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ABSTRACTS

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

Boshuisen K[1], van Schooneveld M[2], Polster T[3], Daehn M[3], Djimjadi S[3], Yalnizoglu D[4], Turanli G[4], Sassen R[5], Hoppe C[5], Kuczaty S[5], Barba C[6], Kahane P[7], Schubert-Bast S[8], Bast T[8,9], Strobl K[9], Mayer H[9], de Saint-Martin A[10], Seegmuller C[10], Cross H[11,12], Arzimanoglou A[13], Uiterwaal C[14], Braun K[1]
[1]Department of Child Neurology, Brain Center Rudolf Magnus, University Medical Center Utrecht, Utrecht, The Netherlands, [2]Department of Child Psychology, Brain Center Rudolf Magnus, University Medical Center Utrecht, Utrecht, The Netherlands, [3]Bethel Epilepsy Center, Bielefeld, Germany, [4]Department of Pediatric Neurology, Hacettepe University Children's Hospital, Ankara, Turkey, [5]University of Bonn Medical Centre, Bonn, Germany, [6]Paediatric Hospital A. Meyer, University Hospital, Florence, Florence, Italy, [7]University Hospital Grenoble, Grenoble, France, [8]University Hospital Heidelberg, Heidelberg, Germany, [9]Epilepsy Center Kork, Kehl-Kork, Kork, Germany, [10]University Hospital Strasbourg, Strasbourg, France, [11]Neurosciences Unit, UCL-Institute of Child Health, Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK, [12]Young Epilepsy, Lingfield, London, UK, [13]Department of Epilepsy, Sleep and Paediatric Neurophysiology, HFME, University Hospitals of Lyon (HCL), Lyon, France, [14]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands

Purpose: Antiepileptic drugs (AEDs) may have cognitive side effects and, particularly in children, have permanent consequences for eventual intellectual functioning. It was recently reported that postoperative AED withdrawal improves reaction times after childhood epilepsy surgery. AED discontinuation was shown to be an important predictor of IQ increase following temporal resections. We aimed to evaluate the effect of AED withdrawal on postoperative total IQ (tIQ), and on the change in tIQ compared to preoperatively (delta IQ, dIQ), and tried to identify other predictors of tIQ and dIQ in a large European pediatric epilepsy surgery cohort.

Method: The TimeToStop study (TTS), (n = 776), showed that timing of AED withdrawal does not influence long term seizure outcomes (Boshuisen et al. Lancet Neurology 2012;11(9):784–91). For this study, tIQ data were collected of children from the TTS cohort who underwent both pre- and postoperative neuropsychological evaluation (n = 346). We analyzed whether reduction of AEDs prior to the latest psychological 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 EEG findings, 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 tIQ 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

Treviño-Peinado C[1], Trzeciak M[1], Barriobero N[1], Echeveste B[1], Viteri C[1]
[1]Clínica Universidad de Navarra, Neurology, Pamplona, Spain

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 bitherapy group, 32 patients (39.5%) are seizure-free and 23 (28.39%) continue presenting seizures. 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

Srikanth R[1], Reshma A[2], Pushkar K[3], Sriram D[2], Yogeeswari P[2]
[1]Pharmacy, Birla Institute of Technology & Science-Pilani, Hyderabad, India, [2]Birla Institute of Technology & Science-Pilani, Hyderabad, India, [3]Dr. Reddy's Institute of Life Sciences, Hyderabad, India

Purpose: Adenosine receptors (AR) play an important role in chemical signaling in both, peripheral and central nervous systems. Four subtypes of Adenosine Receptors have been identified: designated A1, A2A, A2B, and A3. A2A ARs are found in high density in certain brain regions, such as Striatum, Nucleus accumbens, and Olfactory tubercle. Adenosine exhibits high affinity to A2A ARs, which appear to be tonically activated under physiological conditions. A2A AR antagonists have been proposed as novel therapeutics for Epilepsy and Parkinson's disease.

Methods: Human A2A AR bound to ZM241385 with IC_{50} 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 Glu169, 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

Ghosh C[1], Hossain M[1], Spriggs A[1], Boussadia B[1], Marchi N[1], Janigro D[1,2]
[1]Cerebrovascular Research, Biomedical Engineering, Cleveland Clinic, Cleveland, OH, USA, [2]Neurological Surgery, Cleveland Clinic, Cleveland, OH, USA

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

Lotte J[1], Bast T[2], Borusiak P[3], Coppola A[4], Cross H[4], Dimova P[5], Sánchez Fernández I[6], Fogarasi A[7], Graneß I[8], Guerrini R[9], Hjalgrim H[10], Leiz S[11], Linder-Lucht M[12], Loddenkemper T[6], Makowski C[13], Müller A[14], Nicolai J[15], Pellacani S[9], Philip S[16], Ruf S[17], Selch C[13], Schlachter K[18], Striano P[19], Sukhudyan B[20], Vermeulen RJ[21], Staudt M[14], Wolf P[22], Kluger G[23]
[1]Kinderzentrum, Maulbronn, Germany, [2]Epilepsieklinik für Kinder und Jugendliche, Epilepsiezentrum, Kork, Germany, [3]Department of Pediatrics, Witten/Herdecke University, HELIOS Hospital, Wuppertal, Germany, [4]Department of Clinical & Experimental Epilepsy, Great Ormond Street Hospital, University College, London, UK, [5]Clinic of Child Neurology, St. Naum University Hospital of Neurology and Psychiatry, Sofia, Bulgaria, [6]Division of Epilepsy and Clinical Neurophysiology, Boston Children's Hospital, Boston, MA, USA, [7]Neurology Department, Bethesda Children's Hospital, Budapest, Hungary, [8]Neuropädiatrie, Waldklinikum, Gera, Germany, [9]Child Neurology Unit, A. Meyer Children's Hospital, University of Florence, Florence, Italy, [10]Epilepsihospitalet Filadelfia, Danish Epilepsie Center, Dianalund, Denmark, [11]Neuropädiatrie, Kinderklinik Dritter Orden, München, Germany, [12]Servicio de Pediatría y Unidad de Epilepsia, Hospital del Mar, Barcelona, Spain, [13]Kinderklinik der Technischen Universität München, Klinikum Schwabing, München, Germany, [14]Neuropädiatrie, Schön Kliniken, Vogtareuth, Germany, [15]Department of Neurology, Maastricht University Medical Center, Maastricht, The Netherlands, [16]Children's Hospital, Birmingham, UK, [17]Neuropädiatrie, Universitätskinderklinik, Tübingen, Germany, [18]Department of Pediatrics, Landeskrankenhaus, Bregenz, Austria, [19]Pediatric Neurology, Institute Gaslini, University of Genova, Genova, Italy, [20]"Arabkir" Medical Complex, Yerevan, Armenia, [21]Child

*Neurology, VU University Medical Center, Amsterdam, The Netherlands, [22]Department of Neuropediatrics, DRK-Children's Hospital, Siegen, Germany, [23]Neuropä*diatrie, Schön Klinik-en, Vogatreuth, Germany

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 (70%), 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 RFN (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, RFN 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 ANTIEPILEPTIC DRUGS TRANSPORT THROUGH THE BLOOD-BRAIN BARRIER IN CHILDREN

Soares RV[1,2], Jullien V[1], Do M[2], Noyalet G[2], Chhun S[1], Pons G[1], Mabondzo A[2], Chiron C[1]
[1]Unité Inserm U 663 (Epilepsies de l'Enfant et Plasticité Cérébrale), Paris, France, [2]CEA/DSV/iBiTec-S (Service de Pharmacologie et Immunoanalyse), Gif-sur-Yvette, France

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

Rohracher A[1], Dobesberger J[1], Höfler J[1], Huber D[1], Kalss G[1], Kuchukhidze G[1], Leitinger M[1], Trinka E[1]
[1]Department of Neurology, Paracelsus Medical University Salzburg, Salzburg, Austria

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). Sixty-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 (39%) 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%), neuropsychological (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

Schoemaker R[1], Stockis A[2]
[1]SGS Exprimo NV, Mechelen, Belgium, [2]UCB Pharma, Braine-L'Alleud, Belgium

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 0.4/0.8/1.6 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: +40.8%, 95% confidence interval [CI]: 19.9–65.2; CBZ: +47.9%, 95% CI: 27.8–71.2; VPA: −10.1%, 95% CI: −0.8 to 18.5). For most children, BRV C_{ss} values were similar to those observed in adults, although low body weight patients (<15 kg) and young children (<2 years) tended to be underdosed, especially when co-administering BRV with PB or CBZ. Simulations showed that similar C_{ss} may be obtained using an age-independent dosing regimen of up to 2.5 mg/kg bid (≤100 mg bid).

Conclusion: Population pharmacokinetics modelling showed that a BRV dosing regimen similar to that used in study N01263 and further simplified by removing the age criterion, may be adequately used in children with epilepsy.

UCB-sponsored.

009
EVALUATION OF METABOLIC PARAMETERS OVER TIME IN THE PERAMPANEL POOLED PHASE III EPILEPSY STUDIES

Brodie MJ[1], Patsalos PN[2], Bagul M[3], Laurenza A[4]
[1]Western Infirmary, Glasgow, UK, [2]Institute of Neurology, London, UK, [3]Eisai Ltd, Hatfield, UK, [4]Eisai Inc., Woodcliff Lake, NJ, USA

Purpose: Explore metabolic parameter changes in the perampanel pooled Phase III studies.

Method: Patients (≥12 years), with uncontrolled partial-onset seizures despite 1–3 concomitant anti-epileptic drugs (AEDs) were randomised to perampanel (2, 4, 8 mg [study 306]; 8 or 12 mg [studies 304, 305]) or placebo (6-week titration + 13-week double-blind treatment) (Steinhoff et al. Epilepsia 2013;54:1481–1489). Mean (±SD) changes from baseline to end of treatment are reported for cholesterol, triglycerides, glucose (mM) and weight (kg) for the safety analysis set (N = 1,480).

Results: Over 19 weeks, weight increase was greater with perampanel (+1.18 [±3.10]kg overall; change for 2, 4, 8, 12 mg: +0.4, +0.98, +1.34, +1.60, respectively) than placebo (+0.40 [±2.81]kg). Weight increase >7% occurred in 14.6% of perampanel-treated patients (vs. 7.1% of placebo-treated patients). For patients receiving perampanel vs. placebo, cholesterol change was +0.035 (±0.701) vs. −0.046 (±0.602) mM; triglycerides change was +0.082 (±1.378) vs. +0.012 (±0.657) mM, and the change in non-fasting glucose levels was +0.044 (±1.199) vs. −0.018 (±0.928) mM. Metabolic parameters reported as treatment-emergent adverse events (TEAEs) in >1% of patients receiving perampanel vs. placebo were: weight increase (39 [3.8%] 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

Patsalos PN[1], Brodie MJ[2], Bagul M[3], Cartwright K[3], Yang H[4]
[1]Institute of Neurology, London, UK, [2]Western Infirmary, Glasgow, UK, [3]Eisai Ltd, Hatfield, UK, [4]Eisai Inc., Woodcliff Lake, NJ, USA

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 (mM) and body weight (kg) is reported (safety analysis set).

Results: Of 1,186 patients, 1,089 (91.8%), 580(48.9%) 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 mg [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) mM for cholesterol; +0.053 (±0.694) mM for triglycerides, and +0.068 (±0.999) mM 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 (hyponatraemia, diabetic ketoacidosis, hypochloraemia, 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.

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011
EVEROLIMUS LONG-TERM SAFETY AND EFFICACY IN PATIENTS WITH SUBEPENDYMAL GIANT CELL ASTROCYTOMA (SEGA) ASSOCIATED WITH TUBEROUS SCLEROSIS COMPLEX (TSC)

Franz DN[1], Care MM[1], Holland-Bouley K[1], Agricola K[1], Tudor C[1], Berkowitz N[2], Miao S[2], Segal S[2], Peyrard S[3], Krueger DA[1]
[1]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA, [2]Novartis Pharmaceuticals S.A.S., Rueil-Malmaison, France, [3]Novartis Pharmaceuticals, East Hanover, NJ, USA

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/m^2/day (titrated to target blood trough levels of 5–15 ng/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
HYPONATRAEMIA WITH ESLICARBAZEPINE ACETATE (ZEBINIX) ADD IN THERAPY IN EVERYDAY CLINICAL PRACTICE USING A RETROSPECTIVE MULTICENTRE AUDIT

Keogh S[1], McDonald P[2], Lawthorn C[3], Brodie M[4], McLean B[5], Mohanraj R[6], Morrow J[7], Tittensor P[8], Bagary M[1]
[1]BSMHFT, Regional Epilepsy and Sleep Service, Birmingham, UK, [2]BSMHFT, Research and Innovation, Birmingham, UK, [3]Department of Neurology, Royal Gwent Hospital, Swansea, UK, [4]University of Glasgow, Glasgow, UK, [5]Royal Cornwall Hospital, Plymouth, UK, [6]Salford Royal Hospital, Manchester, UK, [7]Royal Victoria Hospital, Belfast, UK, [8]Stafford Hospital, Stafford, UK

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 (17–83) 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% ≥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
Monday, 30th June 2014

013
THE ROLE OF TOLL-LIKE RECEPTOR 3 IN EPILEPSY

Benninger F[1,2,3], Gross A[4], Steiner I[1,3], Offen D[2,3], Okun E[4]
[1]Beilinson Hospital Rabin Medical Center, Neurology, Petah Tikva, Israel, [2]Felsenstein Research Medical Center, Rabin Medical Center, Laboratory of Neuroscience, Petah Tikva, Israel, [3]Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel, [4]The Leslie and Susan Gonda Multidisciplinary Brain Research Center, Bar Ilan University, Ramat Gan, Israel

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 gliosis 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

Iffland PH II[1,2], Trigunaite A[3], Jørgensen TN[3], Janigro D[1,4]
[1]Biomedical Engineering, Cleveland Clinic, Cleveland, OH, USA, [2]School of Biomedical Sciences, Kent State University, Kent, OH, USA, [3]Immunology, Cleveland Clinic, Cleveland, OH, USA, [4]Neurological Surgery, Cleveland Clinic, Cleveland, OH, USA

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 = 20) displayed no extravasation of IgG, suggesting that at these disease stages the BBB is intact. Lupus 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. Intranuclear IgG accumulation may be a mechanism of seizure-induced hippocampal sclerosis.

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015
FEBRILE SEIZURES PERSISTENTLY ALTER HIPPOCAMPAL $GABA_A$ RECEPTOR PHYSIOLOGY

Swijsen A[1], Bernareggi A[2], Schipper S[3], Raijmakers M[1,3], Clynen E[1], Aalbers M[3], Rijkers K[3], Dings J[3], Schijns O[3], Vles H[3], Rigo J-M[1], Hoogland G[3]
[1]Hasselt University, Diepenbeek, Belgium, [2]University of Trieste, Trieste, Italy, [3]University Medical Center Maastricht, Maastricht, The Netherlands

Purpose: Febrile seizures (FS) are the most common type of childhood seizures, affecting 2–3% of the children between 3 months and 5 years. Correlative clinical studies have linked early-life FS to hippocampal sclerosis-associated temporal lobe epilepsy (TLE) later in life. Insight into the cellular mechanisms underlying FS-induced epileptogenesis is crucial for a rational drug design to treat TLE. Our present study aims at elucidating if an altered hippocampal GABAergic signalling can be a link between childhood FS and TLE in adulthood.

Method: We make use of an established animal model for FS-induced epileptogenesis in which FS are elicited in 10-day old rat pups by hyperthermia (core temperature ~41–42.5°C). Normothermia littermates (core temperature ~35°C) serve as control. One week later, $GABA_A$R-mediated neurotransmission is determined by whole-cell patch-clamp of granule cells in acute hippocampal slices. For a translational approach, we collected freshly frozen hippocampal biopsies from 4 TLE patients with and 4 TLE patients without a FS history plus 3 non-neurological human autopsy controls. Hippocampal membranes are isolated from the frozen specimen and transplanted into Xenopus laevis oocytes allowing the incorporation of human $GABA_A$ receptors in the oocyte plasma membrane. GABA-evoked currents are recorded by two micro-electrode voltage clamp on oocytes.

Results: Experimental FS induce persistent alterations in spontaneous inhibitory activity. An increased $GABA_A$-receptor sensitivity and changes in subunit expression are also detected after experimental FS.

Conclusion: This study demonstrates that FS cause a long-lasting alteration in hippocampal $GABA_A$-receptor functioning.

016
PATHOGENIC POTENTIAL OF ANTIBODIES DIRECTED AGAINST AMPAR AND $GABA_BR$ IN AUTOIMMUNE ENCEPHALITIS

Nibber A[1], Pettingill P[1], Waters P[1], Mann E[2], Vincent A[1], Lang B[1]
[1]Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK, [2]DPAG, University of Oxford, Oxford, UK

Purpose: Antibodies directed against AMPAR and $GABA_BR$ 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 $GABA_BR$ 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 $GABA_BR$ subunits and primary neuronal cultures. $GABA_BR$ antibody IgG was acutely applied to horizontal brain slices, and in vitro recordings were taken in the entorhinal cortex.

Results: Both AMPAR and $GABA_BR$ antibodies showed staining on the surface of appropriately transfected cells and to live primary neuronal cultures. The main antibody subclass for AMPAR and $GABA_BR$ 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 $GABA_BR$ 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, $GABA_BR$ antibodies do not activate complement, but may be causing a direct modulating effect of cortical networks.

017

TRANSCRIPTIONAL CHANGES IN AMYLOIDOGENIC AND TAU PATHWAYS IN POST-TRAUMATIC EPILEPTOGENESIS IN APP/PS1 MOUSE MODEL OF ALZHEIMER′S DISEASE

Miszczuk D[1], Debski K[1], Tanila H[2], Lukasiuk K[1], Pitkanen A[2]
[1]Laboratory of Epileptogenesis, Nencki Institute for Experimental Biology, Warsaw, Poland, [2]A. I. Virtanen Institute, University of Eastern Finland, Kuopio, Finland

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 effect 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-mTBI 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 Ctsd ($r = 0.63$).

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 transcriptomics 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?

Marchi N[1,2], Puvenna V[3], Janigro D[2,3,4]
[1]Cerebrovascular Research, Biomedical Engineering, Cleveland Clinic, Cleveland, OH, USA, [2]Molecular Medicine, Cleveland Clinic Lerner College of Medicine, Cleveland, OH, USA, [3]Cerebrovascular Research, Biomedical Engineering, Cleveland Clinic Lerner College of Medicine, Cleveland, OH, USA, [4]Flocel Inc, Cleveland, OH, USA

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 a possible link with TBI-related seizures we tested the hypothesis that blood-brain barrier disruption (BBBD) 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

Mirza N[1], Jorgensen A[1], Sills G[1], Johnson M[2], Pirmohamed M[1], Marson AG[1]
[1]University of Liverpool, Liverpool, UK, [2]Imperial College London, London, UK

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 $< 2.2 \times 10^{-16}$), and (ii) there was a highly significant overlap between the enriched pathways for the discovery and replication cohorts (hypergeometric distribution p-value $< 3.7 \times 10^{-17}$). 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

Lemke JR[1,2], Hendrickx R[3], Geider K[4], Bodo L[4], Schwake M[5], Harvey RJ[6], James VM[6], Pepler A[6,7], Steiner I[7], Hörtnagel K[7], Neidhardt J[8], Ruf S[9], Wolff M[9], Bartholdi D[10], Caraballo R[11], Platzer K[12], Suls A[3], De Jonghe P[3], Biskup S[7,10], Weckhuysen S[3]

[1]University of Leipzig, Leipzig, Germany, [2]University of Bern, Bern, Switzerland, [3]University of Antwerp, Antwerp, Belgium, [4]Technical University Darmstadt, Darmstadt, Germany, [5]University of Bielefeld, Bielefeld, Germany, [6]University College London School of Pharmacy, London, UK, [7]CeGaT GmbH – Center for Genomics and Transcriptomics, Tübingen, Germany, [8]University of Zurich, Zurich, Switzerland, [9]University of Tübingen, Tübingen, Germany, [10]Institute of Clinical Genetics, Klinikum Stuttgart, Stuttgart, Germany, [11]Juan P. Garrahan Pediatric Hospital, Buenos Aires, Argentina, [12]University of Lübeck, Lübeck, Germany

Purpose: NMDA receptors are tetrameric ligand-gated ion channels permeable to Na^+, K^+ and Ca^{2+} 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 Mg^{2+} block, all analysed mutations induced a severely increased influx of Ca^{2+} 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

Dibbens LM[1], Scheffer IE[2], Regan BM[2], Mandelstam S[2], Crompton DE[2], Hodgson BL[1], Licchetta L[3], Provini F[3], Bisulli F[3], Vadlamudi L[4], Gecz J[5], Connelly A[2], Tinuper P[3], Ricos MG[1], Berkovic SF[2], Heron SE[1]

[1]University of South Australia, Adelaide, SA, Australia, [2]University of Melbourne, Melbourne, Vic., Australia, [3]University of Bologna, Bologna, Italy, [4]University of Queensland, Brisbane, Qld, Australia, [5]University of Adelaide, Adelaide, SA, Australia

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 epilepsy 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

Steiner I[1], Döcker M[1], Russ AC[1], Battke F[1], Jüngling J[1], Reicherter K[1], Scheurenbrand T[1], Lemke J[2], Lerche H[3], Biskup S[1], Hörtnagel K[1]

[1]CeGaT GmbH, Tuebingen, Germany, [2]Division of Human Genetics, University Children's Hospital, Inselspital, Bern, Switzerland, [3]Department of Neurology and Epileptology, University of Tuebingen, Tuebingen, Germany

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 *SCN1A*, *SCN2A*, *CACNA1A* and *MECP2* being mutated most frequently. Across the cohort, 69 genes were 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

Kolbjer S[1], Wincent J[2,3], Martin D[4], Luthman A[2], Åmark P[1,5], Dahlin M[1,5], Anderlid B-M[2,3]

[1]Department of Neuropediatrics, Astrid Lindgrens Childrens Hospital, Karolinska University Hospital, Stockholm, Sweden, [2]Department of Molecular Medicine and Surgery and Center for Molecular Medicine, Karolinska Institutet, Stockholm, Sweden, [3]Department of Clinical Genetics, Karolinska University Hospital, Stockholm, Sweden, [4]Department of Neuroradiology, Karolinska University Hospital, Stockholm, Sweden, [5]Department of Women and Child Health, Karolinska Institutet, Stockholm, Sweden

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, polymicrogyria, 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 numbers 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

de Kovel CGF[1], Berghuis B[2], Meisler MM[3], Lindhout D[4], Brilstra EH[1], O'Brien J[3], Estacion M[5], Waxman SG[5], Dib-Hajj SD[5], Koeleman BPC[1]

[1]UMC Utrecht, Utrecht, The Netherlands, [2]SEIN Zwolle, Zwolle, The Netherlands, [3]University of Michigan, Ann Arbor, MI, USA, [4]SEIN, Heemstede, The Netherlands, [5]School of Medicine, Yale University, New Haven, CT, USA

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 6 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

Bartolini E[1], Pesaresi I[2], Fabbri S[1], Cecchi P[1], Giorgi FS[3], Sartucci F[1], Bonuccelli U[1], Cosottini M[4]

[1]Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy, [2]Unit of Neuroradiology, Santa Chiara Hospital AOUP, Pisa, Italy, [3]Unit of Neurology, Santa Chiara Hospital AOUP, Pisa, Italy, [4]Department of Traslational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy

Purpose: Juvenile Myoclonic Epilepsy (JME) is a young onset electroclinical syndrome, characterized by myoclonic, generalized tonic-clonic and possibly typical absence seizures. Interictal 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, thalami 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

Woermann FG[1], Bien CG[2], Schulz R[2], Polster T[2], Kalbhenn T[2], Coras R[3], Blumcke I[3]

[1]MRI Unit, Bethel Epilepsy Center, Mara Hospital, Bielefeld, Germany, [2]Bethel Epilepsy Center, Mara Hospital, Bielefeld, Germany, [3]Neuropathology, University Hospital Erlangen, Erlangen, Germany

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 myelinated 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 white matter atrophy, 2 x faint transmantle sign. No circumscribed marked FLAIR- or MT-hyperintensity. Quantitative image postprocessing (MAP07) was positive in 4 cases. Complete resection of MR-visible lesion was achieved in 3 cases at 6 months after surgery.

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.

027
A VOXEL-BASED MORPHOMETRY STUDY OF POSTOPERATIVE SEIZURE OUTCOME IN TEMPORAL LOBE EPILEPSY

Keller SS[1,2], Richardson MP[2], Schoene-Bake J-C[3,4], Elger C[3], Weber B[3,4]

[1]Department of Molecular and Clinical Pharmacology, Institute of Translational Medicine, University of Liverpool, Liverpool, UK, [2]Department of Clinical Neuroscience, Institute of Psychiatry, King's College London, London, UK, [3]Department of Epileptology, University of Bonn, Bonn, Germany, [4]Department of Neurocognition/Imaging, Life & Brain Research Centre, Bonn, Germany

Purpose: It remains unknown why over 30% of patients with intractable temporal lobe epilepsy (TLE) continue to experience postoperative seizures. We sought to compare brain structure between patients rendered seizure free (SF), those continuing with postoperative seizures (PS), and healthy controls using voxel based morphometry (VBM).

Methods: We studied 81 patients with unilateral TLE and hippocampal sclerosis who were surgically rendered SF using amygdalohippocampectomy (ILAE I-II, n = 51) or continued to experience PS (ILAE III-VI, n = 30), and 79 age-matched healthy controls. T1-weighted MRIs were acquired using the same sequences on a 3T scanner for all participants. VBM (SPM8) was used to map differences in brain structure between groups. MRIs of patients with right TLE were left-right flipped so that abnormalities in patients were considered as ipsilateral and contralateral. Results are reported corrected for multiple comparisons over the whole brain (FWE, $p < 0.05$).

Results: Compared to controls, patients with PS and those rendered SF both had grey matter (GM) atrophy of the ipsilateral hippocampus, extrahippocampal temporal lobe, mesial occipital-parietal cortex and cerebellum. Only patients with PS showed evidence of significant atrophy of the ipsilateral thalamus; thalamic voxels showing atrophy were connected with hippocampal voxels showing atrophy, and corresponded to a hippocampothalamic anatomical pathway via the fornix route. Contralateral thalamus was atrophic in patients with PS using uncorrected statistical thresholds. In direct comparisons between patient groups, patients with PS had significant GM loss of the thalamus bilaterally. An ROI analysis on the hippocampi indicated that GM volume of the contralateral hippocampus was reduced in patients with PS relative to those rendered SF.

Conclusion: Thalamic atrophy is associated with a poor seizure outcome after temporal lobe surgery. Persistent postoperative seizures are also associated with subtle contralateral mesial temporal atrophy.

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

Veersema TJ[1], Ferrier CH[1], van Eijsden P[1], Gosselaar PH[1], Hendrikse J[2], Spliet WGM[3], Aronica E[4], Braun KPJ[1]

[1]Department of Neurology and Neurosurgery, Brain Center Rudolf Magnus, University Medical Center Utrecht, Utrecht, The Netherlands, [2]Department of Radiology, University Medical Center Utrecht, Utrecht, The Netherlands, [3]Department of Pathology, University Medical Center Utrecht, Utrecht, The Netherlands, [4]Department of Pathology, Academic Medical Center, Amsterdam, The Netherlands

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[1]. 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 [2] 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. T_1, T_2, 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 IIb (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)

Strandberg M[1], Ljung H[1], Källén K[1]
[1]Skåne University Hospital, Lund, Sweden

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

Grade M[1], Carmichael DW[2], Chaudhary UJ[1], Lemieux L[1], Diehl B[1]
[1]UCL Institute of Neurology, London, UK, [2]UCL Institute of Child Health, London, UK

Purpose: A number of medication refractory patients with focal epilepsy require invasive monitoring of ictal 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

Mühlebner A[1], Leiner S[1], Gröppel G[1], Dressler A[1], Reiter-Fink E[1], Dorfer C[2], Czech T[2], Hainfellner JA[3], Prayer D[4], Feucht M[1]
[1]Department of Pediatrics, Medical University of Vienna, Vienna, Austria, [2]Department of Neurosurgery, Medical University of Vienna, Vienna, Austria, [3]Institute of Neurology, Medical University of Vienna, Vienna, Austria, [4]Department of Radiology, Medical University of Vienna, Vienna, Austria

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 $\pm$ 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

Boon P[1], van Rijckevorsel K[2], Elger CE[3], Mullatti N[4], Vonck K[5], Schulze-Bonhage A[6], Wagner LG[7], Van Grunderbeek W[8], Mcguire R[9], Begnaud J[9]

[1]University Hospital Ghent, Neurology, Ghent, Belgium, [2]Cliniques Universitaires Saint Luc, Brussels, Belgium, [3]University Hospital Bonn, Bonn, Germany, [4]King's College Hospital, London, UK, [5]University Hospital Ghent, Ghent, Belgium, [6]University Hospital Freiburg, Freiburg, Germany, [7]Kempenhaeghe, Heeze, The Netherlands, [8]Cyberonics BVBA, Diegem, Belgium, [9]Cyberonics USA, Houston, TX, USA

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 AspireSR™ 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

Jin S-H[1], Chung CK[1,2,3]

[1]Department of Neurosurgery, Seoul National University Hospital, Seoul, Korea, [2]Department of Neurosurgery, Seoul National University College of Medicine, Seoul, Korea, [3]Department of Brain and Cognitive Sciences, Seoul National University College of Natural Sciences, Seoul, Korea

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

Milian M[1], Wisniewski I[2], Wendling A-S[2], Gharabaghi A[1], Rona S[1]

[1]University Hospital Tübingen, Tübingen, Germany, [2]Epilepsy Center Kork, Kehl-Kork, Germany

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 OoL 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

Lehtimäki K[1], Möttönen T[1], Öhman J[1], Peltola J[2]
[1]Department of Neurosurgery, Tampere University Hospital, Tampere, Finland, [2]Department of Neurology, Tampere University Hospital, Tampere, Finland

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 SURGICAL RESECTIONS IN FOCAL EPILEPSY

Thom M[1,2], Tachrount M[3], Reeves C[1,2], Eriksson S[2], Yousry T[3]
[1]Department of Neuropathology, UCL Institute of Neurology, London, UK, [2]Department of Clinical and Experimental Epilepsy, UCL Institute of Neurology, London, UK, [3]Department of Brain Repair and Rehabilitation, UCL Institute of Neurology, London, UK

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 T2star ($p = 0.029$). 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 PDGFRβ AND NG2 PERICYTES AFTER SEIZURES

Milesi S[1], Boussadia B[2], Rousset M-C[2], DeBock F[2], Schaeffer M[2], Rigau V[2], Lerner-Natoli M[2], Marchi N[2]
[1]Department of Neurobiology, Institute of Functional Genomic – CNRS, Montpellier, France, [2]Department of Neurobiology, Institute of Functional Genomic, Montpellier, France

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. BL/6 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 autoptic 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, $PDGFR\beta^+$ 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 autoptic control.

Conclusion: The rearrangement of $PDGFR\beta^+$ 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.

038
TARGETING HYPERPHOSPHORYLATED TAU IS A DISEASE-MODIFYING TREATMENT IN A POST-STATUS EPILEPTICUS RAT MODEL OF TEMPORAL LOBE EPILEPSY

Zheng P[1], Shultz SR[1], Liu S[1], Wright D[2], Hovens C[3], Jones N[1], O'Brien TJ[1]

[1]Medicine, Royal Melbourne Hospital, Melbourne, Vic., Australia, [2]Royal Melbourne Hospital, Melbourne, Vic., Australia, [3]Surgery, Royal Melbourne Hospital, Melbourne, Vic., Australia

Purpose: To investigate whether treatment with sodium selenate, a drug that reduces the pathological hyperphosphorylation of tau by increasing protein phosphatase 2A (PP2A) activity, would reduce spontaneous seizures, neurodegeneration and glial activation in a post- status epilepticus (SE) rat model of temporal lobe epilepsy (TLE).

Method: After 4 h of SE induced by systemic kainic acid (KA) injections, or control-saline injections, young-adult male Wistar rats (n = 9/group) were given continuous sodium selenate treatment (1 mg/kg/day), with a subcutaneous osmotic mini-pump for 2 months. In-vivo MRI and MRS was used to assess neuronal damage and glia activation 1 month post-injury. Video-EEG recording was used to evaluate the seizure frequency and duration both during the treatment and after the treatment. Molecular tests were used to assess levels of hyperphosphorylated tau and related pathologies.

Results: During the treatment, the post-SE rats with saline treatment got 1.4 seizures/day, and selenate treatment could reduce the frequency to 0.1 seizures/day. After the drug washout, the effect was sustained (8.6 seizures/day in saline group vs. 2.6 seizures/day in selenate group). Selenate treatment also decreased the neurodegeneration and glial activation reflected by MRS imaging and further confirmed by immunofluorescence imaging. The selenate treatment also reduced the volume of ventricles and increased the volume of hippocampus in post-SE rats.

Conclusion: Sodium selenate treatment can reduce spontaneous seizures and biomarkers for neurodegeneration and glial activation in a post-SE rat model of TLE.

039
THE EFFECT OF DEXAMETHASONE ON ABSENCE SEIZURES OF RATS WITH GENETIC ABSENCE EPILEPSY

Eryigit T[1], Ravizza T[2], Vezzani A[2], Onat Yılmaz F[1]

[1]School of Medicine, Marmara University, Istanbul, Turkey, [2]Department of Neuroscience, Mario Negri Institute for Pharmacological Research, Milano, Italy

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 LITHUIM-PILOCARPINE IN ADULT RATS

Landgrave-Gómez J[1], Mercado-Gomez O[1], Guevara-Guzmán R[1]

[1]Physiology, Universidad Nacional Autónoma de México, Distrito Federal, Mexico

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 determinated whether a feeding restiction 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 β-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 scopololamine 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 β-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 has significant anticonvulsant activity resembling some features of calorie restiction model, such as an increase in ketone body levels, activation of AMPK signaling pathway and decreasing activity of Akt signaling pathway. Moreover, we establish that alimentary restriction prove its efficacy decreasing drastically seizure duration, percentage of status epilepticusand seizure score.

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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

Balosso S[1], Liu J[2], Bianchi ME[2], Vezzani A[1]
[1]IRCCS-Istituto di Ricerche Farmacologiche "Mario Negri," Milano, Italy, [2]San Raffaele Scientific Inst and San Raffaele University, Milano, Italy

Purpose: HMGB1 is a "danger signaling" protein released by glia and neurons following experimental brain injuries, upregulated in human epilepsy 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 μg 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 $Tlr4^{-/-}$ neurons. These pathologic effects were mediated by Src-dependent phosphorylation of NR2B subunit which increases NMDA receptor Ca^{2+} permeability.

Conclusion: *Oxidized* HMGB1 activates a molecular pathway in neurons that contributes to seizures and neurodegeneration. Antioxidant treatments and antagonists of HMGB1-TLR4 signaling represent promising anti-seizures and neuroprotective drugs.

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

Thyrion L[1], Raedt R[1], Ydens E[2,3], Janssens S[3], Kips J[1], van Loo P[1], Portelli J[1], Lambrecht B[3], Meurs A[1], Vonck K[1], Boon P[1]
[1]Department of Neurology, Ghent University, Ghent, Belgium, [2]Department of Molecular Genetics, University of Antwerp, Antwerp, Belgium, [3]Inflammation Research Center, University of Ghent, Ghent, Belgium

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.

Platform Session: Antiepileptic Drugs 2
Tuesday, 1st July 2014

043
THE IMPACT OF THE OVERALL DRUG LOAD ON MEMORY AND EXECUTIVE FUNCTIONS: NUMBER OF ANTIEPILEPTIC DRUGS VS. TOTAL DAILY DEFINED DOSE (WHO)

Witt J-A[1], Elger CE[1], Helmstaedter C[1]
[1]Department of Epileptology, University Clinic of Bonn, Bonn, Germany

Purpose: The study was set up to disclose the impact of the overall drug load of antiepileptic pharmacotherapy on cognition.

Method: Analyses were performed in 834 patients with epilepsy who underwent a brief routine cognitive assessment (EpiTrack Plus) at our

department before an intended change of medication. The applied Epi-Track 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

French JA[1], Kowalski J[2], Maciejowski M[3], Ilankumaran P[4], Kamin M[4]

[1]New York University School of Medicine, New York, NY, USA, [2]NZOZ VITO-MED Sp. Ltd, Gliwice, Poland, [3]NZOZ Diagnomed, Katowice, Poland, [4]SK Life Science Inc., Fair Lawn, NJ, USA

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 (≥3/28 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 ≥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). Nervous system/GI adverse events included balance disorder (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.

Study sponsored by SK Life Science Inc.

045
FROM EARLY ADD-ON LACOSAMIDE TO MONOTHERAPY CONVERSION: RESULTS OF REALLY STUDY

Villanueva V[1], Garcés M[1], López Gomáriz E[2], Serratosa JM[3], González-Giráldez B[3], Parra J[4], Rodríguez-Uranga J[5], Toledo M[6], Salas-Puig J[6], López González FJ[7], Bermejo P[8], Giner P[9], Torres N[9], Castillo A[10], Molins A[11], Mauri JA[12], Campos D[13], on behalf of REALLY Group

[1]Hospital Universitario y Politécnico La Fe, Valencia, Spain, [2]Hospital Lluis Alcanyis, Xátiva, Spain, [3]Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain, [4]Hospital San Rafael, Madrid, Spain, [5]IENSA-Clinica Sagrado Corazón, Sevilla, Spain, [6]Hospital Universitario Vall d'Hebron, Barcelona, Spain, [7]Hospital Clinico Universitario Santiago, Santiago Compostela, Spain, [8]Hospital Universitario Puerta de Hierro, Madrid, Spain, [9]Hospital Universitario Dr. Peset, Valencia, Spain, [10]Consorcio Hospital General Universitario, Valencia, Spain, [11]Hospital Universitario Josep Trueta, Girona, Spain, [12]Hospital Clinico Universitario, Zaragoza, Spain, [13]Hospital Clinico Universitario, Valladolid, Spain

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 5) Patients with at least 1 partial seizure in the year before inclusion. Conversion to LCM monotherapy was assessed.

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 (67.3%) 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.

Abstracts

046
STEREOSELECTIVE ANTICONVULSANT AND PHARMACOKINETIC ANALYSIS OF VALNOCTAMIDE, A CNS-ACTIVE DERIVATIVE OF VALPROIC ACID WITH LOW TERATOGENIC POTENTIAL

Shekh-Ahmad T[1], Hen N[1], Yagen B[1], McDonough JH[2], Wlodarczyk BJ[3], Bialer M[1]
[1]School of Pharmacy, Institute for Drug Research, The Hebrew University of Jerusalem, Jerusalem, Israel, [2]Pharmacology Branch, Research Division, US Army Medical Research Institute of Chemical Defense, Aberdeen, MD, USA, [3]Department of Nutritional Sciences, Dell Pediatric Research Institute, The University of Texas at Austin, Austin, TX, USA

Purpose: Valnoctamide-(VCD), a CNS-active chiral constitutional isomer of valpromide, 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 ED_{50} 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-ED_{50} 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

Wechsler RT[1], Li G[2], O'Brien T[3], D'Cruz O[4], Williams P[4], Goodson R[4], Brock M[4]
[1]Consultants in Epilepsy and Neurology, PLLC, Boise, ID, USA, [2]Medsol Clinical Research Center, Port Charlotte, FL, USA, [3]The Royal Melbourne Hospital, University of Melbourne, Melbourne, Vic., Australia, [4]UCB Pharma, Raleigh, NC, USA

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 ≥1 exit criterion by Day 112 was 30.0% (95% CI: 24.6%, 35.5%) and 27.3% (95% CI: 18.4%, 36.3%), respectively, both were lower than the historical control exit percentage of 65.3%. In post-hoc analyses on the safety set, ≥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.

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

Wide KA[1], Wallander M[2], Linder C[2], Pohanka A[2], Beck O[2], Gustafsson LL[3]
[1]Division of Pediatrics, Karolinska Institute, CLINTEC, Stockholm, Sweden, [2]Karolinska University Hospital, Stockholm, Sweden, [3]Karolinska Institutet, Stockholm, Sweden

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 of30 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 mikroL) samples dried on filter paper (whatman-903 protein saver cards), hematocrit, and an ordinary 500 mikroL capillary sample were collected from each patient.

Results: The LCMS/MS method was fully validated according to guidelines from European Medecines Agency for VPA, LTG and CBZ for DBS samples)The method were 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

Del Felice A[1], Arcaro C[2], Manganotti P[1,2,3]
[1]Section of Neurology, Department of Neurological and Movment Sciences, University of Verona, Verona, Italy, [2]Department of Neurophysiology, IRCCS San Camillo, Venezia, Italy, [3]Clinical Neurophysiology and Functional Imaging Unit, Section of Neurology, University of Verona, Verona, Italy

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 to 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

Schwind J[1], Dümpelmann M[2], Mader M[1], Schulze-Bonhage A[2], Jacobs J[1]
[1]Department of Neuropediatrics, Univeristy of Freiburg, Freiburg, Germany, [2]Epilepsy Center, University of Freiburg, Freiburg, Germany

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 6–025 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?

Evangelista E[1], Bénar C-G[2,3], Carron R[4], Bartolomei F[2,3,5]
[1]Aix-Marseille University, Marseille, France, [2]INSERM UMR 1106, Marseille, France, [3]Institut de Neurosciences des Systèmes, Aix Marseille Université, Marseille, France, [4]Service de Neurochirurgie Fonctionnelle et Stéréotaxique, APHM, Hôpital Timone, Marseille, France, [5]Service de Neurophysiologie Clinique, APHM, Hôpital Timone, Marseille, France

Purpose: The role of synchronized thalamo-cortical networks in focal seizures has not yet been thoroughly studied. Moreover the exact mechanisms 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.

Abstracts

052
SYNCHRONIZATION AND BRAIN CONNECTIVITY IN PATIENTS WITH FOCAL PERIODIC ACTIVITY IN SCALP EEG: ICTAL FEATURES

Maestro Saiz I[1], Lopetegui Alba E[2], O'Toole JM[2], García Zapirain B[2], Anaya-Chen AB[3], Yurrebaso Santamaría I[3]
[1]Clinical Neurophysiology, Epilepsy Unit, Cruces University Hospital, Barakaldo, Spain, [2]Deusto Tech-LIFE, University of Deusto, Bilbao, Spain, [3]Clinical Neurophysiology, Cruces University Hospital, Barakaldo, Spain

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 underdiagnosed non-convulsive status *epilepticus*.

053
AUDITORY-VERBAL REMINISCENCE EXPERIENCES SUGGESTING A FUNCTIONAL INTERACTION OF INSULAR-TEMPORAL NETWORKS: CORTICAL STIMULATION DATA IN EPILEPTIC PATIENTS

Scholly J[1], Valenti Hirsch MP[1], Bartolomei F[2], Seegmuller A-C[1], Boulay C[1], De Saint-Martin A[3], Benmekhbi M[4], Kehrli P[4], Hirsch E[1]
[1]Department of Neurology, University of Strasbourg, Strasbourg, France, [2]Service de Neurophysiologie Clinique, Hôpital Timone, University Aix-Marseille II, Marseille, France, [3]Department of Paediatrics, University of Strasbourg, Strasbourg, France, [4]Department of Neurosurgery, University of Strasbourg, Strasbourg, France

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 anatomo-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, temporo-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 vecus. All AVR were characterised by non lateralized brief "hearing" of human voices, often with emotional connotation and with an 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 vecus, 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

Maliia MD[1], Barborica A[2,3], Donos C[2], Ciurea J[4], Mindruta I[1,5]
[1]Neurology Clinic/Epilepsy and Sleep Center, University Emergency Hospital Bucharest, Bucharest, Romania, [2]Faculty of Physics, Electricity and Biophysics, University of Bucharest, Bucharest, Romania, [3]FHC Inc, Bowdoin, ME, USA, [4]Neurosurgery, Bagdasar-Arseni Hospital, Bucharest, Romania, [5]Clinical Neurology, University of Medicine and Pharmacy "Carol Davila," Bucharest, Romania

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.

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

055

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

Vogt VL[1], Becker AJ[1], Elger CE[1], von Lehe M[2], Helmstaedter C[1]
[1]University of Bonn Medical Center, Bonn, Germany,
[2]University Hospital Bochum, Bochum, Germany

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 benign with respect to survival. Several factors, including size, side and specific tumor growth patterns may contribute to this phenomenon.

056

EMOTION'S RECOGNITION IN MEDIAL TEMPORAL LOBE EPILEPSY: A SYSTEMATIC REVIEW

Monti G[1], Meletti S[1]
[1]Department of Biomedical, Metabolism, and Neuroscience, University of Modena and Reggio Emilia, Modena, Italy

Purpose: To analyse current literature on emotion recognition (ER) in temporal lobe epilepsy (TLE). In particular, we aim to analyse whether differences (if any) in ER performance could be explained by disease-related factors.

Method: We included cross-sectional studies comparing TLE or temporal lobectomy (ATL) patients respect with healthy volunteers (HV) or/and clinical control groups (CCG, such as extra-MTLE, IGE). The few longitudinal studies comparing the same patients before and after ATL were also considered. Studies using all types of ER stimuli (facial expressions, prosody, visual dynamic stimuli and music) were considered. Disease related variables: age of epilepsy onset, duration of disease, types and number of antiepileptic drugs, side of seizure focus, pathology, pre/post-surgery status.

Results: Thirty-six studies meet full inclusion criteria. Most of the studies (33 out of 36) showed severe ER impairment in MTLE and ATL patients 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

Meekes J[1,2], van Schooneveld M[1], Braams OB[1,2], Braun KPJ[1], Jennekens-Schinkel A[1,2], van Rijen PC[1], Hendriks MPH[3,4], van Nieuwenhuizen O[1]
[1]University Medical Center Utrecht, Utrecht, The Netherlands,
[2]Bio Research Center for Children, Arnhem, The Netherlands,
[3]Epilepsy Centre Kempenhaeghe, Heeze, The Netherlands,
[4]Radboud University, Nijmegen, The Netherlands

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.

Methods: 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 ($F_{2,115} = 3.25$, $p = 0.04$, adjusted $R^2 = 0.04$). 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 age at surgery, duration of epilepsy, etiology, and type of surgery best predicted pre-surgical IQ ($F_{9,108} = 17.8$, $p < 0.001$, adjusted $R^2 = 0.56$). The best model for post-surgical IQ ($F_{2,115} = 465.2$, $p < 0.001$, adjusted $R^2 = 0.89$), however, included only pre-surgical IQ and PE 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

Tonberg A[1], McLellan A[2,3], Harden J[3], Chin R[2,3], Duncan S[3,4]
[1]Epilepsy Scotland, Glasgow, UK, [2]Neurology, Royal Hospital for Sick Children, Edinburgh, UK, [3]University of Edinburgh, Edinburgh, UK, [4]National Health Service, Edinburgh and South East Scotland Epilepsy Service, Edinburgh, UK

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 disclosure. 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 difficulties. 14/22 (64%) thought it should not be done immediately at diagnosis, but soon after. 4/22 (18%) personally favoured disclosure at diagnosis, but did not think this was best for the general epilepsy population. 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

Giovagnoli AR[1], Parente A[1], Deleo F[1], Didato G[1], D'Incerti L[1], Tringali G[2], Villani F[1]
[1]Diagnostics and Applied Technology, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy, [2]Neurosurgery, Fondazione I.R.C.C.S. Istituto Neurologico Carlo Besta, Milan, Italy

Purpose: Temporal lobe epilepsy (TLE) surgery bears the risk of loosing memory and language, which may counteract the benefits of seizure control. 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 functionally eloquent areas, involving the anterior lateral and medial temporal lobe encompassing the uncus, amygdala, and part of the hippocampus. The faux pas 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 preoperative and postoperative test scores obtained 6 months and a year after surgery, 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 distinction of these cognitive domains.

060
INTERICTAL EPILEPTIC ACTIVITY INTERFERES WITH FRONTAL LOBE FUNCTION IN TEMPORAL LOBE EPILEPSY

Dinkelacker V[1,2], Xin X[1,3], Baulac M[1,2], Samson S[4], Dupont S[1,2]
[1]Epilepsy Unit, Hôpital Pitié-Salpêtrière, Paris, France, [2]Institut du Cerveau et de la Moelle (ICM), Paris, France, [3]Laboratory of Neural Engineering/SFNC, Tsinghua University, Beijing, China, [4]Laboratoire de Neurosciences Fonctionnelles, Lille University, Lille, France

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. Temporal 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 correlated with diminished performance in a large range of executive functions. We suggest that epileptic discharge has a genuine impact on cognitive functions beyond the temporal lobe, most likely via alterations of frontotemporal interplay.

Platform Session: Epilepsy Surgery
Tuesday, 1st July 2014

061
THE USE OF 3D MULTIMODALITY IMAGING IN THE PRESURGICAL EVALUATION OF EPILEPSY

Nowell M[1,2], Rodionov R[1,2], Zombori G[3], Ourselin S[3], Micallef C[1], Diehl B[1], Wehner T[1], Miserocchi A[4], McEvoy A[4], Duncan J[1,2]

[1]Department of Epilepsy, University College London, London, UK, [2]MRI Unit, Epilepsy Society, Chalfont St Peter, UK, [3]Centre for Medical Image Computing, University College London, London, UK, [4]Department of Nerosurgery, National Hospital for Neurosurgery and Neurology, London, UK

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 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

Reinholdson J[1], Lundgren J[1], Edelvik A[2], Flink R[3], Hallbook T[4], Olsson I[4], Rydenhag B[2], Malmgren K[2]

[1]Department of Paediatrics, Institution of Clinical Sciences, Lund University, Lund, Sweden, [2]Epilepsy Research Group, Institute of Neuroscience and Physiology, Sahlgrenska Academy at the University of Gothenburg, Gothenburg, Sweden, [3]Department of Clinical Neurophysiology, Akademiska University Hospital, Uppsala, Sweden, [4]Institute of Clinical Sciences, Sahlgrenska Academy at the University of Gothenburg, Gothenburg, Sweden

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

Barba C[1], Sylvain R[2], Minotti L[3], Isnard J[2], Hoffmann D[4], Chabardes S[4], Guenot M[5], Ryvlin P[6,7], Kahane P[3,8]

[1]Pediatric Neurology Unit, Children's Hospital Meyer, Florence, Italy, [2]Functional Neurology and Epileptology UNIT, Neurological Hospital, Hospices Civils de Lyon, Lyon, France, [3]Neurology, Grenoble University Hospital, Grenoble, France, [4]Neurosurgery, University Hospital Grenoble, Grenoble, France, [5]Neurosurgery, Neurological Hospital, Hospices Civils de Lyon, Lyon, France, [6]Functional Neurology and Epileptology, Hospices Civils de Lyon, Lyon, France, [7]CRNL, TIGER, Lyon, France, [8]GIN INSERM U 836, Grenoble, France

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 statiscally 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

Goellner E[1], Bianchin MM[2], Burneo JG[3], Parrent AG[3], Steven DA[3]

[1]Hospital Mãe de Deus, Porto Alegre, Brazil, [2]Ciências Médicas, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil, [3]Clinical Neurological Sciences, Western University, London, ON, Canada

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 surgical 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 < 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

Golovteev A[1], Shishkina L[1], Arkhipova N[1], Grinenko O[1], Pronin I[1], Kozlova A[1], Vorobyev A[1], Kuszel Y[1], Melikyan A[1]

[1]Burdenko Neurosurgical Institute, Moscow, Russian Federation

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 extra-temporal 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). Pre-operative evaluation included assessment of clinical history, seizure semiology, video-EEG and MRI. Electrocorticography (ECOG) was used intraoperatively 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

Rydenhag B[1], Flink R[2], Malmgren K[3], Epilepsy Surgery Group

[1]Neurosurgery, Göteborg, Sweden, [2]Department of Clinical Neurophysiology, Uppsala, Sweden, [3]Institute of Clinical Neurocience, Sahlgrenska Academy, Göteborg, Sweden

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 Tuesday, 1st July 2014

067

THE EMERGING PHENOTYPE OF *SCN8A* ENCEPHALOPATHY

Larsen J[1,2,3], Carvill GL[4], Gardella E[1], Kluger G[5], Schmiedel G[6], Barisic N[7], Depienne C[8,9,10], Brilstra E[11], Mang Y[2], Klint JE[12], Kirkpatrick M[13], Goudie D[14], Goldman R[13], Jähn JA[15], Jepsen B[1], Gill D[16], Döcker M[17], Biskup S[17], McMahon JM[18], Koeleman B[11], Braun K[11], de Kovel CCF[19], Marini C[20], Specchio N[21], Djémié T[22,23], Weckhuysen S[22,23], Tommerup N[2], Troncoso M[24], Troncoso L[24], Bevot A[25], Wolff M[25], Hjalgrim H[1,3], Guerrini R[21], Scheffer IE[18,26,27], Mefford HC[4], Møller RS[1,3], EuroEPINOMICS RES CRP

[1]Danish Epilepsy Centre, Dianalund, Denmark, [2]ICMM, Panum Institute, University of Copenhagen, Copenhagen, Denmark, [3]Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark, [4]Division of Genetic Medicine, Department of Pediatrics, University of Washington, Seattle, WA, USA, [5]Schön Klinik Vogtareuth, Clinic for Neuropediatrics and Neurorehabilitation, Epilepsy Center for Children and Adolescents, Vogtareuth, Germany, [6]Clinic for Children and Adolescents, Esslingen, Germany, [7]Department of Pediatrics, University Hospital Centre Zagreb, Zagreb, Croatia, [8]Faculté de Médecine, Université Pierre et Marie Curie, Paris, France, [9]INSERM UMRS 975, CNRS UMR 725, Paris, France, [10]Institut für Humangenetik, Universität Würzburg, Würzburg, Germany, [11]Department of Medical Genetics, Medical Center Utrecht, Utrecht, The Netherlands, [12]Department of Clinical Medicine, Roskilde Hospital, Roskilde, Denmark, [13]Tayside Children's Hospital, Dundee, UK, [14]Ninewells Hospital and Medical School, Dundee, UK, [15]University Medical Center Schleswig-Holstein, Christian-Albrechts University, Kiel, Germany, [16]The Children's Hospital at Westmead, Sydney, NSW, Australia, [17]CeGaT GmbH – Center for Genomics and Transcriptomics, Tübingen, Germany, [18]Epilepsy Research Centre, University of Melbourne, Melbourne, Vic., Australia, [19]Medical Genetics Research, UMC Utrecht, Utrecht, The Netherlands, [20]Child Neurology Unit, Pediatric Hospital Bambino Gesú, Rome, Italy, [21]Child Neurology Unit, Children's Hospital A. Meyer and University of Florence, Florence, Italy, [22]Department of Molecular Genetics, Neurogenetics Group, University of Antwerp, Antwerp, The Netherlands, [23]Laboratory of Neurogenetics, University of Antwerp, Antwerp, The Netherlands, [24]Child Neurology Service Hospital San Borja Arriarán, University of Chile, Santiago, Chile, [25]Department of Pediatric Neurology, University Children's Hospital, Tübingen, Germany, [26]Florey Institute Melbourne, Melbourne, Vic., Australia, [27]Department of Paediatrics, University of Melbourne, Melbourne, Vic., Australia

Purpose: *SCN8A* encodes a voltage-gated sodium channel ($Na_v1.6$) 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.

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LONG TERM CLINICAL AND COGNITIVE OUTCOME IN SUBJECTS WITH PCDH19 MUTATION

Darra F[1], Offredi F[1], Cantalupo G[1], Fontana E[1], Fiorini E[1], Dalla Bernardina B[1]

[1]Life and Reproduction Sciences, Verona, Italy

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 49.6).

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.

Abstracts

069
AEDS EFFICACY IN THE DRAVET SYNDROME: A CROSS-SECTIONAL STUDY

De Liso P[1,2], Chemaly N[2,3,4], Dulac O[2,3,4], Chiron C[2,3,4], Nabbout R[2,3,4]
[1]Department of Pediatrics and Child Neurology and Psychiatry, Sapienza University of Rome, Rome, Italy, [2]Centre de Référence des Epilepsies Rares (CRéER), Hôpital Necker Enfants Malades, Paris, France, [3]Unité Inserm U 1129 Infantile Epilepsies and Brain Plasticity, Université Paris Descartes, Necker Enfants Malades, Paris, France, [4]Service de Neuropédiatrie, Hôpital Necker Enfantes Malades, Paris, France

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 fever sensitive. In the oldest patients (>10y) compared to youngers (6–10 years), seizures were most 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 epileptics and long lasting seizures with tritherapy (STP, VPA, 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

Tohyama J[1,2], Akasaka N[1], Kobayashi Y[1], Magara S[1], Kawashima H[1], Kato M[3], Matsumoto N[4], Saitsu H[4]
[1]Department of Child Neurology, Nishi-Niigata Chuo National Hospital, Niigata, Japan, [2]Bioscience Medical Research Center, Niigata University Medical and Dental Hospital, Niigata, Japan, [3]Department of Pediatrics, Faculty of Medicine, Yamagata University, Yamagata, Japan, [4]Department of Human Genetics, Yokohama City University Graduate School of Medicine, Yokohama, Japan

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 stereotypies. 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 stereotypies are heterogeneous. More precise evaluations for genotype-phenotype study would be necessary to establish the proper diagnostic approach to IEE.

071
TREATMENT OF ENCEPHALOPATHY WITH ELECTRICAL STATUS EPILEPTICUS IN SLEEP (ESES) – META-ANALYSIS AND UPCOMING RANDOMIZED CONTROLLED TRIAL

Van den Munckhof B[1], Van Dee V[1], Liukkonen E[2], Sagi L[3], Loddenkemper T[4,5], Sánchez Fernández I[6], Caraballo R[7], Veggiotti P[8], Buzatu M[9], Bulteau C[10], Perucca E[8], Arzimanoglou A[11], Braun KP[1], Jansen FE[1]
[1]Pediatric Neurology, Brain Center Rudolf Magnus, University Medical Center Utrecht, Utrecht, The Netherlands, [2]Pediatric Neurology, Helsinki University Central Hospital, Helsinki, Finland, [3]Pediatric Neurology, Tel Aviv Medical Center, Tel Aviv, Israel, [4]Cleveland Clinic, Epilepsy Center, Cleveland, OH, USA, [5]Children's Hospital Boston and Harvard Medical School, Neurology, Boston, MA, USA, [6]Children's Hospital Boston and Harvard Medical School, Boston, MA, USA, [7]Neurology, Hospital de Pediatría "Prof. DR. Juan P. Garrahan," Buenos Aires, Argentina, [8]C. Mondino National Neurological Institute and University of Pavia, Pavia, Italy, [9]Pediatric Neurology, ULB-Hôpital Erasme, Brussels, Belgium, [10]Pediatric Neurosurgery, Fondation Rothschild, Paris, France, [11]Epilepsy, Sleep and Pediatric Neurophysiology, University Hospital of Lyon (HCL) Lyon and Lyon Neuroscience Research Center (CRNL), Lyon, France

Purpose: Epileptic encephalopathy with ESES is a rare pediatric epilepsy syndrome with sleep-aggravated epileptic discharges and acquired impairment of cognition or behavior. The goal of treatment of ESES syndrome is to improve cognitive outcome. The aim of this meta-analysis is to create an overview of the current evidence for different treatment regimens in children with ESES syndrome.

Method: A broad literature search using Pubmed and Embase was performed. Articles were selected if they contained original treatment data of patients with ESES syndrome. Authors were contacted for additional information. Individual patient-data were collected, coded and analyzed using logistic regression.

Results: The literature search yielded 1,766 articles. After excluding duplicates and applying in- and exclusion criteria, 114 articles remained that described 950 treatments in 575 patients. Antiepileptic drugs (AEDs, n = 495) were associated with any (i.e. cognitive and/or EEG) improvement in 49% of patients, benzodiazepines (n = 171) in 68% and steroids

(n = 166) in 81%. Surgery (n = 62, e.g. multiple subpial transection and focal resection) resulted in any improvement in 90%. We subsequently performed a subgroup analysis, including only patients who were consecutively reported (n = 585) and found any improvement in a smaller proportion of patients (AEDs 34%, benzodiazepines 59%, steroids 75% and surgery 93%, respectively). Possible predictors of improved outcome were treatment category, normal development before ESES onset and the absence of structural abnormalities.

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

McGinnity CJ[1], Tyson AL[2], Gammerman A[1], Gerbase SW[3], Elmasri M[4], Reed TK[5], Said MA[1], Pina M[6], Barker GJ[7], Smith AB[1], Richardson MP[1], Pal DK[1]

[1]Department of Clinical Neuroscience, King's College London, London, UK, [2]Immunology Infection and Inflammatory Disease Research Division, King's College London, London, UK, [3]Department of Psychological Medicine, King's College London, London, UK, [4]Department of Biomedical Sciences, King's College London, London, UK, [5]School of Psychology and Clinical Language Sciences, University of Reading, Reading, UK, [6]Department of Clinical Neurophysiology, King's College Hospital, London, UK, [7]Centre for Neuroimaging Sciences, King's College London, London, UK

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/mm^2) 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 ($p \leq 0.05$ 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 scoresand FA and sentence comprehension scores ($p \leq 0.05$ 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.

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073
DOSE-DEPENDENT TERATOGENICITY OF VALPROATE IN MONO- AND COMBINATION THERAPY

Tomson T[1], The EURAP Study Group

[1]Karolinska Institutet, Clinical Neuroscience, Stockholm, Sweden

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

Pickrell WO[1,2], Lacey AS[2,3], White CP[2,4], Rees MI[1,2], Natarajan J[5]

[1]Neurology and Molecular Neuroscience, College of Medicine, Swansea University, Swansea, UK, [2]Wales Epilepsy Research Network, College of Medicine, Swansea University, Swansea, UK, [3]Health Informatics Research Unit, Swansea University, Swansea, UK, [4]Morriston Hospital, Abertawe Bro Morgannwg University Health Board, Swansea, UK, [5]Royal Glamorgan Hospital, Cwm Taf Health Board, Llantrisant, UK

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) databank. 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; 26–45; 45–65 and 66+. 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 REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION APPLICATION ON REFRACTORY TEMPORAL EPILEPSY

Kistsen V[1], Evstigneev V[2], Kilin S[3]
[1]Neurology and Neurosurgery, Belarusian Medical Academy of Post-Graduate Education, Minsk, Belarus, [2]Belarusian Medical Academy of Post-Graduate Education, Minsk, Belarus, [3]National Academy of Sciences of Belarus, Minsk, Belarus

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; $p = 0.00011$). 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

Baftiu A[1], Landmark CJ[2], Neslein I-L[2], Johannessen SI[3], Perucca E[4]
[1]The Norwegian Medicines Agency, Oslo, Norway, [2]Oslo and Akershus University College of Applied Sciences, Oslo, Norway, [3]National Center for Epilepsy, Sandvika and Oslo University Hospital, Sandvika, Norway, [4]University of Pavia, Pavia, Italy

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 varies 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 MODELLED IN JME

Timmings P[1,2], Kasteleijn-Nolst Trenité DGA[3]
[1]Waikato Clinical School, University of Auckland, Auckland, New Zealand, [2]Neurology Deparment, Waikato Hospital, Hamilton, New Zealand, [3]University Medical Center Utrecht, Utrecht, The Netherlands

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 lamortigine 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.

078
META-ANALYSIS OF NEURODEVELOPMENTAL OUTCOME FOLLOWING PRENATAL EXPOSURE TO ANTIEPILEPTIC DRUGS

Bromley RL[1,2], Pulman JL[3], Adab N[4], Sanniti A[3], Greenhalgh J[3], McKay A[3], Tudur-Smith C[3], Marson AG[5]
[1]University of Manchester, Manchester, UK, [2]Central Manchester University Hospitals NHS Foundation Trust, Manchester, UK, [3]University of Liverpool, Liverpool, UK, [4]University Hospitals Coventry and Warwickshire NHS Trust, Coventry, UK, [5]Molecular and Clinical Pharmacology, University of Liverpool, Liverpool, UK

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.

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

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079
TWENTY-FOUR HOURS QUANTITATIVE-EEG AND IN VIVO GLUTAMATE BIOSENSOR DETECTS ACTIVITY AND CIRCADIAN RHYTHM DEPENDENT BIOMARKERS OF PATHOGENESIS IN MECP2 KO MOUSE MICE

Kadam SD[1,2], Ammanuel S[3], O'Driscoll C[4], Wozniak A[5], Naidu S[6], Johnston MV[6]
[1]Neuroscience, Kennedy Krieger Institute, Baltimore, MD, USA, [2]Neurology, Johns Hopkins University School of Medicine, Baltimore, MD, USA, [3]Biomedical Engineering, Johns Hopkins University, Baltimore, MD, USA, [4]Johns Hopkins Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA, [5]Biostatistics Center, Johns Hopkins University School of Medicine, Baltimore, MD, USA, [6]Pediatric Neurology, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Purpose: Mutations in the X-linked gene encoding methyl-CpG-binding protein 2 (MeCP2) cause most cases of Rett syndrome (RTT). Currently there is no cure or viable treatment for RTT. Abnormal EEGs are found in a 100% of the RTT cases and are associated with severe sleep dysfunction, the cause of which is not well understood. Mice that are deficient in MeCP2 show neuropathological and behavioural deficits similar to those reported for RTT. To study the non-ictal EEG correlates in symptomatic MeCP2 KO mice and determine novel biomarkers of the progressive neurodegeneration

Method: We used 24 h video-EEG/EMG with synchronous in-vivo cortical glutamate biosensors in the frontal cortex. We scored the EEG for activity states and did spectral analysis to evaluate correlations to the synchronous extracellular glutamate fluctuations underlying MeCP2 inactivation as compared to controls.

Results: Glutamate peaks and troughs tightly correlated with wake and sleep cycles respectively. However significant alterations in sleep structure, poor quality of slow wave sleep (SWS) and impaired activity dependent glutamate homeostasis was detected in KO mice that were also associated with a significant increase in glutamate loads per activity cycle. Colorimetric quantitation of absolute glutamate levels in the frontal cortices also showed significantly higher levels.

Conclusion: This study found that chronic sleep deprivation associated with glutamate toxicity may underlie the progressive neurodegeneration and fatality in the MeCP2 KO mice. Identification of these quantitative biomarkers will be valuable to evaluate the efficacy of novel interventions in-vivo to help guide the design of therapeutic approaches in the clinic.

Abstracts

080
MOLECULAR IMAGING OF INFLAMMATION REVEALS DIFFERENCES BETWEEN DRUG-RESISTANT AND DRUG-SENSITIVE ANIMALS IN A CHRONIC MODEL OF TEMPORAL LOBE EPILEPSY

Potschka H[1], Bogdanovic RM[1], Syvänen S[2], Michler C[1], Russmann V[1], Eriksson J[3], Windhorst AD[4], Lammertsma AA[4], de Lange EC[5], Voskuyl RA[5,6]

[1]Institute of Pharmacology, Toxicology, and Pharmacy, Ludwig-Maximilians-University, Munich, Germany, [2]Department of Public Health and Caring Sciences, Uppsala University, Uppsala, Sweden, [3]Department of Medicinal Chemistry, Preclinical PET Platform, Uppsala University, Uppsala, Sweden, [4]Department of Radiology and Nuclear Medicine, VU University Medical Center, Amsterdam, The Netherlands, [5]Division of Pharmacology, LACD, Leiden University, Leiden, The Netherlands, [6]SEIN – Epilepsy Institutes of the Netherlands Foundation, Heemstede, The Netherlands

Purpose: Activation of glia cells can promote ictogenesis 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 *(R)*-[^{11}C]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)*-[^{11}C]PK11195 brain uptake rates did not differ from those in control animals. In contrast, enhanced *(R)*-[^{11}C]PK11195 brain uptake was evident in different brain regions including the hippocampus, occipital cortex, parietal cortex, and caudate putamen. Standardized uptake values of *(R)*-[^{11}C]PK11195 showed no correlation with seizure frequencies during the last 72 h before PET scanning.

A trend towards increased TSPO expression was observed in the hippocampus of drug-resistant rats as compared to drug-sensitive rats. In both groups of rats microglia activation was confirmed based on ED1 immunostainings.

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

Genovesi S[1], Cerri C[2], Püntener U[3], Perry VH[3], Caleo M[2], Bozzi Y[1]

[1]Centre for Integrative Biology (CIBIO), University of Trento, Trento, Italy, [2]CNR Neuroscience Institute, Pisa, Italy, [3]Centre for Biological Sciences, University of Southampton, Southampton, UK

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

Mercado-Gómez OF[1], Landgrave-Gómez J[1], Arriaga-Ávila V[1], Guevara-Guzmán R[1]

[1]Physiology, Facultad de Medicina, Universidad Nacional Autónoma de México, Mexico City, Mexico

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 able 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

Teocchi MA[1], D'Souza-Li L[1]
[1]Center for Investigation in Pediatrics, University of Campinas, Campinas, Brazil

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 (NFkB) 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 immunohistochemitry 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 NFkB 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 REFRACTORINESS IN IMMATURE RATS

Pařízková M[1], Ben Salem Z[2], Mares P[1]
[1]Institute of Physiology, Academy of Sciences of Czech Republic, Prague, Czech Republic, [2]Institute of Anatomy and Physiology, Academy of Sciences of Czech Republic, Prague, Czech Republic

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 exhibitng 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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085
PROGNOSIS AND MORTALITY OF EPILEPSY IN A RURAL DISTRICT OF VIETNAM

Tuan NA[1], Thinh LV[1,2]
[1]Neurology, Hanoi Medical University, Hanoi, Vietnam, [2]Clinical Neurology, Bach Mai Hospital, Hanoi, Vietnam

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 determined 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-exiting diseases 5 cases and unknown etiology (possible SUDEP) 5 cases.

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

086
LONG-TERM PROGNOSIS OF JUVENILE MYOCLONIC EPILEPSY

Pietrafusa N[1], La Neve A[1], Amoroso MG[1], Francavilla T[1], Durante V[1], Luisi C[1], Pontrelli G[1], Boero G[2]
[1]Department of Neurology, University of Bari, Bari, Italy, [2]Department of Neurology, "SS. Annunziata" Hospital, Taranto, Italy

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 yy (range 16–53)]; in 4 cases JME was an evolution of Childhood Absence Epilepsy. 43(81%) patients showed generalized tonic-clonic seizures (gtcs) and 19 (36%) absence seizures.

Mean follow-up was 95 ± 60 months (16–239). 40(75%) patients resulted seizure-free for at least 2 years; a higher likelihood of refractoriness of JME was associated to: family history of epilepsy and febrile convulsions, gtcs 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 yy (15–49); seizures relapse was observed in 20 (95%) cases and the patient who remained seizure-free was the only one who withdrew drug treatment after the fourth decade of life (49 yy).

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

Voll AR[1], Buckley S[2], Hernadez Ronquillo L[1], Tellez-Zenteno JF[1]
[1]Neurology, University of Saskatchewan, Saskatoon, SK, Canada, [2]University of Saskatchewan, Saskatoon, SK, Canada

Purpose: To identify risk factors for development of drug resistant epilepsy (DRE) in an adult cohort of patients with generalized epilepsy. The identification of specific risk factors would allow patients to receive earlier 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 significantly younger than controls at the onset of epilepsy (6.5 vs. 18.8 $p \leq 0.001$). 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 epilepsy.

088
DEVELOPMENT OF EPILEPSY IN PATIENTS WITH POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (PRES)

Datar S[1], Rabinstein A[1], Hocker S[1]
[1]Neurology, Mayo Clinic, Rochester, MN, USA

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 diagnosed 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 analysis of which 80 were women (68%). The most common clinical associations 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 discontinued 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.

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

Simola M[1], Nevalainen O[2], Auvinen A[3,4], Isojärvi J[1,5], Ansakorpi H[1]

[1]Medical Research Center Oulu, Oulu University Hospital and University of Oulu, Oulu, Finland, [2]Medical School, University of Tampere, Tampere, Finland, [3]School of Health Sciences, University of Tampere, Tampere, Finland, [4]Pediatric Research Center, Tampere University Hospital and University of Tampere, Tampere, Finland, [5]Lundbeck, Deerfield, IL, USA

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.

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EPILEPSY-RELATED CLINICAL CHARACTERISTICS AND MORTALITY: A SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL COHORT STUDIES

Nevalainen O[1], Ansakorpi H[2], Simola M[2], Raitanen J[3,4], Isojärvi J[2,5], Artama M[6], Auvinen A[4,7]

[1]School of Medicine, University of Tampere, Tampere, Finland, [2]Medical Research Center Oulu, Oulu University Hospital and University of Oulu, Oulu, Finland, [3]UKK Institute for Health Promotion, Tampere, Finland, [4]School of Health Sciences, University of Tampere, Tampere, Finland, [5]Lundbeck, Deerfield, IL, USA, [6]University of Helsinki, Helsinki, Finland, [7]Pediatric Research Center, Tampere University Hospital and University of Tampere, Tampere, Finland

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% (R^2, $p < 0.001$) 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.

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091

A GENETIC BASIS FOR RESPONSE TO THE KETOGENIC DIET

Schoeler N[1,2], Cross JH[2], Leu C[1], Sander JW[1], Sisodiya S[1]

[1]UCL Institute of Neurology, London, UK, [2]UCL Institute of Child Health, London, UK

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 and no responders harboured a variant. There were other genes of interest, but none reached significance on any measure. The BIOCARTA "PTC1" (patched 1) pathway reached suggestive significance for association with unfavourable KD response. The REACTOME pathway "Tri-

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

DjÕmié T[1,2], EuroEPINOMICS-RES Consortium, EPGP Consortium, Epi4K Consortium
[1]Department of Molecular Genetics, VIB, Antwerp, Belgium, [2]Institute Born-Bunge, Antwerp, Belgium

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 EE 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, entailing a large amount of genetic results of unknown significance. Collaborative efforts that share resources will greatly increase the speed by 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

Licchetta L[1,2], Bisulli F[1,2], Vignatelli L[3], Claudia R[1,2], Trippi I[1,2], Di Vito L[1,2], Naldi I[1], Mostacci B[1,2], Bernabè G[1,2], Plazzi G[1,2], Provini F[1,2], Tinuper P[1,2]
[1]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy, [2]Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy, [3]Local Health Trust of Bologna, Bologna, Italy

Purpose: To evaluate the prognosis of NFLE in terms of 5-year seizure freedom (SF).

Methods: Cohort study with both retrospective and prospective recruitment. We included consecutive patients attending our Institute, diagnosed with NFLE on clinical and video-polisomnographic (VPSG) 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 MYOCLONIA WITH ABSENCES

Vaudano AE[1], Ruggieri A[1], Tondelli M[1], Avanzini P[1,2], Benuzzi F[1], Gessaroli G[1], Cantalupo G[3], Mastrangelo M[4], Vignoli A[5], Di Bonaventura C[6], Canevini MP[5], Dalla Bernardina B[3], Nichelli PF[1], Meletti S[1]
[1]Department of Biomedical Science, Metabolism, and Neuroscience, NOCSE Hospital, University of Modena and Reggio Emilia, Modena, Italy, [2]Department of Neuroscience, University of Parma, Parma, Italy, [3]Department of Life and Reproduction Sciences, University of Verona, Verona, Italy, [4]Paediatric Neurology Unit, V. Buzzi Hospital, Milan, Italy, [5]Department of Health Sciences, Epilepsy Centre, San Paolo Hospital, University of Milan, Milan, Italy, [6]Department of Neurological Sciences, University of Rome "La Sapienza," Rome, Italy

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;

2 Higher fMRI decrements in the bilateral posterior cortex in relation to the alpha rhythm;
3 Increments in the grey matter concentration at the lingual gyrus, superior colliculus and thalamus while decrements were observed in the anterior cingulate and frontal eye field.

Conclusion: We provide evidences of altered anatomo-functional properties of the visual system in EMA. These abnormalities involve a complex circuit spanning from the occipital cortex to the cortical/subcortical systems physiologically involved in the volitional and attentional control of eye-closure and gaze.

095
INVESTIGATION OF GENETIC CAUSES OF EPILEPSY IN CHILDREN WITH NON-SPECIFIC INTELLECTUAL DISABILITY USING ACGH-BASED TECHNOLOGY

Budisteanu M[1,2], Tutulan-Cunita A[1], Papuc SM[1], Iliescu C[2], Burloiu C[2], Minciu I[2], Butoianu N[2], Sandu C[2], Craiu D[2], Arghir A[1]
[1]"Victor Babes" National Institute of Pathology, Bucharest, Romania, [2]"Prof. Dr. Alex Obregia" Clinical Hospital of Psychiatry, Bucharest, Romania

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: *CDKL5* 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, *MFSD8* 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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SCN2A-RELATED EPILEPTIC ENCEPHALOPATHIES: EXTENDED PHENOTYPE AND RESPONSE TO SODIUM CHANNEL BLOCKERS

Wolff M[1], Loddenkemper T[2], Jillella D[2], Döcker M[3], Wong-Kisiel LC[4], Møller RS[5,6], Weckhuysen S[7], Ceulemans B[8], Klepper J[9], Baumeister FA[10], Koolen DA[11], Kluger G[12]
[1]Department of Pediatric Neurology, University Children's Hospital, Tübingen, Germany, [2]Division of Epilepsy and Clinical Neurophysiology, Harvard Medical School, Boston Children's Hospital, Boston, MA, USA, [3]CeGaT – Center for Genomics and Transcriptomics, Tübingen, Germany, [4]Division of Child and Adolescent Neurology, Department of Neurology, Mayo Clinic, Rochester, MN, USA, [5]Danish Epilepsy Centre, Dianalund, Denmark, [6]Institute for Regional Health Services, University of Southern Denmark, Odense, Denmark, [7]VIB Department of Molecular Genetics, Neurogenetics Group, University of Antwerp, Antwerp, Belgium, [8]Pediatric Neurology, Department of Neurology, University Hospital of Antwerp, Antwerp, Belgium, [9]Children's Hospital, Klinikum Aschaffenburg, Aschaffenburg, Germany, [10]Children's Hospital, RoMed Klinikum, Rosenheim, Germany, [11]Department of Human Genetics, Radboud University Medical Center, Nijmegen, The Netherlands, [12]Clinic for Neuropediatrics and Neuro-Rehabilitation, Epilepsy Center for Children and Adolescents, Schön Klinik, Vogtareuth, Germany

Purpose: *SCN2A* mutations most often have been associated with benign epileptic phenotypes such as benign familial neonatal-infantile seizures. Several de novo *SCN2A* mutations have been described with more severe phenotypes, such as early infantile epileptic encephalopathies. In these, both gain and loss of function of the sodium channel have been found. Accordingly, positive and negative effects of sodium channel blockers (SCB) on epileptic seizures might be expected. Here, we aim to describe the phenotypic spectrum and the effect of SCB on epileptic seizures in a cohort of children with *SCN2A*-related epileptic encephalopathies.

Method: Children with epileptic encephalopathies, i.e. drug resistant epilepsies and developmental delay were screened for *SCN2A* mutations across multiple centers using Next Generation Sequencing. Positive cases were analyzed with respect to clinical data and treatment response to SCB.

Results: 10 children were included with de novo *SCN2A* mutations. The age of seizure onset ranged from 1 day to 3 years. Four children had multifocal seizures with neonatal onset. Sodium channel blockers were effective in all of them. Six children presented with tonic-clonic or hemiclonic seizures, atypical absences, myoclonic, myoclonic-tonic, atonic and focal seizures of later onset (mean age 2 years) resembling Dravet or Lennox-Gastaut phenotypes. In these, SCB either worsened seizures (N = 2), were ineffective (N = 3) or were not used for treatment (N = 1).

Conclusion: *SCN2A* mutations can cause epileptic encephalopathies with variable phenotypes. While early onset seizures did respond to sodium channel blockers, these were not effective in later onset seizures, probably reflecting different effects of the mutations on the sodium channel.

Platform Session: Status Epilepticus
Wednesday, 2nd July 2014

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

Zelano J[1], Möller F[1], Dobesberger J[2], Trinka E[2], Kumlien E[1]
[1]Uppsala University, Uppsala, Sweden, [2]Paracelsus Medical University, Salzburg, Austria

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 RESPOSE TO THE TREATMENT OF SUPERREFRACTORY STATUS EPILEPTICUS IN CHILDREN: A 15-YEAR A SINGLE CENTER EXPERIENCE

Kravljanac R[1,2], Djuric M[1,2], Pekmezovic T[2,3]
[1]Neurology Department, Institute for Mother and Child Healthcare of Serbia, Belgrade, Serbia, [2]Faculty of Medicine, University of Belgrade, Belgrade, Serbia, [3]Institute for Epidemiology, Belgrade, Serbia

Purpose: Evaluation of etiology, clinical course and respose 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 anaesthetic therapy, including those cases that recur on the reduction or withdrawal of anaesthesia. Etiology was summarized according to Shinnar'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, thiopenthal (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. Levetiracetam was effective (3/3), but in one case with neuronal lipofuscinosis caused severe bradicardia. 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 SuperRefrSE is very chalingable and those patients require a particular therapeutic approach.

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A GLOBAL AUDIT OF TREATMENT OF REFRACTORY AND SUPER-REFRACTORY STATUS EPILEPTICUS

Ferlisi M[1], Hocker S[2], Grade M[3], Trinka E[4], Shorvon S[3]
[1]Unit of Neurology, Department of Neuroscience, University Hospital of Verona, Verona, Italy, [2]Department of Neurology, Mayo Clinic, Rochester, MN, USA, [3]UCL Institute of Neurology, National Hospital for Neurology and Neurosurgery, London, UK, [4]Department of Neurology, Christian-Doppler-Clinic, Paracelsus Medical University, Salzburg, Austria

Purpose: There is a remarkable dearth of information about the various therapies used in refractory status epilepticus (RSE). Randomized or controlled studies are extremely difficult to perform in this situation. We proposed an international case registry to collect informations on cases of RSE around the world.

Method: De-identified data on etiologies, treatments and outcomes of RSE cases are collected in a prospective manner through a standardized, web-based data collection form.

Results: To date, 210 cases of RSE have been collected from 33 different countries. Midazolam was the anaesthetic of first choice in most of the cases (60.4%), followed by propofol (29.5%) and barbiturates (7.6%). For 157 cases there were data on the outcome of the status: 73.2% recovered, 22.9% died during the course of anaesthesia, 3.8% had the therapy withdrawn. The outcome was not different depending on which anaesthetic was used as first. 158 patients were classified according to the modified Rankin scale (mRS) on termination of anaesthesia: outcome was good (mRS: 1–3) in 37.6% of patients and poor (mRS: 4–06) in 62.3%. Patients treated with barbiturates as first choice seems to have a poorer outcome than those treated with propofol ($p = 0.04$), but the small numbers and influence of etiology mean that no conclusions can be drawn at present.

Conclusion: This is the first multinational case registry for cases of RSE. Validity of the results depends mainly on the adhesion rate. We do hope as many doctors from as many world-wide centres as possible will take part in this study, which should provide important information about the range of treatments used and the outcome of this severe condition. To participate, simply register with the online system at www.staus-epilepticus.net.

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

Santamarina E[1], Toledo M[1], Sueiras M[1], Rodríguez N[1], Gonzalez M[1], Guzman L[1], Quintana M[1], Alvarez-Sabín J[1], Salas-Puig X[1]
[1]Hospital Vall Hebron, Barcelona, Spain

Many questions have arisen of how aggresive 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

symptomatic (41 lesional, 12 toxic-metabolic, 17 hypoxic), 9 remote symptomatic and 9 cryptogenic. A total of 43(48.3%) required more than 2 AEDs, with a median recovery time of 24 h (30 min–360 h). In-hospital mortality was 28% (n = 25). After a median follow-up of 8 months, 50% of survivors (n = 32) showed seizures at follow-up.Subsequently, we analyzed which factors might be related to the development of epilepsy during follow-up and finding that SE duration had been significantly longer (74 vs. 24 h, p = 0.003); furthermore, the development of chronic seizures was correlated with etiology (remote symptomatic, p = 0076) and the use of more than 2 AEDs (p = 0.084).Regarding the duration of SE, a cutoff above 16 h was clearly related to chronic seizures (p = 0.014). After a logistic regression, only a duration longer than 16 h (OR 8.309 (1.612–42.8), p = 0.011) and a remote symptomatic etiology (OR 9.396 (1.19–77.73), p = 0.03) were found to be independent predictors of development of epilepsy.

Conclusion: In NCSE patients, the longer duration of NCSE and etiology (no acute lesions) are associated with an increased risk of subsequent epilepsy at follow-up. A more aggressive treatment might arise in this group to avoid this possibility.

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STATUS EPILEPTICUS PROGNOSIS: A 4-YEAR RETROSPECTIVE ANALYSIS IN A TERTIARY CENTER

Mendes A[1,2], Rocha H[2,3]
[1]Neurology, Unidade Local de Saude do Alto Minho, Viana do Castelo, Portugal, [2]Clinical Neurosciences and Mental Health, School of Medicine, University of Porto, Porto, Portugal, [3]Neurology, Centro Hospitalar S. Joao, Porto, Portugal

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 in 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 and nonconvulsive with clinical signs; valproate or levetiracetam to nonconvulsive without clinical signs). The number of AED (3.30 ± 0.15) used to stop the SE did not differ between the SE groups. Both variables do not influence the prognosis.

The mRankin is significantly worst at discharge (p = 0.002), namely for nonconvulsive cases without clinical signs and to older patients. Global mortality was 18.6%.

Conclusion: This study cannot confirm the etiology as a main prognostic factor; multiple concurrent causes in the majority of patients may contribute to that observation. The first AED had not a major significance in the final outcome. The nonconvulsive cases without clinical signs had worst prognosis, perhaps because a latter diagnosis, reinforcing the need to identify high risk patients and monitor them with EEG.

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CONTINUOUS EEG RECORDING IS USEFUL TO PREDICT RESPONSE TO IV KETAMINE IN CHILDREN WITH REFRACTORY CONVULSIVE STATUS EPILEPTICUS

Ilvento L[1], Rosati A[1], L'Erario M[2], Mirabile L[2], Guerrini R[1]
[1]Child Neurology Unit, Children's Hospital A. Meyer, University of Florence, Firenze, Italy, [2]Intensive Care Unit, Children's Hospital A. Meyer, University of Florence, Firenze, Italy

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 5/8, BS pattern was stable and persistent with a 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.

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

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MICE AND RATS SHOW OPPOSING CHANGES IN NEURONAL EXCITABILITY FOLLOWING AN EPILEPTOGENIC BRAIN INSULT

Bröer SC[1,2], Pilawski I[3], Löscher W[1,2], Bernard C[3,4]
[1]Department of Pharmacology, Toxicology, and Pharmacy, University of Veterinary Medicine Hannover Foundation, Hannover, Germany, [2]Center for Systems Neuroscience, Hannover, Germany, [3]Inserm, UMR_S 1106, Marseille, France, [4]Aix Marseille Université, INS, Marseille, France

Purpose: Various brain insults, including status epilepticus (SE), can trigger epileptogenesis. In order to prevent this process, it is important to understand its early steps. Using the pentetrazole (PTZ) seizure threshold as a surrogate marker for changes in neuronal excitability after SE, we found different responses in rats and mice. This provides an ideal experi-

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.

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

Raijmakers M[1,2], Hoogland G[2], Clynen E[1], Smisdom N[1], Rigo J-M[1], Swijsen A[1]
[1]Biomedical Research Institute BIOMED, Hasselt University, Hasselt, Belgium, [2]Maastricht University Medical Center, Maastricht, The Netherlands

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.

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

Ali I[1,2], Chugh D[1,2], Ekdahl CT[1,2]
[1]Division of Clinical Neurophysiology, Department of Clinical Sciences, Lund University, Lund, Sweden, [2]Department of Clinical Sciences, Lund Epilepsy Center, Lund University, Lund, Sweden

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.

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ADULT NEUROGENESIS AND BRAIN INFLAMMATION AS POTENTIAL BIOMARKERS OF EPILEPTOGENESIS

Chugh D[1,2], Bakochi A[1,2], Ali I[1,2], Etholm L[3], Ekdahl CT[1,2]
[1]Division of Clinical Neurophysiology, Department of Clinical Sciences, Lund University, Lund, Sweden, [2]Department of Clinical Sciences, Lund Epilepsy Center, Lund University, Lund, Sweden, [3]Section of Clinical Neurophysiology, Department of Neurology, Oslo University Hospital, Oslo, Norway

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.

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

Häussler U[1], Marx M[1], Janz P[1], Haas CA[1,2,3]

[1]Experimental Epilepsy Research, Department of Neurosurgery, University of Freiburg, Freiburg, Germany, [2]Bernstein Center Freiburg, University of Freiburg, Freiburg, Germany, [3]BrainLinks-BrainTools, University of Freiburg, Freiburg, Germany

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 C57Bl/6 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.

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

Kilias A[1,2,3], Froriep UP[4], Häussler U[5], Kumar A[2,3], Haas CA[2,5], Egert U[1,2]

[1]Department of Microsystems Engineering – IMTEK, Faculty of Engineering, Laboratory for Biomicrotechnology, University of Freiburg, Freiburg, Germany, [2]Bernstein Center Freiburg, University of Freiburg, Freiburg, Germany, [3]Faculty of Biology, University of Freiburg, Freiburg, Germany, [4]Bioelectronics Group, Research Laboratory of Electronics, Massachusetts Institute of Technology, Cambridge, MA, USA, [5]Experimental Epilepsy Research, Department of Neurosurgery, Faculty of Medicine, University of Freiburg, Freiburg, Germany

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

could tune the hippocampal network towards seizure susceptibility via pathological plasticity.

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A RETROSPECTIVE EVALUATION OF RETIGABINE IN PATIENTS WITH HIGHLY THERAPY-RESISTANT EPILEPSY

Huber B[1], Bocchicchio M[1]
[1]Von Bodelschwingsche Stiftungen Bethel, Bethel.regional, Bielefeld, Germany

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, range18–54 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 with a 3 months baseline period. Tolerability was assessed using information provided by the patient, staff, and the neurologist 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%: 1 patient; 25–50%: 4 patients; unchanged: 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. Ophthalmological 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

Thampratankul L[1], Khongkhatithum C[1], Visudtibhan A[1]
[1]Department of Pediatrics, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

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

Murena L[1], Lawden M[1]
[1]Neurology Department, University Hospitals of Leicester NHS Trust, Leicester, UK

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.

p112
EFFICACY AND SAFETY OF USL255, ONCE-DAILY EXTENDED-RELEASE TOPIRAMATE, IN ADULTS WITH PARTIAL ONSET SEIZURES: THE PREVAIL STUDY

Blatt I[1], Chung SS[2], Hogan RE[3], Clark A[4], Anders B[4], Halvorsen M[4], on behalf of the PREVAIL Study Group
[1]The Chaim Sheba Medical Center, Ramat Gan, Israel, [2]Barrow Neurological Institute, Phoenix, AZ, USA, [3]Washington University in St. Louis, St. Louis, MO, USA, [4]Upsher-Smith Laboratories, Inc., Maple Grove, MN, USA

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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p113
PREVALENCE OF METABOLIC SYNDROME IN VALPROATE-TREATED ADULT PATIENTS WITH EPILEPSY

Rakitin A[1], Eglit T[2], Kõks S[3], Lember M[2], Haldre S[1]
[1]Department of Neurology and Neurosurgery, Tartu University, Tartu, Estonia, [2]Department of Internal Medicine, Tartu University, Tartu, Estonia, [3]Department of Physiology, Tartu University, Tartu, Estonia

Purpose: No study has explored the prevalence of metabolic syndrome (MS) in patients with epilepsy treated with valproate (VPA) at the population level. The aim of study was to compare the prevalence of MS and its components in VPA-treated patients and the general population.

Method: This study involved 118 patients with epilepsy (63 men, 55 women) receiving VPA monotherapy. MS was diagnosed according to National Cholesterol Education Program Adult Treatment Panel III criteria. Data were compared with the results of a population-based study of the prevalence of MS in the same geographic region (N = 493; 213 men, 280 women).

Results: The weighted prevalence of MS in adults with epilepsy receiving VPA monotherapy (25.8%) was similar to that in the control group (27.9%). Multiple logistic regression analysis showed positive correlations between MS development and body mass index (BMI; odds ratio [OR]=1.47; 95% confidence interval [CI], 1.25–1.73) and VPA treatment duration (OR=1.01; 95% CI, 1.0–1.02), but no correlation with VPA dosage or homeostasis model assessment index (HOMA). In control subjects, BMI and HOMA had similar predictive abilities for MS occurrence; in VPA-treated patients, the predictive ability of HOMA-IR was significantly lower than that of BMI, with areas under the receiver operating characteristic curves of 0.808 and 0.897 ($p = 0.05$), respectively.

Conclusion: MS is not more prevalent in patients with epilepsy who have received VPA treatment than in the general population. HOMA is an inferior predictor of MS in VPA-treated patients in comparison with the general population.

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

Italiano D[1], Ferrara R[1], Trifiro' G[1], Cannata A[1], Capuano A[2], Pagliaro C[3], Tari DU[3], Tari M[3], Arcoraci V[1], Spina E[1]
[1]Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy, [2]Pharmacology Section, Department of Experimental Medicine, Second University of Napoli, Napoli, Italy, [3]Local Health Unit, Caserta, Italy

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.

p116
LACO-EXP, A RETROSPECTIVE STUDY OF LACOSAMIDE: DOSAGE-RESPONSE ANALYSIS ON PATIENTS ON A LACOSAMIDE DOSE ≤400 MG

Villanueva V[1], Garcés M[1], López FJ[2], Serratosa JM[3], González-Giráldez B[4], Campos D[5], Molins A[6], Rodriguez-Uranga J[7], Mauri JA[8], Salas-Puig J[9], Toledo M[9], Sánchez-Alvarez JC[10], Moreno A[11], Serrano-Castro PJ[12], Saiz-Diaz RA[13], González de la Aleja J[13], de la Peña P[13], Asensio M[14]
[1]Hospital Universitario y Politécnico La Fe, Valencia, Spain, [2]Hopital Clinico Universitario Santiago, Santiago de Compostela, Spain, [3]Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain, [4]Hospital Universitario y Politécnico La Fe, Madrid, Spain, [5]Hospital Clinico Universitario, Valladolid, Spain, [6]Hospital Universitario Josep Trueta, Girona, Spain, [7]IENSA-Clinica Sagrado Corazón, Sevilla, Spain, [8]Hospital

Clinico Universitario Lozano Blesa, Zaragoza, Spain, [9]Hospital Universitario Vall d'Hebron, Barcelona, Spain, [10]Hospital Clinico Universitario San Cecilio, Granada, Spain, [11]Hospital Universitario Son Espases, Palma de Mallorca, Spain, [12]Hospital Universitario Torrecárdenas, Almeria, Spain, [13]Hospital Universitario 12 de Octubre, Madrid, Spain, [14]Hospital General Universitario, Alicante, Spain

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.

p117
EFFECTS OF OXCARBAZEPINE AND LEVETIRACETAM AS A MONOTHERAPY ON CALCIUM AND VITAMIN D METABOLISM

Aksoy D[1], Ataklı D[2], Arpaci B[2], Guveli B[2], Un Candan F[2]
[1]Dr. Burhan Nalbantoglu State Hospital, Nicosia, Cyprus, [2]Bakirköy Neurological and Psychiatric Disease Teaching and Research Hospital, Istanbul, Turkey

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

Mrabet H[1], Kefi M[1], Ktari M[1], Manai R[1], Mrabet A[2]
[1]Neurological Department, Soukra Clinic, La Soukra, Tunisia, [2]Belvedre Medical, Tunis, Tunisia

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

Kelly K[1], Stephen LJ[1], Parker P[1], Brodie MJ[1]
[1]Epilepsy Unit, Western Infirmary, Glasgow, UK

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–

15 (median 3) schedules. At this early stage, PER (4–12 mg [median 4 mg] daily) has benefitted 4 (18.2%) patients, with 1 remaining seizure-free, 1 having a ≥50% and 2 demonstrating a <50% seizure reduction. One other patient succumbed to SUDEP. The AED has been withdrawn in 17 (41.5%) patients (2 lack of efficacy; 15 side effects), the majority of whom (n = 14) took 4 mg daily. Common side effects leading to PER withdrawal included nausea, vomiting, ataxia and depression. Weight gain occurred in 3 (7.3%) patients (1 withdrawal).

Conclusion: Adjunctive PER can be a useful AED in patients with highly drug-resistant localization-related epilepsy. Side effects occurred mainly at low doses. Outcomes will be assessed when the drug is introduced as an earlier schedule.

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INFLUENCE OF ANTIEPILEPTIC DRUGS IN THE LIPID PROFILE OF VASCULAR EPILEPSY

Rodríguez Villatoro N[1], Santamarina E[1], Toledo M[1], Quintana M[1], Aller JS[1], Bejr-Kasem H[1], Alvarez-Sabín J[1], Salas-Puig J[1]
[1]Vall d'Hebron University Hospital, Universitat Autonoma de Barcelona, Barcelona, Spain

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) ($p = 0.026$). 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 triglycerides 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

Kishi T[1], Fujii Y[1,2], Kobayashi Y[1,2], Ishikawa N[1,2]
[1]Department of Pediatrics, KKR Hiroshima Memorial Hospital, Hiroshima, Japan, [2]Department of Pediatrics, Hiroshima University Hospital, Hiroshima, Japan

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.

p122
LEVETIRACETAM IN REFRACTORY CHILDHOOD EPILEPSY: EFFICACY AND TOLERABILITY

Zaveckienė K[1], Karandienė J[2], Endzinienė M[1,2], Vaičienė-Magistris N[1,2], Laurynaitienė J[1,2]
[1]Hospital of Lithuanian University of Health Sciences, Kaunas, Lithuania, [2]Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

Purpose: Levetiracetam (LEV) is widely used in the treatment of refractory childhood epilepsy. Clinical studies have confirmed its efficacy in both generalized and focal epilepsy with minimal adverse effects. The aim of study to evaluate an efficacy and tolerability of LEV as an add-on therapy in children with refractory epilepsy.

Method: Retrospective review of medical records of children with refractory epilepsy followed at the Hospital of Lithuanian University of Health Sciences in Kaunas within October 2009–December 2013.

Results: LEV as add-on therapy was introduced in 60 children (age range 1–17 years, mean age 9.2 ± 4.7), 48.3% of them having refractory focal cryptogenic/symptomatic epilepsy, 26.7% generalized symptomatic, 11.7% generalized idiopathic, and 3.3% focal idiopathic epilepsy. Concomitant developmental disorders (mental retardation, behavioral, speech or motor disorder) prior to LEV treatment were found in 42 (70.0%) cases. Most patients were on polytherapy (mean number of antiepileptic drugs used before LEV was 5.2 ± 2.4). Treatment improved seizure control and was therefore continued in 36 (60.0%) cases without any significant differences regarding separate types of epilepsy ($p = 0.22$). Overall, 27 (45.0%) patients had adverse effects, the most common ones being behavioral/emotional problems 18/27, somnolence and nausea. Nineteen out of 27 patients who experienced adverse effects had concomitant developmental disorders prior to LEV treatment.

Conclusion: LEV proved to be sufficiently (>50%) and comparatively effective in different types of drug-resistant childhood epilepsies. Adverse effects were more common in patients with developmental disorders, mainly the behavioral ones.

Abstracts

p123
SENSORINEURAL HEARING LOSS AFTER ADMINISTRATION OF SODIUM VALPROATE

Akrioti M[1], Bregianni M[1], Paraskevoulakos E[1], Rizou C[1], Saravakos P[2], Papavasiliou A[1]
[1]Neurology, Pendeli Children's Hospital, Athens, Greece, [2]Otolaryngology, Pendeli Children's Hospital, Athens, Greece

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

Greshake B[1], Straub H-B[1]
[1]Epilepsiezentrum Berlin-Brandenburg, Klinik Tabor, Bernau, Germany

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 polytherapie (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 were reported, 3 had a marked increase of body weight. Comedikation 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 comedikation 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 patiens with IGE, LGS and in 1 Patient with Progressive Myoclonusepilepsy.

p125
PERAMPANEL AND RUFINAMIDE SHOW COMPARABLE INITIAL EFFECTIVENESS AND TOLERABILITY IN PEDIATRIC PATIENTS WITH REFRACTORY EPILEPSIES – FIRST EUROPEAN EXPERIENCES AFTER MARKETING

Biro A[1], Stephani U[2], Tarallo T[2], Bast T[3], Kurlemann G[4], Fiedler B[4], Schlachter K[5], Fleger M[5], Leiz S[6], Nikanorova M[7], Wolff M[8], Haberlandt E[9], Müller A[1], Selch C[1], Jansen C[1], Fiedler A[10], Staudt M[1], Kluger G[1]
[1]Epilepsy Center for Children and Adolescents, Clinic for Neuropediatrics and Neurorehabilitation, Schön Klinik Vogtareuth, Vogtareuth, Germany, [2]Department of Neuropediatrics, University Medical Center Schleswig-Holstein, Christian-Albrechts University, Kiel, Germany, [3]Epilepsy Center Kork, Kehl, Germany, [4]Department of Neuropediatrics, University Children's Hospital Münster, Münster, Germany, [5]Department of Pediatrics, LKH Bregenz, Bregenz, Austria, [6]Department of Pediatrics, Dritter Orden Clinic, München, Germany, [7]Danish Epilepsy Centre, Dianalund, Denmark, [8]Department of Pediatric Neurology, University Children's Hospital Tübingen, Tübingen, Germany, [9]Department of Pediatrics, Innsbruck Medical University, Innsbruck, Austria, [10]Pediatric Clinic St. Marien, Amberg, Germany

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

Philip S[1], Concannon B[1], Morris D[1], Seri S[1], Agrawal S[1]
[1]Paediatric Neurology, Birmingham Childrens Hospital, Birmingham, UK

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 adjunct. 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 dizzy spells 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

Dash A[1], Singh J[2], Gopal CH[3], Abbas A[4], Satyanarayana G[5], Kaur D[1], Mishra S[1]
[1]Eisai Pharmaceuticals India Private Limited, Mumbai, India, [2]Sanjivini Hospital, Ahmedabad, India, [3]Prime Hospital, Hyderabad, India, [4]Neurocare & Research Centre, Lucknow, India, [5]Vijaya Health Care Hospital, Secunderabad, India

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.

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

Nankovic S[1], Hajnsek S[1], Bujan Kovac A[1], Sulentic V[1], Kovacevic I[1], Petelin Gadze Z[1], Rados M[2]
[1]Department of Neurology, University Hospital Centre Zagreb, Zagreb, Croatia, [2]Croatian Institute for Brain Research, Zagreb, Croatia

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 discontinuitation 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 secondary 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 hyperintense 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

Hajnsek S[1], Sulentic V[1], Kovacevic I[1], Bujan Kovac A[1], Nankovic S[1], Petelin Gadze Z[1]
[1]Department of Neurology, University Hospital Centre Zagreb, Zagreb, Croatia

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.

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OUR EXPERIENCE OF LACOSAMIDE FOR DRUG RESISTANT EPILEPSY AT THE BURDEN CENTRE – A TERTIARY NEUROPSYCHIATRIC SERVICE

Mohan M[1], Perera S[1], Isaac L[1]
[1]North Bristol NHS Trust, Neurosciences, Bristol, UK

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 slow inactivation of voltage gated sodium channels and has been shown to have a good balance of safety and tolerability (Chung, S *Epilepsia*, 2010;*51*(6):958–967).

Recent literature has recommended that more work is needed to investigate the impact of lacosamide in real life clinical practice (Simoens, S *Current Medical Research & Opinion* 2011; *27*(7):1329–1338).

Our aim was to discover more about the real life population that have been prescribed Lacosamide within our tertiary neuropsychiatric centre both in terms of the patient background, dosage, tolerability and efficacy.

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 54% Female 46%
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 ESLICARBAZEPINE

Camacho Velasquez JL[1], Mauri Llerda JA[1], Rivero Sanz E[1], Santos Lasaosa S[1], Suller Marti A[1], Bellosta Diago E[1], Pardiñas Baron B[1], Sanabria Sanchinel A[1]
[1]Neurology, Hospital Clinico Universitario Lozano Blesa, Zaragoza, Spain

Purpose: To determine the efficacy and safety of high dose eslicarbazepine 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 eslicarbacepine 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 eslicarbazepine.

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

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GALACO STUDY: 6 MONTHS EXPERIENCE WITH LACOSAMIDE FOR FOCAL EPILEPSIES IN GALICIA, SPAIN

Rodríguez Osorio X[1], López González FJ[2], Pato Pato A[3], Fernández Pajarín G[2], Corredera García E[2], Rubio Nazábal E[4],

Abella J[5], Marey J[4], Rodríguez Regal A[6], Yáñez R[7], Cebrián E[6], Lema T[4], Pego R[8], Rodríguez M[1], Alberte M[1], García-Estévez D[1], Rodríguez R[1], García-Bargo D[1], Castro D[1], Amigo C[1], González-Ardura J[1], López M[1], Cimas I[1], Lorenzo JR[1], Raña N[1], Piñeiro R[1], Aguado M[1], Rodríguez JR[1], Cabo I[1]
[1]Neurology, Complexo Hospitalario Universitario de Santiago de Compostela, Santiago de Compostela, Spain, [2]Complexo Hospitalario Universitario de Santiago de Compostela, Santiago de Compostela, Spain, [3]Hospital POVISA, Vigo, Spain, [4]Complexo Hospitalario Universitario de A Coruña, A Coruña, Spain, [5]Hospital Arquitecto Marcide, Ferrol, Spain, [6]Complexo Hospitalario de Pontevedra, Pontevedra, Spain, [7]Complexo Hospitalario Universitario de Ourense, Ourense, Spain, [8]Hospital Lucus Augusti, Lugo, Spain

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 ³50% 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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CONSCIENTIOUS PERSONALITY, BELIEFS ABOUT ANTIEPILEPTIC DRUGS AND MEDICATION ADHERENCE IN PEOPLE WITH EPILEPSY

Margolis SA[1,2], Nakhutina L[2], Grant AC[2], Kunnakkat S[2], Coleman M[2], Gonzalez JS[1,3]
[1]Ferkauf Graduate School of Psychology, Yeshiva University, Bronx, NY, USA, [2]Department of Neurology, SUNY Downstate Medical Center, Brooklyn, NY, USA, [3]Albert Einstein College of Medicine, Yeshiva University, Bronx, NY, USA

Purpose: Nonadherence to antiepileptic drugs (AEDs) is a major source of preventable seizures and associated morbidity and mortality in people with epilepsy (PWE). Conscientiousness has been linked to treatment adherence in other chronic illnesses; its role in epilepsy has not been explored. Concerns about negative effects of AEDs and perceived necessity of taking AEDs have been associated with adherence in our prior work. The relative impact and interaction between conscientious personality traits and these beliefs has not been examined.

Method: In this study, predominantly ethnic minority, low-income PWE (N = 50; 56% Female; 52% African-American, 26% Caribbean-American, 16% Latino) completed validated questionnaires of personality (NEO-FFI-3), beliefs about AEDs (Beliefs about Medicines Questionnaire), and AED adherence (Morisky Medication Adherence Scale). Beliefs about AEDs were represented by a differential of perceived necessity minus concerns. Age, gender, education, illness duration, and number of prescribed AEDs were assessed as potential covariates; only gender showed a trend-level relationship. Controlling for gender, multiple linear regression assessed the independent effects of conscientiousness and AED beliefs on adherence. Moderation analyses explored significant interactions.

Results: Lower conscientiousness and greater AED concerns relative to perceived necessity were each independently associated with nonadherence ($\beta = 0.36$, $p = 0.005$, $\Delta R^2 = 0.17$; $\beta = 0.36$, $p = 0.005$, $\Delta R^2 = 0.12$, respectively). Significant moderation indicated that the relationship between AED beliefs and adherence was significant only at low and average levels of conscientiousness; when conscientiousness was high, beliefs did not relate to adherence. Conscientiousness was consistently associated with AED adherence, except when AED necessity greatly outweighed concerns.

Conclusion: Results suggest that successful AED adherence may depend both on positive beliefs about treatment and personality traits involving organization, deliberateness, persistence and self-discipline. Replication of these findings would suggest that attention should be paid to both personality characteristics and beliefs about treatment in the clinical management of PWE. Findings could inform interventions to improve AED adherence.

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RETENTION, DOSING, TOLERABILITY AND PATIENT REPORTED SEIZURE OUTCOME OF ZONISAMIDE AS ONLY ADD-ON TREATMENT UNDER REAL-LIFE CONDITIONS IN ADULT PATIENTS WITH PARTIAL ONSET SEIZURES: RESULTS OF THE NON-INTERVENTIONAL STUDY ZOOM

Hamer H[1], Baulac M[2], Bagul M[3], Kockelmann E[4]
[1]University Hospital Erlangen, Erlangen, Germany, [2]Universite PARIS VI, Paris, France, [3]Eisai Europe Ltd, Hatfield, UK, [4]Eisai GmbH, Frankfurt, Germany

Purpose: The choice of antiepileptic drugs (AED) for add-on therapy is often difficult due to individual drug profiles and possible interactions. Zonisamide (ZNS) is licensed for adjunctive therapy for partial-onset seizures (POS) with or without secondary generalization in patients 6 years and older, and as monotherapy for the treatment of POS in adult patients with newly diagnosed epilepsy. ZNS shows a favorable pharmacokinetic profile with low interaction potential with other drugs. The non-interventional study ZOOM aimed to gather real-life data on ZNS treatment in a European setting.

Method: Patients (N = 93, 46.2% male) with uncontrolled POS under AED monotherapy were offered participation in this study. Retention, dosing, tolerability and reported efficacy were assessed over 6 months in private practice and out-patient clinic settings.

Results: 31.2% of patients were ≥60 years. Median seizure frequency within 3 months prior to baseline was 6. The 6-month retention rate was 82.8%. Mean daily dose after titration was 219.0 ± 101.4 mg. Levetiracetam was the most frequently preferred combination partner

(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 by 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.

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LIMITED BENEFIT OF PERAMPANEL IN INSTITUTIONALIZED COGNITIVELY IMPAIRED PATIENTS WITH HIGHLY THERAPY-RESISTANT EPILEPSY

Schmid G[1], Huber B[1]
[1]Bodelschwinghsche Stiftungen Bethel, Bielefeld, Germany

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% of seizure reduction and a very good effect on CGI- Scale). 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.

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EFFECTS OF PRENATAL ANTIEPILEPTIC DRUG EXPOSURE ON NEWBORN BRAIN ACTIVITY

Videman M[1], Tokariev A[2], Stjerna S[3], Roivainen R[4], Gaily E[1], Vanhatalo S[5,6]
[1]Helsinki University Central Hospital (HUCH), Children's Hospital, Helsinki, Finland, [2]Neuroscience Center, Helsinki University, Helsinki, Finland, [3]Helsinki University, Helsinki, Finland, [4]Department of Neurology, HUCH, Helsinki, Finland, [5]HUCH, Helsinki, Finland, [6]Marie Curie Research Fellow Program, Helsinki, Finland

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 neurotropic 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.

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EFFICACY AND TOLERABILITY OF PERAMPANEL IN PATIENTS WITH REFRACTORY PARTIAL EPILEPSY IN A TERTIARY EPILEPSY CENTRE

Sieradzan KA[1], Hodgson H[2]
[1]Neurology, North Bristol NHS Trust, University of Bristol, Bristol, UK, [2]Neurology, North Bristol NHS Trust, Bristol, UK

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.

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PERAMPANEL IN SOUTH WALES: A MULTI-CENTRE CLINICAL EVALUATION

Lawthom C[1], Powell R[2], Hillman E[3], John K[3], Talbert A[4], Hamandi K[4]

[1]Neurology, Aneurin Bevan Health Board, Newport, UK, [2]Morriston Hospital, Swansea, UK, [3]Aneurin Bevan Health Board, Newport, UK, [4]Alan Richens Epilepsy Unit, University Hospital of Wales, Cardiff, UK

Purpose: Perampanel is currently the only licensed anti-epileptic drug (AED) acting at the AMPA receptor approved by the EU in September 2012. Pragmatic information is often forthcoming in post-marketing authentic clinical use. We evaluated our cohort looking for clinical predictors of successful perampanel patient experiences.

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). Titration 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.

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PERAMPANEL – EFFECTIVE AND SAFE VIA PERCUTANEOUS GASTRIC TUBE IN HIV EPILEPTIC PATIENT WITH CONCOMITANT HIGHLY ACTIVE ANTIRETROVIRAL THERAPY

Caravias G[1], Geit M[2], Vosko M[1], Ransmayr G[1]

[1]Department of Neurology, Linz General Hospital, Linz, Austria, [2]Department of Dermatology, Linz General Hospital, Linz, Austria

We present a 56 year old male patient with a 13 years history of HIV infection. Due to HIV encephalopathy he suffered from symptomatic epilepsy with repeated dyscognitive status epilepticus twice a year. Our patient receives highly active antiretroviral therapy (HAART) with raltegravir, abacavir and lamivudine.

After the last episode of status epilepticus under levetiracetam and valproate we decided to use perampanel as add-on due its novel anticonvulsive mechanism of action and favourable pharmacological profile in respect of side effects and interactions. Perampanel is a non-competitive antagonist of the glutamate AMPA receptor showing high selectivity to this receptor.

All three HAART substances are neither inducers, nor inhibitors of CYP3A. Raltegavir and abacavir are metabolized via UDP-glucuronosyltransferase (UGT), lamivudine is excreted renally. Perampanel is metabolized by the CYP3A enzyme and is neither a strong inducer nor inhibitor of any UGT enzymes in vitro.

Due to severe ultra long Barrett oesophagus the nutrition in our patient is administered via percutaneous gastric tube (PEG). Up to now there is no specific information available in respect of administration of pulverized and dissolved perampanel film-coated tablets.

Therapy with 2 mg of perampanel was started. Pulverized and dissolved film-coated tablets were administered via PEG. The dosage could be increased up to 6 mg/day and levetiracetam could be tapered off. Ten months follow up showed a seizure free patient and no side effects were detected. The optimized anticonvulsive medication did not influence the effectiveness of anti HIV therapy. PCR of HIV in serum remains negative and absolute count of CD4, as a marker of HAART effectiveness, is still unchanged. Perampanel plasma level was measured once at 0.44 µg/ml 16 h after the last dose.

p140
ESLICARBAZEPINE ACETATE AS ADD-ON TREATMENT TO ANTIEPILEPTIC MONOTHERAPY IN ADULTS WITH PARTIAL-ONSET SEIZURES: REAL-WORLD DATA ON RETENTION, DOSING, PATIENT REPORTED SEIZURE OUTCOME AND SAFETY FROM AN INTERIM ANALYSIS OF THE OPEN-LABEL NON-INTERVENTIONAL STUDY EPOS

Holtkamp M[1], Bagul M[2], Kockelmann E[3]

[1]Charité – Universitätsmedizin Berlin, Berlin, Germany, [2]Eisai Europe Ltd, Hatfield, UK, [3]Eisai GmbH, Frankfurt, Germany

Purpose: Eslicarbazepine acetate (ESL) is approved as adjunctive therapy in adults with partial onset seizures (POS), with or without secondary generalization. The aim of the non-interventional study EPOS (Eslicarbazepine acetate in Partial-Onset Seizures) was to assess retention rate, effectiveness, safety and tolerability of ESL as only add-on to monotherapy in everyday clinical practice across six European countries.

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 109 evaluable patients (data cut-off December 2013) are 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 ± 300.0 mg. Levetiracetam (32.1%) and Lamotrigine (23.9%) were the most frequently preferred combination partners. Adverse events (AE, n = 47) occurred in 29 patients; two serious AE were reported for 2 patients. The most frequently reported AE were dizziness (6.4%), headache (5.5%) and fatigue (4.6%). Seizure freedom over the observation period of 6 months was reported by 47.8% of the patients.

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

Stern WM[1,2], Sander JW[1,2,3], Rothwell JC[4], Sisodiya SM[1,2]
[1]Department of Clinical and Experimental Epilepsy, Institute of Neurology, University College London, London, UK, [2]Epilepsy Society, Chalfont St Peter, UK, [3]Stichting Epilepsie Instellingen Nederland, Heemstede, The Netherlands, [4]3Sobell Department of Motor Neuroscience and Movement Disorders, University College London, London, UK

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 even when added to two or more concurrent antiepileptic medications (with different modes of action). Whether there is a correlation between excitability change and efficacy remains to be seen. Further cases are being recruited. TMS may prove a useful tool for drug-based studies, including pharmacogenomics.

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EPILEPSY CO-MORBIDITY IN ADULT PATIENTS

Ndoja D[1], Buda L[1], Kuqo A[1], Ibro E[2], Mijo S[1], Seferi A[3], Rroji A[4], Perolli A[5], Kollcaku A[6], Kruja J[1]
[1]Neurology, UHC Mother Theresa, Tirana, Albania, [2]Emergency Center, UHC Mother Theresa, Tirana, Albania, [3]Neurosurgery, UHC Mother Theresa, Tirana, Albania, [4]Neuroradiology, UHC Mother Theresa, Tirana, Albania, [5]Hematology, UHC Mother Theresa, Tirana, Albania, [6]Rheumatology, UHC Mother Theresa, Tirana, Albania

Object: Thirty-five patients with epilepsy in co existence 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, 3% mixed colagenosis) or hematologic diseased 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 neurologic 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

Lotfinia M[1,2]
[1]Shefa Neuroscience Research Center, Tehran, Iran, [2]Shahid Beheshti University of Medical Sciences, Tehran, Iran

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

Costa C[1], Morelli E[2], Ghiglieri V[2], Pendolino V[2], Bagetta V[2], Fejtova A[3], Pignataro A[4], Ammassari-Teule M[4], Gundelfinger ED[3], Picconi B[2], Calabresi P[1,2]
[1]S. Maria della Misericordia Hospital, University of Perugia, Perugia, Italy, [2]Laboratory of Neurophysiology, Fondazione Santa Lucia, IRCCS, Rome, Italy, [3]Leibniz Institute for Neurobiology, Magdeburg, Germany, [4]Laboratory of Psychobiology, Fondazione Santa Lucia, IRCCS, Rome, Italy

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 (BsnΔEx4/5) 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 therapeutic effects of EE. The mutant bsn mouse represents a possible model to investigate the role of the hippocampus in early onset epilepsy.

Reference 1. Altrock WD et al. (2003) Functional inactivation of a fraction of excitatory synapses in mice deficient for the active zone protein bassoon. Neuron 37:787–800.

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

Lotfinia AA[1]
[1]*Shefa Neuroscience Research Center, Tehran, Iran*

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 DNXQ 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 glutamatergic 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 ADMINSTRATION DISCLOSED POST TRAUMATIC ENHANCED SEIZURE SUSCEPTIBILITY FOLLOWING A NEW FOCAL BRAIN INJURY MODEL

Ghadiri Garjan T[1,2], *Sharifzadeh M*[2], *Gorji A*[3]
[1]*Shefa Neuroscience Research Center, Tehran, Iran,* [2]*School of Advanced Technologies in Medinice, Tehran University of Medical Sciences, Tehran, Iran,* [3]*Muenster University, Muenster, Germany*

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, ECoG 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

Thomas MG[1], *Covington JA*[1], *Wall MJ*[1]
[1]*University of Warwick, Coventry, UK*

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 mm^2) 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-

mised the mixing of the two perfusing solutions. The effectiveness of the chamber was characterised both by measuring the mixing of fluorescent dyes and by confirming the isolated effect of TTX on Purkinje cell firing in slices of cerebellar vermis. Finally, electrographic seizure activity was induced, in isolated regions of tissue.

Results: 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.

p148
THE EFFECTS OF ENTORHINAL CORTEX LESION ON EPILEPTOGENESIS IN A TOXIN-FREE ANIMAL MODEL OF TEMPORAL LOBE EPILEPSY

Meyer M[1], Bauer S[1], Rosenow F[1], Norwood B[1]
[1]Neurology, Philipps University, Marburg, Germany

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: 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 during the latent period is not supported. Additional experiments are needed, however, to determine whether lesions of the entorhinal cortex are an effective antiepileptic treatment.

p149
PROGRESSIVE BRAIN DAMAGE, SYNAPTIC REORGANIZATION AND NMDA ACTIVATION IN A MODEL OF EPILEPTOGENIC CORTICAL DYSPLASIA

Colciaghi F[1], Finardi A[1], Nobili P[1], Locatelli D[1], Spigolon G[2,3], Battaglia GS[1]
[1]IRCCS Neurological Institute Carlo Besta, Milano, Italy, [2]Neuroscience Institute Cavalieri Ottolenghi (NICO), University of Torino, Torino, Italy, [3]Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden

Purpose: Whether severe epilepsy could be a progressive disorder remains as yet unresolved. We previously demonstrated in a rat model of acquired focal cortical dysplasia, the methylazoxymethanol/pilocarpine rats (MAM-PILO), that the occurrence of status epilepticus (SE) and subsequent seizures fostered a pathologic process capable of modifying the morphology of cortical pyramidal neurons and NMDA receptor expression/localization (Colciaghi, Brain 2011;134:2828–43). We have here extended our analysis by evaluating neocortical and hippocampal changes in MAM-PILO rats at different time-points after the onset of the first spontaneous seizure.

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

1. is steadily progressive, deeply altering neocortical and hippocampal morphology, with atrophy of neocortex and CA regions and progressive increase of granule cell layer dispersion;
2. changes dramatically the fine morphology of neurons in neocortex and hippocampus, by increasing cell size and decreasing both dendrite arborization and spine density;
3. induces reorganization of glutamatergic and GABAergic networks in both neocortex and hippocampus, favoring excitatory vs. inhibitory input;
4. 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.

p150
GYKI 52,466 DELAYED AMPA-INDUCED SEIZURE SUSCEPTIBILITY IN NEONATAL RATS

Dhir A[1], Chopra K[2]
[1]Pharmacology, Institute of Research and Development, Gujarat Forensic Sciences University, Gandhinagar, India, [2]Pharmacology, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh, India

Purpose: Ionotropic glutamatergic receptors [AMPA (alpha-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid), NMDA (*N*-methyl-D-asparate) and kainate] maintain excitatory synaptic transmission. These receptor sub-types play an important role in the pathophysiology of neonatal seizures. AMPA-induced seizures in neonatal rats is not a well-characterized animal model to screen antiepileptic drugs for neonatal seizures.

Method: Here, we evaluate various behavioral seizure abnormalities in neonatal rats after intraperitoneal administration of AMPA. Further, we explored whether acute administration of GYKI 52,466, a highly selective, non-competitive AMPA receptor antagonist, could protect against different phases of convulsions induced by AMPA.

Results: Exogenous administration of AMPA (4 mg/kg., i.p.) in Sprague Dawley neonatal rats (P9–P11) resulted in wagging of the tail/jerks (112.33 ± 30.76 s), forelimb/hindlimb clonus (277.50 ± 13.90 s), hyperlocomotion with periodic loss of righting reflex, hindlimb tonic extension (384.83 ± 15.07 s), followed by permanent loss of righting reflex and death. A lower dose of AMPA (2 mg/kg., i.p.) resulted in similar phases of convulsions; the onset of tail wagging/jerks (219 ± 38.32 s)

but not clonus (264.00 ± 35.89 s) and tonic extension (438.00 ± 52.87s) 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.

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p151
AUTOANTIBODIES TO THE *N*-METHYL-D-aspartate receptors and seizure susceptibility in mice

Wright S[1], Hashemi K[2], Pettingill P[1], Lang B[1], Vincent A[1], Upton L[1]

[1]Universtity of Oxford, Oxford, UK, [2]Brandeis University, Boston, MA, USA

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

Noe' FM[1], Librizzi L[1], Bellistri E[1], deCurtis M[1]

[1]Fondazione IRCCS Istituto Neurologico 'Carlo Besta', SOSD Experimental Neurophysiology and Epilettology, Milano, Italy

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 hippocampi (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

Byeon JH[1], Kim G-H[1], Kim MK[1], Kim SW[1], Eun B-L[1]

[1]Department of Pediatrics, Korea University College of Medicine, Seoul, Korea

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 relavant 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.

p154
CHARACTERIZATION AND MODIFICATION OF THE FOCAL KAINATE MODEL IN MICE AS A SUITABLE MODEL FOR STUDIES ON ANTIEPILEPTOGENESIS

Twele F[1,2], Töllner K[1,2], Brandt C[1,2], Löscher W[1,2]
[1]University of Veterinary Medicine, Hannover, Germany,
[2]Center for Systems Neuroscience, Hannover, Germany

Purpose: Symptomatic epilepsies, particulary 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

Yuen E[1], Troconiz I[2]
[1]Eli LIlly & Co., Global PK/PD & Pharmacometrics, Windlesham, UK, [2]Universidad de Navarra, Pamplona, Spain

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 (ED_{50}) 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. ED_{50}s were recorded and rodent exposures at these ED_{50}s 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 ED_{50} (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.

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SEIZURE PROGRESSION AND SISCOM PERFUSION CHANGES IN THE AMYGDALA KINDLING MODEL IN THE RHESUS MONKEY

Cleeren E[1,2], Casteels C[3], Goffin K[3], Janssen P[1], Van Paesschen W[2]
[1]Laboratory for Neuro- and Psychophysiology, KU Leuven, Leuven, Belgium, [2]Laboratory for Epilepsy Research, KU Leuven, Leuven, Belgium, [3]Nuclear Medicine and Molecular Imaging, KU Leuven, Leuven, Belgium

Amygdala kindling is a widely used animal model to study mesial temporal lobe epileptogenesis. In the macaque monkey, kindling develops slowly and represents, therefore, a unique opportunity to study neural changes associated with epileptogenesis using electrophysiology and functional imaging.

We implanted two rhesus monkeys with low impedance electrodes in the right amygdala. Electrical kindling consisted of daily stimulation with a 1 s, 60 Hz sine wave at the intensity of the afterdischarge threshold, while the animal was monitored by video-EEG. Brain perfusion was measured by ^{99m}Tc-ECD SPECT scanning 2 months postoperatively and during the four clinical seizure stages. To measure ictal brain perfusion, the monkeys were injected with approximately 222 MBq ^{99m}Tc-ECD 10s before a seizure was elicited. Images were analyzed using the SISCOM (Subtraction Ictal SPECT Co-registered to MRI) technique.

After discharge duration increased slowly over 477 days for monkey K and 515 days for monkey S (18 ± 8 s in stage I −52 ± 13 s in stage IV) while the animals experienced four clinical stages ranging from interrupting ongoing behavior to bilateral convulsions. Ictal SPECT imaging showed hyperperfusion in the stimulated temporal lobe and hypoperfusion of frontal lobes. Seizures of monkey K were accompanied by hypoperfusion in the right putamen and hyperperfusion in the right insula and thalamus, while for these structures, monkey S showed opposite results. Comparing different stages within monkeys revealed no major changes in the SISCOM perfusion network.

SISCOM showed temporal lobe hyperperfusion and frontal lobe hypoperfusion 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 electroclinical evolution of seizures within this network during kindling remain to be established.

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REDUCTION OF THE NMDA RECEPTOR NR_{2B} SUBUNIT EXPRESSION IN CORTICAL AND SUBCORTICAL AREAS OF WAG/RIJ RATS

Karim Zadeh F[1], Lotfinia M[1]
[1]*Shefa Neuroscience Research Center, Tehran, Iran*

Purpose: Glutamatergic NMDA receptors modulation could affects the synchronization of spike discharges in in WAG/Rij rats, a valid genetic animal model of absence epilepsy. In present study, we describe the alteration of NR_{2B} 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 NR_{2B} receptors was assessed by immunohistochemical staining in WAG/Rij and compared to age-matched Wistar rats.

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

Conclusion: The reduction of NR_{2B} 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.

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

Kim DW[1], Ryu N-Y[1]
[1]*Pediatrics, Inje University Ilsan Paik Hospital, Goyang, Korea*

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.

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

Hong Z[1], Yang T[1], Zhou D[1]
[1]*Department of Neurology, Sichuan University, Chengdu, China*

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 immunochemistry 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-kindling) 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.

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EPILEPTIC SEIZURES AT PATIENTS WITH MODERATE AND SEVERE HEAD INJURY

Trifonov I[1], Krylov V[1], Talypov A[1]
[1]*Moscow Health Care Department, Scientific Research Institute of Emergency Care named after N. V. Sklifosovsky, Moscow, Russian Federation*

Abstracts

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 till 13 scores). The cerebral contusion of moderate severity was seen at 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 hematomas (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 leucocytes amount in CSF more than 100 cells per 1 μl.

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

Ferlazzo E[1], Gasparini S[1], Sofia V[2], Bellavia MA[1], Mumoli L[3], Cianci V[1], Latella MA[1], Fatuzzo D[2], Labate A[3], Arcudi L[4], Gambardella A[3,5], Aguglia U[1]

[1]Regional Epilepsy Center, Catanzaro University, Reggio Calabria, Italy, [2]Neurologic Clinic, University of Catania, Catania, Italy, [3]Neurologic Clinic, Catanzaro University, Catanzaro, Italy, [4]Stroke Unit Azienda Ospedaliera Bianchi Melacrino Morelli, Reggio Calabria, Italy, [5]Institute of Neurological Sciences, National Research Council, Mangone, Italy

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: recent stroke, insufficient imaging data, coexistence of nonvascular cerebral lesions or psychogenic seizures. Subjects were divided in two groups: Post-Stroke Epilepsy (PSE: large vessel disease involvement), and Epilepsy associated with Small Vessel Disease only (ESVD). Epileptogenic focus was identified in both groups, on the basis of ictal semiology and interictal/ictal EEG. Univariate and multivariate logistic regression was performed to assess differences between groups.

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

Andreev V[1]

[1]Moscow State Medical Stomatology University, Moscow, Russian Federation

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 clonic 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 locus, 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

Abubakr A[1], Wambacq I[2]

[1]Neurology, University of Mississippi Medical Center, Jackson, MS, USA, [2]Montclair State University, Montclair, NJ, USA

Purpose: We assessed the lateralizing value of clonic Asymertic 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 ascertained. 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 (25.2%) 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. Seizures 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.

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SEMIOLOGICAL ETIOLOGICAL ELECTROENCEPHALOGRAPHIC FINDINGS IN FLE

Ndoja D[1], Kuqo A[1], Agolli D[1], Xhaxho S[1], Dobi D[1], Mijo S[1], Kruja J[1], Buda L[1]
[1]UHC 'Mother Theresa', Tirana, Albania

Purpose: Semiological etiological electroencephalographic findings in FLE.

Objects: Thirty eights 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 fibrilation in 8% respectively. Surgery, Tension Type headache, Arterial Hypertension and Febrile Convulsions in 3% respectively. Heredity was positive in 10%, whilst (40%; 26%) had psychiatric or memory impairment. Seizures were rare in 40%, monthly or daily equally reported in 24%, weekly in 12%, whilst only 13% of the entire population presented new onset epilepsy. Refractory seizures etiology was; vascular in 40%, post-traumatic, inaugural tumors, cerebral palsy and non-lesional in 15% respectively. Right laterality prevailed in 40% compare to 34% left sided, 26% had unlateralized seizures. Semiology: 29% showed immediate GTCS (16% nocturnal),18% had versive +/− partial motor onset with secondary generalization, partial motor or sensory onset only (18%; 3%), tonic seizures with aura, automatisms or limbic signs 11%, hyperactive seizures 11%, only automatisms or staring 3%. EEG: lateralized IEDs 22%, anterior bilateral or unilaterally dominated (23%; 20%), focal anterior localized or contralaterally spreaded (17%; 12%), diffuse but prevaling unilaterally and normal or unrealized exams in 3% respectively.

Diagnosis: Non-lesional 34% (hereditary FLE 1%), tumoral (meningeoma, hydrocefaly from carcinomatos meningitis (24%; 1%), post-traumatic and cortical traumatic hemyspheric edema (11%; 1%), post-stroke 11%, natal hypoxia 3%, cerebral palsy and cicatricial lesions in 3% respectively. Lastly dementia, cortical hematoma, pineal 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 semeiology; non lesional, tumoral, post-traumatic, vascular and natal hypoxia in etiology; and bilateral anterior IEDs in EEG prevailed more.

p166
VISUAL EPILEPTIC PHENOMENA: SEMIOLOGY AND CLINICAL IMPLICATIONS

Gonzalez-Cuevas GM[1], Toledo M[2], Santamarina E[2], Fernandez A[3], Sarria-Estrada S[4], Sueiras-Gil M[5], Cambrodí R[5], Alvarez-Sabín J[1], Salas-Puig J[2]
[1]Neurology Department, Vall d'Hebron University Hospital, Universitat Autonoma de Barcelona, Barcelona, Spain, [2]Epilepsy Unit, Neurology Department, Vall d'Hebron University Hospital, Universitat Autonoma de Barcelona, Barcelona, Spain, [3]Neurology, Sant Creu y Sant Pau Hospital, Barcelona, Spain, [4]Magnetic Resonance Unit, Radiology Department, Vall d'Hebron University Hospital, Universitat Autonoma de Barcelona, Barcelona, Spain, [5]Neurophysiology Department, Vall d'Hebron University Hospital, Universitat Autonoma de Barcelona, Barcelona, Spain

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 symptoms were 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.

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LOCALIZING VALUE OF ICTAL EXTRAPYRAMIDAL MOTOR SYMPTOMS

Kalss G[1], Fruehwald U[2], Bauer G[2], Trinka E[1]
[1]Neurology, Christian Doppler Klinik, Paracelsus Medical University Salzburg, Salzburg, Austria, [2]Neurology, Medical University of Innsbruck, Innsbruck, Austria

Abstracts

Purpose: The basal ganglia form circuits with frontal and temporal neocortices. Among established ictal extrapyramidal motor symptoms (EPMS) are dystonic limb posturing and gyratory 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.

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NONCONVULSIVE STATUS EPILEPTICUS ASSOCIATED WITH CEFEPIME IN A PATIENT WITH RENAL FAILURE

Kim SH[1], Yoon BA[1], Son SW[1], Kim JK[1]
[1]Department of Neurology, Dong-A University Hospital, Busan, Korea

Background: Cephalosporins widely used in clinical practice have some adverse effect, including neurotoxicity, however only few cases have reported about cephalosporins induced nonconvulsive status epilepticus (NCSE).

Case: A 57 year old woman with bilateral optic neuritis, lung abscess and chronic kidney disease was referred to our epilepsy clinic because of her decreased mentality. She had been hospitalized for treatment of her visual disturbance and taken 1 g methyl-prednisolone pulse therapy for 2 days. Two weeks later, she suddenly showed abnormal behaviors like sang a strange song, stared into space, and did not response to verbal stimulation. Brain MRI revealed only a small (about 3 mm of diameter) cortical infarction in right parietal cortex with mild diffuse cerebral atrophy. Spinal fluid examination was normal and EEG demonstrated continuous 2 Hz generalized sharp and slow wave discharges which was compatible with NCSE. Although she received full dose of valproic acid, levetiracetam and topiramate, all these antiepileptic drugs were of no effect. She was mildly responsive to intravenous midazolam, only. We prescribed intravenous midazolam 5 mg in every 6 h for 1 week, and tapering to 2.5 mg every 8 h because of her vital instability. While treating equal dose of midazolam, we discontinued her intravenous antibiotics cefepime which was prescribed for management of lung abscess. Thereafter, her mentality was recovered dramatically.

Discussion: In renal failure, increased urea induces BB disruption and significant quantity of cephalosporins can cross BBB. Decreased clearance of cephalosporins also results in the buildup of toxic levels of drug or its toxic metabolites. Increased level of cephalosporins blocks GABA-A receptor and leads to electrical excitability in neurons.

Conclusion: The diagnosis of NCSE should be considered in all patients with unexplained mental changes and on treatment with intravenous cephalosporins, particularly when these patients have some degree of renal dysfunction.

p169
ABDOMINAL PAIN: DON'T ASK THE STOMACH, ASK THE BRAIN

Pardo-Parrado M[1], Rodríguez-Osorio X[1], Domínguez-Vivero C[1], Rodríguez-Castro E[1], López-Dequidt I[1], Saavedra Piñeiro M[1], López-González J[1]
[1]Neurology, Hospital Clínico Universitario de Santiago de Compostela, Santiago de Compostela, Spain

Purpose: Abdominal pain usually corresponds to focal causes. Paroxysmal recurrence, associated manifestations, EEG findings and response to AEDs suggest an epileptic origin. Isolated refractory abdominal auras with no electrical activity in surface EEG recordings are difficult to diagnose.

Method: We present a right-handed woman who suffered an abdominal Burkitt lymphoma at the age of ten. After the first treatment regimen with metotrexate, vincristine and cyclophosphamide, she presented with kidney failure and needed hemodialysis. In addition, she experienced an episode of loss of awareness, skin pallor and muscle weakness with secondary generalization. She had no previous history of febrile seizures. Brain CT and CSF analysis were normal. EEG showed spikes and sharp-wave complexes in the right mid-temporal region. Phenobarbital was started and substituted by carbamazepine afterwards. Several schemes of AEDs were tried unsuccessfully. At the age of 20 she was transferred to the Neurology Department with episodes of isolated acute epigastralgia with nausea and her usual complex partial seizures.

Results: Presurgical evaluation included VideoEEG showing 2-min-episodes of isolated upper abdominal painful sensations with no electrical activity in surface recordings and complex partial seizures preceded by the same aura, showing ictal activity arising from the right temporal lobe. MRI evidenced right mesial temporal sclerosis (MTS). Surgery was proposed and amigdalohippocampectomy with resection of the anterior right temporal lobe was performed. A year later the patient is seizure free including abdominal auras.

Pain abdominal auras represent 5% of all the abdominal auras and they frequently arise from temporal mesial structures. MTS is the most frequent cause of refractory epilepsy. Although it is uncommon, it has been described as a result of hematologic cancer.

Conclusion: We would like to raise the awareness of abdominal pain as an epileptic manifestation. This specific semiology points to a mesial temporal origin, as the case we present.

p170
JAPANESE ENCEPHALITIS PRESENTING AS NONCONVULSIVE STATUS EPILEPTICUS WITH EXCELLENT RECOVERY

Kim S-H[1], Shim DH[1], Yoon BA[1]
[1]Department of Neurology, Dong-A University Hospital, Busan, Korea

Background: <1% of people infected with Japanese encephalitis (JE) virus develop clinical disease. Mental changes, seizures, focal neurologic deficits, and generalized weakness typically develop in the JE. The seizures in most of JE cases are convulsive seizure pattern. The clinical outcome of JE usually show poor prognosis.

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 disappered 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 callosum splenium which was 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.

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NOCTURNAL FRONTAL LOBE EPILEPSY WITH HYPERMOTOR SEIZURES ASSOCIATED WITH AUDITORY SYMPTOMS: ANATOMOELECTRO-CLINICAL DESCRIPTION OF 11 PATIENTS

Ferri L[1,2], Bisulli F[1,2], Nobili L[3], Tassi L[3], Licchetta L[1,2], Mostacci B[1,2], Stipa C[1,2], Manieri G[1,2], Trippi I[1,2], Provini F[1,2], Tinuper P[1,2]

[1]IRCCS Institute of Neurological Science of Bologna, Bologna, Italy, [2]Department of Biomedical and Neuro-Motor Science, University of Bologna, Bologna, Italy, [3]'C. Munari' Epilepsy Surgery Center, Niguarda Hospital, Milano, Italy

Purpose: We aim to describe the anatomo-electroclinical data of a population of patients with nocturnal hypermotor seizures (NHS) associated with auditory symptoms, in order to evaluate the localizing value of auditory aura.

Method: We reviewed all patients from our database of Nocturnal Frontal Lobe Epilepsy (NFLE) cases, with diagnosis confirmed by videopolysomnographic (VPSG) recording of the attacks; we selected those who reported an auditory aura as initial ictal symptom at least in two nocturnal hypermotor seizures (NHS) during their lifetime. The localization of the epileptogenic zone was based on the analysis of anatomo-electroclinical data.

Results: A total of 11 out of 165 subjects were selected (7 M and 4 F). Seven patients reported simple auditory aura, clearly lateralized in 5 cases. According to VPSG recording of NHS, semeiological features were: tonic/dystonic seizures (6 pts), hyperkinetic seizures (3 pts), both in 2 patients.

Three patients were studied with stereo-EEG: in 2 patients the epileptogenic zone lay in the left superior temporal gyrus, in 1 patient seizures arose from a lesion located between the posterior insula and the left temporal lobe; one of these patients underwent Heschl's gyrus resection and he is currently seizure free. In 3 patients the anatomo-electroclinical data pointed to a presumed epileptogenic zone: in the left temporal lobe in 2 of them and between the insula and the left temporal lobe in 1. In 5 patients the anatomo-electroclinical correlations were not conclusive.

Conclusion: Our study suggests that auditory aura may be a helpful anamnestic feature to suspect an extra-frontal origin. It could guide secondary investigations and intracerebral studies, in order to improve diagnostic definition and to perform surgical treatment.

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Monday, 30th June 2014

p172
HIGH-GRADE GLIOMAS: ARE EPILEPTIC SEIZURES MORE SENSITIVE THAN NEUROIMAGING IN PREDICTING DISEASE RECURRENCE?

Fattouch J[1], Fanella M[1], Albini M[1], Casciato S[1], Lapenta L[1], Morano A[1], D'Elia A[2], Salvati M[2], Berardelli A[1], Giallonardo AT[1], Di Bonaventura C[1]

[1]Neurological Sciences, University of Rome 'La Sapienza', Rome, Italy, [2]Neurosurgery Unit, Department of Neurological Sciences, University of Rome 'Sapienza', Rome, Italy

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/m^2) and then with chemotherapy alone (Temozolomide 200 mg/m^2 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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CLINICAL AND HISTOPATHOLOGICAL CHARACTERISTICS OF TEMPORAL LOBE EPILEPSY PATIENTS MANIFESTING WITH HYPERMOTOR SEIZURES

Elisak M[1], Martinkovic L[1], Amlerova J[1], Musilova K[2], Kuba R[2,3], Brazdil M[2,3], Marusic P[1]

[1]Department of Neurology, 2nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Prague, Czech Republic, [2]Brno Epilepsy Centre, First Department of Neurology, Faculty of Medicine, St. Anne's University Hospital, Masaryk University, Brno, Czech Republic, [3]Central European Institute of Technology (CEITEC), Masaryk University, Brno, Czech Republic

Abstracts

Purpose: To identify characteristics of temporal lobe epilepsy (TLE) patients who manifest with hypermotor seizures.

Method: Retrospectively we have reviewed data of 438 adult refractory TLE patients and selected those who had hypermotor seizures (HMS) recorded during preoperative video-EEG monitoring. Electro-clinical data, neuroimaging findings, histopathology, type of resection and outcome were analyzed.

Results: We identified 22 patients (5%) from our series. HMS type 1 (marked agitation with a facial expression of fear) had 72% of them, the rest presented with type 2 (mild agitation, horizontal movements or rotation of trunk or pelvis). Typical temporal lobe seizure semiology (epigastric/auditory aura, oroalimentary automatisms) was observed in 90% of patients and this preceded, followed or was independent on HMS. MRI showed temporal lobe abnormality in 77%, PET in 90% of patients, and both were concordant with electro-clinical localization. Hypermotor seizures were frequently associated with malformation of cortical development (64%) and with speech non-dominant temporal lobe (91%). Outcome of this subgroup of patients was comparable to the outcome of TLE surgery in general – 17 patients (77%) were seizure free 1 year after surgery. Unfavourable epilepsy surgery outcome was not influenced by history, epilepsy duration, EEG, MRI/PET findings, extent of resection or histopathological finding.

Conclusion: Temporal lobe epilepsy manifesting with HMS is often associated with malformation of cortical development – a lesion affecting the development of the temporal lobe. More often we found hypermotor seizures in patients with TLE originating from speech non-dominant hemisphere.

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CASE PRESENTATION OF 26-YEAR OLD WOMAN WITH FOCAL EPILEPSY DUE TO FOCAL CORTICAL DYSPLASIA IN THE RIGHT TEMPORAL LOBE

Bograkou M[1,2], Vigren P[1,2,3], Richter J[3], Lindehammar H[2,4], Gauffin H[1,2]

[1]Department of Neurology, University Hospital of Linköping, Linköping, Sweden, [2]Department of Clinical and Experimental Medicine, Linköping University, Linköping, Sweden, [3]Department of Neurosurgery, University Hospital of Linköping, Linköping, Sweden, [4]Department of Clinical Neurophysiology, University Hospital of Linköping, Linköping, Sweden

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. Interictal 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 lesionectomi 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: This case demonstrates the diagnostic difficulties in a patient with initially MRI negative neocortical temporal lobe epilepsy. The semiology included ipsilateral limb automatisms.

p175
SEIZURES MIMICKING STROKES

Gómez A[1], Ley M[1], Jimenez J[1], Puig A[1], Roquer J[1], Rocamora R[1]

[1]Neurology, Hospital del Mar, Barcelona, Spain

Purpose: To assess the frequency of seizures mimicking strokes defined as events in which the initial symptoms lead to the primary diagnosis of stroke at the Emergency Room. To compare the demographic and clinical characteristics between patients with seizures mimicking stroke and real acute ischemic events.

Method: We analyzed the demographic data, medical history and initial clinical condition from the Stroke Database of our hospital (BASICMAR) from January 2005 to June 2013. This database included 3,688 patients that were evaluated by the neurologist at the ER and were oriented as acute ischemic stroke as the initial diagnosis; no hemorrhages were included. We found 403 stroke mimic cases. From these patients, 67 cases were known to be seizures mimicking a stroke. The univariate and multivariate analysis were done with IBM SPSS.19 Statistics software

Results: We found 10.9% of stroke mimics of different etiologies in the acute ischemic stroke group. 16.6% of the stroke mimic cases were found to be epileptic seizures. 1.8% of the total patients that we initially oriented as acute ischemic stroke were seizures mimicking a stroke. After the multivariate analysis, factors indicative for seizures were the presence of isolated aphasia without other focal neurological symptom; factors indicative of ischemic stroke were previous cardioembolic diseases, high cholesterol, and D-dimer over 200 ng/ml ($p < 0.05$). The ROC curve demonstrated AUC = 0.738 ($p < 0.001$).

Conclusion: Isolated aphasia is associated with the final diagnosis of seizures mimicking stroke. Cardioembolic 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.

p176
ANALYSIS OF SEIZURE SEMIOLOGY IDENTIFIES PATIENTS WITH BILATERAL TEMPORAL LOBE EPILEPSY

Loesch AM[1], Feddersen B[1], Tezer I[2], Hartl E[1], Rémi J[1], Vollmar C[1], Noachtar S[1]

[1]Epilepsy Center, Department of Neurology, University of Munich, Munich, Germany, [2]Department of Neurology, Faculty of Medicine, Hacettepe University, Ankara, Turkey

Purpose: We investigated whether the analysis of seizure semiology including lateralizing seizure phenomena identifies bilateral independent temporal lobe seizure onset.

Method: We investigated the seizure semiology in 17 patients in whom invasive EEG-video-monitoring documented bilateral temporal seizure onset. The results were compared to 20 left and 20 right consecutive temporal lobe epilepsy (TLE) patients who were seizure free after anterior temporal lobe resection. The seizure semiology was analyzed using the semiological seizure classification with particular emphasis on the sequence of seizure phenomena over time (i.e. aura -> automotor seizure-> versive seizure-> generalized tonic-clonic seizure) and lateralizing seizure phenomena (hand dystonia, version, ipsilateral nose rubbing, sign of 4 etc.) (c^2 analysis or Fisher's exact test).

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 independent clinical information to EEG and imaging in the selection of patients considered for resective temporal lobe epilepsy surgery.

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AUTOMATISMS IN POSTERIOR CORTEX EPILEPSIES: A STEREO-ELECTROENCEPHALOGRAPHY STUDY

Craciun L[1], Nica Pasnicu A[2], Mindruta I[3], Taussig D[4], Haegelen C[5], Ciurea J[6], Barborica A[7,8], Malaia MD[1], Biraben A[9]

[1]Neurology, Emergency Universitary Hospital of Bucharest, Bucharest, Romania, [2]Centre Hospitalier Universitaire de Rennes, Service d'Explorations Fonctionnelles, Rennes, France, [3]Epilepsy Monitoring Unit, Emergency Universitary Hospital of Bucharest, Bucharest, Romania, [4]Fondation Ophtalmologique Adolphe de Rothschild, Service de Neurochirurgie, Paris, France, [5]Centre Hospitalier Universitaire de Rennes, Service de Neurochirurgie, Rennes, France, [6]Neurosurgery, Bagdasar-Arseni Hospital, Bucharest, Romania, [7]Faculty of Physics, Electricity and Biophysics, University of Bucharest, Bucharest, Romania, [8]FHC Inc, Bowdoin, ME, USA, [9]Centre Hospitalier Universitaire de Rennes, Service de Neurologie, Rennes, France

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 automatisms occurrence was found in the two groups (Fisher's exact test, $p < 0.05$). Regarding the incidence of various automatisms, we were able to find a significant preponderance of these clinical manifestations during seizures originating in the temporo-occipital territories. Anatomo-electro-clinical correlation during SEEG studies showed that automatisms occurred during the ictal as well as postictal period when involved different structures that were distributed usually bilaterally and mainly comprised temporo-basal structures.

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.

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INTERICTAL EPILEPTIFORM DISCHARGES IN NEW-ONSET EPILEPSY IN THE ELDERLY

Toyota T[1], Akamatsu N[1]

[1]Neurology, University of Occupational and Environmental Health School of Medicine, Kitakyushu, Japan

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 $\pm$ 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

Yoshioka S-I[1], Kuyama K[2]

[1]Faculty of Medicine, School of Health Science, Tottori University, Yonago, Japan, [2]Faculty of Nursing, Baika Women's University, Ibaragi, Japan

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

Landmark CJ[1], Karouni M[2], Feet SA[1], Larsson PG[3], Henning O[4], Sætre E[5], Johannessen SI[6]

[1]Department of Pharmacy and Biomedical Science, Oslo and Akershus University College of Applied Sciences, Oslo, Norway, [2]Varhaug Apotek, Jæren, Norway, [3]Department of Neurosurgery, Oslo University Hospital, Oslo, Norway, [4]National Center for Epilepsy, Oslo University Hospital, Sandvika, Norway, [5]National Center for Epilepsy, Oslo University Hospital, Oslo, Norway, [6]National Center for Epilepsy, Department of Pharmacology, Oslo University Hospital, Sandvika, Norway

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 comedication was 27% and 22%, in elderly and younger patients with epilepsy, respectively, with 2–7 CNS-active drugs. The most frequently used AEDs with a potential for significant interactions were phenytoin and phenobarbital in the elderly and lamotrigine and valproate in younger patients with epilepsy.

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

Del Felice A[1], Broggio E[2], Valbusa V[2], Gambina G[2], Arcaro C[1], Manganotti P[1,3,4]

[1]Department of Neurological and Motor Sciences, Section of Neurology, University of Verona, Verona, Italy, [2]USO Centro Alzheimer e Disturbi Cognitivi, Neurologia d.O, AOUI, Verona, Italy, [3]Clinical Neurophysiology and Functional Imaging Unit, Section of Neurology, University of Verona, Verona, Italy, [4]Department of Neurophysiology, IRCCS San Camillo, Venezia, Italy

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 Mental 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. TEA incidence may be underestimated in mild cognitive impairment and high-density EEG improved the detection rate of epileptiform abnormalities.

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A CASE OF ANTI-GLUTAMIC ACID DECARBOXYLASE ANTIBODY ASSOCIATED LIMBIC ENCEPHALITIS WITH TEMPORAL LOBE EPILEPSY

Gelener P[1], Keskiner F[2]

[1]Nicosia State Hospital, Nicosia, Cyprus, [2]Or-Ahayim Balat Hospital, Istanbul, Turkey

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 enchantment 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 immunglobulin 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 temporal lobe epilepsy in the elderly.

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

Bouma HK[1], Labos C[1], Gore G[1], Keezer MR[1]
[1]Neurology, McGill University, Montreal, QC, Canada

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.

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

Duez L[1], Beniczky S[1,2], Tankisi H[1], Sidenius P[3], Sabers A[4], Fuglsang-Frederiksen A[1]
[1]Department of Neurophysiology, Aarhus University Hospital, Aarhus, Denmark, [2]The Danish Epilepsy Center, Department of Neurophysiology, Dianalund, Denmark, [3]Department of Neurology, Aarhus University Hospital, Aarhus, Denmark, [4]Department of Neurology, Rigshospitalet, Copenhagen, Denmark

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

Noertjahjani S[1], Susanto A[2], Hidayat R[2], Wibowo S[3]
[1]Department of Electronical Engineering and Information Technology, Engineering Faculty, Gadjah Mada University, Yogyakarta, Indonesia, [2]Department of Electronical Engineering and Information Technology, Gadjah Mada University, Yogyakarta, Indonesia, [3]Neurology, Medical Faculty, Gadjah Mada University, Yogyakarta, Indonesia

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, skewneses, kurtosises, 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 6.94, mean standard deviations 126.31, mean skewneses 0.52, mean kurtosises 4.45, mean entropies 1.16 from normal person and means −153.85, mean standard deviations 404.52, mean skewneses −0.89, mean kurtosises 3.72, mean entropies 3.72 from epileptic patients. Besides, this algorithm can achieve the sensitivity of 98.70% and specificity of 98.25% total accuracy of 99.78%.

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

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EEG ANALYSIS IN PRETERM INFANTS WITH ISCHEMIC BRAIN DAMAGE

Melashenko TV[1], Guzeva VV[2]
[1]Neonatal Intensive Care Unit, Saint Petersburg Pediatric Medical University, Saint Petersburg, Russian Federation,
[2]Neurology Department, Saint Petersburg Pediatric Medical University, Saint Petersburg, Russian Federation

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 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 interventricular 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-awake 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

Melin A[1], Erlandsson I[1], Fajersson Nilsdotter A[1], Ebrahimi Tajadod A[1]
[1]Clinical Neurophysiology, University Hospital in Lund, Lund, Sweden

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 Tc^{99m}-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-examinated 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 electrode 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

Nakagawa E[1,2], Koichihara R[1], Sugai K[1], Sasaki M[1], Inagaki M[2]
[1]Department of Child Neurology, National Center of Neurology and Psychiatry, National Center Hospital, Tokyo, Japan,
[2]Department of Developmental Disorders, National Institute of Mental Health, National Center of Neurology and Psychiatry, Tokyo, Japan

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.

p191
AN APPROACH TO STAGING SLEEP IN POLYSOMNOGRAPHIC STUDIES IN CHILDREN WITH FOCAL EPILEPSY

Chan S[1,2], Chevalier-Riffard C[1], Pressler R[1,2], Baldeweg T[3], Cross H[1,2]
[1]Neurosciences Unit, UCL Institute of Child Health, London, UK, [2]Great Ormond Street Hospital for Children, London, UK, [3]Developmental Cognitive Neurosciences Unit, UCL Institute of Child Health, London, UK

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

Romigi A[1], Toschi N[2], Albanese M[1], Placidi F[1], Izzi F[1], Liguori C[1], Guerrisi M[2], Campagna N[1], Mercuri NB[1], Marciani MG[3]
[1]Neurophysiopathology, University of Rome Tor Vergata, Rome, Italy, [2]Medical Physics Section, Faculty of Medicine, University of Rome Tor Vergata, Rome, Italy, [3]Neurology, University of Rome Tor Vergata, Rome, Italy

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). Cardiovagal index (CVI), cardiosympathetic index (CSI), and approximate entropy (ApEn) were also calculated from Poincarè 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/HF ratio vs. INT and PRE. Time domain variables showed a statistically lower ICT RR interval (vs. PRE) and RMSDD (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/HR 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.

p193
IS HOME VIDEO-TELEMETRY (HVT) SUPERIOR TO INPATIENT VIDEO-TELEMETRY (VT)?

Manidakis I[1], Singh R[1], Amin D[1], Richardson M[1], Brunnhuber F[1]
[1]King's College Hospital, London, UK

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 repeat 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).

p194
PROLONGED PERI-ICTAL CLINICAL-EEG ALTERATIONS IN PATIENTS WITH PCDH19 MUTATION

Terney D[1], Jepsen B[1], Hjalgrim H[1], Stendevad P[1], Nikanorova M[1], Møller R[1], Beniczky S[1], Gardella E[1]
[1]Danish Epilepsy Centre, Dianalund, Denmark

Purpose: Protocadherin coding gene (PCDH19) is a major gene in female patients with infantile onset epilepsy, associated with variable

degree of mental retardation and autistic features with obsessive/hyperactive traits. PCHD-19-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 PCHD19-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 morpheic 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.

p195
CATAMENIAL EPILEPSY IS A PREDICTOR OF DISEASE RESISTANCE

Odintsova GV[1], Koroleva NY[2], Guzeva VI[3], Saykova LA[4]
[1]Neurology, Institute of Human Brain of RAS, Saint Petersburg, Russian Federation, [2]Institute of Human Brain of RAS, Saint Petersburg, Russian Federation, [3]Neurology, Saint Petersburg State Paedistric Medical University, Saint Petersburg, Russian Federation, [4]Neurology, North-Western State Medical University n.a.I.I. Mechnikov, Saint Petersburg, Russian Federation

Purpose: To study clinical value of catamenial epilepsy in assessment of disease resistance.

Method: The work was the part of prospective observation uncontrollable one-center research of antiepileptic drugs (AEDs) side effects on reproductive health (RH) at 155 women at the age of 16 – 45. 3 groups were allocated: 1gr. – AEDs monotherapy, 2 gr. – polytherapy, 3 gr. – without AEDs. Reproductive health in women with epilepsy was estimated as complex social, physical wellbeing and absent reproductive system problem. Physical wellbeing was defined by clinical picture and AEDs complications. Catamenial epilepsy characterized disease clinic. Frequency was determined and compared separately in groups. STATISTICA for Windows system (version 5.5) was used.

Results: Average age of the surveyed women made 25 years. Quantity in groups was presented: the first group included 68 patients (44%), the second – 67 (43%). Control third group made 20 women (13%). Women were included in group of control didn′t receive AEDs during last 12 months. Approximately the peer number of patients on mono – and polytherapy differed from average data at epilepsy and was caused by the contingent of patients of specialized epileptological center Statistically reliable differences in qualitative characteristics of groups weren′t taped. The general indicator of a catamenialnost in cohort made 32%. Dominance of the catamenial epilepsy was noted into 2 group (43%) in comparison with 1(24%) and 2 (25%) groups. Differences were statistically significant above at polytherapy group ($p < 0.001$).

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**.**

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IDIOPATHIC GENERALIZED EPILEPSIES AND SEIZURE CONTROL

Kiteva-Trenchevska G[1]
[1]University Clinic of Neurology, Skopje, Macedonia

Purpose: Idiopathic generalized epilepsies (IGE) are pharmacorensponsive 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.

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ROLE OF AMPLITUDE-INTEGRATED EEG MONITORING DURING THERAPEUTIC HYPOTHERMIA AFTER CARDIAC ARREST

Lee Y[1], Cho Y-J[1], Lee BI[1], Heo K[1]
[1]Neurology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

Purpose: Therapeutic hypothermia (TH) has been regarded as a standard treatment option after cardiac arrest. We compared the prognostic value of conventional EEG (cEEG) and amplitude-integrated EEG (aEEG) monitoring during TH in the adult patients with hypoxic ischemic encephalopathy.

Method: A total of 81 patients from our prospective TH registry between September 2011 and October 2013 were enrolled to the study. All patients completed 24 h mild hypothermia and managed according to our institutional standard protocol. Continuous EEG monitoring, which enables simultaneous recoding of both cEEG and aEEG was done in all patients. cEEG was graded as between 1 and 5 similar to the Bassetti group, and aEEG with normal voltage continuous pattern was set as favorable.

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 not always indicating grave prognosis and withdrawal of life support. Development of standard EEG grade systems will be required.

p198
PERSISTENT LOCAL BRAIN ACTIVITY DURING POSTICTAL GENERALIZED EEG SUPPRESSION

Altenmüller D-M[1], Schulze-Bonhage A[1], Elger CE[2], Surges R[2]
[1]Epilepsy Center Freiburg, Freiburg, Germany, [2]Department of Epileptology, Bonn, Germany

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.

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DIAGNOSTIC VALUE OF SLEEP-DEPRIVED EEG OVER ROUTINE EEG IN JUVENILE MYOCLONIC EPILEPSY (JME) AND TEMPORAL LOBE EPILEPSY (TLE)

Khan M[1,2], Jawaid A[1], Brohi H[1,3]
[1]Department of Clinical Neurophysiology, Aga Khan University, Karachi, Pakistan, [2]French Medical Institute for Children, Professional Services, Kabul, Afghanistan, [3]Department of Neurology, Aga Khan University, Karachi, Pakistan

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 SDE where as rest of 23 (13%) were still normal. 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.

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INTERICTAL ELECTROENCEPHALOGRAPHY IN PATIENTS WITH EPILEPSY IN NORTHWESTERN NIGERIA

Owolabi LF[1], Sale S[2], Epilepsy Study Group
[1]Department of Medicine, Bayero University, Kano, Nigeria, [2]Psychiatry, Bayero University, Kano, Nigeria

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 hyperventilation (HV) and response to HV was unremarkable in 1,286 (76%) of them. Out of 405 who had remarkable changes on hyperventilation; 302 had increase in epileptiform discharges, while 103 had abnormal discharges only on hyperventilation. Seventeen out of 19 (89.5%) patients with 3 Hz spike and wave complexes had activation by hyperventilation. Most common interictal epileptiform activities were focal spike/sharp and wave and generalized spike/sharp and slow waves. More AED naïve (678) than those that were on AED (500) had EEG abnormality and the difference was statistically significant, $p = 0.0001$.

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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ARTERIAL SPIN LABELING MRI: A STEP FORWARD IN NON-INVASIVE DELINEATION OF FOCAL CORTICAL DYSPLASIA IN CHILDREN

Blauwblomme T[1], Boddaert N[1], Chemaly N[1], Chiron C[2], Bourgeois M[1], Bahi-Buisson N[1], Kaminska A[1], Grevent D[1], Brunelle F[1], Archambaud F[2], Sainte-Rose C[1], Nabbout R[1]
[1]Hopital Necker, Paris, France, [2]INSERM U836, Paris, France

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 ^{18}FDG-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.

p202
GENE EXPRESSION PROFILING OF FOCAL CORTICAL DYSPLASIA SHOWS REDUCED EXPRESSION OF MYELIN-ASSOCIATED GENES IN DYSPLASTIC TEMPORAL LOBE

Donkels C[1], Pfeifer D[2], Huber S[1], van Velthoven V[3], Weyerbrock A[3], Zentner J[3], Haas CA[1]
[1]Experimental Epilepsy Research, University of Freiburg, Freiburg, Germany, [2]Department of Hematology, Oncology and Stem Cell Transplantation, University of Freiburg, Freiburg, Germany, [3]Department of Neurosurgery, University of Freiburg, Freiburg, Germany

Purpose: Focal cortical dysplasias (FCD) are local malformations of the human neocortex, originating during pre- and perinatal brain development. They are frequent causes of medically intractable focal epilepsy, associated with a high seizure frequency. To date little is known about the pathomechanisms leading 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 neocortex 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.

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BRAIN MALFORMATIONS AS A FACTOR OF EPILEPSY DEVELOPMENT IN CHILDREN AT AN EARLY AGE

Stetsenko T[1]
[1]Child Neurology, National Medical Academy of Postgraduate Education named after P.L.Shupyk, Kiev, Ukraine

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 electrophysiologic findings in brain malformation (lyssencephaly, heterotopia, focal cortical dysgenesis and polymicrogiria, 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 group 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

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 35% 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 ophtalmoplegia, 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 anamnesis: 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: Lyssencephaly 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

Nakagawa JM[1,2], Donkels C[2], Fauser S[3,4], Beckervordersandforth J[5,6], Prinz M[5], Zentner J[1], Haas CA[2]
[1]Department of Neurosurgery, University Hospital Freiburg, Freiburg, Germany, [2]Experimental Epilepsy Research, University Hospital Freiburg, Freiburg, Germany, [3]Epilepsy Center, University Hospital Freiburg, Freiburg, Germany, [4]Department of Neurology, University Hospital Ulm, Ulm, Germany, [5]Department of Neuropathology, University Hospital Freiburg, Freiburg, Germany, [6]Department of Pathology, University Hospital Maastricht, Maastricht, The Netherlands

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 epileptogenicity 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). Neuron-specific protein levels were analyzed by quantitative Western blot analysis. Following systematic quantification of neocortical neuronal 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 assignment 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 neocortical neuronal composition in FCD.

p206
CHARACTERISTICS OF EPILEPSY CHILDREN WHO OVERLAP WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD)

Lee IG[1], Choi HY[1], Hahn JY[1], Kim SJ[2], Eom TH[3], Bin JH[4], Kim YH[5], Chung SY[6]
[1]Pediatrics, Seoul St. Mary's Hospital, the Catholic University of Korea, Seoul, Korea, [2]Pediatrics, St. Vincent Hospital, the Catholic Univerity of Korea, Suwon, Korea, [3]Pediatrics, Yeouido St. Mary's Hospital, the Catholic Univerity of Korea, Seoul, Korea, [4]Pediatrics, Bucheon St. Mary's Hospital, the Catholic University of Korea, Bucheon, Korea, [5]Pediatrics, Uijeongbu St. Mary's Hospital, the Catholic University of Korea, Uijeongbu, Korea, [6]Pediatrics, Incheon St. Mary's Hospital, the Catholic University of Korea, Incheon, Korea

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.

p207
A 256-DENSE ARRAY EEG SPECTRAL ANALYSIS IN MESIAL SCLEROSIS AND NEOCORTICAL TEMPORAL EPILEPSY PATIENTS: A COMPARISON AMONG DIFFERENT SPIKE DISTRIBUTIONS

Arcaro C[1], Del Felice A[2], Storti SF[2], Mai R[3], Manganotti P[2,4,5]
[1]University of Verona, Verona, Italy, [2]Department of Neurological, Neuropsychological, Morphological and Movement Sciences, Section of Neurology, University of Verona, Verona, Italy, [3]Epilepsy Surgery Center, Niguarda Hospital,

Milan, Italy, [4]Clinical Neurophysiology and Functional Neuroimaging Unit, AOUI of Verona, Verona, Italy, [5]Department of Neurophysiology, IRCCS Fondazione Ospedale San Camillo, Venezia, Italy

Purpose: To describe the different topographical distributions of epileptic spikes in mesial sclerosis and neocortical temporal epileptic patients through the use of a topographical 2D map and an EEG spectral analysis of all the 256 derivations.

Method: Three mesial sclerosis patients (mean age 41.3 years) and 3 neocortical temporal patients (mean age 37.3 years) were recruited. Spikes were marked off line on the high-density EEG. For each patient a spike average and a grand average were calculated. Number of spikes averaged was 31.3 in mesial sclerosis patients and 36.3 in the neocortical ones. The peak of the event was used as a trigger for averaging in epochs of 500 ms. A Fast Fourier Transform (FFT) was applied to the grand average ranging between 0.1 and 30 Hz. The same event was visually considered on a topographical 256 derivations topoplot map labeled with the same numeration.

Results: In all 3 patients affected by mesial temporal epilepsy the grand average spike showed an anterior temporal and zygomatic topographical distribution. The maximum delta and theta peak ranges were recorded over the zygomatic anterior derivations (0.1–5 Hz and 5–7.5 Hz). In neocortical temporal patients slow frequencies were present as well, but a higher range of frequencies (10–25 Hz) was present over the temporal posterior derivations.

Conclusion: We suggest the use of a 256 channel EEG for a better distinguish between the anterior zygomatic distribution of mesial sclerosis patients and the temporal posterior distribution in temporal neocortical ones by the presence of zygomatic derivations all over the jaw for the former and the plus channels for the latter. This is confirmed by the relative distribution of the spectral analysis. It suggests, in addition, a different recognition in frequency terms for sharp waves rhythms rather than pure spiking ones.

p208
THE CASE OF MULTIPLE CONGENITAL MALFORMATIONS OF THE BRAIN (HEMIMEGALENCEPHALY, LYSSENCEPHALY, LEFT-SIDED CEREBELLAR DYSPLASIA, AGENESIS OF THE CORPUS CALLOSUM) AND PIERRE ROBIN SYNDROME IN COMBINATION WITH EPILEPTIC SYNDROME WITH POLYMORPHIC ATTACKS

Shevchenko AA[1]

[1]*Pediatric Psychoneurology, Institute of Pediarics, Obstetrics and Gynecology of the National Academy of Medical Sciences of Ukraine, Kiev, Ukraine*

Purpose: Necessity of timely diagnosis of congenital malformations of the brain with the use of MRI for prenatal diagnostics.

Method: Further is presented case of the multiple congenital malformations of the brain. The child was born from the first pregnancy. Child's parents are somatically healthy. During pregnancy- toxicosis in the first half of pregnancy.

Results: Hydramnion was diagnosed by an ultrasound study on the 22–23 week of pregnancy, through week- cysts of cerebrum. Fetal MRI (Conclusion): MR features of fetal hemimehalencephaly on the left. It was rejection of interruption of pregnancy. After delivery- severe birth asphyxia, cardio-pulmonary resuscitation, central nervous system depression syndrome, frequent tonic-clonic convulsions, muscular hypotonia. The child received supportive care in the newborn resuscitation and intensive care unit of the district hospital in the home area. In the age of 2 years the child was hospitalized in our Clinic with the severe developmental delay, tonic-clonic convulsions in the limbs several times a day. Treatment before hospitalisation: depakin (400 mg/day), phenobarbital (0.01) three times a day. Magnetic resonance imaging.

Conclusion: MR features of the multiple congenital malformations: hemimegalencephaly, lissencephaly, left-sided cerebellar dysplasia, agenesis of the corpus callosum, abnormalities of the facial skull and soft tissues of the face on the left, Pierre Robin syndrome. As a result of anticonvulsive therapy (abolition of the phenobarbital, dose reduction of Depakine (300 mg) and gradual titration of topiramate (5 mg/kg), diazepam – at the status development of the epileptic seizures), the frequency of the seizures was considerably reduced-1-2 attacks per month.

Prenatal ultrasound examination does not always provide sufficient information. Fetal MRI is optimal standard for diagnostics of the congenital anomalies of the Brain (from 20 weeks of pregnancy) for optimization of prenatal diagnostics, clinical and prognostic evaluation and reduction of mortality and childhood disability.

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OVERTREATMENT OF CRYING SPELLS WITH ANTIEPILEPTIC DRUGS AS A FORM OF MUNCHHAUSEN BY PROXY: THE ALBANIAN EXPERIENCE

Haruni A[1], *Vyshka G*[2], *Tashko V*[3]

[1]*Pediatric Neurology, Polyclinic of Specialties No. 3, Tirana, Albania,* [2]*Neurology, UHC Mother Theresa, Tirana, Albania,* [3]*Pediatric Neurology, Hygeia Hospital, Tirana, Albania*

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 policlinic 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 inexistent ′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.

p211
ONE-YEAR SEIZURE OUTCOME FOLLOWING KETOGENIC DIET FOR PEDIATRIC REFRACTORY EPILEPSY: A SINGLE CENTER EXPERIENCE FROM SINGAPORE

Chiam EPJ[1], Lim KJ[2], Wang FS[1], Ong HT[1]
[1]Khoo Teck Puat – National University Children's Medical Institute, National University Hospital, Singapore, Singapore, [2]National University of Singapore, Pediatrics, Yong Loo Lin School of Medicine, Singapore, Singapore

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.

p212
HEALTH-RELATED QUALITY OF LIFE (HRQOL) IN SCHOOL-AGED CHILDREN WITH "ACTIVE" EPILEPSY: A POPULATION-BASED SAMPLE

Reilly C[1,2], Atkinson P[3], Gillberg C[2], Scott RC[4,5,6], Chin RM[7], Das KB[1,5,6], Burch V[1], Aylett S[5], Neville BG[1]
[1]Young Epilepsy, Lingfield, UK, [2]Gillberg Neuropsychiatry Centre, Gothenburg, Sweden, [3]Crawley Child Development Centre, Crawley, UK, [4]University of Vermont, Burlington, VT, USA, [5]Great Ormond Street Hospital, London, UK, [6]Institute of Child Health, London, UK, [7]University of Edinburgh, Edinburgh, UK

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.

p213
RESEARCH OF CONCENTRATION OF ZINC IN CHILDREN WITH EPILEPSY

Guzeva OV[1], Guzeva VI[1]
[1]Neurology Department, Saint-Petersburg Pediatric Medical University, Saint-Petersburg, Russian Federation

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 month–17 years. Group with epilepsy consist of 56 boys and 48 girls, control group – 14 boys and 14 girls. Zinc content in heirs 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.

p214
RESULTS OF THE RESEARCH OF TRIIODOTHYRONINE HORMONE CONCENTRATION IN BLOOD OF GIRLS WITH DIFFERENT FORMS OF EPILEPSY

Guzeva VV[1], Guzeva VI[2]
[1]Neurology Deparment, Saint-Petersburg Pediatric Medical University, Saint-Petersburg, Russian Federation, [2]Saint-Petersburg Pediatric Medical University, Saint-Petersburg, Russian Federation

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 (1group), 11 girls- generalized symptomatic epilepsy (2 group), 15 girls- focal symptomatic temporal epilepsy (3group), 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 nм, in group 2 – 2.67 ± 0.26 nм, in group 3 – 2.07 ± 0.44 nm, in group 4 – 2.56 ± 0.22 nм. 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 ($p \geq 0.90$) 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 nм), and at generalized symptomatic, then at focal symptomatic temporal epilepsy (0.60 ± 0.54 nм), and at others forms of focal symptomatic epilepsy, then at focal symptomatic temporal epilepsy (0.49 ± 0.44 nм).

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?

Nickels K[1], *Kenney D*[1], *Wong-Kisiel LC*[1], *Wirrell E*[1]
[1]*Mayo Clinic, Rochester, MN, USA*

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 electroclinical 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 ($p = 0.064$, χ^2). However, when only those with presumed genetic etiology (idiopathic generalized epilepsy) were included in this group, there was a significantly increased response rate ($p = 0.031$, χ^2, 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

Dumitru MM[1]
[1]*Socola Psychiatric Hospital, Iasi, Romania*

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 simptomathology, 77% of pacients.

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 pacients.

Conclusions: There is a higher occurnes of attempts in girls rather than boys, comparing to the accomplished suicide, where the rate is swiched. 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

Gniatkowska-Nowakowska A[1]
[1]*Outpatient Clinic of Child Neurology and Epileptology, Kielce, Poland*

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.

p219
CHILDRENS' EPILEPSY AND SLEEP DISORDER BREATHING

Khayat N[1], Galli S[1]
[1]Unit EEG-Epilepsy, CHU Besancon, Besancon, France

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 adenoidectomy 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 oximetries' 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 oximetries 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 childrens' epilepsy.

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p220
A CHILD WITH KLINEFELTER'S SYNDROME PRESENTING WITH MENTAL RETARDATION AND EPILEPTIC SEIZURES

Kim E-H[1], Yum M-S[1], Ko T-S[1]
[1]Department of Pediatrics, Asan Medical Center, Asan Medical Center Children's Hospital, University of Ulsan College of Medicine, Seoul, Korea

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, XXY. 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.

p221
TOPIRAMATE IN EPILEPTIC SYNDROMES OF CHILDHOOD WITH CONTINUOUS SPIKE-AND-WAVE DURING SLEEP: RETROSPECTIVE STUDY OF 23 CASES

Vrielynck P[1], Ghariani S[1], Lienard F[1], de Borchgrave V[1], Delmelle F[1], van Rijckevorsel K[1], Bonnier C[1]
[1]William Lennox Neurological Hospital, Université Catholique de Louvain, Ottignies, Belgium

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

Dehlin EE[1], Linden-Mickelsson P[2], Svensson E[2], Undren AK[1]
[1]Child Neurology, Skane University Hospital, Lund, Sweden, [2]Neurophysiology, Skane University Hospital, Lund, Sweden

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.

A long term follow-up regarding surgery in children in Lund show results comparable to other international centers. (Hallböök et al. Acta Neurol Scand 2013;128: 414–421).

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

Cekic B[1], Jovic N[1]
[1]Clinic of Neurology and Psychiatry for Children and Youth, University Belgrade, Belgrade, Serbia

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 restrospectively analyzed for epilepsy and EEG characteristics.

Results: Epilepsy developed in 8 (19%) 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.

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THE PRACTICES IN EMERGENCY AND RESCUE MEDICATION FOR EPILEPSY MANAGED WITH COMMUNITY ADMINISTERED THERAPY (PERFECT) INITIATIVE: INSIGHTS FROM HEALTHCARE PROFESSIONALS, CHILDREN AND THEIR CARERS

Vigevano F[1], Lagae L[2], Panahloo Z[3], on behalf of the PERFECT Investigators (FV) & Steering Committee (LL)
[1]Bambino Gesù Children's Hospital, Rome, Italy, [2]University of Leuven, Leuven, Belgium, [3]ViroPharma SPRL, Brussels, Belgium

Purpose: The PERFECT initiative was undertaken to determine how prolonged, acute, convulsive seizures (PACS) in children are managed in the community.

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 enrolment 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

Voitenkov V[1], Skripchenko N[2], Klimkin A[3], Krivosheenko E[3], Ivanova M[3]
[1]Functional Diagnostics, Institute for Children's Infections, Saint Petersburg, Russian Federation, [2]Neuroinfections, Institute for Children's Infections, Saint Petersburg, Russian Federation, [3]Institute for Children's Infections, Saint Petersburg, Russian Federation

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 thorougly 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

Brand CM[1], McLellan AE[1], Joseph S[1], Chin RF[1,2]
[1]Neurology, Royal Hospital for SIck Children, Edinburgh, UK,
[2]Child Life and Health, University of Edinburgh, Edinburgh, UK

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.

Consideration should be given to provide year-long vitamin D supplementation in all children on AEDs and to all Scottish children during wintertime.

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EPILEPSIA PARTIALIS CONTINUA IN TICK-BORNE RUSSIAN SPRING-SUMMER ENCEPHALITIS

Mukhin KY[1], Mironov MB[1], Kvaskova NE[1]
[1]Svt. Luka's Institute of Child Neurology and Epilepsy, Moscow, Russian Federation

Purpose: Epilepsia partialis continua (EPC) has numerous possible etiologies. We describe EPC in the tick-borne Russian spring-summer encephalitis (TBRSSE) and compare it with Kozhevnikov-Rasmussen syndrome.

Method: We included 10 patients with EPC in TBRSSE. The diagnosis was verified by immunology (antibodies against TBRSSE 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 TBRSSE, 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 TBRSSE or the tick bite to seizure onset was 3–10 months. We identified 3 phases of clinical course of EPC in TBRSSE: (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 TBRSSE is relatively frequent in the Eastern part of the Russian Federation but not west of the Urals. Unlike Kozhevnikov-Rasmussen encephalitis, EPC with TBRSSE 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.

p229
DOES COEXISTANCE OF CLINICAL RISK FACTORS AND MOLECULAR MARKERS INCREASE A RISK OF DRUG-RESISTANCE IN EPILEPSY?

Emich-Widera E[1], Kazek B[1], Likus W[2], Niemiec P[3], Balcerzyk A[3], Sieroń AL[4], Żak I[3]
[1]Department of Neuropediatrics, Medical University of Silesia, Katowice, Poland, [2]Department of Human Anatomy, Medical University of Silesia, Katowice, Poland, [3]Department of Biochemistry and Medical Genetics, School of Health Care, Medical University of Silesia, Katowice, Poland, [4]Department of General and Molecular Biology and Genetics, Medical University of Silesia, Katowice, Poland

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-pharmalogical 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 CYP 3A5*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 (IR/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 isoforms 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 (IR/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.

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Monday, 30th June 2014

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ASSOCIATION OF ABCB AND SCN1A GENE POLYMORPHISMS TO LAMOTRIDGINE AND CARBAMAZEPINE IN UKRAINIAN PATIENTS WITH EPILEPSY

Oros M[1], Dubenko A[2], Yevtushenko O[3], Reynolds G[4]
[1]Clinic 'Vodolij', Khust, Ukraine, [2]Institute of Neurology, Psychiatry and Narcology of NAMS of Ukraine, Kharkiv, Ukraine, [3]Inctitute of Pharmacology and Toxicology AMS Ukraine, Kiev, Ukraine, [4]Sheffield Hallam University, Biomedical Research Centre, Sheffield, UK

Purpose: In spite of variety AED, treatment remains inffective 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 lamotridgine (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-resistart 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 60% 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.

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ASSOCIATION OF A *GABRG2* POLYMORPHISM WITH EPILEPSY: IN SILICO REPLICATION STUDY

Baum L[1], Kwan P[1], Cherny SS[2]
[1]The Chinese University of Hong Kong, Hong Kong, China, [2]The University of Hong Kong, Hong Kong, China

Purpose: The gamma-aminobutyric acid receptor subunit gamma-2 (*GABRG2*) gene encodes GABRγ2 protein, which is one of five subunits comprising the GABA-A receptor, the most common receptor in the mammalian brain. *GABRG2* has been implicated in susceptibility to epilepsy. Several studies have investigated whether rs211037, a synonymous polymorphism in exon 5 of *GABRG2*, is a risk factor for epilepsy, however results have been inconsistent. Therefore, we sought to examine association of this polymorphism with epilepsy.

Method: Subjects were ethnic Chinese from genome-wide association studies. Epilepsy patients were recruited from neurology clinics of five regional hospitals in Hong Kong. Controls were from three sources: healthy blood donors contributed by the Hong Kong Red Cross, participants recruited for other studies conducted in the University of Hong Kong, and healthy individuals recruited in Taiwan. Written informed consent was given by all patients or by their guardians in the case of a child. Genotypes of rs211037 were analyzed in 488 symptomatic epilepsy and 2,844 control subjects.

Results: The T allele was less common in patients than controls: 57% vs. 62%, odds ratio = 0.82 (95% confidence interval: 0.71–0.94), p = 0.005. The TT genotype was less frequent in patients than controls: 33% vs. 37%, odds ratio (compared to CC) = 0.64 (95% confidence interval: 0.48–0.86), p = 0.002.

Conclusion: The T allele of the *GABRG2* rs211037 polymorphism may be associated with decreased susceptibility to epilepsy.

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TWO SISTERS WITH STRIKINGLY SIMILAR PHOTOSENSITIVITY, BUT DISCORDANT FOR SCN1A-POSITIVE DRAVET SYNDROME

Kasteleijn-Nolst Trenité DGA[1], Verbeek NE[1], Gutter T[2], Sonsma ACM[1], Brilstra EH[1], Wegner I[2], Gunning WB[2], de Weerd AI[2]
[1]Medical Genetics, University of Utrecht, Utrecht, The Netherlands, [2]SEIN – Epilepsy Institutes of the Netherlands Foundation, Zwolle, The Netherlands

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 p.Gly1433Glu SCN1A-mutation. At age 2 parents noticed frequent blinking and myoclonic jerks: EEG registrations under multiple AEDs showed irregular background, epileptiform discharges (ED) over the 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.

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MOLECULAR CHARACTERIZATION OF A FAMILIAL CHROMOSOME 9Q22.2-22.32 DELETION IN A PATIENT WITH CORPUS CALLOSUM AGENESIS AND INTRACTABLE EPILEPSY

Hiz S[1], Agilkaya S[2], Bayram E[1], Cingoz S[2]
[1]Pediatric Neurology, Dokuz Eylül University, Izmir, Turkey, [2]Medical Biology and Genetics, Dokuz Eylül University, Izmir, Turkey

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. EEG 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.

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NEXT GENERATION SEQUENCING STRATEGIES FOR MENDELIAN EPILEPSY DISORDERS: A HYPOTHESIS-BASED GUIDELINE FOR PATIENT SELECTION

Hardies K[1,2], Weckhuysen S[1,2], De Jonghe P[1,2,3], Suls A[1,2]
[1]VIB Department of Molecular Genetics, Neurogenetics Group, Antwerp, Belgium, [2]Institute Born-Bunge, Antwerp, Belgium, [3]University Hospital Antwerp, Antwerp, Belgium

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 using NGS tools in their search for new mutations and causal gene defects. The accessibility of NGS has made the analysis and interpretation of large data sets a daily practice for every geneticist. But before acquiring this data, a crucial step in a cost-efficient NGS project lies in the selection of the "to be sequenced" individuals. The earliest NGS studies showed that an increasing number of family members gives considerably more power to any study (e.g. Roach et al., 2010). If researchers envision to identify all causal gene mutations in all patients, it could be stated that everyone should simply be sequenced. NGS projects remain a costly effort though. Thus it remains an important question to ask from which individual an extra exome or genome will truly enlarge your chances to identify a monogenic gene defect? Depending on the phenotype, inheritance pattern and rational behind the project different strategies can be put forward. By summarizing and discussing different NGS project strategies, which led to the identification of new epilepsy causing mutations, we will give an overview of the latest breakthroughs in Mendelian epilepsy disorders with NGS technologies. Moreover, by troubleshooting different study designs we will put forward a hypothesis-based guideline to determine which individuals should be selected to conduct a cost-efficient NGS project.

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DE NOVO LOSS-OF-FUNCTION MUTATIONS IN CHD2 CAUSE A FEVER-SENSITIVE MYOCLONIC EPILEPTIC ENCEPHALOPATHY SHARING FEATURES WITH DRAVET SYNDROME

Suls A[1], Jaehn JJ[2], Kecskés A[3], Weber Y[4], Weckhuysen S[1], Craiu DC[5], Siekierska A[3], Djémié T[1], Afrikanova T[3], Gormley P[6], von Spiczak S[2], Kluger G[7], Iliescu CM[5], Talvik T[8], Talvik I[8], Meral C[9], Caglayan HS[10], Giraldez BG[11], Serratosa J[11], Lemke JR[12], Hoffman-Zacharska D[13], Szczepanik E[13], Barisic N[14], Komarek V[15], Hjalgrim H[16], Møller RS[16], Linnankivi T[17], Dimova P[18], Striano P[19], Zara F[19], Marini C[20], Guerrini R[20], Depienne C[21], Baulac S[21], Kuhlenbäumer G[22], Crawford AD[3,23], Lehesjoki A-E[24], de Witte PAM[3], Palotie A[6,25,26], Lerche H[4], Esguerra CV[3], De Jonghe P[1,27], Helbig I[22], EuroEPINOMICS RES Consortium
[1]VIB-DMG/University of Antwerp, Antwerp, Belgium, [2]University Medical Center Schleswig-Holstein, Christian-Albrechts Universit, Kiel, Germany, [3]University of Leuven, Leuven, Belgium, [4]Hertie Institute for Clinical Brain Research, University of Tübingen, Tübingen, Germany, [5]"Carol Davila" University of Medicine, Bucharest, Romania, [6]Wellcome Trust Sanger Institute, Hinxton, UK, [7]Epilepsiezentrum für Kinder und Jugendliche, Tagesklinik für Neuropädiatrie, Schön Klinik Vogtareuth, Vogtareuth, Germany, [8]University of Tartu/Tartu University Hospital, Tartu, Estonia, [9]GATA Haydarpasa Teaching Hospital, Istanbul, Turkey, [10]Bogazici University, Istanbul, Turkey, [11]Centro de Investigación Biomédica en Red de Enfermedades Raras (CIBERER), Hospital Universitario Fundación Jiménez Diaz, Madrid, Spain, [12]University Children's Hospital Inselspital, Bern, Switzerland, [13]Institute of Mother and Child, Warsaw, Poland, [14]University of Zagreb/University Hospital Centre Zagreb, Zagreb, Croatia, [15]University Hospital Motol, Praha, Czech Republic, [16]Danish Epilepsy Centre, Dianalund, Denmark, [17]Pediatric Neurology, Children's Hospital, University of Helsinki and Helsinki University Central Hospital, Helsinki, Finland, [18]St. Naum University Hospital of Neurology and Psychiatry, Sofia, Bulgaria, [19]Gaslini Institute, University of Genova, Genova, Italy, [20]Children's Hospital A. Meyer, University of Florence, Florence, Italy, [21]Hôpital Pitié-Salpêtrière, Paris, France, [22]Christian-Albrechts-University Kiel, Kiel, Germany, [23]32 Luxembourg Center for Systems Biomedicine, University of Luxembourg, Esch-sur-Alzette, Luxembourg, [24]Molecular Neurology and Neuroscience Center, Folkhälsan Institute of Genetics, University of Helsinki, Helsinki, Finland, [25]Institute for Molecular Medicine Finland (FIMM), University of Helsinki, Helsinki, Finland, [26]The Broad Institute of MIT and Harvard, Cambridge, MA, USA, [27]Antwerp University Hospital, Antwerp, Belgium

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.

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ADENOSINERGIC SYSTEM IN MESIAL TEMPORAL LOBE EPILEPSY

Leal B[1], Zenatti L[1], Rangel R[2], Chaves J[2], Carvalho C[1], Bettencourt A[1], Santos A[3], Magalhães T[3], Correia-de-Sá P[1], Martins da Silva A[1,2], Costa PP[1,4], Martins da Silva B[1]
[1]UMIB – ICBAS-UP, Porto, Portugal, [2]Centro Hospitalar do Porto, Hospital de Santo António, Porto, Portugal, [3]Instituto de Medicina Legal, Delegação do Porto, Porto, Portugal, [4]Instituto Nacional de Saúde Dr. Ricardo Jorge, Porto, Portugal

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 pathological conditions such as epilepsy. Evidence from experimental studies support a role for ADK overexpression in brain injury associated with astrogliosis, 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 $2^{-\Delta\Delta C}{}_{t}$ method. Differences in ΔCt 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.

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T1174S *SCN1A* MUTATION IS ASSOCIATED WITH SEIZURE AND MIGRAINE – MAY IT ALSO CHANGE THE EPILEPTIC ENCEPHALOPATHIES' COURSE?

Hoffman-Zacharska D[1], Terczynska I[2], Górka P[1], Winczewska-Wiktor A[3], Steinborn B[3], Mazurczak T[2], Goral J[4], Charzewska A[1], Tataj R[1], Szczepanik E[2]
[1]Department of Medical Genetics, Institute of Mother and Child, Warsaw, Poland, [2]Clinic of Neurology of Child and Adolescents, Institute of Mother and Child, Warsaw, Poland, [3]Pediatric Neurology of Developmental Age Clinic, Poznan University of Medical Sciences, Poznan, Poland, [4]Department of Medical Genetics, Institute of Mother and Child Developmenta Neurology and Pediatrics, SPS ZOZ-Zdroje, Szczecin, Poland

Purpose: Mutations, in *SCN1A* are causative for Dravet Syndrome and GEFS+ 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 encephalopaties; 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 (refereed 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 NI/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 $Na_v1.1$, and probably not only causes the epilepsy/migraine but and 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

Tuychibaeva N[1], Prokhorova A[1]
[1]Tashkent Medical Akademy, Tashkent, Uzbekistan

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 T/T was over 4 times reliably higher than in the controls (χ^2 = 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.

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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

Weckhuysen S[1], Suls A[1], Djemie T[1], Sterbova K[2], Hoffman-Zacharska D[3], Talvik T[4], Caglayan H[5], Striano P[6], Marini C[7], Koeleman B[8], Serratosa J[9], Lemke J[10], Depienne C[11], Helbig I[12], De Jonghe P[13], EuroEPINOMICS-RES

[1]VIB-DMG, University of Antwerp, Antwerp, Belgium, [2]University Hospital Motol, Prague, Czech Republic, [3]Institute of Mother and Child, Warsaw, Poland, [4]Tartu University Hospital, Tartu, Estonia, [5]Bogazici University, Istanbul, Turkey, [6]University of Genova/Gaslini Institute, Genova, Italy, [7]Meyer's Children Hospital, Florence, Italy, [8]University Medical Center Utrecht, Utrecht, The Netherlands, [9]Fundacion Jimenez Diaz, Madrid, Spain, [10]University Children's Hospital Inselspital, Bern, Switzerland, [11]INSERM UMRS 975, CNRS UMR 7225, Paris, France, [12]University Medical Center Schleswig-Holstein, Christian-Albrechts Universit, Kiel, Germany, [13]University of Antwerp, Antwerpen, Belgium

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 *SCN8A*, 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

Sarecka-Hujar B[1], Kopyta I[2], Zak I[3], Emich-Widera E[2]

[1]Department of Applied Pharmacy, Medical University of Silesia, Sosnowiec, Poland, [2]Department of Neuropediatrics, School of Medicine in Katowice, Medical University of Silesia, Katowice, Poland, [3]Department of Biochemistry and Medical Genetics, Medical University of Silesia, Katowice, Poland

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 poststroke 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-RFLP 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 *677*T 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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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

Vadapalli RSV[1], Sattaluri SJ[2], Panigrahi M[3]
[1]Vijaya Diagnostics and Research, Radiology and Imaging, Hyderabad, India, [2]Neurology, KIMS, Hyderabad, India, [3]Neurosurgery, KIMS, Hyderabad, India

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 s) 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 1B 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.

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HYPERCONNECTIVITY IN JUVENILE MYOCLONIC EPILEPSY – A NETWORK ANALYSIS

Powell R[1,2,3], Caeyenberghs K[4,5], Jones D[2], Hamandi K[2,3,6]
[1]Department of Neurology, Morriston Hospital, Swansea, UK, [2]Cardiff University Brain Research Imaging Centre (CUBRIC), Cardiff University, Cardiff, UK, [3]Welsh Epilepsy Research Network, Wales, UK, [4]Department of Physical Therapy and Motor Rehabilitation, Faculty of Medicine and Health Sciences, University of Ghent, Ghent, Belgium, [5]Department of Movement and Sports Sciences, University of Ghent, Ghent, Belgium, [6]The Alan Richens Welsh Epilepsy Centre, University Hospital of Wales, Cardiff, UK

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.

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VOLUME INCREASE OF THE AMYGDALA IN ANTIBODY-ASSOCIATED LIMBIC ENCEPHALITIS REVEALED BY VOXEL-BASED MORPHOMETRY

Wagner J[1,2], Elger CE[1,2], Weber B[1,2]
[1]Epileptology, University of Bonn Medical Center, Bonn, Germany, [2]Life & Brain NeuroImaging, University of Bonn Medical Center, Bonn, Germany

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.

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VARIATIONS OF CLINICAL COURSE OF REFRACTORY EPILEPSY CONDITIONED BY BRAIN TRACTS CHARACTERISTICS

Sakovich R[1], Kistsen V[1], Evstigneev V[1]
[1]Belarusian Medical Academy of Post-Graduate Education, Minsk, Belarus

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 parameters was carrying out.

Results: Subjects with epilepsy, as compared to healthy controls, demonstrated four patterns of tracts reduce: in frontal lobe, lateral parts of hemisphere mono- or bilaterally, anterior and/or posterior commissure, complex of several tracts changes. Epilepsy subjects have reduced FA, predominately in the epileptogenic cerebral hemisphere ($p < 0.05$). MD increasing and pattern of tracts reduce in frontal lobe typified for pharmacoresistant course of disease ($p < 0.05$). Pattern of tracts reduce in lateral parts of hemisphere monolateraly 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.

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VULNERABILITY OF THE VENTRAL LANGUAGE NETWORK IN CHILDREN WITH FOCAL EPILEPSY

Croft LJ[1], Baldeweg T[1], Sepeta LS[2], Zimmaro LA[2], Berl MM[2], Gaillard WD[2]
[1]Institute of Child Health, University College London, London, UK, [2]Children's National Medical Center, Washington, DC, USA

Purpose: Children with focal epilepsy are at increased risk of language impairment, yet the neural substrate of this dysfunction is not yet known. Using functional magnetic resonance imaging we aimed to investigate the impact of focal epilepsy on the developing language system using measures of network topology (spatial organisation of activation) and synchrony (functional connectivity).

Method: We studied healthy children ($n = 48$, 4–12 years, 24 females) and children with focal epilepsy ($n = 21$, 5–12 years, 9 females) with left hemisphere language dominance. Participants performed an age-adjusted auditory description decision task during functional magnetic resonance imaging, to identify perisylvian language regions. Mean signal change was extracted from eight left perisylvian regions of interest and compared between groups. Paired region-of-interest functional connectivity analysis was performed on time course data from the same regions, to investigate left network synchrony. Two principal component analyses were performed to extract

1. patterns of activation (using mean signal change data) and
2. patterns of synchronised regions (using functional connectivity data). For both principal component analyses two components (networks) were extracted, which mapped onto the functional anatomy of dorsal and ventral language systems. Associations among network variables, age, epilepsy-related factors and verbal ability were assessed.

Results: Activated networks were affected by age and epilepsy ($F(2.60) = 3.74$, $p = 0.03$): Post-hoc analyses showed, for healthy children, activation in both ventral and dorsal networks decreased with age ($p = 0.02$). Regardless of age, children with epilepsy showed reduced activation of the ventral network ($p < 0.001$) and a trend for increased activation of the dorsal network ($p = 0.08$). Crucially, decreased activation of the ventral network in patients predicted poorer language outcome ($R^2_{adjusted} = 0.47$, $p = 0.002$).

Conclusion: Childhood onset epilepsy preferentially alters maturation of the ventral language system, and this is related to poorer language ability.

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LEVETIRACETAM REDUCES ABNORMAL NETWORK ACTIVATIONS IN TEMPORAL LOBE EPILEPSY

Wandschneider B[1], Stretton J[1,2], Sidhu M[1], Centeno M[1,3], Kozak L[4], Symms M[1], Thompson P[1], Duncan J[1], Koepp M[1]
[1]Department of Clinical and Experimental Epilepsy, UCL Institute of Neurology, London, UK, [2]MRC Cognition and Brain Science Unit, University of Cambridge, Cambridge, UK, [3]UCL Institute of Child Health, London, UK, [4]MR Research Center, Semmelweis University, Budapest, Hungary

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.

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CHILDREN OF WOMEN WITH EPILEPSY HAVE REDUCED GREY MATTER AND TOTAL BRAIN VOLUME BY VOXEL BASED MORPHOMETRY

Thomas SV[1], Sreedharan RM[2], Kesavadas C[3]
[1]Department of Neurology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, India,

[2]Department of Radiodiagnosis, Trivandrum Medical College, Trivandrum, India, [3]Sree Chitra Tirunal Institute for Medical Sciences and Technology, ISIR, Trivandrum, India

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 (1,308 ± 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.

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EPILEPSY RELATED BRAIN NETWORKS IN RING CHROMOSOME 20 SYNDROME. AN EEG-FMRI STUDY

Ruggieri A[1], Vaudano AE[1], Vignoli A[2], Avanzini P[1,3], Benuzzi F[1], Gessaroli G[1], Nichelli PF[1], Darra F[4], Cantalupo G[4], Mastrangelo M[5], Dalla Bernardina B[4], Canevini MP[2], Meletti S[1]
[1]Department of Biomedical Sciences, Metabolism, and Neuroscience, University of Modena and Reggio Emilia, Modena, Italy, [2]Epilepsy Centre, Department of Health Science, University of Milan, San Paolo Hospital, Milan, Italy, [3]Department of Neuroscience, University of Parma, Parma, Italy, [4]Department of Life and Reproduction Sciences, University of Verona, Verona, Italy, [5]Pediatric Neurology Unit, Buzzi Hospital, Milan, Italy

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 3–7 Hz rhythm that characterize this condition.

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

Lascano AM[1], Spinelli L[1], Perneger T[2], Vulliemoz S[1], Brodbeck V[3], Garibotto V[4], Vargas MI[5], Momjian S[6], Schaller K[6], Michel CM[7], Seeck M[1]
[1]Neurology, University Hospitals of Geneva, Geneva, Switzerland, [2]Division of Clinical Epidemiology, University Hospitals of Geneva, Geneva, Switzerland, [3]Brain Imaging Center, Department of Neurology, University of Frankfurt, Frankfurt a.M, Germany, [4]Department of Nuclear Medicine, University Hospitals of Geneva, Geneva, Switzerland, [5]Neuroradiology, University Hospitals of Geneva, Geneva, Switzerland, [6]Neurosurgery, University Hospitals of Geneva, Geneva, Switzerland, [7]Functional Brain Mapping Laboratory, Department of Neurology, University Hospitals of Geneva and University Medical Center, Geneva, Switzerland

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 postoperative outcome. The chances to be seizure-free are >90% if MRI and ESI-HR agree.

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VISUALIZING MEYER'S LOOP BEFORE TEMPORAL LOBE RESECTION USING DETERMINISTIC AND PROBABILISTIC TRACTOGRAPHY

Lilja Y[1], Ljungberg M[2], Starck G[2], Malmgren K[1], Rydenhag B[1], Nilsson D[1]
[1]Institute of Neurosciences and Physiology, Sahlgrenska Academy at Gothenburg University, Gothenburg, Sweden, [2]Institute of Clinical Sciences, Gothenburg, Sweden

Purpose: Postoperative visual field defects are common after temporal lobe resection due to injury to the most anterior part of the optic radiation, Meyer's loop. 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 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.

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TUMOUR LOCALISATION AND SECONDARY GENERALISATION: MRI LESION MAPPING IN OLIGODENDROGLIOMA PATIENTS

Wieshmann UC[1], Milinis K[2], Keller S[3]
[1]Neurology, The Walton Centre for Neurology and Neurosurgery, Liverpool, UK, [2]The Walton Centre for Neurology and Neurosurgery, Liverpool, UK, [3]University of Liverpool, Liverpool, UK

Purpose: Some patients with oligodendrogliomas have generalised tonic clonic seizures (GTCS) while 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

Menzel A[1], Le Van P[2], Ramantani G[3], Schulze-Bonhage A[3], Hennig J[2], Jacobs J[1]
[1]Department of Neuropediatrics, University of Freiburg, Freiburg, Germany, [2]Medical Physics, University of Freiburg, Freiburg, Germany, [3]Epilepsy Center, University of Freiburg, Freiburg, Germany

Purpose: EEG-fMRI 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-MREG. 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-fMRI in epilepsy, and facilitates time-series analysis to improve the interpretation of results.

Abstracts

p253
DIFFUSION TENSOR IMAGING ABNORMALITIES OF THE CORPUS CALLOSUM IN MALFORMATIONS OF CORTICAL DEVELOPMENT

Andrade CS[1], Leite CC[1], Otaduy MCG[1], Lyra KP[1], Valente KDR[2], Yasuda CL[3], Beltramini GC[3], Beaulieu C[4], Gross DW[5]
[1]Radiology, University of Sao Paulo, Sao Paulo, Brazil, [2]Psychiatry, University of Sao Paulo, Sao Paulo, Brazil, [3]Radiology, University of Campinas, Campinas, Brazil, [4]Biomedical Engineering, University of Alberta, Edmonton, AB, Canada, [5]Medicine, University of Alberta, Edmonton, AB, Canada

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.

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ANATOMICAL NETWORKS AMONG EPILEPTIC AND NON-EPILEPTIC DÈJÀ-VÙ: A VBM STUDY

Labate A[1], Cerasa A[2], Mumoli L[1], Ferlazzo E[1], Aguglia U[1], Gambardella A[1], Quattrone A[1]
[1]University of Catanzaro, Catanzaro, Italy, [2]Imaging Research Unit, Institute of Neurological Sciences, National Research Council, Catanzaro, Italy

Purpose: Dèjà-vù (DV) can occur as a seizure of mesial temporal lobe epilepsy (MTLE) and in almost 80% of healthy individuals. The remarkable similarity between epileptic DV and DV in healthy individuals raises the possibility that DV might sometimes be an ictal phenomenon in apparently normal individuals. Thus, we thought to study a group of healthy subjects vs. patients with benign MTLE (bMTLE) both suffering of DV.

Methods: 63 epileptic patients with bMTLE and 39 healthy controls at Catanzaro University were recruited. Participants completed the Inventory for Déjà Vu Experiences Assessment (IDEA) test, underwent asleep electroencephalogram, MRI of the brain using a 3T scanner and whole brain voxel-based morphometry (VBM). bMTLE patients with DV and nonDV were also matched for the presence of hippocampal sclerosis.

Results: Our controls had no history of neurological or psychiatric illness, epilepsy or had history of febrile convulsions. Neurological and cognitive examinations were normal. Electroencephalographic procedures were unremarkable in all subjects. In bMTLE group, the direct comparison between DV patients vs. nonDV revealed abnormal anatomical changes in the left hippocampus, parahippocampal gyrus and visual cortex. Healthy controls with DV showed abnormal anatomical changes in the left insular cortex.

Conclusions: Our VBM results clearly demonstrate a structural correlate of epileptic DV involving the memory circuit while DV in healthy subjects is associated with brain abnormalities in the cerebral regions taking part of the limbic system.

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SPATIAL RESOLUTION EVALUATION OF DOUBLE-DENSITY FUNCTIONAL NEAR-INFRARED SPECTROSCOPY FOR THE DIAGNOSIS OF FUNCTIONAL CORTEX

Yokota H, Oguro K, Mizutani T, Dhuha A, Watanabe E
Neurosurgery, Jichi Medical University, Shimotsuke, Japan

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 signal averaging method with five trials of tapping and pricking tasks. On the other hands, five patients with brain tumor seated on close to central sulcus had the examination with the same tasks pre- and/or post- operatively. 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

Linden-Mickelsson P[1], Rosen I[1], Källen K[2]
[1]Neurophysiology, Skane University Hospital, Lund, Sweden, [2]Neurology, Skane University Hospital, Lund, Sweden

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 (CURRY/s-Loreta).

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 coregistred 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 patients (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

Oguro K[1], Yokota H[1], Mizutani T[1], Edison RE[1], Hirai M[2], Dan I[3], Watanabe E[1]
[1]Neurosurgery, Jichi Medical University, Tochigi-ken, Japan, [2]Functional Brain Science Lab, Center for Development of Advanced Medical Technology Jichi Medical University, Tochigi-ken, Japan, [3]Research and Development Initiatives, Applied Cognitive Neuroscience Lab, Chuo University, Tokyo, Japan

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 caliculated 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 OxHb and 9/12 in DeoxyHb showed increase on the correct epileptogenic side. There was a strong positive correlation between increase in OxHb and DeoxyHb. Duration of EEG and fNIRS changes showed negative correlation with extent of OxHb increase.

Conclusion: fNIRS is 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)

Gonzalvez GG[1], Haag A[2], He C[2], Koepp M[2], Thompson P[2], Duncan JS[2]
[1]Epilepsy Department, UCL Institute of Neurology, London, UK, [2]UCL Institute of Neurology, London, UK

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.

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EMOTION PROCESSING IN PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY AND AMYGDALA LESIONS

Kuchukhidze G[1,2], Zamarian L[1], Schmid E[2], Koppelstaetter F[3], Siedentopf C[3], Delazer M[1], Gizewski E[4], Luef G[1], Unterberger I[1], Trinka E[1,2]
[1]Neurology, Innsbruck Medical University, Innsbruck, Austria, [2]Neurology, Christian Doppler Klinik, Paracelsus Medical University Salzburg, Salzburg, Austria, [3]Radiology, Innsbruck Medical University, Innsbruck, Austria, [4]Neuroradiology, Innsbruck Medical University, Innsbruck, Austria

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 post-surgical deficits in patients with drug resistant mTLE.

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DISTINGUISHING EPISODIC MEMORY PROCESSES FAMILIARITY AND RECOLLECTION BY USING EXTAOPERATIVE TEMPOROPARIETAL STIMULATION

Hendriks M[1,2], Daselaar S[2], Van Kranen-MastenbroekV[3], Colon A[1], Schijns O[3]
[1]Epilepsy Centre Kempenhaeghe, Heeze, Netherlands,, [2]Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, Nijmegen, Netherlands, [3]Maastricht University Medical Center, Maastricht, Netherlands

Purpose: The MTL and lateral temporparietal 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 lesionedhippocampus were impaired in the recollection-like processes

Method: We recently used this approach in a pilot-study with 31 years old epilepsysurgery 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 pilotstudy we found an indication that direct stimulating familiarity regions reduces familiarity, not recollection. Further research with this procedure to test a suggested double dissocation whether stimulating recollection regions reduces recollection, not familiarity.

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INTERICTAL EPILEPTIFORMIC DISCHARGES (IED) AND MEMORY FUNCTION IN TEMPORAL LOBE EPILEPSY

Kostylev A, Pizova N, Novozhilova S
Yaroslavl State Medical Academy, Yaroslavl, Russian Federation

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» test 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 epileptiformic discharges with temporal lobe epilepsy registered in the routine EEG record are more associated with impaired memory than with attention.

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SEMANTIC MEMORY IMPAIRMENT IN TEMPORAL LOBE EPILEPSY OF ANTERIOR-NEOCORTICAL OR HIPPOCAMPAL ORIGIN

Campo P[1], Poch C[2], Toledano R[3], García-Morales I[3,4], Igoa JM[1], Belinchón M[1], Gil-Nagel A[3]
[1]Basic Psychology, Universidad Autonoma de Madrid, Madrid, Spain, [2]Department of Biological and Health Psychology, Universidad Autónoma de Madrid, Madrid, Spain, [3]Neurology,

Hospital Ruber International, Madrid, Spain, [4]Neurology, Hospital Universitario Clinico San Carlos, Madrid, Spain

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. encephalocele) 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 -anterior 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 during 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 align 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

Hermsen A[1], Chen Y-M[1], Böhringer M[1], Leonhard S[2], Belke M[1], Knake S[1], Rosenow F[1]

[1]Departement of Neurology, Epilepsy Centre, Philipps-University Marburg, Marburg, Germany, [2]Neurology, Bad Wildungen, Germany

Purpose: Mesial temporal lobe (mTL) structures play a key role in explicit memory (ExM). Patients with mTLE have impaired ExM function. There is conflicting data on role of the mTL 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 ± 0.9; $p = 0.008$). Performance on first vs. last sequence-bloc 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 hemispheric difference in ImM.

Conclusion: All patient groups showed a learning effect, however all patients performed worse than healthy controls. Patients with eTLE 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

Rösche J[1], Rühle N[1], Schley A[1], Pohley I[1,2], Kampf C[1], Benecke R[1]

[1]Klinik für Neurologie und Poliklinik, Universitätsmedizin Rostock, Rostock, Germany, [2]Klinik für Psychiatrie, Psychotherapie und Psychosomatik, Sana Hanse-Klinikum Wismar, Wismar, Germany

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

Donath V[1], Kocurova M[2]

[1]F.D. Roosevelt University Hospital, Banska Bystrica, Slovakia, [2]Neurology, F.D. Roosevelt University Hospital, Banska Bystrica, Slovakia

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 (Preiss, 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

Hermans E[1], Hendriks M[1,2], Ossenblok P[2], Hofman P[2,3], Colon A[2], Frankenmolen NL[1]

[1]Cognition and Behaviour, Donders Institute for Brain, Radboud University Nijmegen, Nijmegen, Netherlands, [2]Epilepsy Centre Kempenhaeghe, Heeze, Netherlands, [3]Maastricht University Medical Center, Maastricht, Netherlands

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 (LI), 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 and right TLE patients (LI: $M = 0.36$, SD = 0.26) showed more left over right hippocampal activation ($t(8) = 2.15$, $p < 0.05$, 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 ($t(4) = 2.72$, $p < 0.05$, 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

Demichelis G, Pal DK, McGinnity C, Smith AB

Department of Clinical Neuroscience, Institute of Psychiatry, King's College London, London, UK

Purpose: Children with Rolandic 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

Di Folco S[1], Guerriero V[1], Mittica A[2], Panunzi S[2], Brinciotti M[2], Matricardi M[2]

[1]Department of Dynamic and Clinical Psychology, Sapienza, University of Rome, Rome, Italy, [2]Department of Pediatric and Child Neuropsychiatry, Sapienza, University of Rome, Rome, Italy

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 patients, 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 seizure 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

van Iterson L[1,2], Davelaar S[3], Augustijn PB[4]
[1]Neuropsychology, SEIN-Epilepsy Institute in the Netherlands Foundation, Heemstede, Netherlands, [2]De Waterlelie, Neuropsychology, Cruquius, Netherlands, [3]Psychology, SEIN-Epilepsy Institute in the Netherlands Foundation, Heemstede, Netherlands, [4]Neurology, SEIN-Epilepsy Institute in the Netherlands Foundation, Heemstede, Netherlands

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*s > 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 youngster once, was retold immediately (IR), after 20–30 min (DR20), and when the youngster returned at Day 2 (Day2; *N*s = 8 + 8) *or* Day 7 (Day7; *N*s = 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, η_p^2 = 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

Bouman Z[1,2], Hendriks MPH[1,2], Kessels RPC[2,3], Aldenkamp AP[1,4]
[1]Kempenhaeghe, Academic Center of Epileptology, Heeze, Netherlands, [2]Cognition and Behaviour, Donders Institute for Brain, Radboud University Nijmegen, Nijmegen, Netherlands, [3]Nijmegen Medical Centre, Radboud University, Nijmegen, Netherlands, [4]Maastricht University Medical Center, Maastricht, Netherlands

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

Gómez Caravaca MT, Martínez Agredano PM, Suárez González A
Department of Neurology, University Hospital Virgen del Rocio, Seville, Spain

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 differences in 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.

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A META-ANALYSIS OF LITERACY AND LANGUAGE IN CHILDREN WITH ROLANDIC EPILEPSY

Smith A, Bajomo O, Pal D
Clinical Neuroscience, Institute of Psychiatry, King's College London, London, UK

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: 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

Said MA[1], McGinnity CJ[2], Pal DK[1], Smith AB[2]
[1]Clinical Neuroscience Department, King's College London, Denmark Hill, UK, [2]Clinical Neuroscience Department, King's College London, London, UK

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 subtests 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.

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THE EFFECTS OF MEMORY, EXTRA-MEMORIAL FUNCTIONS AND NEURO-IMAGING, ON THE PROGNOSIS OF TEMPORAL LOBE EPILEPSY PATIENTS

Bora İ[1], Bican Demir A[1], Cantürk V[2], Bekar A[3], Hakyemez B[4], Tamgaç F[2], Türkeş N[5]
[1]Neurology, Uludag University, Bursa, Turkey, [2]Uludag University, Bursa, Turkey, [3]Neurosurgery, Uludag University, Bursa, Turkey, [4]Radiology, Uludag University, Bursa, Turkey, [5]Neuropshylogy, Uludag University, Bursa, Turkey

Purpose: Epilepsy is a common disease effecting 0.5–1% of all community. 30–35% of epileptic patients stil have seizures even if they are on new antiepileptic drugs. The success rate of epilepsy surgery shows variability between 33 and 90% in drug resistant TLE patients. We aimed to evaluate memory and extra-memorial functions in operated and nonoperated TLE patients (for operated group presurgical and postsurgical). The relation between neuropsychological test results and age, sex, disease duration, frequency of seizures, focus of seizures, medication, neuroimaging methods and prognosis was investigated.

Method: In this study we investigated files of 90 patients retrospectively and s prospectively who were diagnosed as TLE in Uludag University Department of Neurology, Neurology Clinic between 2002 and 2011. All patients were hospitalized in video-EEG unit of Neurology Department. All cases seizure follow-up, Video-EEG, cranial magnetic resonance imaging (MRI) and Pozitron Emission tomography (PET), neuropsychometric testing (NPT) were performed to all patients. 37 of these patients were performed amygdala hippocampectomy + anterior temporal lobec-

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 beter cognitive functions.

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TREND OF SELECTIVE REMINDING PERFORMANCES BEFORE AND AFTER TEMPORAL LOBE EPILEPSY SURGERY

Parente A, Tarallo A, Villani F, Didato G, Deleo F, D'Incerti L, Tringali G, Giovagnoli AR
IRCCS Neurological Institute Carlo Besta, Milan, Italy

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

Olusanya AW[1], Danesi M[2], Ojinni F[2], Okubadejo N[2], Ojo D[2], Mallum C[3]
[1]Neurology, Internal Medicine, Babcock University Teaching Hospital, Ilisan-Remo, Nigeria, [2]Neurology, Internal Medicine, Lagos University Teaching Hospital, Idi-Araba, Nigeria, [3]Neurology, Internal Medicine, Jos University Teaching Hospital, Jos, Nigeria

Purpose: To identify inter-ictal morbidities in adult epileptic patients attending the Lagos Universtity 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 are 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.

Based on aetiology 65 (63.1%) had seizures of unknown aetiology, 29 (28.2%) had of symptomatic while 9(8.7%) was possibly genetic due to the positive family history of epilepsy. Of the structural/metabolic aetiology 8 (7.76%) had inter-ictal morbidities while 24 (23.3%) of patients with unknown aetiology had.

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.

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PROFILING OF METHYLOME AND TRANSCRIPTOME IN EXPERIMENTAL TBI IN RATS

Huusko N[1], Lipponen A[1], Dębski K[2], Kaspi A[3], Harikrishnan KN[3], Khurana I[3], Ziemann M[3], El-Osta A[3], Lukasiuk K[2], Pitkänen A[1,4]
[1]A.I. Virtanen Institute for Molecular Sciences, University of Eastern Finland, Kuopio, Finland, [2]The Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland, [3]Epigenetics in Human Health and Disease, Baker IDI Heart and Diabetes Institute, The Alfred Medical Research and Education Precinct, Melbourne, VIC, Australia, [4]Department of Neurology, Kuopio University Hospital, Kuopio, Finland

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 methylome 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.

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STIGMA, TREATMENT AND OTHER PERCEPTIONS TOWARDS EPILEPSY IN NORTHWEST INDIA: A MEDICAL-ANTHROPOLOGICAL STUDY

Pal SK[1,2], Prabhakar S[1], Sharma K[3], Pathak A[4]
[1]Neurology, Postgraduate Institute of Medical Education & Research, Chandigarh, India, [2]RFSL, Northern Range, Home, Dharamshala, India, [3]Anthropology, Panjab University, Chandigarh, India, [4]Neurosurgery, Fortis Hospital, Mohali, India

Purpose: To study the therapies, existence of diverse myths, beliefs, and perceptions regarding epilepsy prevalent in northwest India from anthropological perspective.

Method: 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 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 SEIZURES SCORE BY REPARATIVE PRETREATMENT BY TRANSCRANIAL MAGNETIC STIMULATION ON RAT MODEL

Khodaie B[1,2,3], Saba V[1], Lotfinia AA[1,2]
[1]Medical, AJA University of Medical Science, Tehran, Iran, [2]Neuroscience, Shefa Neuroscience Research Center, Tehran, Iran, [3]Pathology, Faculty of Veterinary Medicine, Azad Islamic University, Karaj, Iran

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 hyperexcitablity in epilepsy models.

Method: 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) intrapersonal 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

Medici D, Foschi N
Department of Neurologic Sciences, Polytechnic University of Marche, Torrette di Ancona, Italy

Purpose: Lacosamide is indicated for the treatment of epilepsy focal-onset seizures in patients aged >16 years.

Objective: To evaluate the efficacy and safety of lacosamide monotherapy for treatment failure and/or side effects of drugs previously used.

Method: 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.

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CARBAMAZEPINE INHIBITORY EFFECTS IN EPILEPSY ASSOCIATED DISORDER IN RAT

Khodaie B[1], Lotfinia AA[1], Ahmadi M[1], Lotfinia M[1,2]
[1]Shefa Neuroscience Research Center, Tehran, Iran, [2]Shahid Beheshti University of Medical Sciences, Tehran, Iran

Purpose: Carbamazepine is a well-known drug in treatment of epilepsy. Previously scientists have found near correlation of some neural dysfunction with epilepsy. Cortical spreading depression (CSD) is nominated for pathogenesis of epilepsy. CSD refers to a wave of mass cellular depolarization associated with net influx of captions and water. CSD is characterized by near-complete breakdown of ion gradients. This followed by a massive depression of the neuronal bioelectrical activity, which play role in some neurodegenerative disorders such as Migraine and epilepsy. Theories defined elevated potassium and/or glutamate in the extracellular space as major corresponded for CSD initiation. However, mean changes responsible for the generation and propagation of spreading depression (SD) remain unknown. But, activated persistent Na+ current and NMDA-controlled current could trigger SD-like depolarization. Therefore it have been suggested that inhibition of action potential could ameliorate depolarization initiation or propagation and consequently related disorders.

Method: In the 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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CELLULAR PROTECTION OF TRANSCRANIAL MAGNETIC STIMULATION IN SEIZURES INDUCED RAT

Khodaie B[1], Saba V[2], Lotfinia AA[1], Karimzadeh F[1]
[1]Shefa Neuroscience Research Center, Tehran, Iran, [2]AJA University of Medical Science, Tehran, Iran

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. Recently, numerous electrical stimulation practices have been established for animal models of epilepsy. TMS was endorsed by many clinical observations as a non-invasive method for investigation of the excitability functions in the brain. TMS have revealed, diagnostic, research, and even therapeutic applications. Repetitive TMS application showed suppressing cortical hyperexcitablity in epilepsy models.

Method: In present study 24 male Wistar rat (150–200 g) were used to investigate repetitive TMS role in epilepsy score. TMS was performed and animals' epilepsy was induced by Pentylenetetrazole (PTZ) intrapersonal injection.

Results: Present data revealed by histological analysis demonstrated that seizures were significantly disrupted by TMS application. Furthermore, cellular damages significantly decreased by TMS application.

Conclusion: We conclude that electrical distribution during PTZ injection could interfere with epilepsy induced cell damages.

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MODIFIED ATKINS DIET MAY REDUCE SERUM CONCENTRATIONS OF ANTIEPILEPTIC DRUGS IN ADULTS WITH REFRACTORY EPILEPSY – REPORT OF FOUR CASES

Kverneland M[1], Taubøll E[2,3], Selmer KK[3,4], Iversen PO[3,5], Nakken KO[1]
[1]Department of Refractory Epilepsy, Oslo University Hospital, Sandvika, Norway, [2]Department of Neurology, Oslo University Hospital, Oslo, Norway, [3]Faculty of Medicine, University of Oslo, Oslo, Norway, [4]Department of Medical Genetics, University of Oslo, Oslo, Norway, [5]Department of Nutrition, University of Oslo, Oslo, Norway

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 and 12 weeks on the modified 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 pre-diet 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

Sitges M[1], Garza-Morales S[2]
[1]Instituto de Investigaciones Biomédicas, Universidad Nacional Autónoma de México, Biología Celular y Fisiología, Distrito Federal, Mexico, [2]Hospital Infantil de México Federico Gómez, Secretaría de Salud, Mexico City, Mexico

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?

Stubbings V, Nielsen H, Jepsen BS
Paediatric Department, The Danish Epilepsy Center, Dianalund, Denmark

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 spasm 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.

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DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL OF THE ANTICONVULSANT EFFECTS OF N-3 PUFAS IN PATIENTS WITH EPILEPSY

Burnham MW[1,2], Hwang PA[3,4], EpLink-OBI
[1]Pharmacology, University of Toronto Epilepsy Research Program, Toronto, ON, Canada, [2]Ontario Brain Institute, EpLink-OBI, Toronto, ON, Canada, [3]Paediatrics, Medicine & Institute of Medical Science, Paediatrics, Medicine & Institute of Medical Science, University of Toronto Epilepsy Research Program, Toronto, ON, Canada, [4]Paediatrics & Medicine, North York General Hospital, Toronto, ON, Canada

Purpose: A prospective randomised controlled clinical trial of n-3 fish-oils (DHA and EPA) as add-on therapy for persons with epilepsy refractory to standard AEDs.

Method: Patients with medically refractory epilepsy, partial and generalised, having 3 or more seizures monthly, on 2 or more AEDs, were recruited into a randomised double-blind placebo-controlled study with signed consent, approved by the research ethics board. After a baseline period keeping a seizure calendar (modified NIH), they were randomised into treated and controlled groups, taking either 3 g DHA + 5 g EPA, or similar placebo-containing capsules, together with stable AED drug levels, hemogram and biochemistry. Regular visits verified the seizures, pill counts, adverse effects and blood tests.

After 3 months of the blinded phase, subjects not improved were offered the alternative treatment with active DHA + EPA, in an open-label maintenance phase.

Results: The initial 12 months of recruitment identified 12 subjects who qualified for the study and 10 who failed to qualify due to low seizure frequency or premature entry.

Almost all subjects tolerated the n-3 PUFAs well without adverse effects or drug interactions with AEDs. Two subjects had complete cessation of seizures, four had only auras and the rest had >50% reduction in seizure frequency. No severe ADRs were noted nor EEG findings of note. A larger RCT is planned.

Conclusion: This ongoing prospective RCT of n-3 PUFAs for epilepsy refractory to AEDs showed good tolerability and absence of severe adverse effects in subjects with refractory epilepsy and good quality of life.

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DETERMINATION OF THE CONCENTRATION OF THE INHIBITORY NEUROTRANSMITTER – GAMMA-AMINOBUTYRIC ACID (GABA) IN CHILDREN WITH CONGENITAL ANOMALIES OF THE CENTRAL NERVOUS SYSTEM

Shevchenko AA
Pediatric Psychoneurology, Institute of Pediarics, Obstetrics and Gynecology of the National Academy of Medical Sciences of Ukraine, Kiev, Ukraine

Relationship between inhibitory neurotransmitter – gamma-aminobutyric acid (GABA) and excitatory neurotransmitters – glutamate and aspartate has a leading role for epileptogenesis with the presence of sustained pathological focus of bioelectrical activity in certain brain structures.

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

Bunoza B[1], Barišić N[2], Grđan P[2], Lehman I[2], Benjak V[2], Kostović I[2], Radoš M[2]
[1]Department of Pediatrics, Clinical Medical Center Zagreb, Zagreb, Croatia, [2]Clinical Medical Center Zagreb, Zagreb, Croatia

Purpose: White matter lesions associated with periventricular leucomalacia and intraventricular haemorrhage are serious neurological complications of praematurity. 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

Günay P, Akşahin E, Kekilli A, Karabiber C, Yananlı HR, Demirkapu M, Topkara B
Marmara University, Istanbul, Turkey

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 Wistar 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 initated 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 NALand 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

Kravtsova SV, Stepanova TS, Kasumov VR, Kasumov RD, Bersnev VP, Ulitin AY
Russian A.L. Polenov Neurosurgical Institute, St. Petersburg, Russian Federation

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-elecrtosubcorticography-stereoelectroencephalography 79% of our patients were found to have combined damage of the temporal lobe neocortex and limbic structures (hippocampus, amygdale). 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 he disease: monotemporal, bitemporal and "intermediate" (monotemporal with initial formation of the mirror focus). The morphofunctional basis of the extratemporal links of epileptogenesis was made by the integral adative 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

Neef M[1], Donkels C[1], Häussler U[1], Bechstein M[2], Kirsch M[3], Haas CA[4]

[1]Department of Neurosurgery, Experimental Epilepsy Research, Freiburg, Germany, [2]Department of Neurosurgery, University Medical Center Freiburg, Freiburg, Germany, [3]Neuroanatomy, Institute of Anatomy and Cell Biology, University of Freiburg, Freiburg, Germany, [4]Department of Neurosurgery/BrainLinks-BrainTools, Cluster of Excellence, Experimental Epilepsy Research, University of Freiburg, Freiburg, Germany

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 epilepsy-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 rapid and sustained activation of astrocytes reflected by up-regulation of 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 glutamate 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

de Weerd AL

SEIN Zwolle, Zwolle, Netherlands

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

Noergaard K, Andersen Becser N

Department of Neurology, Glostrup Hospital, University Hospital of Copenhagen, Epilepsy Clinic, Glostrup, Denmark

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 retrospectively 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)

Hopia L[1], Andersson ML[1], Svenungsson E[2], Piehl F[1], Tomson T[1]
[1]Department of Clinical Neuroscience, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden,
[2]Department of Medicine, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden

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

Bruno E[1], Quattrocchi G[1], Crespo Gómes EB[2], Sofia V[1], Padilla S[2], Camargo M[3], Zappia M[1], Bartoloni A[4], Nicoletti A[1]
[1]University of Catania, Catania, Italy, [2]Servicio Departmental de Salud, Santa Cruz, Bolivia, [3]Bolivian League against Epilepsia, Santa Cruz, Bolivia, [4]University of Florence, Florence, Italy

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 PACIENTS WIH GLIOMA

Vivanco Hidalgo RM[1,2], Gomez A[3], Martinez M[4], Villalba G[5]
[1]Hospital del Mar, Barcelona, Spain, [2]Institut Mar d'Investigacions Mèdiques (IMIM), Grup Neuvas, Barcelona, Spain, [3]Neurology, Hospital del Mar, Barcelona, Spain, [4]Oncology, Hospital del Mar, Barcelona, Spain, [5]Neurosurgery, Hospital del Mar, Barcelona, Spain

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.

Method: We reviewed clinical histories of patients with glioma presented at the Committee between January 2006 and December 2012Variables 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 hig-grade glioma patients.

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EPILEPSY BEYOND SEIZURES. A NATIONWIDE REGISTRY STUDY OF COMORBIDITY IN CHILDHOOD EPILEPSY

Aaberg KM[1,2], Surén P[1,2], Søraas CL[2], Bakken IJ[2], Gunnes N[2], Håberg SE[2], Lossius MI[1], Stoltenberg C[2], Chin R[3]
[1]National Center for Epilepsy, Oslo University Hospital, Oslo, Norway, [2]Norwegian Institute of Public Health, Oslo, Norway, [3]Muir Maxwell Epilepsy Centre, University of Edinburgh, Edinburgh, UK

Purpose: 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: We included children 0–16 years registered with an epilepsy diagnosis (G40) from 2009 through 2012, in the Norwegian Patient Register (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 enrolled. The prevalence of epilepsy increased by age stabilizing at 0.8% from age 11 years.

22% had gastrointestinal disorders, including 9% constipation and 9% gastro-esophageal reflux. There were 9% with malnutrition or eating difficulties and 15% with musculoskeletal problems, including 5% with scoliosis. Chronic lower respiratory conditions occurred in 11%, urinary tract disorders in 8%, cardiovascular conditions in 5%, endocrinological conditions in 4%, and brain tumors in 2%. Congenital/neuronal malformations were found in 17%, chromosomal abnormalities in 5% and inborn errors of metabolism in 2%.

Neurological and psychiatric conditions were frequent; 14% had cerebral palsy, 6% headaches, 4% sleep disturbances, 4% hydrocephalus, 23% visual problems, 5% hearing loss and 35% developmental delay, while 12% had ADHD, 8% autism and 14% other psychiatric conditions.

Non-neurological comorbidities were considerably more frequent in children with developmental delay or other neurological conditions plus epilepsy.

Conclusion: Childhood epilepsy has high disease burden. A low threshold for screening for medical non-neurological as well as neurological comorbidities is needed, in addition to optimizing seizure control.

p300
SLEEP DISORDERS AND EPILEPSY: THE ROLE OF SEIZURES AND ANTIEPILEPTIC DRUGS

Öztürk İ, Aslan K, Bozdemir H
Department of Neurology, Faculty of Medicine, Çukurova University, Adana, Turkey

Purpose: Poor sleep quality or quantity may worsen seizure control. On the other hand, seizures and epilepsy may worsen the sleep quality. In addition, antiepileptic drugs have an effect on sleep architecture. Sleep complaints are common in patients with epilepsy. In this study we aim to evaulate the sleep complains, quality or quantity properties of sleep. And role of seizure frequency on sleep of epileptic patients.

Method: Totally, 225 patients with epilepsy (61.8% [n:139] of female and 38.2% [n:86] male, the mean age 33.3 ± 12.3 [17–77]) were being followed in the epilepsy polyclinic of our clinic were included in the study. Sleep properties were evaluated with Pittsburgh sleep quality index (PUKI) and Epworth sleep quality inventories.

Results and conclusion: The frequency of sleep complains of 225 epileptic patients were 50.2%. These complains 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 monotheraphy. 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.

p302
SUICDE IN EPILEPSY: A POPULATION-BASED STUDY

Sveinsson O[1], Hesdorffer D[2], Tomson T[1]
[1]Department of Neurology, Karolinska University Hospital, Stockholm, Sweden, [2]Gertrude H Sergievsky Center and Department of Epidemiology, Columbia University, New York, NY, USA

Purpose: To study the contribution of suicide to the overall mortality of people with epilepsy, and to describe clinical characteristics of people with epilepsy committing suicide.

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 population during 2008 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: Out 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

Varley J, Haaker G, Toms N, Diehl B
UCH, London, UK

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, neuroimaging 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 hyperglycaemia 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

Choezom T, Bonito J, Hirsch L, Detyniecki K
Yale University, New Haven, CT, USA

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 medications, seizure severity, and quality of life at baseline.

Results: Overall, 30 out of 100 (30%) patients reported seizure clustering in the year prior to enrollment and of those, 9 (30%) had prescribed rescue medication whereas 21 (70%) did not. There were no significant difference in the mean total QOLIE-31score ($p = 0.881$) 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

Bankole IA, Erameh CO, Igetei SO
Internal Medicine, Irrua Specialist Teaching Hospital, Irrua, Nigeria

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 neuroimaging 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 neuroimaging 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

Wagner RG[1,2], Ibinda F[3], Newton CR[3,4,5,6], Tollman S[1,2], Lindholm L[1], Bertram MY[7], Studies of the Epidemiology of Epilepsy in the Demographic Surveillance Sites (SEEDS), INDEPTH Network, Accra, Ghana
[1]Epidemiology & Global Health, Umeå University, Umeå, Sweden, [2]MRC/Wits Agincourt Research Unit, University of the

Witwatersrand, Johannesburg, South Africa, [3]KEMRI/Wellcome Trust Research Programme, Centre for Geographic Medicine Research-Coast, Kilifi, Kenya, [4]Department of Psychiatry, Oxford University, Oxford, UK, [5]Neurosciences Unit, Institute for Child Health, University College London, London, UK, [6]Clinical Research Unit, London School of Hygiene and Tropical Medicine, London, UK, [7]World Health Organization, Geneva, Switzerland

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.

p307
THE PREVALENCE AND SUBJECTIVE HANDICAP OF EPILEPSY IN ILIE: A RURAL RIVERINE COMMUNITY IN SOUTHWEST NIGERIA

Mustapha AF[1], Preux PM[2]
[1]Medicine, Lautech Teaching Hospital, Osogbo, Nigeria, [2]Institute of NeuroEpidemiology and Tropical Neurology, UMR INSERM 1094, Limoges, France

Purpose: Epilepsy is one of the commonest neurological disorders worldwide affecting all races and ages. The prevalence of epilepsy is high in tropical countries, particularly in Africa with an estimated mean prevalence of 15 per 1000. There is lack of recent data on epilepsy prevalence in Nigeria.

The main objective of the study was to determine the prevalence of epilepsy in Ilie South West (SW) Nigeria.

Secondary objectives were to determine the clinical characteristics and the seizure types with electroencephalography (EEG) recording,the pattern of treatment of epilepsy and to evaluate the subjective handicap of people living with epilepsy (PWE) in Ilie.

Materials and methods: The study which was descriptive cross-sectional, was carried out in Ilie, a rural community in South west Nigeria using a simple random sampling technique. The survey was done in 2 phases from January 2013 to April 2013.

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 houeseholds 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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THE EFFECT OF SPINAL CORD STIMULATION ON CHEMICALLY-INDUCED SPIKE-AND-WAVE SEIZURES IN RATS

Jiao J, Jensen W, Harreby KR, Sevcencu C
Health Science and Technology, Aalborg University, Aalborg, Denmark

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 pentylenetetrazole 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 it's pro-convulsive effect.

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UNILATERAL VS. BILATERAL HIPPOCAMPAL DBS IN A RAT MODEL FOR TEMPORAL LOBE EPILEPSY

Van Nieuwenhuyse B[1], Raedt R[1], Delbeke J[1], Wadman W[2], Boon P[1], Vonck K[1]
[1]Laboratory for Clinical and Experimental Neurophysiology, Neurobiology and Neuropsychology, Ghent University, Ghent,

Belgium, [2]Swammerdam Institute of Life Sciences, University of Amsterdam, Amsterdam, Netherlands

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

Andersen Becser N, Schmidt DM, Petrenaite V
Department of Neurology, Epilepsy Clinic, Glostrup Hospital, University Hospital of Copenhagen, Glostrup, Denmark

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 8/13 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 benne 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 presurgical 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.

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LONG LASTING MEMORIES SCRUTINIZED FROM ELECTRICAL BRAIN STIMULATION: A REVIEW AND ANALYSIS OF 80 YEARS OF LITERATURE IN EPILEPTIC PATIENTS

Curot J[1,2], Busigny T[2], Valton L[1,2], Bartolomei F[3,4,5], Chauvel P[3,4,5], Vignal J-P[6], Maillard L[6], Denuelle M[1], Barbeau E[2,7]
[1]CHU Rangueil, Service de Neurologie et d'Explorations Fonctionnelles Neurologiques, Toulouse, France, [2]Centre de Recherche Cerveau et Cognition and CNRS UMR 5549, CerCo, Toulouse, France, [3]CHU Timone, Service de Neurophysiologie Clinique, Marseille, France, [4]Faculté de Médecine, Université de la Méditerranée, Marseille, France, [5]INSERM, U 751, Laboratoire de Neurophysiologie et Neuropsychologie, Marseille, France, [6]Hopital Central, CHU de Nancy, Service de Neurologie, Nancy, France, [7]Université de Toulouse, UPS, Toulouse, France

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

Mannino S, Colicchio G, Di Bonaventura R, Fuggetta F, Mattogno P, Peraio S, Schiano di Cola M, Cioni B
Catholic University, Roma, Italy

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.

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THE EFFECT OF TUBEROMAMMILLARY NUCLEUS HIGH-FREQUENCY ELECTRICAL STIMULATION ON EPILEPTIC ACTIVITY AND SLEEP-WAKE CYCLE OF WAG/RIJ RATS

Blik VA[1,2]

[1]Institute of Higher Nervous Activity and Neurophysiology of RAS, Moscow, Russian Federation, [2]Faculty of Biology, Lomonosov Moscow State University, Moscow, Russian Federation

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.

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DEEP BRAIN STIMULATION AS A TREATMENT OF FOCAL ONSET INTRACTABLE EPILEPSY: A CASE SERIES

Gupta P, Gupta A, Gupta D, Jain R, Trivedi A

Neurology, Artemis Hospitals, Gurgaon, India

Purpose: To test the efficacy of deep brain stimulation in focal onset intractable epilepsy in clinical setting.

Method: We performed bilateral anterior thalamic Deep brain stimulation surgery in 5 patients with intractable focal onset epilepsy who were not candidates for resective surgery.

Results: The median age was 27 years with epilepsy duration of 17 years with seizure frequency ranging from 7/month to 60/month. All of the n five patients had intractable complex partial epilepsy without clear EEG localization or localized lesions on MRI and had been evaluated and refused resective surgery earlier. All patients have more than 6 months of follow up. Of the five patients two patients became seizure free in over 6 months of follow up one patient has occassional seizures and two had 60% seizure reduction. All patients achieved more than 50% seizure reduction with mean 90 seizure reduction and 40% became seizure free.

Conclusion: Deep Brain stimulation is an effective treatment for intractable partial onset epilepsy and represents a significant advance for patients who are not candidates for resective surgery.

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CLINICAL EXPERIENCES WITH TACHYCARDIA-TRIGGERED VAGUS NERVE STIMULATION (VNS)

Hirsch MJ, Schulze-Bonhage A

Center for Epilepsy, University Clinic of Freiburg, Freiburg, Germany

Purpose: To evaluate performance and tolerability of Automated Magnet Mode (AMM) stimulation with a VNS pulse generator that triggers stimulation on detection of ictal tachycardia detection.

Method: We report our experience with three patients implanted with the Model 106 pulse generator (Cyberonics) in the E36-study. The device includes six seizure detection (SD) settings with thresholds of 20–70% heart rate increase above baseline.

This study used video-EEG monitoring (vEEG) to assess performance. During the stay, patients were randomized to one of three SD thresholds: 20%, 40% or 60% with AMM only. We report sensitivity, detection latency, and specificity that include periods of standardized physical (stepping) exercise (STEX).

Results: Patient 1 (63 year, female, TLE) with SD 60%, 6 seizures with heart rate changes <42%, hence none triggered. No stimulation occurred during STEX and false positives (FP)/12 h were low, increasing to 4 FP/12 h when SD reduced to 40%. After vEEG, a SD change to 50% was well tolerated.

Patient 2 (23 year, male, multifocal) with SD 40%, 5/5 seizures recorded while AMM was active triggered stimulation, 12s to 44s after clinical onset. Stimulation occurred in STEX; there were 51 FP/12 h with good tolerability.

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.

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EFFECTIVENESS OF VAGUS NERVE STIMULATION (VNS) IN SEVERE NONSURGICAL CANDIDATES AND FAILED INTRACRANIAL EPILEPSY SURGERY PATIENTS

Limotai C, Deesudchit T, Lochalernkul C, Srikijvilaikul T
King Chulalongkorn Memorial Hospital, Bangkok, Thailand

Purpose: To delineate the effectiveness of VNS in highly selective non-surgical 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 Moya-Moya disease. Mean age was 27.65 $\pm$ 10.47 years. Mean duration of epilepsy was 17.53 $\pm$ 8.79 years. Mean seizure per day was 2.36 $\pm$ 3.38. Mean number of exposed antiepileptic drugs was 7.2 $\pm$ 1.36. Mean percentage of seizure reduction was 7.63%, 19.3%, 3.03%, and 6.33% at 3, 12, 18, 24 months, but increased 1.6% at 6 months after stimulation. The maximal seizure reduction was found at 12 months after stimulation in both methods of analyses. In LGS patients, the seizure frequency was reduced with the maximal reduction (30.88%) once again at 12 months.

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.

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LEAD MALFUNCTION IN VAGUS NERVE STIMULATION: CLINICAL EFFECT, DIAGNOSIS AND OUTCOME AFTER LEAD REVISION

Evsiukova T, Kostov H, Henning O
National Center for Epilepsy, Oslo University Hospital, Oslo, Norway

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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THE IMPORTANCE OF STIMULATION CYCLE IN VAGUS NERVE STIMULATION FOR DRUG-RESISTANT EPILEPSIES

Colicchio G[1], Montano N[1], Fuggetta MF[1], Nucci CG[1], Papacci F[1], Meglio M[2]
[1]Catholic University, Roma, Italy, [2]University Hospital, Verona, Italy

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 $\pm$ 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.

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EFFICACY AND SAFETY OF TRIGEMINAL NERVE STIMULATION: AN EXPERIENCE IN 8 PATIENTS WITH DRUG-RESISTANT EPILEPSY

Sierra-Marcos A, Giráldez BG, Serratosa JM
Department of Neurology, Fundación Jiménez Díaz University Hospital, Madrid, Spain

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.

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EXTERNAL TRIGEMINAL NERVE STIMULATION (ETNS) FOR EPILEPSY: EARLY CLINICAL EXPERIENCE

Slaght SJ[1,2], Said M[1], Hughes E[1], Ramdas S[1], Richardson M[1], Elwes R[1], Nashef L[1]
[1]Neurology, King's College Hospital, London, UK, [2]Neurology, Wessex Neurological Centre, Southampton, UK

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-QOL, 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.

Two adults discontinued within 2 weeks (disliked sensation/unhappy with seizure pattern) and one after 15 weeks (efficacy). The remaining tolerated eTNS well, completing 18 weeks; eight chose to continue use (so far 116–277 days). One had transient forehead reddening when hot. The device was worn for 6½–12 h/night (median 10) with a median current of 5 mA (range 2.6–7.6). Efficacy could not be assessed in four (two improved but had significant concurrent medication changes; two: uncountable absences).

Of the remaining 10, data was analysed at 18 weeks. Mean seizure rate reduced from a baseline of 2.9 ± 1.9–2.2 ± 1.5 ($p = 0.07$). Five patients had a >30% reduction in seizure frequency of whom one had a 50% reduction. QOLIE-10 weighted score improved significantly from 37 ± 26 (n = 12) to 18 ± 17 (n = 10), $p = 0.02$, and BDI significantly from 12 ± 8 (n = 12) to 6 ± 5 (n-10), $p = 0.01$. There was also an improvement in both sleep scales (Pittsburgh 7 ± 4 (n = 12) to 4 ± 2 (n = 10);

Epworth 11.0 ± 7.9 (n = 12) to 10.8 ± 6.0 (n = 10).

Conclusion: These data support the safety, efficacy and tolerability of eTNS.

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YIELD AND PREDICTORS OF EPILEPSY SURGERY CANDIDACY IN CHILDREN ADMITTED FOR SURGICAL WORKUP

Wirrell E[1], Wong-Kisiel LC[1], Wetjen N[2], Nickels K[1]
[1]Child and Adolescent Neurology, Mayo Clinic, Rochester, MN, USA, [2]Neurosurgery, Mayo Clinic, Rochester, MN, USA

Purpose: To review yield and predictors of surgical candidacy in children admitted to EMU.

Methods: Children admitted for presurgical assessment from 11/2010 to 11/2013 at Mayo Clinic were identified. Charts were reviewed for demographic data, seizure details, developmental status, neurological exam findings, MRI and outpatient EEG results. Surgical candidates were defined as those recommended for surgery following epilepsy surgical conference.

Results: 130 children underwent presurgical workup (52% male) and 119 (92%) had typical events recorded. Sixty five (55%) were defined as surgical candidates. Of these, 45 underwent surgery (40 resective, 4 callosotomy alone, 1 resective + callosotomy), 7 had surgery pending, 2 underwent grid placement without resection (1-inadequate localization, 1-focus involved eloquent cortex), and in 11, the family chose not to pursue surgery. Of the 54 non-surgical candidates, ictal onset was multifocal in 24, generalized in 7 and nonlocalizing in 15. Seven had focal ictal onset but extensive or bilateral imaging abnormalities and 1 had non-epileptic events. Excluding those undergoing corpus callosotomy alone, favorable predictors of surgical candidacy included focal EEG slowing ($p = 0.001$), ≥1 interictal foci all in the same hemisphere ($p < 0.001$), focal/hemispheric abnormality on MRI ($p < 0.001$), normal development ($p = 0.04$), single ictal semiology on history ($p < 0.001$) and structural or structural-genetic etiology ($p = 0.005$). Surgical candidacy was found in only 30% (20/67) with ≤3 favorable prognostic factors vs. 85% (41/48) with ≥4 factors.

Conclusions: More than half of children admitted for presurgical workup are considered surgical candidates. Factors identifiable on clinical history, interictal EEG and MRI prior to EMU admission are significantly predictive of candidacy.

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BILATERAL INTRAHYPOTHALAMIC HAMARTOMA – INDICATION FOR RESECTIVE SURGERY?

Staack AM[1], Strobl K[1], Wendling A-S[1], Wisniewski I[1], Scholly J[2], Valenti MP[2], Benmekhbi M[2], Hirsch E[2], Bast T[1], Kehrli P[2], Steinhoff BJ[1]

[1]Kork Epilepsy Centre, Kehl-Kork, Germany, [2]University Hospital of Strasbourg, Strasbourg, France

Purpose: Hypothalamic Hamartomas (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 dacrystic seizures, different kinds of auras (epigastric, 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 mamillary bodies of each side were detected on MRI, again more voluminous on the right side.

Since drug-resistancy 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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VALPROATE ASSOCIATED COAGULOPATHY AND PLATELET DYSFUNCTION: CLINICAL RELEVANCE FOR EPILEPSY SURGEON

Kurwale NS, Garg K, Chandra SP, Tripathi M

All India Institute of Medical Sciences, New Delhi, India

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 $\pm$ 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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CLUSTER ORGANIZATION OF THE IRRITATIVE ZONE IN NEOCORTICAL EPILEPSY: IMPLICATIONS FOR PATHOPHYSIOLOGY, SURGERY PLANNING AND OUTCOME

Janca R[1], Krsek P[2], Jezdik P[1], Cmejla R[1], Tomasek M[3], Jefferys JGR[4], Komarek V[2], Marusic P[3], Jiruska P[3,4,5]

[1]Department of Circuit Theory, Faculty of Electrical Engineering, Czech Technical University in Prague, Prague, Czech Republic, [2]Department of Paediatric Neurology, 2nd Faculty of Medicine, Motol University Hospital, Charles University in Prague, Prague, Czech Republic, [3]Department of Neurology, 2nd Faculty of Medicine, Motol University Hospital, Charles University in Prague, Prague, Czech Republic, [4]Neuronal Networks Group, School of Clinical and Experimental Medicine, University of Birmingham, Birmingham, UK, [5]Department of Developmental Epileptology, Institute of Physiology, Academy of Sciences of Czech Republic, Prague, Czech Republic

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 $\pm$ 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 $\pm$ 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.

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NEUROPSYCHIATRIC COMORBIDITIES IN PATIENTS WITH VNS FOR INTRACTABLE EPILEPSY IN A TERTIARY NEUROPSYCHIATRY SERVICE

Mohan M, Isaac L, Perera S, McConnell K, Sandeman D, Bird J
Neurosciences, North Bristol NHS Trust, Bristol, UK

Purpose: Vagal Nerve Stimulation (VNS) is a neurosurgical 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.

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HEALTH-RELATED QUALITY OF LIFE, MOOD AND PATIENT SATISFACTION AFTER EPILEPSY SURGERY IN SWEDEN – A PROSPECTIVE CONTROLLED OBSERVATIONAL STUDY

Malmgren K[1], Sager Magnusson E[1], Ekstedt G[1], Taft C[2]
[1]Department of Clinical Neuroscience and Rehab, Institute of Neuroscience and Physiology, Sahlgrenska Academy at Gothenburg University, Göteborg, Sweden, [2]Institute of Health and Care Sciences, Sahlgrenska Academy at Gothenburg University, Göteborg, Sweden

Purpose: To evaluate health-related quality of life (HRQOL) in Swedish epilepsy surgery candidates before and 2 years after surgery or presurgical investigation.

Method: In this study 141 patients participated, 96 were operated and 45 were not. Questionnaires completed at baseline and 2-year follow-up included the SF-36 health survey, the Hospital Anxiety and Depression scale (HAD), operated patients also answered patient satisfaction questions. SF-36 scores were compared with scores from a matched sample from the Swedish norm population. Numbers of patients achieving minimum important change (MIC) were calculated for the SF-36 Physical Composite Summary (PCS) and Mental Composite Summary (MCS).

Results: At baseline patients had significantly lower values than norm on all SF-36 domains. At follow up, seizure-free patients reached the same levels as the norm in all SF-36 domains except Social Function. Operated patients with continued seizures and non-operated patients had unchanged scores. 51% of seizure-free patients had an improvement reaching MIC in PCS, 45% in MCS. Corresponding results for patients with continued seizures were 28% in PCS and 28% in MCS, for non-operated 33% in PCS and 29% in MCS. Seizure-free patients had significantly lower anxiety levels. Of all operated patients, 80% were satisfied with having had surgery, 86% considered that they had benefited, 20% thought that surgery caused some harm.

Conclusion: While HRQOL normalised in seizure-free patients there was no change in patients with continued seizures or non-operated at group level although a proportion in both groups improved. Still, the majority of all patients were satisfied with surgery.

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EPILEPSY SURGERY IN THE POSTERIOR PART OF THE BRAIN IN 96 CHILDREN AND ADOLESCENTS WITH SEVERE DRUG RESISTANT EPILEPSIES

Holthausen H[1], Pieper T[1], Hartlieb T[1], Pascher B[1], Bluemcke I[2], Staudt M[1], Kudernatsch M[3]
[1]Neuropediatrics, Schoen-Klinik, Vogtareuth, Germany, [2]Neuropathology, University Clinic of Erlangen, Erlangen, Germany, [3]Neurosurgery, Schoen-Klinik, Vogtareuth, Germany

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 2013 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, O 7, TP 4. *Etiologies:* FCD 46, HIE/ulegyria 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/ulegyria 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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COGNITIVE IMPAIRMENT IN EPILEPSY: THE EFFECT OF DRUG THERAPHY

Sahin S, Cakmak MA, Cinar N, Iscen P, Karsidag S
Neurology Department, Maltepe University Medical School, Istanbul, Turkey

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 polytheraphy 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 monotheraphy group; backward and forward digit span, abstraction and word counting impairments were found significant in polytheraphy group when compared to the controls. There were no significant difference of cognitive test scores between two groups.

Conclusion: Various factors may affect cognition in patients with epilepsy. The cognitive impact of AEDs can not be ignored. Physicians should consider evaluating cognitive function prior to starting or adding an AED.

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ADJUNCTIVE LACOSAMIDE – 5 YEARS' CLINICAL EXPERIENCE

Stephen LJ, Kelly K, Parker P, Brodie MJ
Epilepsy Unit, Western Infirmary, Glasgow, UK

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 generalisation, regardless of concomitant treatment. Commonest dose-related side effects were neurotoxic in nature.

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SAFETY AND EFFICACY OF ZONISAMIDE AS FIRST ADD-ON THERAPY TO CARBAMAZAPINE IN INDIAN ADULT PATIENTS DIAGNOSED WITH EPILEPSY: A SUBANALYSIS

Dash A[1], Abbas A[2], Ravat S[3], Satyanarayana G[4], Kaur D[1], Mishra S[1], Demudubabu B[5]
[1]Eisai Pharmaceuticals India Private Limited, Mumbai, India, [2]Neurocare & Research Centre, Lucknow, India, [3]KEM Hospital, Mumbai, India, [4]Vijaya Health Care Hospital, Secunderabad, India, [5]Caring Hand Neuro Centre, Vishakapatnam, India

Purpose: Evaluation of safety & efficacy of zonisamide as first add-on therapy to carbamazapine 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 carbamazapine. 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 carbamazapine 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.

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SAFETY AND EFFICACY OF ZONISAMIDE AS ADD-ON TO EXISTING ANTI-EPILEPTIC THERAPY: AN EVALAUTION IN INDIAN ADULT POPULATION

Dash A[1], Divatia R[2], Srinivasan A[3], Biniwale AA[4], Varkey B[5], Narayana R[6], Achtani R[7]
[1]Eisai Pharmaceuticals India Private Limited, Mumbai, India, [2]Shrey Hospital, Ahmedabad, India, [3]Trinity Acute Care Hospital, Chennai, India, [4]Biniwale Clinic, Pune, India, [5]Lourdes Hospital, Kochi, India, [6]Seven Hills Hospital, Vishakapatnam, India, [7]Mata Chanan Devi Hospital, New Delhi, India

Abstracts

Purpose: To evaluate the tolerability & efficacy of zonisamide as add-on to existing anti-epileptic therapy-an evalaution 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 carbamazapine 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: As add-on to existing anti-epileptic therapy, zonisamide is an effective treatment option with a good tolerability profile. Minimal pharmacokinetic interactions and better compliance due to once daily dosing because of long half life confer an additional advantage.

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EXPERIENCE WITH LACOSAMIDE IN TREATING FOCAL EPILEPSY PATIENTS IN ROMANIA: EFFICACY, SAFETY AND TIME TO REACH RESPONSE

Mindruta IR[1], Bajenaru OA[2], Panea CA[3], Lacramioara Perju-Dumbrava, Cristian Dinu Popescu, Ruxandra Dana Chirileanu, Dan Iulian Cuciureanu, Corina Roman- Filip, Ionela Codita, Sanda Petrutiu, Diana Nicoleta Hodorog, Dan Filip, Edith Sisak, Daniela Reisz, Izabela Popa, Anca Gogu, Do
[1]Neurology, University Emergency Hospital of Bucharest, University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania, [2]Neurology, University Hospital, University of Medicine and Pharmacy, Bucharest, Romania, [3]Neurology, Elias Hospital of Bucharest, University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania

Purpose: Lacosamide is a new antiepileptic drug (AED) that interferes the sodium channel with a novel mechanism of action, approved as adjunctive therapy in patients with focal epilepsy. We aimed to assess responders and seizure freedom rate, time to reach response and tolerability of a patient population with drug resistant epilepsy that received lacosamide in real life clinical practice.

Method: We conducted a retrospective, observational analysis including 158 patients in 13 centers, over 2 years.

Inclusion criteria: patients over 16 years of age, uncontrolled monthly focal seizures with or without secondary generalization, treated with at least 1 AED.

Exclusion criteria: progressive causes of epilepsy or substance abuse, pregnancy or breast feeding mothers, patients taking AED in low doses, that could obtain control by increasing the daily dose, patients with severe hepatic or renal failure.

Results: We included 49% women and 51% men with a mean age of 38 years. The responder rate (more than 50% reduction of seizure frequency) was 56.6% and seizure freedom rate was 13.1%. Responder's population reached this status in the first 4 months of treatment in 78% of cases. Adverse events occurred in 29.12% of patients. 8.22% of patients (13 patients) were withdrawn from the medication due to adverse events. Retention rate was 75% with a mean follow-up period of 9.2 months. The most common adverse events were dizziness and nausea.

No significant difference in the tolerability profile was observed between patients taking lacosamide in association with sodium channel blockers or non-sodium channel blockers.

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.

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COSMETIC ADVERSE EFFECTS OF ANTIEPILEPTIC DRUGS IN ADULTS WITH EPILEPSY

Chen B[1], Detyniecki K[1], Hirsch L[1], Choi H[2], Buchsbaum R[2], Bausell R[2]
[1]Yale University, New Haven, CT, USA, [2]Columbia University, New York, NY, USA

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

Parrett MP[1], McLean BN[1], Shankar R[2], Cox D[2]
[1]Neurology Department, Royal Cornwall Hospital, Truro, UK, [2]Neuropsychiatry, Cornwall Partnership NHS Foundation Trust, Epilepsy and Memory Service, Truro, UK

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.

Method: Preliminary retrospective data collection of 24 patients from Oct 2012 to January 2014.

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.

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p335
A SERVICE EVALUATION OF PERAMPANEL (FYCOMPA) AT LEEDS GENERAL INFIRMARY

Goulding PJ, Wright E, Geldard J, Maguire M
Neurology, Leeds General Infirmary, Leeds, UK

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

Auvin S, Papon A, Bellavoine V, Storme T, Merdariu D, Ilea A, Bourdon O, Corny J
Child Neurology Department & Inserm U 1141, Hôpital Robert Debré, Paris, France

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.

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p337
MUST DIFFERENT MECHANISMS OF ACTION BE CONSIDERED IN THE ANTIEPILEPTIC POLYTHERAPY?

Rovira Sirvent D, Juárez Torrejón N, Hernando Requejo V
Neurology, Severo Ochoa University Hospital, Leganés, Spain

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 voltaje-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.

Results: Groups 1 and 9 were MoDA more used. Antiepileptic drugs (AEDs) with GABAergic action were more present in the AE group (7.32%) 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

Atugonza R, Idro R, Kakooza-Mwesige A
Paediatrics and Child Health, Makerere University, College of Health Sciences, Kampala, Uganda

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[a] 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

Belyaev O, Volkova E
Volgograd State Medical University, Volgograd, Russian Federation

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 (finlepsin 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 ESLICARBAZEPINE ACETATE TREATMENT IN ELDERLY PATIENTS

Costa R[1], Oliveira C[1], Lopes N[1], Gama H[1], Sousa R[1], Nunes T[1], Soares-da-Silva P[1,2]
[1]Bial – Portela & C[a], S.A., São Mamede do Coronado, Portugal,
[2]University of Porto, Porto, Portugal

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 & C[a], S.A.

p341
SAFETY OF ESLICARBAZEPINE ACETATE AFTER 4 YEARS OF POST-MARKETING EXPERIENCE IN EUROPE

Gama H[1], Vieira M[1], Costa R[1], Sousa R[1], Pinto R[1], Soares-da-Silva P[1,2]
[1]Bial – Portela & C[a], S.A., São Mamede do Coronado, Portugal, [2]University of Porto, Porto, Portugal

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 SOCs 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 & C[a], S.A.

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PREFERRED FLAVOUR OF ESLICARBAZEPINE ACETATE ORAL SUSPENSION TO PAEDIATRIC EPILEPTIC SUBJECTS

Lima R[1], Moreira J[1], Pinto R[1], Sousa R[1], Nunes T[1], Soares-da-Silva P[1,2]
[1]Bial – Portela & C[a], S.A., São Mamede do Coronado, Portugal, [2]University of Porto, Porto, Portugal

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 & C[a], S.A.

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SEIZURE RESPONSE TO PERAMPANEL IN A SEVERE REFRACTORY GROUP OF EPILEPSY PATIENTS

Flynn C, Delanty N
Beaumont Hospital, Dublin, Ireland

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.

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LONG-TERM NON-INTERVENTIONAL STUDY OF LACOSAMIDE SAFETY AS ADD-ON THERAPY IN PATIENTS WITH EPILEPSY AND UNCONTROLLED PARTIAL-ONSET SEIZURES

Steinhoff BJ[1], Eckhardt K[2], Doty P[3], De Backer M[4], Brunnert M[2], Schulze-Bonhage A[5]
[1]The Kork Epilepsy Centre, Kork, Germany, [2]UCB Pharma, Monheim am Rhein, Germany, [3]UCB Pharma, Raleigh, NC, USA, [4]UCB Pharma, Brussels, Belgium, [5]University Hospital Freiburg, Freiburg, Germany

Abstracts

Purpose: To compare incidence of certain cardiovascular and psychiatric treatment-emergent adverse events (TEAEs) in patients with epilepsy initiating adjunctive lacosamide or other approved AEDs.

Method: In this non-interventional post-authorization safety study (NCT00771927), 1005 epilepsy patients with uncontrolled partial-onset seizures were assigned to one of two groups (lacosamide or other approved AED) at the discretion of the treating physician and followed for 12 months. Results are presented for the safety set per treatment initiation.

Results: Mean age was 41.0 ± 14.5 years (6.9% ≥65 years). 256/511 [50%] lacosamide and 256/493 [52%] Other-AED patients completed 12 months treatment. Overall modal lacosamide dose was 200 mg/day. Four patients (0.8%) in each group (all aged <65 years) reported predefined cardiovascular-related TEAEs; none were considered serious TEAEs or led to discontinuation. One event each of sinus bradycardia (lacosamide), AV-block first-degree (lacosamide), and syncope (Other-AED) were judged to be treatment-related. Predefined psychiatric-related TEAEs were reported by 21 (4.1%) lacosamide patients and 27 (5.5%) Other-AED patients. Five patients reported predefined psychiatric-related TEAEs that were considered serious TEAEs (depression in 2 lacosamide patients and 1 Other-AED patient, and suicide attempt in 2 lacosamide patients). Depression was most frequently reported, by 15 (2.9%) lacosamide patients (7 judged to be treatment-related) and 21 (4.3%) Other-AED patients (12 judged to be treatment-related). Two lacosamide (depression [n = 2]) and 4 Other-AED patients (depression [n = 3]; depressed mood [n = 1]) discontinued due to a psychiatric-related TEAE. Seven patients died, 3 had initiated lacosamide treatment (SUDEP, fall, malignant glioma) and 4 initiated Other-AED (left-ventricular failure, unknown death cause, road traffic accident, grand mal convulsion). All deaths were considered unrelated/unlikely related to study medication.

Conclusion: Comprehensive evaluation of predefined cardiovascular- and psychiatric-related TEAEs did not reveal any increased incidence of these events for patients treated in real-life medical practice with adjunctive lacosamide vs. other approved AEDs.

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p345
LACOSAMIDE ADDED TO A MONOTHERAPY IN EPILEPSY PATIENTS WITH PARTIAL-ONSET SEIZURES: FINAL ANALYSIS OF THE VITOBA STUDY

Noack-Rink M[1], Irrgang V[1], Ramirez F[1], Mayer T[2], Arnold S[3], Runge U[4]

[1]UCB Pharma, Monheim am Rhein, Germany, [2]Sächsisches Epilepsiezentrum, Radeberg, Germany, [3]Neurozentrum Nymphenburg, Munich, Germany, [4]Neurologische Universitätsklinik, Greifswald, Germany

Purpose: This prospective non-interventional study (Clinicaltrials.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.

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DIFFERENCES IN USAGE OF CLOBAZAM VS. CLONAZEPAM FOR EPILEPSY

Isojarvi J[1], Jones D[1], Guiraud-Diawara A[2], Shen V[1], Verpillat P[2]

[1]Lundbeck LLC, Deerfield, IL, USA, [2]Lundbeck SAS, Issy-les-Moulineaux, France

Purpose: Clobazam is FDA-approved for seizures associated with Lennox Gastaut Syndrome in patients ≥2 years. Clobazam (a 1,5-benzodiazepine) and 1,4-benzodiazepines such as clonazepam have been used in Europe for a variety of epilepsy disorders and anxiety. The Clinical Practice Research Datalink (CPRD), a longitudinal primary care database, consists of electronic medical records from general practitioners in the United Kingdom (UK). We analyzed data from the CPRD to compare use of clobazam and clonazepam in UK clinical practice.

Methods: All patients with ≥1 incident prescription of clobazam or clonazepam within the study period (Jan. 1, 2001, to Dec. 31, 2010) with a diagnosis of epilepsy or anxiety disorders were included. Dates of patients' first prescriptions were termed index date. Patients must have had ≥182 days of history in the database before index date, all without any clobazam or clonazepam prescriptions to ensure no previous clobazam or clonazepam had been prescribed. Patients must also have had a diagnosis of epilepsy or anxiety any time prior to or ≤90 days after index dates. Patients were followed until end of clobazam or clonazepam therapy, or until Feb. 28, 2013.

Results: 8,249 patients met the inclusion criteria. Of these, 2,870 received clobazam and 5,379 received clonazepam. 95% of clobazam patients received clobazam for epilepsy (5% for anxiety). Conversely, 72% of clonazepam patients received clonazepam for anxiety (28% for epilepsy). Clobazam patients treated for epilepsy were younger than those receiving clonazepam (mean ± SD: 34.9 ± 18.6 years vs. 43.6 ± 21.0 years, $p < 0.0001$). 93% of epilepsy patients receiving clobazam were also receiving concomitant AED therapy (76% for clonazepam).

Conclusions: Clobazam is primarily an adjunctive therapy for epilepsy in the UK, while clonazepam is used for anxiety. This is further supported by the younger patients, on average, being treated with clobazam, as well as the greater percentage of clobazam-treated patients receiving concomitant AEDs.

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A CASE OF MYCOSIS FUNGOIDES LIKE LESIONS DEVELOPING AFTER LEVETIRACETAM THERAPY

Bora İ, Bican Demir A, Bülbül Başkan E
Uludag University, Bursa, Turkey

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 pyrimidione, 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 literatüre. 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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PERAMPANEL AS ADD-ON TREATMENT IN PATIENTS WITH DRUG-RESISTANT FOCAL EPILEPSY: THE CLINICAL EXPERIENCE OF THE DANISH EPILEPSY CENTER

Juhl S, Rubboli G
The Danish Epilepsy Center, Dianalund, Denmark

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

Ristic ST[1], Djordjevic GM[1], Ristic DT[2], Marinkovic IM[3]
[1]Department of Neurology, Clinic Centre of Nis, Nis, Serbia, [2]Institut of Pulmonary Disaeses, Nis, Serbia, [3]Medical Faculty of Nis, Nis, Serbia

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 advese 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 lamotrigin in patients with newly- diagnosed epilepsy as a monotherapy.

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ASSESSING LONG-TERM EFFECTS OF ESLICARBAZEPINE ON LIVER VALUES AND LIPID METABOLISM PROFILE

Ley Nácher M, Principe A, Planellas Giné L, Rocamora Zúñiga RA
Neurology, Epilepsy Monitoring Unit, Hospital del Mar, Barcelona, Spain

Purpose: Efficacy, safety and tolerability of eslicarbazepine has been assesed 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.

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LONG-TERM EXPERIENCE WITH LACOSAMIDE IN PEDIATRIC EPILEPSY PATIENTS – A RETROSPECTIVE EUROPEAN MULTICENTRE REPORT

Feucht M[1], Haberlandt E[2], Ošlejšková H[3], Ramos Rivera GA[4]
[1]Department of Pediatrics, Medical University of Vienna, Vienna, Austria, [2]Department of Pediatrics, Medical University of Innsbruck, Innsbruck, Austria, [3]Department of Child Neurology, University Hospital Brno, Brno, Czech Republic, [4]Department of Pediatric Neurology, Children University Hospital of Bratislava, Bratislava, Slovakia

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 >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.

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EUROPEAN NON-INTERVENTIONAL REGISTRY STUDY OF ANTIEPILEPTIC DRUG USE IN PATIENTS WITH LENNOX-GASTAUT SYNDROME: INTERIM ANALYSIS

Panzer A[1], Auvin S[2], Hauser E[3], Bagul M[4]
[1]DRK Kliniken, Epilepsiezentrum/Neuropädiatrie, Berlin, Germany, [2]Child Neurology Department & Inserm U1141, Hôpital Robert Debré, Paris, France, [3]Hospital Mödling, Mödling, Austria, [4]Eisai Ltd, Hatfield, UK

Purpose: Interim analysis of an ongoing European registry study, designed to capture long-term data (≥18 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

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EVALUATION OF ANTIEPILEPTIC DRUG USE IN THE PREGNANT PATIENTS WITH EPILEPSY IN A UNIVERSITY HOSPITAL IN ISTANBUL

Idriz Oglu Gulcebi M, Kucukibrahimoglu E, Demirkapi M, Gulhan R, Karaalp A, Goren Z, Onat F
Pharmacology, Marmara University, School of Medicine, Istanbul, Turkey

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. Of the 2 premature newborns, one who exposed to lamotrigine had low birth weight, respiratory distress and stayed under intensive care for 5 days. Thirty-four percentage of the patients were still on the pregnancy period.

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

Cumbo E, Ligori LD
A.S.P. 2 Caltanissetta, Alzheimer and Dementia Unit-Neurodegenerative Disorders O.U., Caltanissetta, Italy

Purpose: To evaluate the long-term efficacy and tolerability of lacosamide (LCM) monotherapy in Alzheimer's disease patients with AEDs-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 month. 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 month's treatment the first group was switched to LCM monotherapy, the second group continued on a bitherapy. LEV, LTG, OXC were 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 change 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

Benna P, Rovera A, Montalenti E
Neuroscience Department, Università di Torino, Torino, Italy

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

Romigi A[1], Placidi F[1], Izzi F[2], Albanese M[1], Marchi A[1], Marciani MG[2], Cerminara C[3], Mercuri NB[2]
[1]Neurophysiopathology, University of Rome Tor Vergata, Rome, Italy, [2]Neurology, University of Rome Tor Vergata, Rome, Italy, [3]Child Neurology Department, University of Rome Tor Vergata, Rome, Italy

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 paraesthesias followed by hypoesthesia 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 die). After 1 month the patient showed focal seizures with secondarily generalization under a stable treatment with levetiracetam (3000 mg/die), therefore he received phenobarbital (50 mg per day) as add-on treatment. The

patient became stuporous and mental status fluctuated. In addition breakthrough seizures later developed. EEG showed generalized 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 temporo-parieto-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 offers 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 ESLICARBAZEPINE ACETATE (ZEBINIX) WITH CARBAMAZEPINE IN EVERYDAY CLINICAL PRACTICE USING A RETROSPECTIVE MULTICENTRE AUDIT

Keogh S[1], McDonald P[2], Lawthorn C[3], Brodie M[4], McLean B[5], Mohanraj R[6], Morrow J[7], Tittensor P[8], Bagary M[1]

[1]BSMHFT, Regional Epilepsy and Sleep Service, Birmingham, UK, [2]BSMHFT, Research and Innovation, Birmingham, UK, [3]Department of Neurology, Royal Gwent Hospital, Swansea, UK, [4]University of Glasgow, Glasgow, UK, [5]Royal Cornwall Hospital, Plymouth, UK, [6]Salford Royal Hospital, Manchester, UK, [7]Royal Victoria Hospital, Belfast, UK, [8]Stafford Hospital, Stafford, UK

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% ≥2) 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 (Zebinex) with a slow titration regime for eslicarbazepine acetate (Zebinex) to maximise tolerability.

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THE EFFICACY AND TOLERABILITY OF PERAMPANEL (FYCOMPA) IN EVERYDAY CLINICAL PRACTICE USING A RETROSPECTIVE MULTICENTRE AUDIT

Keogh S, Greenhill L, O'Donnell M, McCorry D, Bagary M

BSMHFT, Regional Epilepsy and Sleep Service, Birmingham, UK

Purpose: Perampanel is a non-competitive antagonist of α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) glutamate receptor on post-synaptic neurons. We report our initial findings on the efficacy and tolerability in routine clinical practice.

Method: A retrospective audit of outcomes following treatment with perampanel for localisation-related epilepsy. 16 patients with median values for age 42 (24–59) years; duration of epilepsy 30 (7–53) years; 2 (2–3) concomitant AEDs; 11 (3–16) previous AED exposures and 7–285 days duration of perampanel treatment. Perampanel dosage ranged from 4 to 12 mg/day.

Results: 18.8% (3/16) of subjects experienced a 50% improvement in seizure control with the addition of perampanel. Thus far, no subjects have achieved seizure freedom or moved to monotherapy. 7/16 (43.8%) subjects remain on perampanel (duration 7–153 days). Perampanel was withdrawn in 9 subjects, 7 (77.8%) for tolerability problems and 2 (22.2%) for lack of efficacy. The most common side effects were behavioural disturbance (37%), sedation 18.8%, dizziness (18.8%) and unsteadiness (12.5%).

Conclusion: In this initial data from this on-going audit the median previous AED exposures was 11, indicating a very pharmacoresistant cohort of subjects. 18.8% (3/16) have experienced improved seizure control. Tolerability issues were in keeping with the summary of product characteristics. Further data will be incorporated into the audit as more subjects are recruited.

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EXPERIENCE WITH BUCCAL MIDAZOLAM FOR SEIZURE CLUSTERS IN ADULTS

Fraga V[1], Falip M[2], Donaire A[1], Aparicio J[1], Carreño M[1]

[1]Hospital Universitari Clínic Barcelona, Barcelona, Spain, [2]Hospital Universitari de Bellvitge, Barcelona, Spain

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 inmediate 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 experience 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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EXPERIENCE WITH BUCCAL MIDAZOLAM FOR SEIZURE CLUSTERS IN ADULTS

Fraga V[1], Falip M[2], Donaire A[1], Aparicio J[1], Carreño M[1]
[1]Hospital Universitari Clínic Barcelona, Barcelona, Spain, [2]Hospital Universitari de Bellvitge, Barcelona, Spain

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 inmediate 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 experience 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

Russo E, Citraro R, Aiello R, Chimirri S, Donato G, De Sarro G
Science of Health Department, School of Medicine, University of Catanzaro, Catanzaro, Italy

Purpose: Several studies have demonstrated the involvement of mTOR pathway in epilepsy and the process of epileptogenesis[1;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 seizures[2;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 areas[4]. 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 neural 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 ANTIEPILEPTICS ON GAMMA OSCILLATIONS – DERIVATION OF AN ANALYTICAL EQUATION FROM DYNAMIC CLAMP EXPERIMENTS

Zeberg H[1], Robinson HPC[2], Århem P[1]
[1]Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden, [2]Department of Physiology, Development and Neuroscience, University of Cambridge, Cambridge, UK

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

in-depth understanding of how pharmacological agents modulates the rhythm of the brain is of great clinical importance.

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THE IMPACT OF THE ANTIEPILEPTIC DRUGS LAMOTRIGINE, TOPIMARATE AND LACOSAMIDE ON GLIAL PROPERTIES IN AN IN VITRO CO-CULTURE MODEL OF INFLAMMATION

Dambach H[1], Moinfar Z[1,2], Angersbach L[1], Corvace F[1], Hinkerohe D[3], Prochnow N[1,2], Faustmann PM[1,2]
[1]Department of Neuroanatomy and Molecular Brain Research, Ruhr-University Bochum, Bochum, Germany, [2]International Graduate School of Neuroscience (IGSN), Ruhr-University Bochum, Bochum, Germany, [3]Department of Neurology, Knappschafts-Hospital, Bochum, Germany

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 connexin 43 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 mictoglia 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 in vivo and further in human to benefit from AEDs therapy.

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THE ANTIEPILEPTIC AND NEUROPROTECTIVE EFFECTS OF PERIODIC FASTING ON PENTYLENETETRAZOL-INDUCED SEIZURES IN RATS

Karimzadeh F, Modarres Mousavi SM, Lotfinia AA
Shefa Neuroscience Research Center, Tehran, Iran

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 pentylenetetrazol (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.

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A COMPARATIVE STUDY OF PERFORANT PATHWAY STIMULATION IN C57BL/6 MICE AND SPRAGUE-DAWLEY RATS

Kienzler-Norwood F[1,2], Rosenow F[1], Norwood BA[1]
[1]Neurology, Philipps University Marburg, Marburg, Germany, [2]Johann Wolfgang Goethe-University Frankfurt am Main, Frankfurt am Main, Germany

Purpose: Perforant pathway stimulation (PPS) in rats is a long-standing and well-established method of modeling temopral 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 induces 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 intracellular "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.

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THE EFFECT OF CARBAMAZEPINE ON NEURONAL DAMAGE IN PENTYLENTETRAZOL MODEL OF EPILEPSY

Jafarian M[1], Alipour ME[1,2], Lotfinia AA[1]
[1]Shefa Neuroscience Research Center, Tehran, Iran, [2]Tehran University of Medical Sciences, School of Advanced Medical Technology, Tehran, Iran

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 carbamazpine 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 Cabamazepine 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 PENTYLENETETRAZOLE (PTZ) INDUCED CONVULSIONS IN MICE: POSSIBLE BEHAVIORAL, BIOCHEMICAL AND MITOCHONDRIAL ALTERATIONS

Mishra J, Lalitha S, Kumar A
University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh, India

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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LONG-TERM PROFILE AND SEIZURE CLUSTERING IN THE TETANUS TOXIN MODEL OF TEMPORAL LOBE EPILEPSY

Jiruska P[1,2], Otahal J[1], Cmejla R[3], Kudlacek J[1,3], Vlk P[1,3], Palus M[4], Hlinka J[4], Marusic P[2], Jefferys JGR[5]
[1]Department of Developmental Epileptology, Institute of Physiology, Academy of Sciences of the Czech Republic, Prague, Czech Republic, [2]Department of Neurology, 2nd Faculty of Medicine, Motol University Hospital, Charles University in Prague, Prague, Czech Republic, [3]Department of Circuit Theory, Faculty of Electrical Engineering, Czech Technical University, Prague, Czech Republic, [4]Department of Nonlinear Modeling, Institute of Computer Science, Academy of Sciences of the Czech Republic, Prague, Czech Republic, [5]Neuronal Networks Group, School of Clinical and Experimental Medicine, University of Birmingham, Birmingham, UK

Rationale: Epileptic seizures are characterized as sudden and unpredictable events. The inability to predict the occurrence of the next seizure represents the main disabling factor of epilepsy. Recent studies have demonstrated that seizures do not occur randomly, nor are they uniformly distributed in time. Periods of increased and decreased probability of seizure occurrence were observed in patients and in chronic models of epilepsy. In the current study, we examined long-term seizure dynamics in the tetanus toxin model of temporal lobe epilepsy.

Methods: Tetanus toxin was stereotaxically injected into the right hippocampal CA3 area of eight adult rats, and silver ball electrodes were implanted epidurally above the hippocampi. Continuous video-EEG monitoring started on day four and continued for 2 weeks to monitor the development of spontaneous seizures. Semiautomatic seizure detectors were applied to long-term recordings to extract the following parameters: seizure frequency, interval between seizures and seizure duration.

Results: All animals developed spontaneous seizures characterized as complex partial seizures, some of which became secondarily generalized. Average seizure frequency was 8.3 $\pm$ 1.7/day and seizure duration was 73.9 $\pm$ 0.94 s. In all animal seizures did not occur randomly and periods of high seizure frequency (clusters) were interspersed with periods of seizure absence or low seizure frequency. Examination of the cluster dynamics showed that in certain cases a progressive change in the seizure parameters marked an approaching termination of the seizure clustering.

Conclusion: This study demonstrates that seizures in the tetanus toxin model occur in temporally distributed clusters, which also display internal dynamics. Studies focused on the mechanisms which underlie changes in long-term probability of seizure occurrence can open new ways for the development of seizure forecasting techniques.

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REGULATION OF BRAIN P450 CYTOCHROME EXPRESSION IN A MOUSE MODEL OF SEIZURES

Boussadia B[1], Plaud C[1], Rousset M-C[1], Milesi S[1], DeBock F[1], Lakhal L[2], Pascussi J-M[3], Janigro D[4], Ghosh C[4], Marchi N[1]
[1]Department of Neurobiology, Institute of Functional Genomic – CNRS, Montpellier, France, [2]INRA, Toulouse, France, [3]Department of Oncology, Institute of Functional Genomic – CNRS, Montpellier, France, [4]Cleveland Clinic, Biomedical Engineer, Cleveland, OH, USA

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

Kapur J, Sun J
Neurology, University of Virginia, Charlottesville, VA, USA

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

Fabera P, Mares P
Department of Developmental Epileptology, Institute of Physiology, Academy of Sciences of Czech Republic, Prague, Czech Republic

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 harddisc. 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 epileptic 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")

Librizzi L, Noè FM, Bellistri E, de Curtis M
Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy

Purpose: To reconstruct the patterns of generation and propagation of epileptiform activity and to analyze the putative role of blood brain bar-

rier (BBB) permeability and inflammatory mediators release in seizure occurrence and maintainance.

Method: In the isolated brain preparation the tri-dimensional connectivity among brain structures as well as functional preservation of neuronal/glial, vascular and BBB compartments is maintained.

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-1b from astrocytes, reflecting cerebral inflammation. A rapid increase in $[K^+]_o$ and extravasation of intravascular FITC-albumin are observed, suggesting BBB impairment. IL-1b 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 underlie ictal events.

This abstract is presented for the FORUM SESSION "Integrated models for the study of seizure mechanisms".

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MOTOR COMPENSATION OF HEMISPHERIC LESIONS

Rüber T[1], Schoene-Bake J-C[1], Lindenberg R[2], Schramm J[3], Weber B[1], Elger CE[1]

[1]Department of Epileptology, Bonn University Hospital, Bonn, Germany, [2]Department of Neurology, Charité – University Medicine, Berlin, Germany, [3]Department of Neurosurgery, Bonn University Hospital, Bonn, Germany

Purpose: It has been hypothesized that motor compensation of hemispheric lesions is mediated by the reinforcement of contralesional uncrossed fibers of the pyramidal tract (PT_c), 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 PT_c and aMF in patients after hemispherectomy. We hypothesized that, if PT_c 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 PT_c and aMF separately.

Results: Voxel-wise analyses within delineated tracts revealed significantly lower FA values in patients as compared to controls along PT_c. Comparably higher FA values were solely found within aMF. Furthermore, voxel-wise analyses yielded significant motor function↓— FA↓ correlations along PT_c. 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 PT_c 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.

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AUTOIMMUNE EPILEPSY: THE ROLE OF ANTIBODIES

Tabrizi N, Abedini M

Mazandaran University of Medical Sciences, Sari, Iran

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 decarbodylase 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.

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ANTIEPILEPTIC DRUG BINDING TO POTASSIUM CHANNELS: ROLE OF AROMATIC RESIDUES

Nilsson J, Sahlholm K, Århem P

Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden

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 anaesthetics (e.g. bupivacaine) bind to Kv channels with a considerable affinity.

To explore the role of aromatic residues for local anaesthetic 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.

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.

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EISENMAN SELECTIVITY SERIES APPROACH TO EXPLAIN ABILITY FOR THE ONE-VALENCE SALTS OF THE INHIBITORY AMINO ACIDS (GLYCINE, β-ALANINE AND GABA) TO PASS THROUGH BBB

Shilau G

Byelorussian Medical Academia Postgraduate Education, Minsk, Belarus

Purpose: To search for the new anticonvulsants that could be devoid of the ususal 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 introventrical injection of GABA, glicine and β-alanine and their intraperitonial injection on the cerebral neurophisiological 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, pentylenetetrazol 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 (introventrical 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 (intraperitonial 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 (pentylenetetrazol 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).

p376
DISTURBANCES OF PARASYMPATHETIC SYSTEM IN SEIZURES WITH OXYGEN DESATURATION

De Jonckheere J[1], Troussière A-C[2], Derambure P[3], Logier R[1], Szurhaj W[3]

[1]Unité INSERM CIC-IT 807, Lille, France, [2]Lille Medical Center, Lille, France, [3]Lille2 University/Lille Medical Center, Lille, France

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: 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.

p377
MOTOR MAPS AREA ENLARGE IN CONDITIONS OF THE CHRONIC EPILEPSIES MODELS

Vastyanov RS, Shandra AA

Physiology, National Medical University, Odessa, Ukraine

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 postkinled 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 postkinling period no differences in the forelimbs motor cortical representation were seen. These results allow to conclude that brain chronic epileptization mechanisms involve certain cortical neurons reorganization into the principally new network with the new synaptic connections between different groups of the neurons.

p378
EFFECTS OF IL-1β SIGNALING ON SYNAPTIC PROTEINS AND STRUCTURAL INTEGRATION OF NEWBORN NEURONS IN THE ADULT MOUSE BRAIN

Avdic U, Chugh D, Ekdahl Clementson C
Department of Clinical Sciences, Lund University, Lund, Sweden

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), neurologin-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

Akman O[1], Gulcebi Idrisoglu M[2], Eryigit T[2], Yilmaz Onat F[2]
[1]Physiology, Istanbul Bilim University, Istanbul, Turkey,
[2]Pharmacology, Marmara University, Istanbul, Turkey

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 generalization of focal limbic seizures induced by kindling. We found that lidocaine injections into the SNRposterior obliterate the resistance to 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 and SNRanterior 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 animals. 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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USING THE STIGMA SCALE OF EPILEPSY (SSE) TO ASSESS EFFECTIVENESS OF AN EPILEPSY IN-SERVICE PROGRAMME FOR EDUCATORS

Mifsud J[1], Dimech V[2]
[1]Department of Clinical Pharmacology and Therapeutics, University of Malta, Msida, Malta, [2]Caritas Malta Epilepsy Association, Floriana, Malta

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 have 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.

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EPILEPSY AND ANTIEPILEPTIC DRUGS TREATMENT IN ELDERLY

Govori V[1], Vranica S[1], Berisha M[2], Zajmi D[2], Halilaj G[3], Koliqi R[4], Shala A[5]
[1]Neurology, Medical Faculty, University Clinical Center of Kosovo, University of Pristina, Pristina, Albania, [2]Social Medicine, Medical Faculty, National Institute of Public Health

of Kosova, University of Pristina, Pristina, Albania, [3]Ministry of Health of Kosovo, Pristina, Albania, [4]Farmacy, Medical Faculty, University of Pristina, Pristina, Albania, [5]Neurology, University Clinical Center of Kosovo, Pristina, Albania

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%, Insufficiencia 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

Conti G[1], Bresolin N[2]

[1]Department of Neuroscience, Fondazione I.R.C.C.S. Ospedale Maggiore Policlinico, Mangiagalli e Regina Elena, Milan, Italy, [2]Fondazione I.R.C.C.S. Ospedale Maggiore Policlinico, Mangiagalli e Regina Elena, Milan, Italy

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 having 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.

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REDUCED GREY MATTER VOLUME AND PROLONGED ARTERIAL ARRIVAL TIME IN AN MRI STUDY OF OCCULT CEREBROVASCULAR DISEASE IN LATE ONSET EPILEPSY

Hanby MF[1], Al-Bachari S[2], Vidyasagar R[3], Parkes L[4], Emsley H[5]

[1]Cardiovascular Sciences, University of Leicester, Leicester, UK, [2]Biomedical Imaging Institute, University of Manchester, Manchester, UK, [3]School of Cancer and Enabling Sciences, University of Manchester, Manchester, UK, [4]Imaging Sciences, University of Manchester, Manchester, UK, [5]Department of Neurology, Royal Preston Hospital, University of Manchester, Manchester, UK

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% O_2 and 79% CO_2), 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 $ETCO_2$.

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.

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CORRELATIONS BETWEEN EEG AND CT SCAN IN VASCULAR EPILEPSY

Sisak E[1]

[1]Emergency Hospital St.George, Neurology, Sf.-Gheorghe, Romania

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 attacks, 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?

Sone D[1,2], Taniguchi G[3], Mogi T[4], Murata Y[1], Watanabe Y[1], Okazaki M[1], Watanabe M[1]

[1]Department of Psychiatry, National Center of Neurology and Psychiatry, Epilepsy Center, Tokyo, Japan, [2]Department of Neuropsychiatry, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, [3]Department of Neuropsychiatry, The University of Tokyo Hospital, Tokyo, Japan, [4]Department of Psychiatry, National Defense Medical College, Saitama, Japan

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 ^{11}C-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

Chepreganova-Changovska T[1], Sazdova-Burneska S[2], Cvetkovska E[2]

[1]Department of Epilepsy, University Clinic of Neurology, Skopje, Macedonia, the Former Yugoslav, [2]University Clinic of Neurology, Skopje, Macedonia, the Former Yugoslav

Purpose: The aim of this study was to evaluate the clinical, and anatomo-morfological 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. MNR 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.

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DIFFICULTIES IN DIAGNOSING TRANSIENT LOSS OF CONSCIOUSNESS IN THE ELDERLY

El Tawil S[1], Duodu Y[1]

[1]Milton Keynes Hospital NHS Foundation Trust, Milton Keynes, UK

Purpose: Episodes of transient loss of consciousness may be caused by either syncope or epilepsy. Both conditions are common in the elderly and the clinical presentation may overlap. Unjustified use of antiepileptic medication can potentially worsen symptoms be provoking cardiac arrhythmias. This case demonstrates the practical difficulties in making a definite diagnosis in these situations

Method: Case report.

Results: A 94 years old man was admitted to hospital with global dysphasia and minimal right sided weakness secondary to an acute left frontal infarction. ECG and 24 h tape showed atrial fibrillation with a slow ventricular response. Few days after onset, he developed recurrent attacks of unresponsiveness with drop of GCS to 3/15. Attacks had no clear precipitant, and no relation to posture. Blood pressure was stable during episodes and heart rate was within his usual range. Episodes lasted 10–20 min, with gradual recovery over several hours. He was started on

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.

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HYPERPROLACTINEMIA AMONG WOMEN WITH EPILEPSY

Zhidkova I[1], Karlov V[1], Kaznacheeva T[1], Kunkina U[1], Berseneva V[1]
[1]Moscow State University of Medicine and Dentistry named after A.I.Evdokimov, Moscow, Russian Federation

Introduction: Hormonal abnormalities among women with epilepsy (WWE) are due to epilepsy-related 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).

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 ± 0.6 years) were enrolled in the study. Group I included 14 WWE using valproate; group II consisted of 16 WWE taking carbamazepine; group III – included 21 WWE using new AEDs (oxcarbazepine, lamotrigine, levetiracetam, topiramate); group IV – 11 WWE taking polytherapy. All women were investigated: sex hormones – luteinizing hormone (LG), follicle-stimulating hormone (FSH), prolactin (PRL), estradiol (E), progesteron (P), testosterone (T).

Results: Hyperprolactinemia was revealed among 23% of women using valproate (786 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 (olygomenorrhea) 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.

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POSTNATAL CONCERNS IN CHILDREN BORN TO WOMEN WITH JUVENILE MYOCLONIC EPILEPSY

Babić M[1,2], Jovic N[1,2]
[1]School of Medicine, University of Belgrade, Belgrade, Serbia,
[2]Clinic of Neurology and Psychiatry for Children and Youth, Belgrade, Serbia

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 levetiracetame-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. Caesarean 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.

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CORRELATION OF THE DEVELOPMENT OF MIGRAINE AND EPILEPSY IN WOMEN

Litovchenko T[1], Iakubenko I[1], Zinchenko O[1]
[1]Department of Neurology, Kharkiv Medical Academy of Postgraduate Education, Kharkiv, Ukraine

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, cardiography 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 affect 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

Andersen Becser N[1], Hansen R[1]
[1]Department of Neurology, Glostrup Hospital, Epilepsy Clinic, University Hospital of Copenhagen, Glostrup, Denmark

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 paient 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

Weckesser A[1], Denny E[2]
[1]Faculty of Health, Birmingham City University, Birmingham, UK, [2]Birmingham City University, Birmingham, UK

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 will 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

Pulman JL[1], Bromley RL[2,3], Marson AG[1]
[1]Molecular and Clinical Pharmacology, University of Liverpool, Liverpool, UK, [2]University of Manchester, Manchester, UK, [3]Central Manchester University Hospitals NHS Foundation Trust, Manchester, UK

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

Farmen AH[1], Grundt JH[2], Tomson T[3], Nakken KO[4], Nakling J[5], Lossius M[6]
[1]Department of Neurology and Clinical Neurophysiology, Innlandet Hospital Trust Lillehammer, Lillehammer, Norway, [2]Department of Pediatrics, Innlandet Hospital Trust Lillehammer, Lillehammer, Norway, [3]Department of Neurology, Karolinska Institutet, Stockholm, Sweden, [4]National Center for Epilepsy, Oslo University Hospital, Oslo, Norway, [5]Department of Gynecology and Obstetrics, Innlandet Hospital Trust Lillehammer, Lillehammer, Norway, [6]National Center for Epilepsy, Oslo, Norway

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 χ^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 ($p < 0.044$). 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

Odintsova GV[1]
[1]Neurology, Institute of Human Brain of RAS, Saint Petersburg, Russian Federation

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 uncontrollable 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 intaken 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

Vlasov P[1], Petrukhin V[2], Karlov V[1], Krasnopolski V[2], Melnikov A[2], Tsivtsivadze E[2]
[1]Department of Neurology of General Medical Faculty, Moscow State University of Dentistry and Medicine, Moscow, Russian Federation, [2]Moscow Region's Scientific Research Institute of Obstetrics and Gynecology, Moscow, Russian Federation

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 38 patients – 77.5% (cryptogenic – 46.9%, symptomatic – 30.6%), idiopathic generalized epilepsy in 6 patients – 12.2% and undetermined epilepsy in 5 patients – 10.2% of all cases in 1998 year. Respectively focal epilepsy was in 86 women – 76.1% (cryptogenic – 54.0%, symptomatic – 22.1%), idiopathic generalized epilepsy in 25 women 22.1% and undetermined epilepsy in 2 – 1.8% of all cases in 2013 year. 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%); bitherapy 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.

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THE EFFECTS OF ANTIEPILEPTIC DRUGS ON TRANSPORTER EXPRESSION IN HUMAN PLACENTA

Tetro N[1], Wohl D[2], Eisenberg I[2], Yagel S[2], Shmuel M[1], Rubinchik-Stern M[1], Eyal S[1]
[1]Institute for Drug Research, Hebrew University of Jerusalem, Jerusalem, Israel, [2]Hadassah Medical Center, Jerusalem, Israel

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.

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JUVENILE MYOCLONIC EPILEPSY PROGRESSION IN WOMEN OF REPRODUCTIVE AGE

Vlasov P[1], Petruhin V[2], Magzhanov R[3], Nurmukhametova S[3], Anisimova D[3]
[1]Moscow State University of Medicine and Dentistry named after A.I.Evdokimov, Moscow, Russian Federation, [2]Moscow Region's Scientific Research Institute of Obstetrics and Gynecology, Moscow, Russian Federation, [3]Bashkir State Medical University, Ufa, Russian Federation

Female epilepsy holds a specific place in epileptology, as woman's body has a more complicated structure, while epileptic seizures and long-term treatment with antiepileptic drugs may cause female reproductive system malfunctions.

Purpose: Aiming to study peculiarities of juvenile myoclonic epilepsy (JME) progression in women of childbearing age, we examined 35 women suffering from JME aged between 18 and 30. Average age of our patients was 24.47 ± 0.65. Average age of the disease onset was 14.26 ± 0.82. Average duration of the disease amounted to 10.21 ± 0.94.

Method: All patients filled in a specialized questionnaire. The next stage of the survey was blood sampling for hormonal investigations. Women with 28 days menstrual period duration were submitted to a blood test twice, on the 7th and 21th day respectively. We investigated the level of luteinizing hormone, follicle-stimulating hormone, estradiol, testosterone at the first phase of menstrual period and progesterone level at the second phase.

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 myoclonias, although only 17.6% of patients observe that their myoclonia 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 luteinizing 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.

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DEVELOPMENT OF METHODOLOGY FOR IMAGING THE EFFECTS OF ANTIEPILEPTIC DRUGS ON THE PLACENTAL BARRIER IN VIVO

Meir M[1], Bishara A[1], Portnoy E[1], Shmuel M[1], Eyal S[1]
[1]Institute for Drug Research, The Hebrew University of Jerusalem, Jerusalem, Israel

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 infra-red (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.

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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)

Mostacci B[1,2], Piccinni C[3], Bisulli F[1,2], Poluzzi E[3], Naldi I[1,3], Accetta G[1], Cocchi G[4], Curti A[5], D'Alessandro R[1], Tinuper P[1,2], ESPEA Group
[1]IRCCS Institute of Neurological Sciences of Bologna, Bologna, Italy, [2]Department of Biomedical and Neuromotor Sciences,

University of Bologna, Bologna, Italy, [3]Department of Medical and Surgical Sciences DIMEC, University of Bologna, Bologna, Italy, [4]Department of Maternal and Paediatric Sciences, Neonatology, St. Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy, [5]Division of Prenatal Medicine, Department of Medical and Surgical Sciences DIMEC, St. Orsola Malpighi Hospital, University of Bologna, Bologna, Italy

Purpose: To assess the prevalence of AntiEpileptic 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: Phenobarbital, Primidone, 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

Midi I[1], Bulut B[1], Ozbek D[1], Ozden HO[1], Agan K[1]
[1]Department of Neurology, Marmara University Hospital, Istanbul, Turkey

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 polyterapy 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 abnomaly 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

Molokwu OA[1], Onwuekwe I[1], Nwabueze A[1], Ezeala-Adikaibe B[1]
[1]Medicine, University of Nigeria Teaching Hospital (UNTH), Enugu, Nigeria

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 periovulation 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

Mantoan Ritter L[1], Kovac S[1], Miserocchi A[2], Valente I[1], Scott C[1], McEvoy A[2], Wehner T[1], Diehl B[1]

[1]Telemetry Department, National Hospital for Neurology and Neurosurgery, University College London Hospitals NHS Foundation Trust, London, UK, [2]Department of Neurosurgery, National Hospital for Neurology and Neurosurgery, University College London Hospitals NHS Foundation Trust, London, UK

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 $\pm$ 10 years) implanted with a total of 78 $\pm$ 17.5 electrode contacts: 66.2 $\pm$ 17.6 grid, 8.9 $\pm$ 6.8 strip and 13.4 $\pm$ 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 post-surgically at 1.87 $\pm$ 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

Jeong W[1,2], Jin S-H[1,3], Kim M[1], Kim JS[1], Chung CK[1,3,4]

[1]Department of Neurosurgery, MEG Center, Seoul National University Hospital, Seoul, Korea, [2]Interdisciplinary Program in Neuroscience, Seoul National University College of Natural Science, Seoul, Korea, [3]Neuroscience Research Institute, Seoul National University Medical Research Center, Seoul, Korea, [4]Department of Brain and Cognitive Sciences, Seoul National University College of Natural Sciences, Seoul, Korea

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 networ3k 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

Dalvit C[1], Valenti MP[1], Seegmuller C[2], Boulay C[1], De Saint-Martin A[3], Kherli P[4], Bartolomei F[5], Hirsch E[1]

[1]Neurologie, CHU Strasbourg, Strasbourg, France, [2]Neuropsychologie, CHU Strasbourg, Strasbourg, France, [3]Pediatrie, CHU Strasbourg, Strasbourg, France, [4]Neurochirurgie, CHU Strasbourg, Strasbourg, France, [5]Neurologie, CHU Timone, Marseille, France

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 develpmental malformation (MCD), 3 had DNET, 1 patient had hippocampal sclerosis, 1 had vascular malformation and 1 had Tuberosis Sclerosis. Mean age at epilepsy onset ranged from 6 months to 12 years. All patients who benefifed 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 disappearence 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 differenciate the two EEG traits. The co-existence of a these two EEG patterns does not preclude favorable outcome.

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ASYMMETRIC SEIZURE-RELATED MODULATION OF ATRIOVENTRICULAR CONDUCTION IN PEOPLE WITH BILATERAL MESIAL TEMPORAL LOBE EPILEPSY

Basili LM[1,2], Elger CE[1], Surges R[1]
[1]University Hospital Bonn, Bonn, Germany, [2]Department of Neurology, University of Rome "La Sapienza", Rome, Italy

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.

p408
FREQUENCY AND CLINICAL CORRELATES OF FRONTAL INTERMITTENT RHYTHMIC DELTA ACTIVITY IN THE ADULT NEUROLOGICAL INTENSIVE CARE UNIT

Dericioglu N[1], Arsava EM[1], Topcuoglu MA[1]
[1]Department of Neurology, Faculty of Medicine, Hacettepe University, Ankara, Turkey

Purpose: Frontal intermittent rhythmic delta activity (FIRDA) is characterized by transient rhythmic delta waves localized mainly over frontopolar 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 hyponatremia; 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.

p409
THE SENSITIVITY OF SHORT SLEEP EEG IN NEW ONSET EPILEPSIES

Yeni NS[1], Benbir G[1], Yavuz Demiray D[1], Delil Ş[1]
[1]Neurology, Istanbul University Cerrahpasa Medical School, Istanbul, Turkey

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.

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AUTOMATIC ANALYSIS AND TRENDING OF LONG-TERM SCALP EEG USING NEUROTREND

Fürbass F[1], Hartmann M[1], Perko H[1], Weinkopf M[1], Baumgartner C[2], Koren J[2], Herta J[3], Gruber A[3], Kluge T[1]
[1]AIT Austrian Institute of Technology GmbH, Vienna, Austria, [2]2nd Neurological Department, General Hospital Hietzing with Neurological Center Rosenhuegel, Vienna, Austria, [3]Department of Neurosurgery, Medical University of Vienna, Vienna, Austria

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 where detected correctly. The detection sensitivity did not rise significantly when periodic patterns were incorporated in addition (mean 82%, 95% CI 74–87.5%).

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.

p411
HIGH FREQUENCY (GAMMA ACTIVITY) EVOKED BY 50 HZ STIMULATION DURING SEEG PRESURGICAL EVALUATION

Bellistri E[1], Gnatkovsky V[1], Sartori I[2], Francione S[2], De Curtis M[1]
[1]Fondazione I.R.C.C.S. Istituto Neurologico C. Besta, Epilettologia Clinica e Neurofisiologia Sperimentale, Milano, Italy, [2]Ospedale Niguarda Ca Granda, Centro per la Chirurgia dell'Epilessia "C. Munari", Milano, Italy

Purpose: Epilepsy is ultimately a disease of functionally and structurally aberrant connections between neurons and groups of neurons at the systems level. Application of network analysis in epilepsy has provided valuable information both on seizure dynamics and on the interictal state of functional networks. Among data obtained from invasive studies with intracelebral electrodes during sEEG, we focused on response to high frequency (50 Hz) stimulation performed for diagnostic purposes to evaluate its dynamic of propagation through epileptic and normal brain.

Method: An automatic algorithm was developed with LabView in order to eliminate high frequency (HF) stimulation artifact and reveal the underlying signal oscillations. A semi-authomatic algorithm developed in MatLab was used to classify relationship between stimulation and response contacts according to the appearing of a specific pattern within the stimulation window. Signal power spectrum was computed using a multitaper function with a not-overlapping window of 1 s. Based on this classification, the connectivity between epileptogenic zone and surround tissue was evaluated by network analysis.

Results: Eliminating the HF stimulation artifact, different patterns can be recognized within the stimulation window: no change from the baseline, oscillation with a frequency locked to the frequency of stimulation, slow high amplitude oscillation followed by a HF oscillation not locked to the frequency of stimulation. Power spectrum analysis reveals a relative peak around 60–70 Hz in the latter oscillation pattern followed by an afterdischarge. Preliminary results obtained from n = 3 patients show a topology of the connectivity network that reflects the classification between epileptic and non-epileptic tissue performed by clinicians.

Conclusion: HF stimulation during sEEG recording induces different oscillation patterns within the stimulation window and across different brain regions, revealing a functional connectivity between them. A preliminary network analysis suggests that evaluation of network parameters can help to understand basic mechanisms of ictogenesis and seizure propagation.

p412
INCREASED VARIABILITY IN BACKGROUND SENSORIMOTOR NEURAL ACTIVITY IN BECTS

Koelewijn L[1], Brindley L[1], Routley B[1], Muthukumaraswamy S[1], Brookes M[2], Singh K[1], Hamandi K[3]
[1]CUBRIC, School of Psychology, Cardiff University, Cardiff, UK, [2]Sir Peter Mansfield Magnetic Resonance Centre, University of Nottingham, Nottingham, UK, [3]The Alan Richens Welsh Epilepsy Centre, University Hospital Wales, Cardiff, UK

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 to 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?

Guzmán García LC[1], Thonon VC[1], Sueiras Gil M[1], Santamarina E[2], Quintana M[2], Toledo M[2], Matinez R[1], Salas X[2]
[1]Clinical Neurophysiology, Hospital Universitari Vall d'Hebron, Barcelona, Spain, [2]Neurology, Hospital Universitari Vall d'Hebron, Barcelona, Spain

Purpose: SE is a neurogical emergency that requires immediate diagnosis and care. We aim to describe electrical and clinical features in a serie 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* standed 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.

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POSTICTAL GENERALIZED EEG SUPPRESSION AND PERIICTAL CARDIAC AUTONOMIC INSTABILITY IN PEDIATRIC PATIENTS WITH CONVULSIVE SEIZURES

Serino D[1], Flaccaveno B[2], Mattei E[2], Calcagnini G[2], Specchio N[1], Vigevano F[1], Fusco L[1]
[1]Child Neurology, Bambino Gesù Pediatric Hospital, Rome, Italy, [2]Italian Institute of Health, Rome, Italy

Purpose: Postictal generalized electroencephalographic suppression (PGES) might have a significant pathophysiological relationship with sudden unexpected death in epilepsy (SUDEP). Studies on the association between PGES and periictal cardiac autonomic instability have already been conducted in the adult population and have yielded conflicting results. Scarce data exists however regarding such association in the pediatric population. Purpose of this study was to evaluate the role of PGES as a possible risk factor for SUDEP in pediatric patients with convulsive seizures (CS).

Method: We conducted a retrospective study in 9 pediatric patients with CS recorded on digital video-electroencephalography (EEG): 6 patients with PGES and 3 patients without PGES. Patient age ranged between 6 months and 17 years. One CS per individual was reviewed. Heart rate (HR) variability was analyzed using time and frequency domain indexes. LF/HF ratio, computed as the ratio between the spectral power in the low frequency band (LF: 0.04–0.15 Hz) and the spectral power in the high frequency band (HF: 0.15–0.4 Hz), was used to evaluate the sympathetic vs. parasympathetic balance. HR variability analysis was performed over 4 min long heart period segments.

Results: In 5 out of 6 patients with PGES, HR was lower in the 5–10 min postictal period than in the preictal period and autonomic balance (LF/HF ratio) progressively increased after PGES. Patients without PGES showed a similar trend in the LF/HF ratio, but no changes in HR were observed.

Conclusion: The presence or absence of PGES did not have a significant impact on measures of cardiac autonomic instability in our patients. Such data suggests that PGES may not be considered as a reliable risk factor for SUDEP in the pediatric population.

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INTERICTAL EEG IN EILEPTIC CHILDREN

Khachidze I[1], Maloletnev V[1], Gugushvili M[2]
[1]Centre of Experimental Medicine and Tbilisi Medical Center, Tbilisi, Georgia, [2]Centre of Experimental Medicine, Tbilisi, Georgia

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.

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DIFFERENTIATION OF EEG PATTERNS IN PATIENTS WITH NONCONVULSIVE STATUS EPILEPTICUS FROM EEG PATTERNS IN PATIENTS WITH TRIPHASIC WAVE USING WAVELET ANALYSIS

Kang JK[1], Mullen T[2], Lee EM[3], Lee G-H[4], Jung K-Y[5], Makeig S[2]
[1]Department of Neurology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, [2]Swartz Center for

Computational Neuroscience, Institute for Neural Computation, University of California at San Diego, San Diego, CA, USA, [3]Department of Neurology, Ulsan University Hospital, Ulsan, Korea, [4]Department of Neurology, Pusan National University Hospital, Pusan, Korea, [5]Department of Neurology, Anam Hospital, Korean University College of Medicine, Seoul, Korea

Purpose: Distinguishing nonconvulsive status epilepticus (NCSE) from triphasic 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 triphasic 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.

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A ROBUST LOW COMPLEXITY ALGORITHM FOR REAL-TIME EPILEPTIC SEIZURE DETECTION

Bandarabadi M[1], Dourado A[1], CISUC Adaptive Computation Group (ACG)
[1]Informatics Engineering, University of Coimbra, Coimbra, Portugal

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.

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STATNET EEG A FAST AND RELIABLE OPTION IN PATIENTS SUSPECTED FOR NCSE

Ladino LD[1,2], Moien-Afshari F[2], Tellez-Zenteno JF[2]
[1]Hospital Pablo Tobon Uribe, Medellin, Colombia, [2]University of Saskatchewan, Saskatoon, SK, Canada

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.

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THE LONGITUDINAL STUDY OF FOCAL EEG FINDING IN TEMPORAL LOBE EPILEPSY: IS IT AGE-DEPENDENT?

Vojvodic NM[1], Nikolic DM[2], Vojvodic LM[3], Ristic AJ[1], Jankovic S[1], Kovacevic M[1], Sokic D[1]
[1]Epilepsy Center, Neurologi Clinic, Belgrade, Serbia, [2]Neurology, University Children's Hospital, Belgrade, Serbia, [3]St. Sava Hospital, Belgrade, Serbia

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; 37.90 ± 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.

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EEG CHRONOLOGICAL CHANGES DURING THE COURSE OF ANTI-NMDA RECEPTORS ENCEPHALITIS: A FOUR CASES STUDY

Rosenberg SD[1,2], Chanson E[1], Bicilli E[1], Brotelle T[3], Chabanne R[4], Lauxerois M[1], Rieu L[1], Dionet E[1], Beudin P[1], Clavelou P[1]

[1]Neurology - Neurophysiology, CHU Clermont-Ferrand, Clermont-Ferrand, France, [2]IGCNC - EA 7282, Université d'Auvergne, Clermont-Ferrand, France, [3]Oncology, CHU Clermont-Ferrand, Clermont-Ferrand, France, [4]Intensive Care, CHU Clermont-Ferrand, Clermont-Ferrand, France

Purpose: A specific EEG pattern in Anti-NMDA receptors (NMDAR) encephalitis, the extreme delta-brush (EDB) activity, has recently been 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. All drugs administered during EEG acquisition was carefully mentioned and taken into account for interpretation.

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: 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.

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DIFFERENCES IN CORTICAL EXCITABILITY BETWEEN WELL-CONTROLLED AND POORLY-CONTROLLED PATIENTS WITH EPILEPSY

Pawley AD[1], Nashef L[1], Ceronie B[1], Elwes R[1], Valentin A[1], Richardson MP[1]

[1]King's College London, London, UK

Purpose: 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 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 interosseus 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.

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p422
IS RASMUSSEN'S ENCEPHALITIS A NMDA ENCEPHALITIS? A CASE REPORT AND REVIEW OF LITERATURE

Proteasa S[1], Vargas L[1], Karkare S[1]

[1]NSH/LIJ Hospital, New Hyde Park, NY, USA

Objective: Challenging differential diagnosis.

Background: We describe the case of a 2 years old girl with no significant past medical history, who developed subacute onset of right hemiparesis, speech regression and epilepsia partialis continua on the right side of her body. Her EEG showed continuous delta slowing in the left hemisphere while her contrast brain MRI was normal. Rasmussen's Encepha-

litis (RE) was considered based on her clinical presentation. PET scan with FDG indicated diffuse hyper metabolism on the left and hypo metabolism 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 larger 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.

p423
TEMPORAL LOBE EPILEPSY SURGERY IN CHILDREN – ELECTROCLINICAL PROFILES AND OUTCOMES ACCORDING TO ETIOLOGY

Pereira CD[1], Jiménez MÁP[1], Del Castillo CF[1], Melero J[1], Budke M[1], Fernández MG[1], Linera JÁ[1], Ortega FV[1]
[1]Epilepsy Unit, Hospital Universitario Infantil Niño Jesús, Madrid, Spain

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. Postsurgically, 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

Ong H-T[1,2], Chiam EPJ[1], Low PC[1], Wang FS[1], Lim KJ[2]
[1]Khoo Teck Puat-University Children's Medical Institute, National University Health System, Singapore, Singapore, [2]Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore

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 hypsarrhythmia) 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

Elzbieta S[1], Iwona T[1], Dorota A-M[1], Alicja G-C[1], Paulina G[2], Renata T[2], Dorota H[2]
[1]Institute of Mother and Child, Clinic of Children and Adolescents Neurology, Warsaw, Poland, [2]Medical Genetics Department, Institute of Mother and Child, Warsaw, Poland

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.

Abstracts

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 Panayotopoulous syndrome (1 case per each respectively). Mutations were not detected in children with isolated febrile seizures, family febrile seizures nor in patients with myoclonic – astatic 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 Panayotopoulous 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.

p426
SELF-PERCEIVED CHANGES IN PSYCHOSOCIAL FUNCTIONING AND QUALITY OF LIFE IN CHILDREN AFTER RESECTIVE EPILEPSY SURGERY, A LONG-TERM FOLLOW-UP

Hallböök T[1], Tideman P[1], Rosén I[2], Lundgren J[3], Tideman E[4]
[1]Department of Pediatrics, Institution of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, [2]Department of Clinical Neurophysiology, Skane University Hospital, Lund, Sweden, [3]Department of Pediatrics, Skane University Hospital, Lund, Sweden, [4]Department of Psychology, Lund University, Lund, Sweden

Purpose: This follow-up study present long-term outcome (5–21 years) of changes in self-perceived psychosocial functioning and QoL after epilepsy-surgery in all children operated at Skanes University Hospital, Lund, Sweden 1991–2007.

Method: 44 children were assessed by a semi-structured interview, in which self-perceived changes in different aspects of psychosocial functioning were tapped by asking the patients to compare before and after surgery. QoL was assessed by a VAS-scale (1–10, 7 is mean-score in health-surveys). Occupations were described. In this presentation we focus on 21/44 without mental-retardation before surgery. Three had autism-spectrum-diagnosis, eight depression or contact with psychiatric-care. Fifteen were seizure-free; ten had stopped AED′s.

Results: In self-perceived mood, 8 (38.1%) scored better and 11 (52.4%) same. In self-perceived well-being 6 (28.6%) scored better and 13 (61.9%) same. Two, diagnosed with depression and not seizure-free, still on AED′s scored worse in both aspects. Eight (38.1%) scored better and 13 (61.9%) same in ability to maintain relationship. Eight (38.1%) made a clear statement that they had a satisfying number of friends. Thirteen (61.9%) reported too few friends, ten of these had a psychiatric diagnosis or a regular contact with psychiatric-care. Regarding QoL, 61.9% rated ≥7. Among those with seizure-freedom 73.3% rated ≥7. In the six without seizure-freedom two rated ≥7.

Of the 14/21 > 20 years, 10 (71.4%) were employed and four unemployed; one lived with parents, three had independent living. All 7 < 20 years went to ordinary school and lived with parents.

Conclusion: In this follow-up study a clinically meaningful change in self-perceived well-being and psychosocial function was demonstrated. Bad outcome was associated with psychiatric problems. Higher QoL-assessments were associated with seizure-freedom and no AED's. Epilepsy surgery in children offers suitable candidates a good chance of significantly improved seizure outcome and low rates of complications and seems to be compatible with good life prospects in a long-term perspective.

p427
OUT-OF-HOSPITAL MANAGEMENT OF CHILDREN WITH PROLONGED, ACUTE, CONVULSIVE SEIZURES IN SWEDEN

Hallböök T[1]
[1]Department of Pediatric Neurology, University of Gothenburg, Gothenburg, Sweden

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 neurologists, 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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p429
MEDICAL REDUCTION OF ROLANDIC SPIKES AND SPEECH DISORDERS REDUCTION. IS IT EQUAL?

Zaytsev DY[1], Titov NA[2]
[1]Psychiatry, Zaytsev's Neuropsychiatric Center, St.Petersburg, Russian Federation, [2]Neurology, Zaytsev's Neuropsychiatric Center, St.Petersburg, Russian Federation

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 Sultiame 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 inducted rolandic spikes reduction.

Conclusion:
1 Antiepileptic therapy does not lead to a reduction of speech disorders in children with rolandic spikes at different ages.
2 Sulthiame should not be recommended as a treatment for speech disorders in rolandic epilepsy.

p430
WEST SYNDROME: CLINICAL-ELECTROENCEPHALOGRAPHY CORRELATION

Fomina M[1]
[1]*Pediatric Clinic St. Marien Medical University, St Petersburg, Russian Federation*

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 angiomatosis 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-extensione). Hypsarrhythmia was an obligate interictal pattern. A classic option is indicated by 21 patients, 11 – modified version of hypsarrhythmia (asymmetric, hypsarrhythmia with episodes of voltage attenuation with pattern «flash-suppression», hypersynchronous). 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.

p431
A CHILD WITH ICTAL VOCALIZATIONS AND GENERALIZED EPILEPSY

Kurian M[1], *Korff C*[1]
[1]*Pediatrics, University Hospital, Geneva, Switzerland*

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 non-speech 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.

p432
NEURODEVELOPMENT IN PRESCHOOL CHILDREN OF FIFE AND LOTHIAN EPILEPSY STUDY: NEUROPROFILES – A POPULATION-BASED STUDY

Hunter MB[1,2], *Sumpter R*[1,2], *Verity K*[1,2], *Chin RF*[1,2]
[1]*Muir Maxwell Epilepsy Centre, University of Edinburgh, Edinburgh, UK,* [2]*Royal Hospital For SIck Children, Edinburgh, UK*

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 Responsiveness Scale-2, Adaptive Behaviour Assessment System-II, Infant Toddler Social Emotional Assessment, and Behaviour Rating Inventory of Executive Function-Preschool. Matched controls are being recruited through public advertisement. Eye-tracking and brain MRI correlates with psychometric findings 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.

p433
THE CHARACTERISTICS OF EPILEPTIC CHILDREN HOSPITALIZED IN EPILEPSY CENTER FOR CHILDREN IN POLAND

Winczewska-Wiktor A[1], Malendowicz- Major B[1], Steinborn B[1]
[1]Department of Developmental Neurology, University of Medical Sciences, Poznan, Poland

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%), neurasthenia (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 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 microgryia 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

Gumbelevičienė L[1], Endzinienė M[1,2], Vaičienė-Magistris N[1,2]
[1]Neurology Department, Hospital of Lithuanian University of Health Sciences Kaunas Clinics, Kaunas, Lithuania, [2]Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

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

Prato G[1], Mancardi MM[1], Janis S[1], Gagliardi A[1], Baglietto MG[1]
[1]Epilepsy Centre, Child Neuropsychiatry Unit, Giannina Gaslini Children's Hospital, Genoa, Italy

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

Kim W-S[1]
[1]Chungbuk National University, Cheongju, Korea

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 neurological outcomes of the subjects.

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

Globa O[1], Gromyko O[2], Averianova N[2], Kuzenkova L[1], Pinelis V[2], Savost'yanov K[2]
[1]Neurology, Scientific Center of Children Health, Moscow, Russian Federation, [2]Genetic, Scientific Center of Children Health, Moscow, Russian Federation

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* S1(T341C), S2 (G598A), S3(G857A) 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 (G681A)-9 hetero and 1 homozygous (30%), CYP2D6 (G1934A)-hetero 11, homo 2 (39.4%), CYP2D6 (DelA2637)-6 (18.2%) – totally on CYP2D6-19 (57.6%). The 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 increases not depending of the dose of VPA. Eight children from these group didn't have the CYP450 polymorphisms, only in GSTM1, GSTT1 and 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.

p439
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

Ebus SCM[1], den Boer JT[1], van de Does A[1], Debeij-van Hall MHJA[1], Boon PJ[1,2], Aldenkamp AP[1,3,4], Arends JBAM[1,4]
[1]Kempenhaeghe/Academic Center of Epileptology, Heeze, The Netherlands, [2]Ghent University Hospital, Ghent, Belgium, [3]Maastricht University Medical Center, Maastricht, The Netherlands, [4]University of Technology Eindhoven, Eindhoven, The Netherlands

Purpose: We prospectively determined the 2-year time-course of the IED frequency in children with benign focal epilepsies (BFE) and/or typical EEG. 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 wakefulness and 30 pages in sleep were categorized as: [No IEDs], [10–50%], [50–80%] or [80–100%] on the page (1 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 yet 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.

p440
ENDOSCOPIC DISCONNECTION OF HYPOTHALAMIC HAMARTOMA IN CHILDREN WITH DRUG RESISTANT EPILEPSY: TECHNIQUE AND RESULTS REGARDING A POPULATION OF 94 PATIENTS

Fohlen MJ[1], Dorfmuller G[2], Ferrand-Sorbets S[2], Bulteau C[2], Taussig D[2], Chipaux M[2], Delalande O[2]
[1]Chidl Neurosurgery, Fondation Rothschild, Paris, France, [2]Fondation Rothschild, Paris, France

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 term 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 dacrystic seizures as first seizure type. Mental retardation was present in 58.5%. 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 (1).

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.

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EPILEPSY OUTCOME IN ACUTE ENCEPHALOPATHY WITH INFLAMMATION-MEDIATED STATUS EPILEPTICUS (AEIMSE): REPORT OF FOUR CASES

Janis S[1], Mancardi M[1], Granata T[2], Ragona F[2], Giribaldi G[3], Prato G[1], Gagliardi A[1], Baglietto MG[1]
[1]Neuropsychiatry, Istituto Giannina Gaslini, Genova, Italy,
[2]Neuropsychiatry, Istituto Neurologico C. Besta, Milano, Italy,
[3]Intensive Care Unit, Istituto G. Gaslini, Genova, Italy

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 immunoistochemical 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 response was poor in all cases, one case responded to intravenous immunoglobulins (IVIG), one responded to IVIG and high dose steroids (Prednisone), the other two presented a surprising response to plasmapheresis (performed after IVIG and high dose steroids). After acute phase, patients presented different degrees of cognitive impairment associated, in three of them, with drug-resistant epilepsy and, in one case, with relevant paroxysmal abnormalities rebound after 2 years (no seizure to date). The neuropsychological evaluation after the acute phase and characteristics of EEG and seizures at follow-up are described.

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.

p442
EFFICACY AND SAFETY OF LACOSAMIDE IN EPILEPTIC SYNDROMES WITH CONTINUOUS SPIKE AND WAVES DURING SLOW SLEEP (CSWS)

Grosso S[1], Parisi P[2]
[1]Department of Pediatrics, University of Siena, Siena, Italy,
[2]NESMOS Department, Faculty of Medicine and Psychology, Child Neurology, Chair of Pediatrics, "Sapienza University", Rome, Italy

Purpose: Epileptic syndromes with continuous spikes-waves during sleep (CSWS) represent a wide spectrum of epileptic disorders having CSWS as a common EEG-feature. Defined therapeutic strategies are still lacking. We evaluated the efficacy of lacosamide add-on therapy on the EEG, behavior, and cognition in children with CSWS.

Method: Twelve children with CSWS refractory to other conventional antiepileptic drugs were included in the study. A 24-h EEG recording was performed at 6 month-interval in all patients. The spike-wave index (SWI) was obtained in each 24-h EEG recording. Neuropsychological data were obtained before lacosamide introduction and after a minimum of 12 months of therapy.

Results: After a 8-month period of therapy, 66.6% of patients was defined as responder, 16.6% as partial responder and another 16.6% as non-responder. In particular, 24-h EEG normalized in 4 cases (33.3%). After a minimum of 12 months, 24-h EEG normalized in another two patients. Neuropsychological functions slightly improved in 25% of patients.

Conclusion: Although further studies are needed to validate our observations, this study suggests that lacosamide add-on therapy may be safe and effective in children affected by CSWS.

p443
NOCTURNAL FRONTAL LOBE EPILEPSY IN MUCOPOLYSACCHARIDOSIS

Bonanni P[1], Negrin S[1], Antoniazzi L[1], Rendazzo G[1], Nobili L[2]
[1]Epilepsy and Clinical Neurophysiology Unit, IRCCS Eugenio Medea, Conegliano, Italy, [2]'Claudio Munari" Epilepsy Surgery Centre, Niguarda Ca'Granda Hospital, Milan, Italy

Purpose: Nocturnal frontal lobe epilepsy (NFLE) is an epileptic syndrome that is primarily characterized by seizures with motor signs occurring almost exclusively during sleep.

Method: We describe 2 children with mucopolysaccharidosis (MPS) who were referred for significant sleep disturbance.

Results: Long term video-EEG monitoring (LT-VEEGM) demonstrated sleep-related hypermotor seizures consistent with NFLE.

Conclusion: No case of sleep-related hypermotor seizures has ever been reported to date in MPS. However, differential diagnosis with parasomnias has been previously discussed. The high frequency of frontal lobe seizures causes sleep fragmentation, which may result in sleep disturbances observed in at least a small percentage of MPS patients. We suggest monitoring individuals with MPS using periodic LT-VEEGM, particularly when sleep disorder is present.

Moreover, our cases confirm that NFLE in lysosomal storage diseases may occur, and this finding extends the etiologic spectrum of NFLE.

p444
COULD VAGUS NERVE STIMULATION SERVE AS FIRST LINE OF TREATMENT FOR EPILEPSY IN RETT SYNDROME?

Anghelescu C[1], Butoianu N[1], Tarta-Arsene O[1], Leanca M[1], Dica A[1], Brehar F[2], Tascu A[2], Craiu D[1]
[1]Pediatric Neurology Department, Alexandru Obregia Hospital, Bucharest, Romania, [2]Neurosurgery Department, Bagdasar-Arseni Hospital, Bucharest, Romania

Purpose: Rett Syndrome (RTT) is an X-linked neurodevelopmental disorder characterized by decelaration oh 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 Stimulatior (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 as 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 spams, 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 neccesary to confirm this hypothesis.

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EPILEPSY IN RETT SYNDROME: LESSONS FROM THE RETT NETWORKED DATABASE

Nissenkorn A[1,2], Bondi O[3], Levi Drumer R[3], Renieri A[4], Villard L[5], Mari F[4], Mencarelli MA[4], Lo Rizzo C[4], Meloni I[4], Pineda M[6], Armstrong J[6], Clarke A[7], Bahi-Buisson N[8], Mejaski Bosnjak V[9], Djuric M[10], Craiu D[11], Djukic A[12], Pini G[13], Bisgaard AM[14], Melegh B[15], Vignoli A[16], Russo S[17], Anghelescu C[11], Veneselli E[18], Hayek J[19], Ben-Zeev B[1]
[1]Sheba Medical Center, Tel Hashomer, Israel, [2]Tel Aviv University, Tel Aviv, Israel, [3]Bar Ilan University, Givat Shmuel, Israel, [4]University of Siena, Siena, Italy, [5]Inserm, Marseille, France, [6]Hospital Sant Joan de Deu, Barcelona, Spain, [7]Cardiff University, Cardiff, UK, [8]Universite Paris Descartes, Paris, France, [9]University of Zagreb Medical School, Zagreb, Croatia, [10]University of Belgrade, Belgrade, Serbia, [11]Carol Davila University of Medicine, Bucharest, Romania, [12]Albert Einstein College of Medicine, Yeshiva University, New York, NY, USA, [13]Tuscany Rett Center Versilia Hospital, Lido di Camaiore, Italy, [14]Rigshospitalet, Copenhagen, Denmark, [15]University Medical School, Pecs, Hungary, [16]University of Milan, Milan, Italy, [17]Instituto Auxologico Italiano, Milan, Italy, [18]G Galini Hospital, Genova, Italy, [19]University Hospital AOUS of Siena, Siena, Italy

Purpose: Rett syndrome is an X linked dominant neurodevelopmental disorder with autistic regression, loss of hand usage and midline hand stereotypies. Epilepsy is a core symptom, but literature is controversial regarding genotype phenotype correlation. Analyzing data from a large cohort should overcome these shortcomings.

Method: Data from 1248 female patients from The Rett Networked Database was included. Phenotypic and genotypic parameters, age of onset and severity of epilepsy, type of seizures were collected. Statistical analysis was done using the IBM ™SPSS™ Version 21 software.

Results: Epilepsy was present in 67% of patients, in 32.3% of them epilepsy was difficult to control. Age of onset of epilepsy was 4.68 ± 3.5 years. There was a marginal negative correlation between age of onset of epilepsy and severity of epilepsy (Spearman correlation $r = -1.4$, $p < 0.01$). Patients with late truncating mutation were less likely to have epilepsy. Compared to them, patients with p.R133C mutation, associated with a clinical forme fruste, had an increased risk for epilepsy (OR 2.46, 95% CI 1.3–4.66), but was mild (OR 2.59, 95% CI 1.33–5.02). The p.R255X mutation conferred an increased risk for epilepsy (OR 2.07, 95% CI 1.2–3.59) as well as for severe epilepsy (OR 3.4, 95% CI 1.6–7.3). The p.T158M and p.C306C mutations had increased risk for severe epilepsy (OR 3.09/2.69, 95% CI 1.48–6.4/1.19–6.05, but not for epilepsy.

Conclusion: These results are different from previously reported in literature, possibly due to epigenetic factors and modifier genes. Further investigation of these mechanisms should promote better understanding of epileptogenesis in Rett syndrome.

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EPILEPSY IN 16P11.2 MICRODELETION: DESCRIPTION OF EPILEPTIC PHENOTYPE IN 5 CHILDREN

Ragona F[1], Freri E[1], Zibordi F[1], Rizzo A[2], Sciacca F[2], Girgenti V[2], Casellato S[3], Matricardi S[4], Binelli S[5], Granata T[1]
[1]Pediatric Neuroscience, Foundation I.R.C.C.S. Neurological Institute C. Besta, Milan, Italy, [2]Unit of Clinical Pathology and Medical Genetics, Foundation I.R.C.C.S. Neurological Institute C. Besta, Milan, Italy, [3]Child Neuropsychiatry Unit, University Hospital, Sassari, Italy, [4]Department of Pediatric, University of Chieti, Chieti, Italy, [5]Clinical Neurophysiology and Epilepsy Center, Foundation I.R.C.C.S. Neurological Institute C. Besta, Milan, Italy

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 stereotypies. The 16p11.2 microdeletion included the following genes with a potential role in epileptogenesis: QPRT (quinolinate phosphoribosyltranferase), DOC2A

(double C2-like domain-containing protein alpha) e SEZ6L2 (seyzure related 6 homolog mouse-like). The region also included PRRT2 gene, that may explain the presence of paroxysmal kinesigenic dyskinesia observed in one patient.

Conclusion: In our series, differently from what reported in literature, epilepsy was the presenting symptom of 16p11.2 microdeletion syndrome. Associated symptoms, such as mental retardation and dysmorhisms were present at our first observation, albeit mild and therefore overlooked. The presence of non-epileptic paroxysmal disorders in 2 out of 5 patients adds a new finding that can explain the co-occurrence of epilepsy and movement disorder through a common genetic background.

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EPILEPSY IN CHILDREN WITH RARE GENETIC DISORDERS

Jotovska O[1]

[1]*Institute for Mental Health of Children and Youth, Skopje, Macedonia, the Former Yugoslav*

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, comobrid 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-Hirschhron 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-Hirschhron 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 antiepileptics 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.

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OUTCOME OF INFANTILE SPASMS WITH ACTH TREATMENT IN HOLOPROSENCEPHALY PATIENTS-CASE REPORTS

Sandu C[1], *Butoianu N*[1], *Barca D*[1], *Iliescu C*[1]

[1]*Alexandru Obregia Clinical Hospital, Bucharest, Romania*

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 holoprosencehaly 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 6 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.

p450
DRUG-RESISTANT EPILEPSY AND EPILEPTIC SYNDROMES IN CHILDREN

Myrzaliyeva B[1], *Lepessova M*[1]

[1]*Child Neurology and Medical Genetics, Almaty State Institute of Advanced Medical Education, Almaty, Kazakhstan*

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 3 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

in-depth study of cerebral metabolism, genetic research and application of high resolution MRI and EEG.

p451
EFFECT OF MODIFICATIONS OF THE NATIONAL VACCINATION PROGRAM ON SEIZURE RISK FOLLOWING PERTUSSIS VACCINATION IN DRAVET SYNDROME PATIENTS IN THE NETHERLANDS

Verbeek NE[1], Sonsma A[1], Ippel E[1], Vermeer-de Bondt PE[2], Gunning WB[3], Jansen FE[4], Kempen M[1], Knoers N[1], Lindhout D[1], van der Maas NAT[2], Brilstra EH[1]

[1]Department of Medical Genetics, University Medical Center Utrecht, Utrecht, The Netherlands, [2]RIVM, Bilthoven, The Netherlands, [3]The Epilepsy Institutes of the Netherlands Foundation (SEIN), Zwolle, The Netherlands, [4]Department of Child Neurology, University Medical Center Utrecht, Utrecht, The Netherlands

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 (9%, 3 of 33, resp. 8%, 2 of 24 vaccinations) than for wP-vaccines (37%, 16 of 43 vaccinations). Likewise, regression analysis showed Odds of 0.18 (0.05–0.71) and 0.11 (0.02–0.59), for aP- and non-pertussis vaccines, after adjustment for potential confounders (wP set as reference).

Conclusion: Replacement of whole-cell by acellular pertussis vaccine in the national vaccination program, led to fewer vaccination-associated seizures in DS-patients, whereas earlier start of vaccinations did not induce earlier seizure onset.

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BITEMPORAL EPILEPSY: A SPECIFIC PHENOTYPE IN THE TEMPORAL LOBE EPILEPSY SPECTRUM?

Villani F[1], Chiesa V[2], Didato G[1], Pelliccia V[3], Deleo F[1], Gozzo F[3], Canevini MP[2], Mai R[3], Spreafico R[1], Cossu M[3], Tassi L[3]

[1]Clinical Epileptology, Foundation Neurological Institute C. Besta, Milano, Italy, [2]Neurology 2 Unit, Epilepsy Center, San Paolo Hospital, Milano, Italy, [3]Epilepsy Surgery Centre C. Munari, Milano, Italy

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: 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.

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EFFICACY OF THE KETOGENIC DIET IN DRAVET SYNDROME VS. OTHER THERAPIES- WHEN TO START WITH?

Dressler A[1], Trimmel- Schwahofer P[1], Reithofer E[1], Mühlebner A[1], Gröppel G[1], Reiter-Fink E[1], Benninger F[2], Grassl R[2], Feucht M[1]

[1]Abteilung für Allgemeine Pädiatrie und Neonatologie, Universitätskinderklinik, Medizinische Universität Wien, Wien, Austria, [2]Abteilung für Kinderpsychiatrie, Universitätsklinik für Kinderpsychiatrie, Medizinische Universität Wien, Wien, Austria

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

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 Levetiracetam (70%: 30%) ($p = 0.037$). 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.

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INCREASED FREQUENCY OF PRE-EXISTING SEZURES DUE TO VOLTAGE-GATED POTASSIUM CHANNELS (VGKC) – COMPLEX-ASSOCIATED LGI1 AUTOANTIBODIES ENCEPHALITIS

Gross-Paju K[1,2], Sorro U[1], Reitsnik A[1], Kannel K[1], Vahter L[1]
[1]Neurology, West-Tallinn Central Hospital, Tallinn, Estonia, [2]Institute of Clinical Medicine, Tallinn University of Technology, Tallinn, Estonia

35 year old female patient was admitted on 27.03.2013 with spells of „tingling feeling" on the 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-injurying 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 brasilian 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 LGI 1 antibodies were positive (LGI 1 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 i/v. After the treatment all her symptoms resolved and her repeated EEG was normal.

p455
NMDA RECEPTOR ENCEPHALITIS PRESENTING AS PARTIAL STATUS EPILEPTICUS: CASE REPORT AND DISCUSSION

Proteasa S[1], Lajoie J[1], Maytal J[1]
[1]NSH/LIJ Hospital, New Hyde Park, NY, USA

Objective: Challenging differential diagnosis.

Background: Anti-NMDA receptor encephalitis develops in 5 distinct phases:

1 The Prodrom.
2 The Psychotic phase.
3 The Non-responsiveness.
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 noncontrast 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

Kopyta I[1], Sarecka-Hujar B[2], Balcerzyk A[3], Niemiec P[3], Zak I[3], Emich-Widera E[1]
[1]Department of Neuropediatrics, School of Medicine, Medical University of Silesia, Katowice, Poland, [2]Department of Applied Pharmacy, Medical University of Silesia, Sosnowiec, Poland, [3]Department of Biochemistry and Medical Genetics, Medical University of Silesia, Katowice, Poland

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, 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, OR = 2.53 [0.79–8.14]) and 20% (p = 0.002, 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.

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p457
IDENTIFICATION OF VARIANTS IN MICRORNA GENES INVOLVED IN EPILEPTIC ENCEPHALOPATHIES

Roovers J[1,2], Cammaerts S[1,2], Strazisar M[1,2], Lemke J[3], Weckhuysen S[1,2], De Jonghe P[1,2,4], Del-Favero J[1,2,5], Suls A[1,2], RES-EuroEPINOMICS

[1]VIB-DMG, Antwerp, Belgium, [2]University of Antwerp, Antwerp, Belgium, [3]University Children's Hospital Inselspital, Bern, Switzerland, [4]Antwerp University Hospital, Antwerp, Belgium, [5]Multiplicom NV, Niel, Belgium

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 of EE. Using multiplex PCR combined with massively parallel sequencing, we will screen microRNAs and microRNA biogenesis genes in patients with EE.

Method: Two "Multiplex Amplification of Specific Targets for Resequencing" (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 (*AGO2*, *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.

p458
OCCURRENCE OF GLUT1 DEFICIENCY SYNDROME IN PATIENTS TREATED WITH KETOGENIC DIET

Selmer KK[1], Ramm-Pettersen A[2], Nakken KO[2]

[1]National Centre for Rare Epilepsy-Related Disorders, Oslo University Hospital, Oslo, Norway, [2]Refractory Epilepsy, Oslo University Hospital, Sandvika, Norway

Purpose: GLUT1 deficiency syndrome (GLUT1-DS) is a treatable metabolic encephalopathy caused by a mutation in the SLC2A1 gene. This mutation causes a compromised transport of glucose across the blood-brain barrier. The treatment of choice is ketogenic diet, with which most patients become seizure free. At the National Centre for Epilepsy, we have since 2005 offered treatment with ketogenic diet (KD) and modified Atkins diet (MAD) to children with difficult-to-treat epilepsy. As we believe many children with GLUT1-DS are unrecognized, the aim of this study was to search for GLUT1-DS patients among those who had been responders (>50% reduction in seizure frequency) to KD or MAD.

Method: We retrospectively reviewed the medical records of all children (0–16 years) treated with KD and MAD at the epilepsy centre in the period February 2005-February 2012.

Results: Of the 130 children included, 58 (44%) were defined as responders. Among these, 11 were already diagnosed with GLUT1-DS. No mutations in the SLC2A1 gene were detected in the remaining patients. However, the clinical features of these patients differed considerably from the patients diagnosed with GLUT1-DS. While 9 out of 10 GLUT1-DS patients became seizure free with dietary treatment, only 3 out of 33 of the remaining patients were seizure free with KD or MAD treatment.

Conclusion: 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.

p459
RARE EPILEPTIC SYNDROMES STUDIED WITH EXOME SEQUENCING

Fjaer R[1,2], Brodtkorb E[3,4], Chaudhry FA[5], Aaberg KM[6], Vigeland MD[1,2], Sheng Y[1], Øye A-M[1], Hjorthaug H[1], Selmer KK[1,2]

[1]Department of Medical Genetics, Oslo University Hospital, Oslo, Norway, [2]Department of Medical Genetics, University of Oslo, Oslo, Norway, [3]Norwegian University of Science and Technology, Trondheim, Norway, [4]Neurology and Clinical Neurophysiology, St Olavs Hospital, Trondheim University Hospital, Trondheim, Norway, [5]Institute of Basic Medical Sciences, University of Oslo, Oslo, Norway, [6]Department of Refractory Epilepsy, SSE, Oslo University Hospital, Oslo, Norway

Purpose: The purpose of the study was to discover disease-causing genes in patients with rare epilepsy syndromes.

Method: Small families with rare epileptic syndromes were selected. These were studied with exome sequencing of trios or sib-ships. Findings were validated with Sanger sequencing.

Results: At the beginning of 2014, 6 families had been exome-sequenced (3 trios and 3 sib-ships). A probable genetic cause had been identified in half of them. In a sib-ship of two affected sisters with generalized tonic-clonic seizures and basal ganglia calcifications, a heterozygous missense mutation in *SLC20A2* was found. A 13 year old girl with multiple seizure types, ataxia and developmental regression, with a

suspected metabolic disorder, was found to have a heterozygous *de novo* missense 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 *KCTD7*. In two sib-ships 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.

p460
SCN2A MUTATIONS: EXPANDING THE PHENOTYPE TO AUTISM, LATE-ONSET SEIZURES AND ACUTE ENCEPHALITIS WITH REFRACTORY, REPEATED PARTIAL SEIZURES

Korff CM[1], Gaiser U[2], Turner A[3], Grasshoff U[4], Wolff M[2]
[1]University Hospitals, Geneva, Switzerland, [2]University Children's Hospital, Tübingen, Germany, [3]Sydney Children's Hospital, Randwick, NSW, Australia, [4]Eberhard-Karls University, Tübingen, Germany

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 multiple 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 (AERRPS). 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.

p461
RARE COPY NUMBER VARIATION IS COMMON IN ROLANDIC EPILEPSY AND DISRUPTS KNOWN EPILEPSY GENES

Addis L[1], Newhouse S[1], Topp SD[1], Carabello R[2], Pruna D[3], Thomas S[4], Pal DK[1]
[1]Insititute of Psychiatry, King's College London, London, UK, [2]Hospital de Pediatria "Prof Juan P Garrahan", Buenos Aires, Argentina, [3]Clinica di Neuropsichiatria Infantile, Cagliari, Italy, [4]Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, India

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 Omni-Express arrays. CNVs were called using PennCNV whilst incorporating GC correction. Cut-offs for CNV calling; >15 SNPs and >20 Kb in size. CNVs were further validated by >90% overlap with QuantiSNP 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.

p462
CHD2 MUTATIONS PRODUCE AN EARLY CHILDHOOD ENCEPHALOPATHY WITH PROMINENT PHOTOSENSITIVE SEIZURES

Thomas RH[1,2], Zhang LM[1,3], Carvill GL[4], Archer JS[1], Heavin SB[1], Mandelstam SA[5,6], Craiu D[7], Berkovic SF[1], Gill DS[8], Scheffer IE[1,6,9], EuroEPINOMICS-RES
[1]Epilepsy Research Centre, University of Melbourne, Melbourne, Vic., Australia, [2]MRC Centre for Neuropsychiatric Genetics & Genomics, Cardiff University, Cardiff, UK, [3]Children's Hospital of Fudan University, Shanghai, China, [4]University of Washington, Seattle, WA, USA, [5]Departments of Radiology and Paediatrics, University of Melbourne, Melbourne, Vic., Australia, [6]Florey Institute Melbourne, Melbourne, Vic., Australia, [7]Pediatric Neurology Clinic, Carol Davila' University of Medicine, Bucharest, Romania, [8]TY

Nelson Department of Neurology, The Children's Hospital at Westmead, Sydney, NSW, Australia, [9]Departments of Paediatrics, Royal Children's Hospital, Melbourne, Vic., Australia

Purpose: To delineate the phenotype of early childhood epileptic encephalopathy associated with *de novo* mutations of *CHD2*, which encodes the chromodomain-helicase-DNA-binding protein 2.

Methods: The medical history, MRI and video-EEG recordings of nine individuals with *de novo CHD2* mutations and one with a *de novo* 15q26 deletion encompassing *CHD2* were analysed.

Results: The 10 patients had a mean age of 17.9 years (range 6–36 years) at last contact. Seizures began at a mean of 26 months (12–42) with myoclonic seizures in all ten cases. 7 exhibited exquisite clinical photosensitivity; 6 self-induced with the television. Absence seizures occurred in 9 including typical (5), atypical (2) and absence seizures with eyelid myoclonias (4). Generalised tonic-clonic seizures occurred in 9/10 with mean onset 5.8 years. Convulsive and non-convulsive status epilepticus were later features (6/10, mean onset 9 years). Tonic (40%) and atonic seizures (30%) occurred. In 3 cases an unusual seizure type, the atonic-myoclonic-absence was captured on video. A phenotypic spectrum was identified with 7 cases having moderate to severe intellectual disability and refractory seizures including tonic attacks. Their mean age of onset was 23 months. Three cases had a later age of onset (34 months), relative preservation of intellect and initially seizures were responsive to anti-epileptic medication. Imaging showed posteriorly predominant atrophy with particular involvement of the splenium of the corpus callosum.

Conclusion: The phenotypic spectrum of *CHD2* encephalopathy has the distinctive features of myoclonic epilepsy, marked clinical photosensitivity, atonic-myoclonic-absence and intellectual disability ranging from mild to severe. Recognition of this genetic entity will permit earlier diagnosis and enable the development of targeted therapies.

p463
GENOME WIDE ASSOCIATION STUDY FOR CUTANEOUS ADVERSE REACTION OF LAMOTRIGINE

Kim W-J[1], Kim SW[2], Lee JH[2], Heo K[1], Lee MG[2], Lee BI[1]
[1]Neurology, Yonsei University College of Medicine, Seoul, Korea, [2]Pharmacology, Yonsei University College of Medicine, Seoul, Korea

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 for lamotrigine with genome wide association study.

Method: Thirty-three Korean epilepsy patients with skin rash derived by LTG was genotyped with Affynetrix 500k sNp array and age matched l2 l4 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
LGI1 EXPRESSION IN GLIOBLASTOMA MULTIFORME WITH AND WITHOUT EPILEPSY

Michelucci R[1], Dazzo E[2], Pasini E[1], Furlan S[2], De Biase D[3], Nobile C[2]
[1]IRCCS Institute of Neurological Science of Bologna, Bologna, Italy, [2]CNR Neuroscience Institute, Padova, Italy, [3]DIMES, University of Bologna, Bologna, Italy

Purpose: LGI1, 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, LGI1 disruptions can be partly responsible for two such different conditions such as GBM and epilepsy. We hypothesized that the expression of LGI1 in GBM could be influenced by the coexistence of epilepsy.

Method: We studied the expression of LGI1 in tumoral specimens of 23 patients with GBM, 10 of them showing epilepsy and 13 displaying other clinical features. The expression of LGI1 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 LGI1 expression in tumor tissues of both subgroups with or without epilepsy and no overall significant difference between them. Western blot analysis detected Lgi1 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 Lgi1.

Conclusion: These data suggest that LGI1 expression in GBM tumoral 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

Chaves J[1], Leal B[2], Barreira A[2], Carvalho C[2], Bettencourt A[2], Lopes J[1], Ramalheira J[1], Martins da Silva A[1,2], Costa PP[2,3], Martins da Silva B[2]
[1]Hospital de Santo António - Centro Hospitalar do Porto, Porto, Portugal, [2]UMIB - ICBAS-UP, Porto, Portugal, [3]Instituto Nacional de Saúde Dr.Ricardo Jorge, Porto, Portugal

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 (HTR)1A 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.

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 FS antecedents).

Conclusion: This study indicates that rs6295CC genotype may be a risk factor for MTLE-HS development, which is different from previous studies (Stefulj 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.

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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

Hoshida T[1], Maruyama N[1], Sawai Y[1], Kawata K[1], Hirabayashi H[1]

[1]Epilepsy Center, Nara Medical Center, National Hospital Organization, Nara, Japan

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 × 15 × 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

Sepeta LN[1], Berl MM[1], Theodore WH[2], Xu B[2], Roopchansingh V[2], Shih S[1], Barrett L[3], Terwilliger V[1], Emery E[1], Germeyan S[2], Suthana N[4], Bookheimer SY[4], Gaillard WD[1,2]

[1]Children's National Medical Center, Washington, DC, USA, [2]National Institutes of Health, Bethesda, MD, USA, [3]Tulane University School of Medicine, New Orleans, LA, USA, [4]University of California, Los Angeles, CA, USA

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 ($n = 10$; $r = 0.554$, $p = 0.097$).

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 SUBSTRACTION SPECT ANALYSIS BY STATISTICAL PARAMETRIC MAPPING (ISAS) ON REFRACTORY STRUCTURAL EPILEPSY

Quesada CM[1,2], Hampel K[1], Weber B[1,2], Ahmadzadehfar H[3], Essler M[3], Elger CE[1,2]

[1]Department of Epileptology, University of Bonn, Bonn, Germany, [2]Department of NeuroCognition/Imaging, Life & Brain Center, Bonn, Germany, [3]Department of Nuclear Medicine, University of Bonn, Bonn, Germany

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 substraction 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 (exTLE, 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.

p469
EARLY RADIOLOGICAL SIGNS OF PIAL ANGIOMA IN STURGE-WEBER SYNDROME

Rener-Primec Z[1,2], Hertz-Pannier L[3], Laffond C[4], Boddaert N[5], Nabbout R[4]

[1]Department of Child Neurology, University Children Hospital, Ljubljana, Slovenia, [2]Medical Faculty University Ljubljana, Ljubljana, Slovenia, [3]UMR 663, INSERM-CEA-Paris Descartes, UNIACT- NeuroSpin, Gif-sur-Yvette Cedex, France, [4]Paediatric Neurology, Centre for Rare Epilepsies, Necker Hospital, Paris, France, [5]Paediatric Radiology, Necker Hospital, University Paris Descartes, Paris, France

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 the 1 st MRI was 87% and specificity 80% and for T1 hypersignal 67% and 80%, respectively.

Conclusion: Hyposignal of WM on T2 and hypersingnal 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

Mirandola L[1], Ballotta D[1], Zucchelli M[1], Ruggieri A[1], Ferrari E[1], Vaudano AE[1], Nichelli PF[1], Meletti S[1], Benuzzi F[1]

[1]Department of Biomedical, Metabolic and Neural Sciences, University of Modena e Reggio Emilia, Modena, Italy

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) onset 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 *onset* vs. *offset* of GSWD 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

Coito A[1], Plomp G[1], Wiest R[2], Abela E[2], Seeck M[3], Michel C[1], Vulliemoz S[1,3]

[1]Functional Brain Mapping Lab, University of Geneva, Geneva, Switzerland, [2]Bern University Hospital, Bern, Switzerland, [3]Epilepsy Unit, Geneva University Hospital, Geneva, Switzerland

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).

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 82 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.

p472
SIMULTANEOUS EEG-FMRI: POSTERIOR SLOW-WAVES COMPARED WITH OCCIPITAL ALPHA IN CHILDHOOD ABSENCE EPILEPSY

Perani S[1,2], Centeno M[2], Cross H[2], Carmichael DW[2], Richardson M[1]
[1]King's College London, London, UK, [2]UCL Institute of Child Health, London, UK

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 thalamus 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 × 3 × 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.

p473
VERBAL AND VISUAL MEMORY FUNCTION IN TEMPORAL LOBE EPILEPSY: RESULTS OF A BLOCKED VS. EVENT-RELATED ANALYSIS

Bonelli SB[1,2], Yogarajah M[2], Powell R[2], Thompson PJ[2], Samson R[2], Symms M[2], Koepp M[2], Duncan JS[2]
[1]Department of Neurology, Medical University of Vienna, Vienna, Austria, [2]Department of Clinical and Experimental Epilepsy, Institute of Neurology, Queen Square, London, UK

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 lateralization 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.

p474
DURATION OF TEMPORAL LOBE EPILEPSY IN CHILDREN IS ASSOCIATED WITH LOSS OF HIPPOCAMPAL TISSUE AND MEMORY DYSFUNCTION

Skirrow C[1,2], Cross JH[2,3], Cormack F[1,4], Harrison S[2], Vargha-Khadem F[1,2], Baldeweg T[1,2]
[1]Developmental Cognitive Neuroscience Unit, Institute of Child Health, University College London, London, UK, [2]Great Ormond Street Hospital for Children NHS Trust, London, UK, [3]Neurosciences Unit, Institute of Child Health, University

College London, London, UK, [4]MRC Cognition and Brain Science Unit, Cambridge, UK

Purpose: Hippocampal volume loss has been associated with temporal lobe seizures. In adults progressive reduction in hippocampal volume has been linked to continuing seizures. Similarly, in infants multiple epileptic insults may be predictive of hippocampal injury. The current cross-sectional study investigates the relationship between duration of epilepsy, hippocampal volumes and verbal memory in children who are candidates for temporal lobe surgery.

Method: Twenty-eight children with focal temporal lobe abnormalities (hippocampal sclerosis: N = 19, dysembryoplastic neuroepithelial tumours: N = 9) underwent investigations for temporal lobe surgery. These included assessment of delayed story recall (Wechsler Memory Scale-Revised), and IQ (Wechsler Intelligence Scales) and structural MRI. Ten subjects later underwent right, and eighteen underwent left temporal lobectomy, at a mean age of 14.3 years. MRI analysis included manual hippocampal tracing, and automatic whole brain segmentation of grey and white brain matter.

Results: Duration of epilepsy was the strongest clinical predictor of brain structural and verbal memory outcome. Longer duration of epilepsy was (1) associated with poorer delayed story recall ($\rho = -0.46$, $p = 0.015$), significant after controlling for IQ and age at epilepsy onset; and (2) correlated with reduction of ipsi-lesional hippocampal volume ($\rho = -0.74$, $p < 0.001$), significant after controlling for intracranial volume, and (3) associated, at trend level, with lower global grey matter volume ($\rho = -0.34$, $p = 0.08$). In turn, smaller ipsi-lesional hippocampal volumes were correlated with lower delayed story recall ($r = 0.53$, $p = 0.006$), significant after controlling for intracranial volume and IQ. These effects were stronger in children with left ($r = 0.68$, $p = 0.003$) than right-sided seizure foci ($\rho = 0.42$, $p = 0.27$). Memory function was not predicted by frequency of seizures.

Conclusion: Findings provide preliminary evidence of the deleterious effect of chronic, medication-resistant seizures: longer duration of epilepsy was associated with memory dysfunction and ipsi-lesional hippocampal volume reduction. Results indicate a potential meditational effect of hippocampal volumes for the effects of epilepsy duration on memory outcome.

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Tuesday, 1st July 2014

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TUBER-SEGA: THE IMPORTANCE OF EARLY DIAGNOSIS OF A NEW NEUROLOGIC FINDING ON BRAIN MRI OF TS PATIENTS

Tzadok M[1], Roth J[2], Cagnano E[3], Ben-Zeev B[1]
[1]Pediatric Neurology Unit, Sheba Medical Center, Edmond and Lili Safra Childrens' Hospital, Ramat-Gan, Israel, [2]Department of Pediatric Neurosurgery, Tel Aviv Medical Center, Dana Children's Hospital, Tel Aviv, Israel, [3]Department of Pathology, Tel Aviv Medical Center, Tel Aviv, Israel

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 (SEGA). 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.

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 SEGA 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 seizures free with normal development. Both patients had a rare pathological finding consistent with SEGA tissue within the tuber.

We describe a new type of lesion in TS patients "Tuber SEGA" 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 workup is inconclusive m-TOR inhibitor treatment should be strongly considered for epilepsy because of the SEGA component.

p476
ALTERED WHITE MATTER INTEGRITY IS ASSOCIATED WITH DRUG USAGE IN EPILEPSY PATIENTS, A TRACT-BASED SPATIAL STATISTICS STUDY

Ding J[1], Mao L[1], Jiang Y[2], Xu D[3], Wang X[1]
[1]Neurology, Zhongshan Hospital, Fudan University, Shanghai, China, [2]Key Laboratory of Brain Functional Genomics, Shanghai Key Laboratory of Magnetic Resonance, Institute of Cognitive Neuroscience, East China Normal University, Shanghai, China, [3]MRI Unit & Epidemiology Division, Department of Psychiatry, Columbia University/New York State Psychiatric Institute, New York, NY, USA

Purpose: Previous studies have proven that white matter integrity is altered in epilepsy patients. However, few studies have investigated whether it is affected by AED drugs.

Method: Diffusion tensor images were acquired from epilepsy patients and age- sex-matched controls using 3T MRI. Brain voxel-wise analysis of fractional anisotropy (FA) was performed by tract-based spatial statistics (TBSS) to localize abnormal white matter regions between groups.

Results: We totally enrolled 114 epilepsy patients with a diagnosis of idiopathic epilepsy or epilepsy with unknown causes and 51 age- sex-matched controls. Among all patients, 20 patients did not take any AEDs, 64 patients received monotherapy, and 30 patients took 2 and more than 2 types of AEDs. There were no significant differences among three groups in terms of age, gender, disease duration, age of onset, frequency, seizure type and seizure severity scores. TBSS demonstrated that patients received more than 2 types of AEDs had significantly lower FA than patients received monotherapy, patients did not take any AEDs and controls throughout the brain, including the bilateral orbito-frontal white matter, uncinate fasciculus, corpus callosum, cingulum, inferior fronto-occipital fasciculus and corona radiation while exhibiting no areas of higher FA. Patients received monotherapy had significantly lower FA than patients did not take any AEDs and controls in left orbito-frontal white matter and forceps minor of corpus callosum. There were no significant differences between patients did not take any AEDs and controls.

Conclusion: Tract-based spatial statistics revealed significant reductions of FA in epilepsy patients who took 2 and more than 2 types of AEDs. The results of our analyses suggest that changes in FA may be related to anti-epileptic drug usage. Our preliminary results merit further investigation.

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PROTON SPECTROSCOPY (^{1}H-MRS), IN PATIENTS WITH NOCTURNAL FRONTAL LOBE EPILEPSY (NFLE)

Naldi I[1], Bisulli F[1], Tonon C[2], Rizzo G[2], Gramegna LL[2], Testa C[2], Licchetta L[1], Ferri L[1], Lodi R[2], Tinuper P[1]
[1]Department of Biomedical and NeuroMotor Sciences (DiBiNeM), IRCCS Istituto delle Scienze Neurologiche Bologna, University of Bologna, Bologna, Italy, [2]Functional MR Unit, Department of Biomedical and NeuroMotor Sciences (DiBiNeM), University of Bologna, Bologna, Italy

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 (^{1}H-MRS). In particular, ^{1}H-MRS was performed on two regions of interest: the thalami 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.Analysis of correlation, performed using multiple regression models, showed that the [NAA]/[Cr] in the anterior cingulated gyrus correlated with seizure frequency ($p = 0.048$), being lower in patients with very frequent seizures.

Conclusion: Our preliminary data on ^{1}H-MRS in NFLE patients showed hypometabolism of cingulated cortex that correlates with high seizure frequency, confirming its role in pathophysiology of NFLE.

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MICROSTRUCTURAL CONNECTIVITY AND GREY MATTER STUDY IN BITEMPORAL LOBE EPILEPSY

Miró J[1,2], Gurtubay A[2,3], Ripollés P[2,3], Sierpowska J[2,3], Juncadella M[4], Fuentemilla L[2,3], Santurino M[1], Sanchez-Sanchez V[5], Jaraba S[1], Falip M[1], Rodríguez-Fornells A[2,3,6]
[1]Epilepsy Unit, Neurology Department, L'Hospitalet de Llobregat, University Hospital of Bellvitge, Spain, [2]Bellvitge Biomedical Research Institute- IDIBELL, Cognition and Brain Plasticity Group, L'Hospitalet de Llobregat, Spain, [3]Department of Basic Psychology, L'Hospitalet de Llobregat, University of Barcelona, Spain, [4]Neurology Department, L'Hospitalet 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 bitemporal 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 interhemispehric 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.

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REFLEX TRAITS IN IDIOPATHIC GENERALIZED EPILEPSIES: AN EEG-FMRI STUDY

Pappalardo I[1], Vaudano AE[2], Ruggieri A[2], Meletti S[2]
[1]Section of Neurosciences, Department GF Ingrassia, University of Catania, Catania, Italy, [2]Department of Biomedical Sciences, Metabolic and Neuroscience, University of Modena and Reggio Emilia, Modena, Italy

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.

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MORPHOMETRIC MRI ANALYSIS ENHANCES VISUALIZATION OF CORTICAL TUBERS IN TUBEROUS SCLEROSIS

House PM[1], Lanz M[1], Voges B[1], Lindenau M[1], Kohl B[2], Osseforth J[1], Martens T[3], Holst B[4], Stodieck SRG[1], Huppertz H-J[5]

[1]Department of Neurology and Epileptology, Protestant Hospital Alsterdorf, Hamburg, Germany, [2]Department of Neuropediatrics, Catholic Children's Hospital Wilhelmstift, Hamburg, Germany, [3]Department of Neurosurgery, University Hospital Hamburg-Eppendorf, Hamburg, Germany, [4]Department of Neuroradiology, University Hospital Hamburg-Eppendorf, Hamburg, Germany, [5]Swiss Epilepsy Centre, Zürich, Switzerland

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.

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SURGICAL OUTCOMES OF PATIENTS WITH MAGNETIC RESONANCE (MRI)-NEGATIVE AND POSITRON EMISSION TOMOGRAPHY (PET/CT) POSITIVE TEMPORAL LOBE EPILEPSY

Rysz A[1], Mączewska J[2]

[1]Department of Neurosurgery, Epilepsy Service, Medical University of Warsaw, Warszawa, Poland, [2]Department of Nuclear Medicine, Medical University of Warsaw, Warszawa, Poland

Purpose: The aim of this study was to assess the usefulness of routine fluoro-2-deoxyglicose 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 seizures 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 seizures 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.

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WHITE MATTER TRACT CHANGES WITH AGE IN TEMPORAL LOBE EPILEPSY WITH UNILATERAL HIPPOCAMPAL SCLEROSIS

Yasuda CL[1,2], Beltramini GC[1,2], Min L[1,3], Campos BM[2], Coan AC[2], Araujo PV[2], Morita ME[2], Beaulieu C[4], Gross DW[1], Cendes F[2]

[1]Neurology, University of Alberta, Edmonton, AB, Canada, [2]Neurology, University of Campinas, Campinas, Brazil, [3]University of Montreal, Montreal, QC, Canada, [4]Biomedical Engineering, University of Alberta, Edmonton, AB, Canada

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 cingulum ($p = 0.54$). The trajectories were parallel for CC, anterior cingulum, IFO and ILF for TLE and controls. A steeper trajectory for TLE was observed for the fornix, CST, uncinate and posterior cingulum.

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.

p483
A CLINICAL APPLICATION FOR MR-BASED NEURONAL CURRENT IMAGING – PRELIMINARY RESULTS IN FOCAL EPILEPSY

Wiest R[1], Abela E[1,2], Weisstanner C[1], Rummel C[1], Schindler K[2], Kiefer C[1]

[1]Support Center for Advanced Neuroimaging (SCAN), Institute for Diagnostic and Interventional Neuroradiology, University Hospital and University of Bern, Bern, Switzerland, [2]Department of Neurology, Inselspital, University Hospital Bern and University of Bern, Bern, Switzerland

Purpose: To develop a new approach to neuronal current imaging (NCI) based on effectively lowering the Larmor frequency in high-field MR systems using the spin-locking (SL) mechanism, and to test whether it can detect SL-effects (SLE) induced by interictal epileptiform discharges (IED) in patients with focal epilepsies.

Method: During a spin-lock, the magnetization is locked in the rotating frame by an RF field ("spin-lock field $B_{1,lock}$"). Neuronal currents produce a resonant saturation effect on the MR signal in the rotating frame during the spin-lock state. The latter can be tuned to be sensitive to a frequency of interest by adjusting $\gamma B_{1,lock}$. We adjusted the $\gamma B_{1,lock}$ to high-frequency oscillations at 120 Hz to sensitize the sequence to high frequency oscillations that appear during IED. B1, BOLD and phase dependency effects were minimized. Standardized Z-score maps were used to visualize SLE.

Results: We present three patients with focal extra-temporal epilepsies (2 female, age range 24–47) investigated with NCI. All had presurgical intracranial EEG recordings available, and two underwent resective surgery. Multimodal image coregistration was used to identify intracranial electrode positions and to visually record the spatial relationship of IED and seizure-onset zone (SOZ) relative to peak SLE. In all patients, peak SLE co-localized with the IED and SOZ at the sub-lobar level. One patient had already undergone surgery without improvement (Engel Class IV), and SLE could be detected immediately behind the resection zone. SLE were no longer detectable in two newly operated patients; one remained seizure-free (Class IA), the other had one seizure (Class IIB) during a 6 month follow-up period.

Conclusion: SLE can be measured non-invasively on a routine MR scanner using a modified SL technique. Co-localization of SLE with IED and SOZ indicates that the proposed NCI sequence might be capable of mapping epileptogenic tissue in patients with focal epilepsies.

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DEVELOPMENTAL CHANGES OF LANGUAGE CONNECTOME IN CHILDREN

Vydrova R[1], Komárek V[1], Kynčl M[1], Šanda J[1], Krsek P[1]

[1]2nd Faculty of Medicine in Motol, Charles University, Prague, Czech Republic

Purpose: Language associated tracts, identified in presurgical assessment of children with epileptogenic zone in related regions, can be affected by developmental changes or underlying structural/functional pathology. Besides dorsal pathway of arcuate fascicle (AF), we also studied ventral language streams, i.e. inferior fronto-occipital fascicle (IFOF), uncinate fascicle (UF) and inferior longitudinal fascicle (ILF) as identified by diffusion tensor imaging (DTI), in healthy children and children with developmental dysphasia (DD).

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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COGNITIVE OUTCOME 2 YEARS AFTER FRONTAL LOBE EPILEPSY SURGERY

Ljunggren S[1], Andersson Roswall L[1], Samuelsson H[1,2], Malmgren K[1]

[1]Department of Clinical Neuroscience and Rehab, Institute of Neuroscience and Physiology, Sahlgrenska Academy at Gothenburg University, Göteborg, Sweden, [2]Department of Psychology, Gothenburg University, Göteborg, Sweden

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 wheras 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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PREDICTORS OF NEUROPSYCHOLOGICAL DYSFUNCTION IN CHILDREN WITH INTRACTABLE EPILEPSY DUE TO TUBEROUS SCLEROSIS

Maulisova A[1,2], Krsek P[3], Korman B[4], Rey G[4], Jaykar P[5], Miller I[6], Reznik T[7], Duchowny M[7,8]

[1]Motol Faculty Hospital, Prague, Czech Republic, [2]Faculty of Arts, Charles University, Prague, Czech Republic, [3]Department of Pediatric Neurology, 2nd Faculty of Medicine, Motol University Hospital, Charles University, Prague, Czech Republic, [4]Neuropsychology Section, Brain Institute and Behavioral Medicine, Miami Children's Hospital, Miami, FL, USA, [5]Neuroscience Center, Brain Institute, Miami Children's Hospital, Miami, FL, USA, [6]Neuro Network Partners, Miami, FL, USA, [7]Department of Neurology and Comprehensive Epilepsy Program, Brain Institute, Miami, FL, USA, [8]Department of Neurology, University of Miami Miller School of Medicine, Miami, FL, USA

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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EMOTION RECOGNITION AND FAUX-PAS IDENTIFICATION IN TEMPORAL LOBE EPILEPSY PATIENTS: CORRELATION OF PERFORMANCE WITH AMYGDALAR AND HIPPOCAMPAL VOLUMES

Martinkovic L[1], Amlerova J[1], Marusic P[1]

[1]2nd Faculty of Medicine, Motol University Hospital, Charles University, Prague, Czech Republic

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 hippocampus 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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ATTENTION DEFICIT IN PATIENTS WITH TEMPORAL LOBE EPILEPSY: CLINICAL, NEUROPHYSIOLOGICAL AND NEUROIMAGING CHARACTERISTICS

Jovanovic M[1], Buder N[1]

[1]Department for Epilepsy and Neurophysiology, Institute of Mental Health, Belgrade, Serbia

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 posttraumatic or tumorous) in AD group – 20/36 (55%) than in the other one – 8/

21 (38%), We found diagnostically significant reduction of attention index, mostly visual, but also verbal attention span.

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.

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PATTERN OF PSYCHOACTIVE SUBSTANCE USE AMONG PEOPLE LIVING WITH EPILEPSY IN SOUTH-WESTERN NIGERIA

Babalola EO[1]
[1]*Aro, Psychiatry, Neuropsychiatric Hospital, Abeokuta, Nigeria*

Purpose: To determine the prevalence and pattern of psychoactive substance use among people living with epilepsy, and evaluate socio-demographic and clinical variables associated with substance use.

Method: A descriptive cross sectional study was conducted between June and December 2013 among people living with epilepsy attending the outpatient clinic of the Neuro-psychiatric Hospital Aro, Abeokuta in South Western Nigeria. The MINI - Plus questionnaire was used to evaluate for substance use among respondents.

Results: One hundred and thirty six people living with epilepsy participated in the study. Seventy six (56%) were males. Thirty (22%) had used psychoactive substances in their lifetime. Alcohol was the commonest psychoactive substance used, with 20 (14.7%) currently abusing alcohol and 6(4.4%) dependent on it. Twelve (8.8%) patients currently abusing tobacco with 4 (2.9%) dependent on it. Six (4.4%) were currently abusing cannabis, with 2(1.4%) currently dependent on it. Psychoactive substance use was significantly associated with younger age and unemployment.

Conclusion: Psychoactive substance use 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.

p490
THE DIAGNOSTIC RELATIONSHIP OF INTERICTAL DYSPHORIC DISORDER WITH MOOD AND ANXIETY DISORDERS

Yoshino A[1], *Tatsuzawa Y*[1], *Mogi T*[1], *Suda T*[1]
[1]*Department of Psychiatry, National Defense Medical College, Tokorozawa, Japan*

Purpose: Some patients with localization-related epilepsy are suffered from a pleomorphic affective syndrome named interictal dysphoric disorder (IDD) whose episodes last up to a few days and recur in a uniform manner. However, the relationship of IDD with current psychiatric diagnostic categories has been unclear. We examined whether the diagnosis of IDD was dependent or not of mood and anxiety disorders.

Method: This study was approved by the Ethics Committee of the National Defense Medical College. Subjects were 99 patients with localization-related epilepsy (median age 39 years; female, 48; TLE, 61; remission, 49). All patients provided written informed consent after they were explained in detail the purpose and methods of the study. IDD was diagnosed using the IDD Inventory (IDDI). The diagnosis of any mood and anxiety disorders was established using the Mini International Neuropsychiatric Interview (MINI). IDDI total score and severity were analyzed using ANOVA concerning two independent factors, the diagnoses of IDD and any mood and anxiety disorders.

Results: 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 IDDI 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.

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ARE THERE DEPRESSIVE AND ANXIETY SYMPTOMS SPECIFICALLY RELATED TO CHILDREN WITH EPILEPSY?

Stevanovic D[1], *Lakic A*[1], *Jancic J*[1]
[1]*Clinic for Neurology and Psychiatry for Children and Youth, Belgrade, Serbia*

Purpose: To evaluate whether children with epilepsy experience different depressive and anxiety symptoms than other children do.

Method: In the study participated 60 children with epilepsy [26 (43.4%) males, age mean 13.8 (2.8) years], 67 children with juvenile idiopathic arthritis (JIA) [19 (28.4%) males, age mean 13.6 (2.9) years], and 75 healthy children [46 (61.6%), age mean 13.6 (3.1) years]. The Screen for Child Anxiety Related Emotional Disorders (SCARED) was used for anxiety and the Mood and Feeling Questionnaire (MFQ) for depressive symptoms assessment.

Results: In a series of multivariate analyses, controlled for gender due to significant differences between the groups ($p < 0.01$), it were observed negligible differences between the groups in expressing particular depressive and anxiety symptoms. Only one of 33 depressive and two of 41 anxiety symptoms differed among children with epilepsy than among the other two. However, several depressive symptoms specifically clustered among children with epilepsy such as “feeling upset”, “thinking about death or dying”, “feelings being a bad person”, “feelings working things wrongly, and “sleeping more than usual”. Considered together, they accounted for 95.6% of the total variance in levels of all depressive symptoms expressed. Additionally, several anxiety symptoms also specifically clustered among children with epilepsy such as “when frightened, hard to breathe”, “worry about being good”, “told that worry too much”, “don’t like to be away from the family”, “worry that something bad might happen to the parents”, and “worry about what is going to happen”. They accounted for 95% of the total variance in levels of all anxiety symptoms expressed.

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.

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ANXIETY AND DEPRESSION AMONG CAREGIVERS OF CHILDREN AND ADOLESCENTS WITH SEIZURE DISORDERS IN SOUTH WESTERN NIGERIA

Babalola EO[1], *Onifade PO*[2], *Adebowale TO*[2]
[1]*Neuropsychiatry, Neuropsychiatric Hospital Aro, Abeokuta, Nigeria,* [2]*Clinical Services, Neuropsychiatric Hospital Aro, Abeokuta, Nigeria*

Purpose: The aim of this study was to assess the prevalence and correlates of anxiety and depression among caregivers of children with seizure disorders in south western Nigeria.

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 1 Diagnosis (SCID) was used for diagnosis of Generalized Anxiety Disorder and Major Depression.

Results: One hundred and forty six (72%) of the carers 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.

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SHOULD WE USE A SCALE IN NOCTURNAL BEHAVIOUR? THE RESULTS OF OUR SLEEP UNIT

Demir AB[1], *Bora İ*[1]
[1]*Neurology, Uludag University, Bursa, Turkey*

Purpose: Parasomnias are clinical disorders which don't cause disorders in stages of sleep and wakefulness but primarily emerge during the sleep with undesirable physical phenomena. Changes of the autonomic nervous system and skeletal muscle activity frequently accompany the disorder.Most of paroxysmal events during sleep are confused with epileptic seizures during sleep especially frontal lobe seizures and as a result the majority of patients are diagnosed with epilepsy.

Method: We used the scale of the studies made in 2006 by Derry and his friends about their specificity and sensitivity study of the Frontal Lobe Epilepsy (FLE) and Parasomnias (FLEP). Ninety-three patients, forty-nine with Frontal Lobe Epilepsy and forty-four with Parasomnias were studied. The scale applications were done by a video-EEG monitoring sleep technician and a physician who didn't have any information about the patients. In total scores epilepsy +1 and over, zero and values below zero were seen as supporting Parasomnias.

Results: The average total score of patients with FLE was 4.8 ($\pm$ 1.96), patients with Parasomnias -3.92 ($\pm$ 1.83). The average age of patients with FLE was 32 (19–47) while the average age of patients with Parasomnias was (18–80). Statistically both values between the two groups were significant. The most important result was the answer for the question of FLE patients the Dystonic posture and tonic contractions and the talk during sleep and not remembering it afterwards for Parasomnias.

Conclusion: It is difficult to distinguish Parasomnias and nocturnal epileptic seizures. In this case, the current method is video-polysomnography. We think that it could be helpful to use the FLEP-scale, which is a reliable scale, with video-polysomnography from the positive results of our patients.

p495
PECULIAR PSYCHOGENIC NONEPILEPTIC SEIZURES (PNES) CHARACTERISTICS IN PATIENTS WITH BORDERLINE INCTELLECTUAL FUNCTIONING OR MENTAL RETARDATION

Chiesa V[1], *Savini M*[1], *Vignoli A*[2], *Turner K*[1], *Oggioni G*[1], *La Briola F*[1], *Zambrelli E*[1], *Canevini MP*[2]
[1]*Epilepsy Center, Neurology 2 Unit, San Paolo Hospital, Milan, Italy,* [2]*Epilepsy Center, Neurology 2 Unit, San Paolo Hospital, University of Milan, Milan, Italy*

Purpose: Psychogenic nonepileptic seizures (PNES) are a relatively common disorder, often misdiagnosed as epilepsy. Expecially when epileptic seizures coexist. the diagnosis might be difficult. The gold standard for PNES diagnosis is video-EEG recording of a tipical attack.

PNES are referred to be common in patients with low I.Q. The aim of our study is to clarify PNES semiology and characteristics in this population.

Method: We analized demographic and clinical characteristics of 25 patients with mental retardation or borderline inctellectual functioning (BIF), with a certain diagnosis of PNES, recorded by Video-EEG. Then we examinated 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 tecniques, which showed a sensitivity of 100% in our patients. A clear psychiatric comorbidity was present in 60% of patients; almost 50% was treated with psychiatic 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 tecniques.

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PROVOCATION OF NON EPILEPTIC SEIZURES BY SUGGESTION IN CHILDREN AND ADOLESCENTS POPULATION

Starczewska M[1], *Steinborn B*[1]
[1]*Department of Developmental Neurology, University of Medical Sciences, Poznań, Poland*

Purpose: To evaluate the method of saline provocation during video EEG recording in patient with patient in 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 developmental age. Saline provocation is a sensitive method of identification of PNES.

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INCIDENCE OF OXYGEN DESATURATION IN PSYCHOGENIC NON-EPILEPTIC SEIZURES

Teasdale E[1], Derry C[1,2], Brotherstone R[3,4], Duncan S[1,2]
[1]Department of Clinical Neurosciences, Edinburgh and South East Scotland Epilepsy Service, Western General Hospital Edinburgh, Edinburgh, UK, [2]University of Edinburgh, Edinburgh, UK, [3]Department of Clinical Neurophysiology, Western General Hospital Edinburgh, Edinburgh, UK, [4]Department of Clinical Neurosciences, Western General Hospital Edinburgh, Edinburgh, UK

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 apnoeic episodes in individuals with OSA. Caution should be used when interpreting oxygen desaturation as evidence of an epileptic basis to seizures.

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LONG TERM FOLLOW-UP (10 YEARS) OF LIMBIC ENCEPHALITIS ASSOCIATED WITH VGKC-COMPLEX LGI1 ANTIBODIES

Agazzi P[1], Gobbi C[1]
[1]Neurologia, Ospedale Civico, Lugano, Switzerland

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-inactived-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 (Phenytoin, Carbamazepin, Levetiracetam, Zonisamide, Valproic Acid, Pregabalin). Since the last relapse (6.3013) 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.

p499
CAN WE DISTINGUISH SEIZURES FROM SYNCOPE BASED ON HISTORY DATA – EXTERNAL VALIDATION OF SCREENING QUESTIONNAIRE?

Stojanov A[1], Spasic M[1], Peric Z[1], Lukic S[1]
[1]Clinic of Neurology, University Clinical Center Nis, Nis, Serbia

Purpose: To perform external validation of the screening questionnaire, proposed by Sheldon et al 2002, designed to distinguish seizure from syncope based on historical criteria.

Method: Alongside to the standard clinical observation, screening questionnaire with 9 historical questions was performed in all patients evaluated due to transient loss of consciousness. Score results were compared to final diagnosis based on detailed neurology, electrophysiology and cardiology assessment. Analyses were performed with and without inclusion of additional clinical variables, using multiple regression models. Discrimination values were tested with classification tables and receiver-operator characteristic (ROC) analysis. Calibration characteristics were tested with Hosmer-Lemeshow chi square statistic.

Results: From July 2013 to December 2013, 63 patients (31M, 32 F) have been evaluated due to transient loss of consciousness. Final diagnosis of epileptic seizures has made in 51 patients (22M, 29F) and syncope in 12 patients (9M, 3F). Patients with epileptic seizures have been significantly younger (median 36.5 years, IQR 23–65.5) than patients with syncope (median 59, IQR 50-65). However, only screening questionnaire score has significant effect in multivariate logistic regression model (OR 60.6). Screening questionnaire correctly classified 87.3% patients with sensitivity 86.27% and specificity 91.67%. Area under ROC curve was 0.89, and Hosmer-Lemeshow c^2 (8) = 12.97, $p = 0.11$.

Conclusion: Screening questionnaire based on historical criteria could be useful additional tool for differentiate seizure from syncope. Regarding the pretest probability, questionnaire's overall gain in diagnostic accuracy is moderate. Potential improvement for the use in the tertiary academic centers could be considered in future studies.

p501
PAROXYSMAL NON-EPILEPTIC EVENTS OF CHILDHOOD

Delic JV[1], Bogicevic D[1,2], Dedijer S[1], Milivojevic T[1], Cuk VV[3], Nikolic D[1,2]
[1]School of Medicine, University of Belgrade, Belgrade, Serbia, [2]University Children's Hospital, Belgrade, Serbia, [3]Clinical Center Zvezdara, Belgrade, Serbia

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.

Others 4
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p502
REPEATED MILD BRAIN TRAUMA AND EPILEPSY

Malenica M[1], Kukuruzovic M[1], Cvitanovic-Sojat L[1]
[1]Department of Neuropediatrics, University Hospital Centre Sestre Milosrdnice, Zagreb, Croatia

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.

p503
SEIZURE PRECIPITANTS IN A COMMUNITY-BASED EPILEPSY COHORT

Wassenaar M[1,2], Kasteleijn-Nolst Trenité DGA[3,4], de Haan G-J[1], Carpay HA[5,6], Leijten FSS[2], OPPEC Study Group
[1]SEIN-Epilepsy Institute in the Netherlands Foundation, Heemstede, The Netherlands, [2]Department of Neurology and Neurosurgery, Brain Center Rudolf Magnus, University Medical Center Utrecht, Utrecht, The Netherlands, [3]Department of Medical Genetics, University Medical Center Utrecht, Utrecht, The Netherlands, [4]Department of Neuroscience, University Sapienza, Rome, Italy, [5]Department of Neurology, Tergooi Hospitals, Blaricum, The Netherlands, [6]Department of Neurology, Leiden University Medical Center, Leiden, The Netherlands

Purpose: Epileptic seizures can be provoked by several factors. Better understanding of these factors may improve a patients 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 auras 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.

p504
NON-ADHERENCE TO AEDS IS A MAJOR CAUSE OF ACUTE HOSPITALIZATION IN PATIENTS WITH EPILEPSY

Samsonsen C[1], Reimers A[2,3], Bråthen G[1,4], Helde G[4], Brodtkorb E[1,4]
[1]Department of Neurology and Clinical Neurophysiology, St Olav's Hospital, Trondheim University Hospital, Trondheim,

Norway, [2]Department of Clinical Pharmacology, St Olav's Hospital, Trondheim University Hospital, Trondheim, Norway, [3]Department of Laboratory Medicine, Children's and Women's Health, Norwegian University of Science and Technology, Trondheim, Norway, [4]Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway

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.

p505
SPECIAL REFLEX FEATURES IN TWO EPILEPTIC PATIENTS WITH PHENYLKETONURIA

Yıldız Çelik Ş[1], Bebek N[1], Samancı B[1], Akçay Hİ[1], Gürses C[1], Baykan B[1], Gökyiğit A[1]
[1]Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey

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 hypersyncrony in the first patient. Seizures were continuing despite multiple antiepileptic drug combinations.

Conclusion: Although some clinical and electrophysiological features have been described, photosentivity 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

Chahidi A[1,2,3], Adali N[2,4], Louhab N[2,4], Kissani N[2,4]
[1]ED268, Sorbonne University Paris, Paris, France, [2]Basic and Clinical Neurosciences Researches Laboratory, Medical University School of Marrakech, Marrakech, Morocco, [3]Department of Neurology, Moroccan Epilepsy Association AMCEP, Ibn Tofail University Hospital, Marrakech, Morocco, [4]Department of Neurology, Ibn Tofail University Hospital, Marrakech, Morocco

Purpose: The post stroke epilepsy defined by the occurrence of at least two unprovoked seizures usually in late stroke suites, 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 department 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.

p507
EPILEPTIC ASYSTOLE: A CLUE TO THE INTERPRETATION OF SYNCOPE-LIKE ATTACKS IN ADULTS

Pasini E[1], Riguzzi P[1], Rubboli G[1], Volpi L[1], Borghi A[1], Michelucci R[1]
[1]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy

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.

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 syncope-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 syncope-like episodes preceded by mesial temporal auras. These cases rise problems of differential diagnosis and require expert neurological and cardiological evaluation.

p508
AN ALTERNATIVE TO COLLODION

Wagner EE
Clinic of Dr. Carlos H. Gama, Baptist Neurolog, Baptist Neurology, Jacksonville, FL, USA

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 3MT™ Micropore™ Microporus 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 head, which is very convenience, especially for children. Eight patients per week were monitored and evaluated for diagnosis of Epileptic seizures vs. non epileptic spells.

Results: This method is fast, easy and convenient with no Collodion odor, no skin breakdown and easy electrode removal with just water. The electrodes remain secured on patients with severe epileptic seizures and autistic children. Electrodes continue with low impedance and practically no repairs on patients monitored for 3 to 4 days. This procedure is also for patients who are allergic to Collodion

Conclusion: Most of the recordings are of high quality and the Epileptologists are able to see the beginning, evolution and end of the seizure.

p509
ON THE RELATIONSHIP BETWEEN HEADACHES WITH SOMATIC AND PSYCHIATRIC COMORBIDITY IN PATIENTS WITH EPILEPSY

Mar'yenko LB
Lviv National Medical University named after Danylo Halitsky, Neurology, Lviv, Ukraine

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-resistance).

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. Additionaly 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 ($r = 0.20$, $p < 0.01$) arterial hypertension ($r = 0.24$, $p < 0.01$). Patients in remission without HAs had no significant somatic ($r = 0.14$, $p < 0.01$) 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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BECTS INCIDENCE IN WALES – UNREPORTED OR OVERESTIMATED?

Saxena A[1], Gibbon F[2], te Water Naude' J[2], Hamandi K[3]
[1]Institute of Medical Genetics, Cardiff University School of Medicine, Cardiff, UK, [2]Paediatric Neurology, Children's Hospital for Wales, Cardiff, UK, [3]The Alan Richens Welsh Epilepsy Centre, University Hospital of Wales, Cardiff, UK

Purpose: Benign Epilepsy with Centrotemporal spikes (BECTS) is reported to be one of the commonest 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 31/12/12012). 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 recognise 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

Mierlovan P, Snoeijen-Schouwenaars F, Veendrick M, Erpvan G, Louwde A, Tan F, Schelhaas J
Kempenhaeghe/Academic Center of Epileptology, Heeze, The Netherlands

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.

p512
EPILEPSY AND AUTISM IN SIBLINGS

Christensen J[1], Overgaard M[2], Parner ET[2], Vestergaard M[3], Schendel D[2]
[1]Aarhus University Hospital, Neurology, Aarhus, Denmark, [2]Aarhus University, Department of Biostatistics, Institute of Public Health, Aarhus, Denmark, [3]MEPRICA, Research Unit and Section for General Practice, Department of Public Health, Aarhus University, Aarhus, Denmark

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

Andrade LI[1], Aranguiz JL[2], Acevedo K[3], Venegas V[4], Jeldres E[5], Cuadra L[6], Bustos A[7]
[1]Hospital Carlos Van Buren, Pediatria, Valparaiso, Chile, [2]Hospital de Vallenar, Vallenar, Chile, [3]Pontificia Universidad Católica de Chile, Neurología, Santiago, Chile, [4]Hospital San Rafael Juan de Dios, Santiago, Chile, [5]Hospital de Rancagua, Rancagua, Chile, [6]Instituto Asenjo, Santiago, Chile, [7]Hospital Arquitecto Van Buren, Valparaíso, Chile

Purpose: Evaluate the risk factors associated to epilepsy and refractory epilepsy subsecuent 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 promp epilepsy GEF`lus or Dravet syndrome.

p514
NEUROCYSTICERCOSIS: A CASE REPORT

Mukonde F
MCDMCH, Chambishi, Zambia

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 subcutaneous nodules on the face, recurrent headache and epileptic seizures. The headache was primarily frontal and the subcutaneous 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 cores seen in all cerebral slices. Cerebral sulcus and gyrus are normal. Lateral third and fourth ventricles and cistern are not dilated. The midline structures are not shifted. The brain stem, cerebellum and puitary glands are normal. Praziquantel 1500 mg bd (50 mg/kg) was given for 6 weeks together with prednisolone. Treatment was given according 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

Šimić Klarić A[1,2], Šimić Ž[1], Tesari Crnković H[1,2], Matoković D[1,2]

[1]General County Hospital, Požega, Croatia, [2]Medical School, University of Osijek, Osijek, Croatia

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 COMPRESSIVE FRACTURES FOLLOWING A CLUSTER OF GTCS – IN AN OSTEOPOROTIC YOUNG ADULT MALE

Ndoja D[1], Buda L[2], Perolli A[2], Hysi G[2], Tafaj A[2], Mijo S[2], Koci S[2], Kuqo A[2]

[1]UHC 'Mother Theresa', Department of Neurology, Tirana, Albania, [2]UHC 'Mother Theresa', Tirana, Albania

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 admittion he presented prolonged post -ictal confusion, not recalling the episodes of LOC and unable to mobilize. On objective examination he showed muscles tender from D5–D10 with inferior paraparesis but no sphincters 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 evocating 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 tirocalcitonina but no sign of thyroid malignancy at doppler imaging. Free serum calcium level, urinary calcium dosage, and PTH resulted normal as well. A current 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.

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EPILEPSY WITH ONSET WITHIN 3 YEARS OF AGE: ELECTROCLINICAL CHARACTERIZATION AND LONG TERM OUTCOME

Vignoli A[1,2], Scornavacca G[1], Fergnani V[1], Oggioni G[1], Turner K[1], Chiesa V[1], La Briola F[1], Zambrelli E[1], Savini MN[1], Canevini MP[1,2]

[1]Centro Epilessia AO San Paolo, Milan, Italy, [2]University of Milan, DISS, Milan, Italy

Purpose: To outpoint prevalence, electroclinical characteristics and long term outcome of infantile and early childhood onset epilepsies, according to the new proposal for Epilepsy Classification (ILAE, 2010).

Method: We reviewed clinical records of patients referred to Epilepsy Center, San Paolo Hospital, Milan, Italy since 1992 to 2012, searching for infantile onset epilepsies (<3 years).

Results: From 3096 screened records, we selected 266 patients (144 M), mean age at onset was 17.5 months (147 onset <1 year). Mean age at follow up was 29.4 years, mean follow-up 8.7 years .Most of the patients (100) presented with non syndromic epilepsy (57 structural abnormalities, 19 genetic, 7 metabolic, 7 neurocutaneous syndrome, 7 cortical development abnormalities, 3 tumors); 90 presented an electroclinical syndrome; 76 presented distinctive costellations.On the basis of etiology 31 were genetic, 12 metabolic, 23 cortical development abnormalities, 73 structural, 3 tumoral, 10 neurocutaneous syndromes .At follow-up 117 patients (66.5%) had intellectual disability (29.7% severe). Neurological examination was abnormal in 137 patients.173 (65%) had pharmacoresistant epilepsy according to ILAE criteria and 113 patients were seizure free (at least 2 years follow-up).

Conclusion: In our population prevalence of drug-resistant epilepsy and severe neurocognitive delay is higher than observed by other groups, this is probably due to the selection of a population of very early onset epi-

lepsy. 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?

Rummel C[1], Abela E[1,2], Hauf M[1,3], Zubler F[2], Weisstanner C[1], Wiest R[1], Schindler K[2]
[1]Inselspital, University Institute for Diagnostic and Interventional Neuroradiology, Bern, Switzerland, [2]Inselspital, Department of Neurology, Bern, Switzerland, [3]Epilepsy Clinic Bethesda, Tschugg, Switzerland

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 $p > 0.3$) and 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

Mihu N
NSH/LIJ Hospital, Manhasset, NY, USA

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 the question was 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.

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p520
100 CASES IN THE TREATMENT OF STATUS EPILEPTICUS WITH INTRAVENOUS LEVETIRACETAM

Eue S[1], Dragut-Ivan M[2], Grumbt M[2], Knörnschild A[2], Latsch A[2], Irimie A[2], Millig L[2], Müller M[2], Schulze A[2], Sepsi O[2]
[1]AMEOS Klinikum Bernburg, Neurology, Bernburg, Germany, [2]AMEOS Klinikum Bernburg, Bernburg, Germany

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 the 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

Melikyan GR[1,2], Deleu D[1,2], Uthman B[1,3]
[1]Hamad Medical Corporation, Neurology, Doha, Qatar, [2]Weill Cornell Medical College in Qatar, Clinical Neurology, Doha,

Qatar, [3]Weill Cornell Medical College in Qatar, Neurology, Doha, Qatar

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 anticonvulsant 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

Marks D[1,2], Bhat A[1], Sharer L[3]
[1]Rutgers-NJ Medical School, Newark, NJ, USA, [2]Neurosciences, Rutgers-NJ Medical School, Newark, NJ, USA,
[3]Neuropathology, Rutgers-NJ Medical School, Newark, NJ, USA

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

Nikic PM, Grkic I
Special Hospital for Cerebrovascular Diseases 'Sveti Sava', Belgrade, Serbia

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 PEDs 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

Tiamkao S[1,2], Pranbul S[3], Thepsuthammarat K[4], Sawanyawisuth K[1]
[1]Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand, [2]Khon Kaen University, Integrated Epilepsy Research Group, Khon Kaen, Thailand, [3]Nursing Division, Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand, [4]Clinical Epidemiology Unit, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

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.

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 improved and 1,045 patients (8.4%) died. The most common co-morbid diseases were hypertension (1,790 patients, 14.5%); DM (1,064 patients, 8.6%) and stroke (819 patients, 6.6%).Pneumonia was the most common complication 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

Tatishvili N[1], Shatirishvili T[1], Kipiani T[1], Tatishvili S[2]
[1]M.Iashvili CCH, Neuroscience, Tbilisi, Georgia,
[2]Neurodevelopment Centre, Tbilisi, Georgia

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 as death, 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, recurrent CSE, existence of neurological abnormality before CSE and their influence on morbidity and mortality. Was 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 artificial 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 statuss:

Conclusion: Non Standardized pre hospital treatment of pediatric CSE in Tbilisi had statistically significant negative influence on outcome of CSE in children.

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INCIDENCE OF PERI-ICTAL DIFFUSION MRI CHANGES AND THEIR ROLE IN ADULT PATIENTS WITH STATUS EPILEPTICUS

Yi H, Cho Y-J, Lee BI, Heo K
Severance Hospital, Yonsei University College of Medicine, Neurology, Seoul, Korea

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 (AJ Cole).

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 diaschisis 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%, epilepsia 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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p527
SURGERY FOR MESIAL TEMPORAL LOBE EPILEPSY DUE TO HIPPOCAMPAL SCLEROSIS: 4 YEARS EXPERIENCE FROM EPILEPSY CENTER ZAGREB, CROATIA

Sajko T[1], Hečimović H[2], Bedek D[3], Divošević S[4]
[1]Neurosurgery, UHC 'Sestre Milosrdnice', Zagreb, Croatia,
[2]Neurology, UHC 'Sestre Milosrdnice', Zagreb, Croatia,
[3]Radiology, UHC 'Sestre Milosrdnice', Zagreb, Croatia,
[4]Nuclear Medicine, UHC 'Sestre Milosrdnice', Zagreb, Croatia

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), neuropsyhological 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 occured 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
INTRAOPERATIVE 1.5T MR IMAGING AND FUNCTIONAL NEURONAVIGATION IN RESECTIVE EPILEPSY SURGERY: EXPENSIVE HYPE OR FUTURE TECHNOLOGY? CONCLUSIONS FROM 10 YEARS' EXPERIENCE IN 400 PATIENTS

Roessler K[1], Sommer B[2], Hofmann A[2], Grummich P[2], Coras R[3], Kasper B[4], Hamer HM[1], Blumcke I[1], Stefan H[4], Buchfelder M[2]
[1]University Hospital Erlangen, Erlangen, Germany, [2]Neurosurgery, University Hospital Erlangen, Erlangen, Germany, [3]Neuropathology, University Hospital Erlangen, Erlangen, Germany, [4]Neurology, University Hospital Erlangen, Erlangen, Germany

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 (for 18.3 years mean) were extensively investigated preoperatively using a level IV epilepsy center protocol to define epileptogenic and functional brain tissue. Intraoperative MR imaging and neuronavigation including functional risk maps, electro-corticography and magneto-encephalography were employed for lesionectomy, tailored or lobar resection.

Results: In 82% of patients (n = 328), temporal resections were performed, 18% (n = 72) had extra-temporal surgery. Most common entities included hippocampal sclerosis (HS, n = 151, 37.8%), long term epilepsy associated tumors (LEAT, n = 60, 15%), cavernous malformations (CM, n = 34, 8.5%) and focal cortical dysplasia (FCD, n = 23, 5.8%). Resection amount of neocortical/ hippocampal removal in HS was 5.1 cm/ 2.6 cm mean. Percentages of complete resection in LEAT and CM were 80.8% and 92%, respectively. Intraoperative underestimation of resection amount verified by iopMR imaging occurred in 12.5%, which was successfully corrected intraoperatively by second look surgery. Altogether, surgery achieved an Engel Grade I seizure outcome in 71% of patients with 57.6% being actually seizure free (Follow-up 2.5 years mean in 280 patients). Main surgical complications were visual field defects (10%), speech or memory decline (2%) and hemiparesis (1%).

Conclusion: Intraoperative MR imaging combined with functional neuronavigation seems to enhance resection amount in lesional epilepsy surgery, resulting in high percentages of seizure free patients. Additionally, implementation of functional risk maps may lead to lesser complications. Thus, both methods may serve as future technology for resective epilepsy surgery.

p529
STEREOTACTIC RADIOFREQUENCY THERMOCOAGULATION OF HYPOTHALAMIC HAMARTOMA IN 100 CONSECUTIVE PATIENTS

Shirozu H, Masuda H, Murakami H, Ito Y, Sonoda M, Kameyama S
Nishi-Niigata Chuo National Hospital, Hypothalamic Hamartoma Center, Department of Functional Neurosurgery, Niigata, Japan

Purpose: To clarify the characteristics of seizures due to hypothalamic hamartoma (HH) and to validate our surgical strategy of stereotactic radiofrequency thermocoagulation (SRT), we retrospectively reviewed surgical and functional outcomes.

Methods: Clinical records of 100 consecutive cases of HH that underwent SRT between 1997 and 2013 were reviewed.

Results: Thirty-four patients were female. 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 intrahypothalamic 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 multistaged surgeries. In 82 patients with follow-up for ³1 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

Medvedovsky M[1,2], Artzi M[1,3], Zadicario E[4], Levy Y[4], Tlusty T[4], Foroni R[5], Ricciardi GK[5], Nicolato A[5], Aizenstein O[1], Fahoum F[1], Kipervasser S[1,3], Hendler T[1,3], Klovatch I[1], Gazit T[1], Neufeld MY[1,3], Frid I[1,3,6], Ben Bashat D[1,3]
[1]Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, [2]University of Helsinki, Helsinki, Finland, [3]Tel Aviv University, Tel Aviv, Israel, [4]InSightec.Ltd, Tirat Hacarmel, Israel, [5]University of Verona, Verona, Italy, [6]UCLA, Los Angeles, CO, USA

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. Leksel 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 girus 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 JJr 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 cm^3. MRgFUS could ablate 8.06 cm^3 (62.05%). The remaining 4.93 cm^3 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

Bjellvi J, Lindblom B, Rydenhag B, Malmgren K
Sahlgrenska Academy, University of Gothenburg, Institute of Neuroscience and Physiology, Göteborg, Sweden

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 vigabatrin use) were excluded. Of the remaining 87 patients, 45 (52%) had no VFD, 25 had a partial homonymous quadrantanopia (29%), 15 (17%) had a complete homonymous quadrantanopia, and two (2%) had a homonymous hemianopia postoperatively. In 15/87 patients (17%), the postoperative VFD was judged to preclude driving. Of these 15 patients, eight (53%) had been seizure-free for 1 year at follow-up.

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 STEREO ELECTRO ENCEPHALOGRAPHY AFTER A FIRST FAILED EPILEPSY SURGERY

Vaugier L[1], Bonini F[1,2], Mc Gonigal A[1], Gavaret M[1,2], Trebuchon A[1,2], Regis J[1], Carron R[1], Scavarda D[1], Chauvel P[1,2], Bartolomei F[1,2]
[1]APHM, Hôpital Timone, Marseille, France, [2]Université de la Méditérranée, INSERM, U 1106, Brain Dynamic Institute, Marseille, France

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 Stereo-electro-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, latero-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.

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LESION FOCUSSED STEREOTACTIC THERMO-COAGULATION INSTEAD OF OPEN RESECTION: A NEW WAY IN EPILEPSY SURGERY?

Wellmer J[1], Kopitzki K[2], Voges J[2]
[1]Department of Neurology, Ruhr-Epileptology, University Hospital Knappschaftskrankenhaus, Bochum, Germany, [2]Department of Stereotactic Neurosurgery and Leibnitz Institute for Neurobiology, University Hospital Magdeburg, Magdeburg, Germany

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 mininmal invasive epilepsy surgery approach which can contribute to solving this question.

Method: Two patients with pharmacoresistant 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: Ceasing 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

Cukiert A[1], Rydenhag B[2], Harkness W[3], International Pediatric Epilepsy Surgery Panel
[1]Department of Neurosurgery, Faculdade de Medicina do ABC, Sao Paulo, Brazil, [2]Department of Neurosurgery, Sahlgrenska University Hospital, Göteborg, Sweden, [3]Department of Neurosurgery, London, UK

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, hemosthasis 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 withdraw valproate 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 surgicel for hemosthasis, 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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PEDIATRIC EPILEPSY SURGERY TECHNIQUES SPECIFIC ISSUES: INTER-CENTER WORLDWIDE VARIABILITY

Harkness W[1], Rydenhag B[2], Cukiert A[3], International Pediatric Epilepsy Surgery Panel
[1]Department of Neurosurgery, London, UK, [2]Department of Neurosurgery, Sahlgrenska University Hospital, Göteborg, Sweden, [3]Department of Neurosurgery, Faculdade de Medicina do ABC, Sao Paulo, Brazil

Purpose: There is a wide variability of surgical techniques used among the different pediatric epilepsy surgery centers. A web-based questionnaire was sent to several centers with a wide geographical representation in order to try to understand the present practice status around the world. In this paper we describe the findings related to specific surgical issues.

Method: A web-based survey comprising 13 questions was filled up by 52 centers representing all continents. Questions investigated the different technical aspects for kids undergoing temporal lobe resection, hemispherectomy or callosotomy. These included: positioning, peroperative imaging, peroperative neurophysiology, surgical instruments, skin incision, bone flap, and surgical extension. Complication rates and types were evaluated for all types of surgical procedures.

Results: Regarding temporal lobe resections, 90% of the surgeons used head fixation, 61% image guidance, 67% ultrasonic aspiration, 50% electrocorticography; all used the surgical microscope. Sixty-six percent of the surgeons used a question-mark skin incision, and 82% used free bone flaps. While performing callosotomy, 80% of the surgeons used a supine, neck-flexed position, 34% used U-shaped skin incisions, 76% put bone flaps over the midline, 80% used bipolar coagulation for the callosal section itself and 46% used neuronavigation. In hemispheric surgery, 63% used ultrasound aspiration, 58% used the microscope only, 38% used both the loupe and the microscope, 53% performed insular resection, 32% performed insular disconnection, 25% performed basal ganglia disconnection, 44% used a question mark skin incision, and 76% used a free bone flap.

Conclusion: There was wide variability throughout most of the items investigated. There were no clear geographic or country specific differences. Some of that might be related to the "surgical school" where the surgeon was trained. On the other hand, many of these issues should not be "school"-related, and would need adequate RCTs to be further investigated.

p536
SURGICAL STRATEGIES OF FLE WITH CORTICAL DYSPLASIA IN TERMS OF EXTENT OF RESECTION

Son E-I
Keimyung University, Neurosurgery, Daegu, Korea

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 acute recording (ECoG) and functional brain mapping techniques to identify the epileptic and essential areas could be a procedural option especially for cortical dysplasias.

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

Ozanne A[1], Graneheim UH[2], Ekstedt G[1], Malmgren K[1]
[1]Department of Clinical Neuroscience and Rehab, Institute of Neuroscience and Physiology, Sahlgrenska Academy at Gothenburg University, Gothenburg, Sweden, [2]Department of Nursing, Umeå University, Umeå, Sweden

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

Gröppel G[1], Dorfer C[2], Czech T[2], Dressler A[1], Mühlebner-Fahrngruber A[1], Porsche B[1], Prayer D[3], Feucht M[1]
[1]Medical University Vienna, Child and Adolescent Medicine/EMU, Vienna, Austria, [2]Neurosurgery, Medical University Vienna, Vienna, Austria, [3]Radiology, Medical University Vienna, Vienna, Austria

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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EMPLOYMENT OUTCOME AFTER RESECTIVE EPILEPSY SURGERY IN SWEDEN 1995–2010 – A LONGITUDINAL OBSERVATIONAL STUDY

Edelvik A[1], Rydenhag B[1], Flink R[2], Malmgren K[1]
[1]Institute of Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden, [2]Department of Neuroscience, Uppsala University, Uppsala, Sweden

Purpose: To explore long-term employment outcome after resective epilepsy surgery in adults in a national, population-based cohort.

Method: The Swedish National Epilepsy Surgery Register encompasses data on all epilepsy surgery procedures in Sweden since 1990. Data are collected longitudinally before and at surgery, and after 2, 5, 10 and 15 years. 496 adult patients (>18 years) underwent resective epilepsy surgery in Sweden 1995–2010. In this prospective, population-based study vocational outcome was analysed after surgery and related to seizure outcome at each time point. In the cohort 473/496 had 2-year follow-up, 220/240 had 5-year follow-up, 240/278 had 10-year follow-up and 85/109 had 15-year follow-up. Employment status at each time-point was classified into full-time work (FW), part-time work (PW), full- or part-time studies (S), or benefits/unemployment (B), and patients were categorized according to their employment status pre-operatively.

Results: For patients in FW at baseline who were seizure free the last year before follow-up, 79%, 79%, 57% and 47% were still in FW after 2, 5, 10 and 15 years. Around 80% of patients with ≥75% seizure reduction continued PW or FW after surgery. For students who became seizure free 58% and 59% were in FW after five and ten years, respectively. Patients with B at baseline had the least favorable results; of seizure free patients around 30% had FW at long-term follow-up ($p = 0.004$ at 10-year follow-up).

Conclusion: Employment outcome after resective epilepsy surgery with good seizure outcome is favorable for those patients who have full-time work or are students preoperatively, but with time fewer patients stay in full-time employment. However, many can continue to work part-time. Patients who are entirely on benefits at baseline have more difficulty getting employment even after seizure freedom. A significant proportion does, however, come back to work to some extent.

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DO ANTIEPILEPTIC DRUG CHANGES AFFECT COGNITIVE OUTCOME AFTER EPILEPSY SURGERY?

Helmstaedter C, Witt J-A
Epileptology, University of Bonn, Bonn, Germany

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, clobazame, 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

Gras-Combe G[1,2], Minotti L[3], Hoffmann D[2], Krainik A[4], Kahane P[3], Chabardes S[2]
[1]CHU Montpellier, Neurosurgery, Montpellier, France, [2]CHU Grenoble, Functional Neurosurgery Unit, Grenoble, France, [3]CHU Grenoble, Epilepsy Monitoring Unit, Grenoble, France, [4]CHU Grenoble, Neuroradiology, Grenoble, France

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, dysarthria).

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

Grinenko O[1,2], Golovteev A[1,2], Dorofeeva M[3], Koptelova A[4], Vorobyev A[1], Kozlova A[1], Korsakova M[1], Nagorskaya I[1], Arkhipova N[1], Pronin I[1], Stroganova T[4], Melikyan A[1]
[1]Burdenko Neurosurgical Institute, Moscow, Russian Federation, [2]Kazaryan Clinic of Epileptology and Neurology, Moscow, Russian Federation, [3]State Medical University, Institute of Pediatrics, Neurology & Epileptology, Moscow, Russian Federation, [4]Centre of Neurocognite Research (MEG-centre) of MSUPE, Moscow, Russian Federation

Purpose: Surgical treatment of epilepsy patients with tuberous sclerosis complex (TSC) is a challenge due to multiple brain lesions and multiregional 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 subtotal 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 are 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.

Abstracts

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

Kochen S[1], Oddo S[2], Pereyra de SN[3], Seifer G[3], Campora N[3], Solis P[3], Medel N[3], Munera C[3], D'Alessio L[3], Knopka H[4], Seoane E[5]

[1]Neurosciences Clinic and Applicated Center, Epilepsy, Cognition and Behavioural, Hosp. 'R.Mejía' – IBCN, School of Medicine, Univ. Buenos Aires – National Council for Scientific and Technical Research (CONICET), Epilepsy Center, Buenos Aires, Argentina, [2]Section of Epilepsy, Neurology Div, Hosp. 'R.Mejía'- IBCN-CONICET, School of Medicine, Univ. of Buenos Aires, Buenos Aires, Argentina, [3]Neurosciences Clinic and Applicated Center, Epilepsy, Cognition and Behavioural, Hosp. 'R.Mejía' – IBCN, School of Medicine, Univ. Buenos Aires – National Council for Scientific and Technical Research (CONICET), Buenos Aires, Argentina, [4]Neurosciences Clinic and Applicated Center, Epilepsy, Cognition and Behavioural, Hosp. 'R.Mejía' – IBCN, School of Medicine, Univ. Buenos Aires – National Council for Scientific and Technical Research (CONICET), Pathological Anatomy, Buenos Aires, Argentina, [5]Neurosciences Clinic and Applicated Center, Epilepsy, Cognition and Behavioural, Hosp. 'R.Mejía' – IBCN, School of Medicine, Univ. Buenos Aires – National Council for Scientific and Technical Research (CONICET), Neurosurgery Div., Buenos Aires, Argentina

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.

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INSULAR AND INSULO-OPERCULAR EPILEPSY IN CHILDHOOD: PRESURGICAL STEREOEEG EXPLORATION AND SURGICAL OUTCOME

Chipaux M[1], Taussig D[1], Dylgjeri S[1], Lebas A[1,2], Fohlen M[1], Bulteau C[1,3], Ternier J[1], Ferrand-Sorbets S[1], Delalande O[1], Isnard J[4], Dorfmuller G[1,3]

[1]Rothschild Foundation, Paediatric Neurosurgery Department, Paris, France, [2]Department of Neurophysiology, Rouen University Hospital, Rouen, France, [3]INSERM U 663, University Paris Descartes, Paris, France, [4]Department of Functional Neurology and Epileptology, Neurological Hospital, Lyon, France

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.

p545
FEASIBILITY OF USING AN ONLINE TOOL TO ASSESS APPROPRIATENESS FOR AN EPILEPSY SURGERY EVALUATION

Hrazdil CT[1,2], Roberts JI[1,3], Wiebe S[1,3], Sauro K[1,3], Federico P[1,4], Hanson A[1], Pillay N[1], Murphy W[1], Jetté N[1,3]

[1]Department of Clinical Neurosciences and Hotchkiss Brain Institute, University of Calgary, Calgary, AB, Canada, [2]Division of Neurology, Department of Medicine, University of British Columbia, Vancouver, BC, Canada, [3]Department of Community Health Sciences and Calgary Institute for Population and Public Health, University of Calgary, Calgary, AB, Canada, [4]Department of Radiology, University of Calgary, Calgary, AB, Canada

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-

priateness scores are concordant with the clinical judgment of epilepsy specialists.

Method: We prospectively applied the tool in 107 consecutive patients with focal epilepsy seen in an epilepsy outpatient clinic. Variables collected included: seizure type, epilepsy duration, seizure frequency, seizure severity, number of antiepileptic drugs (AEDs) tried, AED-related side effects, and the results of investigations. Appropriateness ratings were then compared to retrospectively collected information concerning whether a surgical evaluation had been considered and/or performed.

Results: Thirty-nine patients (36.4%) were rated as appropriate for an epilepsy surgical evaluation, all of whom had adequately tried two or more appropriate AEDs. The majority of patients (84.6%) rated as appropriate had previously been considered or referred for an epilepsy surgical evaluation. Approximately half of participants (49.5%) were rated as inappropriate for a surgical evaluation, nearly all (98%) of who had less than two adequate trials of AEDs, were currently seizure free, or had non-disabling seizures. Tool feasibility of use was high, with the exception of assessing whether previous AED trials had been adequate and discrepancies between physician and patient reports of AED side effects.

Conclusion: Our evidence-based, online clinical decision tool is easily applied and able to determine whether patients with focal epilepsy are appropriate for a surgical evaluation. The tool successfully distills epilepsy clinical complexities into a concise and practical referral device which has the potential to improve clinical decision-making more effectively than clinical practice guidelines alone. The tool must next be validated through prospective application in different settings.

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LONG-TERM FOLLOW-UP AFTER HEMISPHEROTOMY FROM THE PATIENTS' PERSPECTIVE

Verdinelli C[1], Olsson I[1], Edelvik A[1], Flink R[2], Hallböök T[1], Rydenhag B[3], Malmgren K[3]

[1]Department of Pediatrics, Institute of Clinical Sciences, Sahlgrenska Academy at the University of Gothenburg, Gothenburg, Sweden, [2]Department of Clinical Neurophysiology, Uppsala University, Uppsala, Sweden, [3]Sahlgrenska Academy, University of Gothenburg, Institution of Neuroscience and Physiology, Gothenburg, Sweden

Purpose: To report long-term seizure outcome and parents'/patients' perception of outcome after hemispherotomy.

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 3 cases, Rasmussen 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. 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 childrens' 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

Itkonen E[1], Halkoaho A[2], Pietilä A-M[3], Kälviäinen R[4], Keränen T[5]

[1]Faculty of Health Sciences, University of Eastern Finland, Kuopio, Finland, [2]Science Service Center, Kuopio University Hospital, Finland, [3]Faculty of Health Sciences, University of Eastern Finland, Kuopio Social and Health Care Services, Kuopio, Finland, [4]Kuopio Epilepsy Center, Department of Neurology, Kuopio University Hospita, Kuopio, Finland, [5]Kuopio University Hospital, Science Service Center, Kuopio, Finland

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.

Abstracts

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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

Lukic S[1], Jovic N[2], Ćojbasić Ž[3], Popović M[4], Milošević Z[5], Bjelaković B[6], Spasić M[1]

[1]Clinic of Neurology, Clinical Centre, University of Nis, Medical School, Nis, Serbia, [2]Medical School, Clinic of Neurology and Psychiatry for Children and Youth, University of Belgrade, Belgrade, Serbia, [3]Faculty of Mechanical Engineering, University of Nis, Nis, Serbia, [4]School of Electrical Engineering, University of Belgrade, Belgrade, Serbia, [5]Department of Medical Statistic and Informatics, Institute of Public Health, University of Nis, Medical School, Nis, Serbia, [6]Medical School, Clinic of Pediatrics, Clinical Center, Univesity of Nis, Nis, Serbia

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

Sivkova S[1], Zaykova F[1], Mukhin K[2]

[1]Kazan Children Municipal Hospital 8, Kazan, Russian Federation, [2]Institute of Children Neurology named St. Luka, Moscow, Russian Federation

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 (aggression, dysphoria, excitability, hysteric reactions) were noted in 7 (21%) of patient, treated by phenobarbital and in 2 (6%) of patient, treated by topiramate. In 1 (3%) patient, treated by 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

Müller A[1], Jansen C[1], Selch C[1], Bast T[2], Lotte J[3], Guerrini R[4], Albers J[5], Muhle H[5], Auvin S[6], Korenke GC[7], Philip S[8], Keimer R[9], Striano P[10], Wolf NI[11], Püst B[12], Thiels C[13], Fogarasi A[14], Waltz S[15], Kurlemann G[16], Kovacevic-Preradovic T[17], Ceulemans B[18], Berweck S[1], Staudt M[1,19], Kluger G[1,20]

[1]Schön Klinik Vogtareuth, Vogtareuth, Germany, [2]Epilepsy Center Kork, Kehl-Kork, Germany, [3]Kinderzentrum Maulbronn, Maulbronn, Germany, [4]A. Meyer Children`s Hospital, Child Neurology Unit, University of Florence, Florence, Italy, [5]Klinik für Neuropädiatrie, UKSH, Campus Kiel, Kiel, Germany, [6]Service de Neurologie Pédiatrique et des Maladies Métaboliques-Hôpital Robert Debré-Paris, Paris, France, [7]Neuropädiatrie, Zentrum für Kinder- und Jugendmedizin, Klinikum Oldenburg, Oldenburg, Germany, [8]Children`s Hospital Birmingham, Birmingham, UK, [9]Neuropädiatrie, Pädiatrie 1, Klinikum Stuttgart, Stuttgart, Germany, [10]Pediatric Neurology, Institute Gaslini, University of Genova, Genova, Italy, [11]Child Neurology, VU University Medical Center Amsterdam, Amsterdam, The Netherlands, [12]Neuropädiatrie, Kath. Kinderkrankenhaus Wilhelmsstift, Hamburg, Germany, [13]Neuropädiatrie, Klinik für Kinder- und Jugendmedizin, Klinik der Ruhr Universität, Bochum, Germany, [14]Neurology Department, Bethesda Children's Hospital, Budapest, Hungary, [15]Neuropädiatrie, Kinderklinik Amsterdamer Straße, Kliniken der Stadt Köln, Köln, Germany, [16]Kinderklinik Münster, Neuropädiatrie, Münster, Germany, [17]Epilepsiezentrum Radeberg-Kleinwachau, Radeberg, Germany, [18]University Hospital and University of Antwerp, Antwerp, Belgium, [19]Neuropädiatrie Universitätskinderklinik, Tübingen, Germany, [20]Paracelsus Medical University, Salzburg, Austria

Purpose: Mutations in the X-linked Cyclin-dependent kinase-like 5 gene (CDKL5 gene) cause an epileptic encephalopathy, intractable seizures and an early onset severe neurological impairment. Currently there is no concept how to treat these patients. Aim of the study was to evaluate the effectiveness of different antiepiletic drugs (AED) and ketogenic diet (KD) in patients with CDKL5 mutations.

Method: We retrospectively evaluated the effectiveness of multiple AED in 40 children (female: n = 35, male: n = 5, age: 0.4–22.4 years (mean: 7.1 years)) with CDKL 5 mutations 3, 6 and 12 months after introduction of each drug. Drug response was defined as at least 50% seizure reduction.

Results: The response rate to at least one AED was 68% after 3, 43% after 6 and 23% after 12 months. The highest rate of seizure reduction after 3 months was reported during treatment with FBM (3/3), CLB (7/14), VGB (8/26), VPA (7/35) and steroids (5/26). 13 patients (33%) experienced a seizure aggravation to at least one AED.

Conclusion: Considering several limitations of our ongoing study the long-term efficacy of multiple AED and KD in patients with CDKL5 mutation was low. Our data may help to define realistic treatment goals together with the parents focusing not only on epilepsy- specific variables such as seizure frequency and epilepsy severity but on the overall health-related quality of life.

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LACOSAMIDE IN MESIAL TEMPORAL LOBE EPILEPSY (MTLE) WITH HIPPOCAMPAL SCLEROSIS (HS)

Labate A[1], Mumoli L[1], Gambardella A[1], Quattrone A[1], Kraenzel AS[2], Li W[2], Heinze HJ[2], Schmitt F[2]
[1]University of Catanzaro, Catanzaro, Italy, [2]Otto-von-Guericke-University, Magdeburg, Germany

Purpose: Traditional believe was that MTLE accompanied by HS was synonymous to druf-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 convulsion. 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/4 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 particular 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

Clemente De V
Catholic University, Paediatric Neurology Unit, Rome, Italy

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 pharmacoresistent 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), vascular (13 pts), infective (3 pts), brain tumor (3 pts), metabolic (1 pts) and various (9 pts). Co-AEDs (sodium channels blockers – SCB): SCB+ (79 pts) and SCB- (31 pts). Assessment of efficacy and safety: change from baseline in seizure frequency and presence of side effects.

Results: At the end of follow up 52% of our patients were responders (12% seizure-free). Was observed better results in children than in young adults (61% in <16 years; 43% in >16 years). We find no differences in use SCB+ or SCB- in our patients.LCM was more effectiveness in treatment of focal epilepsy (54%).It is well tolerate in 50% of patients. 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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TWO YEAR DATA ON EFFICACY AND TOLERABILITY OF LACOSAMIDE AS ADD-ON THERAPY IN PATIENTS WITH REFRACTORY FOCAL ONSET EPILEPSY AT A TERTIARY EPILEPSY CENTER

Kkolou E[1], Christou YP[1], Flourentzou A[2], Malikkidou A[3], Papacostas SS[1]
[1]The Cyprus Institute of Neurology and Genetics, Nicosia, Cyprus, [2]Nicosia General Hospital, Nicosia, Cyprus, [3]Limassol General Hospital, Limassol, Cyprus

Purpose: To investigate the efficacy and tolerability of Lacosamide (LCM) in Cypriot patients with refractory focal onset epilepsy.

Method: Thirty-one adult patients (mean age 40.8 years, 54.8% female, mean epilepsy duration 23.3 years, mean seizure rate 11.3/month) were treated with LCM as add-on therapy to ≥2 antiepileptic drugs and studied retrospectively for 2 years. Mean seizure frequency was compared for a 3-month period prior to and 2 years after LCM introduction.

Results: Two patients (6.5%) became seizure free. Three patients (9.7%) had seizure reduction by ≥75%. Seven patients (22.6%) had seizure reduction by ≥50%. Eight patients (25.8%) had no significant change from baseline. A significant reduction in the number of seizures ($p = 0.16$) and the number of concomitant AEDs ($p = 0.004$) was observed in patients completing 2 years of LCM treatment compared to baseline.

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.

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LONG-TERM EFFICACY OF ZONISAMIDE VS. CARBAMAZEPINE MONOTHERAPY FOR TREATMENT OF ADULTS WITH NEWLY DIAGNOSED PARTIAL EPILEPSY: ANALYSIS BY BASELINE SEIZURE TYPES

Baulac M[1], Patten A[2], Giorgi L[2]
[1]Hôpital Pitié-Salpêtrière, Paris, France, [2]Eisai Limited, Hatfield, UK

Purpose: To assess the long-term efficacy of once-daily zonisamide vs. twice-daily controlled-release carbamazepine monotherapy 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% [14/74] 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.

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AN OVERALL AND DOSE-RESPONSE META-ANALYSIS OF EFFICACY OF NEWER GENERATION ANTIEPILEPTIC DRUGS IN THE TREATMENT OF SECONDARILY GENERALIZED TONIC-CLONIC SEIZURES

Russo E[1], Copetti M[2], Franco V[3], Grillo E[4], Zaccara G[5]
[1]University of Catanzaro, School of Medicine, Catanzaro, Italy, [2]IRCCS Casa Sollievo della Sofferenza, Foggia, Italy, [3]University of Pavia, Pavia, Italy, [4]Medical School, University of Milan, Milan, Italy, [5]Florence Health Authority, Florence, Italy

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).

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ZONISAMIDE AND RETINAL VASCULITIS – A CAUSAL RELATIONSHIP?

Leitão-Marques M[1], Proença R[2], Luzeiro I[1]
[1]Coimbra University Hospitalar Center, Neurology, Coimbra, Portugal, [2]Coimbra University Hospitalar Center, Ophthalmology, Coimbra, Portugal

Purpose: Zonizamide 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 hypersinchronisation fenomena. Was approved in 2005 in Europe for the treatment of partial seizures with current level of evidence A in monotherapy. Occlusive retinal vasculitis is an inflammatory disease of retinal vessels, charac-

terized by microenfartes, 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 3id 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 ophtalmology, 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 decribed, we decided for the immediate suspension of the drug, and switch to eslicarbamazepina.

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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EFFECTS OF ADJUNCTIVE ZONISAMIDE TREATMENT ON WEIGHT AND BODY MASS INDEX IN PAEDIATRIC PATIENTS WITH PARTIAL EPILEPSY

Lagae L[1], Giorgi L[2], Patten A[2], Bagul M[2]
[1]University of Leuven, Leuven, Belgium, [2]Eisai Limited, Hatfield, UK

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; 31/64 (48.4%) had normal weight at study entry, compared with 42/64 (65.6%) at study end. Three patients were underweight at start of treatment and four more became underweight 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.

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IMPACT OF ADJUNCTIVE PERAMPANEL ON BEHAVIOUR IN ADOLESCENTS WITH REFRACTORY PARTIAL-ONSET SEIZURES

Lagae L[1], Velkey I[2], Bagul M[3], Yang H[4], Laurenza A[4], Kumar D[4]
[1]University Hospitals, Leuven, Belgium, [2]Regional Hospital Borsod-Abaúj-Zemplén, Miskolc, Hungary, [3]Eisai Ltd, Hatfield, UK, [4]Eisai Inc., Woodcliff Lake, NJ, USA

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.

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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

Reed RC[1], Kasteleijn-Nolst Trenité DGA[2,3]
[1]Department of Pharmacy Practice, Husson University, School of Pharmacy, Bangor, ME, USA, [2]Epilepsy, Sapienza University of Rome, Roma, Italy, [3]Medical Genetics, Utrecht University, Amsterdam, The Netherlands

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 pentylenetetrazol, 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

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 (Kasteleijn-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
EFFICACY 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

Dimova S[1], McShea C[2], Doty P[2], Werhahn KJ[3], Backer De M[1]
[1]UCB Pharma, Brussels, Belgium, [2]UCB Pharma, Raleigh, NC, USA, [3]UCB Pharma, Monheim am Rhein, Germany

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

p561
TOLERABILITY OF LACOSAMIDE CONVERSION TO MONOTHERAPY: A HISTORICAL-CONTROLLED MULTICENTER, DOUBLE-BLIND, RANDOMIZED TRIAL

Wechsler RT[1], Li G[2], O'Brien T[3], D'Cruz O[4], Williams P[4], Goodson R[4], Brock M[4]
[1]Consultants in Epilepsy and Neurology, PLLC, Boise, ID, USA, [2]Medsol Clinical Research Center, Port Charlotte, FL, USA, [3]The Royal Melbourne Hospital, University of Melbourne, Melbourne, Vic., Australia, [4]UCB Pharma, Raleigh, NC, USA

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

Manidakis I[1], Cock H[2], Loszardi D[2], Moran N[3], Nashef L[1], Richardson M[1], Elwes R[1]
[1]King's College Hospital, London, UK, [2]St George's Hospital, London, UK, [3]East Kent and Canterbury Hospitals, Canterbury, UK

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.

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.

p563
CLINICAL EXPERIENCE WITH PERAMPANEL IN A REGIONAL EPILEPSY CLINIC

Coyle H[1], Mohanraj R[1,2]
[1]Greater Manchester Neurosciences Centre, Salford Royal Hospital, Greater Manchester, UK, [2]University of Manchester, Manchester, UK

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 – 59). 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 63.33%). 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.

p564
CLINICAL TRIAL FEASIBILITY AND UK PRACTICE SURVEY OF ROLANDIC EPILEPSY AND PANAYIOTOPOULOS SYNDROME

Mellish L[1], Dunkley C[2], Ferrie C[3], Pal DK[4]
[1]King's College London, Clinical Neurosciences, London, UK, [2]Sherwood Forest Hospitals, Nottingham, UK, [3]Leeds General Infirmary, Leeds, UK, [4]King's College London, London, UK

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 summating 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.

p565
LACOSAMIDE FOR UNCONTROLLED PRIMARY GENERALIZED TONIC-CLONIC SEIZURES: AN OPEN-LABEL PILOT STUDY WITH 59-WEEK EXTENSION

Wechsler RT[1], Yates S[2], Leroy R[3], Beller C[2], Doty P[2]
[1]Consultants in Epilepsy and Neurology, PLLC, Boise, ID, USA, [2]UCB Pharma, Raleigh, NC, USA, [3]Neurological Clinic of Texas, Dallas, TX, USA

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[NCT01118949]) 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 [NCT01118962]) 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

(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.

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EFFECTS ON QUALITY OF LIFE OF LACOSAMIDE AS FIRST AND LATER ADJUNCTIVE TREATMENT FOR UNCONTROLLED PARTIAL-ONSET SEIZURES: A MULTICENTER OPEN-LABEL TRIAL

Escartin A[1], Tzvetanov P[2], Waldman Zadeh W[3], Byrnes W[4], Tennigkeit F[5], Li T[4], Werhahn KJ[5], Dedeken P[6], Backer De M[6], Borghs S[7]

[1]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, [2]Military Medical Academy, Hospital Base for Active Treatment (HBAL), Pleven, Bulgaria, [3]Broadlawns Medical Center, Des Moines, IA, USA, [4]UCB Pharma, Raleigh, NC, USA, [5]UCB Pharma, Monheim am Rhein, Germany, [6]UCB Pharma, Brussels, Belgium, [7]UCB Pharma, Slough, UK

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 with either monotherapy at ≤24 months since diagnosis (Group 1) or ≥2 previous AEDs at ≥5 years since diagnosis (Group 2). Patients received lacosamide in a 6-week fixed titration to 400 mg/day, followed by a 24-week Maintenance Phase. QOL was assessed using the Quality of Life Inventory in Epilepsy-31-P (QOLIE-31-P) at Baseline and at end of treatment.

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 in the FAS was 2.7 (SD 15.18, 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).

Conclusion: Lacosamide up to 400 mg/day resulted in improvements in QOLIE-31-P subscales with marked improvements in those receiving lacosamide after first monotherapy.

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EFFICACY AND SAFETY OF LACOSAMIDE AS FIRST ADJUNCTIVE TREATMENT FOR UNCONTROLLED PARTIAL-ONSET SEIZURES: A MULTICENTER OPEN-LABEL TRIAL

Tzvetanov P[1], Waldman Zadeh W[2], Escartin A[3], Byrnes W[4], Tennigkeit F[5], Borghs S[6], Li T[4], Werhahn KJ[5], Dedeken P[7], BackerDe M[7]

[1]Military Medical Academy, Hospital Base for Active Treatment (HBAL), Pleven, Bulgaria, [2]Broadlawns Medical Center, Des Moines, IA, USA, [3]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, [4]UCB Pharma, Raleigh, NC, USA, [5]UCB Pharma, Monheim am Rhein, Germany, [6]UCB Pharma, Slough, UK, [7]UCB Pharma, Brussels, Belgium

Purpose: To evaluate the efficacy and safety of lacosamide as first adjunctive treatment for partial-onset seizures (POS).

Method: This open-label trial (NCT00955357) enrolled patients with uncontrolled seizures (≥3 POS during 3 months before 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: 456 patients received at least one dose of lacosamide (96 Group 1, 360 Group 2), 444 had at least one post-baseline seizure assessment (FAS), and 333 completed 12 weeks. Overall, 19.8% of 12-week completers (66/333) were seizure-free after 12 weeks. Among Group 1 completers, 37.5% (27/72) were seizure-free for 12 weeks, with 26.5% (18/68) seizure-free for 24 weeks. Corresponding percentages of seizure-free patients in Group 2 were 14.9% (39/261) and 11.6% (29/249). At 12 weeks, 76.4% (55/72) of Group 1 completers achieved ≥50% reduction and 66.7% (48/72) ≥75% reduction in seizure frequency compared with Baseline. Among Group 2 completers, ≥50% and ≥75% reductions in seizure frequency were achieved by 53.3% (139/261) and 36.0% (94/261). Treatment-emergent adverse events (TEAEs) led to discontinuation in 12.5% of Group 1 and 19.2% of Group 2. Overall, the most common TEAEs were dizziness (31.3% Group 1, 33.6% Group 2), somnolence (6.3% and 15.0%) and headache (13.5% and 11.4%).

Conclusion: Lacosamide initiated as first adjunctive treatment was efficacious in achieving seizure freedom and was well-tolerated in patients with uncontrolled POS.

Supported by: UCB Pharma

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PRAGMATIC LONG-TERM OPEN-LABEL STUDY ON THE EFFECTIVENESS OF LACOSAMIDE AS ADD-ON THERAPY IN REFRACTORY PARTIAL EPILEPTIC PATIENTS

La Neve A[1], Boero G[2], Internò S[2], Pietrafusa N[1], Amoroso MG[1], Durante V[1], Luisi C[1], Amoroso N[3]
[1]Department of Neurology, University of Bari, Bari, Italy, [2]Division of Neurology SS. Annunziata Hospital, Taranto, Italy, [3]Department of Physics, University of Bari, Bari, Italy

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 responsives to at least two adequate antiepileptic drugs (AEDs).

After 3 months with stable therapy lacosamide was administrated 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 performed in order to evaluate 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 datas 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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BRIVARACETAM BIOAVAILABILITY/ BIOEQUIVALENCE COMPARISON BETWEEN 10, 50, 75 AND 100 MG TABLETS AND 100 MG INTRAVENOUS BOLUS IN HEALTHY VOLUNTEERS

Stockis A[1], Singh P[1], Hartstra J[2], Hadi S[2]
[1]UCB Pharma, Braine-L'Alleud, Belgium, [2]PRA International, Zuidlaren, The Netherlands

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 (C_{max}, $AUC_{(0\text{-}inf)}$ and $AUC_{(0\text{-}t)}$), were analysed by ANOVA.

Results: Twenty-five participants (age: 20–54 years; 13 male) were randomised. The 90% confidence intervals (CIs) around the C_{max}, $AUC_{(0\text{-}inf)}$ and $AUC_{(0\text{-}t)}$ 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 $AUC_{(0\text{-}inf)}$ and $AUC_{(0\text{-}t)}$ (90% CIs: 0.95–1.01), but iv C_{max} 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.

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CLINICAL EXPERIENCE WITH THERAPEUTIC DRUG MONITORING OF ESLICARBAZEPINE ACETATE IN NORWAY

Landmark CJ[1], Svendsen T[2], Reimers A[3], Brodtkorb E[4], Sætre E[2], Molden E[5], Johannessen SI[6]
[1]Department of Pharmacy and Biomedical Science, Oslo and Akershus Unviersity College of Applied Sciences, Oslo, Norway, [2]National Center for Epilepsy, Oslo University Hospital, Sandvika, Norway, [3]Pharmacology, St. Olav's Hospital, Trondheim, Norway, [4]Neurology, St. Olav's Hospital, Trondheim, Norway, [5]Center for Psychopharmacology, Diakonhjemmet Hospital, Oslo, Norway, [6]Department of Pharmacology, National Center for Epilepsy, Oslo University Hospital, Sandvika, Norway

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.

Abstracts

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PATIENTS' VS. PRESCRIBERS' VIEW OF ANTIEPILEPTIC MEDICATION

Mevåg MA[1], Landmark CJ[2], Nakken KO[3], Henning O[3]
[1]South-East Norway Pharmaceutical Trust, Radium Hospital, Oslo, Norway, [2]Oslo and Akershus University College of Applied Sciences, Oslo, Norway, [3]National Center for Epilepsy, Sandvika, Oslo University Hospital, Sandvika, Norway

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
LENNOX-GASTAUT SYNDROME AND VAGUS NERVE SIMULATOR: CASE REPORT OF 5 YEAR FOLLOW UP

Meira ID[1,2], Baltar AC[3], Pereira V[4], Leon S[4]
[1]Neurology, Rio de Janeiro Federal University, Rio de Janeiro, Brazil, [2]Instituto Estadual do Cerebro Paulo Niemeyer, Epilepsy Center, Rio de Janeiro, Brazil, [3]Instituto Estadual do Cerebro Paulo Niemeyer, Rio de Janeiro, Brazil, [4]Hospital Universitario Clementino Fraga Filho, Rio de Janeiro, Brazil

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. Became with uncontrolled seizures, with severe electroencephagrafic 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

Kottmel K, Geiblinger S, Pirker S, Freydl E, Langenberger E, Riederer F, Sedlacek C, Baumgartner C
Neurological Center Rosenhuegel, Karl Landsteiner Institute for Clinical Epilepsy Research and Cognitive Neurology, 2nd Neurological Department, Vienna, Austria

Purpose: Perampanel (PER), an oral selective antagonist of a-amino-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, suicidality in 1 patient, vertigo and gait disorder in 3 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 EpiTracks. 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, OXCARBAZEPINE, AND THEIR ACTIVE METABOLITES CARBAMAZEPINE-10,11-EPOXIDE AND LICARBAZEPINE IN HUMAN PLASMA

Ferreira AF[1,2], Rodrigues M[1,2,3], Rosado L[4], Rosado P[4], Falcão A[2,3], Alves G[1,2]

[1]CICS-UBI – Health Sciences Research Centre, University of Beira Interior, Covilhã, Portugal, [2]CNC – Centre for Neuroscience and Cell Biology, University of Coimbra, Coimbra, Portugal, [3]Faculty of Pharmacy, University of Coimbra, Coimbra, Portugal, [4]Hospital Centre of Cova da Beira, Covilhã, Portugal

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® Star C18 column (55 mm × 4 mm, 3 µm) at 35°C 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 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 ($r^2 > 0.9946$) 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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THERAPEUTIC DRUG MONITORING OF ANTICONVULSANTS IN CLINICAL PRACTICE IN RUSSIA

Leonova M[1], Belousov Y[1], Shteynberg L[1], Tischenkova I[1], Sokolov A[2]

[1]Russian State Medical University, Clinical Pharmacology, Moscow, Russian Federation, [2]Moscow Medical Academy, Clinical Pharmacology, Moscow, Russian Federation

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 (C_{min}, C_{max}) 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, C_{max} 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, C_{min} 13.5 ± 0.2 mg/l, C_{max} 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 C_{min} and C_{max}, only by C_{max} – 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.

p576

THE EFFECT OF ORAL CONTRACEPTIVES ON THE LAMOTRIGINE CONCENTRATION DEPENDS ON COMEDICATION*

Wegner I[1,2], Wilhelm AJ[3], Lambrechts DAJE[4], Sander JW[1,5], Lindhout D[1,2]

[1]SEIN – Stichting Epilepsie Instellingen Nederland, Zwolle, The Netherlands, [2]University Medical Centre Utrecht, Utrecht, The Netherlands, [3]VU Medical Centre, Amsterdam, The Netherlands, [4]Epilepsy Centre Kempenhaeghe, Heeze, The Netherlands, [5]UCL Institute of Neurology, London, UK

Purpose: We prospectively evaluated the influence of cyclic oral contraceptive (OC) use on lamotrigine (LTG) serum levels when used in combination therapy.

Method: We used a dried blood spot sampling method to evaluate antiepileptic drug concentrations every other day in women with epilepsy using LTG in combination with valproate (VPA) (n = 7), carbamazepine (CBZ) (n = 3) or oxcarbazepine (OXC) (n = 1). Results were compared with women on LTG monotherapy and OCs (n = 12). NONMEM software was used for population pharmacokinetic analysis.

Results: The final model estimated the mean study population value of LTG clearance 3.17 l/h (relative standard error 12%). Introduction of covariates for co-medication (VPA, CBZ, OXC and OC) significantly reduced the between subject variability. We found a significant influence of OC comedication on LTG clearance in both LTG monotherapy (clearance with OC 4.02 ± 0.38 l/h, OC free week 3.03 ± 0.39 l/h) and in LTG-CBZ combination (clearance with OC 4.95 ± 0.15 l/h, OC free week 4.15 ± 0.26 l/h). We found no influence of OC in the LTG-VPA combination (clearance with OC 0.99 ± 0.16 l/h, OC free week 0.90 ± 0.15 l/h).

Conclusion: We found no significant influence of cyclic OC use on LTG or VPA clearance when used in combination therapy. Adding OCs to LTG monotherapy or the combination LTG-CBZ, significantly increased the LTG clearance and thus reduced LTG serum levels. In the combination LTG-CBZ, OCs had a non-significant effect on CBZ clearance.

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EFFECT OF DOSING INTERVALS ON THE PHARMACOKINETIC PROFILE OF USL255, ONCE-DAILY EXTENDED-RELEASE TOPIRAMATE

Gidal B[1], Clark AM[2], Anders B[2]
[1]University of Wisconsin Madison, School of Pharmacy, Madison, WI, USA, [2]Upsher-Smith Laboratories, Inc., Maple Grove, MN, USA

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 (C_{min}) and maximum plasma concentrations (C_{max}) were evaluated for 96 h.

Results: The impact of a missed dose on C_{min} 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 C_{min} 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; C_{max} values were between 2.1–11.8% higher than steady-state and C_{min} 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 C_{max} 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

Pisarenco I, Agazzi P
Neurocenter, Lugano, Switzerland

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 emergent 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 MR) 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 of Levonoregestrel 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

Ahmadi M[1,2], Khodaie B[1], Lotfinia M[1,3], Lotfinia AA[1], Jafarian M[1]
[1]Shefa Neuroscience Research Center, Tehran, Iran, [2]Islamic Azad University, Karaj, Iran, [3]Shahid Beheshti University of Medical Sciences, Tehran, Iran

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 reduce 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

Lai Y, Li N, Lawrence W, Wehrens XHT, Anderson AE
Baylor College of Medicine, Houston, TX, USA

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 observation that epileptic individuals exhibit resting tachycardia and prolonged QTc. However, whether these changes predispose to stimulation-induced ventricular tachycardia (VT) and whether b 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 b 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

Brewster AL[1], Nguyen LH[2], Anderson AE[3]
[1]Department of Psychological Sciences, Purdue University, West Lafayette, IN, USA, [2]Department of Neuroscience, Baylor College of Medicine, Houston, TX, USA, [3]Department of Pediatrics-Neurology, Baylor College of Medicine, Houston, TX, USA

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 epilepsy 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 astroglia in the hippocampus of NS-PTEN KO mice, and hyperativation 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 immunosuppressant treatments have seizure-attenuating effects in this model of CD.

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p582
INCREASED ACTIVITY OF HYDROGEN PEROXIDE-REMOVING ENZYMES IN HIPPOCAMPI OF THE PATIENTS WITH MESIAL TEMPORAL LOBE EPILEPSY DUE TO HIPPOCAMPAL SCLEROSIS

Ristić AJ[1], Sokić D[1], Bogdanović Pristov J[2], Baščarević V[3], Nestorov J[4], Vojvodić N[1], Kovačević M[1], Spasojević I[2]
[1]Epilepsy Center, Neurology Clinic, Clinical Center of Serbia, Belgrade, Serbia, [2]Department of Life Sciences, Institute for Multidisciplinary Research, University of Belgrade, Belgrade, Serbia, [3]Neurosurgery Clinic, Clinical Center of Serbia, Belgrade, Serbia, [4]Department of Biochemistry, Institute for Biological Research "Siniša Stanković", University of Belgrade, Belgrade, Serbia

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 tempolal 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 to 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 HIPPOCAMPI IN PATIENTS WITH DRUG-RESISTANT MESIAL TEMPORAL LOBE EPILEPSY

Ristić AJ[1], Sokić D[1], Baščarević V[2], Spasić S[3], Vojvodić N[1], Savić S[4], Raičević S[2], Kovačević M[1], Savić D[5], Spasojević I[6]
[1]Epilepsy Center, Neurology Clinic, Clinical Center of Serbia, Belgrade, Serbia, [2]Neurosurgery Clinic, Clinical Center of Serbia, Belgrade, Serbia, [3]Department of Chemistry, Institute of Chemistry, Technology, and Metallurgy, University of Belgrade, Belgrade, Serbia, [4]Institute of Forensic Medicine, Medical School, University of Belgrade, Belgrade, Serbia, [5]Department of Neurobiology, Institute for Biological Research "Siniša Stanković", University of Belgrade, Belgrade, Serbia, [6]Life Sciences Department, Institute for Multidisciplinary Research, University of Belgrade, Belgrade, Serbia

Purpose: Altered hippocampal metallome 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 metallome, copper and manganese deficiency, and the absence of iron accumulation.

p584
RETINAL NERVE FIBER LAYER THICKNESS: A POSSIBLE BIOMARKER OF DRUG RESISTANCE IN EPILEPSY

Balestrini S[1,2], Bartman AP[1], Clayton LM[1], Chinthapalli KV[1], Novy J[1], Coppola A[1], Wandschneider B[1], Koepp MJ[1], Stern W[1], Acheson J[3], Bell GS[1], Sander JW[1], Sisodiya SM[1]
[1]NIHR University College London Hospitals Biomedical Research Centre, Department of Clinical and Experimental Epilepsy, UCL Institute of Neurology, London, UK, [2]Neuroscience Department, Polytechnic University of Marche, Ancona, Italy, [3]Department of Neuro-Ophthalmology, National Hospital for Neurosurgery and Neurology, London, UK

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, $p = 0.03$). 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.

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ACONITUM COCHLEARE WOROSCHIN-OIL ATTENUATES THE MOLECULAR MARKERS OF EPILEPTOGENESIS IN PENTYLENETETRAZOLE INDUCED KINDLED MICE WITH SAFE TOXICITY PROFILE

Malhi SM[1], Mazhar F[1], Zeeshan M[1], Chaudhary MI[1], Shaheen F[1], Simjee SU[1,2]
[1]HEJ Research Institute of Chemistry, University of Karachi, Karachi, Pakistan, [2]Dr. Panjwani Center for Molecular Medicine and Drug Research, International Center of Chemical and Biological Sciences, University of Karachi, Karachi, Pakistan

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. Neurtrophic 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.

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PROTEOMIC PROFILING OF THE HIPPOCAMPUS OF RATS SUBJECTED TO THE PILOCARPINE MODEL OF EPILEPSY PRESENTING STATUS EPILEPTICUS OR NOT

Persike DS[1], Lima ML[2], Amorim RP[3], Araújo MGL[1], Sierra LF[1], Cavalheiro EA[1], Schenkman S[2], Fernandes MJDS[1]

[1]Escola Paulista de Medicina, Neurologia e Neurocirurgia, São Paulo, Brazil, [2]Escola Paulista de Medicina, Microbiologia, Imunologia e Parasitologia, São Paulo, Brazil, [3]Escola Paulista de Medicina, São Paulo, Brazil

Purpose: The temporal lobe epilepsy (TLE) is the most common type of partial complex seizure in adulthood. High doses of pilocarpine to rats induce *status epilepticus* (SE) and reproduce the main characteristics of TLE. This model appears to be highly isomorphic with the human disease. We employed a two-dimensional gel electrophoresis (2-DE) to study differential expression of proteins in the hippocampus of rats exhibiting SRS induced by pilocarpine. We also assessed the proteomic profile of rats that not presented SE after pilocarpine administration.

Method: Male Wistar rats (weight~250 g). Groups: PILO SE: animals treated with pilocarpine (360 mg/kg, N = 6) presenting SE and PILO SE free (same dose of pilocarpine but without SE). Control: Saline (N = 6). Both groups were analyzed 90 days after SE onset or pilocarpine administration. Hippocampi were dissected and homogenized in a lysis buffer. Homogenates were used to perform 2-DE. Protein spots were analyzed by PDQuest software revealing forty proteins differentially expressed in the hippocampus of epileptic rat compared to control ($p < 0.05$, Student's test). LC MS/MS results were analyzed with MASCOT.

Results: Thirty-one of the identified proteins were up-regulated in epileptic rat, among them dihydropyrimidinase, 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 phosphatidylethanolamine-binding protein. In the free SE group were identified twenty-five differentially expressed proteins compared with epileptic and control animals, between them dihydropyrimidinase 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 dihydropyrimidinase-related protein 2 is related to schizophrenia. Animals SE free also exhibit alterations in protein expression.

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EFFECT OF THE ANTI-SEIZURE DRUGS VINPOCETINE, CARBAMAZEPINE AND VALPROIC ACID ON IL-1β AND TNF-α EXPRESSION IN THE HIPPOCAMPUS

Gómez CD, Buijs RM, Sitges M

Instituto de Investigaciones Biomédicas/Universidad Nacional Autónoma de México, Biología Celular y Fisiología, México, Mexico

Purpose: Pro-inflammatory cytokines are known to be increased by seizures or in epileptic like conditions in the brain. However studies directed to explore the effects of anti-seizure drugs on brain inflammation are missing. Therefore, in the present study the effects of the two classical antiepileptic drugs, carbamazepine and valproic acid, and the non-classical anti-seizure drug, vinpocetine were investigated on pro-inflammatory cytokines expression in the hippocampus, a brain structure particularly epileptogenic.

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, pentylenetetrazole 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, pentylenetetrazole 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.

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

Song HK[1], Choi HC[2], Shin DJ[3], Suh SW[4]

[1]Neurology, Hallym University Medical Center Kangdong Hospital, Seoul, Korea, [2]Neurology, Hallym University Choonchun Hospital, Seoul, Korea, [3]Gacheon University Ghil Hospital, Incheon, Kuwait, [4]Physiology, Hallym University Medical College, Choonchun, Korea

Purpose: Citicoline (CDP-choline; cytidine 5′-diphosphocholine) is an important intermediate in the biosynthesis of cell membranes phospholipids. Citicoline serves as a choline donor in the metabolic pathways for biosynthesis of acetylcholine and neuronal membrane phospholipids, mainly phosphatidylcholine. The ability of citicoline to reverse the neuronal injury has been tested in animal models of cerebral ischemia and also has been performed clinical trial in stroke patients. However, no previous report has examined the effect of citicoline on seizure-induced neuron death. To clarify the therapeutic potency of citicoline on seizure-induced neuron death, we used an animal model of pilocarpine-induced epilepsy.

Method: Temporal lobe epilepsy (TLE) was induced by intraperitoneal injection of pilocarpine (25 mg/kg) in male adult rats. Citicoline (100 or 300 mg/kg) was injected into the intraperitoneal space 2 h after seizure onset and a second injection was performed 24 h after the seizure. Superoxide production was detected by dehydroethidium at 3 h after the seizure. Neuronal injury and microglia activation was evaluated at 1 week after the seizure.

Results: Here we found that post-treatment of citicoline showed no protection of superoxide production. Even citicoline treatment increased

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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MEMORY IMPAIRMENT CAUSED BY SPREADING DEPRESSION MODULATED BY INJECTION OF NIFEDIPINE

Lotfinia M[1,2]
[1]*Shefa Neuroscience Research Center, Tehran, Iran,* [2]*Shahid Beheshti University of Medical Sciences, Tehran, Iran*

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

Gey L[1,2], *Gernert M*[1,2], *Löscher W*[1,2]
[1]*University of Veterinary Medicine Hannover, Foundation, Department of Pharmacology, Toxicology and Pharmacy, Hannover, Germany,* [2]*Center for Systems Neuroscience, Hannover, Germany*

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.

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ELECTROGRAPHIC AND BEHAVIORAL CHARACTERIZATION OF EP-80317 ANTICONVULSANT EFFECTS IN PILOCARPINE-TREATED RATS

Curia G[1,2], *Lucchi C*[1,2], *Torsello A*[3], *Biagini G*[1,2]
[1]*Department of Biomedical, University of Modena and Reggio Emilia, Metabolic and Neural Sciences, Modena, Italy,* [2]*Department of Neurosciences, NOCSAE Hospital, Modena, Italy,* [3]*Department of Health Sciences, University of Milano-Bicocca, Monza, Italy*

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 ± 1.16; 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: 44.7% 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 anticonvulsant properties in the pilocarpine model of SE, and suggest the presence in the rat population of full responders and non-responders.

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THE EFFECT OF RAPAMYCIN (SIROLIMUS) ON PENICILLIN-INDUCED EPILEPTIFORM ACTIVITY IN RATS

Ankarali S[1], Beyazcicek E[1], Demir S[1], Taka S[1], Ankarali H[2]
[1]Physiology, Institute of Health Sciences/Duzce University, Duzce, Turkey, [2]Biostatistics, Institute of Health Sciences/Duzce University, Duzce, Turkey

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 the 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 urethane, 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 THYMOQUINONE ON PENICILLIN-INDUCED EPILEPTIFORM ACTIVITY IN RATS

Beyazcicek E[1], Ankarali S[1], Beyazcicek O[1], Ankarali H[2], Demir S[1], Ozmerdivenli R[1]
[1]Physiology, Duzce University/Institute of Health Sciences, Duzce, Turkey, [2]Biostatistic, Duzce University/Institute of Health Sciences, Duzce, Turkey

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 anticonvulsant, anticancer, 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 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 acitivty 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-ARACHIDONOYLGLYCEROL MEDIATES CANNABINOID-DEPENDENT EFFECTS IN A MOUSE MODEL OF TEMPORAL LOBE EPILEPSY

Rüden von E-L[1,2], Bogdanovic RM[1,2], Wotjak CT[3], Potschka H[1]
[1]Institute of Pharmacology, Toxicology and Pharmacy, Ludwig-Maximilians-University, Munich, Germany, [2]Graduate School of Systemic Neurosciences, Munich, Germany, [3]Max Planck Institute of Psychiatry, Munich, Germany

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:CremophorEL: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 afterdischarge 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 ISOBOLOGRAPHIC ANALYSIS

Kondrat-Wróbel M[1], Mazurkiewicz LP[1], Wróbel J[1], Łuszczki JJ[1,2]

[1]Medical University of Lublin, Lublin, Poland, [2]Institute of Rural Health, Lublin, Poland

Purpose: To isobolographically 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, 500V, 50 Hz, 0.2s stimulus duration) delivered via auricular electrodes. Type I isobolographic 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 + phenobarbital + 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?

Lipatova L[1], Serebryanaya N[2], Sivakova N[1]

[1]V.M. Bekhterev Psychoneurological Research Institute, St. Petersburg, Russian Federation, [2]North-Western State Medical University named after I.I. Mechnikov, St. Petersburg, Russian Federation

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 rIL-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 (Roncoleukinum®) – 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 Roncoleukinum®. 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-8, 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 (U) <0.01, respectively), by more than 4 times decreased the concentration of pro-inflammatory cytokine IL-8 after Roncoleukinum® treatment of PE. Changes of these immunological parameters correlated with clinical improvement of PE: reduction of seizure frequency and positive EEG changes.

Thus Roncoleukinum® 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

Kubová H[1], Mares P[2], Mikulecká A[3]

[1]Institute of Physiology, Academy of Sciences of Czech Republic, Prague, Czech Republic, [2]Institue of Physiology, Academy of Sciences CR, Prague, Czech Republic, [3]Institute of Physiology Academy of Sciences CR, Prague, Czech Republic

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 ANTIEPILEPTIC DRUGS (AEDS) IN EXPERIMENTAL SEIZURE MODELS

Katyal JPK, Kumar H, Gupta YK
All India Institute of Medical Sciences, Pharmacology, New Delhi, India

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 Pentylenetetrazole (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, Malanodialdehyde (MDA) and reduced glutathione (GSH) andzinc 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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p599
A COMPARISON OF TREATMENT AND EMERGENCY CARE USE FOR PROLONGED SEIZURES IN CHILDREN OCCURRING IN THE COMMUNITY IN ITALY: A MODEL BASED ANALYSIS

Vigevano F[1], Beccaria F[2], Beghi E[3], Franzoni E[4], Minicucci F[5], Romeo A[6], Striano S[7], Verrotti A[8]
[1]Bambino Gesù Pediatric Hospital, Neurology Unit, Rome, Italy, [2]Azienda Ospedaliera "C. Poma", Mantova, Italy, [3]Istituto di Ricerche Farmacologiche Mario Negri, Milano, Italy, [4]Azienda Ospedaliera di Bologna, Bologna, Italy, [5]Ospedale San Raffaele, Milano, Italy, [6]AO Fatebenefratelli e Oftalmico, Milano, Italy, [7]Ospedale Policlinico Federico II, Napoli, Italy, [8]Clinica Pediatrica, Università di Perugia, Perugia, Italy

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.

Sponsor: ViroPharma SPRL-BVBA.

p600
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 BEHAVIOURLY DISTRESSED WHEN ATTEMPTS WERE MADE TO HAVE OVERNIGHT EEGS

Shankar R[1,2], Jory C[1], Hagnow K[3], Cox D[1], Tripp M[1]
[1]Cornwall Foundation NHS Trust, Truro, UK, [2]Exeter Medical School, Truro, UK, [3]Just Checking, Lapworth, UK

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

Markovic I, Sporis D, Susak I, Basic S
University Hospital Dubrava, Department of Neurology, Zagreb, Croatia

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 in ED, but it is strongly indicated in older patients with first partial seizure. There is no need for preventive parenteral administration of AET. The study strongly indicates the need for guidelines for seizure workup in the ED.

p602
MEMORY & EPILEPSY: WHAT FACTORS DETERMINE THE SEVERITY OF MEMORY DECLINE IN EPILEPTIC PATIENTS?

Bray EL
Cardiff University, Cardiff, UK

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 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.

p603
EPILEPSIWEBBEN- AN OPEN INTERNETBASED INFORMATION SITE FOR ADOLESCENTS WITH EPILEPSY

Neideman M[1], Adolfsson T[2], Wide K[2]
[1]Karolinska Universitetssjukhuset, Astrid Lindgrens Barnsjukhus i Huddinge, Neuropediatriken B66, Stockholm, Sweden, [2]Karolinska Universitetssjukhuset, Astrid Lindgrens Barnsjukhus, Neuropediatriken B66, Stockholm, Sweden

Purpose: To develop a website intended 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.

p604
THE POEM STUDY: TESTING THE IMPACT OF A DIGITAL HEALTH PLATFORM IN U.S. VETERANS WITH EPILEPSY

Hixson JD
University of California San Francisco, Neurology, San Francisco, CA, USA

Purpose: The purpose of the POEM (Policy for Optimal Epilepsy Management) study was to assess the impact of a digital health management platform in a population of U.S. Veterans with epilepsy. The digital intervention included a social media forum, condition-specific tracking tools, and educational resources.

Method: We conducted a pragmatic clinical trial in U.S. Veterans with epilepsy that had not previously used the PatientsLikeMe platform (www.patientslikeme.com). We utilized mixed recruiting techniques,

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, were 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?

Dogan Ak P[1], Ataklı HD[2], Yüksel B[3], Güveli B[2], Sarı H[2]
[1]Neurology Department, Fatih Sultan Mehmet Education and Research Hospital, Istanbul, Turkey, [2]Bakirkoy Psychiatry, Neurology and Neurosurgery Research and Training Hospital, I.Neurology Department, Istanbul, Turkey, [3]Neurology Department, Antalya Education and Research Hospital, Antalya, Turkey

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) 0.30.3% 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%20.6 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

Braams O[1], Meekes J[1], Braun K[2], Schappin R[1], Jennekens-Schinkel A[3], Nieuwenhuizen OV[3], Dutch Collaborative Epilepsy Surgery Programme (DuCESP)
[1]Psychology, Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, The Netherlands, [2]Neurology, Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, The Netherlands, [3]Bio Research Center for Children, Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, The Netherlands

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

Aydemir N[1], Kaya B[2], Yıldız G[2], Baklan B[3], Öztura İ[4]
[1]Department of Psychology, Izmir University of Economics, Izmir, Turkey, [2]Izmir University of Economics, Izmir, Turkey, [3]Department of Neurology, Dokuz Eylül University, Izmir, Turkey, [4]Dokuz Eylül University, Izmir, Turkey

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 previously developed epilepsy stigma, overprotection in epilepsy and concerns 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 ($t = 3.15$, $p = 0.01$) which was higher in females. Number of seizures created significant 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

Giráldez BG[1], Sierra-Marcos A[1], Sopelana D[2], Sáez Pinel R[1], Serratosa JM[1]
[1]Department of Neurology, Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain, [2]Deparment of Neurology, Hospital General de Albacete, Albacete, Spain

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 occasional 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 recognized 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 syndromic diagnosis has relevant diagnostic and therapeutic practical implications (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 epilepsies as the history and/or routine EEG studies may not be enough to reach a diagnosis of reflex epilepsy.

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p609
PERFORMANCE OF A MULTIDISCIPLINARY SPECIALIST SERVICE FOR ADULT PATIENTS WITH EPILEPSY AND INTELLECTUAL DISABILITY

Tan IY[1], Linden van der P[1], Erp van G[2], Schelhaas J[2], Majoie M[2]
[1]Kempenhaeghe, Long Stay, Heeze, The Netherlands,
[2]Kempenhaeghe, Heeze, The Netherlands

Purpose: Patients have difficulty finding the appropriate care service when they suffer from both epilepsy and ID (Intellectual Disability). Epilepsy-centre Kempenhaeghe started a specialised clinic in 2008 for adult outpatients with refractory epilepsy and ID. Care was provided by a multidisciplinary 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 inital 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 specialist, while 21% remained in care of the Epilepsy centre and a minority was referred to another specialist, e.g. a geneticist or a rehabilitation specialist.

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

Mishra VN
Institute of Medical Sciences, Banaras Hindu University, Neurology, Varanasi, India

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 profarma 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 Neurologists 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 a excellent media tool in North India, for epilepsy education.

p611
SOCIODEMOGRAPHIC DISPARITIES IN ADMINISTRATION OF ANTIEPILEPTIC DRUGS TO ADULTS IN GERMANY

Hamer HM[1], Kostev K[2]
[1]University of Erlangen, Neurology/Epilepsy Center, Erlangen, Germany, [2]IMS Health GmbH, Epidemiology & Pharmacovigilance, Frankfurt, Germany

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 0.72–0.92; $p < 0.001$) were frequently administered in rural areas. Living in an urban community raised the likelihood to be treated with levetiracetam (OR 1.23; 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

Salawu FK[1], Danburam A[2], Popoola A[3], Martins OF[2]
[1]Federal Medical Centre, Internal Medicine-Neurology, Yola, Nigeria, [2]Federal Medical Centre, Internal Medicine, Yola, Nigeria, [3]Federal Medical Centre, Paediatrics, Gombe, Nigeria

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

Guerriero V[1], Di Folco S[1], Matricardi M[2], Brinciotti M[2], Zavattini GC[1]
[1]Sapienza, Department of Dynamic and Clinical Psychology, University of Rome, Rome, Italy, [2]Sapienza, Department of Pediatric and Child Neuropsychiatry, University of Rome, Rome, Italy

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: $t = 0.14$, $p > 0.05$; family: $t = -0.24$, $p > 0.05$; other: $t = 0.87$, $p > 0.05$). 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 influent 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.

Abstracts

p615
HOW DOES THE LABEL "EPILEPTIC" INFLUENCE ATTITUDES TOWARDS EPILEPSY?

Friedrich L[1], Taslak M[2], Bielen I[1]
[1]University Hospital "Sveti Duh", Zagreb, Croatia, [2]Faculty of Humanities and Social Sciences, Psychology Department, Zagreb, Croatia

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

Allmenvon A[1], Nirkko A[2], Goette J[3], Mathis J[2], Krestel H[2]
[1]University Hospital, and University of Bern, Neurology, Engineering and Information Technology, Bern, Switzerland, [2]Neurology, Bern University Hospital, Bern, Switzerland, [3]Engineering and Information Technology, Bern University, Bern, Switzerland

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

Strzelczyk A[1], Hermsen A[1], Belke M[1], Oertel WH[1], Knake S[1], Rosenow F[1], Hamer HM[2]
[1]Philipps-University Marburg, Marburg, Germany, [2]Friedrich-Alexander-University, Erlangen, Germany

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, zygomatic 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

Chen J[1], Yan B[2], Zhou D[1]
[1]West China Hospital, Sichuan University, Neurology, Chengdu, China, [2]West China Hospital, Sichuan University, Chengdu, China

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.

p620
FEASIBILITY OF WHOLE BODY VIBRATION TRAINING IN PEOPLE WITH EPILEPSY, OSTEOPENIA AND AN INTELLECTUAL DISABILITY

Snoeijen-Schouwenaars F, Tan I, Verschuure P
Kempenhaeghe, Heeze, The Netherlands

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 bonemarkers CTx and P1NP.

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

Prosperetti C, Zellini F, Abbafati M, Pisarenco I, Agazzi P
Ospedale Civico, Neurologia, Lugano, Switzerland

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

Gardella E[1], Larsen J[1,2,3], Wolff M[4], Schmiedel G[5], Kirkpatrick M[6], Barisic N[7], Depienne C[8,9], Troncoso M[10], Jepsen B[11], Nikanorova M[11], Troncoso L[10], Bevot A[4], Hjalgrim H[3,12], Beniczky S[1,13], Møller RS[3,12]
[1]Danish Epilepsy Center, Department of Clinical Neurophysiology, Dianalund, Denmark, [2]ICMM, Panum Institute, University of Copenhagen, Copenhagen, Denmark, [3]Faculty of Health Sciences, Institute of Regional Health Services Research, University of Southern Denmark, Denmark, [4]Department of Pediatric Neurology, University Children's Hospital, Tübingen, Germany, [5]Clinic for Children and Adolescents, Esslingen, Germany, [6]Tayside Children's Hospital, Dundee, UK, [7]Department of Pediatrics, University Hospital Centre Zagreb, Zagreb, Croatia, [8]Faculté de Médecine, Université Pierre et Marie Curie, Paris, France, [9]INSERM UMRS 975, CNRS UMR 725, Paris, France, [10]Child Neurology Service Hospital San Borja Arriarán, University of Chile, Santiago, Chile, [11]Danish Epilepsy Center, Child Neurology, Dianalund, Denmark, [12]Danish Epilepsy Center, Dianalund, Denmark, [13]Aarhus University Hospital, Department of Clinical Neurophysiology, Aarhus, Denmark

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-temporal 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

Cieza Ortiz SI[1], Urrestarazu Bolumburu E[1], Alegre Esteban M[1], Valencia Ustarruz M[2], Artieda Gonzalez-Granda J[1], Sanchez-Carpintero R[3]
[1]Neurophysiology, Clínica Universidad de Navarra, Pamplona, Spain, [2]Centro de Investigación Medica Aplicada, Pamplona, Spain, [3]Clinica Universidad de Navarra, Neuropediatrics, Pamplona, Spain

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

Ferrari-Marinho T, Perucca P, Mok K, Olivier A, Hall J, Dubeau F, Gotman J
Montreal Neurological Institute and Hospital, McGill University, Montreal, QC, Canada

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 HFO 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. HFOs (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 HFO 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 HFOs. 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 HFOs.

p625
EEG COHERENCY IN CHILDREN WITH AUTISM

Radivojevic V, Car M, Milovanovic M, Pejovic-Milovancevic M
Institute of Mental Health, Belgrade, Serbia

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.

p626
WHITE BLOOD CELL COUNT IN PATIENTS WITH EPILEPTIC SEIZURES

Papaliagkas V, Kazis D, Mavroudis I, Daglis I, Kolios S, Papagiannopoulos S, Bostantjopoulou S
Aristotle University of Thessaloniki, Third Department of Neurology, Thessaloniki, Greece

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. Papanikolaou" 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.

p627
THE ROLE OF EEG IN EPISODES OF LOSS OF COSCIOUSNESS: ONE OR MORE RECORDINGS?

Kazis DA[1], Papaliagkas V[1], Mavroudis I[1], Daglis I[1], Rossopoulos N[2], Kolios S[1], Bostantjopoulou S[1]
[1]Third Department of Neurology, Aristotle University of Thessaloniki, Thessaloniki, Greece, [2]Technological Educational Institute, Informatics & Communication Department, Serres, Greece

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 $\pm$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.

p628
NON-CONVULSIVE STATUS EPILEPTICUS IN PATIENTS WITH POST COMA UNCONSCIOUSNESS AT SEVERE CRANIOCEREBRAL INJURY

Aleksandrov M[1], Ulitin A[2], Schcerbinin A[1], Kuznecova L[1], Aleksandrova T[1]
[1]Saint Petersburg I.I. Dzhanelidze Research Institute of Emergency Medicine, Saint Petersburg, Russian Federation, [2]Russian Polenov Neurosurgical Institute, Saint Petersburg, Russian Federation

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 epilepticus 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 phenomena. 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 «spike – 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

clear consciousness has occurred in 48 patients; in 4 cases the permanent vegetative condition was formed.

Conclusion: Epileptic activity is registered in approximately 80% of patients with severe craniocerebral injury in the post coma period. However a distinction needs to be drawn between the status epilepticus and the epileptiform activity which does not determine a severity of the patient condition. Basic "axes" of distinction are the index and prevalence of epileptic activity. When the epileptic activity index is more than 30% the pattern should be considered as non-convulsive status epilepticus.

p629
COGNITIVE FUNCTIONS IN PATIENTS WITH FRONTAL LOBE EPILEPSY DURING TOPIRAMATE AND DEPAKINE THERAPY

Selitskii GV[1], *Sorokina ND*[2]
[1]*Neurology, Moscow State Medical and Dental University, Moscow, Russian Federation,* [2]*Physiology, Moscow State Medical and Dental University, Moscow, Russian Federation*

Purpose: The study was aimed to analyse the cognitive effects of topamax (TPM) in patients with symptomatic frontal lobe epilepsy (left and right-sided epileptic foci) manifested by focal seizures with secondary generalization as compared with depakine (VPA) effect and control group.

Method: Three groups of epilepsy patients and control group (healthy subjects) were administered neuropsychological and cognitive tests for attention, psychomotor speed, memory, frontal lobe functions (Wisconsin Card Sorting Test), emotion and others. The 1-d and 2-d groups included patients with symptomatic frontal lobe epilepsy with focal secondarily generalized seizures (left and right-sided foci, 79 and 74 subj.). All patients had a medication change from DPA to TPM 1.5 $\pm$ 0.5 years ago. They were free from seizures and had medium TPM dosage of 200 mg/day. The patients of 3-d group had the same form of epilepsy and had long-term VPA therapy without withdrawn, mean DPA dosage of 400 mg/day (162 subject). The statistical intergroup comparisons were analysed for all tests in double-blind study.

Results: The statistically significant differences on measures of attention and frontal lobe associated functions were obtained for groups of patients and control. Higher scores in cognitive performance and tests for frontal lobe associated functions were obtained in 1 and 2 TPM groups as compared the VPA group. Results demonstrate the distinct improvement in patients of the TPM-1 group as compared the TPM-2 and DPA groups: in scores for temporal ordering, sorting of cards etc.

Conclusion: In symptomatic partial epilepsy with secondarily generalized seizures, the VPA therapy displayed the adverse cognitive effects in the cognitive test, 1 and 2 groups only mild negative effects in psychomotor speed (compared with the control group). Data obtained in 1 group demonstrated the positive alterations in left frontal lobe associated functions (this may be explained by activating psychotropic effects of TPM).

p630
CORTICAL ACTIVITY IN TINNITUS PATIENTS AND ITS MODIFICATION BY PHONOSTIMULATION

Pawlak-Osińska K[1], *Wierzchowska M*[2], *Kaźmierczak H*[1], *Matuszewska I*[1]
[1]*Department of Pathophysiology of Hearing and Balance System, Collegium Medicum Nicolaus Copernicus University, Toruń, Poland,* [2]*Department of Otolaryngology and Laryngological Oncology, Collegium Medicum Nicolaus Copernicus University, Toruń, Poland*

Objective: 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 otoneurologic 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 phonostimulation 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. Phonostimulation 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-h wave amplitudes, and pathologic patterns. Cortical activity modifications occurred predominantly in the temporal region. Phonostimulation 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

Viteva E
University of Medicine, Department of Neurology, Plovdiv, Bulgaria

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

Petrenaite V, Schmidt DM
Glostrup University Hospital, Neurological, Glostrup, Denmark

Purpose: The efficacy and safety of lacosamid (LCM) has been showed in previous studies in patients with refractory partiel-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 uptitration than suggested should be considered to reduce the risk of side-effects.

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THE MODIFIED ATKINS DIET IN PATIENTS WITH REFRACTORY EPILEPSY AND SEVERE INTELLECTUAL DISABILITY – DESIGN OF A RANDOMIZED CONTROLLED TRIAL

Hulshof HM[1,2], Carpay JA[1,3,4], Jansen FE[2], Braun KPJ[2]
[1]Neurology, Tergooi Hospitals, Blaricum, The Netherlands, [2]Brain Center Rudolf Magnus, Pediatric Neurology, University Medical Center Utrecht, Utrecht, The Netherlands, [3]Amerpoort Clinic for People with Learning Disabilities, Neurology, Baarn, The Netherlands, [4]Leiden University Medical Center, Neurology, Leiden, The Netherlands

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

Kumar FA[1,2], Das K[1,3], Das D[1,4], Hards A[1], Lax-Pericall T[5,6]
[1]Young Epilepsy (NCYPE), Paediatric Neurology and Epilepsy, Lingfield, UK, [2]Great Ormond Street Hospital for Children, Honarary Specialist Registrar Department of Paediatric Neurology, London, UK, [3]Great Ormond Street Hospital for Children, Paediatric Neurology, London, UK, [4]King's College Hospital, General Paediatric and Paediatric Neurology, London, UK, [5]Young Epilepsy (NCYPE), Child and Adolescent Mental Health, Lingfield, UK, [6]South London and Maudsley NHS Trust, Child and Adolescent Mental Health, London, UK

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

Auce P[1], Brodie MJ[2]

[1]Department of Molecular and Clinical Pharmacology, University of Liverpool, Liverpool, UK, [2]Epilpesy Unit, Western Infirmary, Glasgow, UK

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?

Smeyers PM[1], Rosello B[2]

[1]Hospital Universitario y Politécnico La Fe, Valencia, Spain, [2]Child Neurology, Hospital Universitario y Politécnico La Fe, Valencia, Spain

Purpose: To analyze cognitive and behaviour functioning of a serie 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 Psicolinguistic 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 questionary and IPE (Inventory of Problems at School), Miranda 1993 were used.

Results: The cognitive domains that showned high prevalence of disturbances were verbal memory (37.5%), alertness (37.5%), selective attention, (45.8%) and cognitive flexibilitiy (47.82%). The behaviour domains that showned higher prevalence were attention, (33.4%), hiperactivity, (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.

p637
FEATURES OF SYMPTOMATIC MESIAL TEMPORAL LOBE EPILEPSY RELATED TO THE AGE OF ITS MANIFESTATION

Kirillovskikh O[1], Myakotnykh V[1]

[1]Ural State Medical University, Ekateriburg, Russian Federation

Aim: 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 (55.8%). 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 dialeptic (38.8%) and automotoric (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

Montolio M[1], Isla J[1], Aras LM[1], Mingorance- Le Meur A[1]
[1]Dravet Syndrome Foundation, Madrid, Spain

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

Krysl D[1,2], Elisak M[1], Martinkovic L[1], Krijtova H[1], Marusic P[1]
[1]Department of Neurology, 2nd Faculty of Medicine, Charles University in Prague, Motol University Hospital, Prague, Czech Republic, [2]Department of Clinical Neurophysiology, Sahlgrenska University Hospital, Göteborg, Sweden

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 (Euroimmun 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 mediotemporal 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 mediotemporal 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 electrocoagulation. 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

Hagebeuk EEO[1], Marcelis CL[2], Alders M[3], de Weerd AL[4]
[1]SEIN, Pediatric Neurology, Zwolle, The Netherlands, [2]Department of Genetics, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands, [3]Department of Clinical Genetics, Academic Medical Center, Amsterdam, Netherlands, [4]Stichting Epilepsie Instellingen Nederland, Clinical Neurophysiology, Zwolle, Netherlands

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 encepalopathy, 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 Othahara pattern, and with increasing age into hypsarithmia. 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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LENNOX-GASTAUT SYNDROME IN ADULT PATIENTS

Milovanovic M[1], Martinovic Z[2]
[1]Institute of Mental Health, Epilepsy and Clinical Neurophysiology, Belgrade, Serbia, [2]Medical Faculty, University of Belgrade, Belgrade, Serbia

Purpose: To study the long-term clinical and electroencephalographic outcome of Lennox – Gastaut syndrome (LGS) from the childhood till adulthood.

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, atonic, 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 predominated 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 psychosis 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.

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INVESTIGATION OF INTERICTAL CARDIAC RHYTHM ABNORMALITIES, HEART RATE VARIABILITY AND RELATED FACTORS IN UNTREATED PATIENTS WITH IDIOPATHIC GENERALIZED EPILEPSY

Kilinc O[1], Pehlivan A[1], Cincin A[2], Midi I[1], Agan K[1]
[1]Neurology, Marmara University School of Medicine, Istanbul, Turkey, [2]Cardiology, Marmara University School of Medicine, Istanbul, Turkey

Epilepsy is a disease known to occur with autonomous phenomenons. 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, Transthoracic 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.

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LAFORA DISEASE SIMILAR TO JUVENILE MYOCLONIC EPILEPSY

Tan M[1], Canpolat ET[2]
[1]Neurology Department, Adana Research and Training Center, Başkent University, Adana, Turkey, [2]Pathology Department, Adana Research and Training Center, Başkent University, Adana, Turkey

Purpose: Lafora disease (LF) is a type of progressive myoclonic epilepsy with poor prognosis, but different from the Juvenil 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 carbamezapin 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-valproat 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.

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EYELID MYOCLONIA WITH ABSENCES: A RETROSPECTIVE FOLLOW-UP STUDY OF CLINICAL AND ELECTROPHYSIOLOGICAL CHARACTERISTICS

Tsirka V[1,2], Stefanatou M[1], Sakellariou D[3], Richardson M[2], Kostopoulos G[3], Koutroumanidis M[1,2]
[1]Guys and St Thomas' Foundation NHS Trust, London, UK, [2]King's College London, London, UK, [3]University of Patras, Patra, Greece

Purpose: Eyelid myoclonia with absences (EMA) is a distinct syndrome of Idiopathic Generalized Epilepsies (IGE) characterized by

eyelid myoclonia, with or without absences, 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 analysed.

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 pyknoleptic 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)

El-Naggar H[1], McCormack M[1], Delanty HN[1]
[1]Beaumont Hospital, Epilepsy Research Group, Dublin, Ireland

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 etiologic 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 diagnoses with generalised epilepsy (23.6%), 112 with non epileptic seizure (5%) and no specific diagnosis was given in 142 patients (6.4%).

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CLINICAL FEATURES AND EVOLUTION OF EPILEPSY IN HEMICONVULSION-HEMIPLEGIA-EPILEPSY (HHE) SYNDROME

Marjanovic D[1], Juhl S[1], Jaegergard J[1], Madsen CG[2], Leffers A-M[2], Rubboli G[1]
[1]Danish Epilepsy Center, Dianalund, Denmark, [2]Radiological Department MR-Team, Hvidovre Hospital, Hvidovre, Denmark

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.

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A DIFFERENT TYPE REFLEX EPILEPSY: EPILEPSY INDUCED BY COLD WEATHER

Akyol A[1], Ozkul A[1], Gokcil Z[2], Gulluoglu H[3]
[1]Neurology, Adnan Menderes University Faculty of Medicine, Aydin, Turkey, [2]GATA Haydarpasa Teaching Hospital, Ankara, Turkey, [3]Izmir University, Izmir, Turkey

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 triggerin 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 pharmacological 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 similiar 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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PSYCHIATRIC DISTURBANCE IN CHILDREN WITH EPILEPSY

Besag FMC[1], Aldenkamp A[2], Caplan R[3], Dunn D[4], Gobbi G[5], Sillanpaa M[6]
[1]SEPT, South Essex Partnership NHS Trust, Child and Adolescent Mental Health Services, Bedford, UK, [2]Epilepsy Centre Kempenhaeghe, Heeze, The Netherlands, [3]UCLA, Los Angeles, CA, USA, [4]Indiana University, Indianopolis, IN, USA, [5]Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy, [6]University of Turku, Turku, Finland

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.

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PRIMARY SYSTEMIC CARNITINE DEFICIENCY CAUSING INFANTILE ONSET SEIZURES

Christodoulou L[1], Kinali M[1]
[1]Chelsea and Westminster Hospital NHS Trust, Paediatrics, London, UK

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 Phenytoin, Phenobarbitone and Midazolam infusion until finally controlled. Her Carnitine levels were low so she was started on oral carnitine. An echocardiogram suggested possible cardiomyopathy and septal hypertrophy. When tried to wean her anti-convulsants she developed eyelid flickering and eye rolling episodes with right hemiclonic 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 are 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)

Kazis DA[1], Papaliagkas V[1], Papagiannopoulos S[1], Argyropoulou O[1], Lialias I[2], Thanos N[1], Bostantjopoulou S[1]
[1]Third Department of Neurology, Aristotle University of Thessaloniki, Thessaloniki, Greece, [2]Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece

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)

Redfern P[1], Jory C[1], Shankar R[1,2], Tripp M[1], Cox D[1]
[1]Cornwall Foundation NHS Trust, Truro, UK, [2]Exeter Medical School, Exeter, UK

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.

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NITRAZEPAM AS FIRST LINE TREATMENT IN WEST SYNDROME

Shetty J[1], Eunson P[1], Mcwilliam K[1], Tallur K[1], Chin R[1], Mclellan A[1]
[1]Department of Paediatric Neurosciences, Royal Hospital for Sick Children, NHS Lothian, Edinburgh, UK

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 5(70%) 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.

p654
LENNOX-GASTAUT SYNDROME IN ADULTHOOD: CLINICAL FEATURES FROM A LONG TERM FOLLOW-UP

Oggioni GD[1], Scornavacca G[1], Allaria F[1], Zambrelli E[1], Chiesa V[1], Vignoli A[1,2], Canevini MP[1,2]
[1]A. O. San Paolo, Centro Regionale Epilessia – Neurologia II, Milano, Italy, [2]Università degli Studi di Milano, D.I.S., Milano, Italy

Background: Lennox-Gastaut syndrome (LGS) is a rare and severe epileptic encephalopathy, with heterogeneous etiology. Clinical and electroencephalografic (EEG) features at disease onset are well defined, but few data about its evolution and characteristics in adulthood are available.

Method: We reviewed clinical records of the period 1992–2012, searching for patients with LGS.

Results: From 3096 records we identified 28 adult LGS patients (average age 41.2 years; range 20–55). Average follow up was 14.4 years (range: 2–40 years). Mean age at seizure onset was 33.3 months (range: 1–228 months), 10 patients had onset after age 3 (2 after age 8). 7 had a previous West syndrome. Etiology was unknown in 11 patients, genetic in 2 (1 Angelman syndrome, 1 duplication 15 q13p14), structural in 15 (5 perinatal sufferance, 2 infective, 3 neurocoutaneous syndrome, 3 cortical abnormalities, 2 metabolic). 12 patients had neurological deficits. All patient had drug resistant epilepsy and 22 were on therapy with 3 or more AEDs (2 with rufinamide), 3 had VNS. Atypical absences and tonic seizure in sleep were the most common seizures reported. All patients had mental retardation (3 mild, 9 moderate, 15 severe). 7 patients had behavioural abnormalities and 2 had psychogenic non epileptic seizures. EEG at follow up showed paroxysmal abnormalities in all but 5 patients (1 normal EEG, 4 slow activity only).

Conclusion: In a wide series of adult LGS patients, we confirm the severe long term outcome both respect of seizure control and of cognitive/behavioural problems, irrespective of its etiology.

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EPILEPTIC ENCEPHALOPATHIES: COMORBIDITY OR A CAUSE OF AUTISTIC SPECTRUM DISORDERS IN EARLY CHILDHOOD

Kirilova LG[1], Miroshnikov OO[1], Grabovenska IO[1], Lisica VV[1], Silaeva LY[1], Shevchenko OA[1], Shevchenko TB[1], Tkachuk LI[1], Gaydai SS[1]

[1]Department Psychoneurology for Children with Perinatal Lesions of the Nervous System (0 to 3 years), State Institution 'Institute of Pediatrics, Obstetrics and Gynecology of NAMS of Ukraine', Kyiv, Ukraine

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-resistent epileptic seizures or persistent epileptiform activity.

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ENCEPHALOPATHY RELATED TO STATUS EPILEPTICUS DURING SLOW SLEEP (ESES): ELECTROCLINICAL FEATURES AND EVOLUTION IN A COHORT OF IDIOPATHIC CASES

Pavlidis E[1,2], Gardella E[2], Kölmel MS[2], Hjalgrim H[2], Møller RS[2], Alving J[2], Beniczky S[2], Rubboli G[2]

[1]Neuroscience Department, Child Neuropsychiatry Unit, University of Parma, Parma, Italy, [2]Danish Epilepsy Center 'Filadelfia', Dianalund, Denmark

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: 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 social/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%. EEG 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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CORTICAL SOURCES OF MAGNETIC SPIKE-WAVES IN 60 CHILDREN WITH ELECTRIC STATUS EPILEPTICUS DURING SLEEP (ESES) WITH SUSPECTED ENCEPHALOPATHY

Paetau RA[1]

[1]Pediatric Neurology, Helsinki University Central Hospital, Helsinki, Finland

Purpose: To study the generator areas of epileptic spikes in different clinical epileptic encephalopathies and ESES.

Method: The anatomical sources of epileptic magnetoencephalography (MEG) spikes were retrospectively analysed of 60 patients with ESES and epileptic encephalography, or who were suspected to develop encephalopathy. MEG was collected during a nap or light thiopental anaesthesia. Networks of epileptic spikes were modelled with equivalet current dipoles, and the dipole locations were displayed on the subjets' 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 porencefalic cysts,

perinatal hemispheric infarction, thalamic lesions, hypoxis-ischemic encephaopathy 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

Coqué N[1,2,3], Chemaly N[4,5], Nabbout R[4,5]
[1]Alliance Syndrome de Dravet, Brest, France, [2]AgroParisTech, UMR MIA, Paris, France, [3]INRA, UMR 518 MIA, Paris, France, [4]Department of Pediatric Neurology, Necker-Enfants Malades Hospital, AP-HP, National Referral Center for Rare Epilepsies, Paris, France, [5]INSERM U 663, University Paris V – Paris Descartes, Paris, France

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' medications: medecines 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 98%, 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 medications. 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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THE ENCEPHALOPATHY IN DRAVET SYNDROME IS NOT A DIRECT CONSEQUENCE OF EPILEPSY

Chemaly N[1,2], Nabbout R[1,2], Chipaux M[1], Barcia G[1,2], Bouis C[1], Dubouch C[1], Leunen D[1], Jambaque I[1,2], Dulac O[1,2], Dellatolas G[3], Chiron C[1,2]
[1]Departement of Neuropediatrics, Necker Hospital, Paris Descartes University, Paris, France, [2]INSERM U 663, Paris Descartes University, Paris, France, [3]Maison de Solenn, Inserm U 669, Paris Descartes University, Paris, France

Purpose: Dravet syndrome (DS) is considered as an epileptic encephalopathy, a condition in which epilepsy and EEG abnormalities cause cognitive delay. Our aim was to prospectively analyse the neuropsychological features in a large cohort of DS patients in relation to epilepsy and SCN1A mutation.

Method: We included 67 patients with typical DS (9 months to 24 years, 15). They had 81 examinations using Brunet-Lezine (developmental/intelligence quotient [DQ/IQ] and DQ sub-scores), Achenbach, Conners, and a semi-quantitative psychomotor score (SQPS). We studied the correlation between DQ/IQ/SQPS and age, epilepsy characteristics, and the presence of SCN1A mutation.

Results: DQ/IQ significantly decreased with age ($r = -0.53$, $p < 0.001$), from normal before 2 years (mean 80, range 64–105) to low after 3 yeras (mean 48, range 30–69). Hyperactivity and attention disorders impacted learning abilities especially up to 6 years. However, raw (not age-adjusted) DQ sub-scores increased with age during the first decade, showing no regression. We did not find any significant correlation between DQ/IQ at last evaluation and epilepsy characteristics except for myoclonus and focal seizures which were associated with a lower QD/IQ after 3 years. SCN1A mutated patients (n = 58) seemed to exhibit worse psychomotor course than non-mutated ones (n = 9) (severe SQPS in 26% vs. 0%), although their epilepsy tended to be less severe. DQ subscores were dissociated throughout the course: hand-eye coordination was significantly lower than language, posture and sociability ($p < 0.01$).

Conclusion: Although psychomotor/cognitive delay declines with age, patients with DS showed no regression. Encephalopathy seems not a pure consequence of epilepsy but SCN1A mutation might play an additional role.

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INCIDENCE OF NEONATAL SEIZURES: A PROSPECTIVE STUDY

Espeche AL[1], Hoffmann M[1], Travaini V[2], del Barco M[3]
[1]Neurology, Hospital Publico Materno Infantil de Salta, Salta, Argentina, [2]Hospital Publico Materno Infantil de Salta, Salta, Argentina, [3]Neonatology, Hospital Publico Materno Infantil de Salta, Salta, Argentina

Seizures are the most frequent clinical manifestation of neurolgical 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).

Materials and Methods: Prospective study, collecting all infants born alive at HPMI, between January 1, and December 31, 2010. Inclusion criteria: clinical seizures occuring 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 (37/8,092), 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 1,500 g (49.69/1,000 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.

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PHARMACOLOGIC TREATMENT OF NEONATAL SEIZURE IN CHUNGBUK, KOREA

Kim WS[1]
[1]*Pediatrics, Chungbuk National University, Chungju, Korea*

Purpose: Neonatal seizures are the most important indicator of neurologic dysfunction in the neonatal period. A mainstay in the therapy of neonatal seizures is the diagnosis and treatment of underlying etiology. So we studied treatment of neonatal seizure in Chungbuk Korea.

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 hemorrage is 1 and hypoxic ischemic encephalopathy is 1. The Brain sono is that germinal matrix hemorrhage with IVH is 1 and diffuse echogenecity 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 Korea. The further study is necessary about other antiepileptic drug.

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EXPANDING THE CLINICAL, GENETIC, AND PATHOGENIC SPECTRUM OF NEONATAL EPILEPSIES ASSOCIATED WITH KCNQ2 MUTATIONS

Aharoni S[1,2], *Goldberg-Stern H*[2,3], *Berkovic SF*[4]
[1]*Epilepsy Center, Schneider Children's Medical Center of Israel, Petach Tikva, Israel,* [2]*Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel,* [3]*Schneider Children's Medical Center of Israel, Epilepsy Center, Petach Tikva, Israel,* [4]*Department of Medicine, PSY Research Center, The University of Melbourne, Austin Health, Heidelberg, Qld, Australia*

Purpose: Mutations in KCNQ2 and KCNQ3 genes encoding for potassium channel subunits underlie the M-current and cause benign familial neonatal seizures (BNFS). This is an autosomal dominant disorder, occurring in the first days of life. Although BFNS is considered a benign epileptic disorder, recently, several families have been described in whom some individuals show benign neonatal convulsions and favorable prognosis, while others present with epileptic encephalopathy. The purpose of our study is to highlight the phenotypic heterogeneity in KCNQ2 mutation cases.

Method: We describe a 4-generation family with BFNS with 7 affected members in different generations. Six of them had a benign course while one 2-year-old girl had epileptic encephalopathy with difficult-to-control seizures and developmental delay, despite carrying the exact same mutation as the other family members.

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.

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TREATMENT OF STATUS EPILEPTICUS AND SEIZURES IN PATIENTS WITH *KCNQ2* ENCEPHALOPATHY

Pisano T[1], *Numis A*[2], *Heavin S*[3], *Weckhuysen S*[4], *Angriman M*[5], *Suls A*[4], *Guerrini R*[1], *Scheffer I*[3], *Marini C*[1], *Cilio MR*[2]
[1]*Neurology Unit and Laboratories, A. Meyer Children's Hospital, Florence, Italy,* [2]*Epilepsy Unit, Benioff Children's Hospital, University of California, San Francisco, CA, USA,* [3]*Department of Medicine, Florey Institute, University of Melbourne, Melbourne, Vic., Australia,* [4]*Epilepsy Centre Kempenhaeghe, Institute Born-Bunge, University of Antwerp, Antwerp, Belgium,* [5]*Central Hospital of Bolzano, Bolzano, Italy*

Purpose: 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 onset-phase and ongoing intractable seizures in patients with *KCNQ2* encephalopathy.

Methods: Review of the clinical, ictal and interictal video-EEG data and AED treatment of 7 patients with heterozygous *KCNQ2* missense mutations: 6 *de novo* and 1 inherited from a mosaic father.

Results: Seizure onset 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)

Pressler RM[1], Boylan G[2], De Vries LS[3], Marlow N[4], Vanhatalo S[5], Jullien V[6], Zohar S[7], Mats B[8], Hallberg B[9], Cross JH[10], Chiron C[11], Levene M[12], Mangum B[13], Pons G[14], Hellström-Westas L[15], Murphy B[16], Murray D[17], Rennie J[10], Swarte R[18], Toet M[19], NEMO Consortium

[1]Neurosciences Unit, Institute of Child Health UCL, London, UK, [2]Neonatal Brain Research Group & Neonatal Unit, University College Cork, Cork, Ireland, [3]Neonatology, University Medical Centre Utrecht, Utrecht, The Netherlands, [4]Neonatal Unit (IWH), University College London, London, UK, [5]Helsinki University Central Hospital, Helsinki, Finland, [6]Pharmacology, U 663 Necker Paris Descartes, Paris, France, [7]U 663 Necker Paris Descartes, Paris, France, [8]Neonatology, Karolinska University Hospital, Stockholm, Sweden, [9]Neonatology, Karolinska University Hospital, Stockholm, Sweden, [10]Institute of Child Health UCL, London, UK, [11]Paediatric Neurology, INSERM U 663, Paris, France, [12]Neonatology, Leeds General Infirmary, Leeds, UK, [13]Duke Clinical Research Institute, Duke, NC, USA, [14]Pharmacology, U 663 Necker Paris Descartes, Paris, France, [15]Neonatology, Uppsala University Hospital, Upsala, Sweden, [16]Neonatal Unit, University College Cork, Cork, Ireland, [17]Neonatology, University College Cork, Cork, Ireland, [18]Erasmus Universitair MC Rotterdam, Rotterdam, The Netherlands, [19]Neonatology, University Medical Centre Utrecht, Utrecht, The Netherlands

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 phenobarbitone were allocated via bivariate continual reassessment method to one of 4 dose levels (0.05–0.3 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 aminoglycosides. 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 ($GABA_AR$)-MEDIATED EXCITATION IN PROPOFOL-INDUCED ELECTROENCEPHALOGRAPHIC SEIZURES IN NEONATAL RATS

Martynyuk A[1,2], Seubert C[1], Gravenstein N[1,2]

[1]University of Florida, Gainesville, FL, USA, [2]McKnight Brain Institute, Gainesville, FL, USA

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 of $GABA_AR$ activity, administered to neonatal rats, causes an increase in serum levels of corticoids, electroencephalographic seizures, and abnormal behavior later in life. To test the hypothesis that altered LHPA activity and $GABA_AR$-mediated excitation are involved in mediation of neonatal-anesthesia caused electroencephalographic seizures, the effects of propofol and etomidate – anesthetics with similar $GABA_AR$-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 ($F_{(1,21)} = 4.975$, $p < 0.05$).

Conclusion: Our results suggest that an increase in corticoid levels along with $GABA_AR$-mediated excitation is required for propofol-induced electroencephalographic seizures in neonatal rats.

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MITOCHONDRIAL DNA PROFILING VIA GENOMIC ANALYSIS IN MESIAL TEMPORAL LOBE EPILEPSY PATIENTS WITH HIPPOCAMPAL SCLEROSIS

Gurses C[1], Azakli H[2], Alptekin A[3], Arikan M[4], Cakiris A[4], Abaci N[4], Kursun O[3], Gokyigit A[1], Ustek D[4]

[1]Neurology, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey, [2]Institute for Experimental Medicine, Istanbul University, Genetics, Istanbul, Turkey, [3]Computer Engineering, Istanbul University, Istanbul, Turkey, [4]Genetics, Institute for Experimental Medicine, Istanbul, Turkey

Purpose: Mithochondrial genome analysis is rarely carried out in the investigation of some diseases. The aim of this study is to show mito-

chondrial dysfunctions using genome analysis in patients with MTLE-hippocampal sclerosis (HS).

Method: 44 patients with MTLE-HS 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.

p667
NO EVIDENCE FOR A ROLE OF CYSTATIN ß GENE IN JUVENILE MYOCLONIC EPILEPSY

Mumoli L[1], Labate A[1], Tarantino P[2], Gagliardi M[2], Annesi G[2], Michelucci R[3], Bianchi A[4], Gambardella A[1]
[1]Institute of Neurology, University of Magna Graecia, Catanzaro, Italy, [2]Institute of Molecular Bioimaging and Physiology, National Research Council, Catanzaro, Italy, [3]Division of Neurology, Bellaria Hospital, Bologna, Italy, [4]Division of Neurology, Ospedale S. Donato, Arezzo, Italy

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 ß, 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: Forthy-four 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 ß gene in patients with JME.

p668
SODIUM CHANNEL MUTATIONS AND GENERALIZED EPILEPSY WITH FEBRILE SEIZURES PLUS

Almendra R[1], Velon AG[1], Guimarães P[1], Silva MR[1]
[1]Centro Hospitalar Tras-os-Montes e Alto Douro, EPE, Vila Real, Portugal

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 peritrigonal 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.

p669
METHYLATION PATTERNS IN HUMAN FRONTAL LOBE EPILEPSY OF UNKNOWN ORIGIN

Coppola A[1], Karpathakis A[2], Liu J[1], Miserocchi A[1], Morris T[2], Diehl B[1], Thom M[1], Thirlwell C[2], Sisodiya SM[1]
[1]UCL Institute of Neurology, National Hospital for Neurology and Neurosurgery, London, UK, [2]UCLCancer Institute, London, UK

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 ictal 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 0.6441988, Average beta value controls 0.5975810, 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

Bhatnagar M[1], Shorvon S[2]
[1]University College London, Institute of Neurology, London, UK, [2]UCL Institute of Neurology, London, UK

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.

p671
INTER-RATER RELIABILITY OF MULTICENTRE PHENOTYPING FOR GENOMIC ASSOCIATION STUDIES IN EPILEPSY

Borghei M[1], Avbersek A[2], Krause R[3], Sisodiya S[2], Depondt C[1,4], for the EpiPGX Consortium
[1]Laboratory for Experimental Neurology, Université Libre de Bruxelles, Brussels, Belgium, [2]Department of Clinical and Experimental Epilepsy, Institute of Neurology, London, UK, [3]Luxembourg Centre for Systems Biomedicine, University of Luxembourg, Esch-sur-Alzette, Luxembourg, [4]Department of Neurology, Université Libre de Bruxelles, Brussels, Belgium

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: 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 multicentre studies that involve large-scale phenotyping.

p672
GENE EXPRESSION IN CHILDHOOD AND JUVENILE ABSENCE EPILEPSY

von Deimling M[1], Häsler R[2], Volz V[1], Holterhus P-M[3], von Spiczak S[1], Stephani U[1], Helbig I[1], Muhle H[1]
[1]Department of Neuropediatrics, Christian-Albrechts-University of Kiel, Kiel, Germany, [2]Institute of Clinical Molecular Biology, Christian-Albrechts-University of Kiel, Kiel, Germany, [3]Department of Pediatrics, Christian-Albrechts-University of Kiel, Kiel, Germany

Purpose: Childhood and Juvenile Absence Epilepsies (CAE, JAE) are among the most common epilepsies of childhood and represent well-defined and clearly delineated epilepsy syndromes. In CAE, seizures often start rapidly with a high seizure frequency of several hundred seizures per day. So far, the mechanism behind the sudden onset remains entirely unclear. A genetic contribution for absence epilepsies has been demonstrated in various studies. However, with a few exceptions in large families, the genetic basis of CAE/JAE remains to be resolved. In order to obtain further information with respect to the underlying molecular mechanisms, we performed genome-wide gene expression analysis in patients with new-onset CAE/JAE prior to medication compared to age-matched controls.

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 transcriptome 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

Lund C[1], Heimdal KR[2], Wangensteen T[2], Sheng Y[2], Øye A-M[2], Rødningen O[2], Kulseth MA[2], Selmer KK[1,2]
[1]National Centre for Rare Epilepsy-Related Disorders, Oslo University Hospital, Sandvika, Norway, [2]Department of Medical Genetics, Oslo University Hospital and the University of Oslo, Oslo, Norway

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 100×.

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

van Kempen M[1], Brilstra E[1], van der Zwaag B[1], Verbeek N[1], Elferink M[1], Jansen F[1], van Zon P[1], Lindhout D[2], Ploos van AmstelHK[1]
[1]UMC Utrecht, Utrecht, The Netherlands, [2]Epilepsy Institute of the Netherlands SEIN, UMC Utrecht, Utrecht, The Netherlands

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 (MPS) 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.

p675
KCNT1 MUTATIONS IN SEIZURE DISORDERS AND SUDDEN UNEXPLAINED DEATH IN EPILEPSY (SUDEP)

Møller RS[1,2], Heron S[3,4], Gardella E[1], Larsen L[5], Nikanorova M[1,2], Bayly MA[3,4], Dahl HA[5], Larsen J[1], Hjalgrim H[1,2], Gellert P[1], Scheffer IE[6,7,8], Berkovic SF[6], Dibbens LM[3,4]
[1]Danish Epilepsy Centre, Dianalund, Denmark, [2]Institute for Regional Health Services, University of Southern Denmark, Odense, Denmark, [3]Epilepsy Research Program, School of Pharmacy and Medical Sciences, University of South Australia, Adelaide, SA, Australia, [4]Sansom Institute for Health Research, University of South Australia, Adelaide, SA, Australia, [5]Amplexa Genetics, Odense, Denmark, [6]Epilepsy Research Centre, University of Melbourne, Melbourne, Vic., Australia, [7]Florey Institute, Melbourne, Vic., Australia, [8]Department of Paediatrics, University of Melbourne, The Royal Children's Hospital, Parkville, Vic., Australia

Purpose: Autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE) and malignant migrating focal seizures of infancy (MMFSI) are phenotypically distinct epileptic disorders. The causation of these two differing disorders by mutations in *KCNT1*, suggests that they may be part of a larger spectrum of disorders associated with mutations in this gene, which may include focal epilepsies associated with psychiatric disorders and other severe forms of focal epilepsy. The study aimed to investigate the role of *KCNT1* in focal epilepsy.

Method: One family with ADNFLE and 96 patients/families with focal epilepsies, including 22 with psychiatric co-morbidities, were screened for mutations in *KCNT1* either by targeted next generation sequencing or high resolution melting-curve analysis.

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.Gly228-Ser 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 arrythmia 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

Larsen LHG[1], Dahl HA[1], Olofsson K[2], Uldall P[2,3], Frangu M[4], Born PA[3], Gellert P[2], Nikanorova M[2], Jepsen B[2], Marjanovic D[2], Kragh-Olsen B[5], Brusgaard K[1], Hjalgrim H[2,6], Møller RS[2,6]
[1]Amplexa Genetics, Odense C, Denmark, [2]Danish Epilepsy Centre, Dianalund, Denmark, [3]Pediatric Clinic 1, Copenhagen University Hospital, Copenhagen, Denmark, [4]Department of Pediatrics, Holbæk Hospital, Holbæk, Denmark, [5]Department of Pediatrics, Aarhus University Hospital, Aarhus, Denmark, [6]Institute for Regional Health Services, University of Southern Denmark, Odense, Denmark

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 such as PolyPhen2, SIFT, mutation taster etc. Variants were verified by Sanger sequencing and parents were included for segregation or *de novo* analysis. We analyzed this panel on a cohort of 29 patients. The majority of the patients in this cohort had epileptic encephalopathies (EE) and a few patients suffered from milder epilepsy syndromes such as GEFS+ or ADNFLE.

Results: We identified a presumed disease-causing variation 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.

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p677
TWO NOVEL AND THREE KNOWN EPM2A AND NHLRC1 (EPM2B) GENE VARIANTS LEADING TO LAFORA DISEASE IN TURKISH PATIENTS

Bebek N[1], Ozdemir O[2], Öre ÖE[1], Uğur İşeri S[2], Tutkavul K[3], Ayta S[4], Baykan B[1], Gürses C[1], Gökyiğit A[1], Özbek U[2]
[1]Faculty of Medicine, Istanbul University Istanbul, Istanbul, Turkey, [2]Research Institute for Experimental Medicine, Istanbul University, Istanbul, Turkey, [3]Neurology, Haydarpaşa Numune Education and Research Hospital, Istanbul, Turkey, [4]Child Neurology, Maltepe University Medical School, Istanbul, Turkey

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?

Tarta-Arsene O[1], Iliescu C[1], Motoescu C[1], Barca D[1], Butoianu N[1], Budisteanu M[1], Dica A[1], Anghelescu C[1], Leanca M[1], Craiu D[1]
[1]Department of Pediatric Neurology, Clinical Hospital 'Al Obregia', Bucharest, Romania

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 spams (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

Dica AD[1], Tarta-Arsene O[2], Leanca M[2], Budisteanu M[2], Anghelescu C[2], Craiu D[2]
[1]Pediatric Neurology,Alexandru Obregia Hospital, Bucharest, Romania, [2]Alexandru Obregia Hospital, Bucharest, Romania

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 autozomal 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 continous 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 crests abnormalities), moderate mental retardation and epilepsy. Seizures started at the age of 14 months, as focal motor seizures on the right hemibody 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, 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.

p680
EPILEPSY IN ANGELMAN SYNDROME

Kholin A[1,2], Il`ina E[2], Kolpakchi L[2], Fedonyuk I[2], Zavadenko N[1]
[1]Department of Neurology, Neurosurgery and Medical Genetics, Russian National Research Medical University, Moscow, Russian Federation, [2]Department of Psychoneurology N2, Russian Children Clinical Hospital, Moscow, Russian Federation

Purpose: The study of the age of epilepsy debut, characteristics of epileptic seizures and the effectiveness of antiepileptic therapy of epilepsy in children with Angelman syndrome.

Method: At Department of Psychoneurology N2 of RCCH and Department of Neurology, Neurosurgery and Medical Genetics of RNRMU at the period of 2005–2013 were studied 7 pediatric patients with genetically identified Angelman syndrome. For all the children were provided dynamic video-EEG monitoring.

Results: Angelman syndrome manifested with epilepsy in 100% of cases. Age debut of epilepsy varied from 4.5 months to 3 years 10 months (on average 18 months). Only one girl has a 1 type of attacks, in 1 case – 2, in 3 cases – 3 and one – 4 types. The most frequent seizure types were: atypical absences – 4 (57.1%), myoclonic – 3 (42.9%), generalized tonic-clonic – 3 (42.9%), tonic versive – 3 (42.9%), rarely – serial infantile spasms – 1 (14.3%), axorhyzomelic tonic – 1 (14.3%), myoclonic-astatic – 1 (14.3%), atonic-astatic – 1 (14.3%), pharyngo-oral – 1 (14.3%) and hemiconvulsive types – 1 (14.3%). Persistent clinical remission was achieved in 3 children (42.9%), but the clinical and the electroencephalography only for one child; and 4 children (57.1%) showed a significant decrease of seizures with persistence of epileptiform discharges with high index. The most effective drugs were valproates in combination with ethosuximide.

Conclusion: Epilepsy is an obligate symptom of the Angelman syndrome and characterized by early onset and highly polymorphic seizure types. Positive prognosis for epileptic seizures (clinical remission or significant decreasing of seizure frequency) is combined with a poor prognosis for the persistence of epileptiform discharges on EEG, severe cognitive deficits and manifestations of atypical autism.

p681
EXOME SEQUENCING IN MYOCLONIC ASTATIC EPILEPSY IDENTIFIES KNOWN EPILEPSY GENES AND INTERESTING CANDIDATE GENES

von Spiczak S[1], EuroEPINOMICS RES Consortium
[1]Department of Neuropediatrics, University Medical Center Schleswig-Holstein, Kiel, Germany

Purpose: Myoclonic astatic (atonic) epilepsy is a childhood epilepsy syndrome characterized by myoclonic-astatic seizures that often occur together with generalized tonic-clonic, atonic, myoclonic and absence seizures. Developmental problems might occur with seizure onset. Although a strong genetic contribution to the epilepsy is assumed, no causal genes have been identified for the majority of patients so far. The aim of this study was to unravel the genetics of myoclonic astatic (atonic) epilepsy.

Method: Whole exome sequencing was performed on 38 patients with MAE and their unaffected parents by the EuroEPINOMICS-RES consortium. All patients were thoroughly phenotyped to exclude atypical MAE cases.

Results: 4/38 patients carried *de novo* mutations in a known epilepsy gene (1 *SCN1A* mutation, 1 *SCN2A* mutation, 1 *SYNGAP1* mutation and 1 *CHD2* mutation). No mutations were identified in *GLUT1* (*SLC2A1*), a gene previously identified in up to 5% of patients with MAE. 2/38

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

Montalvo J[1], Rios-Motta M[2], Acevedo K[3], Vazquez - Correa M[1], Echegaray M[4], Pita I[2]

[1]Neurology- Child Neurology Section, University of Puerto Rico Medical Sciences Campus, San Juan, Puerto Rico, [2]Neurology, University of Puerto Rico Medical Sciences Campus, San Juan, Puerto Rico, [3]Pediatrics, University of Puerto Rico Medical Sciences Campus, San Juan, Puerto Rico, [4]University of Puerto Rico at Cayey, Cayey, Puerto Rico

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) ($\chi^2 = 4.093$, 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 ($\chi^2 = 0.764$, 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)

El Tawil S[1], Gaber A[1], Fouad A[1], El Nahhas N[1], Hemeda M[1], El Etribi MA[1]

[1]Neurology, Ain Shams University, Cairo, Egypt

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 psychotic episode and substance misuse.

Conclusion: FFEVF is rare, with about 10 families described in literature since it was first identified in by Schaeffer 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?

Barcia G[1,2], Kaminska A[1,2], Boddaert N[3], Chemaly N[1,2], Colleaux L[4], Dulac O[1,2], Nabbout R[1,2]

[1]Department of Pediatric Neurology, Centre de Reference Epilepsies Rares, Hôpital Necker Enfants Malades, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, France, [2]Inserm U 663, Université Paris Descartes, PRES Sorbonne Paris Cité, Hôpital Necker Enfants Malades, Paris, France, [3]Departement of Pediatric Radiology, Hôpital Necker Enfants Malades, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, France, [4]INSERM U 781, PRES Sorbonne Paris Cité, Institut IMAGINE, Hôpital Necker-Enfants Malades, Paris, France

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 generalized 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*.

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p686
MRI FINDINGS IN REFRACTORY EPILEPSY

Thacker AK[1], Singh V[2]
[1]Neurology, Dr RML Institute of Medical Sciences, Lucknow, India, [2]BRD Medical College, Gorakhpur, India

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, electrophysiological & 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 T_1, T_2, FLAIR, DWI, Sagittal T_2, Oblique Coronal T_2 FLAIR, T_1 FLAIR, Volume 3 DMPGR, SWI, & T_2 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 13 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

Seynaeve L[1], Adamczuk K[2], Kovacs S[3], Sunaert S[3], Vandenberghe R[2], Dupont P[2,3], Van Paesschen W[1]
[1]Laboratory for Epilepsy Research, KU Leuven, Leuven, Belgium, [2]Laboratory for Cognitive Neurology, KU Leuven, Leuven, Belgium, [3]Medical Imaging Research Center, UZ Leuven and KU Leuven, Leuven, Belgium

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 Pcor < 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 PTT might be better to predict cognitive decline after TLE surgery than fMRI using the verb-to-noun paradigm.

p688
ADDED VALUE OF MULTIMODAL STRUCTURAL AND FUNCTIONAL IMAGING IN DUAL PATHOLOGY

Weisstanner C[1], Rummel C[1], Schindler K[2], Wiest R[1], Abela E[1,3]
[1]Support Center for Advanced Neuroimaging (SCAN), Institute for Diagnostic and Interventional Neuroradiology, University Hospital and University of Bern, Bern, Switzerland, [2]Neurology, University Hospital 'Inselspital' Bern, Bern, Switzerland, [3]Department of Neurology, Inselspital, University Hospital Bern and University of Bern, Bern, Switzerland

Purpose: To map structural changes and effective connectivity within an exemplary epileptogenic network with multiple potential epileptogenic lesions and to identify its critical nodes.

Method: We acquired high-resolution T1-weighted imaging data with high-contrast between GM and WM (MDEFT), Diffusion Spectrum Imaging (DSI) and simultaneous EEG-fMRI in a 26 year old male patientwith long-standing pharmacoresistant structural mesial temporal lobe epilepsy (MTLE) and extended biparietal polymicrogyria. Structural images were statistically compared to 16 healthy male controls (age range 22–30 years, mean 26.4, SEM ± 0.7) using a fully automated procedure. Cortical curvature and thickness as well as the sulcus depth were evaluated. Structural connectivity was assessed by DSI. In-scanner EEG data were preprocessed to eliminate scanner, pulse and ballistocardiogramm-related artifacts. Blood-oxygen level dependent (BOLD) signal changes correlated with interictal epileptiform discharges were identified using finite-impulse response (FIR) modelling in SPM8 between 5 seconds before to 17 seconds after IED. Stochastic Dynamic Causal Modeling (sDCM) followed by fixed-effects Bayesian Model Selection (BMS) was used to analyze the effective connectivity within significant BOLD clusters. All statistical maps were thresholded with False Discovery Rate (FDR) $q < 0.05$.

Results: Morphological analysis revealed extended increases of cortical thickness in postcentral gyrus posterior medial temporal gyrus, superior parietal lobule and frontoorbitalgyrus. Aberrant sulcus depth was found around the central sulcus and medial occipital lobe. We found clusters of IED-related BOLD responses in the right superior parietal lobe and left mesial temporal lobe. DSI confirmed the integrity of the cingulate pathways connecting the clusters between the hemispheres. sDCM revealed increased effective connectivity between right (dysplastic) parietal lobe an left hippocampus.

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

Hammers A[1,2,3,4], Riaño Barros DA[1,2], McGinnity CJ[1,2], Rosso LA[1], Heckemann RA[1,5], Egerton A[6], Bhattacharyya S[6], Howes OD[2,6], Brooks DJ[1], Duncan JS[3], Turkheimer FE[7], Koepp MJ[3]
[1]Department of Experimental Medicine, Imperial College London, London, UK, [2]MRC Clinical Sciences Centre, Hammersmith Hospital, London, UK, [3]Department of Clinical and Experimental Epilepsy, Institute of Neurology, University College London, and Epilepsy Society, Chalfont St Peter, London, UK, [4]Neurodis Foundation, Lyon, France, [5]MedTech West at Sahlgrenska University Hospital, Gothenburg University, Gothenburg, Sweden, [6]Department of Psychological Medicine, King's College London, London, UK, [7]Centre for Neuroimaging Sciences, King's College London, London, UK

Purpose: Activation of the cannabinoid receptor type 1 (CB_1) has been associated with both anti- and pro-convulsant effects. A post-ictal increase in the availability of CB_1 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 CB_1 receptor availability, assessed with a novel PET radioligand, [^{11}C]MePPEP (Terry GE et al. NeuroImage 2009;48:362–370).

Method: Eight participants with refractory TLE (five females; median / range 42 / 30–60 years) and 20 healthy controls (eight females; median / range 29 / 20–66 years), were scanned on two separate days after an intravenous bolus injection of ~370 MBq of [^{11}C]MePPEP. Parametric volume-of-distribution images (V_T) were created using spectral analysis. V_T was compared on a voxel-by-voxel basis by ANCOVA using Statistical Parametric Mapping (SPM8).

Results: At the group level, CB_1 availability in TLE was higher in the ipsilateral temporal lobe in postictal scans than in controls ($p < 0.005$ uncorrected), as hypothesised. Focal decreases were seen in the parietal and occipital lobes. CB_1 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, CB_1 availability in TLE was higher in the ipsilateral temporal lobe in postictal scans than in controls ($p < 0.005$ uncorrected), as hypothesised. Focal decreases were seen in the parietal 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 ANTIEPILEPTIC DRUGS WITHDRAWAL DURING VIDEO-EEG TELEMETRY

Sokic D[1,2], Lavrnic S[3], Ristic A[1], Bascarevic V[4], Vojvodic N[1]
[1]Department of Epileptology, Clinic of Neurology, Clinical Centre of Serbia, Belgrade, Serbia, [2]School of Medicine, University of Belgrade, Belgrade, Serbia, [3]Clinical Center of Serbia, Center for MRI, Belgrade, Serbia, [4]Clinic of Neurosurgery, Clinical Centre of Serbia, Belgrade, Serbia

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 hypocalcemic 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

Centeno M[1,2], Croft L[1], Cross H[1,2], Pressler R[1,2], Clark C[1], Baldeweg T[1], Carmichael DW[1]
[1]UCL Institute of Child Health, London, UK, [2]Epilepsy Department, Great Ormond Street Hospital for Children, London, UK

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 have 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.

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.

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LANGUAGE LATERALISATION BEFORE AND AFTER EPILEPSY SURGERY IN CHILDREN: RELATIONSHIP TO COGNITIVE FUNCTION

Coleman RV[1], Skirrow C[1], Harrison S[2], Cross JH[1,2], Rankin P[1,2], Sanfilippo P[2], Liegeois F[1,2], Harkness W[2], Clayden J[1], Clark CA[1], Vargha-Khadem F[1,2], Baldeweg T[1,2]
[1]UCL Institute of Child Health, London, UK, [2]Great Ormond Street Hospital for Children NHS Trust, London, UK

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. Seizure localisation varied between patients; 10 temporal, 5 extra-temporal and 5 multi-lobar, but was predominantly left-sided (70% of cases vs. 30% right-sided). 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).

Results: 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.

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BRAIN METALS IN EPILEPSY: FIRST INSIGHTS FROM ATOMIC NEUROSCIENCE IN POST-SURGICAL TISSUE

Lam A[1,2,3], Florez CM[2], Mylvaganam S[2], Valiante T[2,3], Carlen PL[2,3], Ohayon EL[1,2,3]
[1]Neurolinx Research Institute, Green Neuroscience Laboratory, San Diego, CA, USA, [2]Toronto Western Research Institute, Toronto, ON, Canada, [3]University of Toronto Epilepsy Research Program, Toronto, ON, Canada

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 post-surgical 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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DIFFUSION TENSOR IMAGING AND TRACTOGRAPHY IDENTIFY STRUCTURAL CHANGES IN CRYPTOGENIC FOCAL EPILEPSY

Vollmar C[1], Goc J[1], Hartl E[1], Catarino C[1], Loesch A-M[1], Jan R[1], Noachtar S[1]
[1]Department of Neurology, Epilepsy Center, University of Munich, Munich, Germany

Purpose: To investigate the contribution of Diffusion Tensor Imaging (DTI) and Diffusion Tensor Tractography (DTT) in identifying abnormalities in MRI negative patients with cryptogenic extramesiotemporal focal epilepsies.

Method: 14 patients with cryptogenic extramesiotemporal focal epilepsy were investigated. DTI data was acquired on a GE Signa HDx 3T Scanner, using an acquisition scheme with 64 diffusion weighted directions, a b-value of 1,000 m/s^2, 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 DTI findings.

Conclusion: These preliminary data show the potential role of DTI and DTT as complementary lateralizing and localizing imaging modality in cryptogenic extramesiotemporal 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

Ciumas C[1], Laurent A[1], Saignavongs M[1], Ilski F[1,2], de Bellescize J[2], Panagiotakaki E[2], Ostrowsky-Coste K[2], Ryvlin P[2]

[1]INSERM U 1028, CNRS UMR 5292, Centre de Recherche en Neuroscience de Lyon, Translational and Integrative Group in Epilepsy Research (TIGER), Université Lyon-1, Lyon, France, [2]Department of Paediatric Sleep, Epilepsy, and Clinical Neurophysiology, Department of Functional Neurology, Hospices Civils de Lyon, Lyon, France

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 misclassified happy and neutral emotional faces as stimuli of negative valence. Our preliminary findings demonstrate impairment in social cognition in BCECTS.

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READING, LISTENING AND MEMORY-RELATED BOLD SIGNAL RESPONSE IN CHILDREN WITH EARLY-STAGE TEMPORAL LOBE EPILEPSY OF UNKNOWN CAUSE – AN FMRI STUDY

Mankinen K[1], Ipatti P[2], Harila M[3], Nikkinen J[2], Paakki J-J[2], Rytky S[4], Starck T[2], Remes J[2], Tokarie M[5,6], Carlson S[5,6], Tervonen O[2], Rantala H[1], Kiviniemi V[2]

[1]Department of Paediatrics, Oulu University Hospital, Oulu, Finland, [2]Clinic of Diagnostic Radiology, Oulu University Hospital, Oulu, Finland, [3]Department of Neurology, Oulu University Hospital, Oulu, Finland, [4]Department of Clinical Neurophysiology, Oulu University Hospital, Oulu, Finland, [5]Brain Research Unit, O.V. Lounasmaa Laboratory, Aalto University School of Science, Aalto, Finland, [6]Neuroscience Unit, Institute of Biomedicine/Physiology, University of Helsinki, Helsinki, Finland

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

Okazaki M[1], Takahashi A[2], Otsuki T[2]

[1]Department of Psychiatry, National Center Hospital of Neurology and Psychiatry, Kodaira, Japan, [2]Department of Neurosurgery, National Center Hospital of Neurology and Psychiatry, Kodaira, Japan

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.

p698
PSYCHIATRIC COMORBIDITY AND SEIZURE CONTROL IN PATIENTS WITH TUBEROUS SCLEROSIS COMPLEX

Jovic N[1], Belacevic M[2], Babic M[1], Karaklic D[1]
[1]Neurology, Clinic for Neurology and Psychiatry for Children and Youth, Belgrade, Serbia, [2]Medical School, University of Belgrade, Belgrade, Serbia

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 relation 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.

p699
VALIDATION OF THE GENERALIZED ANXIETY DISORDER-7 IN PEOPLE WITH EPILEISY: A MEPSY STUDY

Park S-P[1], Seo J-G[1]
[1]Department of Neurology, School of Medicine, Kyungpook National University, Daegu, Korea

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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THE ANTIDEPRESSANT SERTRALINE DIMINISH THE EXPRESSION OF IL-1β AND TNF-α MRNA INDUCED BY SEIZURES IN THE HIPPOCAMPUS

Sitges M[1], Gómez CD[1], Aldana BI[1]
[1]Instituto de Investigaciones Biomédicas, Universidad Nacional Autónoma de México, Biología Celular y Fisiología, Distrito Federal, Mexico

Purpose: Recently we found that the antidepressant sertraline was an effective inhibitor of hippocampus presynaptic Na^+ channels permeability in vitro and of tonic-clonic seizures in the animal in vivo. Since 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-

zures and the increase in the expression of 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 brain inflammatory processes might importantly contribute to both, the anti-depressive and the anti-seizure action of sertraline.

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EPILEPSY AND DEPRESSION COMORBIDITY IN ADOLESCENTS

Sieracka J[1], Mazurkiewicz-Beldzinska M[1], Szmuda M[1], Agnieszka M[1]
[1]Developmental Neurology, Medical University of Gdańsk, Gdansk, Poland

Purpose: The comorbidity of depression and epilepsy is estimated at about 33%, compared with 6% in the general population. Clinical presentation of depression in these patients is usually more severe and often atypical symptoms are observed. It has been suggested that depressive disorders affect antiepileptic therapy and occur more frequent in patients with poorly controlled or severe epilepsy. The aim of this research was to assess prevalence of depression among adolescents suffering from epilepsy.

Method: The group of epilepsy adolescents (115) admitted to the Out and Inpatients Developmental Neurology Department during one year period and control group – healty adolescents (65) The groups were examined using standardized tests for depression, epilepsy, quality of life. Exclusion criteria in the study were e.g. severe general condition, abusion of alcohol, drugs, psychiatric disorders (other than depression) and chronic diseases requiring constant pharmacotherapy. Patient selection was aimed at creating a homogeneous group, in order to eliminate the influence of other variables on the occurrence of depression.

Results: The prevalence of depression in sudied group was 23% vs. 3% in control group, the correlations between the type of epilepsy and treatment and depression occurence were performed. Interstingly we did not find correlation between seizures severity and depressions as well as number of drugs in therapy and depression. The quality of life in the depression group was not-suprisingly statisticaly lower than in non-depression group.

Conclusion: There is high prevalence of depression in adolescents with epilepsy. Not necessary the severity of epilepsy in this age group predispose to depression.

p702
THE INCIDENCE OF MENTAL RETARDATION AND BEHAVIORAL DIFFICULTIES AT CHILDREN WITH EPILEPSY

Diaconu G[1], Ioana G[1]
[1]University of Medicine, Gr. T. Popa', Iasi, Romania

Purpose: The aim of this study was to assess the incidence of mental retardation and behavioral problems in children with epilepsy.

Method: During 4 years the study followed 83 children aged between 4 and 17 years, diagnosed with various forms of epilepsy (27 with symptomatic/cryptogenic localization-related epilepsy, 17 with idiopathic localization-related epilepsy, 14 with idiopathic generalized epilepsy and 25 with symptomatic generalized epilepsy). The study protocol included: EEG, brain CT / MRI, Wechsler Intelligence Scale for Preschool Period and Wechester 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 EEG 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 JUVENILE MYOCLONIC EPILEPSY

Japalak S[1], Jovic N[2,3]
[1]Hospital for Psychiatric Disorders 'Dr Laza Lazarevic', Belgrade, Serbia, [2]School of Medicine University of Belgrade, Belgrade, Serbia, [3]Clinic for Neurology and Psychiatry for Children and Youth, Belgrade, Serbia

Purpose: We evaluated the prevalence of psychiatric disorders among our patients with juvenile myoclonic epilepsy (JME).

Method: The diagnosis of JME was based on the criteria of the International Classification of Epilepsies. We enrolled 87 patients (49 female, 38 male) aged from 17.5 to 43.5 years (mean 27.6), with mean seizure onset of 14.3 ± 2.9 years (range 8.3–20.5) who had been followed up for a mean of 13.3 ± 5.8 years (range 5–28 years). The Epilepsy Department is a part of a University Clinic of Neurology and Psychiatry for Children and Adolescents. All patients were assessed according the Tenth Revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) criteria for mental and behavioural disorders. Current and lifetime psychiatric diagnoses were assigned.

Results: The twenty-five percent of the JME patients (22 patients, 11 female, 11 male) aged between 20 and 43.5 years (mean 26.8) suffered from one or more psychiatric disorders at any time of their life. Mental and behavioural disorders due to psychoactive substance use (F10–F19) were present in 4.5%, mood [affective] disorders (F30–F39) in 31.8%, neurotic, stress-related and somatoform disorders (F40–F49) in 36.3%, behavioural syndromes associated with physiological disturbances and physical factors (F50–F59) in 4.5%, disorders of adult personality and behavior (F60–F69) in 50%, behavioural and emotional disorders with onset usually occurring in childhood and adolescence in 18.2%. The eighteen patients with psychiatric disorders (81.8%) received psychiatric treatment (15 patients (83.3%) received the ambulatory care, 3 patients (16.7%) received the inpatient care). The psychiatric treatment included pharmacotherapy and psychotherapy.

Conclusion: Patients with JME have an increased incidence of personality disorders, neurotic, stress-related and somatoform disorders and mood disorders. The management of psychiatric disorders among patients with JME required timely and appropriate psychiatric treatment.

Keywords: Juvenile myoclonic epilepsy; psychiatric disorders; ICD-10

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PSYCHIATRIC DISORDERS IN PATIENTS WITH EPILEPSY

Mijo S[1], Zekja I[1], Grabova S[1], Doci H[1], Muslymi F[1], Papajani M[1], Stefanidhi L[1], Elezi F[2], Kruja J[1]

[1]Service of Neurology, UHC Mother Theresa, Tirana, Albania, [2]Service of Psychiatry, UHC Mother Theresa, Tirana, Albania

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%) particulary 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.

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SUBSTANCE USE DISORDERS AND PSYCHOTIC DISORDERS IN EPILEPSY: A POPULATION-BASED REGISTRY STUDY

Bakken IJ[1], Revdal E[2], Nesvåg R[1], Brenner E[2], Knudsen GP[1], Surén P[1], Ghaderi S[1], Gunnes N[1], Magnus P[1], Reichborn-Kjennerud T[1], Stoltenberg C[1], Trogstad L[1], Håberg SE[1], Brodtkorb E[2]

[1]The Norwegian Institute of Public Health, Oslo, Norway, [2]St Olavs Hospital, Trondheim, Norway

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.

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FAST DETECTION OF DEPRESSION IN EPILEPSY

Hansen CP[1], Amiri M[1]

[1]Department of Neurology, Copenhagen University Hospital North Zealand, Hillerød, Denmark

Purpose: To validate a Danish version of the Neurological Disorder Depression Inventory for Epilepsy (NDDI-E).

Method: Epilepsy outpatients were included according to the following criteria: Age above 18 years, epilepsy diagnosis, MRI or CT- scan of the brain, EEG, constant level of antiepileptic treatment in the past month and ability to read and speak Danish. Patients filled out the Neurological Disorder Depression Inventory for Epilepsy (NDDI-E) which was translated from English to Danish. NDDI-E in English is sensitive and specific for the diagnosis major depression when the sum for the 6 questions is above 15. For comparison the patients also filled out the World Health Organization Well-being Index (WHO-5). A score below 50 in WHO-5 is considered indicative of depression. All patients came for a Mini International Neuropsychiatric Interview version 5 (MINI 5.0.0). Patients were included from October 1, 2013.

Results: By January 20, 2014 we have included 43 epilepsy patients. According to MINI two patients had a depression (4.7%), and two had other psychiatric disorders. Five of the 43 patients had a score above 15 on NDDI-E, including the two patients with a diagnosis of depression according to MINI, whereas 38 patients had a score of 15 or less. Eight patients had a score on WHO-5 below 50, including the two with a depression, and 35 had a score of 50 or higher. With these preliminary data the Danish version of NDDI-E as a diagnostic tool for major depression in epilepsy has a sensitivity of 100% and a specificity of 93%, whereas WHO-5 has a sensitivity of 100% and a specificity of 85%. Results based on a larger number of patients will be presented.

Conclusion: Based on these preliminary results the Danish version of NDDI-E seems to be sensitive and specific in detecting depression in epilepsy patients.

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VAGUS NERVE STIMULATION HAS ANTIDEPRESSANT EFFECTS IN THE KAINIC ACID MODEL FOR TEMPORAL LOBE EPILEPSY

Grimonprez A[1], Raedt R[1], Dauwe I[1], Mollet L[1], Meurs A[1], De Herdt V[1], Wadman W[2], Delbeke J[1], Vonck K[1], Boon P[1]

[1]Neurology, Ghent University, Ghent, Belgium, [2]Neurobiology, Amsterdam University, Amsterdam, Netherlands

Purpose: Although vagus nerve stimulation (VNS) is used in clinical practice to treat refractory epilepsy and depression, efficacy is variable, predictors for response are unknown and the mechanism of action is unclear. Furthermore, studies on the antidepressant effects of VNS in patients with epilepsy are confounded by multiple factors, including antiepileptic drug therapy. We investigated whether VNS affects anhedo-

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 ELECTROENCEPHALOGRAM IN CHILDREN WITH AUTISM SPECTRUM DISORDER AND SPEECH DISTURBANCES

Gamirova RG[1,2], Belousova MV[2], Zaikova FM[2]
[1]Kazan Federal University, Kazan, Russian Federation, [2]Department of Pediatric Neurology, Kazan State Medical Academy, Kazan, Russian Federation

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% и 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 centrotemporal [Rolandic] and temporal-occipital areas).

Conflicts of Interest: None.

p709
SLEEP DISORDERS IN PATIENTS WITH DRUGRESISTANT FOCAL EPILEPSIES

Ley Nácher M[1], Principe A[1], Rocamora Zúñiga RA[1], Planellas Giné L[1]
[1]Neurology, Epilepsy Monitoring Unit, Hospital del Mar, Barcelona, Spain

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?

Socanski D[1], Herigstad A[2]
[1]Division of Psychiatry, Department of Child and Adolescent Psychiatry, Neuropsychiatric Department, Stavanger University Hospital, Stavanger, Norway, [2]Department of Clinical Neurophysiology, Stavanger University Hospital, Stavanger, Norway

Purpose: The purpose of this retrospective study was to investigate whether epileptiform abnormalites (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.

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

Vujisic S[1], Vodopic S[1], Radulovic L[1]
[1]Neurology, University of Montenegro, Podgorica, Montenegro

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

Kurth C[1], Steinhoff B[1]
[1]Epilepsy Centre Kork, Kork, Germany

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 hypermotor 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

Kapidzic A[1]
[1]Department of Neurology, Faculty of Medicine, University Clinical Centre Tuzla, University of Tuzla, Tuzla, Bosnia and Herzegovina

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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CHANGE IN ASTROCYTIC CA^{2+} RESPONSE DURING THE LATENT PERIOD OF EPILEPTOGENESIS IN THE ADULT MOUSE

Heuser K[1], Szokol K[1], Steinhäuser C[2], Jensen V[3], Enger R[3], Tang W[3], Taubøll E[1], Nagelhus EA[3]
[1]Neurology, Oslo University Hospital, Oslo, Norway, [2]Medical School, Institute of Cellular Neurosciences, University of Bonn, Bonn, Germany, [3]Institute of Basic Medical Sciences, University of Oslo, Oslo, Norway

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 uclear.

Method: Parahippocampal kainate injection in C57Bl6 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.

p716
EPILEPTIC SEIZURES IN NEURO-BEHCET DISEASE

Kutlu G[1], Semercioglu S[1], Ucler S[1], Erdal A[2], Inan LE[1]
[1]Neurology, Ministry of Health Ankara Research and Training Hospital, Ankara, Turkey, [2]Aksaray State Hospital, Aksaray, Turkey

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 NBD, 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 freqently 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.

p717
HYPOGLYCAEMIA AND RISK OF SEIZURES: A RETROSPECTIVE CROSS-SECTIONAL STUDY

Halawa I[1], Zelano J[1], Kumlien E[1]
[1]Department of Neuroscience, Uppsala University, Uppsala, Sweden

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 ≤3.5 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.

p718
IMMUNOLOGICAL PARAMETERS IN EPILEPSY

Rakhimbaeva G[1], Azizova R[1]
[1]Tashkent Medical Akademy, Tashkent, Uzbekistan

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, BMP, 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, ð < 0.001). The levels of AAB to MBP were high in the first group (14.9 ± 4.9 CU, ð < 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, ð < 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) (ð < 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

Azizova R[1], Rasulova K[2]
[1]Neurology, Tashkent Medical Akademy, Tashkent, Uzbekistan, [2]Tashkent Pediatric Institut, Tashkent, Uzbekistan

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

Azizova RB[1], Rakhimbaeva GS[1]
[1]Neurology, Tashkent Medical Akademy, Tashkent, Uzbekistan

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 41.2% 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

Ossenblok P[1], Hermans K[1,2], Spisak T[3], de Munck J[2], van Houdt P[1,2], Colon A[1], Boon P[1]
[1]Kempenhaeghe / Academic Center of Epileptology, Heeze, The Netherlands, [2]VU University Medical Center, Amsterdam, The Netherlands, [3]University of Debrecen, Debrecen, Hungary

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; 75:238–48]. 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 (IC) analysis. 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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p722
CASE REPORT OF ASYSTOLE AND REACTIVE ANOXIC SEIZURES DUE TO EXTRA-ADRENAL PHEOCHROMOCYTOMA

Mkhitaryan L[1], Melikyan G[2,3]
[1]Yerevan State Medical University, MC 'Erebouni', Neurology, Yerevan, Armenia, [2]Hamad Medical Corporation, Doha, Qatar, [3]Weill Cornell Medical College in Qatar, Clinical Neurology, Doha, Qatar

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. Carbamazepine started in 200 mg TID with therapeutic serum level but frequency of seizures were increased. Interictal and Ictal EEG showed diffuse polymorphic delta slowness. Baseline ECG and Echo was normal. Glucose was 9.1 mmol/ 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 asystoly in duration of 24–29 s preceded by blood pressure elevation. MRI of adrenal glands did not reveal tumor or hyperplasia. Scintgraphy 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 hypertention and causing bradycardia and even cardiac arrest.

p723
SEXUAL DYSFUNCTION AND SEXUAL WELL-BEING IN PEOPLE WITH EPILEPSY IN NORWAY

Henning O[1], Træen B[2], Nakken KO[1]
[1]National Epilepsy Centre, Oslo University Hospital, Sandvika, Norway, [2]Department of Psychology, University of Oslo, Oslo, Norway

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

Zisimopoulou V[1], Mamali M[1], Siatouni A[2], Verentzioti A[2], Tavernarakis A[1], Gatzonis S[2]
[1]Department of Neurology, Evaggelismos General Hospital, Athens, Greece, [2]Department of Neurosurgery, Evaggelismos General Hospital, Athens, Greece

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 Evaggelismos 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 concentration (>5/mm^3) and 2 had abnormal CSF leukocyte 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

Doneva AP[1], Petreska J[1], Pili Kuzeva K[2], Velinova V[1]
[1]Department of Neurology, GCH 8th September, Skopje, Macedonia, the Former Yugoslav, [2]Department of Neurology, CH Bitola, Bitola, Macedonia, the Former Yugoslav

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 myoclonic 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).

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LITERATURE ABOUT EPILEPSY 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

Tuft M[1], Aamold G[1], Hem ML[1], Gonder M[1], Stavn I[1]
[1]Oslo University Hospital, Bærum, Norway

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 ment be a tool for making good conversations, and to empower patients and families to tell their own stories, to give associations to their own lifes and to open up for conversations about epilepsy. Children with epilepsy, siblings of children with epilepsy, parents, friends, kindergardens, schools and health personell have been informed in different ways. 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), individual talks with children and siblings on a non-regular basis, courses for health personell and for the childrens′ grandparents on a non-regular basis.

Children with epilepsy have so far responded that they find the stories nice to listen to. After listening to the stories, they often tell about their own experiences with epilepsy, and how they inform friends and relatives about epilepsy.

The parents have appreciated to listen to examples from children about their experiences about having epileptic seizures, reactions from the social community, and how it feels to be a sibling to a child with epilepsy. They specifically valued the direct and honest language, reflecting the children′s own voices, and they learn that their own- and their children′s conceptions of epilepsy are different. The families are also happy to be able to bring the book "Epilepsy- children tell their stories" home for free, to show their relatives, friends, kindergarden or school.

The project will last for at least two more years. From April 2014 a new book exclusively for siblings to children with epilepsy, is added to the project. (Books will be on display)

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BRAIN NETWORK ORGANIZATION IN FOCAL EPILEPSY: A SYSTEMATIC REVIEW AND META-ANALYSIS

Van Diessen E[1], Zweiphenning W[1], Jansen FE[1], Stam CJ[2], Braun KP[1], Otte WM[1]
[1]UMC Utrecht, Utrecht, The Netherlands, [2]VU University Medical Center, Amsterdam, The Netherlands

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 contradictive 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.

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HEADACHE AND EPILEPSY: PREVALENCE AND CLINICAL FEATURES OF 398 PATIENTS

Bisulli F[1,2], Mainieri G[1,2], Leta C[1,2], Broli M[1,2], Giannini G[1,2], Ferri L[1,2], Santucci M[1,2], Avoni P[1,2], Cortelli P[1,2], Tinuper P[1,2], Cevoli S[1,2]
[1]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy, [2]Department of Biomedical and Neuro-Motor Science, University of Bologna, Bologna, Italy

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 epileptologists (FB, PT, MS, PA). Clinical variables in patients with and without IIH and PIH were analysed:χ^2-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 migrainous 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.

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TWO CASES OF CHOREA-ACANTHOCYTOSIS WITH EPILEPSY

Kaleagasi H[1], Fidanci H[1], Ozgur A[2], Dogu O[1]
[1]Neurology, Mersin University School of Medicine, Mersin, Turkey, [2]Radiology, Mersin University School of Medicine, Mersin, Turkey

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 frontocentral spikes and oxcarbazepine was started. After the four years of follow-up, chorea and involuntary oral biting occured. 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.

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NATIONAL REGISTRY OF DRAVET'S SYNDROME AND OTHER SYNDROMES CORRELATED WITH GENES SCN1A AND PCDH19

Dalla Bernardina B[1,2], Brambilla I[2], Bianchi F[3], Paoli D[4], Pierini A[3], Lipucci M[5]
[1]Life and Reproduction Sciences, University of Verona, Verona, Italy, [2]Dravet Syndrome Foundation Italia Nonprofit Association, Verona, Italy, [3]Institute of Clinical Physiology, CNR, Pisa, Italy, [4]Fundation Tuscany G. Monasterio CNR Region of Tuscany, Pisa, Italy, [5]Eurordis, Pisa, Italy

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 beta-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.

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EPILEPTIC SEIZURES IN PEDIATRIC POPULATION WITH BACTERIAL MENINGITIS IN A DEVELOPING COUNTRY

Esposito A[1], Hirose M[1], Lo DS[1], Ragazzi SL[1], Guilhoto LM[1,2]
[1]Divisao de Clinica Pediatrica, Hospital Universitario da Universidade de Sao Paulo, Sao Paulo, Brazil, [2]Neurology, UNIFESP, Sao Paulo, Brazil

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 in-patients 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 (18.5×10^9/l [IQR 17.3–26.8] vs. 15.8×10^9/L [IQR 12.0–19.2]; $p < 0.001$), higher median CSF leukocyte (3.498/dl [IQR 264–8.800] vs. 672/dL [IQR 161–2.545]; $p = 0.03$) and higher median CSF protein levels (257 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.

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HYPOMAGNESEMIA AND HYPOCALCEMIA MIMICKING SYMPTOMATIC FOCAL EPILEPSY: A CASE REPORT

Ihle JB, Caporale C, Nedeltchev K, Biethahn S
[1]*Neurology, Cantonal Hospital Aarau, Aarau, Switzerland*

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 myoclonus with preserved consciousness and an overall duration of around 30 s. The episodes were triggered by startling phenomena without evident external stimulus. The physical examination revealed fasciculations in both legs as well as a (preexistent) mild right-sided hemiparesis (NIHSS = 4). The episodes were initially interpreted as symptomatic focal epileptic seizures, possibly due to post-stroke lesions. Antiepileptic treatment with Levetiracetam was established. Laboratory results showed severe depletion of magnesium and calcium, most likely due to the prolonged diarrhea. Over the next two days, a progressive decline of consciousness, a worsening of the hemiparesis (NIHSS = 13), and a nonfluent aphasia occurred. Repeated EEGs did not show epileptic activity. Symptoms ceased with normalization of electrolyte levels.

Conclusion: Severe depletion of magnesium and calcium can present with a broad spectrum of neurologic manifestations including neuromuscular hyperexcitability, seizures, and coma. As both electrolytes are not routinely tested in most emergency wards, it is meaningful to consider dyselectrolitemia in cases of predisposing diseases such as persisting diarrhea.

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VIEWS OF YOUNG PEOPLE TOWARD EPILEPSY IN VOJVODINA

Ivetic VP[1]*, Vasic VI*[2]
[1]*Medical Faculty, Department of Physiology, Novi Sad, Serbia,*
[2]*Department of Physiology, University of Novi Sad, Novi Sad, Serbia*

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.

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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PREVENTION OF DEVELOPMENT OF TOLERANCE TO PHENOBARBITONE IN MICE USING HERBAL EXTRACTS

Katyal JPK[1]*, Vijaykumar AE*[1]*, Gupta YK*[1]
[1]*Pharmacology, All India Institute of Medical Sciences, New Delhi, India*

Purpose: Phenobarbitone (PHB) maintains its position as one of the most widely prescribed AED in developing as well as in some developed countries inspite of its side effects. Besides development of tolerance has been another limitation with its use. We studied the effect of aqueous extract of *Withania somnifera* (WS) (500, 750, 1,000 mg/kg) an Indian medicinal plant on development of tolerance to phenobarbitone (PHB).

Method: Male Swiss albino mice (25–30 g) were screened for 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: While WS (500 mg/kg) treated mice showed 80% incidence of tolerance, the higher dose (750 and 1000 mg/kg) caused a significant decrease in development of tolerance (< 20%). The MDA levels decreased and GSH levels increased significantly after the treatment with different dose of the WS when compare with phenbarbitone treated mice. Higher dose of WS in mice also showed significant improvement in cognitive functions.

Conclusion: The findings suggests that aqueuos extract of WS (750, 1,000 mg/kg) as adjuvant to PHB may delay tolerance development and also cognitive impairment.

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STATUS EPILEPTICUS AS A PROGNOSTIC INDICATOR IN TUBERCULAR MENINGITIS

Mishra VN[1]
[1]*Neurology, Banaras Hindu University, Varanasi, India*

Purpose: To find out the incidence and importance of Status epilepticus as 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 satges 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. Satutus epilepticus and development of hydrocephalus were the two independent prognostic indicator in the outcome of Tubercular Meningitis.

Conclusion: Status epilepticus is an independent prognotic indicator in management of Tubercular Meningitis.

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ARE ALL THE PATIENTS WITH TEMPORAL LOBE EPILEPSY SURGICAL CANDIDATES?

Hernandez Ronquillo L[1], Bukcley S[1], Ladino Malagon L[1], Tellez-Zenteno JF[1]
[1]Medicine, University of Saskatchewan, Saskatoon, SK, Canada

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.

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PROGNOSIS OF EPILEPSY IN PATIENTS WITH SEVERE MOTOR AND INTELLECTUAL DISABILITIES: A 10-YEAR FOLLOW-UP

Momosaki K[1,2], Matsubasa T[2], Kimura A[2], Endo F[1]
[1]Pediatrics, Graduate School of Medical Science, Kumamoto University, Kumamoto, Japan, [2]Pediatrics, Ashikita Institution for Developmental Disabilities, Ashikita-cho, Kumamoto, Japan

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.

Methods: 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).

Conclusions: 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.

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HEMISPHEROTOMY IN RASMUSSEN ENCEPHALITIS: LONG-TERM OUTCOME IN AN ITALIAN SERIES OF 16 PATIENTS

Matricardi S[1,2], Freri E[1], Ragona F[1], Casazza M[3], Villani F[4], Deleo F[4], Tringali G[5], Gobbi G[6], Tassi L[7], Lo Russo G[7], Marras CE[8], Specchio N[9], Vigevano F[9], Fusco L[9], Granata T[1]
[1]Department of Pediatric Neuroscience, Carlo Besta Neurological Institute, Milan, Italy, [2]Department of Pediatrics, University of Chieti, Chieti, Italy, [3]Department of Neurophysiology, Carlo Besta Neurological Institute, Milan, Italy, [4]Carlo Besta Neurological Institute, Clinical Epileptology and Experimental Neurophysiology Unit, Milan, Italy, [5]Department of Neurosurgery, Carlo Besta Neurological Institute, Milan, Italy, [6]IRCCS Istituto delle Scienze Neurologiche di Bologna, Local Health Trust of Bologna, Child Neurology Unit, Bologna, Italy, [7]Epilepsy Surgery Centre C. Munari, Milan, Italy, [8]Neurosurgery Unit, Bambino Gesù Children's Hospital, Rome, Italy, [9]Department of Neuroscience, Bambino Gesù Children's Hospital, Rome, Italy

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-

connection of the affected hemisphere (hemispherotomy, with different techniques).

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.

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CLINICAL HETEROGENEITY OF JUVENILE MYOCLONIC EPILEPSY: FOLLOW-UP AFTER AN INTERVAL OF MORE THAN 20 YEARS

Syvertsen M[1,2], Thuve S[2], Stordrange B[2], Brodtkorb E[2,3]
[1]Department of Neurology, Drammen Hospital, Drammen, Norway, [2]Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway, [3]Department of Neurology and Clinical Neurophysiology, St. Olav's University Hospital, Trondheim, Norway

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.

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LONG TERM OUTCOME IN CHILDREN WITH INFANTILE SPASMS TREATED WITH VIGABATRIN: A COHORT OF 180 PATIENTS

Djuric ML[1,2], Kravljanac R[1,2], Tadic B[3], Mrljes-Popovic N[3], Appleton R[4,5]
[1]Neurologic, Mother and Child Health Care Institute of Serbia 'Dr Vukan Cupic', Belgrade, Serbia, [2]Medical Faculty, University of Belgrade, Belgrade, Serbia, [3]Mother and Child Health Care Institute of Serbia 'Dr Vukan Cupic', Belgrade, Serbia, [4]Alder Hey Children's Hospital, Neurologic, Liverpool, UK, [5]University of Liverpool, Liverpool, UK

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 disfunction, 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% & 81.6% vs. 14.9% &0%, $p = .001$) Idiopathic patients treated with vigabatrin were all intellectually normal, except the youngest one, who was evaluated as borderline case with normal neurological status.

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

Deleo F[1], Didato G[1], Tringali G[2], Antozzi C[3], Beretta S[1], Garbelli R[1], Granata T[4], Matricardi S[4], Villani F[1]
[1]Clinical Epileptology & Experimental Neurophysiology, Foundation IRCCS Neurological Institute 'Carlo Besta', Milano, Italy, [2]Division of Neurosurgery III, Foundation IRCCS Neurological Institute 'Carlo Besta', Milano, Italy, [3]Neuroimmunology and Neuromuscular Diseases, Foundation IRCCS Neurological Institute 'Carlo Besta', Milano, Italy, [4]Division of Child Neurology, Foundation IRCCS Neurological Institute 'Carlo Besta', Milano, Italy

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 hemisyndrome) 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, IVIg, 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

Eeg-Olofsson O[1]

[1]*Department of Women's and Children's Health/ Neuropediatrics, Uppsala University, Uppsala, Sweden*

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 Empirically 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

Doležalová I[1,2], *Brázdil M*[1,2], *Hermanová M*[3], *Kojan M*[1,2], *Kuba R*[1,2]

[1]*First Department of Neurology, St. Anne's University Hospital and Faculty of Medicine, Masaryk University, Brno, Czech Republic,* [2]*Central European Institute of Technology (CEITEC), Masaryk University, Brno, Czech Republic,* [3]*First Department of Pathological Anatomy, Faculty of Medicine, St. Anne's University Hospital, Masaryk University, Brno, Czech Republic*

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 disconcordant (i.e. <90% in SOZ). The scalp EEG was evaluated for number (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 oroalimentary 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

Olusanya AW[1], *Danesi M*[2], *Ojinni F*[2], *Okubadejo NU*[2], *Ojo D*[2]

[1]*Neurology, Internal Medicine, Babcock University Teaching Hospital, Ilisan -Remo, Nigeria,* [2]*Neurology, Internal Medicine, Lagos University Teaching Hospital, Idi-Araba, Nigeria*

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

Pujar S[1,2,3], Seunarine K[1], Martinos M[1], Neville B[1,3], Chin R[1,4], Scott R[1,2,3,5], Clark C[1]

[1]UCL Institute of Child Health, London, UK, [2]Great Ormond Street Hospital for Children, London, UK, [3]Young Epilepsy, Lingfield, UK, [4]Muir Maxwell Epilepsy Centre, University of Edinburgh, Edinburgh, UK, [5]Geisel School of Medicine, Hanover, NH, USA

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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p747
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME INFLUENCES SHORT-TERM MORTALITY IN STATUS EPILEPTICUS

Stragapede L[1], Furlanis G[1], Belluzzo M[1], Monti F[1]

[1]Azienda Ospedaliero-Universitaria 'Ospedali Riuniti' Trieste, Triest, Italy

Purpose: Short-term status epilepticus outcome is determined mainly by age and etiology. Recently, the role infectious comorbidity 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 neurophysiologic 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

Handouk Y[1], Passarin MG[1]

[1]Ospedale Maurizio Bufalini, Cesena, Italy

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 neurological deterioration with an EEG pattern of a non convulsive status epilepticus (NCSE). He was treated in intensive care unit with intravenous 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

generally been attributed to microvascular occlusive disease, but NCSE is a treatable condition that can cause similar symptoms. Aggressive treatment with RTX, PE and antiepileptic drugs may prevent permanent neurologic deficits.

p749
EPIDEMIOLOGY BASED MORTALITY SCORE IN STATUS EPILEPTICUS - A RETROSPECTIVE EXPLORATORY COMPARISON

Leitinger M[1], Höller Y[1], Kalss G[1], Rohracher A[1], Novak H[1], Höfler J[1], Dobesberger J[1], Trinka E[1]
[1]Department of Neurology, Paracelsus Medical University Salzburg, Salzburg, Austria

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 $p \leq 0.0044$).

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

Giovannini G[1,2,3], Monti G[1,2,3], Mirandola L[1,2,3], Girardis M[1,2,3], Marudi A[1,2,3], Pinelli G[1,2,3], Valzania F[1,2,3], Nichelli PF[1,2,3], Meletti S[1,2,3]
[1]NOCSAE Hospital, University of Modena and Reggio Emilia, Modena, Italy, [2]AO Policlinico, Modena, Italy, [3]NOCSAE Hospital AUSL, Modena, Italy

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 Phenitoin (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

Milivojevic T[1], Bogicevic D[1,2], Delic J[1], Dedijer S[1], Nikolic D[1,2]
[1]Pediatrics/Neurology, School of Medicine, University of Belgrade, Belgrade, Serbia, [2]Department of Neurology, University Children's Hospital, Belgrade, Serbia

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. Ventriculomegalia 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 occured 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

Dedijer SS[1], Dragana B[1,2], Delic J[1], Milivojevic T[1], Dujovic M[1], Nikolic D[1,2]

[1]School of Medicine, University of Belgrade, Belgrade, Serbia, [2]University Children Hospital, Belgrade, Serbia

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

Kantanen A-M[1], Ruokonen E[2], Reinikainen M[3], Parviainen I[4], Kälviäinen R[5]

[1]Neurocenter/Epilepsy Center, Kuopio University Hospital, Kuopio, Finland, [2]Intensive Care, Kuopio University Hospital and Institute of Clincal Medicine, University of Eastern Finland, Intensive Care Unit, Kuopio, Finland, [3]Intesive Care Unit, North-Karelia Central Hospital, Joensuu, Finland, [4]Intensive Care Unit, Kuopio University Hospital, Kuopio, Finland, [5]Neurology, Kuopio University Hospital and Institute of Clinical Medicine, University of Eastern Finland, Neurocenter/Epilepsy Center, Kuopio, Finland

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 aetiology, 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.

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PREDICTING SUCCESSFUL ANTIEPILEPTIC DRUG WITHDRAWAL IN CHILDREN AFTER EPILEPSY SURGERY

Krsek P[1], Dvorak J[2], Jahodova A[3], Kudr M[1], Komarek V[1], Sebronova V[1], Tichy M[2]

[1]Department of Pediatric Neurology, Charles University, 2nd Faculty of Medicine, Motol University Hospital, Prague, Prague, Czech Republic, [2]Department of Neurosurgery, Charles University, 2nd Faculty of Medicine, Motol University Hospital, Prague, Prague, Czech Republic, [3]Department of Neurology, Charles University, 2nd Faculty of Medicine, Motol University Hospital, Prague, Prague, Czech Republic

Purpose: To assess variables influencing successful antiepileptic drug (AED) discontinuation after pediatric excisional epilepsy surgery.

Methods: Data of 103 children who underwent excisional epilepsy surgery at Motol Epilepsy Centre between 2002 and 2011 were retrospectively analyzed. All patients were followed up for more than two postoperative years. We statistically compared subjects who became seizure-free and drug-free for at least 1 year with children experiencing seizure recurrence during tapering-down medications.

Results: AEDs were postsurgically preserved in 27, reduced in 52 and completely withdrawn in 24 children. Seizure recurrence experienced 23/27(85%) subjects with preserved AEDs, 13/52(25%) patients with reduced AEDs and 4/24(16.6%) children after AED discontinuation. Seizure-free drug-free patients (n = 20) significantly differed from subjects experiencing seizures during or after AED discontinuation (n = 17) in: age at seizure onset (7.7 vs. 3.3 years), seizure frequency (30% vs. 76.5% patients with daily seizures), mental disability (20% vs. 53% mentally-disabled subjects), need of long-term intracranial EEG study (10% vs. 35% cases), localization of resections (95% vs. 29% temporal lobe surgeries), extent of surgeries (0% vs. 41% of multilobar resections), incidence of postoperative EEG spikes (present in 25% vs. 65% of cases) as well as etiology (prevailing hippocampal sclerosis and benign tumors vs. cortical dysplasia).

Conclusions: Successful AED withdrawal was predicted by later seizure onset, less frequent seizures, normal intelligence, temporal lesion other than cortical dysplasia, need of less extensive resection without long-term intracranial EEG study. Assessing completeness of resections at the time of surgery does not reliably predict patient's chances to become postoperatively seizure-free and drug-free.

p756
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

Francione S[1], Liava A[1], Tassi L[1], Mai R[1], Nobili L[1], Sartori I[1], Castana L[1], Cardinale F[1], Cossu M[1], Lo Russo G[1]
[1]Ospedale Niguarda Ca' Granda, Neuroscience, Milano, Italy

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 and 10.3% in class IV. AEDs were stopped in 35.7% and tapered in further 18% of cases. A relapse was observed in 10 cases. An MRI-identifiable discrete lesion represented a statistically-significant favourable predictor, whereas early epilepsy onset (<5 years), the necessity to perform Stereo-EEG, an extra temporal resection and FCDI at histology statistically correlated with a negative outcome.

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%.

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A KNOCK-OUT TO THE IMMUNOMODULATORY APPROACH: A SUCCESSFUL DOMINANT HEMISPHEROTOMY IN RASMUSSEN ENCEPHALITIS

Goldberg-Stern H[1,2], Fried I[3]
[1]Epilepsy Center, Schneider Children's Medical Center of Israel, Petach Tikva, Israel, [2]Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel, [3]Neurosurgery, Sourasky Medical Center, Tel Aviv, Israel

Purpose: Rasmussen encephalitis (RE) is an inflammatory unihemispheric brain disorder with intractable epilepsy and progressive brain atrophy. Hemispherotomy offers a very high chance of seizure freedom, however, at the price of irreversible loss of functions located with the affected hemisphere. In a proportion of patients, long-term immunotherapy slows down the hemispheric tissue loss, but generally does not improve the epilepsy. A dilemma in choosing the appropriate therapeutic approach may emerge in those with severe epilepsy, but still preserved hemispheric function, or in those with dominant hemisphere involvement, since hemispherotomy may lead to mutism or severe speech abnormality in addition to expected hemiparesis. The purpose of this presentation is to highlight the importance of early hemispherotomy even in a dominant hemisphere RE.

Method: We present a right-handed 7-year-old girl with RE in the left hemisphere, manifested by intractable epilepsy with epilepsia partialis continua (EPC) since 4-years old. Due to dominant hemisphere involvement, the patient had been receiving immunomodulatory treatment, including steroids, repeated courses of intravenous immunoglobulin, and tacrolimus for about 2 years, and surgery was deferred, but there was no seizure control despite multiple anti-epileptic drugs. Magnetic resonance imaging (MRI) showed progressive left hemisphere atrophy. Finally, after functional MRI findings of right hemisphere dominancy of speech, the patient underwent successful left hemispherotomy.

Results: At the 6-month follow-up, she is seizure-free, with mild right hemiparesis and preserved speech. Anti-epileptic drugs are being tapered off gradually with no seizure recurrence.

Conclusion: Hemispherotomy is the preferred therapy for RE and should be considered early even in cases of dominant hemisphere involvement. We will review the therapeutic approach of RE, emphasizing the advantages and disadvantages of immunomodulatory protocols vs. surgical approach and discuss the yield of functional MRI in this case.

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EPILEPSY SURGERY IN ADULT-ONSET RASMUSSEN'S ENCEPHALITIS: CASE SERIES AND REVIEW OF THE LITERATURE

Casciato S[1], Di Bonaventura C[1], Giallonardo AT[1], Fattouch J[1], Lapenta L[1], Fanella M[1], Albini M[1], Morano A[1], Esposito V[2], Berardelli A[1], Quarato P[2], D'Aniello A[2], Di Gennaro G[2]
[1]Department of Neurology and Psychiatry, University of Rome 'La Sapienza', Rome, Italy, [2]Department of Neurological Sciences, Epilepsy Surgery Unit, IRCCS Neuromed, Pozzilli, Italy

Purpose: Rasmussen's Encephalitis (RE) is a rare immunomediate 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.

Methods: 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 to 1 to 6 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 fronto-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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PSYCHO-SOCIAL OUTCOMES FOLLOWING EPILEPSY SURGERY: RESULTS FROM THE EPILEPSY PSYCHO-SOCIAL EFFECTS SCALE (EPSES)

Chaplin JE[1], Malmgren K[2]
[1]Institute of Clinical Sciences, Sahlgrenska Academy at the University of Gothenburg, Clinical Sciences, Gothenburg, Sweden, [2]Department of Clinical Neuroscience and Rehab, Institute of Neuroscience and Physiology, Sahlgrenska Academy at Gothenburg University, Gothenburg, Sweden

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.

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TEMPORAL ANTEROINFERIOR ENCEPHALOCELE: AN UNDER-RECOGNIZED ETIOLOGY OF TEMPORAL LOBE EPILEPSY?

Saavalainen T[1], Jutila L[2], Mervaala E[3], Kälviäinen R[2], Vanninen R[1], Immonen A[4]
[1]Department of Clinical Radiology, Kuopio University Hospital, Kuopio, Finland, [2]Department of Neurology, Kuopio University Hospital, Kuopio, Finland, [3]Department of Clinical Neurophysiology, Kuopio University Hospital, Kuopio, Finland, [4]Department of Neurosurgery, Kuopio University Hospital, Kuopio, Finland

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.

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FUNCTIONAL HEMISPHERECTOMY IN CHILDREN AND YOUNG ADULTS WITH MEDICALLY INTRACTABLE EPILEPSY: INFLUENCE OF UNDERLYING PATHOLOGY ON OUTCOME

Mundil N[1,2], Kulkarni G[1], Silva D[1,2], Kayello R[2], Walsh R[1,2]
[1]Department of Neurosurgery, Birmingham Childrens Hospital, Birmingham, UK, [2]Department of Neurosurgery, Queen Elizabeth Hospital, Birmingham, UK

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 years) 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-septicaemia 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 most 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

Galego PHC[1], Ghizoni E[1], Campos BM[1], Filho AA[1], Yasuda CL[1], Joaquim AF[1], Oliveira E[1], Tedeschi H[1], Cendes F[1]
[1]Neurology, University of Campinas, Campinas, Brazil

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 amygdalohyppocampectomy 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 amygdalohippocampectomy 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

Papandreou A[1], Tisdall MM[2], Harkness WF[2], Cross HJ[1], Varadkar SM[1]
[1]Paediatric Neurology, Great Ormond Street Hospital for Children, London, UK, [2]Paediatric Neurosurgery, Great Ormond Street Hospital for Children, London, UK

Purpose: To describe the first case in the literature of complication free epilepsy surgery in a patient with COL4A1 mutation.

Method: Case report: 6 year old female, COL4A1 (collagen type IV alpha 1) mutation positive, with drug resistant epilepsy characterized by multiple seizure types, bilateral spastic dystonic cerebral palsy and developmental delay. COL4A1 mutations disrupt integrity of the vascular basement membrane, so predisposing to a broad spectrum of intracranial disorders including white matter changes, periventricular leucomalacia, haemorrhagic stroke, aneurysm formation, epilepsy and developmental delay Intracranial haemorrhage is reported, but the risk is unclear, though may be recurrent and associated with trauma and anticoagulant therapy In children, an increased risk of stroke with general anaesthesia has been reported.

Results: Following pre-surgical evaluation, our patient was a candidate for for corpus callosotomy. Previous general anaesthesia had been un complicated. Pre-operative full blood count and coagulation studies were normal. Peri-operatively, normotension was maintened anticoagulation was avoided. A complete corpus callosotomy was performed with no subsequent intracranial haemorrhage or other complications. 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

Kishima H[1,2], Oshino S[1,2], Tani N[1,2], Khoo HM[1,2], Yanagisawa T[1,2], Maruo T[1,2], Inoue Y[1,2], Hirata M[1,2], Yoshimine T[1,2]
[1]Department of Neurosurgery, Osaka University Graduate School of Medicine, Suita, Japan, [2]Epilepsy Center, Osaka University Hospital, Suita, Japan

Purpose: We developed the selective amygdalohippocampectomy (SAHT) via the inferior temporal gyrus using neuronavigation system to preserve the temporal stem. This precedure provides excellent epilepsy control for patients with rmesial 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 verbal, visual, 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

van Schooneveld M[1], Jennekens-Schinkel A[1], Braun K[1], Engelhart M[1], van Nieuwenhuizen O[1]
[1]University Medical Center Utrecht, Utrecht, The Netherlands

Purpose: To know health-related quality of life (HrQoL), evaluated by (former) patients at least one year after epilepsy surgery in childhood,

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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 Euroquol 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.