Actual age, epilepsy duration, frequency of epileptic seizures were determined. The depression level was measured by Hamilton’s Depression Scale, and data were analysed by appropriate statistical tests (F test, Pearson Correlation Coefficient).

Results: Actual age, average age on time of the first seizure, average duration of illness, in both group were similar. In first group, there was no gender significant difference according to medium value of depression level (p > 0.05). Frequency of seizures was in positive correlation with depression level in both sexes, (r = 0.64 in female; r = 0.51 in male). In second group, the average score value of Hamilton Scale at males was 8.3 ± 5.9, in comparison to 8.3 ± 6.0 at females, while there was no significant difference (p = 0.97). Having no symptoms of depression there were 31 males (62%) and 32 females (64%). Less expressed depression was at 16 (32%) males and 12 (24%) females, while 6 (12%) females had strong depression symptoms in comparison to 3 (6%) males, which has no statistical importance (p = 0.238).

Conclusion: Patients with epilepsy suffered mainly with mild depressive symptoms. Frequency of seizures is in positive significant correlation of depression level.

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p715 CHANGE IN ASTROCYTIC CA2+ RESPONSE DURING THE LATENT PERIOD OF EPILEPTOGENESIS IN THE ADULT MOUSE
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Purpose: Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis (MTLE-HS) is associated with perturbed ion and water homeostasis and neuronal cell death, possibly due to impaired function of glial cells. Pro-
tein level changes of AQP4, the main water channel in the brain and Kir4.1, the main Kir channel expressed by astrocytes have been associated with chronic epilepsy. Beside water and ion homeostasis astrocytes are also involved in the signal processing of the brain due to their Ca$$^{2+}$$ based excitability. Increase in cytosolic Ca$$^{2+}$$ levels in astrocytes may lead to glutamate release which under pathological conditions may lead to epilepsy. These changes have been associated with epileptic conditions like MTLE-HS but whether they are cause or consequence and at which time point they occur is yet unclear.

Method: Parahippocampal kainate injection in C57B16 WT vs. rAAV coding GCaMP5 (genetically encoded Ca$$^{2+}$$ indicator) injected mice with GCaMP5 expressed in hippocampal astrocytes, were used. We focused on changes at day 1, 3 and 7 representing the latent period of epileptogenesis and the early chronic phase, respectively.

Results: For validation of the model we performed AQP4 and Kir4.1 immunostaining and found an initial decrease at 1d followed by a gradual increase. Optical imaging of stimulation evoked network activity in hippocampal astrocytes in adult animals showed an increase in amplitude and duration of Ca$$^{2+}$$ responses of cell bodies and processes at 1 and 3d post SE. This increase could be attenuated by metabotropic glutamate receptor (mGlur) antagonists, alpha-methyl (4-carboxy-phenyl) glycine (MCPG) and 2-methyl-6-(phenylethynyl)-pyridine (MPEP).

Conclusion: Enhanced astrocytic Ca$$^{2+}$$ signaling in the early phase after SE may contribute to excitotoxicity and epileptogenesis in MTLE-HS. The latent period of epileptogenesis may provide an important target for pharmacological intervention.

EPILEPTIC SEIZURES IN NEURO-BEHÇET DISEASE
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Purpose: Behcet Disease (BD) is a chronic relapsing inflammatory disorder. Neuro BD (NBD) is seen in approximately 5% of all patients. In this article, we evaluated the frequency and type of seizure in NBD

Method: A total forty-two patients with NBD were evaluated between 2006 and 2012 retrospectively. The demographic data, the presentation of NB, clinical findings including seizures, EEG and neuroimaging findings were reviewed.

Results: The mean age of patients was 35.02 ± 8.43. Thirty (71.4%) patients were male; the remaining twelve of them were female. Twenty-four patients had parenchymal involvement; sixteen patients had non-parenchymal involvement. Spinal involvement was seen in two patients. Seven patients had epileptic seizures (six partial seizure). Five of them had dural sinus thrombosis. Four patients had a seizure as the first symptom of the thrombosis. One patient had late onset seizure due to chronic venous infarct. The other patient with seizure had parenchymal involvement. The remaining one was diagnosed as juvenile myoclonic epilepsy before NBD.

Conclusion: The seizure may be observed during the course of NBD. Seizures frequently were due to the dural sinus thrombosis in NBD. Seizures may also observe in parenchymal involvement. Behçet disease and JME was seen in the same patients, it was co- incidental or not. Further investigation should be necessary.

HYPOGLYCAEMIA AND RISK OF SEIZURES: A RETROSPECTIVE CROSS-SECTIONAL STUDY
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Purpose: Few studies have been dedicated to assess neurological symptoms in relations to hypoglycaemia. In this study we investigated the association between different levels of hypoglycaemia and the occurrence of epileptic seizures in patients without a prior diagnosis of epilepsy.

Method: A retrospective cross-sectional study.

Results: From a laboratory database in a Swedish regional hospital we identified 388 patients who between January and December 2009 were found to have a glucose value of ≤5.5 mm. Cases were obtained by a search in the database for all values of serum glucose. Hypoglycaemia was defined at three different categories according to the International League Against Epilepsy’s cut of value for hypoglycaemia; 0–2 mm, 2.1–3 mm and 3.1–3.5 mm. 40 patients were identified in the interval 0–2 mm and 154 patients between 2.1 and 3 mm. In the interval 3.1–3.5 mm 194 patients were randomly selected from a group of 486 patients. Medical records of every patient were carefully scrutinized for information about clinical variables, seizures or other disturbances of consciousness within 24 h of sampling time. When glucose levels dropped below 2.0 mm nine patients out of 40 had coma and only one had a generalized tonic-clonic seizure. One patient with focal seizure was identified in the interval 2.1–3 mm and one between 3.1 and 3.5 mm. The absolute risk (95% confidence interval) for having major neurological symptoms at glucose levels ≤2.0 mm was 0.25 (0.13–0.41), 0.020 CI (0–0.06) at 2.1–3.0 mm and 0.01 (0–0.03) at 3.1–3.5 mm.

Conclusion: Coma is the major neurological symptom related to hypoglycaemia. Epileptic seizures are rare and not as common as previously assumed.

IMMUNOLOGICAL PARAMETERS IN EPILEPSY
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Purpose: 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, BNP, and S100β) 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 ± 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 S100β in epilepsy patients, greater in idiopathic epilepsy, compared to control (54.3 ± 10.3; 39.4 ± 10 and 5.8 ± 1.3 CU, respectively, \( p < 0.001 \)). The levels of AAB to MBP were high in the first group (14.9 ± 4.9 CU, \( p < 0.001 \)), while in the second group were low (2.6 ± 4.3 CU), in comparison with control (8.0 ± 4.7 CU). The levels of AAB to GFAP were higher in symptomatic epilepsy (13.9 ± 7.9 CU, \( p < 0.001 \)). Patients with idiopathic epilepsy had higher (22.0 ± 6.7 CU) levels of AAB to
NF-200 vs. patients with symptomatic epilepsy (11.4 ± 6.4 CU) (0 < 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.

**p719**

**POSTSTROKE EPILEPSY AND FUNCTIONAL OUTCOME**

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**Purpose:** To determine the influence of post-stroke epilepsy on long-term functional outcome in stroke survivors.

**Method:** This study is a prospective cohort study among 140 stroke survivors with a first-ever TIA, ischemic stroke, or intracerebral hemorrhagic (ICH) stroke, aged 18–90 years. After a mean follow-up of 10 years, we performed a follow-up assessment that included an evaluation for post-stroke epilepsy and functional outcome. Odds ratios for poor outcome on the modified Rankin Scale (mRS) (score>2) and Instrumental Activities of Daily Living (IADL) (score< 8) were calculated using logistic regression analysis.

**Results:** One hundred twelve patients (80%) with ischemic stroke, 4 patients (2.8%) with TIA, and 28 patients (20%) with ICH developed post-stroke epilepsy. Ischemic stroke patients with epilepsy more often had a poor functional outcome than those without, both on the mRS and IADL (mRS score>2: 24.5% vs. 9.2%, p = 0.001; IADL< 8: 28.8% vs. 14.6%, p = 0.02). In this case, epilepsy occurred in 24.5% of patients with cardioembolic stroke. Epilepsy was not related to functional outcome in patients with TIA and ICH. Multiple regression analysis revealed that epilepsy was an independent predictor of poor functional outcome after ischemic stroke assessed by mRS (mRS score>2: odds ratio 4.02, 95% confidence interval 1.33–8.60). In contrast, there was no such relation for IADL.

**Conclusion:** Epilepsy after stroke is a common problem that negatively affects functional outcome, even more than 10 years after ischemic stroke.

**p720**

**INFLUENCE OF OXCARBAZEPINE (OXAPINE) ON COGNITIVE FUNCTIONS IN EPILEPSY**

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**Purpose:** Oxcarbazepine (a keto-homologue of carbamazepine), like lamotrigine, acts through modulation of the voltage-dependent sodium channels.

**Objective:** To study effect of oxcarbazepine on cognitive functions in adult patients with epilepsy.

**Method:** We studied 48 patients with partial seizures (mean age – 33.8 ± 15.3 y.o.) who had not previously treated with other AEDs. All patients received monotherapy with oxcarbazepine in different doses (300; 600 and 1200 mg/day). The patients were followed-up for over six weeks. We conducted EEG, assessed cognitive functions by using MMSE scale, test to memorize five words, clock drawing test and test for speech activity. The primary measure of effectiveness was a between-group comparison of the percentage of patients meeting exit criteria.

**Results:** The results were statistically significant in favor of the oxcarbazepine 1200 mg/day group (on 14.2% and 14.8%) compared to the oxcarbazepine 300 mg/day and 600 mg/day group (p = 0.0001). The time to meeting one of the exit criteria was also statistically significant in favor of the oxcarbazepine 2400 mg/day group, (p = 0.0001), however, we observed CNS side effects in ≥5% of patients treated with oxcarbazepine 2,400 mg/day. The best results on cognitive functions were observed in the oxcarbazepine 1,200 mg/day group. The worse effect by influence as on seizures, as on cognitive functions was marked in the oxcarbazepine 300 mg/day group.

**Conclusion:** Treatment with oxcarbazepine should be initiated with a dose of 600 mg/day, given in a BID regimen. If clinically indicated, the dose may be increased by 300 mg/day at approximately weekly intervals to a dose of 1,200 mg/day. Daily doses above 1,200 mg/day show somewhat greater effectiveness in controlled trials, but most patients were not able to tolerate the 2,400 mg/day dose, primarily because of CNS effects. Thus, oxcarbazepine is effective at a dose of 600–1200 mg/day and improves cognitive functions in most epilepsy patients.

**p721**

**CLINICAL VALUE OF SIMULTANEOUS EEG AND FUNCTIONAL MRI FOR EPILEPSY DIAGNOSIS AND TREATMENT**

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**Purpose:** EEG correlated functional MRI (EEG-fMRI) studies revealed substantial predictive value compared to invasive EEG and surgical outcome [van Houdt P et al. Neuroimage 2012; 60 (4):2042–53. 2013; 75:238–75]. The goal of the present study was to deal with limited sensitivity of EEG-fMRI [van Houdt P et al. MRI 2012; 28 (8):1078–86] by applying network analysis strategies to elaborate the clinical usefulness in epilepsy.

**Method:** EEG-fMRI data have been acquired for 10 patients with focal epilepsy. The patients were scanned twice: before the start of pre-surgical video-EEG and at the end, after medication withdrawal. fMRI activation maps were created with the general linear model and with independent component analysis (ICA). In addition, sliding-window based functional connectivity mapping was applied to model the fMRI brain network alterations that co-occur with interictal epileptic discharges (IEDs).

**Results:** EEG-fMRI was successful for only 3 out of 10 patients before the start of the video-EEG session, while an EEG-fMRI correlation map was obtained for all patients at the end of the session. Spatial correlation of this map with the ICs revealed an epileptic IC which coincided for both conditions with the electroclinically identified epileptogenic region. Dynamic mapping of the network alterations indicated, furthermore, that increased functional connectivity in the epileptogenic region is proportional to the number of IEDs in the given interval.

**Conclusion:** In case there is no a priori information available, the increased occurrence of IEDs at the end of a video-EEG session is essential to identify both position and dynamical changes of the epileptogenic region.

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CASE REPORT OF ASYSTOLE AND REACTIVE ANOXIC SEIZURES DUE TO EXTRA-ADRENAL PHEOMOCROMOCYTOMA

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Purpose: This is a rare case of reactive anoxic (due to asystole) seizures triggered by extra-adrenal pheochromocytomas localized in common carotid artery and aortic arch.

Method: 68 years old female, known to have DM, HTN, old CVA presented repetitive episodes of starings (motor arrest with eye up rolling for max 10 s) mainly triggered by neck positioning. Frequency of attacks was 10 per day. Seizures were associated with high blood pressure up to 260/140 mmHg. Brain MRI showed right basal ganglia old lacunar stroke. Carbazepine started in 200 mg TID with therapeutic serum level but frequency of seizures were increased. Interictal and Ictal EEG showed diffuse polymorphic delta slowing. Baseline ECG and Echo was normal. Glucose was 9.1 mmol/l during and after the attacks. Blood work up for CBC, Biochemistry, Immunology, TFT, Vitamin B12 were normal.

Results: Total catecholamines, vanillylmandelic acid, and metanephrines were significantly elevated in 24-hour urine. ECG Holter monitoring showed frequent patterns of asystole in duration of 24–29 s preceded by blood pressure elevation. MRI of adrenal glands did not reveal tumor or hyperplasia. Sцинтigraphy showed evidence of extra-adrenal pheochromocytoma localized in common carotid artery and aortic arch. Patient was implanted with cardiac pacemaker and started on alpha blockers.

Conclusion: Extra-adrenal pheochromocytomas or paragangliomas affecting the carotid artery stretching the carotid baroreceptors along with hypertension and causing bradycardia and even cardiac arrest.

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SEXUAL DYSFUNCTION AND SEXUAL WELL-BEING IN PEOPLE WITH EPILEPSY IN NORWAY

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Purpose: To investigate the prevalence and type of sexual problems and sexual well-being in patients with epilepsy compared to a representative sample of the Norwegian population.

Method: 175 of 202 consecutive adult patients with epilepsy (response rate 87%) and their neurologist at an epilepsy centre participated in a questionnaire based survey about epilepsy, sexual problems and well-being. Data from a representative study among 594 adult Norwegians was eligible for comparison (response rate 54%).

Results: Compared to the general population, patients with epilepsy reported statistically significant (p < 0.001) higher prevalence of sexual problems (11% vs. 69%) and lower sexual well-being (65% vs. 47%). Commonly reported problems among the patients were reduced sexual desire (women 52%, men 26%), orgasm problems (women 35%, men 13%), erection problems (men 34%), vaginal dryness (women 31%), pain during intercourse (women 27%, men 1%) and premature ejaculation (men 16%). There was a significant correlation between sexual problems and quality of life (p < 0.05) as well as having had epilepsy more than 10 years (p < 0.05). We found no correlation between sexual problems and type of epilepsy, age of epilepsy onset or use of enzyme inducing antiepileptic drugs was found.

Conclusion: Sexual problems are common in patients with epilepsy and their sexual well-being is reduced. The type of epilepsy or antiepileptic treatment was not directly associated with sexual problems and well-being. Psychosocial factors may be of greater importance. The study sheds light on an important but often neglected aspect of epilepsy.

p724

THE VALUE OF LUMBAR PUNCTURE IN THE DIAGNOSTIC EVALUATION OF A FIRST UNPROVOKED SEIZURE

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Purpose: Few studies have evaluated the contribution of lumbar puncture (LP) in the diagnostic workup of a first unprovoked seizure. Data concerning its routine use in such cases is conflicting. This retrospective study aimed to collect and analyze data regarding the diagnostic value of LP in the investigation of the first unprovoked seizure in adult patients.

Method: A LP was routinely performed in every patient with a first unprovoked seizure admitted to the Department of Neurology of Evangelismos General Hospital between 1.1.2011 and 31.8.2013. We retrospectively recorded demographic data, seizure type, LP results (cell count, CSF/serum glucose ratio, total protein), anti-epileptic drug treatment and final diagnosis. A LP was considered as either significantly or non-significantly abnormal (SA or NSA, respectively) depending on whether its abnormal results contributed to the etiologic diagnosis of seizures or not.

Results: We recorded 78 patients (49 male, 29 female). The mean age was 37.8 ± 16.9 years. Thirty-four patients (43.6%) had a NSA and 6 (7.7%) a SA-LP. Among those with a SA-LP, 4 had an abnormal CSF leukocyte count (<5/mm³) and 2 had abnormal CSF leucocyte count and CSF protein concentration (<0.45 g/l). Compared to patients with normal LP, those with NSA-LP are older (42.8 ± 17.3 vs. 34.1 ± 15.8 years, p = 0.025) and have a higher in-hospital mortality rate (8.8% vs. 0.0%, p = 0.044). Patients with SA-LP stay in hospital longer compared to those with normal LP (15.5 ± 13.0 vs. 6.0 ± 5.2 days, p < 0.001).

Conclusion: LP had possible diagnostic and relevant prognostic value in 7.7% of adult patients with a first unprovoked seizure. Considering that the results of the SA-LPs did not lead to treatment modification, but only contributed to a possible etiologic diagnosis (encephalitis), we should not suggest the routine use of lumbar puncture in all adult patients with a first unprovoked seizure.

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INJURIES IN EPILEPSY-SEIZURE RELATED

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Purpose: Seizure-related injuries are defined as any injury-trauma, resulting from a seizure, sufficient for the patient to seek medical atten-
tion. We evaluated the risk, type and circumstances of injuries due to epileptic seizures.

**Method:** A questionnaire regarding the traumatic consequences due to seizures we administered to 298 consecutive patient with epilepsy (newly diagnose patient were excluded), 154 female and 144 male, on age up to 18 years admitted to bout departments. Generalized tonic-clonic seizures, complex partial, partial with secondary generalization and myo-clonic seizures, were the most common seizure types.

**Results:** Out of 298 patients, 119 (39.9%) had had at least one traumatic event due to seizures, most of them reported head trauma (65.2%) as follow: cranial soft tissue- contusions or lacerations, dental fractures, epidural hematoma, subdural hematoma and cranial fracture 1 patient. Burns experienced 10%, blunt injury 44%, body wounds 32, bone fractures and dislocations 8%, and traffic accidents 2%, an poly traumas. Domestic accidents prevailed (63.4%), followed by street (27.1%) and work accidents (9.5%).

**Conclusion:** Data showed significant risk associated with seizure-related injuries and facilitate patient counseling how the risk could be minimized. Due to seizure, head trauma (contusions and lacerations) are commonest types of injuries, mostly occurred at home (unemployment, stigma, social isolation).

### Abstracts

**p727 BRAIN NETWORK ORGANIZATION IN FOCAL EPILEPSY: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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**Purpose:** Normal brain functioning is presumed to depend upon the complex though efficient interplay of interacting regions within large-scale neuronal networks. There is increasing evidence for an association between interictal network alterations and cognitive and behavioral deficits in people with focal epilepsy. Nevertheless, previously reported network alterations differ between individual network studies and the results are often contradictory in nature. We therefore conducted a meta-analysis to analyze and summarized the existing literature.

**Method:** We systematically reviewed studies focusing on differences in functional and structural networks between healthy controls and patients with focal epilepsy. We summarized the two measures most commonly used in whole-brain interictal network studies: path length (represents network integration) and clustering coefficient (represents network segregation). Summary statistics were determined using random effects meta-analysis. Heterogeneity between included studies was characterized using meta-regression with the average age and epilepsy duration.

**Results:** We included 12 focal epilepsy network studies (in total, 404 patients and 330 controls). The pooled effect showed that networks in focal epilepsy were significantly less integrated (increased path length) as compared to controls, with a standardized mean difference summary estimate of 0.26 (95% confidence interval (CI): 0.10-0.42, p = 0.001). Epilepsy networks were also more segregated (increased clustering coefficient), with a standardized mean difference of 0.35 (CI: 0.05-0.65, p = 0.02). The integrity and segregation effects were similar in extent and direction for functional and structural networks. We found no effect of mean age or epilepsy duration on the effect sizes.

**Conclusion:** These quantitative data supports the suggestion that frequent epileptic seizures in patients with focal epilepsy have widespread detrimental effects on the interictal brain network organization. These network alterations may relate to the co-morbid cognitive and behavioral impairments.

**p726 LITERATURE ABOUT EPILEPSY STORIES FOR CHILDREN. THE USE OF EPILEPSY STORIES AT A NATIONAL EPILEPSY HOSPITAL IN NORWAY. THE PURPOSE OF THE ONGOING PROJECT (2010–2017) IS TO SPREAD CHILDREN’S EXPERIENCES WITH EPILEPSY, PRIMARILY IN CONVERSATIONS WITH CHILDREN AND THEIR PARENTS. THE PROJECT ARE RUN BY EXPERIENCED EPILEPSY NURSES**

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The purpose of the project has been to spread children’s own experiences with epilepsy, informing children about epilepsy in their own language. Also, it is meant to be a tool for making good conversations, and to empower patients and families to tell their own stories, to give associations to their own experiences with epilepsy, informing children about epilepsy in their own language. Also, it is meant to be a tool for making good conversations, and to empower patients and families to tell their own stories, to give associations to their own experiences with epilepsy. They specifically valued the direct and honest language, comparing categorical and continuous variables respectively.

The methods used, in the period between December 2010 and January 2014 have been: educating parents at the hospital every forthnight (60 education sessions), group sessions for children (almost every week), grandmothers (FB, PT, MS, PA). Clinical variables in patients with and without IIH and PIH were analysed:

out IIH and PIH were independently reviewed by headache experts (SC, PC) and epilepsyologists (FB, PT, MS, PA). Clinical variables in patients with and without IIH and PIH were analysed:

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<th>Variable</th>
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<td>PIH</td>
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**Purpose:** To explore the prevalence and the clinical features of interictal (IIH) and peri-ictal headache (PIH) in patients with epilepsy.

**Method:** All patients with epilepsy aged ≥ 17 years were consecutively recruited from March 2011 to May 2011 and from March 2012 to July 2012 at the Epilepsy Center of IRCCS Institute of Neurological Sciences of Bologna. They underwent an ad hoc semi-structured interview assessing the prevalence and clinical features of IIH and PIH. The clinical files were independently reviewed by headache experts (SC, PC) and epilepsyologists (FB, PT, MS, PA). Clinical variables in patients with and without IIH and PIH were analysed: χ²-test and t-test were performed to compare categorical and continuous variables respectively.
Results: Out of 398 enrolled patients (215F, 183M, mean age 41.28 ± 15.68), 48.49% had IIH: 26.58% had migraine (including a few cases of migraine with aura), 20.85% had tension-type headache, a few patients had other types of headache. PIH was observed in 23.36% of patients (93), occurring pre-ictally in 26 cases, ictally in 3 and post-ictally in 75 (11 patients had two different types of PIH). Out of 105 patients with interictal migraine, 47.61% had PIH (p < 0.0001), that was pre-ictal in 17.14% (p < 0.0001) and post-ictal in 39.04% (p < 0.0001). There were no significant associations with the epilepsy syndrome (generalized or focal). Post-ictal headache had migraineous features in 50.66% of patients and tension-type headache-like in 40.00%. The occurrence of post-ictal headache was significantly associated with antiepileptic drug polytherapy (p < 0.0001), high seizures’ frequency (p = 0.001) and the presence of IIH (p < 0.0001).

Conclusion: These data show that migraine is the most represented type of headache in our patients. Subjects with interictal migraine resulted more prone to develop both pre-ictal and post-ictal headache. The occurrence of the latter is higher in patients with polytherapy, high seizures’ frequency and coexistence of IIH.

p729
TWO CASES OF CHOREA-ACANTHOCYTOSIS WITH EPILEPSY
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Purpose: We aimed to present two cases of Chorea-acanthocytosis (ChAc) whose initial manifestations were epileptic seizures. Case 1: A 42-year-old woman with newly onset unprovoked seizures admitted to our clinic and diagnosed as epilepsy with complex partial secondarily generalized seizures. Electroencephalography (EEG) revealed right fronto-central spikes and oxcarbazepine was started. After the four years of follow-up, chorea and involuntary oral biting occurred. Cerebral magnetic resonance imaging (MRI) showed bilateral caudat nucleus atrophy and acanthocytes were detected at blood smear. She was diagnosed as ChAc. Case 2: A 39-year-old woman admitted to our clinic with involuntary movements and gait disorder. Neurologic examination revealed chorea, bizarre gait, involuntary oral biting and tics. She had a history of recurrent seizures and was taking carbamazepine for one year. Seizures were complex partial-secondarily generalized and EEG revealed right temporal spikes. Cerebral MRI showed bilateral caudat nucleus atrophy and acanthocytes were detected at blood smear. She was also diagnosed as ChAc.

Conclusion: Seizures may be the initial manifestation of ChAc. It should be kept in mind in adult onset epilepsy patients with movement disorders like chorea, tics, unstable or bizarre gait and oral mutilation.

p730
NATIONAL REGISTRY OF DRAVET’S SYNDROME AND OTHER SYNDROMES CORRELATED WITH GENES SCN1A AND PCDH19
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Purpose: Epidemiological surveillance of Rare Diseases through Patient Registers has been recognized as one of the priorities in the Public-Health-Programme strategic intervention of the European Commission. Dravet Syndrome (DS), also known as Severe Myoclonic Epilepsy of Infancy, is a rare epileptic encephalopathy with onset in the first year of life with recurrent epileptic seizures, precipitated by fever, and progressive neurodevelopmental disability in the following years. Some clinical features of DS are shared by other rare syndromes due to SCN1A or PCDH19 genes mutations. In order to develop new therapeutic solutions and social-health services to improve patients’ quality of life, the “Dravet Italia” – a Non-profit Association (http://dravetitalia.org/) – promoted the development of the Italian Registry of DS and other Syndromes related with SCN1A or PCDH19 genes mutations (ReSiDraS).

Method: The ReSiDraS has been developed by a multifaceted working group consisting of expert clinicians (www.dravetitalia.org/it/comitato-medico-scientifico), representatives of Patient Associations, and experts in Disease Registries, as well as Information Technologies specialists by the FTGM-CNR (www.ftgm.it). The working group, after careful data analysis, has identified the data needed and the registry structure. The FTGM implemented the registry in a web-based format, accessible through authentication of certified users via username and password. Data will be gathered by users after receiving the patients’ parents informed consent.

Results: The web-based ReSiDraS registry is now ready and the version is currently under evaluation in order to remove any possible bug before the official release. We aim to start collecting data from the entire Italian territory by the end of 2014, reaching a full coverage within few years.

Conclusion: The data collected by ReSiDraS will allow us a better understanding of the clinical, genetic, and epidemiological aspects of the different diseases included, possibly shedding light on genotype-phenotype correlations, drugs currently used and their efficacy, comorbidities, and long-term outcome.

p731
EPILEPTIC SEIZURES IN PEDIATRIC POPULATION WITH BACTERIAL MENINGITIS IN A DEVELOPING COUNTRY
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Purpose: To evaluate occurrence and relevance of seizures in children with community-acquired bacterial meningitis in a public secondary care university hospital in Sao Paulo, Brazil.

Method: A retrospective study in which clinical data of pediatric inpatients with community-acquired bacterial meningitis was reviewed in a 10-year period (2003–2013).

Results: 101 children (70% male), median age 28 months. (IQR 7–69); epileptic seizures occurred in 10 (9.9%). Patients with seizures were younger (median age 15 months [IQR 7–19] vs. 35 months [IQR 7–74]; p = 0.01), had higher median serum leukocyte count (18.5 ± 109/L [IQR 17.3–26.8] vs. 15.8 ± 109/L [IQR 12.0–19.2]; p < 0.001), higher median CSF leukocyte (3.498x10^3 [IQR 264–8,800] vs. 672x10^3 [IQR 161–2,582]; p = 0.03) and higher median CSF protein levels (457 mg/dl [IQR 220–288] vs. 69 mg/dl [IQR 43–157]; p < 0.001) than patients without seizures. From 10 patients with seizures, in 4 pneumococcus (all these cases occurred before implementing free public pneumococcus immunization for infants in 2010 in the country) was isolated in CSF, in 3, meningococcus, in one, type-A Haemophilus and in two, no agent was identified. Neuroimaging was done in 42% of patients and in all episodes with seizures, revealing a focal lesion in 8% of patients, only one who had seizures. EEG was performed in all seizure episodes and was abnormal in 60% showing focal (30%) or diffuse slowing (30%). One patient had interictal epileptiform activity in frontal regions. Antiepileptic drugs
were administered acutely in all patients who present with seizures. Median time of hospitalization was 9 days (IQR 7–10). Death occurred in 5 (4.9%) cases, in which no epileptic seizures were diagnosed.

Conclusions: In this retrospective study, performed in a public secondary care university hospital in Sao Paulo (Brazil) with data of children with community-acquired bacterial meningitis, seizures were more associated with younger age, severe systemic and central nervous system inflammation and pneumococcal meningitis.

**p732**
**HYPMAGNESEMIA AND HYPOCALCEMIA MIMICKING SYMPTOMATIC FOCAL EPILEPSY: A CASE REPORT**
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**Introduction:** Electrolyte disturbance due to prolonged diarrhea can cause a variety of symptoms, which can be misinterpreted in clinical practice. We report a case of severe hypomagnesemia and hypocalcemia that presented with episodes suggestive of focal epileptic seizures.

**Case Presentation:** A 74-year-old male patient was brought to our emergency department with recurrent “epileptic generalized clonic seizures”. Medical history of multiple left middle cerebral artery strokes, systemic borreliosis, coronary heart disease and metabolic syndrome was reported. During the last 2 months, the patient had received treatment for persisting diarrhea and vomiting. On further elaboration, symptoms were described as short clonic jerks of the upper body, followed by generalized tonic extension (HLTE). Animals were divided into 4 groups, Group 1 received PHB (25 mg/kg, i.p.) along with different concentration of Withania somnifera (WS) (750, 1000 mg/kg respectively). MES was induced after 1 hr of extract administration. At the end of 18th day, behavior evaluation was carried out (Elevated plus maze, rota rod, closed field activity and grip strength) and mice sacrificed for estimation of malanodialdehyde (MDA) and reduced glutathione (GSH).

**Results:** While WS (500 mg/kg) treated mice showed 80% incidence of HLTE, H2O2 treated mice showed 100% hind limb tonic extension (HLTE). Animals were divided into 4 groups, Group 1 received PHB (25 mg/kg, i.p.) and after two Hr maximal electric shock (MES) challenge on alternate days for 18 days, HLTE on two consecutive days was taken as endpoint. Group 2, 3 and 4 received PHB (25 mg/kg, i.p.) along with different concentration of Withania somnifera (500, 750 and 1000 mg/kg respectively). MES was induced after 1 hr of extract administration. At the end of 18th day, behavior evaluation was carried out (Elevated plus maze, rota rod, closed field activity and grip strength) and mice sacrificed for estimation of malanodialdehyde (MDA) and reduced glutathione (GSH).

**Results:** The findings suggest that aqueous extract of WS (750, 1000 mg/kg) as adjuvant to PHB may delay tolerance development and also cognitive impairment.

**Conclusion:** The present study included 834 students (ages 19–23; both genders) from Vojvodina. The research was conducted using a questionnaire which consisted of two sections. The first section of the questionnaire was used to determine the socio-demographic characteristics of the study participants, while the second part dealt with student knowledge of epilepsy.

**Results:** The results show that the young people are familiar with epilepsy, to have a basic knowledge of nature of the disease, but due to different subjective attitudes towards epilepsy and patients, can be said that the attitude of the young population toward epilepsy is still based on a low level information and prejudice.

**Conclusion:** We can conclude that there is an adequate level of awareness and knowledge toward epilepsy among the young people in Vojvodina. However, there is still a need for further improvement of certain aspects of knowledge and understanding of the epilepsy.

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**p733**
**VIEWS OF YOUNG PEOPLE TOWARD EPILEPSY IN VOJVODINA**
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**Purpose:** Epilepsy represent a major health and social problem particularly expressed in developing countries. The quality of life of the person affected is significantly compromised due to the negative attitude of general population, which is the result of prejudice, lack of knowledge and awareness of the nature of this condition on the one side or too protective attitude on the other. Society’s attitude is considered as a key obstacle to their equal integration into society. The aim of our research was to estimate the level of subjective attitudes and knowledge about epilepsy.

**Method:** The present study included 834 students (ages 19–23; both genders) from Vojvodina. The research was conducted using a questionnaire which consisted of two sections. The first section of the questionnaire was used to determine the socio-demographic characteristics of the study participants, while the second part dealt with student knowledge of epilepsy.

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Purpose: To find the incidence and importance of Status epilepticus as a prognostic indicator in management of Tubercular Meningitis.

Method: 42 Consecutive Tubercular meningitis cases were registered in 2 year duration (2011 - 2013). Development of hydrocephalus, Status epilepticus, associated hepatotoxicity, concomitant infections were reported within the study interval. With standard biostatistical tools, the prognostic significance was compared with each of these 4 independent factors.

Results: Patients were in various stages of Tubercular Meningitis (TBM) as Stage 1 (15 Patients), stage 2 (21 patients) and stage 3 (6 patients). 9 patients died, during the study interval. Rest 33 patient recovered. Satatus epilepticus and development of hydrocephalus were the two independent prognostic indicator in the outcome of Tubercular Meningitis.

Conclusion: Status epilepticus is an independent prognostic indicator in management of Tubercular Meningitis.

p736 ARE ALL THE PATIENTS WITH TEMPORAL LOBE EPILEPSY SURGICAL CANDIDATES?

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Purpose: There is a notion that a large percentage of patients with Temporal Lobe Epilepsy (TLE) are surgical candidates. The rates of patients with TLE that are well controlled with anti-epileptic drugs (AEDs) are not frequently reported.

Method: We analyzed the seizure outcome of a cohort of adult patients with TLE from the Epilepsy Program in the province of Saskatchewan, Canada from 2007 to 2013. Etiology and epilepsy syndromes were classified according the ILAE criteria.

Results: A total of 172 patients with TLE were identified. The mean age was 21.7 ± 15 and 51% were males. The mean time of follow-up was 40.1 ± 24.1. At the end of the follow-up, 46 patients (27%) were seizure free while receiving medication, 73 (42%) underwent epilepsy surgery (ES), 11 (6%) were waiting for ES, 17 (10%) were undergoing investigations for ES, 10 (6%) were investigated and were not candidates for ES, 8 (5%) refuse ES and 7 (4%) were death. Patients with TLE who were well controlled with medications were older than the rest of the group (51.3 ± 16 vs. 43 ± 13; p: 0.001), also were older at the diagnosis of epilepsy (36.6 ± 21.6 vs. 18.67 ± 15; p: < 0.001); had a good response to the first antiepileptic drugs (AED) (OR = 2.44; CI, 1.5–3.9); with less frequency of seizures per month (0.23 ± 0.84 vs. 3.7 ± 7.3; p: 0.001) and finally they had had less AEDs trials (2.3 ± 1.4 vs. 4.86 ± 1.9; p: < 0.001).

Conclusion: This study supports the notion that a fair percentage of patients (27%) with TLE are seizure free with medications. This study also support that TLE is highly intractable and 67% of patients will require surgery eventually.

p737 PROGNOSIS OF EPILEPSY IN PATIENTS WITH SEVERE MOTOR AND INTELLECTUAL DISABILITIES: A 10-YEAR FOLLOW-UP

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Purpose: New antiepileptic drugs (AEDs) to treat patients with refractory epileptic seizures are available in Japan since 2000. We investigated the prognosis of epilepsy patients with severe motor and intellectual disabilities (SMID) for a 10-year-period.

Method: Long-term prognosis of epilepsy was investigated in 193 hospitalized SMID patients for a 10-year-period (2003–2013). We determined the number of epilepsy patients and seizure frequency each year. We defined active epilepsy as the occurrence of more than one seizure in a patient in the years just before investigation. We analysed the characteristics of two groups: active epilepsy group and seizure-controlled group.

Results: Of 158 epilepsy patients in 2013, 92 (59.0%) had active epilepsy, 107(67.7%) had generalized epilepsy, and 51(32.3%) had symptomatic partial epilepsy. The proportion of active epilepsy patients decreased from 70.9% (2003) to 59.0% (2013) in 10 years. In the active epilepsy group (N = 92), there were more (69.1%) patients with SMID (bedridden and DQ < 20) than those with less severe intellectual disabilities (20 < DQ < 35; 46.2%). Seven of 9 patients with persistent frequent seizures (occurring more often than every other day) showed a high incidence of age-dependent epileptic encephalopathy; cryptogenic Lennox-Gastaut syndrome (LGS; 3 patients) and epilepsy with a history of West syndrome (WS) and LGS (4 patients). However, only 2 of the 4 patients with WS and LGS received ACTH therapy. In the seizure-controlled group (N = 66), 28 patients had newly become seizure-free in ten years. Only 2 of 28 patients were treated with new AEDs (1 with lamotrigine, 1 with levetiracetam).

Conclusion: In the last decade, the proportion of patients with active epilepsy decreased. However, we have to re-evaluate the contribution of new AED therapy to this decrease because of our shortage of experience.

p738 HEMISPHEROTOMY IN RASMUSSEN ENCEPHALITIS: LONG-TERM OUTCOME IN AN ITALIAN SERIES OF 16 PATIENTS

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Purpose: Rasmussen encephalitis (RE) has been treated in the last decade with different immunomodulatory therapies with partial and transient results on seizure control and disease progression. The surgical disconnective treatment is considered the treatment of choice of RE, but the available data on long-term outcome after disconnective surgery in RE is still scant. We report the long-term seizure, cognitive and motor outcomes after disconnective surgery in 16 RE patients.

Method: Pre- and post-operative evaluations included: long-term video-EEG monitoring, MRI, assessment of motor function, and cognitive evaluation. The surgical procedures were based on functional dis-
Abstracts

**Results:** The series includes 16 patients (8M, 8F), aged 12–33 years (mean age ± SD: 22.9 ± 6.8), who have been operated on between 1993 and 2009. The age at onset ranged between 3 and 11.4 years (6.1 ± 2.7); surgery was performed 8 months to 21 years from disease onset (5.3 ± 4.8). Post-surgical follow-up ranged between 3 and 20 years (10 ± 5.3). At the time of surgery patients were treated with two or more AEDs. All but three patients were seizure-free at the end of follow-up period. AEDs were stopped in ten patients, whereas in other six the number and doses of AEDs were significantly reduced. Postural control improved in all patients. Gain in cognitive functioning was significantly related to the duration of the disease (p < 0.002).

**Conclusion:** The outcome results of our disconnective surgical series demonstrate the successfulness of the operative procedures on a long-term basis. The disconnective surgical treatment remains the treatment of choice in RE because of its long-term efficacy in seizure control and improvement in motor and cognitive functions.

**p740**

**CLINICAL HETEROGENEITY OF JUVENILE MYOCLOTONIC EPILEPSY: FOLLOW-UP AFTER AN INTERVAL OF MORE THAN 20 YEARS**

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**Purpose:** The view that juvenile myoclonic epilepsy (JME) is a uniform and life-long disorder is currently being challenged. The aim of this study was to assess the seizure and psychosocial outcome of JME at least 20 years after onset.

**Method:** In 1992, 42 patients with JME were identified. In 2012, 37 agreed to a semi-structured interview. In the remaining five, only medical records were available.

**Results:** Of 40 patients with known seizure outcome, 21 were in remission for >5 years. Seven were off antiepileptic drugs (AEDs), four being seizure-free for >10 years. Myoclonic seizures (MC) evolving to generalized tonic-clonic seizures (GTC) were associated with seizure persistence (p = 0.013), whereas >1 year between MC and GTC onset was associated with a trend to GTC remission (p = 0.069). Of 19 patients with uncontrolled seizures, eight experienced remission with second generation AEDs. Favorable psychosocial outcome by interview was found in a third, whereas another third had psychiatric comorbidity, seven with substance or alcohol abuse. Psychosocial and seizure outcome did not correlate.

**Conclusion:** This study corroborates the heterogeneity of JME in terms of seizure and psychosocial outcome, but without a clear association between the two. It confirms that seizure control may persist after AED withdrawal in some and supports MC evolving to GTC as a predictor of seizure persistence. Moreover, it suggests that newer broad spectrum AEDs may improve the prognosis of JME; their impact should be focus of prospective studies.

**p741**

**LONG TERM OUTCOME IN CHILDREN WITH INFANTILE SPASMS TREATED WITH VIGABATRIN: A COHORT OF 180 PATIENTS**

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**Purpose:** Evaluation of efficacy of vigabatrin in infants with infantile spasms and reporting the long-term outcome.

**Method:** A cohort of 180 infants with infantile spasms treated with vigabatrin as the first drug, from January 1996 to December 2010, in the Institute was included in the single-centre, prospective, observational, uncontrolled study. After two basal days, vigabatrin was given under the same protocol: Assessment of the therapeutic response (primary outcome), was performed after 14 days. The psychomotor development was evaluated before the onset of treatment and during the follow up. Seizure outcomes were followed prospectively, by seizure types and epilepsy syndromes. Long term (secondary) outcome was defined in relation to neurological status, presence of late epilepsy, and intellectual level.

**Results:** Vigabatrin stopped the spasms in 101 (56.9%) patient at an average time of 5.27 days and failed in 79 (43.1%). Patients with normal psychomotor development before infantile spasms responded more frequently with cessation. After follow up of 2.42-18.86 years (M = 10.64; SD = 4.40), 38.7% of responders, treated with vigabatrin, had severe neurologic dysfunction, 42% had epilepsy, and 42.2% had unfavorable intellectual outcome. The difference in frequency of late epilepsy was not significant (p = 0.547) between responders and non-responders (42% vs. 59%). The group with symptomatic etiology and abnormal neurological status at the start had significantly worse prognosis than cryptogenic or idiopathic cases (85.1% vs. 81.6% vs. 14.9% &0%, p = 0.001).

**Conclusion:** The most important prognostic factors in our patients were etiology of the syndrome and preexisting developmental abnormalities. Long-term outcome in the patients treated with vigabatrin was similar to the outcome in patients treated with ACTH or corticosteroids, as reported in earlier studies. Long-term prognosis of idiopathic cases treated with vigabatrin was favorable.

**p742**

**ADULT-ONSET RASMUSSEN ENCEPHALITIS: LONG-TERM COURSE AND TREATMENT OPTIONS**

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**Purpose:** Rasmussen encephalitis (RE) is a progressive inflammatory disorder characterized by brain hemiatrophy, unilateral focal deficits,
and drug-refractory focal epilepsy (DRFE). RE usually starts during childhood, but adult-onset cases (a-RE) are described. The aim of this study is to describe the long term course of 6 a-RE patients and compare different therapeutic strategies.

**Methods:** The study group comprises 5 females and 1 male, mean age at onset 28 years, range 16–49. All patients underwent to an extensive clinical work up. RE diagnosis was set according to the European Consensus statement (Bien CG et al. Brain 2005;128:454–471). In three patients the diagnosis was confirmed by brain biopsy.

**Results:** Mean follow-up period is 12.5 years (range 1–40). The onset was neurological (aphasia and right hemisindrome) in 1 case; seizures were the onset symptom in the remaining cases. In all of the patients a progression of neurological deficits and brain atrophy was always observed. Focal epilepsy was present in 6/6 patients, whereas EPC was observed in 4/6. All patients were severely drug-resistant and underwent to different immunomodulatory treatments (steroids, plasma exchange, protein-A immunoabsorption, IVlg, immunosuppressants). The response to such treatments was always partial and temporary with no significant differences among different therapeutic regimens. Two patients with severe DRFE and EPC were submitted to limited cortical resections. After a mean follow-up of 42.5 months they are seizure free, but disease progression was not stopped in one.

**Conclusions:** A-RE is a chronic and progressive disease with different onset modalities. Immunomodulatory therapies exerted only temporary benefits on seizures and did not stop disease progression. Hemisferotomy is the treatment of choice in typical RE, but it may be not feasible in adult patients. In selected cases limited cortical resections can be effective on seizures and EPC but may not stop disease progression.

**p743**

**10-YEAR OUTCOME OF CHILDHOOD EPILEPSY IN WELL-FUNCTIONING CHILDREN AND ADOLESCENTS – SOCIAL AND PSYCHOLOGICAL FACTORS**

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**Purpose:** From a population based study of childhood epilepsy from a Swedish county (Larsson K, Eeg-Olofsson O, Eur J Paediatr Neurol 2006;10:107–113) a subgroup designated well-functioning treated for epilepsy in 1997 (n = 47; Eur J Paediatr Neurol 2011;15:331–337) was worked up from medical point of view 10 years later. This work describes social and psychological outcome.

**Method:** Thirty-one individuals, 19 females, aged 11–22 years and their parents/partners responded to a questionnaire according to Achenbach System of Emiperically Based Assessment (ASEBA) to evaluate behavioural and emotional problems, and social competence. Seven were <18 years and 24 ≥ 18 years.

**Results:** Active epilepsy, diagnosed in 32%, was related to attention problems, somatic complaints, and school problems. School problems were found in six of seven children. Polytherapy with antiseizure drugs (ASD) used in 16%, was related to attention problems and aggressive behaviour. Internalizing, externalizing, and “other” syndromes were found in 29% of the individuals, but a grouping of these syndromes in the clinical (abnormal) range only in two (6.5%), a girl with generalized tonic-clonic seizures alone, and a boy with unilateral perisylvian polymicrogyria. Both had active epilepsy with sporadic seizures and were treated with polytherapy. All ten individuals with Rolandic epilepsy were classified as normal. The answers to the ASEBA questionnaire of individuals and parents/partners were inconsistent, and parents generally stated more problems than their offspring.

**Conclusion:** This 10-year follow-up study of psychological and social outcome in well-functioning children and adolescents with childhood onset epilepsy shows some emotional, behavioural, and social problems. Thus, early information to children with epilepsy and their families aiming to increase knowledge about epilepsy, its course and treatment, and eventual co-morbidities, is of importance to decrease risk of low self-esteem, social anxiety, and depression later in life.

**p744**

**CLINICAL CHARACTERISTICS OF PATIENTS WITH REFRACTORY MRI-NEGATIVE, PET-POSITIVE TEMPORAL LOBE EPILEPSY**

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**Purpose:** To analyze characteristic of patients with MRI-negative, PET-positive temporal lobe epilepsy (MRI-/PET+ TLE).

**Methods:** We retrospectively evaluated demographic data, interictal/ictal invasive EEG (SEEG), interictal/ictal EEG, and seizure semiology in 20 patients with MRI-/PET+ TLE. According to the localization of the seizure onset zone (SOZ) in SEEG, patients were subdivided into three subgroups: SOZ in the mesial part of the temporal lobe (TL; mesial SOZ), in the temporal pole (polar SOZ), and in the lateral part of the TL (lateral SOZ). According to the concordance between interictal epileptiform discharges (IEDs) and the localization of the SOZ in SEEG, patients were categorized as having concordant IED distribution (i.e. ≥90% in SOZ) or discordant (i.e. <90% in SOZ). The scalp EEG was evaluated for frequency (frequent vs. rare) and distribution (anterotemporal, posterotemporal, or extratemporal) IEDs, for lateralization of ictal activity (lateralized vs. non-lateralized), and for ictal parameters (time to the development of early rhythmic theta/alpha activity, bitemporal propagation time, and ictal activity duration). The ictal semiology was evaluated for the presence of early orofacial automatisms, ictal motor signs, peri-ictal vegetative symptoms, peri-ictal motor signs, and postictal unresponsiveness.

**Results:** There were 12 (60%) patients with mesial SOZ, 2 (10%) patients with polar SOZ, 5 (20%) with lateral SOZ, and 1 (5%) unclassified patient. There was concordance between the maximum of distribution of IEDs and the SOZ localization in SEEG in only 5 (20%) patients. There were no statistically significant differences between the 3 subgroups when evaluating demographic data, interictal/ictal scalp EEG, and seizure semiology.

**Conclusion:** MRI-/PET+ TLE could be subdivided into three subgroups (mesial, polar, and lateral) according to the SOZ localization in SEEG. These three subgroups could not be distinguished on the basis of non-invasive data.

**p745**

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

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**Purpose:** To compare the seizure outcome in epilepsy patients, who were commenced on antiepileptic drugs early and those who had delayed treatment.
Method: Patients with epileptic seizures attending the Neurology Medical Outpatient Clinic of the Lagos University Teaching Hospital were evaluated using a standard proforma. Early treatment referred to patients that were treated within the first two years of seizure onset while delayed treated were those that were treated at 3 years or later. Outcome measure was the level of seizure control, patients were said to be seizure free after six months of seizure freedom, while uncontrolled were those who did not attain six months seizure freedom.

Results: 131 patients were evaluated. The age range was 15–71, median age was 29 years. Of these 86 (65.6%) patients were commenced on antiepileptic medication within the first 2 years of seizure onset while 45 (34.4%) patients commenced between 3 and 28 years after seizure onset. Of the 86 patients who were commenced on early treatment 46 (53.4%) were seizure free and 40 were uncontrolled. Of the 65 patients who started treatment late 19 were seizure free in six months giving a seizure freedom rate of 29.2% (p value = 0.271).

Conclusion: Although the patients who started treatment early had better remission rates, the result was not statistically significant. Early treatment of seizures may be associated with better outcome. A larger study sample and a prospective study may be necessary to confirm this.

p746
WHITE MATTER MICROSTRUCTURAL ABNORMALITIES ARE PRESENT 8 YEARS AFTER PROLONGED FEBRILE SEIZURES: RESULTS FROM A POPULATION-BASED STUDY

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Purpose: Human and animal studies report acute seizure-induced injury in hippocampal and extra-hippocampal gray matter, and in white matter (WM) following prolonged febrile seizures (PFS). Unlike hippocampal changes, the longer-term evolution of WM changes following PFS have not been investigated. Diffusion tensor imaging (DTI) can identify subtle microstructural alterations invisible on conventional MRI. We report DTI WM microstructure alterations of a population-based cohort 8 years after their PFS, compared to healthy controls.

Method: All subjects underwent MRI brain scan performed on an Avanto 1.5T scanner, and images processed using FSL v5.0.2.1 to obtain fractional anisotropy (FA), mean (MD), axial (AD), and radial diffusivity (RD), measures of axonal and myelin organization and integrity. Comparison between the PFS group and controls performed using tract based spatial statistics (TBSS), a robust technique for automated voxel-wise statistical analysis of WM diffusion properties. Age, gender and handedness included as covariates and p value of <0.05 considered significant.

Results: 26 PFS children (11 male, mean age 9.9 years, SD 1.72) and 27 controls (12 male, mean age 10 years, SD 1.74) were enrolled. Mean duration between PFS and follow-up was 8.23 years (range 6.7–9.6). TBSS analysis revealed two patterns of DTI changes: compared with controls, the PFS group had, (1) higher FA in early-maturing deep central WM tracts (cerebral peduncle, posterior limb of internal capsule, and corticospinal tracts) bilaterally, and (2) higher MD, AD, and RD bilaterally in late-maturing peripheral WM tracts. Higher MD was driven primarily by higher AD.

Conclusion: Diffuse WM microstructural alterations are observed 8 years after an episode of PFS. The pattern of diffusion changes indicates differential impact of prolonged seizures determined by the maturity of WM tracts at the time of the insult. We propose seizure-induced diffuse axonal injury, and subsequent neuroplastic reorganization of WM fibres as a biologically plausible explanation.

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Wednesday, 2nd July 2014

p747
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME INFLUENCES SHORT-TERM MORTALITY IN STATUS EPILEPTICUS

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Purpose: Short-term status epilepticus outcome is determined mainly by age and etiology. Recently, the role infectious comorbidities plays in status epilepticus prognosis has gained a lot of attention, which produced conflicting evidence regarding its importance. We aimed to see whether infections, their severity and treatment strategy may influence survival of patients with status epilepticus.

Method: We carried out a retrospective evaluation of clinical, radiologic and neuropsychologic parameters potentially affecting status epilepticus outcome in a cohort of adult patients admitted to our institution between 2003 and 2013. Case definition was based on EEG criteria.

Results: A total of 146 cases fulfilled inclusion criteria (64% female sex), with a mean age of 74 years (range 18–101). Short-term mortality was 38%. Multivariable analysis revealed the following negative prognostic predictors: age (Odds ratio [OR]: 1.1, p < 0.001), acute symptomatic etiology (OR: 5.5, p = 0.007), systemic inflammatory response syndrome (OR: 5.9, p = 0.002). Infectious complications did not emerge as a significant determinant in multivariate analysis, as well as antibiotic regimens established either before or after status epilepticus occurrence.

Conclusion: Our preliminary study supports the hypothesis systemic inflammatory response exerts a major role in short-term status epilepticus prognosis. Infective complications per se do not seem to alter significantly the outcome.

p748
A CASE OF STATUS EPILEPTICUS IN THROMBOTIC THROMBOCYTOPENIC PURPURA

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Purpose: To describe a 30 years old man with thrombotic thrombocytopenic purpura (TTP) who developed status epilepticus (SE).

Method: The patient developed seizures not well controlled with intravenous midazolam (MDZ) and oxcarbazepine. Then he presented a neuropsychiatric syndrome (levetiracetam (LEV) after MDZ bolus for 48 h than switched to oral therapy (total dose of LEV 3000 mg/die), in association with plasma-exchange (PE) and Rituximab (RTX).

Results: His neurological status improved in few weeks and he had a complete neurological recovery. He stopped oral LEV six months after hospitalization.

Conclusion: TTP is a condition characterized by an ischemic vasculopathy frequently associated with fluctuating neurologic symptoms, including confusion, stupor, and seizures. Fluctuating stupor in TTP has
p749
EPIEDEMOLOGY BASED MORTALITY SCORE IN STATUS EPILEPTICUS - A RETROSPECTIVE EXPLORATORY COMPARISON
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Purpose: Status epilepticus (SE) is regarded a neurological emergency with high mortality. Until today, STESS (SE severity score) is the only available score to stratify individual risk of death. We developed an Epidemiology based Mortality score for SE (EMSE) composed of combinations of domains neurophysiology (N), Age (A), comorbidity (M), etiology (E), duration and level of consciousness, and compared its prognostic value to STESS.

Method: One hundred twelve consecutive episodes in 92 non-hypoxic and 11 hypoxic patients of convulsive or non-convulsive SE admitted to neurological intensive care unit of tertiary care university hospital were retrospectively investigated. Scores for domains were obtained from recent publications of specific mortality rates. Cut-off levels of total sum scores were established for each combination of domains from lowest score of non-survivors, i.e. exploratory approach. Sensitivity, specificity, negative (NPV) and positive predictive value (PPV), and number correctly classified of EMSE and STESS (with different cut-off levels: STESS-3, STESS-4) were compared.

Results: EMSE using a combination of neurophysiology, Age, comorbidity and etiology (“NAME-score”) was superior to STESS-3 and STESS-4 in non-hypoxic patients with SE (NPV = 100%, PPV = 68.8%, correctly classified 89.1%, p = 0.0022 or lower) (corrected p-value for multiple testing: significant p ≤ 0.0044).

Conclusion: NAME-score explained mortality in approximately 90% of cases, and was significantly superior to STESS. This explorative study needs external prospective reinforcement. NAME-score can be adapted to different regions and to medical progress over time, epidemiological data presupposed. NAME-score may prove as valid tool for risk stratification in interventional studies on status epilepticus. Comorbidity was an important part for this mortality model in status epilepticus.

p750
A SHORT-TERM MONOCENTRIC PROSPECTIVE OBSERVATIONAL STUDY OF REFRACTORY/SUPER-REFRACTORY STATUS EPILEPTICUS
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Purpose: To evaluate the major clinical characteristics, therapeutic options and outcome of a case series of adult patients presented with refractory/super-refractory (Shorvon et al., 2011) Status Epilepticus (SE) at NOCSAE hospital, the hub center for neurological disorders of the District of Modena, northern Italy.

Method: A mono-centric, prospective, observational study on consecutive patients with S.E. observed from September 2013, the 1st and January 2014, the 1st. Data were collected through a specific “Status Epilepticus form”. Outcome was evaluated at discharge and at 1 month, if available/possible.

Results: 39 patients (age range 16–94 years; age average: 72 years; male, 16) were observed. The majority of patients presented with non-convulsive S.E. (N 22) and the most frequent causes were: brain tumor (N 8), post-anoxic (N 7) and cerebrovascular disease (N 5). 13 cases have been classified as Refractory S.E., 6 of which met the criteria for Super-refractory S.E. Pharmacological treatment: 25 cases out of 29 received Diazepam as the first line AED; the most frequently used second line AEDs were Valproate (N 13), Levetiracetam (N 11) and Phenotin (N 6). Propofol was the most used anesthetic (N 6). Other therapies were used in 3 cases (Steroids).

Outcome: 23 cases out of 39 resolved (3 cases out of 13 among Refractory S.E. and 1 case out of 6 among Super Refractory S.E.). 16 patients (55%) died at one-month follow-up. There were 7 deaths among Refractory S.E. (70%) and 3 deaths among Super Refractory S.E. (100%).

Conclusion: These preliminary data confirms the high 1-month mortality rates in refractory/super-refractory S.E. In particular S.E. related to brain tumors, acute cerebrovascular disease, and above all, anoxia/hypoxia a have high probability of being refractory or even super-refractory and thus have a poorer outcome.

p751
NEUROIMAGING IN THE CHILDREN WITH STATUS EPILEPTICUS
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Purpose: Status epilepticus is an epileptic seizure which last more than 30 min or series of short seizures with no recovery of the consciousness between them. Purpose of this study was to analyze the neuroimaging findings in the patients with status epilepticus.

Method: This retrospective study includes 78 children with status epilepticus and who underwent neuroimaging (CT or MR) during course of disease. Results of neuroimaging were sort in 6 groups:
1 Normal finding
2 Ventriculomegaly and/or hydrocephalus,
3 Cortico-subcortical atrophic changes,
4 Malformation of cortical development
5 Other CNS abnormalities (such as mesial temporal sclerosis, tuberous sclerosis, Sturge/Weber syndrome, gliosis etc.) and
6 The other. Some of them had more than one change on CT/MR.
Also we follow neurological development of this children. We separated them in 2 groups- with normal neurological status and with changes in it.

Results: Normal CT/MR had 41.03% of children. Disorders from the second group have occurred in 24.36%, from the third in 34.62%, from the fourth in 11.54%, from the fifth 11.54% and from the sixth 14.1% of all MR/CT results respectively. Further, 50% of children had neurological abnormalities, whereas 50% had normal neurological status.

Conclusion: Considering that the most of the children had a normal neurological status and normal neuroimaging, in our study group, we can conclude that the most common status epilepticus is idiopathic. The most frequently causes of the symptomatic status epilepticus are cortico-subcortical atrophic, malatic and hypoplastic changes, and was found in the group of patients with neurological abnormalities.
p753
CHARACTERISTICS OF EPILEPSY IN CHILDREN WITH EPILEPTIC STATUS
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Introduction: Epileptic status (ES) is an acute medical condition characterized by continuous seizures (partial or generalized; convulsive or non-convulsive) in a period of at least 30 min, or a series of seizures in shorter time without regaining the consciousness between them.

Material and Methods: The retrospective study included 84 children with ES, hospitalized at the University Children’s Hospital in Belgrade from 2011 to 2013.

Results: Among 84 hospitalized children, 36 (42.86%) were female and 48 (57.14%) male - aged between 5 months and 16 years. Neurological status was normal in 41 patients (48.81%) whereas 36 patients (42.86%) were neurologically impaired. In 61 patients (72.62%), ES was the first epileptic event while in patients who developed various forms of epileptic seizures was noted before ES (idiopathic generalized seizures in 4 (4.76%), idiopathic partial seizures in 3 (3.57%), symptomatic generalized seizures in 4 (4.76%), symptomatic partial seizures in 8 (9.52%) and epileptic encephalopathy in 4 cases (4.76%). The association of fever with ES was noted in the 31 patients (36.9%). 17 patients (20.24%) had ES while they were on monotherapy, 7 (8.33%) were taking two drugs and 5 (5.95%) were taking three or more drugs. After ES, 34 children (40.48%) had no more seizures while others had other types of seizures.

Conclusion: The study has shown that the majority of children had normal neurodevelopmental status prior to ES. The incidence of the recurrence of ES was low. In the most of the cases, ES was the first and sole manifestation of the disease.

p754
MORTALITY AFTER REFRACTORY STATUS EPILEPTICUS
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Purpose: Status epilepticus (SE) is an important neurological emergency potentially associated with significant mortality and morbidity. Annual incidence of SE is considered to be 20 /100 000. Mortality and morbidity rates of SE are influenced by the underlying etiology, patients age and duration of SE. Status epilepticus is considered refractory (RSE) if the first line (benzodiazepines) and second line (fos-phenytoin) treatments fail. The lack of data on outcome of RSE is well established worldwide. The aim of the study is to identify the incidence and mortality of RSE in Kuopio University Hospital (KUH) responsibility area (population 840,000 inhabitants) in Finland.

Methods: We performed a retrospective analysis from the Finnish Intensive Care Consortium database of the RSE patients treated in the hospitals of KUH special responsibility area over three years time period 2010–2012. Patient charts were reviewed in each of the areas central hospitals by a neurologist. We included consecutive adult (16 years or older) RSE patients treated in intensive care units. Patients that have not had RSE or have not been treated with anaesthetics were excluded as were the patients with hypoxic ischaemic brain damage (post anoxic myoclonus).

Results: We identified 79 patients with RSE in the years 2010–2012 in a population of 840,000. 64.6% of the patients were male and the median age was 55 during the time of treatment, range being 18–82 years. Annual incidence of RSE in Kuopio University responsibility area was 3, 1/100 000. Mortality of RSE within 12 months 22% (16 deaths out of 74 incident SE).

Conclusions: The incidence and mortality of RSE in Finland seems to be on the same level as the international data suggests. Determinants of the mortality will be described.
LONG TERM FOLLOW-UP (>10 YEARS) IN A SINGLE EPILEPSY SURGERY CENTRE: A SERIES OF 420 CONSECUTIVE PATIENTS OPERATED ON FOR DRUG-RESISTANT EPILEPSY AT THE “CLAUDIO MUNARI” CENTRE

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Purpose: Epilepsy surgery has been demonstrated a valuable treatment for drug resistant focal epilepsy patients; nonetheless few studies assess the very long-term post-operative outcome of epilepsy surgery. Aim of this study is presenting the long-term outcome of a series of patients who underwent a tailored cortical resection from May 1996 to December 2003.

Method: Assessment of the clinical outcome and of the potentially associated anatomo-electro-clinical variables.

Results: We identified 420 patients (46% females) with at least 10 years follow-up (range: 10–17.6; mean: 13.4 years); 81% of subjects had a seizure onset <14 years of age, 42% <6 years. Surgery was realized in adult age in 80.2%, at a mean age of 27.5 years and a mean duration of 18.7 years. MRI was normal in 10.2% of cases; 41.6% of subjects underwent a pre-surgical Stereo-EEG evaluation. Surgery was performed in the left hemisphere in 44.5% of cases; a lesionectomy was realized in 34 patients, in the remaining a corticectomy, including the eventual lesion, was performed. Surgery was: temporal (58.6%), frontal (19.4%), parietal (4%), occipital and central (0.7% each), multilobar (16.6%). Malformative pathologies represented the commonest histological finding (43.6%). Seizure freedom was achieved by 70% of subjects (Engel class Ia: 42.8%, Ib: 9%, Ic: 12.4%, Id: 5.4%), 10.7% are in class II, 9% in class III.

Conclusion: A very long-term seizure control following individually-tailored epilepsy surgery can be achieved in 70% of the patients, allowing a drug discontinuation in around 50%.

EPILEPSY SURGERY IN ADULT-ONSET RASMUSSEN’S ENCEPHALITIS: CASE SERIES AND REVIEW OF THE LITERATURE

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Purpose: Rasmussen’s Encephalitis (RE) is a rare immunemediated condition characterized by drug-resistant focal epilepsy, progressive neurological and cognitive deficits associated to unilateral hemispheric atrophy. The onset is typically reported in childhood, although adult cases (A-RE) have been described. While surgical strategies in childhood RE are well defined, little is known about usefulness of epilepsy surgery in A-RE patients. We describe clinical features, surgical approach and outcome of five A-RE patients who underwent epilepsy surgery and we review the literature with regard to surgical A-RE cases.

Method: We retrospectively studied five A-RE patients aged 21–38 years (mean age 22.8 years) who were followed after surgery for a period ranging from 1 to 16 years. Demographic, electro-clinical, neuropsychological and neuroimaging data were systematically reviewed. Four out of five subjects underwent invasive EEG monitoring to define epileptogenic zone. Epilepsy outcome was defined according to Engel’s classification.

Results: Surgery consisted of frontal corticectomy in three patients, temporal lobectomy in one, combined temporal lobectomy plus insular and frontal-basal corticectomy in the remaining case. No permanent neurological deficits were observed after surgery. At the last follow-up observation, one patient was seizure-free, two subjects experienced rare disabling seizures, another had moderate seizure reduction, and one had no clinical improvement.

Conclusion: Our experience, although limited to few cases, suggest that resective surgery in A-RE may play a role in the context of multidisciplinary therapeutical approach of this severe condition. Since the lack of specific data about surgical options, this topic seems to deserve further investigations and more targeted studies.

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Abstracts

p759
PSYCHO-SOCIAL OUTCOMES FOLLOWING EPILEPSY SURGERY: RESULTS FROM THE EPILEPSY PSYCHO-SOCIAL EFFECTS SCALE (EPSES)
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Purpose: To evaluate the use of the Epilepsy Psycho-Social Effects Scale (EPSES) as an outcome measure with an epilepsy surgery population.

Methods: 73 adult epilepsy surgery candidates completed the EPSES and the Hospital Anxiety and Depression scale (HAD) before epilepsy surgery and at follow-up two years after surgery. The EPSES based on the subjective quality of life of patients with epilepsy consists of 14 subscales: Attitude towards the attacks, Fear of having seizures, Fear of stigma in employment, Lack of confidence in the future, Lack of confidence about travelling, Adverse reaction on social life, Adverse reaction on leisure pursuits, Change of outlook on life/self, Difficulty in communicating with the family, Problems with taking medication, Distrust of the medical profession, Depression or emotional reactions, Feeling of increased social isolation, Lethargy/lack of energy.

Results: Significant improvements in quality of life domains was noted in all domains with the exception of Difficulty in communicating with the family. Effect sizes were small to medium with the largest differences occurring in Lack of confidence in the future (Cohen’s d = 0.528), Lack of confidence about travelling (Cohen’s d = 0.600), Distrust of the medical profession (Cohen’s d = 0.740).

Conclusion: The EPSES is a sensitive measure of outcome illustrating significant change in thirteen of the fourteen domains of quality of life measured. The results of this investigation suggest that the EPSES will prove to be a useful tool for investigating the psycho-social outcomes after surgery.

p760
TEMPORAL ANTEROINFERIOR ENCEPHALOCELE: AN UNDER-RECOGNIZED ETIOLOGY OF TEMPORAL LOBE EPILEPSY?
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Purpose: To report increasing frequency of temporal anteroinferior encephalocele diagnosis in our tertiary care epilepsy centre and to illustrate the clinical and imaging characteristics of this condition in a series of 23 patients. Previously only 18 similar patients have been reported in the English literature, largest series being 3 patients.

Method: Epilepsy patients diagnosed with temporal anteroinferior encephalocele during the study period (January 2006 - December 2013) in our hospital were included. All patients had MRI examinations (mainly 3T) according to an epilepsy protocol complemented with additional sequences.

Results: Twenty-three epilepsy patients (14 females, mean age 40 years) were diagnosed with temporal anteroinferior encephalocele. Thirteen patients had two or more encephaloceles, bilateral in seven cases. The estimated prevalence of this condition was 0.3% in MRI examinations performed due to newly diagnosed epilepsy (n = 6) and 1.9% in drug-resistant patients referred to our institute as epilepsy surgery candidates (n = 17). High-quality, thin-slice, preferably three-dimensional MRI and computed tomography studies facilitated the detection of this condition. Histologically gliosis was present in temporal lobe samples in all 10 surgically treated patients and some encephaloceles also showed cortical laminar disorganization. Eight patients with local encephalocele disconnection (n = 3) or anterior temporal lobectomy and amygdalohippocampectomy (n = 5) have become seizure free in a mean 2.8 years (range 3 months to 6.2 years) of follow up. Two local encephalocele disconnection patients were almost seizure free or had a worthwhile improvement.

Conclusion: The possibility of temporal encephalocele should be considered when interpreting MRI examinations of patients with medically intractable temporal lobe epilepsy. These patients can significantly benefit from epilepsy surgery.

p761
FUNCTIONAL HEMISPHERECTOMY IN CHILDREN AND YOUNG ADULTS WITH MEDICALLY INTRACTABLE EPILEPSY: INFLUENCE OF UNDERLYING PATHOLOGY ON OUTCOME
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Purpose: Since 1928, hemispherectomy has evolved from a purely anatomical procedure to an increasingly functional one prioritising disconnection over resection. We sought to assess the influence of underlying pathology on outcome in young patients with hemispheric epilepsy syndromes.

Method: A retrospective case-note review of all patients undergoing the Schramm hemispherectomy at Birmingham Children’s Hospital and Queen Elizabeth Hospital between 1996 and 2013. Patients were reviewed at 1, 3 and 5 years post-surgery to assess their Engel outcome scores. Underlying pathology was stratified as congenital/developmental, acquired and progressive.

Results: Our 22 patients included 18 paediatric cases (aged 3 months to 16 years, mean 6 months) and 4 adult cases (21 to 32 years, mean 25). There were 16 male and 6 female patients with a follow-up of 6 months to 6 years (mean 3.2 years). The underlying pathology was acquired in 11 (6 middle cerebral artery infarct, 2 perinatal ischaemic insult, one each of infarction post-subdural haematoma and post-sepcticaemia and one post-neonatal intraventricular haemorrhage), developmental in 9 (7 hemimegalencephaly, 2 diffuse cortical dysplasia) and progressive in 2 (one each of Rasmussen encephalitis and Sturge-Weber syndrome). At follow-up, 17 patients were seizure-free (77% Engel 1), 1 had occasional seizures (Engel 2) and a further 2 had a worthwhile improvement in seizure frequency (Engel 3). 2 patients had no improvement (9% Engel 4). 90% of patients with acquired insults became seizure-free as opposed to 67% with developmental and 50% with progressive pathologies. 2 patients needed revisional surgery (1 hemimegalencephaly, 1 infarct); neither experienced any improvement in seizure burden. There was no reported mortality and the incidence of ventriculoperitoneal shunting was low (4.5%).

Conclusion: In patients with epilepsy arising from one hemisphere, hemispherectomy appears effective when the underlying structural abnormality is acquired, most commonly ischaemic in origin. Patients who fail to respond are unlikely to benefit from re-operation.
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CLINICAL AND MRI EVALUATION OF THE TRANSUNCUS SELECTIVE AMYGDALO-HYPPOCAMPECTOMY
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Purpose: Anatomic reports have described and proposed the transuncus (TU) approach as a very selective route to the amygdala and hippocampus, but this approach has not been validated in the clinical setting yet. The objective of this study is to evaluate the efficiency, safety and selectivity of the TU approach in the surgical treatment of the TLE.

Method: A prospective study of patients submitted to the TU approach was performed. Clinical and MRI (DTI analysis) data were evaluated, and the results were compared with those in our data base operated earlier through two other approaches in our institution, anterior temporal lobectomy (ATL) and selective amygdalohippocampectomy through inferior circular sulcus of the insula (TI).

Results: In 25 patients operated through the TU approach the mean age was 40 ± 8.21 years-old. The mean follow-up was 26.44 ± 12.58 months and 21 (84%) patients were classified as Engel I (good seizure control). The patients submitted to the TU approach, when compared to the patients submitted to the ATL and TI approaches, had significantly less injuries to the temporal stem (TS) (p < 0.001) and to the uncinate fasciculus (UF) (p < 0.001), but no significant difference was found when analysing the inferior fronto occipital fasciculus (IFO) and the optic radiations (OR). There were no mortality and only one patient had permanent morbidity (residual mild hemiparesis) in this series.

Conclusion: The results showed that the transuncus selective amygdalo-hippocampectomy is an efficient and safe approach in the surgical treatment of the TLE. The TU approach showed to be more selective then the ATL and TI approaches with better preservation of the anterior third of the TS and the UF.

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COL4A1 MUTATIONS SHOULD NOT BE A CONTRAINDICATION FOR EPILEPSY SURGERY
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Purpose: To describe the first case in the literature of complication free epilepsy surgery in a patient with COL4A1 mutation. Her immediate post-operative period was uneventful and she was discharged home a few days after the operation. She continued to be seizure free when seen for the initial follow up appointment six weeks after the operation.

Conclusion: Although there is an increased risk of intracranial haemorrhages in COL4A1 patients, this is not clearly quantifiable and there are minimal data in the literature on the subject. COL4A1 mutations should not be a contraindication for pre-surgical evaluation. Each patient should be individually evaluated and assessed. Risks and benefits should be carefully weighed and informed decisions reached after thorough discussions with patients and families.

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RECOVERY OF MEMORY FUNCTION FOLLOWING SELECTIVE AMYGDALOHIPPOCAMPECTOMY VIA THE INFERIOR TEMPORAL GYRUS
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Purpose: We developed the selective amygdalohippocampectomy (SAHT) via the inferior temporal gyrus using neuronavigation system to preserve the temporal stem. This procedure provides excellent epilepsy control for patients with mesial temporal lobe epilepsy (MTLE). We analyzed the outcome of memory function after this surgical procedure.

Method: Nineteen patients with mesial temporal lobe epilepsy have undergone the SAHT procedure for MTLE via the inferior temporal gyrus. Among them, 12 patients used the Wechsler Memory Scale-Revised (WMS-R) score to evaluate memory function both just before and 6–12 months after SAHT. The lesions were located on verbal dominant hemispheres in 5 cases and on verbal non-dominant hemispheres in 7 cases.

Results: The postoperative outcomes of 18 of all 19 cases were seizure free categorized as Engel’s class I. The pathology of these 18 cases was hippocampal sclerosis. The other case resulted in Engel’s class IIa. The pre-operative visual, verbal, and total memory scores were 78.2 ± 7.8 (Ave ± SE), 93.7 ± 8.7, and 79.0 ± 7.8, respectively. Post-operative scores were 87.6 ± 11.0, 101.2 ± 11.5, and 91.3 ± 10.9, respectively. Post-operative scores of all three scales were significantly improved compared to pre-operative scores. The scores of attention and delayed recall were also significantly improved. The cases of verbal dominant hemispheres revealed significant improvement of visual memory. In contrast, the cases of verbal non-dominant hemispheres revealed significant improvement of verbal and total memory. In one case of dominant hemisphere MTLE, about 10% of verbal memory was lost.

Conclusion: Not only good seizure outcome but also improvement of memory function can be expected with SAHT via the inferior temporal gyrus preserving the temporal stem.

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HEALTH-RELATED QUALITY OF LIFE AFTER EPILEPSY SURGERY IN CHILDHOOD
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Purpose: To know health-related quality of life (HRQoL), evaluated by (former) patients at least one year after epilepsy surgery in childhood,
and to explore relations with type of surgery, age at surgery, seizure freedom, number of anti-epilepsy drugs (AED), and postsurgical IQ of the child.

**Method:** Of 177 children who underwent epilepsy surgery between 1992 and 2009 in the University Medical Center Utrecht, 129 could be contacted and were sent the Euroqol EQ-5D. This questionnaire inventories overall HrQoL using a visual analog scale (EQ VAS, minimum 0 - maximum 100) and HrQoL in the domains mobility, self-care, usual activities, pain/discomfort and anxiety/depression using five three-point (no, some or extreme problems) items.

**Results:** Returned were 112 lists (86.8%), of which the 54 filled out by the children (age 11–28, mean 19 years) are focus of the present contribution. Four children (7.4%) expressed severe problems with mobility, self-care or daily activities, 12 (22.2%) expressed some/extreme pain or discomfort and no child expressed extreme anxiousness or depression. Thirty-two children (59.3%) rated overall HrQoL above 75 and 17 (31.5%) between 50 and 75. The five children with a HrQoL between 26 and 50 suffered severe medical and/or psychosocial problems. With a highest mean VAS score = 80.0 in hemispherectomized (n = 8) children and a lowest = 78.93 in children with extra-temporal resection (n = 14), type of surgery was not significantly related to HrQoL. Children with seizure recurrence (n = 11) expressed non-significantly less HrQoL than seizure-free (n = 43) children (Mean VAS scores 70.18 and 81.2 respectively). Age at surgery, number of AED nor post-surgical IQ were significantly related to the children’s HrQoL.

**Conclusion:** The vast majority of children evaluate their long-term health-related quality of life after epilepsy surgery as positive, even in the presence of remaining physical limitations and/or seizure recurrence.