Epilepsia
The Journal of the International League Against Epilepsy

Table of Contents

Volume 54, Supplement 3, 2013

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

Epilepsia, 54(Suppl. 3):4–29, 2013
doi: 10.1111/epi.12228

ABSTRACTS

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

Platform Session: Paediatric Epilepsy 1
Monday, 24th June
14:30–16:00

001
WHAT PREDICTS ENDURING INTRACTABILITY IN CHILDREN WHO APPEAR MEDICALLY INTRACTABLE IN THE FIRST TWO YEARS AFTER DIAGNOSIS?

Wirrell E[1], Wong-Kisiel L[1], Mandrekar J[2], Nickels K[1]
[1]Mayo Clinic, Child and Adolescent Neurology and Epilepsy, Rochester, MN, USA, [2]Mayo Clinic, Biomedical Statistics and Informatics, Rochester, MN, USA

Purpose: In a population-based retrospective cohort of children with newly-diagnosed epilepsy, to (1) determine what proportion meet criteria for early medical intractability, and (2) predictors of enduring intractability.

Methods: Children with newly-diagnosed epilepsy between 1980 and 2009 while resident in Olmsted County, MN, and followed >36 months were stratified into groups, based on both early medical intractability ('apparent' medical intractability in the first 2 years) and enduring intractability (persisting intractability at final follow-up or having undergone surgery for intractable epilepsy), and variables predicting these outcomes were evaluated.

Results: Three hundred and eighty one children were included, representing 81% of our cohort with newly diagnosed epilepsy. Seventy five (19.7%) had early medical intractability, and predictors of this outcome on multivariable analysis were neuroimaging abnormality ($p = 0.001$), abnormal neurological examination at diagnosis ($p = 0.005$) and mode of onset [association was significant for focal vs generalized onset ($p < 0.001$) but not unknown vs generalized onset ($p = 0.67$)]. After a median follow-up of 11.7 years, 49% remained intractable, 8% had rare seizures (≤q6 months), and the remainder were seizure-free. The only factor predicting for enduring intractability on multivariable analysis was neuroimaging abnormality ($p < 0.0001$).

Conclusion: While a significant minority of children with early medical intractability ultimately achieved seizure control without surgery, those with an abnormal imaging study did poorly. For this subgroup, early surgical intervention is strongly advised to limit co-morbidities of ongoing, intractable seizures. Conversely, a cautious approach is suggested for those with normal imaging, as most will remit with time.

002
INCIDENCE, PREVALENCE AND CLINICAL OUTCOME OF RASMUSSEN ENCEPHALITIS IN CHILDREN FROM THE UNITED KINGDOM

Lamb K[1], Scott WJ[2], Mensah A[2], Varadkar S[1], Robinson R[1], Cross HJ[1,2,3]
[1]Department of Neurology, Great Ormond Street Hospital, London, UK, [2]Young Epilepsy, Lingfield, UK, [3]Neurosciences Unit, UCL Institute of Child Health, London, UK

Purpose: Rasmussen Encephalitis (RE) is a progressive inflammatory disorder affecting one cerebral hemisphere, of presumed autoimmune aetiology, with a previously described biphasic course [1]. We aimed to determine the incidence, prevalence, presentation and outcome of children with RE in the UK.

Method: New and existing cases of RE in children <16 years were identified through the British Paediatric Neurology Surveillance Unit, March 2010–2012. Clinical data were provided on cases by clinician completed questionnaire.

Results: Twenty-one cases were identified (12 male, 9 female), including four new diagnoses during the. study period. This indicated an observed incidence of 0.017 per 100,000 person years and prevalence of 0.18 per 100,000. There was no similarity in demography, medical or family history amongst cases. Nineteen percent developed cognitive deficit, 81% hemiplegia and 67% language deficit. Thirteen underwent surgery (5 dominant, 8 non-dominant); 12 hemispherectomy (11 seizure free, 1 > 75% seizure reduction; all have hemiplegia but ambulant; 8/12 remain in mainstream school).

Conclusion: This is the first study to identify prevelance for RE. One previous calculation of incidence in Germany [2] gives a similar rate (0.024 per 100,000 person years) although in a different population (<18 year olds). Clinical presentation is with focal seizures of variable semiology and there is little support for the previous suggestion of a biphasic course. Post-hemispherectomy outcomes are positive but the decision of when and if to operate remains dependent on the individual clinical course.

References: [1] Bien CG et al CE Brain2002;17511759.
[2] Bien CG et al, Epilepsia1-8,2012.

003
THE RELATIONSHIP BETWEEN EPILEPSY SEVERITY AND SOCIAL ACTIVITIES IN CHILDREN WITH NEW-ONSET EPILEPSY: THE ROLE OF CHILD COGNITIVE AND BEHAVIOUR PROBLEMS

Ferro MA[1,2], Speechley KN[3,4,5]
[1]Psychiatry & Behavioural Neurosciences, McMaster University, Hamilton, ON, Canada, [2]Offord Centre for Child Studies, McMaster University, Hamilton, ON, Canada, [3]Paediatrics, Western University, London, QC, Canada, [4]Epidemiology & Biostatistics, Western University, London, QC, Canada, [5]Children's Health Research Institute, Western University, London, QC, Canada

Purpose: The purpose of this study was to examine the association of epilepsy severity at diagnosis with social activities at 24-months in children with epilepsy and to assess the role of child cognitive and behaviour problems in this relationship.

Method: Data were obtained from the Health Related Quality of Life in Children with Epilepsy Study (HERQULES), a prospective multisite study of children 4–12 years old with new-onset epilepsy followed for 24 months. Epilepsy severity was measured using the Global Assessment

for the Severity of Epilepsy (GASE); social activities were measured using the Social Functioning subscale of the Quality of Life in Childhood Epilepsy (QOLCE). Data were analyzed using multiple-group structural equation modeling. Tests of moderation and mediation were conducted to assess the extent to which the association of epilepsy severity and social activities was influenced by child cognitive problems, and whether the relationship was mediated by child behaviour problems.

Results: A total of N = 374 families participated in HERQULES. There was evidence of differential effects between children with (n = 75) and without cognitive problems (n = 299) in the relationship between epilepsy severity and social activities (moderated-mediation). Controlling for the child age and sex, family functioning, and household income, the mediated effect of behaviour problems was significantly larger in children with cognitive problems compared to without ($\alpha\beta = 0.15$ vs. 0.01, $p = 0.001$).

Conclusion: For children with new-onset epilepsy and cognitive problems, the relationship between epilepsy severity at diagnosis and participation in social activities is mediated by the presence of child behaviour problems. Findings may be useful in developing individualized care in epilepsy and call attention to the role of comorbidities in influencing the impact of clinical risk factors on the social functioning of children newly diagnosed with epilepsy.

004

VALIDATION OF LIVERPOOL ADVERSE EVENTS PROFILE IN PEDIATRICS PATIENTS WITH EPILEPSY AND ITS CORRELATION WITH THE LEVEL OF QUALITY LIFE OF CHILDREN WITH EPILEPSY

Lara-Herguedas J[1], Serratosa-Fernández J[2], García-Peñas J-J[3], Ruiz-Falcó Rojas M[3], Gutierrez-Solana LG[3], Cazorla-Calleja R[1], Gutierrez-Cruz N[1], Roman-Riechmann E[1]

[1]Neuropediatrics Unit, Hospital Universitario Puerta de Hierro Majadahonda, Majadahonda, Spain, [2]Department of Neurology, Fundación Jiménez Diaz, Madrid, Spain, [3]Neuropediatrics Unit, Hospital Infantil Universitario Niño Jesús, Madrid, Spain

Purpose: Adverse effects of antiepileptic drugs (AEDs) are common in pediatric patients suffering from epilepsy. In adults there are standardized and validated questionnaires on patients with epilepsy, such as LAEP, but not the pediatric population.

Objective: Adapt and validate the scale LAEP on pediatric population as a means of detecting the adverse effects of AEDs. Analyze the correlation between the modified LAEP and the quality of life scale CAVE.

Method: An observational, cross-sectional multicenter study during a period of 12 months. We adapted LAEP scale to pediatrics patients with 21 item questionnaire. Each item is assessed on a 4-point Likert scale, and a global summary score ranging from 21 to 84. Sociodemographic and clinical (epilepsy etiology, seizure type, and antiepileptic drug treatment) data were collected at the moment of inclusion. The scale was applied in each patient less frequently than every 3 months.

Results: Modified LAEP and CAVE was applied to 550 children under 18 years with epilepsy. We find correlation between the LAEP scale and the CAVE (r Pearson −0.4037). Time for the test was <5 min in 99% and the difficulty level was low in 88% of cases. The effects most frequently found in children under 3 years were agitation, weight loss, drowsiness, and over 3 years, behavior problems and difficulty in concentrating. There was statistical significance between the frequency and intensity of seizures, polytherapy and the high score in LAEP. Improved scores on the LAEP to withdraw the medication and the maintenance dose at the time.

Conclusion: Modified LAEP is the first scale to detect adverse effects of the AEDs applied in children. The systematic use of scales to predict the adverse effects of AEDs and the proper selection of AEDs can improve the quality of life.

005

THE EFFECT OF THE KETOGENIC DIET ON THE DEVELOPING SKELETON

Simm P[1,2,3], Bicknell-Royle J[4], Nation J[5], Draffin K[6], Stewart K G[7], Cameron F[1,2,3], Scheffer IE[2,3,8,9], Mackay M T[2,3,4,9]

[1]Department of Endocrinology and Diabetes, Royal Children's Hospital Melbourne, Parkville, Vic, Australia, [2]Department of Paediatrics, University of Melbourne, Melbourne, Vic., Australia, [3]Murdoch Childrens Research Institute, Melbourne, Vic., Australia, [4]Department of Neurology, Royal Children's Hospital Melbourne, Parkville, Vic., Australia, [5]Department of Nutrition and Food Services, Royal Children's Hospital Melbourne, Parkville, Vic., Australia, [6]Department of Nutrition and Dietetics, Austin Health, Heidelberg, Vic., Australia, [7]Department of Paediatrics, Austin Health, Heidelberg, Vic., Australia, [8]Department of Medicine, Heidelberg, University of Melbourne, Epilepsy Research Centre, Vic., Australia, [9]Florey Neuroscience Institutes, Melbourne, Vic., Australia

Purpose: The ketogenic diet (KD) is a medically supervised, high fat, low carbohydrate and restricted protein diet which has been used successfully in patients with refractory epilepsy. Only one published report has explored its effect on the skeleton. We postulated that KD impairs bone mass accrual and examined skeletal health parameters in this patient group.

Method: Patients commenced on the KD from 2002 to 2009 were enrolled in a prospective, longitudinal study; with monitoring of Dual-energy Xray absortpiometry (DXA) derived bone parameter including bone mineral content and density (BMD). Areal BMD was converted to bone mineral apparent density (BMAD) where possible. Biochemical parameters including Vitamin D and bone turnover markers including osteocalcin and urinary deoxypiridinolone were assessed.

Results: Twenty-nine patients were on the KD for a minimum of 6 months (range 0.5–6.5 years, mean 2.1 years). There was a mean reduction in lumbar spine (LS) BMD Z score of 0.37. Twenty patients (68%) had a lower BMD at the end of treatment. There was no correlation between change in LS BMD and ambulatory status (R = 0.02). Height adjustment was possible for 13 patients, with a mean reduction in BMAD Z score of 0.19 SD. ALP levels were in the normal range but osteocalcin showed a mean 26.5 nM, which was elevated. No patient suffered fractures. Urinary calcium-creatinine ratios were elevated (mean 0.77) but only one patient developed renal calculi.

Conclusion: The KD has a small but significant effect on the developing skeleton, independent of height and ambulatory status. Effects on bone turnover and calcium/creatinine ratios point to abnormal mineral metabolism. Clinicians should be aware of potential skeletal side effects and monitor bone health during KD treatment. Longer term follow up is still required to determine adult/peak bone mass and fracture risk.

006

RANDOMISED CLINICAL TRIAL COMPARING PREDNISOLONE AND ACTH IN REVERSAL OF HYPSARRHYTHMIA IN UNTREATED EPILEPTIC SPASMS

Wanigasinghe J[1], Attanapola GM[1], Arambepola C[1], Liyanage CB[2], Kankanamge PKSJ[2], Sumanasena S[1], Sri Ranganathan S[1]

[1]University of Colombo, Colombo, Sri Lanka, [2]Lady Ridgeway Hospital, Colombo, Sri Lanka

Purpose: Although several anticonvulsants have been shown to effectively improve the clinical outcomes in infantile spasms, no previous study has systamatically shown their effects in the reversal of hypsarrhythmia. This is the first ever randomised clinical trial to assess the role of hormonal therapy on improving hypsarrhythmia.

Method: Seventy-eight newly diagnosed, untreated infantile spasm patients were randomised into two arms of oral prednisolone or intramuscular ACTH for 14 days on doses according to United Kingdom Infantile Spasms Study protocol (2004). Hypsarrhythmia severity was assessed on a sleep electroencephalogram on a 16-point-scale score described by Kramer et al. (1997), prior to treatment and on 14th/15th day of post-treatment. The scoring was performed by a single investigator, blinded to the clinical details and the treatment arm.

Results: Only 69 infants provided EEG evaluations. The mean pre-treatment overall hypsarrhythmia severity scores were 10.43 (SD = 2.8) for prednisolone and 10.38 (SD = 2.6) for ACTH. The mean post-treatment overall severity scores were 2.54 (SD = 2.25) for prednisolone and 4.09 (SD = 2.5) for ACTH. A significant improvement of hypsarrythmia was seen with both prednisolone (mean difference of pre and post-treatment severity scores = 7.886 ± 2.89) and ACTH (mean difference of pre and post-treatment severity scores = 6.29 ± 2.53; $p < 0.01$). This improvement was significantly higher with prednisolone than with ACTH ($p < 0.01$). All individual components of the score i.e. background disorganisation, diffuse delta slowing, voltage of epileptic discharges, spike wave index, electro-decremental pattern, burst suppression, absence of normal sleep patterns and normalisation in wakefulness were significantly improved with both treatments ($p < 0.01$).

Conclusion: Hormonal therapies (prednisolone and ACTH) resulted in significant reversal of hypsarrhythmia in untreated epileptic spasms. Of the two treatment arms tested, overall reduction of the individual scores was better in those treated with oral prednisolone.

Platform Session: Drug Therapy
Monday, 24th June
14:30–16:00

007
A COMBINATION OF THE 5-HTT GENOTYPES IS LINKED WITH HIGHER 5-HTT GENE EXPRESSION AND WITH WORSE RESPONSE TO PHARMACOTHERAPY IN TLE PATIENTS

Hecimovic H[1], Sajko T[2], Popovic Z[3], Rotim K[2], Basic Kes V[4]
[1]Department of Neurology, University Hospital, Zagreb, Croatia, [2]Department of Neurosurgery, University of Zagreb, Zagreb, Croatia, [3]University of Osijek, Osijek, Croatia, [4]Department of Neurology, University of Zagreb, Zagreb, Croatia

Purpose: Temporal lobe epilepsy (TLE) is the most common epilepsy and about 30% of patients have poorly controlled seizures. Neurobiology underlying responsiveness to medical treatment in TLE patients is unclear and there are currently no biological tests to predict course of the disease. Animal and human studies repeatedly suggested serotonergic dysfunction in subjects with TLE. We investigated association of serotonin transporter (5-HTT) gene polymorphisms with medical treatment response in patients with TLE.

Method: We analysed 5-HTT gene linked polymorphic region (5-HTTLPR) in promoter and variable number of tandem repeats in the second intron of the 5-HTT gene (VNTR-2) in 101 consecutive subjects with TLE in a tertiary health center at University Hospital.

Results: TLE patients with the combination of transcriptionally more efficient genotypes, i.e. 5-HTTLPR L/L and VNTR-2 12/12, had increased seizure refractoriness to antiepileptic medication and shorter periods of seizure freedom, than subjects with other combinations of the 5-HTT genotypes. There were no other clinical or demographic differences among patient groups based on the 5-HTT genotypes.

Conclusion: Combination of the 5-HTT genotypes linked with higher 5-HTT gene expression was found to be associated with worse response to optimal drug therapy. Further studies should determine potential role of this 5-HTT genotype polymorphism in epileptogenesis.

008
EFFECTS OF TREATMENT RESPONSE AND SIDE EFFECTS ON OVERALL QUALITY OF LIFE AND DISTRESS

Simons WR[1], Gilliam F[2]
[1]Global Health Technology Assessments, Eisai Co. Ltd, Woodcliff Lake, NJ, USA, [2]Department of Neurology, Pennsylvania State University, Hershey, PA, USA

Objective: To assess the marginal effects of 50%, 75% and 100% responder rates and time spent with mild, moderate and severe side effects on overall quality of life.

Methods: We used pooled quality of life measured with the Quality of Life in Epilepsy (QOLIE) instrument, efficacy (responder rates) and adverse event data collected in three randomized, placebo-controlled trials in patients with refractory partial onset epilepsy. Increases in overall QOLIE are improvements while increases in side-effects are deteriorations. Responder rates were defined as per protocol. Time with treatment-related adverse events were summed by patient and severity- mild, moderate and severe. Linear regressions were employed with percent change in overall QOL as dependent variables and responder rate and days with side-effects by severity as covariates.

Results: 959 of the 1478 intent to treat population had evaluable QOLIE data. The population average improvement in overall QOL was 20 ($p < 0.01$). Fifty-percent responders improved an additional 8.9% ($p < 0.01$) for a total of 28.9% ($p < 0.01$). Moderate and severe side effects decreased QOL by 0.178 ($p = 0.02$) and 0.752 ($p = 0.04$) per day spent with the side effect. Seventy-five and hundred percent responder had incremental and monotonic improvements in their QOL, 13.86% ($p < 0.01$) and 22.36 ($p < 0.01$). Effects on QOL of moderate and severe side effects were the same. Distress decreased with response, −11.08 ($p < 0.01$) for 50%, −11.66 ($p < 0.01$) for 75% and −14.11 ($p < 0.01$). Moderate and severe side effects increased distress (all $p < 0.05$).

Conclusion: Reductions in seizures significantly improve QOL even after adjusting for side effects.

009
THERAPEUTIC DRUG LEVEL MONITORING WITH LEVETIRACETAM IN THE TREATMENT OF EPILEPSY

Stepanova D[1], Beran RG[1,2,3]
[1]Strategic Health Evaluators, Sydney, NSW, Australia, [2]Griffith University, Gold Coast and Brisbane, Qld, Australia, [3]University of New South Wales, Sydney, NSW, Australia

Purpose: This paper investigates a proposed levetiracetam (LEV) therapeutic range and potential drug interactions in people with epilepsy (PWE).

Method: Fifty-two PWE were evaluated. LEV and concomitant AEMs levels [carbamazepine (CBZ), valproate (VPA) and lamotrigine (LTG)]

were measured and compared to seizure activity. Adopted therapeutic ranges: 20–40 mg/L – LEV; 25–50 μM – total CBZ; 6–13 μM – free CBZ; 300–750 μM – total VPA; 30–75 μM – free VPA; 40–60 μM – LTG. Seizure-freedom was assessed for 1–3, 3–6, 6–12 months and >1 year.

Results: 18/52 (35%) used LEV monotherapy and 13/18 (72%) had 'therapeutic' LEV with 11/13 (85%) seizure-free [1/11 (9%) 1–3 months; 1/11 (9%) 3–6 months; 5/11 (45%) 6–12 months; and 4/11 (36%) >1 year]. 34/52 (65%) used polytherapy and 17/34 (50%) had 'therapeutic' LEV with 7/17 (41%) seizure-free [1/7 (14%) 3–6 months; 1/7 (14%) 6–12 months; and 5 /7 (71%) >1 year]. 11/34 (32%) used CBZ: 5/11 (45%), reduced LEV; 4/11 (36%) increased LEV; and 2/11 (18%) no change; 3/11 (27%) LEV increased CBZ; 7/11 (64%) reduced CBZ; and 1/11 (9%) no change. 14/34 (41%) used VPA: 11/14 (79%) VPA increased LEV; 3/14 (21%) reduced LEV; 5/14 (36%) LEV increased VPA; 9/14 (64%) reduced VPA. 13/34 (38%) used LTG: 7/13 (54%) increased LEV; 4/13 (31%) decreased LEV; 2/13 (15%) no change; 3/13 (23%) LEV increased LTG; 9/13 (69%) LEV reduced LTG; 1/13 (8%) no change.

Conclusion: LEV range (20–40 mg/L) proved useful in treating epilepsy (especially with monotherapy). Unpredictable drug interactions diminished benefits with polytherapy.

010
ALTERED CORTICAL THICKNESS IN LANGUAGE CORTEX FOLLOWING PRENATAL EXPOSURE TO SODIUM VALPROATE

Wood AG[1,2,3], Chen J[2], Barton S[2], Nadebaum C[2], Anderson VA[2,4], Reutens DC[5], O'Brien TJ[6,7], Vajda F[6,8]
[1]University of Birmingham, Birmingham, UK, [2]Murdoch Children's Research Institute, Parkville, Vic., Australia, [3]Monash University, Clayton, Vic., Australia, [4]Royal Children's Hospital, Parkville, Vic., Australia, [5]University of Queensland, St Lucia, Qld, Australia, [6]University of Melbourne, Parkville, Vic., Australia, [7]Royal Melbourne Hospital, Parkville, Vic., Australia, [8]Australian Pregnancy Register for Women with Epilepsy and Allied Conditions, Kew, Vic., Australia

Purpose: Language and intellectual impairments are associated with prenatal exposure to sodium valproate, particularly at higher doses. The current study sought to examine the effect of valproate exposure on the development of brain structure.

Method: Participants were 16 children (aged 6–8 years old) exposed to sodium valproate in utero and 16 age-matched controls. High-resolution T1-weighted images were obtained on a Siemens 3 Tesla MRI scanner at the Murdoch Childrens Research Institute, Australia. Written consent was obtained from parents of study participants. The image analysis software, Freesurfer™, was used to obtain regional cortical thickness measurements. Neuropsychological data and prospectively collected pregnancy information were available for the valproate-exposed children.

Results: Analysis of cortical thickness revealed significantly increased thickness in the left frontal operculum and left peri-calcarine regions of valproate-exposed individuals compared to controls once data were corrected for multiple comparisons. Further analysis of thickness data showed a significant interaction between the laterality of thickness of the frontal operculum and group membership. Mean sodium valproate dose during pregnancy (group mean = 885.5 mg; SD 421.4) correlated significantly with thickness in the right but not left frontal operculum ($p < 0.05$). There was a trend-level negative correlation between verbal intellectual abilities and left frontal opercular thickness ($p = 0.1$).

Conclusion: Perturbations in neurodevelopment following prenatal exposure to anticonvulsants impact on the child's brain development. Our findings underscore data from our own and other international prospective studies that demonstrate particularly susceptibility of language skills, demonstrating for the first time regionally specific cortical changes. Valproate is known to increase apoptosis, however our data suggest that there may be abnormalities in cortical pruning. The extent to which these data reflect prenatal influences or postnatal delays in cortical refinement warrants further investigation.

011
HEALTH ECONOMICS OF PHARMACOGENETIC SCREENING FOR NEWLY DIAGNOSED EPILEPSY: ANALYSIS OF REAL-WORLD DATA

Chen Z[1], Liew D[1,2], Kwan P[1,3]
[1]Department of Medicine, University of Melbourne, Parkville, Vic., Australia, [2]Royal Melbourne Hospital, EpiCentre, Parkville, Vic., Australia, [3]Department of Neurology, Royal Melbourne Hospital, Parkville, Vic., Australia

Purpose: HLA-B*15:02 is strongly associated with carbamazepine (CBZ)-induced Stevens-Johnson syndrome (SJS) in Chinese. System-wide mandatory HLA-B*15:02 screening prior to starting CBZ has been implemented across public hospitals in Hong Kong since September 16, 2008. The study aimed to evaluate the impact of the policy on everyday clinical practice and to audit its cost-effectiveness using real-world data.

Method: 16,415 newly diagnosed epilepsy patients were identified in the 6-year study period (3 years for each pre and post-policy period). We constructed a decision tree model that took into account changes in antiepileptic drug (AED) prescription pattern, incidence of AED induced SJS, costs of AED treatments, SJS treatment and HLA-B*15:02 testing, and the quality adjusted life years (QALYs) of patients to calculate the incremental cost-effectiveness ratio (ICER) of the screening policy in 1-year treatment period.

Results: There was no CBZ-SJS (0/262) in the post-policy period compared with 9/996 (0.90%) in the pre-policy period ($p = 0.1242$). The incidence of AED-SJS overall remained unchanged [24/8,186 (0.29%) vs. 22/8,229 (0.27%), $p = 0.7549$]. Only 8% (160/1,953) of the tests performed and 45% (117/262) of CBZ prescriptions in the post-policy period were made in compliance with the policy. The screening policy had an ICER of $768,781/QALY compared with no screening. The ICER of the policy would fall below the conventional $50,000/QALY cost-effective threshold if full compliance is achieved.

Conclusion: CBZ-SJS was prevented after the mandatory HLA-B*15:02 screening policy was implemented, but the overall incidence of AED-SJS was not reduced. CBZ prescription rate was significantly lower post-policy. Poor compliance to the policy and the high testing cost led to the current screening policy being not cost-effective in newly diagnosed epilepsy patients.

012
SCHOOL AGED IQ IN CHILDREN PRENATALLY EXPOSED TO ANTIEPILEPTIC DRUGS

Baker G[1], Bromley RL[1], Rooney C[2], Calderbank R[2], Shallcross R[1], Irwin B[3], Morrow J[3], Liverpool & Manchester Neurodevelopment Group and the UK Epilepsy and Pregnancy Register
[1]University of Liverpool, Liverpool, UK, [2]Walton Centre for Neurology and Neurosurgery, Liverpool, UK, [3]Belfast Health and Social Care Trust, Belfast, UK

Purpose: To investigate IQ levels in school aged children following prenatal exposure to monotherapy levetiracetam, topiramate, gabapentin or sodium valproate.

Method: Children aged 5–9 years, were recruited from the UK Epilepsy and Pregnancy Register. Children enrolled into the register who were born to women with epilepsy who were not taking AEDs were recruited as the control group. Blinded assessments were undertaken in the child's home or school utilising the Wechsler Intelligence Scale-IV. Multiple linear regression analysis, adjusting for maternal and child demographic confounder was undertaken.

Results: Maternal IQ, socioeconomic status and child gender were significantly associated with child IQ. Exposure to monotherapy levetiracetam (n = 42), topiramate (n = 23) or gabapentin (n = 13) was not associated with reduced performance. Conversely, prenatal exposure to sodium valproate (n = 45) was associated with an 8.6 reduction in full scale IQ ($p = 0.001$), a 10.7 point reduction in verbal IQ ($p < 0.001$), and a 5.5 point reduction in speed of processing ($p = 0.038$), following the adjustment for maternal and child demographics. A dose relationship was demonstrated for sodium valproate but not levetiracetam or topiramate and child IQ. No association with maternal epilepsy type or exposure to seizures was demonstrated.

Conclusion: Levetiracetam may be preferential for the treatment of epilepsy in women in their childbearing years. Further research into topiramate and gabapentin are required to confirm findings reported here due to limited group size. Lowering the dose of sodium valproate may also reduce the risk to child IQ. Further research, with larger cohorts is required to investigate dose relationships more comprehensively.

Platform Session: Basic Science
Monday, 24th June
14:30-16:00

013
NEURO-INFLAMMTION AND MESIAL TEMPORAL LOBE EPILEPSY IN THE DEVELOPING BRAIN: FROM TOLL-LIKE RECEPTOR 4 TO INFLAMMATION RELATED MICRORNAS

omran A[1], Peng J[1], Gan N[1], Ashhab MU[1], Yin F[1], He F[1], Lifen Y[1], Kong H[1]

[1]Pediatric Neurology, Central South University, Changsha, China

Purpose: Increasing evidence indicates that neuro-inflammation plays a critical role in the pathogenesis of mesial temporal lobe epilepsy (MTLE). We aimed to investigate the dynamic expressions of Toll-like receptor 4 (TLR-4), nuclear factor kappaB (NF-kB), interleukin-1β (IL-1β), tumor necrosis factor alpha (TNF-α), miR-146a, and miR-155 in the hippocampi of an immature rat model and children with MTLE.

Method: To study the expressions of TLR-4, NF-kB, IL-1β, TNF-α, miR-146a, and miR-155, we performed a reverse transcription PCR, Western blot, EMSA, and real-time quantitative PCR on the hippocampi of immature rats at 25 days of age. Expressions were monitored in the acute, latent, and chronic stages of disease (2 h and 3 and 8 weeks after induction of lithium-pilocarpine status epilepticus, respectively), and in control hippocampal tissues corresponding to the same timeframes. Similar expression methods were applied to hippocampi obtained from children with MTLE and normal controls.

Results: The expression of TLR-4, NF-kB, IL-1β, TNF-α and miR-155 showed upregulation in the acute and chronic stages, while in the latent stage the expressions were nearly equal to the control group. MiR-146a was upregulated in the latent and chronic stage while in the acute stage it was nearly equal to the control. All markers were upregulated in children with MTLE.

Conclusion: MicroRNAs start to emerge as promising novel players in MTLE pathogenesis in the developing brains. Modulation of the signaling pathway starting from TLR-4 level to inflammation-related microRNAs may be a novel therapeutic target in MTLE treatment.

014
DOES BLOCKADE OF THE PROINFLAMMATORY IL-1b/IL-1 RECEPTOR TYPE 1 SIGNALING PREVENT OR MODIFY EPILEPTOGENESIS IN TWO DIFFERENT RAT MODELS OF EPILEPSY?

Frigerio F[1], Polascheck N[2], Noè F[1], Bankstahl M[2], Ravizza T[1], Reschke C[1], Beltrame L[1], Marchini S[1], Loescher W[2], Vezzani A[1]

[1]Mario Negri Institute for Pharmacological Research, Milan, Italy, [2]University of Veterinary Medicine Hannover & Center for Systems Neuroscience, Hannover, Germany

Purpose: IL-1b/IL-1R1 signaling is induced in brain during seizures and status epilepticus (SE)- evoked epileptogenesis. Signaling inhibition has antiictogenic effects and abrogates kindling progression in rodents. We studied the antiepileptogenic effects of specific pharmacologic signaling blockade in two models of symptomatic epilepsy.

Method: SE was induced in adult Sprague-Dawley rats either by electrical stimulation of the ventral hippocampus or intraperitoneal (ip) lithium/pilocarpine injection. A combination of anakinra (IL-1R1 antagonist) given by subcutaneous osmotic minipumps and VX-765 (IL-1b biosynthesis inhibitor) injected ip twice/day, or vehicles, was started 3 h post-SE for 4–7 days to encompass the epileptogenesis phase. VX-765 treatment was the same affording acute and chronic seizures inhibition. EEG recording (24 h/7 days) was done from SE induction until first spontaneous recurrent seizures (SRS) and for additional 2 weeks to quantify SRS in epileptic rats. Microarray analysis of gene transcription was done during epileptogenesis.

Results: Plasma and CSF anakinra levels in SE rats under treatment were comparable with those endowed of neuroprotective effects in stroke models. Cotreatment significantly reduced both the number of IL-1b-positive astrocytes during epileptogenesis and forebrain neurodegeneration in epileptic rats. Transcriptomic analysis of the hippocampus during epileptogenesis showed that cotreatment neither affected the broad inflammatory response induced by SE or modified onset, frequency and duration of SRS.

Conclusion: IL-1b/IL-1R1 signaling blockade during epileptogenesis afforded neuroprotection but was not sufficient to prevent epilepsy development. Transcriptomic analysis indicates that concomitant blockade of parallel inflammatory pathways with proictogenic properties might be required to effectively block post-injury brain inflammation and epileptogenesis.

015
LONG-TERM OUTCOMES IN MULTIPLE-HIT RAT MODEL OF SYMPTOMATIC INFANTILE SPASMS

Akman O[1], Briggs SW[1], Galanopoulou AS[1]

[1]Albert Einstein College of Medicine, Bronx, NY, USA

Purpose: Patients with infantile spasms (IS) commonly develop other types of epilepsies, often intractable. The multiple-hit rat model of IS (DLP model) from structural lesions shows age-specific expression of flexion or extension spasms, other types of early life seizures, and cognitive dysfunction. Here, we evaluated whether adult DLP rats exhibit epilepsy.

Methods: Postnatal day 3 (PN3) male Sprague-Dawley rats received right intracerebral infusions of doxorubicin and lipopolysaccharide, followed by systemic p-chlorophenylalanine (PN5). Controls consisted of

naïve rats. Six bilateral epidural electrodes were placed at PN60-90. Long-term video EEG (24-h epochs, 54.1 ± 6.2 days/rat over the span of 5 months) records were reviewed, scored, and underwent spectral analyses blinded to group assignment.

Results: Spontaneous generalized motor seizures were detected in 4/7 (57.1%) adult DLP rats, starting at PN 127.0 ± 4.5, but in none of the controls. Seizures occurred in sleep with initial background attenuation followed by rhythmic theta slowing and sharp waveforms maximal at the right side. In 2/7 (28.6%) adult DLP rats bursts of atypical spike-and-slow-wave discharges (SWDs; 5.5–6 Hz) were first seen at PN86.5 ± 0.5. In 2/9 control rats, SWDs were detected but had faster (7 Hz) frequency. Interictally, DLP rats showed excessive sleep and continuous right parietal polymorphic slowing with spikes.

Conclusion: Most adult DLP rats (71.4%) manifest epilepsy and/or atypical SWDs. The DLP model is therefore a new model to study epileptogenesis after IS and develop anti-epileptogenic treatments.

Funded by NINDS R01NS020253, NINDS R21 NS078333-01A1, Autism Speaks, Heffer Family Foundation and the Siegel Family Foundation.

016

RNAi-MEDIATED KNOCKDOWN OF NAV1.1 DISRUPTS A COGNITIVE NEURAL NETWORK

Bender AC[1], Luikart BW[2], Holmes GL[1], Scott RC[1,3], Lenck-santini P-P[1]

[1]Department of Neurology, Geisel School of Medicine at Dartmouth, Lebanon, NH, USA, [2]Department of Physiology and Neurobiology, Geisel School of Medicine at Dartmouth, Lebanon, NH, USA, [3]Institute of Child Health, University College London, London, UK

Background: Dravet syndrome (DS) is a childhood-onset epilepsy leading to severe cognitive impairment. Approximately 85% of cases of DS are linked with loss-of-function mutations in the *SCN1A* gene, coding for the type I voltage-gated sodium channel ($Na_v1.1$). However, the impact of $Na_v1.1$ deficits on cognition is not well understood.

Purpose: Here, we used an RNAi approach to investigate the direct effects of $Na_v1.1$ downregulation on a cognitive neural network in vivo.

Methods: The medial septum and diagonal band of Broca (MSDB) of adult rats was injected with either a siRNA complex or a lentivirus expressing shRNA targeted to the *Scn1a* gene, and the impact of $Na_v1.1$ downregulation on the function of the septo-hippocampal network was subsequently tested. Effects on spatial memory, hippocampal theta oscillations, and neuronal firing were assessed.

Results: We found that focal $Na_v1.1$ downregulation in the MSDB caused a spatial memory impairment on a reaction-to-novelty task. Continuous EEG monitoring revealed that this effect was not caused by seizures. Rather, the fundamental neurophysiological properties of this network were altered. Compared to controls, the regulation of hippocampal theta frequency was impaired with a reduction observed during spatial performance. Single-unit recordings of MSDB neurons in vivo further demonstrated that the firing properties of this neuronal population were substantially altered. The average peak firing frequency was reduced and the average action potential width was increased.

Conclusions: Considering the critical role of the MSDB in regulating hippocampal function, we propose that the downregulation of $Na_v1.1$ directly alters the firing of MSDB neurons, which in turn impairs the ability of the MSDB to properly regulate hippocampal theta oscillations and function. Moreover, our results to this point suggest that the loss of function of $Na_v1.1$ in Dravet syndrome may directly impact cognition through mechanisms other than seizures.

017

ABSENCE OF NEUROINFLAMMATION IN HUMAN AND EXPERIMENTAL TEMPORAL LOBE EPILESY

Aalbers MW[1], Rijkers K[2], Majoie M[2,3], de Baets M[1], Dings J[2], Schijns O[2], Hoogland G[2]

[1]Maastricht University, Maastricht, the Netherlands, [2]Maastricht University Medical Center, Maastricht, the Netherlands, [3]Epilepsy Centre Kempenhaeghe, Heeze, the Netherlands

Purpose: In recent years, inflammation has been implicated in various epilepsies, including temporal lobe epilepsy (TLE). However, it is unclear to what extent pro-inflammatory changes are caused by the underlying histopathology. Therefore we aimed to study several inflammatory markers in hippocampi from TLE patients with and without hippocampal sclerosis (HS) and in an animal model without overt neuronal cell loss, i.e. amygdala kindled rats.

Method: Sclerotic hippocampi from 19 TLE patients were compared with histologically normal cortex (available in 6 out of 19 patients) and with histologically normal hippocampi from non-HS TLE patients (n = 4). Brain tissue was analyzed for several cytokine and cytokine receptors by multiplex assay. Amygdala kindled rats were compared to sham rats that were implanted with an electrode, but not stimulated. Hippocampi were analyzed for

(i) activated astrocytes (GFAP), microglia (OX-42), and neuronal cell loss (NeuN) by immunohistochemistry (n = 5 per group);
(ii) cytokine levels by multiplex assay (n = 8 per group); and
(iii) phosphorylated NMDA-receptors by Western blot (n = 10–11 per group).

Results: In TLE patients, IL-1α and IL-1ra were significantly lower in HS than in histologically normal cortex. Kindling was associated with increased GFAP expression. We did not observe overt microglia activation or neuronal cell loss after amygdala kindling. Cytokine levels and phosphorylation of NMDA-receptor were unaltered as well.

Conclusion: These results suggest that HS does not differentially determine cytokine expression and that inflammation, and in particular upregulation of pro-inflammatory brain cytokines, is not necessarily present in epilepsy.

018

MULTI-UNIT ACTIVITY IN THE HUMAN NEOCORTEX AS A PREDICTOR OF SEIZURE ONSET

Rozman PA[1,2], Eskandar E[2,3], Madsen JR[4,5], Thesen T[6], Carlson C[6], Devinsky O[6], Kuzniecky R[6], Doyle WK[6], Ulbert I[7,8,9], Halgren E[10], Cash SS[1,2]

[1]Department of Neurology, Massachusetts General Hospital, Boston, MA, USA, [2]Harvard Medical School, MA, USA, [3]Department of Neurosurgery, Massachusetts General Hospital, Boston, MA, USA, [4]Department of Neurosurgery, Boston Children's Hospital, Boston, MA, USA, [5]Department of Neurosurgery, Brigham and Women's Hospital, Boston, MA, USA, [6]Comprehensive Epilepsy Center, New York University Medical Center, New York, MA, USA, [7]National Institute of Neuroscience, Budapest, Hungary, [8]Hungarian Academy of Sciences, Institute for Psychology, Budapest, Hungary, [9]Department of Information Technology, Péter Pázmány Catholic University, Budapest, Hungary, [10]Departments of Radiology, Neurosciences, and Psychiatry, University of California at San Diego, San Diego, CA, USA

Purpose: The need for lower-risk, more highly-targeted therapies for focal epilepsies has driven decades of research on seizure prediction. While most of these studies have relied on scalp or intracranial EEG, more recent studies have taken advantage of electrodes that capture single- or multi-unit activity. In capturing such activity, we expect to detect preictal phenomena well in advance of ictal EEG changes.

Method: Intracranial recordings were obtained using both clinical ECoG and laminar microelectrodes, which consist of 24 linearly arranged contacts that sample from layers I-VI of the neocortex. Signal power in the multi-unit band (300–5000 Hz) was calculated for 30-min preictal and interictal time windows. Data for this study was obtained from seven patients (11 electrodes) following an approved IRB protocol.

Results: Several parameters characterizing the multi-unit power were compared between preictal and interictal time windows. Parameters included total time (t) spent beyond a threshold (z SDs above or below a 180-s baseline mean) in a number of channels (n). Optimization of these parameters demonstrated that for $t \geq 90$s, $z = +3$ SDs, and $n \geq 10$ channels, we correctly characterized preictal periods with a sensitivity and specificity of 0.45 and 1.00, respectively. Furthermore, for $t \geq 150$s, $z = -3$ SDs, and $n \geq 1$ channel, we obtained a sensitivity and specificity of 0.82 and 0.71, respectively.

Conclusion: Our results demonstrate reproducible increases, and decreases, in multi-unit activity prior to seizure onset. These changes suggest that multi-unit approaches will be useful in the development of future seizure prediction systems, though this would require a continuous dataset and a refined algorithm to be translatable. Areas of active research include optimizing for both location of the electrode with respect to the seizure focus and the cortical layer in which these changes occur.

Platform Session: Neuroimaging
Monday, 24th June
14:30–16:00

019
CONCORDANCE OF EEG-fMRI BOLD RESPONSES AND MAGNETIC SOURCE IMAGING (MSI) OF EPILEPTIC SPIKES IN PATIENTS WITH FOCAL EPILEPSY

Heers M[1], *Hedrich T*[2], *An D*[1], *Gotman J*[1], *Grova C*[2], *Kobayashi E*[1]

[1]*Department of Neurology and Neurosugery, Montreal Neurological Institute, McGill University, Montreal, QC, Canada,* [2]*Department of Biomedical Engineering, McGill University, Montreal, QC, Canada*

Purpose: EEG-fMRI BOLD responses indicate hemodynamic and metabolic changes associated with spikes. Very often, BOLD activations are multifocal rather than circumscribed. Due to the time course of the hemodynamic response function, they might reflect generation, propagation and distant effect of spikes in the brain. In contrast, MSI can depict the time course of generators of spikes along the cortical surface with high temporal resolution. We aimed to evaluate, whether MSI can provide better understanding of the significance of different BOLD responses to similar spikes.

Method: Twenty-two focal epilepsy patients underwent EEG-fMRI and MEG recordings. Ten were excluded due to absence of spikes or BOLD responses. Twelve patients had similar spikes in EEG-fMRI and in MEG, with significant BOLD activations. For fMRI, marked spikes defined an event-related paradigm analyzed within a GLM: resulting t-maps thresholded at $t > 3.1$, cluster: min 5 voxel, $p < 0.05$ corrected. MSI on averaged spikes was performed using the maximum entropy on the mean source model. MSI results at the peak of the averaged spike were visually compared with main BOLD activations. Six patients had their focus defined by invasive recordings.

Results: MSI main sources and main BOLD activations were: MSI within one cluster ($n = 1$), highly concordant/coincident ($n = 5$), regionally concordant and adjacent ($n = 4$) or discordant ($n = 2$). In 4/6 patients, the findings were concordant with intracranial EEG.

Conclusion: MSI and EEG-fMRI results frequently overlap, reinforcing the confidence we have in both. With high temporal resolution, MSI helps interpreting EEG-fMRI, even in patients with multiple or extensive BOLD activations.

Funding: AES, CIHR, CECR, FRSQ, Savoy Foundation.

020
A NEW DATA-DRIVEN METHOD DETECTS WHOLE-BRAIN FUNCTIONAL CONNECTIVITY DIFFERENCES IN IDIOPATHIC GENERALIZED EPILEPSY

Maneshi M[1], *Vahdat S*[2], *Grova C*[1,3], *Gotman J*[1]

[1]*McGill University, Montreal Neurological Institute and Hospital, Montreal, QC, Canada,* [2]*Functional Neuroimaging Unit, Centre de Recherche de l'Institut Universitaire de Gériatrie de Montréal, Montreal, QC, Canada,* [3]*Biomedical Engineering Department, McGill University, Montreal, QC, Canada*

Purpose: Previously we found differences in frontal brain resting-state connections of idiopathic generalized epilepsy (IGE) using seed-based functional connectivity (FC) [Maneshi et al. *PLoS ONE* 2012]. Recently, we proposed a new data-driven method (shared and specific independent component analysis, SSICA) which systematically extracts and classifies differences in brain networks between groups [Vahdat et al. *Neural Computation* 2012]. Here we applied the SSICA on the same IGE/control dataset to investigate whole-brain connectivity differences.

Method: Fourteen controls and 14 IGE patients were scanned (3T scanner, 24 min of resting-state functional MRI). In patients, only data from wakefulness without epileptic discharges were included. Regular preprocessing was performed to remove cardiac and respiratory artifacts. The aggregated data of both groups were then fed to the SSICA algorithm allowing up to three specific components to be extracted for each group (total number of extracted shared and specific components = 30).

Results: The SSICA classified 27 networks as shared between groups and 3 as specific to the IGE patients. Among these 3 networks, only the one including bilateral precentral gyrus showed significantly higher FC in patients compared to controls, between this area and the rest of the network (FC measured by correlation, $p = 0.0002$).

Conclusion: Using the SSICA, IGE patients are found to have a specific network which shows significantly higher FC between its frontal part and the rest of the network. This result is consistent with our previous main finding using seed-based analysis which showed elevated FC with frontal areas in IGE patients.

021
FUNCTIONAL NEUROIMAGING FEATURES DIFFERENTIATE MESIO-NEOCORTICAL TEMPORAL LOBE EPILEPSY FROM NEOCORTICAL TEMPORAL LOBE EPILEPSY

Joo EY[1,2], *Seo DW*[2], *Hong SC*[3], *Hong SB*[2]

[1]*Feinberg School of Medicine, Neurology,Northwestern University, Chicago, IL, USA,* [2]*Department of Neurology,*

Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, [3]Department of Neurosurgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Purpose: The differentiation of temporal lobe epilepsy combined mesial and neocortical temporal onset of seizures (mesio-neocortical TLE, MNTLE) from neocortical TLE (NTLE) or mesial TLE is critical to achieve good surgical outcomes. Numerous studies had investigated it usng intracranial electroencephalography (iEEG), but its differentiation based on neuroimaging features had not been performed yet.

Methods: Eighty-eight TLE patients were enrolled who underwent iEEG and were classified into MNTLE (n = 35) and NTLE (n = 53), which were confirmed by epilepsy surgery according to the site of ictal-onset rhythms on iEEG. Their postsurgical seizure and memory outcomes were evaluated.

Results: The overall mean seizure-free rate was 73.8% (mean follow-up = 9.7; range, 2–16 years). Functional neuroimaging findings showed that MNTLE patients higher frequencies of interictal glucose hypometabolism in FDG-PET and localized ictal hyperperfusion in ipsilateral temporal lobe in ECD-SPECT compared to NTLE patients. MNTLE patients had more frequent auras and less generalized seizures, but other features (demographics, scalp EEG, MRI abnormalities, Wada asymmetry) were not different from NTLE. The postsurgical seizure-free rates were excellent, not different (Engel class I, 74.3% in MNTLE and 73.6% in NTLE). Postsurgical memory outcome was good in MNTLE patients despite sufficient resection of the mesial temporal area.

Conclusion: Functional neuroimaging studies may be superior diagnostic tools for differentiating MNTLE from NTLE than brain MRI. It would be better to evaluate lateral temporal area in the suggestion of involving neocortical area by functional neuroimagings although structural lesions were confined to medial temporal area in temporal lobe epilepsy.

022
PRESURGICAL DIAGNOSIS OF THE EPILEPTOGENIC FOCUS USING NEAR-INFRARED SPECTROSCOPY MAPPING

Watanabe E[1], Yokota H[1], Oguro K[1], Edison E[1], Dan I[1]
[1]Department of Neurosurgery, Jichi Medical Univerisity, Tochigi, Japan

Purpose: Near infrared spectroscopy (NIRS) is a recently developed technique for hemodynamic studies that is particularly suitable for use during epileptic seizures. It uses the specific absorption properties of living brain tissues in the near infrared range to measure changes in the concentrations of hemoglobin. We previously showed the feasibility of focus diagnosis with NIRS mapping during drug induced seizures (Watanabe 2002. The purpose of present study is to investigate the NIRS focus diagnosis during habitual seizures.

Method: We used 48-channel NIRS system (Hitachi, Japan). Thirty seven cases with drug resistant epilepsy (21 temporal, 16 neocortical) admitted for the presurgical evaluation of epilepsy surgery were enrolled in this study. Ictal recording using NIRS has been applied simultaneously with long term scalp video-EEG monitoring. Inter-ictal IMZ SPECT and FDG-PET.

Results: Ictal NIRS showed increase of regional blood flow in the focus area or focus hemisphere in the initial phase of seizures. We utilized this phenomenon to identify the focus localization. Ictal NIRS diagnosed laterality of the epileptogenic focus correctly in 80% of patients which was superior to IMZ SPECT (47.8%) and FDG PET (50%). These results were much more prominent in patients with neocortical epilepsy, as ictal NIRS diagnosed laterality of the epileptogenic focus correctly in all patients (100%) while IMZ SPECT was 50%, and FDG PET was 33.3%. In temporal lobe epilepsy, ictal NIRS has been shown also to be superior to IMZ SPECT and FDG PET in the diagnosis of laterality of the epileptogenic focus in patients with normal MRI results (non-lesional epilepsy), as they were 100%, 44.4% and 40% respectively.

Conclusions: These results augment our previous results that ictal NIRS is a valuable and reliable method to diagnose laterality and location of the epileptogenic focus especially in patients with neocortical epilepsy and patients with non-lesional temporal lobe epilepsy.

023
HIGH RESOLUTION TEMPORAL IMAGING AND HIGH DENSITY EEG IMPROVES EEG-fMRI IN FOCAL EPILEPSY

Jäger V[1], Dümpelmann M[2], Le Van P[3], Georgia R[2], Schulze-Bonhage A[2], Jürgen H[3], Jacobs J[1]
[1]Neuropediatrics and Muscular Disease, University Medical Center Freiburg, Freiburg, Germany, [2]Department of Epileptology, University Medical Center Freiburg, Freiburg, Germany, [3]Section of Medical Physics, University Medical Center Freiburg, Freiburg, Germany

Purpose: Simultaneous EEG-fMRI is used to localize BOLD changes following epileptic spikes. Previous studies in focal epilepsies showed that BOLD change can be widespread and unspecific. We could recently show that a fast fMRI sequence called MREG outperformed classical EEG-fMRI in sensitivity and specificity. Using MREG the present study investigates the influence of different spike topographies on BOLD responses.

Method: Patients underwent EEG-MREG (3T, TR = 0.1s, 3 mm voxels) using a 64-channel cap. Spike voltage maps were generated considering 32 or all 64 channels. Spike extent (defined as number of channels showing >50% of the maximum spike amplitude) and inter-spike variability were correlated with the location and extent of BOLD.

Results: Seventeen patients with 25 distinct spike types were analyzed. In 16/25 the concordance between focal BOLD and EEG maps was more accurate for the 64-channel than the 32-channel-EEG. The spike extent on EEG was significantly correlated with the BOLD activation volume ($p = 0.03$) and the number activated clusters ($p = 0.04$). Spike types with concordant BOLD responses had significantly lower interspike-variability than those without concordant responses ($p = 0.01$).

Conclusion: Classical EEG-fMRI sequences several averaged spikes for analysis, while MREG single spike analysis is possible due to increased statistical power. Our study suggests that a high variability of spike fields may interfere with fMRI results. Therefore single spike analysis may be promising to reduce unspecific BOLD responses. Moreover higher density EEG facilitates the interpretation of resulting BOLD responses and the extent of the latter is directly dependent on the spread of spikes in the EEG.

024
SUBREGIONAL MESIOTEMPORAL PATTERNS OF DISEASE PROGRESSION IN TEMPORAL LOBE EPILEPSY

Bernhardt BC[1,2], Kim H[1], Bernasconi A[1], Bernasconi N[1]
[1]Neuroimaging of Epilepsy Laboratory, Montreal Neurological Institute and Hospital, McGill University, Brain Imaging Center, Montreal, Canada, [2]Department of Social Neurosciences, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

Purpose: In drug-resistant temporal lobe epilepsy (TLE), multiple cross-sectional MRI studies have shown an association between longer

disease duration and decreased mesiotemporal volumes ipsilateral to the seizure focus. A previous study tracking atrophy longitudinally was limited to the hippocampus. Here, we mapped subregional trajectories of progressive hippocampal, entorhinal, and amygdalar atrophy using cross-sectional and longitudinal designs. Furthermore, we assessed the relation between progressive atrophy and post-surgical seizure outcome.

Method: We studied 134 patients with unilateral drug-resistant TLE and 47 controls. To map subregional patterns of atrophy, we generated spherical harmonic shape descriptions of manual mesiotemporal segmentations. A subset of 31 patients had repeated MRI (mean interval of 2.5 years). Ninety patients underwent surgery, including 16 with repeated scans. We assessed effects of disease duration on mesiotemporal volumes using linear models and fitted linear mixed-effects models testing for a negative effect of time from baseline scan.

Results: Cross-sectional and longitudinal analysis showed progressive atrophy in hippocampal CA1, anterolateral entorhinal, and amygdalar laterobasal group bilaterally. These regions also exhibited more marked age-related volume loss in patients compared to controls. Furthermore, we found increased rates of entorhinal cortex atrophy contralateral to the seizure focus in patients with residual seizures relative to those who became seizure free after surgery.

Conclusion: Convergent longitudinal and cross-sectional patterns of subregional mesiotemporal atrophy emphasize the progressive nature of TLE and highlight the importance of early surgery. The adverse impact of progressive entorhinal cortex pathology on post-surgical outcome underlines the key role of this structure within the epileptogenic network.

Platform Session: Social Issues
Monday, 24th June
14:30–16:00

025
MEDICAL SELF-REPORTING TO TRANSPORTATION AUTHORITIES REMAINS LOW AFTER SPECIALIST COUNSELLING FOR FIRST SEIZURE PATIENTS

Siddiqi M[1], Jirsch J[2]

[1]Department of Neurology, University of Alberta Hospital, Edmonton, AB, Canada, [2]Department of Medicine/Neurology, University of Alberta/Stollery Children's Hospital, Edmonton, AB, Canada

Purpose: To study the driving and reporting practices at a First Seizure Clinic (FSC) in a self-reporting province.

Method: A prospective cohort study has been conducted at a FSC at the University of Alberta Hospital in which patients are seen within 2 weeks of the referral date. Patients seen over the course of 1 year with valid drivers′ licences were included in the study. A questionnaire regarding driving and reporting practices was administered by the clinic nurse at the beginning of the initial as well as follow-up visits. We also reviewed ER/primary care physicians' notes from the time of the original referral to our clinic.

Results: Fifty nine patients were included in the study. Twenty five (42.3%) had first unprovoked seizures, 7(11.9%) seizures related to alcohol/illicit drug use, 17/59(28.9%) syncope, 3/59(5.1%) provoked seizures, 6/59(10.2%) recurrent/ breakthrough seizures and 1/59 (1.7%) loss of consciousness related to concussion. At the initial FSC visit 18/59(30.5%) were still driving. Two/59(3.4%) patients had reported themselves to the Ministry of Transportation (MOT) before visiting the FSC, and 4/59(6.8%) had been told prior to visiting the FSC that they needed to notify the MOT. Among 24 patients seen in follow-up, 2/24(8.3%) were still driving, and 12/24(50%) remained unreported.

Conclusion: In this self-reporting jurisdiction, patients with seizures are very seldom advised by referring primary care physicians to report themselves to Transportation authorities prior to a FSC consultation and many are still driving. While the great majority of at-risk patients seen at FSC follow-up are reportedly not driving, approximately half have not reported themselves despite counselling. A FSC provides timely counselling regarding driving laws and fitness, but does not necessarily result in high rates of adherence to medical self-reporting laws among patients.

026
MARITAL ADJUSTMENT FOR EPILEPSY PATIENTS IN CHINA

Chen J[1], Zhang Y[2], Hong Z[2], Sander JW[3,4], Zhou D[5]

[1]Neurology Department, West China Hospital, Sichuan University, Chengdu, China, [2]West China Hospital, Sichuan University, Chengdu, China, [3]SEIN-Epilepsy Institute in the Netherlands Foundation, Heemstede, the Netherlands, [4]Department of Clinical and Experimental Epilepsy, UCL Institute of Neurology, London, UK, [5]Department of Neurology, West China Hospital, Sichuan University, Chengdu, China

Purpose: Marriage is a major source of social support and a predictor of health; however, marriages that involve people with epilepsy are more likely to fail. However, little is known about the effects of epilepsy on marital adjustment and marriage quality or the epilepsy-related factors associated with marital adjustment. Thus, we conducted a cross-sectional study comparing the marital adjustment of PWEs with that of healthy controls and explored the factors associated with this adjustment.

Method: We compared the marital adjustment of epilepsy patients to control subjects using dyadic adjustment scales (DAS) and performed correlation analysis with the disease, psycho-social factors that might associated with DAS.

Results: A total of 136 married persons with epilepsy (PWEs) and 145 healthy control subjects were recruited. The DAS score was significantly lower in people with active epilepsy than in the controls (102.0 ± 17.8 vs. 109.2 ± 15.8, $p < 0.001$). A stepwise multiple regression suggested that the duration of epilepsy, depression scores and support satisfaction scores predicted 38.2% of the variance in marital adjustment.

Conclusion: This suggests that people with active epilepsy in our sample encountered more marital discord than controls. Early remission of seizures, support intervention and control of depression may be important factors for the marital adjustment of PWEs.

027
STIGMA IN EPILEPSY – AN INTERNATIONAL PERSPECTIVE

Jette N[1,2,3], Ali A[4], Austin JK[5], Birbeck GL[6,7], de Boer H[8], Braga P[9], Cross JH[10], Dua T[11], Fernandes PT[12], Lorenzetti DL[1], Mifsud J[13], Moshe S[14], Parko K[15], Tripathi M[16], Vautour M[1], Wiebe S[2,3,17], Jacoby A[18]

[1]Department of Clinical Neurosciences, University of Calgary, Calgary, AB, Canada, [2]Hotchkiss Brain Institute, Calgary, QC, Canada, [3]Institute of Public Health, Calgary, QC, Canada, [4]Kingston Public Hospital and University of the West Indies, Kingston, Jamaica, [5]Indiana University School of Nursing,

Indianapolis, IN, USA, [6]Epilepsy Care Team, Chikanta Hospital, Mazabuka, Zambia, [7]International Neurologic & Psychiatric Epidemiology Program, Michigan State University, East Lansing, MI, USA, [8]Stichting Epilepsie Instellingen Nederland, Heemstede, Netherlands, [9]Institute of Neurology, Montevideo, Uruguay, [10]University College London, London, UK, [11]Department of Mental Health and Substance Abuse, World Health Organization, Geneva, Switzerland, [12]UNICAMP – State University of Campinas, Campinas, Brazil, [13]Department of Clinical Pharmacology and Therapeutics, University of Malta, Msida, Malta, [14]Albert Einstein College of Medicine, Bronx, NY, USA, [15]University of California at San Francisco, San Francisco, CA, USA, [16]All India Institute of Medical Sciences, Delhi, India, [17]Department of Clinical Neurosciences, University of Calgary, Calgary, AB, Canada, [18]Department of Public Health & Policy, University of Liverpool, Liverpool, UK

Purpose: The Stigma in Epilepsy Task Force (n = 15 international members) was created (2010) by the ILAE North American Commission. Its first objective was to carry out an extensive review of the international literature addressing the following topics:
(1) Available tools to measure stigma;
(2) Frequency and nature of stigma;
(3) Factors associated with stigma;
(4) Interventions to reduce stigma.

Method: A comprehensive literature search (1985–2010) was performed in 11 electronic databases (e.g. Medline, Embase) using a broad search strategy developed with guidance from a systematic review expert librarian, to identify papers relating to stigma in people with epilepsy (PWE). Two independent reviewers screened abstracts, reviewed full text articles and extracted data. Included articles were also hand searched for additional references. There were no language exclusions. Basic descriptive statistics were used to report the findings.

Results: The search identified 4,123 abstracts, of which 824 articles were selected for full text review and 287 studies met all eligibility criteria for data abstraction: n = 36 for measurement tools, n = 243 for frequency/nature of stigma, n = 191 for factors associated with stigma and n = 29 addressing interventions for epilepsy-related stigma. Findings in each area will be presented, and gaps in current research will be highlighted.

Conclusion: Although some studies demonstrated a decline in enacted stigma over time, there are numerous studies confirming that stigma is still a major challenge for PWE. The findings from this study will help guide priorities in the area of epilepsy-related stigma research and interventions.

028
LONG-TERM DISCONTINUATION RATES IN AN EXTENSION STUDY OF THE AMPA RECEPTOR ANTAGONIST PERAMPANEL AS AN ADJUNCTIVE TREATMENT FOR REFRACTORY PARTIAL SEIZURES

Zhu J[1], Yang H[1], Squillacote D[2], Laurenza A[1], Satlin A[1], Kramer LD[1]
[1]Eisai Neuroscience Product Creation Unit, Woodcliff Lake, NJ, USA, [2]Eisai Global Medical Affairs, Woodcliff Lake, NJ, USA

Purpose: To examine long-term retention rates and reasons for discontinuation in patients receiving perampanel.

Methods: Patients completing Phase III studies entered an extension of ≤256 weeks (study 307; dose titrated to individual maximum tolerated dose; ≤12 mg/day). Discontinuation rates and reasons for discontinuation were analyzed using data after 24 weeks of treatment and over five 3-month time intervals: >24–36, >36–48, >48–60, >60–72, >72 weeks. Discontinuation rates for each time interval were calculated using the number of patients who remained in the study at the start of that interval.

Results: One thousand and six patients received >24 weeks of treatment. Mean dose was 10.6 mg; most patients (77.6%) were on 10 or 12 mg at the time of data cut-off (Dec 2010).

Of 227 (22.6%) patients who discontinued treatment after 24 weeks, the most common reasons were patient choice, inadequate therapeutic effect, and adverse events (AEs). Total discontinuation rates declined over consecutive time intervals, from 7.9% at >24–36 weeks to 2.0% at >72 weeks; there was a similar decline in rates of discontinuation due to AEs, from 2.6% at >24–36 weeks to 0.8% at >72 weeks.

The overall discontinuation rate at higher doses (10–12 mg) was 19.7%. At 8 mg or lower, discontinuations tended to occur earlier.

Conclusions: This pattern of discontinuations suggests that in this refractory population, patients who could titrate to higher doses tended to stay on those doses, whereas intolerant patients tended to discontinue earlier and at lower doses for one or more of the three reasons above.

Support: Eisai Inc.

029
PARENTAL EXPERIENCES DURING THE PERI-DIAGNOSTIC PERIOD IN EPILEPSY: A CRY FOR HELP

Ramachandran Nair R[1], Jack SM[1]
[1]McMaster University, Hamilton, ON, Canada

Purpose: To understand the range of parental experiences before and during the diagnosis of epilepsy in their children.

Methods: Descriptive and exploratory qualitative study.

Stratified purposeful sample: Parents (i) of children with moderate-severe (ii) of children with mild, and (iii) of children with new onset epilepsy. *Focus group interviews* were conducted using a semi-structured interview guide. Textual analysis using ethnographic software used principles of *directed content analysis*. Codes were subsequently collapsed into broader categories.

Results: 36 parents (21 mothers and 15 fathers) participated. Participants recounted observing symptoms and then seeking answers on the *internet.* The long assessment process was a period of frustration. They were frequently told 'we don't know'. There was a significant sense of relief once they were provided with a diagnosis. Experiences were enhanced they were referred to a tertiary care center. Mothers disclosed, after the diagnosis of epilepsy, a significant number of *mental health issues*: depression, anxiety, fear, exhaustion. Fathers expressed feelings of worry, anger, and concern for spouse and family. Parents expressed a high degree of *concern/worry that their child would die*. This lead them to be highly vigilant of their children. There was a particular fear that the child would have a seizure while sleeping and die at night; as a coping strategy the majority of parents disclosed that the child slept in their bed. A small number of parents disclosed adopting different technologies to take over the *nightly monitor routine* (e.g. therapy dog, monitors).

Conclusion: Parents experience significant stress and anxiety before and around the time of diagnosis of epilepsy. These were related to long waiting period, uncertainty regarding the diagnosis, own mental health issues and fear of the risk of death in epilepsy. Further studies looking at interventions to improve parental experiences in new onset epilepsy is worth considering.

030

THE RELATIONSHIP BETWEEN ADVERSE EVENT BURDEN AND QUALITY OF LIFE IN PATIENTS WITH EPILEPSY IN A COMMUNITY

Al Faqih SS[1]
[1]*National Hosp, Swaida, Syria*

Purpose: To describe the relationship between seizure frequency, patient reported quality of life, and adverse event burden in an outpatient neurology setting.

Background: Quality of life (QoL) in epilepsy is affected by many factors. A recent study in a tertiary care population indicated a lack of correlation between patient reported QoL and seizure control. However, the study did indicate a strong correlation between QoL and patient reported adverse event burden.

Design and methods: Patients age 16 years or older from community neurology practices were recruited to participate in an open-label study of adjunctive lamotrigine if their current antiepileptic drug therapy was inadequate. Patients completed baseline evaluations of QoL and adverse event burden. The Quality of Life in Epilepsy (QOLIE-31) provides scores ranging from zero to 100, with a higher score indicating better quality of life. The Adverse Event Profile (AEP) provides scores ranging from 19 to 76, with a higher score indicating greater AE burden. Correlation analysis was performed between baseline seizure frequency and total score on QOLIE-31 and between QOLIE-31 and AEP total scores.

Results: Five hundred forty-five (545) patients (58% female) completed the baseline assessments. Mean seizure frequency at baseline was 7.6 ± 24 per month. Mean baseline QOLIE-31 total score was 53.1 and mean baseline AEP score was 42.6. Spearman correlation analysis showed no relationship between baseline seizure frequency and QOLIE-31 total score, $r = -0.2$. However, a significant relationship was noted between QOLIE-31 and AEP, $r = -0.67$, $p = 0.0001$.

Conclusions: These data from the community neurology setting confirm the relationship between AE burden and QoL previously reported at a tertiary care center. Systematic screening for antiepileptic drug side effects using a reliable and valid instrument may be an important factor in determining the overall quality of life in patients with epilepsy.

Platform Session: Genetics
Monday, 24th June
14:30–16:00

031

MUTATIONS IN DEPDC5: A MAJOR CAUSE OF FAMILIAL FOCAL EPILEPSY

Dibbens LM[1], *de Vries B*[2], *Donatello S*[3], *Heron SE*[1], *Hodgson BL*[1], *Chintawar S*[3], *Crompton DE*[4], *Hughes JN*[5], *Bellows ST*[4], *Klein KM*[6], *Callenbach PM*[7], *Corbett MA*[8], *Gardner AE*[8], *Kivity S*[9], *Iona X*[1], *Regan BM*[4], *Weller CM*[2], *Crimmins D*[10], *O'Brien T*[11], *Guerrero-López R*[12], *Mulley JC*[5], *Dubeau F*[13], *Licchetta L*[14], *Bisulli F*[14], *Cossette P*[15], *Thomas PQ*[5], *Gecz J*[8], *Serratosa J*[12], *Brouwer OF*[7], *Andermann F*[13], *Andermann E*[13], *van den Maagdenberg AM*[2], *Pandolfo M*[3], *Berkovic SF*[4], *Scheffer IE*[4]
[1]*Epilepsy Research Program, School of Pharmacy and Medical Sciences, University of South Australia, Adelaide, SA, Australia,* [2]*Department of Human Genetics, Leiden University Medical Centre, Leiden, The Netherlands,* [3]*Laboratory of Experimental Neurology, Université Libre de Bruxelles, Brussels, Belgium,* [4]*Epilepsy Research Centre, Department of Medicine, University of Melbourne, Melbourne, Vic., Australia,* [5]*School of Molecular and Biomedical Science, University of Adelaide, Adelaide, SA, Australia,* [6]*Epilepsy Center Hessen, Department of Neurology, University Hospitals Giessen & Marburg, Campus Marburg, Philipps-University Marburg, Marburg, Germany,* [7]*Department of Neurology, University Medical Centre Groningen, University of Groningen, Groningen, The Netherlands,* [8]*Neurogenetics Program, University of Adelaide, Adelaide, SA, Australia,* [9]*Schneider Children's Medical Center of Israel, Petach Tikvah, Israel,* [10]*Central Coast Area Health Authority, Gosford, NSW, Australia,* [11]*Departments of Medicine and Neurology, The Royal Melbourne Hospital, The University of Melbourne, Melbourne, Vic., Australia,* [12]*Epilepsy Unit, Hospital Universitario Fundación Jiménez Diaz and CIBERER, Madrid, Spain,* [13]*Montreal Neurological Institute, McGill University, Montréal, QC, Canada,* [14]*IRCCS, Istituto di Scienze Neurologiche, University of Bologna, Bologna, Italy,* [15]*CHUM Research Center, University of Montreal, Montreal, QC, Canada*

Purpose: The majority of epilepsies are focal in origin. The disorder Familial Focal Epilepsy with Variable Foci (FFEVF) is remarkable since family members have seizures originating from different cortical regions. FFEVF shows autosomal dominant inheritance in large pedigrees. We set out to identify the causative gene and to determine if it contributes more broadly to familial focal epilepsies. We have begun to characterize the DEPDC5 gene.

Method: To idenitfy the gene for FFEVF we used a strategy of genome wide linkage analysis followed by exome sequencing in two families, one Australian and one Dutch, which mapped to Chromosome 22q12. Follow-up mutation analyses of cases of focal epilepsy from smaller families were performed using high resolution melt curve analysis with verification of putative mutations by Sanger sequencing. Expression analyses of DEPDC5 were carried out using RT-PCR and antibody stainings on human and mouse tissues.

Results: We detected DEPDC5 mutations in the two families and subsequently in 5/6 published large families with FFEVF. The analysis of smaller families with focal epilepsy, which were too small for a conventional clinical diagnosis, revealed DEPDC5 mutations in approximately 12% (10/82) families. One de novo mutation in DEPDC5 was also found. DEPDC5 is localized in neurons in humans and in mouse.

Conclusion: Mutations in DEPDC5 account for approximately 12% of cases of non-lesional familial focal epilepsy, becoming the most common known cause of familial focal epilepsy and revealing a new gene pathway in epilepsy. The detection of a de novo mutation indicates that DEPDC5 contributes to sporadic cases of focal epilepsy, as well as to familial cases. Detection of a mutation will aid in patient diagnosis and prognosis. Shared homology with G protein signalling molecules and its localization suggest a role of DEPDC5 in neuronal signal transduction.

032

IDENTIFICATION OF A NEW CAUSAL GENE FOR AUTOSOMAL DOMINANT FOCAL EPILEPSIES

Ishida S[1], *Picard F*[2], *Rudolf G*[3], *Thomas P*[4], *Genton P*[5], *Marescaux C*[6], *Baulac M*[1], *Hirsch E*[6], *Leguern E*[7], *Baulac S*[1]
[1]*ICM, Pitié-Salpetriere Hospital, Paris, France,* [2]*Hôpitaux Universitaires de Genève, Service de Neurologie, Genève, Switzerland,* [3]*Strasbourg University Hospital, Neurology*

Department, Strasbourg, France, [4]Hôpital Pasteur, Service de Neurologie, Nice, France, [5]Centre Saint Paul, Marseille, France, [6]Strasbourg University Hospital, Strasbourg, France, [7]ICM-Pitié-Salpetriere Hospital, Paris, France

Purpose: The main familial focal epilepsies are autosomal-dominant nocturnal frontal lobe epilepsy (ADNFLE), familial mesial temporal lobe epilepsy (FMTLE), familial lateral TLE (FLTLE), and familial focal epilepsy with variable foci (FFEVF). We aimed to identify a new gene in a family with FMTLE.

Method: We performed linkage analysis using a high-density genome-wide scan with 10,000 SNPs followed by exome sequencing in a large family with FMTLE. A cohort of 15 families with focal epilepsies was subsequently analyzed.

Results: A frameshift mutation in a new gene was identified in the FMTLE family. This ancient eukaryotic gene encodes a protein of unknown function.

Subsequent screening of 15 additional families revealed four nonsense mutations and one missense mutation in five families. All mutations were shown to fully segregate within the families. We demonstrated that one nonsense mutation specifically leads to mRNA degradation by nonsense mediated decay system (NMD). The three additional nonsense mutations were predicted to be degraded by the NMD. Mutations were found in families with different phenotypes: ADNFLE, FMLTE and FFEVF.

Conclusion: We report a new gene with frequent loss-of-function mutations (37%) within a broad spectrum of familial focal epilepsies. The implication of this gene will open new avenues for research.

033
DEFECTIVE MICROTUBULE ORGANIZATION DUE TO NOVEL *EFHC1* MUTATIONS LINKED TO JUVENILE MYOCLONIC EPILEPSY

Praveen K Raju P[1], Satishchandra P[2], Radhakrishnan K[3], Anand A[1]

[1]Molecular Biology and Genetics Unit, Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore, India, [2]Department of Neurology, National Institute of Mental Health and Neurosciences, Bangalore, India, [3]Department of Neurology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, India

Purpose: Juvenile myoclonic epilepsy (JME) is clinically well-defined generalized epilepsy characterized by the major seizure types; early morning myoclonic jerks and generalized tonic clonic seizures. Previous studies have identified *EFHC1* (6p12) as a JME-causing gene, in a few Mexican families (Suzuki et al. *Nat Genet* 2004). *EFHC1* encodes a protein called myoclonin1 known to play a role in cell cycle, neuronal migration and apoptosis by interacting with microtubules. EFHC1 loss-of-function interferes with the organization of the mitotic spindle and arrests cell cycle in cortical neurons (de Nijs et al. *Nat Neurosci* 2009). This study was aimed to study if in a geographically and ethnically different Indian population, *EFHC1* is associated with JME.

Method: We have examined the *EFHC1* in 480 JME patients and 200 ethnically matched controls. Functional correlates of the mutations were studied using immunolocalization studies.

Results: Eleven previously unknown rare missense mutations (H89R, E322K, Y355C, R372W, K378E, R436C, Y485H, N519S, V556L, I619S and Y631C) were identified in this study. These mutations account for 5% of the JME cases examined. Six of the mutations identified are clustered in the conserved functional domain of EFHC1. *In vitro* functional consequences of the EFHC1 mutations suggest microtubule abnormalities, spindle pole defects during cell division.

Conclusion: These findings provide further evidence for the role of this gene in causation of JME. The EFHC1 mutant proteins were found to induce mitotic defects *in vitro* indicating that abnormal cell division and cell migration during cortical development might play role in epileptogenesis.

034
IDENTIFICATION OF A FIRST AND MAJOR GENE FOR ACQUIRED EPILEPTIC APHASIA (LANDAU-KLEFFNER SYNDROME) AND RELATED CHILDHOOD FOCAL EPILEPSIES AND ENCEPHALOPATHIES WITH SPEECH AND LANGUAGE DYSFUNCTION

Lesca G[1], Rudolf G[2], Bruneau N[3], Lozovaya N[3], Labalme A[1], Boutry-Kryza N[1], Salmi M[3], Tsintsadze T[3], Addis L[4], Motte J[5], Wright S[6], Tsintsadze V[3], Michel A[7], Doummar D[8], Lascelles K[9], Strug L[10], Waters P[6], de Bellescize J[11], Vrielynck P[12], de Saint Martin A[13], Ville D[14], Ryvlin P[11], Arzimanoglou A[11], Hirsch E[2], Vincent A[6], Pal D[4], Burnashev N[3], Sanlaville D[1], Szepetowski P[3]

[1]INSERM/Lyon University Hospital, Claude Bernard Lyon I University, CRNL, Lyon, France, [2]Department of Neurology, Strasbourg University Hospital, Strasbourg University, Strasbourg, France, [3]INSERM/Aix-Marseille University, INMED, Marseille, France, [4]Department of Clinical Neurosciences, King's College London, London, UK, [5]Reims University Hospital, American Memorial Hospital, Reims, France, [6]Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK, [7]Department of Neurology, CHRU Pontchaillou, Rennes, France, [8]Department of Neuropediatrics, Armand-Trousseau Hospital, Paris, France, [9]Department of Paediatric Neurology, Evelina Children's Hospital, London, United Kingdom, [10]The Hospital for Sick Children Research Institute, University of Toronto, Toronto, ON, Canada, [11]Epilepsy, Sleep and Pediatric Neurophysiology Department, University Hospitals of Lyon, Lyon, France, [12]William Lennox Neurology Centre, Université Catholique de Louvain, Ottignies, Belgium, [13]Pediatric Department I, Strasbourg University Hospital, Strasbourg, France, [14]Department of Neuropediatrics, University Hospitals of Lyon, Lyon, France

Purpose: Acquired epileptic aphasia (Landau-Kleffner syndrome) and the continuous spike and waves during slow-wave sleep syndrome (CSWSS) represent rare and closely related childhood focal epileptic encephalopathies (EEs). They show electroclinical overlaps with Rolandic epilepsy (RE) and can be viewed as different clinical expressions of a single pathological entity situated at the crossroads between epileptic, speech, language, cognitive and behavioral disorders. LKS and CSWSS are of unknown aetiology; a role for autoimmunity and for genetic influence has long been speculated. In this study we aimed at testing the genetic hypothesis by identifying possible genetic cause(s) for LKS and CSWSS.

Method: Genetic screening followed by the appropriate validation experiments and the subsequent functional analyzes were employed.

Results: We demonstrate that about 20% of LKS, CSWSS, and electroclinically atypical RE often associated with speech impairment (verbal dyspraxia, dysphasia), can have a simple genetic origin sustained by de novo or inherited mutations in a single gene. The 18 different mutations occurred in sporadic or in familial cases, and were of various types (three

microdeletions, one splice-site, one nonsense and 13 missense mutations). They were distributed along the different domains of the corresponding protein. The two missense mutations that were analyzed further, had electrophysiological consequences *in vitro*.

Conclusion: After more than 50 years of debate on the elusive cause of LKS and CSWSS, the identification of a first and major gene for this EE spectrum provides crucial insights into the underlying pathophysiology and opens promising avenues towards the possible design of preventive therapeutic strategies.

035
EFFICIENT GENETIC DIAGNOSTIC TESTING OF PATIENTS WITH EPILEPTIC DISORDERS USING PANEL-BASED NEXT GENERATION SEQUENCING

Russ AC[1], Steiner I[1], Döcker M[1], Riesch E[1], Jüngling J[1], Scheurenbrand T[1], Sprecher A[1], Hörtnagel K[1], Lemke JR[2], Biskup S[1]

[1]CeGaT GmbH, Tübingen, Germany, [2]Division of Human Genetics, University Children's Hospital Inselspital, Bern, Switzerland

Purpose: Epileptic disorders are highly heterogeneous and have a strong genetic contribution. Knowing the genetic basis of an epilepsy can be very valuable for diagnosis, treatment decisions and evaluation of recurrence risks. Therefore, we used panel-based Next Generation Sequencing (NGS) to study the underlying genetic heterogeneity of epilepsies.

Method: Three hundred and sixty-one epilepsy genes were selected from the OMIM database and literature, and subdivided into subpanels according to the most relevant epilepsy phenotypes. Following customized target enrichment, NGS was performed using the SOLiD 5500xl platform. Bioinformatics steps comprised mapping using LifeScope software, variant calling (SNPs and small indels) and annotation using Ensembl, dbSNP and inhouse databases. Variants with minor allele frequencies <5% were selected for further investigation. Validation of all identified mutations and resequencing of underrepresented regions was performed using Sanger sequencing.

Results: To date, we have analyzed 254 patients with epileptic disorders. In 23.2% of patients we were able to identify the causative mutation(s) and 20.1% were inconclusive. 56.7% of cases remained unsolved, mostly due to non-segregation of identified variants with the familial disease, implying complex inheritance. We observed mutations in 69 different genes, with *SCN1A*, *CDKL5*, *KCNQ2* and *STXBP1* among the most prevalent mutated genes.

Conclusion: We have developed a reliable and cost-efficient diagnostic NGS panel to analyze the multifaceted genetic causes of epileptic disorders. We have identified mutations in patients with clear and, more importantly, unspecific epilepsies. This enables a better understanding of genotype-phenotype correlations, particularly of less frequently mutated genes, and of complex modes of inheritance.

036
TARGETED RESEQUENCING IN EPILEPTIC ENCEPHALOPATHIES REVEALS MARKED GENETIC HETEROGENEITY AND NOVEL GENES

Carvill GL[1], Heavin SB[2], Yendle SC[2], O'Roak BJ[3], Cook J[4], Khan A[4], Dorschner MO[5], Weaver MA[5], Calvert S[6], Malone S[7], Wallace G[8], Stanley T[9], Bye AM[10], Bleasel A[11], Howell KB[12], Kivity S[13], Mackay MT[14], Rodriguez-Casero V[15], Webster R[16], Korczyn A[17], Zelnick N[18], Lerman-Sagie T[19], Lev D[19], Steensbjerre Møller R[20], Andrade DM[21], Freeman JL[12], Sadleir LG[9], Shendure J[3], Berkovic SF[2], Scheffer IE[2,22,23], Mefford HC[4]

[1]Pediatrics, Seattle, WA, USA, [2]Epilepsy Research Centre, Medicine, Melbourne, Vic., Australia, [3]Genome Sciences, University of Washington, Seattle, WA, USA, [4]Department of Paediatrics, University of Washington, Seattle, WA, USA, [5]Psychiatry & Behavioral Sciences, University of Washington, Seattle, WA, USA, [6]Department of Neuroscience, Royal and Mater Children's Hospitals, Brisbane, Qld, Australia, [7]Department of Neuroscience, Royal Children's Hospital, Brisbane, Qld, Australia, [8]Department of Neuroscience, Children's Health, Brisbane, Qld, Australia, [9]Department of Paediatrics, University of Otago, Wellington, New Zealand, [10]Department of Paediatrics, University of New South Wales, Sydney, NSW, Australia, [11]Westmead Hospital, University of Sydney, Sydney, NSW, Australia, [12]Department of Neurology, The Royal Children's Hospital, Parkville, Vic., Australia, [13]Schneider Children's Medical Center of Israel, Petach Tikvah, Israel, [14]Murdoch Children's Research Institute, Critical and Neurosciences, Melbourne, Vic., Australia, [15]Monash Medical Centre, Melbourne, Vic., Australia, [16]Department of Neurology, The Children's Hospital at Westmead, Sydney, NSW, Australia, [17]Department of Neurology, Tel-Aviv University, Tel-Aviv, Israel, [18]Department of Pediatrics, Carmel Medical Center, Haifa, Israel, [19]Wolfson Medical Center, Metabolic-Neurogenetic, Tel-Aviv, Israel, [20]Danish Epilepsy Centre, Dianalund, Denmark, [21]Department of Neurology, University of Toronto, Toronto, ON, Canada, [22]Florey Institute, Melbourne, Vic., Australia, [23]Department of Paediatrics, Royal Children's Hospital, University of Melbourne, Parkville, Vic., Australia

Purpose: Epileptic encephalopathies (EEs) are a devastating group of epilepsies characterized by refractory seizures, cognitive arrest or regression, associated with ongoing epileptic activity, and a poor prognosis. *De novo* mutations in a number of genes, as well as rare, *de novo* copy number changes, are known to cause EE. However, the vast majority of cases have an unknown etiology.

Method: We performed targeted massively parallel resequencing of 18 known and 47 candidate EE genes in 500 patients to identify novel genes, and investigate the phenotypic spectrum of known genes.

Results: Overall, we identify pathogenic mutations in 10% of our cohort. Pathogenic variants were found in seven of our 47 candidate genes, collectively accounting for 3% of EE in our cohort. Most notably, we identify mutations in 1.2% of our cohort in a novel gene that acts in the chromatin remodeling pathway. Also, *de novo* mutations were detected in 1% of the cohort in *SYNGAP1*, a gene identified in individuals with intellectual disability. The remaining pathogenic variants were detected in known EE genes. For some, including *SCN1A*, *SCN2A*, and *SCN8A*, we expand the phenotypic spectrum, presenting novel clinical features associated with these genes.

Conclusion: We have developed a rapid, cost-effective (~$1/gene/proband) and efficient targeted resequencing approach to define the molecular etiology of EE. These results will transform molecular diagnostic approaches and facilitate the management of families affected by this devastating disorder. Furthermore, we have identified the chromatin remodeling pathway as a novel biological process involved in epileptogenesis. Future studies of this pathway will provide new avenues for development of therapeutic interventions.

Platform Session: Paediatric Epilepsy 2
Tuesday, 25th June
14:30–16:00

037
CHILDREN WITH EPILEPSY AND ANXIETY: SUBCORTICAL AND CORTICAL DIFFERENCES

Jones JE[1], Chambers KL[1], Jackson DC[1], Dabbs K[1], Hsu DA[1], Stafstrom CE[1], Seidenberg M[2], Hermann BP[1]
[1]Department of Neurology, University of Wisconsin, Madison, WI, USA, [2]Department of Psychology, Rosalind Franklin University of Medicine and Science, North Chicago, IL, USA

Purpose: To examine subcortical brain volumes and cortical thinning using structural MRI in children with epilepsy and a current anxiety diagnosis.

Method: Participants were 90 children with epilepsy ages 8–18 with localization-related (LRE; n = 45) or idiopathic generalized epilepsy (IGE). All participants were assessed within 12 months of diagnosis with normal neurological examinations and clinical MRI. Twenty-five participants (M age = 12.1 years, SD = 3.0 years; 15 female) were diagnosed with a current Axis I anxiety disorder via the Kiddie-Schedule for Affective Disorders and Schizophrenia psychiatric interview. The remaining 65 participants (M age = 12.9 years, SD = 3.5 years; 30 female) had no current anxiety disorders. T1 volumetric MRI scans were collected; subcortical volumes and cortical thickness were computed using the FreeSurfer image analysis suite. Analyses focused on measures of intracranial volume- and age-corrected subcortical brain volumes and age-corrected cortical thickness in the frontal lobes and cingulate. Demographic and clinical epilepsy variables were also examined.

Results: Participants with an anxiety disorder had significantly larger bilateral ($p = 0.033$) and right ($p = 0.022$) thalamic volumes than non-anxious participants with trends for larger left amygdala ($p = 0.052$) and left thalamus ($p = 0.089$) volumes. Additionally, anxious participants showed significant thinning in left medial orbitofrontal ($p = 0.001$), right lateral orbital frontal ($p = 0.014$), right frontal pole ($p = 0.011$), and right insula ($p = 0.044$) regions of cortex. There were no differences between groups in age, sex, IQ, age of onset or duration of epilepsy. Children with LRE were more likely to have an anxiety disorder than children with IGE ($p = 0.040$).

Conclusion: In children with epilepsy, individuals with an anxiety disorder had larger thalamus and amygdala volumes compared to non-anxious children. These children also showed a pattern of cortical thinning in frontal lobe regions known to be associated with emotion and anxiety in the general population.

038
THE SURGICALLY-REMEDIABLE, EPILEPTIC SYNDROME ASSOCIATED WITH BOTTOM-OF-THE-SULCUS DYSPLASIA (BOSD) IN CHILDREN

Harvey AS[1,2,3,4], Mandelstam S[2,5], Maixner WJ[4,6], Leventer RJ[1,3,4], Kean M[4,5], Semmelroch M[2], Jackson GD[1,2,7]
[1]Department of Neurology, Royal Children's Hospital, Melbourne, Vic., Australia, [2]Austin Health, Florey Neurosciences Institutes, Melbourne, Vic., Australia, [3]Department of Paediatrics, University of Melbourne, Melbourne, Vic., Australia, [4]Murdoch Children's Research Institute, Melbourne, Vic., Australia, [5]Royal Children's Hospital, Medical Imaging, Melbourne, Vic., Australia, [6]Department of Neurosurgery, Royal Children's Hospital, Melbourne, Vic., Australia, [7]Department of Medicine, University of Melbourne, Melbourne, Vic., Australia

Purpose: To describe the electro-clinical features of epilepsy associated with highly localised focal cortical dysplasia (FCD), especially bottom-of-the-sulcus dysplasia (BOSD).

Method: The epilepsy surgery database of the Royal Children's Hospital, Melbourne was searched for children aged ≤15 years with FCD Type-2 operated between 2004 and 2012. Preoperative MRI scans (23 at high-field) were reviewed and only patients with FCD confined to one sulcus or gyrus were included; patients with normal MRI or multigyral lesions were excluded. Clinical, MRI, surgical, pathology and outcome details were reviewed.

Results: Thirty children (18 female) aged 1.5–15.8 years (median 7.4) at surgery had localised FCD on MRI; 22 were based at the bottom-of-the-sulcus and eight based at the crown-of-the-gyrus. Eight (36%) BOSDs were undetected on initial MRI at our centre. FCD location was frontal 12, temporal 6, insular 4, parietal 4, central 3 and occipital 1. Age at seizure onset was bimodally distributed at 1–18 (peak 3) months and 3–8 (peak 5) years. Seizure onset after 5 years was only with BOSD. Presentation was with spasms in 2 and focal seizures in 28. Ongoing, drug-resitant seizures had highly stereotyped focal semiology in all patients and localised scalp EEG interictal discharges or ictal rhythms in 87%. Seizure frequency was multiple daily/nightly in 90% patients, but with prolonged periods of seizure control in 57%, often following treatment with phenytoin or carbamazepine. Intellect was normal in 67% patients. All patients underwent lesionectomy guided by neuronavigation, gyral-venous maps and ECoG; only one patient had subdural EEG monitoring. Four had reoperation for residual dysplasia. 93% patients are seizure free; one has rare somatosensory seizures and one has nocturnal seizures.

Conclusion: High-frequency, unifocal seizures exhibiting a relapsing-remitting course in a developmentally normal older child with "normal MRI" should suggest an occult BOSD, which if detected and completely resected, should lead to seizure freedom.

039
AN ONGOING OPEN-LABEL UNCONTROLLED STUDY OF THE EFFICACY AND SAFETY OF KETAMINE IN CHILDREN WITH REFRACTORY CONVULSIVE STATUS EPILEPTICUS

Rosati A[1], L'Erario M[1], Ilvento L[1], Pisano T[1], Mirabile L[1], Guerrini R[1]
[1]Children's Hospital A. Meyer, Firenze, Italy

Purpose: To evaluate the efficacy and safety of ketamine (KE) in the management of refractory convulsive status epilepticus (RSE) in children.

Method: Since November 2009 we started using KE for treating all children consecutively referred for RSE. Clinical and treatment data were analyzed.

Results: Between November 2009 and January 2013, 12 children (aged from 3 months to 12 years) with RSE received intravenous KE. In 11 patients SE had persisted for more than 24 h (super-refractory SE) with a median of 13 days (mean 15.5 ± 12.5; range 2–44 days). Prior to KE administration, conventional anesthetics were used, including midazolam, propofol and thiopental in 12, 7 and 6 patients each. Median dose of KE in continuum intravenous infusion was 40 mcg/kg/min (mean 32.5 ± 20.5 mcg/kg/min; range 10–60 mcg/kg/min). Midazolam was administered add-on to prevent emergence reactions. Four patients were treated twice for two different episodes of RSE (16 therapeutic interventions). The use of KE was associated with resolution of RSE in 13 out of the 16 therapeutic interventions.

Amongst the three individuals who did not respond to KE, two were cured by surgical removal of epileptogenic focal cortical dysplasia. None of the patients experienced serious adverse events. In 2/12 children the use of KE instead of propofol and thiopental permitted to avoid tracheal intubation.

Conclusion: This ongoing, open-label, uncontrolled study provides Class IV evidence that intravenous KE can be effective and safe in treating children with RSE.

040
THE ADULT SOCIAL OUTCOME OF CHILDREN WITH "EPILEPSY ONLY" IS OFTEN TROUBLED AND IS AMAZINGLY SIMILAR ACROSS DIFFERENT TYPES OF EPILEPSY: A POPULATION-BASED STUDY WITH 20–35 YEARS FOLLOW UP

Camfield C[1], Camfield P[1]
[1]Dalhousie University and the IWK Health Centre, Halifax, NS, Canada

Purpose: To establish the adult social outcome of children with "epilepsy only" who have epilepsy types characterized by generalized tonic-clonic seizures.

Method: Patients were selected from the Nova Scotia Childhood Population-based Epilepsy Cohort (total n = 692) with "epilepsy only" (normal intelligence and neurological examination without progressive cause) and generalized tonic-clonic seizures (Juvenile Myoclonic Epilepsy, JME n = 24; Generalized Tonic Clonic Alone, GTCA n = 30; Focal with secondary generalization only, SecGen n = 77). Epilepsy onset occurred between 1977 and 1985 and all patients were followed with a structured telephone interview and chart review beyond their 21th birthday. Adverse social outcomes were: no high school graduation, pregnancy outside a stable relationship (<6 months), no close friends, unemployed, a DSM psychiatric diagnosis, criminal conviction, no romantic relationship >3 months, living alone at the end of follow up.

Results: Average age of seizure onset was: JME 10.4 ± 4.3 years, GTCA 6.7 ± 4.2, SecGen 7.3 ± 4.5. Average follow up was JME 25.8 ± 2.4 years, GTCA 22.2 ± 7.6 years, SecGen 27.9 ± 5.4. Average age at follow up was JME 36 ± 4.8 years, GTCA 29 ± 8.7 and SecGen 34.5 ± 8 ≥1 adverse social outcome occurred in JME 74%, GTCA 76%, SecGec 62% and >2 adverse social outcomes were noted in JME 22%, IGE GTC 21%, SecGen 10% (p = ns). Social outcome was not related to epilepsy remission in any group.

Conclusion: For children with "epilepsy only", adult social outcome is equally disrupted in generalized epilepsy (JME and GTCA) and focal epilepsy with seizures that generalize.

041
EPILEPSY SURGERY IN PEDIATRIC INTRACTABLE EPILEPSY WITH FOCAL CORTICAL DYSPLASIA

Kwon HE[1], Kang JW[2], Kang H-C[2], Lee JS[2], Kim DS[3], Kim HD[2]
[1]Department of Pediatrics, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, [2]Department of Pediatric Neurology, Pediatric Epilepsy Clinics, Severance Children's Hospital, Epilepsy Research Institute, Yonsei University College of Medicine, Seoul, Korea, , [3]Division of Pediatric Neurosurgery, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

Purpose: Focal cortical dysplasia (FCD) is the most common pathological finding in pediatric epilepsy surgery. This study aimed to define the clinical characteristics and surgical outcome according to FCD findings.

Method: One-hundred-nineteen intractable pediatric epilepsy patients, who underwent resective surgery and were confirmed with cortical malformation by pathologic findings, were reviewed. Clinical characteristics, and seizure outcome were analyzed according to types of pathology.

Results: Epileptic encephalopathy (EE), which includes infantile spasms and Lennox-Gastaut syndrome, was most frequently found in mild malformation of cortical development (mMCD)/FCD type I patients, with 32 (69.6%) out of 46 cases, than FCD type II or type III cases, in which EE was found only in 30.5% (18/59), and 7.1% (1/14) of each group ($p < 0.001$). Engel class I outcome was achieved in 24 (52.2%) out of 46 cases of mild MCD/FCD type I group, 33 (55.9%) in 59 FCD type II, and 10 (71.4%) in 14 type III. Analyzed according to epileptic syndromes, Engel class I was observed in 34 (66.7%) out of 51 cases of EE, and 42 (61.8%) out of 68 localization related epilepsy cases ($p = 0.582$). Seizure freedom after reoperation was higher in FCD type II (67.8%) than mild MCD/FCD type I (56.5%) ($p = 0.235$). Successful discontinuation of antiepileptic drug was more feasible in type IIb group (61.1%) than other groups (31.0%) among Engel class I patients ($p = 0.022$).

Conclusion: Pathological classification is important to determine the clinical epileptic features and the surgical outcome.

042
CHALLENGE IN THE TREATMENT OF STATUS EPILEPTICUS IN CHILDREN; 16-YEARS' SINGLE CENTER EXPERIENCE

Kravljanac R[1], Djuric M[1], Jankovic B[1], Pekmezovic T[2]
[1]Institute for Mother and Child Heathcare of Serbia, Faculty of Medicine, University of Belgrade, Belgrade, Serbia, [2]Institute for Epidemiology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Purpose: Evaluation of efficacy and adverse events of drugs used in the treatment of SE in children and proposal of algorithm for SE treatment in children.

Method: The study analyzed SE episodes in children aged 0.2–18 years treated in period from 1995 to 2011. SE was defined as an acute epileptic condition characterized by continuous seizures, or intermittent seizures without full recovery of consciousness between seizures for at least 30 min. 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 20 min, without recurrence within next 6 h. The efficacy and adverse affects were compared and statistically analyzed by Chi-square test.

Results: The study included 602 SE episodes in 395 children with mean age of 4.3 ± 4.0 years. The efficacy of commonly used drugs were: midazolam in 90.3%, thiopental in 82.5%, phenobarbital in 64.4%, levetiracetam 64%, diazepam in 33.9%, while propofol, ketamine and lidocain were ineffective. Adverse effects were noticed in 128 (21.3%) episodes, especially in SE treated by continuous infusion of midazolam (58.1%) and thiopental (55.5%). High dosage corticosteroid infusion was frequently beneficial, even in the SE caused by other than immune-mediated etiology. Intensive therapy was required in 244 (40.5%) due to SE, underlying disease or complications of SE treatment.

Conclusion: The most effective drug in SE treatment in children were midazolam and thiopental in high dosage. Side effects were common, especially in SE caused by progressive encephalopathy, and levetiracetam might be right choice in them. The best approach to SE treatment is according to established algorithm, but with special attention in certain etiological groups.

Platform Session: Epilepsy surgery
Tuesday, 25th June
14:30–16:00

043

INTRAOPERATIVE MR IMAGING (IOPMRI) AND FUNCTIONAL NEURONAVIGATION (FN) FOR SURGERY OF LESIONAL TEMPORAL LOBE EPILEPSY (LTLE): LONG TERM SURGICAL AND SEIZURE OUTCOME

Roessler K[1], Sommer B[1], Grummich P[1], Coras R[2], Kasper B[3], Hamer HM[3], Blümcke I[2], Buchfelder M[1]

[1]Department of Neurosurgery, Universitätsklinikum Erlangen, Erlangen, Germany, [2]Department of Neuropathology, Universitätsklinikum Erlangen, Erlangen, Germany, [3]Department of Neurology, Universitätsklinikum Erlangen, Erlangen, Germany

Objective: LTLE results from a heterogeneous group of pathologies, appearing with sometimes ill defined borders. During surgery, FN and iopMRI may be of value to optimize the amount of resection and spare eloquent areas as an optimal requirement for seizure control.

Methods: To clarify the role of iopMRI and FN for long term tumor control and seizure outcome, we performed a retrospective clinical study investigating patients operated on between August 2002 and March 2012 at our department. Altogether, there were 103 patients (57 male, 46 female, mean age 37 years, from 12 to 69 years). Surgery consisted of pure lesionectomy (n = 63) and lesionectomy combined with tailored or standard temporal resection (n = 40). Additionally to FN including speech, motor, and sensory cortical areas and tracts, eighty-nine patients had iopMR imaging and 16 intraoperative electrocorticography (ECoG).

Results: Complete resection of the lesion was achieved in 89 of 103 patients (86.4%). IopMRI revealed total lesionectomy in only 67 of 89 patients (75%), further resection lead to a removal of remnant pathological tissue in 19 more patients. Thus, as a direct effect of intraoperative MR imaging, overall resection rate was improved by 21.3% (19/89). The most common histological diagnoses were: 43 gangliogliomas (41.7%), 26 cavernomas (25.2%), 9 DNTs (8.7%) and 9 FCDs (8.7%). In radically resected tumor patients, no recurrent tumors were detected during the follow-up. Altogether, in 73.8% of re-evaluated patients (76/103) an Engel Class 1 seizure outcome was found (65% Engel Class 1A) during a mean follow-up of 26 months. No severe postoperative complications were seen, superior visual field defects occured in 12.6%.

Conclusion: By using iopMRI and FN, we were able to increase the rate of complete resections in lesional TLE patients by more than 20%, which resulted in an excellent seizure outcome and a low complication rate.

044

EPILEPTOGENICITY MAPS OF INTRACEREBRAL HFO RANGING FROM 60 TO 100 HZ ($HFO_{60–100}$) AT SEIZURE ONSET: CLINICAL RELEVANCE IN EPILEPSY SURGERY CANDIDATES

Job AS[1,2], David O[2,3], Minotti L[1,2], Chabardès S[2,4], Bartolomei F[5,6], Kahane P[1,2]

[1]Grenoble University Hospital, Epilepsy Unit, Grenoble, France, [2]INSERM U836, Grenoble Institut des Neurosciences, Grenoble, France, [3]Université Joseph Fourier, Grenoble, France, [4]Grenoble University Hospital, Neurosurgery Unit, Grenoble, France, [5]CHU La Timone, Neurophysiological Unit, Marseille, France, [6]INSERM U751, Marseille, France

Purpose: To assess in epilepsy surgery candidates undergoing Stereotactic intracerebral EEG (SEEG) recordings the rate and localizing value of $HFO_{60–100}$ at seizure onset.

Method: 21 consecutive patients who underwent SEEG recordings and in whom at least one spontaneous seizure was recorded were included in a 2 years-period. According to a methodology previously described (David et al., 2011), the power of SEEG-recorded $HFO_{60–100}$ was quantified at seizure onset for each seizure recorded, and statistical parametric maps were used to display the cortical areas exhibiting significant changes as compared to interictal baseline. In 11 patients in whom post-operative
3-D T1 post-operative MRI was available, the overlap between the cortical areas displaying the most significant ictal $HFO_{60–100}$, and the extent of surgical resection was quantified and compared to post-surgical outcome.

Results: Epileptogenicity Maps (EM) were obtained for 69 of the 75 seizures recorded, but analysis at the patient level was possible in all the 21 patients. All patients demonstrated EM that showed a significant increase of $HFO_{60–100}$ at seizure onset, whatever was the seizure onset location or the underlying brain lesion. EM were highly reproducible from one seizure to another one in each patient. In the 11 cases in whom analysis was possible, removal of cortex areas which displayed significant ictal $HFO_{60–100}$ was associated to a better post-surgical outcome.

Conclusion: EM can be obtained for all patients studied by SEEG recordings, whatever the type of epilepsy is. The removal of cortex areas exhibiting the most significant $HFO_{60–100}$ changes seems of prognostic significance and will need further large scale studies.

References1. David O, Blauwblomme T, Job AS, Chabardès S, Hoffmann D, Minotti L, Kahane P. Imaging the seizure onset zone with stereoelectroencephalography. Brain 2011; 134: 2898–2911.

045

BILATERAL HIPPOCAMPAL SCLEROSIS: SURGICAL OUTCOMES WITH NONINVASIVE PRESURGICAL EVALUATION

Ravat S[1], Rao P[1], Shah U[2], Godge Y[1], Muzumdar D[3], Shah S[2]

[1]Department of Neurology, Seth GSMC & KEM Hospital, Mumbai, India, [2]Department of Neuropsychology, Seth GSMC & KEM Hospital, Mumbai, India, [3]Department of Neuropsychology, Neurosurgery, Seth GSMC & KEM Hospital, Mumbai, India

Purpose: To study surgical outcomes in patients with bilateral MRI determined, asymmetric and symmetric, mesial temporal sclerosis (MTS) after non-invasive pre-surgical evaluation.

Method: We studied 35 patients with MRI determined bilateral MTS who underwent anterior temporal lobectomy (ATL) after non-invasive pre-surgical evaluation. Clinical history, EEG, neuropsychology profile and symmetry of MTS on MRI were studied between groups of 'seizure free' and 'not seizure free' patients.

Results: 74.3% patients were seizure free at average follow up of 44 months (range 6–110 months). History of febrile seizures, duration of epilepsy and symmetry of MTS on MRI (symmetric vs. asymmetric) did not have a statistically significant association with seizure free outcome (p = 1.00, 0.64 and 1.00 respectively). 57.1% patients had unilateral interictal discharges and 94.3% patients had unilateral ictal EEG onset. Bilateral interictal discharges were significantly associated with 'not seizure free' outcome (p = 0.02). Only two patients had bilateral independent ictal EEG onset and these patients had >70% reduction in seizure frequency. No significant decline in memory was seen in either left or

right surgery groups. Quality of life score improvements were highly significant ($p \leq 0.0005$).

Conclusion: In a setting of limited resources, a non-invasive pre-surgical protocol can be used in bilateral MTS. Our results suggest that with proper patient selection, the outcomes are comparable to those reported with invasive pre-surgical protocols. Patients with unilateral interictal and ictal EEG have the best outcome. Up to 50% patients with bilateral interictal discharges can have a seizure free outcome. Patients with bilateral independent seizure onset have a less favourable prognosis. Patients who are not seizure free can still attain worthwhile improvement in seizure frequency without significant decline in memory and have an improved quality of life.

046
THE TORONTO EXPERIENCE WITH REGARDS TO NEUROCOGNITIVE AND SEIZURE OUTCOMES OF SELECTIVE AMYGDALOHIPPOCAMPECTOMY VS. ANTERIOR TEMPORAL LOBE RESECTION FOR MESIAL TEMPORAL LOBE EPILEPSY

Mansouri A[1], Fallah A[2], Cohn M[2], Valiante TA[1]

[1]University of Toronto, Toronto, ON, Canada, [2]Toronto Western Research Institute, University Health Network, Toronto, ON, Canada

Purpose: To report the Toronto Western Hospital experience (2004–2011), regarding seizure and neuropsychological outcome of patients with mesial Temporal Lobe Epilepsy (mTLE), operated on by a single neurosurgeon (T.A.V) using either Anterior Temporal Lobectomy (ATL) or Selective Amygdalohippocampectomy (SelAH).

Methods: A retrospective analysis of surgical patients with preoperative MRI and postoperative histopathology suggestive of hippocampal sclerosis was performed. Seizure outcome was assessed using Time-to-event analysis; the 'event' was defined as any seizure following resective surgery (not including seizures in the first postoperative week and/or auras). Neuropsychological assessments included language (Boston Naming Test, BNT), verbal memory (Warrington Word Recognition Test, WWRT), visual memory (Warrington Face Recognition Test, WFRT), and Full-scale IQ. Left and right-sided resections were compared separately.

Results: Ninety six patients (75 ATL, 21 SelAH) were analyzed. Mean follow-up was 40.5 m (range 4–102 m). There was no statistical difference in seizure freedom between the two surgical cohorts (HR: 0.85; 95% CI 0.45–1.59; $p = 0.61$). Regarding neuropsychological testing, the results were as follows. Left sided resections: BNT (SelAH −1.7, ATL −3.4), WWRT (SelAH −3.3, ATL −2), WFRT (SelAH −0.55, ATL +1.5), IQ (SelAH +1, ATL +0.78). Right sided resections: BNT (SelAH +2.22, ATL −0.2), WWRT (SelAH +1.33, ATL −1.2), WFRT (SelAH +0.33, ATL −3.04), IQ (SelAH +2.3, ATL +2.1). None of the observed changes reached statistical significance.

Conclusion: Regarding seizures freedom, there was no significant difference between the two respective approaches. In regards to neuropsychological outcome there was a trend towards preservation of memory and language function in patients undergoing right-sided SelAH, although none of the results reached statistical significance. Therefore, ATL and SelAH provide effectively equivalent surgical approaches to mTLE.

047
STEREOTACTIC LASER ABLATION OF HIPPOCAMPUS LEADS TO BETTER COGNITIVE OUTCOME THAN STANDARD TEMPORAL LOBE RESECTION FOR THE TREATMENT OF EPILEPSY

Drane DL[1,2], Loring DW[3], Voets NL[4], Price M[3], Gross RE[5], Willie JT[5], Helmers SL[3], Ojemann JG[6], Phatak V[2], Miller JW[2], Meador KW[3]

[1]Departments of Neurology and Pediatrics, Emory University School of Medicine, Atlanta, GA, USA, [2]Departments of Neurology, University of Washington School of Medicine, Seattle, WA, USA, [3]Departments of Neurology, Emory University School of Medicine, Atlanta, GA, USA, [4]Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK, [5]Departments of Neurosurgery, Emory University School of Medicine, Atlanta, GA, USA, [6]Neurological Surgery, University of Washington School of Medicine, Seattle, WA, USA

Purpose: There is increasing evidence that temporal lobe epilepsy (TLE) patients experience significant deficits in object recognition and category-specific naming following standard surgical approaches (including selective amygdalohippocampectomy). We have suggested that these deficits represent a decoupling of core processing modules (e.g. language, visual processing, semantic memory), and often represent "collateral damage" occurring as the hippocampal region is accessed by the surgeon. We present a small case series of TLE patients who underwent stereotactic laser ablation of the hippocampus, predicting that they will be free from such deficits due to the preservation of critical white matter pathways and other important network regions.

Method: Twelve TLE patients have undergone laser ablation of the hippocampus at Emory University, and we present postsurgical neuropsychological data for those seven reaching 6-month follow-up to date (including four left-sided ablations). Chi square analysis was used to compare this group to a comparable group of TLE patients who underwent either a tailored or selective surgical approach ($n = 30$) on tasks of recognition and naming of man-made objects and famous persons.

Results: None of the seven laser ablation patients experienced any deficits on the administered tasks of recognition and naming, while 23 of the 30 TLE patients undergoing standard surgical approaches experienced significant declines on one or more measures for both object types ($\chi^2 = 14.2$, $p < .001$). Fifteen of 16 left TLE patients declined on one or more naming tasks, while eight of 14 right TLE patients declined on one or more tasks of object recognition and/or familiarity.

Conclusion: These results suggest that: (i) TLE patients undergoing laser ablation of the hippocampus experience a better outcome on naming and recognition tasks than do TLE patients undergoing standard resections, and (ii) The hippocampus does not appear to be an essential component of the neural networks underlying object recognition and name retrieval.

048
CLINICALLY IMPORTANT IMPROVEMENT IN QUALITY OF LIFE IN MEDICALLY AND SURGICALLY TREATED PATIENTS WITH EPILEPSY: RESULTS FROM A RANDOMIZED CONTROLLED TRIAL

Fiest K[1,2], Dykeman J[1,2], Eliasziw M[3], Parrent A[4], Wiebe S[1,2]

[1]Department of Clinical Neurosciences, University of Calgary, Calgary, AB, Canada, [2]Department of Community Health Sciences, University of Calgary, Calgary, AB, Canada, [3]Department of Public Health & Community Medicine, Tufts University School of Medicine, Boston, MA, USA, [4]Department of Clinical Neurological Sciences, University of Western Ontario, London, QC, Canada

Purpose: To compare the proportion of patients with epilepsy, treated medically and surgically, who achieve minimal clinically important differences (MCID) in quality of life (QOL) at 6- and 12-months follow-up.

Method: We analysed QOL data from a randomized controlled trial of temporal lobe epilepsy (Wiebe et al, NEJM 2001). QOL was assessed

using the Quality of Life in Epilepsy Inventory-89 (QOLIE) and the QOLIE-31. The instruments were self-administered at baseline, 6 and 12 months follow-up. MCID for QOLIE-89 and 31 were defined as 10.14 and 11.76, respectively.

Results: Forty patients were randomized to the medical and 40 to the surgical group. At 6 months a significantly greater proportion of patients achieved MCID with surgery than with medical therapy using QOLIE-89 (40.0% vs. 12.5%, $p < .05$, number needed to treat [NNT] = 4), and QOLIE-31 (62.5% vs. 17.5%, $p < .05$, NNT = 2). Significantly more surgical patients achieved small (67.5% vs. 25.0%), medium (62.5% vs. 15.0%) and large (50% vs. 10%) improvements in QOLIE-31. The difference was maintained at 12 months for large improvements.

Conclusion: The results of the trial show that the proportion achieving MCID in QOL is similar to that of seizure freedom (surgical 58% vs. medical 8%). Large improvements in QOL with surgery persist at 12 months.

Platform Session: Epilepsy in the Developing World
Tuesday, 25th June
14:30–16:00

049
EPILEPSY AND HIV IN THE DEPARTMENT OF NEUROLOGY OF FANN TEACHING HOSPITAL

Noutsa LK[1], Mbonda PCC[1], Ould Lemine S[1], Diop AG[1]
[1]Department of Neurology, Fann Teaching Hospital, Dakar, Senegal

Purpose: Seizures are clinical manifestations of many neurological complications in HIV / AIDS.

Method: We conducted a prospective study from the 1st January 2011 to 30th November 2012; all patients who presented with seizures in the outpatient department of Neurology in Fann Teaching Hospital, with a positive HIV serology confirmed later were recruited. Excluded, were patients with a history of neurological disorders.

Results: Seizures were the mode of revelation of HIV infection in all patients. We recruited 17 patients, aged 18–61 years. The average age was 35.23 years and the sex ratio: 0.67, HIV-2 was found in 70.58% of patients. The mean duration of hospitalization was 17.2 ± 1.2 days. The focal motor seizures were observed in 12 patients (70.58%), among which 66.6% were secondarily generalized while 33.3% were simple. We found two cases (11.76%) of status epilepticus. Cerebral toxoplasmosis was the most common etiology (41.17%) followed by tuberculous meningitis (17.64%) and cryptococcal meningitis (11.76%). For 29.41% of the patients no etiology was found.

Conclusion: Epileptic seizures are common manifestations of neurological complications in HIV / AIDS. Sometimes, they are the mode of revelation. Thus, HIV serology should be sought systematically in all adult patients with seizures. In our study, cerebral toxoplasmosis was the more frequent etiology.

050
CLINICAL FEATURES AND CONSEQUENCES OF ACTIVE CONVULSIVE EPILEPSY IN MULTIPLE SITES IN SUB-SAHARAN AFRICA: A POPULATION-BASED STUDY

Kariuki SM[1], Matuja W[2], Akpalu A[3], Kakooza-Mwesige A[4], Chabi M[5], Wagner RG[6], Cannor M[6], Chengo E[1], Ngugi AK[1], Odhiambo R[1], Bottomley C[7], White S[8], Sander JW[9], Neville BG[10], Newton CRJ[11]
[1]Kenya Medical Research Institute, Kilifi, Kenya, [2]Muhimbili University College of Health Science, Dar es Salaam, Tanzania, , [3]Kintampo Health Research Centre, Kintampo, Ghana, [4]Iganga-Mayuge Health and Demographic Surveillance System, Iganga, Uganda, [5]Ministry of Medical services, Nairobi, Kenya, [6]University of the Witwatersrand, Johannesburg, South Africa, [7]London School of Hygiene and Tropical Medicine, London, UK, [8]Great Ormond Street Hospital, London, UK, [9]UCL Institute of Neurology, London, UK, [10]UCL Institute of Child Health, London, UK, [11]University of Oxford, Oxford, UK

Purpose: Epilepsy is common in sub-Saharan Africa (SSA), but the clinical features and consequences are poorly characterized. Most studies are hospital-based; few studies have compared different ecological sites in SSA. We characterized active convulsive epilepsy (ACE) identified in cross-sectional community surveys in SSA, to understand the clinical features and consequences.

Method: A detailed clinical and neurophysiological description of ACE in 2,170 people identified from a community survey of 586,584 people across five sites in Africa: South Africa; Tanzania; Uganda; Kenya and Ghana are provided.

Results: Over half (51%) of ACE occurred in children. Focal features (EEG, seizure types and neurological deficits) were present in 60% of ACE cases. A third of primarily generalised seizures had focal features on EEG. Status epilepticus occurred in 377/1,633 (23%) of people with ACE. Only 786/2,091 (38%) individuals were on antiepileptic drugs. Important comorbidities of ACE were malnutrition (320/2,115 [15%]), cognitive impairment (494/2,131 [23%]) and neurological deficits (319/2,130 [15%]). The consequences of ACE were burns (347/2,125 [16%]), head injuries (post seizures) (25/1,905 [1%]), no education (938/2,135 [44%]) and, in adults, being unmarried (695/1,030 [68%]) or unemployment (646/1,098 (58%); all were more common than in controls. There were significant differences in the co-morbidities across the sites.

Conclusion: Focal features are common in ACE suggesting identifiable and preventable causes. Malnutrition, cognitive and neurological disorders are common in ACE and should be included in the management. There are significant consequences of epilepsy such as burns, lack of education and marriage prospects, which need to be addressed.

051
ENHANCING MEDICAL COMPLIANCE OF PATIENTS WITH CONVULSIVE EPILEPSY IN RURAL WESTERN CHINA: A RANDOMISED INTERVENTION TRIAL

Li J[1], Si Y[1], Liu L[1], Zhou D[1]
[1]Department of Neurology, West China Hospital, Sichuan University, Chengdu, China

Purpose: This randomised intervention trial was designed to determine whether the implementation of a practical intervention was effective in enhancing medical compliance and improving seizure control in rural communities in western China.

Method: Two out of four areas were randomly selected for this study; one was assigned to be the intervention group (IG) and one to be the control group (CG). An intervention package with four components (intensive education, consultation services, maintenance of an epilepsy tracking card and repeated reminders) was formulated. Medical compliance and seizure control were measured and compared between the groups before and after the intervention. In addition, correlation of both changes in medical compliance and seizure frequency were investigated.

Results: After one year of follow-up, 183 patients in the IG (105 males) and 177 in the CG (99 males) remained for the analysis. At the end of the study, the total number of seizures in the intervention group declined

17.8% compared to that prior to the intervention (after 6-month phenobarbital monotherapy), nearly twice as much as in control group (9.6%). The proportion of patients with a reduction in seizures >50% (including those who were seizure-free) rose to 79.8% in the IG compared to 61.0% in the CG ($p < 0.05$). With regard to medical compliance, the majority of the IG members were rated as excellent or very good, but medical compliance remained nearly unchanged after the intervention. A moderate correlation was found between the changes in AED adherence and seizure control ($r = 0.4$, $p < 0.05$), and a weaker correlation was found between lifestyle and seizure control ($r = 0.328$, $p < 0.05$).

Conclusion: This intervention package proved to be efficient in enhancing medical compliance and improving seizure control. It was practical and effective in rural communities in resource-poor areas.

052
DRUG COMPLIANCE IN PATIENTS AT A DESIGNATED TERTIARY EPILEPSY-CARE FACILITY

Mahmud H[1], Mogal Z[1], Aziz H[1]
[1]National Epilepsy Centre, Jinnah Postgraduate Medical Centre, Karachi, Pakistan

Purpose: To assess treatment compliance of patients at a designated tertiary epilepsy-care centre.

Background: Poor drug compliance in epilepsy is a major concern leading to poor seizure control and frequent visits to hospitals; especially in developing countries. In Pakistan, this is attributed to cost, illiteracy, lack of awareness with erroneous socio-cultural beliefs about epilepsy and poor counseling by the care-givers. At National Epilepsy Centre, Karachi (NEC) patients receive phenobarbitone, phenytoin, valproate and carbamezapine, at token cost. Monthly visit includes, assessment of seizure frequency and intense counseling ensuring continued treatment compliance.

Method: From the 5315 registered patients with NEC (April 2007 – Dec 2012) a cohort of new patients was randomly chosen. All patients with epilepsy between November 2010 and February 2011 were included. Patients were reviewed monthly; 30 days supply of appropriate anti-epileptic drugs, direct interviews assessing seizure frequency and drug compliance corroborated with seizure diary and pill count was done. Intensive counseling at each visit was ensured. Patients, who adhered to proper dosage, were punctual and regular, never missing >02 doses in one year were termed compliant.

Results: Total 360 new patients were seen during the study period; 188 were followed up for atleast one year whilst 172 were lost to follow-up and excluded. Despite intense monitoring and counseling, compliance remained poor in 40 (21.3%). In the 148 (78.7%) patients with good compliance, 100% seizures reduction was achieved in 52.14% at 12 months.

Conclusion: Indirect measures showed poor drug compliance in 21.3% as against 36–50% reported in literature. Drug compliance is improved by addressing the reasons, a strict follow-up protocol and intense counseling.

053
NEUROCYSTICERCOSIS PREVALENCE IN FOUR SOUTH-WESTERN PROVINCES OF THE DOMINICAN REPUBLIC

Sanon NT[1], Rivera Mejia D[2], Santos Viloria D[3], Perez Then E[4], Dario Pimentel R[5], Hugo Garcia H[6], Carmant L[1]
[1]Department of Neurology, CHU Ste-Justine, Montréal, Canada, [2]Dominican Epilepsy Surgery Group, Santo Domingo, Dominican, [3]Dominican League Against Epilepsy, Santo Domingo, Dominican, [4]CENISMI-IDEP, Santo Domingo, Dominican, [5]FUNDIMESO, Santo Domingo, Dominican, [6]CWGP, Peruvian University Cayetano Heredia, Lima, Peru

Purpose: In the Dominican Republic, the prevalence of Epilepsy is estimated to be greater than 5%. In parallel, it is known that neurocysticercosis, a parasitic infection of the nervous system by *T. Solium,* is endemic in certain regions of the country and frequently causes Epilepsy. The goal of this study was to determine the prevalence of neurocysticercosis in epileptic patients living in a region bordering Haiti.

Method: A group of 111 epileptic patients were tested to assess whether they had neurocysticercosis. Positive diagnosis for neurocysticercosis was set as a CT scan showing calcifications with or without positive Western Blot analysis for *T. Solium* seral antibodies. Other cases were considered negative for neurocysticercosis. Furthermore a survey was distributed to the patients to make correlations with lifestyle between 04/2009–09/2011.

Results: On clinical history of the 111 epileptic patients, 81.8% experienced generalized seizures and 42.4% reported a positive family history of Epilepsy. Yet, 30% demonstrated a positive diagnostic for neurocysticercosis ($n = 33$). Among this subgroup 60.6% are males, 62.1% are educated and about half live in rural areas. Lifestyle data revealed that only 20% are agricultural workers, 74.2% do not have a porcine industry in their community but 64% get their meat from their backyard.

Conclusion: Our data demonstrate that a third of patients with epilepsy in the South-Western part of the Dominican Republic also test positive for neurocysticercosis. But due to the high prevalence of generalized epilepsy and of a positive family history, a causal link cannot be clearly established. We will subsequently test non-epileptic controls for neurocysticercosis to establish its prevalence in the general population, phase that has already been approved by the North-American Commission of the ILAE. If a similar rate of positivity is found in the controls, genetic studies of that population could help us define new causes of epilepsy.

054
COGNITIVE FUNCTION AND ACADEMIC ACHIEVEMENT IN CHILDREN WITH IDIOPATHIC EPILEPSY FROM A DEVELOPING COUNTRY

Melbourne-Chambers R[1], Chang-Lopez S[2], Morrison-Levy N[3], Tapper J[3], Tulloch-Reid M[2]
[1]Department of Child and Adolescent Health, University of the West Indies, Kingston, Jamaica, [2]Tropical Medicine Research Institute, University of the West Indies, Kingston, Jamaica, [3]Bustamante Hospital for Children, Kingston, Jamaica

Purpose: To compare the cognition and academic achievement of Jamaican children with idiopathic epilepsy with classroom controls without epilepsy.

Method: School children attending a hospital-based clinic with a confirmed diagnosis of idiopathic epilepsy were enrolled as cases. Children with other neurologic illness, severe mental retardation, mixed seizures, hearing disorders or abnormal neuroimaging or receiving special education were excluded. For each case, a classmate, matched for sex and age, was selected as the control. Parents were interviewed to assess socioeconomic status and parental education. One trained psychologist blinded to the participants' disease status assessed the children's cognitive ability and math skills using the Raven's standard progressive matrices (SPM), selected tests from the NEPSY and the Wide Range Achievement Test – Expanded. The Mann Whitney test was used to compare scores by disease status. Conditional logistic regression models were used to adjust for confounders.

Results: Thirty-three children with idiopathic epilepsy were identified. The mean (±SD) age of the sample was 9.5 ± 1.7 years. No differences between the groups were found in the Raven's SPM (cases 23.7 ± 12.6; controls 23.4 ± 8.8) or on tests of attention, executive function and math. Significant differences were found in tests of auditory memory [forward digit span] ($p = 0.004$) and language [word generation] ($p = 0.02$). After adjusting for mothers education, significant differences were also found in narrative memory ($p = 0.04$) and comprehension of instructions ($p = 0.02$).

Conclusion: Jamaican children with idiopathic epilepsy have similar scores on intelligence and math compared with classroom peers but experience deficits in auditory memory and expressive and receptive language function.

Platform Session: Clinical neurophysiology Tuesday, 25th June 14:30–16:00

055

EFFECTIVENESS OF TEST-ENHANCED LEARNING (TEL) AS AN INSTRUCTIONAL METHOD FOR EEG COURSES

Tan N[1], Chin HX[2], Loh NK[1], Chan DW[3], Rathakrishnan R[4], Lim SH[1]

[1]National Neuroscience Institute, Singapore, Singapore, [2]Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore, [3]Department of Paediatrics, KK Women's and Children's Hospital, Singapore, Singapore, [4]Department of Neurology, National University Health System, Singapore, Singapore

Purpose: There are few studies addressing the effectiveness of EEG instructional methods. Repeated testing, termed Test-Enhanced Learning (TEL), is a teaching method that can enhance information retention. We aimed to determine the effectiveness of TEL for EEG interpretation.

Method: This is a pre/post study of a TEL intervention for EEG interpretation. Participants were neurologists, EEG technicians and non-neurology doctors attending a 4-hour course. Participants were given pre-readings before the course, including (a) key features and sample EEG recordings of normal and abnormal EEG patterns (b) pointers on seizure semiology. No formal teaching was offered during the course. The TEL intervention consisted of participants completing five sets of 10 multiple choice questions (MCQ). During each 20-minute set, an EEG page or video of a seizure was shown with 4–5 answer choices; participants had one minute to select the correct answer using an audience response system clicker. The instructor then provided the correct answer and a brief explanation. Participants were given a 3-minute break between sets. The primary outcome measure was score change on a 16-item MCQ test administered just before and just after TEL intervention.

Results: One-hundred and six participants completed the study (58.5% neurologists). The 16-item pre-post test showed acceptable reliability (Cronbach's $\alpha = 0.72$) and good discriminating ability; all discriminant indices were >0.35. Mean pre- and post-test scores were 57.2% and 69.8% respectively; mean improvement in score was +12.6% (95% CI 9.6–15.5%, $p < 0.001$). The improvement in scores was not significantly different between neurologists and EEG technicians ($p = 0.83$). The effect size of the TEL intervention was moderate (Cohen's $D = 0.62$).

Conclusion: TEL used as a teaching method for EEG interpretation is associated with immediate increased ability to interpret EEG. TEL can be employed in EEG courses as an alternative to passive teaching.

056

THE RELATIONSHIP BETWEEN THE PATHOLOGICAL TYPES AND SCALP EEG FEATURES IN PATIENTS WITH FOCAL CORTICAL DYSPLASIA AND INTRACTABLE EPILEPSY

Chen S[1]

[1]Beijing Sanbo Brain Hospital, Capital Medical University, Epilepsy Center, Beijing, China

Purpose: To study the relationship between different pathological types of focal cortical dysplasia and the morphology of epileptiform discharges on electroencephalography (EEG) in the patients with intractable epilepsy.

Method: Case series of 91 patients (male: female = 54:37), aged 12.7 ± 9.76 years, with a histopathological diagnosis of FCD (based on the consensus classification proposed by an ad hoc Task Force of the ILAE Diagnostic Methods Commission). All patients were examined by long-term scalp video EEG mornitoring before operation and some of them were also monitored by long-term intracranial EEG.The morphology of the interictal discharges on scalp EEG were divided into four types:

(1) no epileptiform discharges;
(2) spikes;
(3) spikes and /or polyspikes;
(4) spikes, polyspikes and/or fast rhythms.

The morphology of the seizure onset was divided into four types: spikes, polyspikes and/or fast rhythms, electro-decremental and unclassified. Fisher's exact test was used to evaluate the relationship between different types of FCD and scalp EEG.

Results: Of 91 patients, there were 10 with FCD Ia, 21 with FCD Ib, 19 with FCD IIa, 20 with FCD IIb, and 21 with FCD III. There were significant difference between different types of FCD in the morphology of interictal discharges (Fisher exact test, $p = 0.013$), and spikes and /or polyspikes was more common in FCD IIa and FCD IIb and the type of spikes, polyspikes and/or fast rhythms was more common in FCD IIa. Spikes were more common in FCD I and FCD III. But no relationship was found between the morphology of the seizure onset and FCD types (Fisher exact test, $p = 0.1976$).

Conclusion: In the patients with intractable epilepsy caused by FCD, the morphology of interictal discharges in scalp EEG is probably related to the pathological types of FCD and the pathological type probably can be suggested based on the morphology of interictal discharges.

057

SPIKE ASSOCIATED HIGH FREQUENCY OSCILLATIONS IN MAGNETOENCEPHALOGRAPHY CO-LOCALIZE WITH FOCAL CORTICAL DYSPLASIA TYPE IIB

Heers M[1], Jacobs J[2], Hirschmann J[3], Duempelmann M[2], Aydin U[4], Wolters CH[4], Rampp S[5], Stefan H[5], Schnitzler A[3], Wellmer J[1]

[1]Ruhr-Epileptology/Department of Neurology, Bochum University Hospital, Bochum, Germany, [2]Epilepsy Centre, Freiburg University Hospital, Freiburg, Germany, [3]Institute for Clinical Neuroscience and Medical Psychology, Heinrich-Heine-University, Duesseldorf, Germany, [4]Institute for Biomagnetism and Biosignalanalysis, Muenster University, Muenster, Germany, [5]Department of Neurology/ Epilepsy Centre, Erlangen University Hospital, Erlangen, Germany

Purpose: High frequency oscillations (HFO) in invasive recordings are a marker of epileptogenicity in patients with focal epilepsy. In magnetoencephalography (MEG) high gamma activity and HFO could

be localized to the epileptogenic zone. The aim of the current project is to noninvasively co-localize visually detected HFO in MEG recordings with the MRI positive part of the Focal Cortical Dysplasia (FCD).

Method: In five epilepsy patients with MRI-based diagnosis of FCD simultaneous MEG and scalp-EEG (MEEG) were recorded with a sampling rate 2400 Hz. MEG and EEG data were visually analysed in the frequency band of 3–70 Hz for the occurrence of epileptic spikes and in the frequency band of 70–300 Hz for HFO/High gamma activity. Without filtering frequency domain beamforming was used for the source localization of spikes and HFO.

Results: HFO associated with epileptic spikes were recorded in 3/5 patients in MEG and in 1/5 in EEG. MEG-identified HFO in the frequency band between 70 and 120 Hz could be localized to the epileptogenic lesion. HFO recorded by EEG correlated with the FCD in sensor space. The high frequency component of epileptic spikes localized more accurately to the lesion than low frequency parts of the spikes.

Conclusion: It is possible to visually detect spike-associated HFO in MEG recordings and to localize them in spatial concordance with the FCD using frequency domain beamforming. This approach might allow to noninvasively identify the epileptogenic zone in non-lesional cases.

Funding: DFG, FoRUM Commission Bochum University, Germany.

058
PATHOLOGICAL SUBSTRATES OF INTRACRANIAL EEG SEIZURE-ONSET PATTERNS

Perucca P[1], Dubeau F[1], Gotman J[1]
[1]Montreal Neurological Institute and Hospital, McGill University, Montreal, QC, Canada

Purpose: To investigate intracranial EEG seizure-onset patterns associated with different epileptogenic lesions, and to define the high-frequency oscillation (HFO) correlates of each pattern.

Method: We analyzed representative seizure types from 33 consecutive patients with drug-resistant focal epilepsy and a structural MRI lesion (11 mesial temporal sclerosis – MTS, nine focal cortical dysplasia, six cortical atrophy, three nodular heterotopia, three polymicrogyria, and one tuberous sclerosis complex) undergoing wideband depth-electrode EEG investigations. Patients were included if seizures arose from contacts located in lesional/peri-lesional tissue, and if clinical manifestations followed electrographic onset. Seizure-onset patterns were defined independently by two reviewers blinded to clinical information, and consensus was reached after discussion. For each seizure, preictal and ictal sections were selected for HFO analysis.

Results: In the 53 seizures sampled, seven intracranial EEG seizure-onset patterns were identified: low-voltage fast activity (43%); low-frequency high-amplitude periodic spikes (21%); sharp activity at ≤13 Hz (15%); spike-and-wave activity (9%); burst of high-amplitude polyspikes (6%); burst suppression (4%); delta brush (4%). Each pattern was found across all or several pathologies, except for low-frequency high-amplitude periodic spikes, only observed with MTS, and delta brush, exclusive to focal cortical dysplasia. However, MTS did not always result in low-frequency periodic spikes and focal cortical dysplasia in delta brush. Each pattern was accompanied by a significant increase in HFOs upon seizure-onset.

Conclusion: Although certain epileptogenic lesions may be associated with pathognomonic intracranial EEG signatures at seizure onset, biologically-distinct pathologies share seizure-onset patterns, suggesting that different brain insults affect similarly neuronal networks underlying seizure generation.

059
NETWORK OSCILLATIONS MODULATE NEURONAL ASSEMBLIES AND INTERICTAL EPILEPTIFORM SPIKE FREQUENCY DURING HUMAN MEMORY

Kucewicz M[1], Matsumoto J[1], Bower M[1], Stead M[1], Matsumoto A[1], Peters P[1], Brinkmann B[1], Danstrom J[1], Goerss S[2], Marsh R[2], Meyer F[2], Worrell G[1]
[1]Mayo Clinic, Neurology, Rochester, MN, USA, [2]Mayo Clinic, Neurosurgery, Rochester, MN, USA

Purpose: This study investigated the effect of brain network oscillations underlying cognitive processing on the interictal epileptiform spike (IES) activity, with the objective to elucidate the mechanisms of and relationship between cognition and spiking.

Method: Eleven patients being evaluated with intracranial micro- and macro-electrode recordings for medically resistant temporal lobe epilepsy participated in a visual recognition memory task. The IES count was compared between task epochs preceding and following presentation of images for subsequent recall, together with the changes in power of local field potential oscillations and single unit activity in the hippocampus, amygdala and temporal cortex.

Results: During successful, but not unsuccessful, encoding of the viewed images there was a significant suppression of IES rate in hippocampus, amygdala and temporal cortex. This effect coincided with a wide-spread decrease in the power of low frequency (4–28 Hz) network oscillations in the theta, alpha and beta bands, and focal increase in gamma power (30–150 Hz) emerging early in memory encoding (0–2000 ms after image presentation). The IES suppression was most strongly correlated with the low frequency power decrease of local field potential oscillations. The causal relationship between these slow network oscillations and mechanisms of IES generation was supported by surge of low frequency power consistently preceding spikes emergence by approximately 200 ms.

Conclusion: We conclude that IES discharge is modulated by distinct patterns of network oscillations underpinning human memory offering a new mechanistic insight into the interplay between cognitive processing, local field potential dynamics and epileptogenesis.

060
A COMPARISON OF CONTINUOUS VIDEO EEG MONITORING AND 30 MIN EEG IN AN ICU SETTING

Khan O[1], Azevedo C[2], Hartshorn A[3], Montanye J[4], Gonzalez J[5], Arshad S[6], Natola M[3], Surgenor S[3], Morse R[3], Nordgren R[3], Bujarski K[3], Holmes G[3], Jobst B[3], Scott R[3], Thadani V[3]
[1]St. Luke's Medical Center, Bethlehem, PA, USA, [2]Yale School of Medicine, Hartford, CT, USA, [3]Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA, [4]MidState Medical Center, Meriden, CT, USA, [5]Erlanger Health System, Chattanooga, TN, USA, [6]Sacramento Medical Center, Sacramento, CA, USA

Purpose: Continuous video encephalographic monitoring (cvEEG) is increasingly recommended for use in intensive care units. We aimed to determine whether there is added benefit from prolonged cvEEG when compared to a routine 30-minute study in detecting and treating seizures or epileptiform discharges in critically ill patients.

Methods: One hundred and thirteen consecutive patients in a medical/surgical ICU, for whom an EEG was requested as part of neurological evaluation, were prospectively assigned to either routine a 30-minute EEG or 16–24 h of cvEEG. 34 unselected patients underwent routine 30-minute EEG. 83 unselected patients received cvEEG for 16–24 h. 13 patients with known seizures were deliberately placed on cvEEG. EEG results were reported to the treating team the following day. Charts were

reviewed retrospectively to analyze EEG results and the impact of prolonged EEG recording on subsequent treatment and outcome.

Results: Of the 34 routine 30-minute EEGs, one was normal, 27 were slow and/or poorly reactive, and 6 (18%) showed epileptiform activity. Of the 83 cvEEG recordings all were slow and/or poorly reactive, and 28 (34%) showed epileptiform findings in the first 30 min ($p = 0.002$). In all other respects the two groups appeared to be similar. Of the 83 patients receiving cvEEG, 12/83 (14%) developed additional epileptiform abnormalities overnight, but only 3 (4%) benefited from a change in treatment based on the EEG findings. Of the 13 patients with known seizures who were deliberately placed on cvEEG, nine had epileptiform findings initially, and one had epileptiform abnormalities overnight. 6/13 patients (46%) benefited from a change in treatment based on the EEG ($p < 0.001$).

Conclusion: We concluded that cvEEG in an unselected intensive care setting provides little additional benefit compared to a routine 30-minute EEG. In a selected population, the benefit may be greater.

Platform Session: Clinical epilepsy
Tuesday, 25th June
14:30–16:00

061
ANALYSIS OF RISK FACTORS FOR FIRST TIME SEIZURES AFTER CEREBROVASCULAR ACCIDENTS IN CHINESE PATIENTS

Wang G[1], Chen C[1], Jia H[2], Lang S[3], Liu X[4], Xia C[5], Sun Y[6], Zhang J[1]

[1]Department of Neurology, Provincial Hospital Affiliated to Shandong University, Jinan, China, [2]Department of Neurology, Jinan Military General Hospital, Jinan, China, [3]Department of Neurology, PLA General Hospital, Beijing, China, [4]Department of Neurology, Nanjing General Hospital of Nanjing Military Command, Nanjing, China, [5]Department of Neurology, Shenyang Military General Hospital, Shenyang, China, [6]Department of Cardiovascular Functional Studies, China Meitan General Hospital, Beijing, China

Purpose: The main objective of our study is to assess the risks and predict the early and late occurrence of seizure after first-ever stroke.

Method: We retrospectively studied 2474 consecutive patients with initial stroke in China during an 11-year period (1997–2007). All patients were evaluated and treated as inpatients in the same period after first-ever stroke. We investigated 24 clinical and radiological indexes. Odds ratio (OR) and 95% confidence interval after adjustment for possible confounding variables were calculated by logistic regression.

Results: Two hundred and thirty-two (11.1%) of these stroke patients developed seizures during a mean follow-up period of 18 months, with 123 experienced early-onset and 109 late-onset seizures.The independent risk factors for early post-stroke seizure were large lesion (OR = 9.36), subarachnoid hemorrhage (OR = 5.28), initial electrolyte disturbance (OR = 2.10), andcortical involvement of the stroke (OR = 1.33). The independent risk factors for late post-stroke seizure were cortical involvement (OR = 11.84) and large lesion (OR = 1.87). In theunivariate analysis, hypertension was associated with late seizures (2 = 6.092, $p = 0.014$), whereas it lost its significance as an independent risk factor for late seizures in the multivariate analysis.

Conclusion: The decisive factors associated with early post-stroke seizure are large lesion, subarachnoid hemorrhage and cortical involvement. Surprisingly, electrolyte disturbance in stroke patients also predicts seizure. We attribute these seizures to cerebral cellular biochemical dysfunction associated with stroke. Cortical involvement is the main risk factor for late post-stroke seizure.

062
SEIZURE PHENEMENOLOGY INFERRED FROM CLINICAL DESCRIPTORS OF CAREGIVERS AND ITS CONCORDANCE TO ONLY VIDEO AND VIDEO-EEG RECORDINGS

Tripathi M[1], Padma V[1], Chandra S[2], Mehta S[2], Bhavya G[2]

[1]All India Institute of Medical Sciences, Neurology, Delhi, India, [2]All India Institute of Medical Sciences, Delhi, India

Purpose: The diagnosis of epilepsy and seizure type largely remains a clinical one. Varied education levels in India could cast a difficulty in lateralising and making a clinical judgement of seizure type.The purpose of this study was to assess the accuracy of the seizure phenemenology and descriptors derived from interpretation of the caregiver description in comparison with the semiology derived from only video obtained on mobile phones and digital cameras using the gold standard as video- EEG recordings obtained from the EMU.

Method: Patients were enrolled into the study after taking an informed consent. A detailed history by the resident of pre, post and intraictal phenomenon was taken. Care was taken to document aura, automatisms and sequence of involvement. Any event that had been recorded at home by digital cameras or mobile phones. Video recording were interpreted by MT who was blinded with the details of the clinical history of the patient except the name,age, developmental history and any co existing neurological abnormality.

Results: Six hundred and eighteen seizures in 340 patients with episodes in the epilepsy monitoring unit were evaluated. 241 seizures from 120 patients were analysed on home videos too. For each concordance (four choices) based clinical descriptions and, separately, of the home video recordings (where available) were compared at the end of the diagnostic work-up, and then compared with the video-EEG recordings (gold standard). Concordance was seen more significantly based on the interpretation of video recordings (82%) than on the clinical descriptions (46%), and the overall accuracy was higher for the video recordings (85%) than for the descriptions (44%). Concordance with the VEEG was not much for the descriptions ($k = 0.47$) and almost perfect for the video recordings ($k = 0.93$).

Conclusion: Video recordings significantly increase the accuracy of seizure interpretation where caregiver education and observation may alter the seizure type.

063
UTILITY OF HOME-MADE VIDEOS IN AN EPILEPSY CLINIC

Ojeda J[1], Ivanez V[2], López Gallardo S[3], Gutierrez-Gutierrez G[1], Miralles A[4]

[1]Adult Neurology, Hospital Universitario Infanta Sofía, Madrid, Spain, [2]Neurology, Epilepsy Unit, Hospital Universitario La Paz, Madrid, Spain, [3]Primary Physisian Outpatient Center, Madrid, Spain, [4]Hospital Universitario Infanta Sofía, Madrid, Spain

Purpose: The definition of epilepsy requires the occurrence at least one epileptic seizure(ILAE). Up to 20% of patients diagnosed of epilepsy are not actually epileptic. An accurate diagnosis is necessary for a satisfactory management of epileptic and non-epileptic patients.

New broad access image technologies allow patients and families to record homemade videos helping neurologists in diagnosis.

Method: During a two year period in an epilepsy clinic, consecutive patients/relatives were encouraged to record their events with any available device. Instructions for good-quality videos were given.

Three neurologists/epileptologists watched the videos in clinical session, rated the quality of the recordings following some parameters and made a clinical diagnosis. The seizures were classified according to the ILAE seizure classification.

Results: Three hundred and fourteen consecutive patients(relatives) were encouraged to record events. 52% male. Average age:46 year. 267 patients had video recording devices available(87%)(photo camera:100%, cell-phone:100%, webcam:10%, video-camera:30%). From this group, 135(50%) felt unable to record events. Reasons given: low seizure frequency:60%, seizures short duration:80%, lack of time spent with patient:30%.

Fifty events from 22 patients were recorded. Average age: 35 year. Seizure frequency three months prior to video deposit was 3.5 seizures/patient/month.

Previous epileptic syndrome diagnosed (based on description/neuroimaging/EEG recordings): 15 focal temporal lobe epilepsy, four focal frontal probably symptomatic epilepsy, three epileptic encephalopathy.

Type of seizures recorded: Focal motor with typical automatisms: 14 seizures/11 patients. Focal motor with hyperkinetic automatisms: nine seizures/two patients. Asymmetrical tonic motor seizures: four seizures/one patient. Focal clonic seizure: five seizures/one patient. Atypical absence seizure: six seizures/three patients. Non-epileptic seizure(NES): 13 seizures/3 patients. Postural tremor: one patient.

There was agreement in diagnosis but in one. Eighteen patients were confirmed in their diagnosis. Epilepsy misdiagnosis: 4. Three NES and one postural tremor.

Conclusion: Homemade videos may be of diagnostic value in epilepsy management. Training patients and relatives in performing good-quality videos is necessary.

064

AUTONOMIC FUNCTION IN SYNCOPE AND SEIZURE

Yerdelen D[1], Erol T[2]

[1]Department of Neurology, Baskent University School of Medicine, Adana, Turkey, [2]Department of Cardiology, Baskent University School of Medicine, Adana, Turkey

Purpose: To differentiate syncope and epilepsy may be difficult in clinical practice. Convulsive activity, incontinence, fall and injury associated with this fall may be encountered in both of the conditions. The mostly seen etiology of syncope are vasovagal, cardiogenic and orthostatic hypotension. Also, cardiac arrhythmia and syncope associated with seizure may develop. In this study, it was aimed to assess autonomic function in patients with syncope or seizure.

Method: Nine patients with syncope, 10 with seizure evaluated according to the history and 10 control subjects at a mean age of 29 years were included in this study. The subjects with normal neurological examination and normal cerebral magnetic resonance imaging, electrocardiography and echocardiography findings were selected. The subjects underwent exercise tolerance tests according to the modified Bruce protocol and heart rate recovery (HRR), an index of vagal activity, at 1 and 3 min (HRR1 and HRR3) were calculated. Heart rate variability measurements are gathered from a 24-h electrocardiogram recordings.

Results: The measurements associated with heart rate variability was significantly different among syncope, seizure and control groups ($p < 0.05$). Also, the difference in syncope group was more prominent compared with seizure group. However, HRR1 and HRR3, the heart rate recovery parameters derived by exercise tolerance test, were similar among groups. However, peak systolic and peak diastolic blood pressure were found decreased in seizure group compared with conrtol and syncope groups ($p < 0.05$).

Conclusion: The established changes in autonomic function including sympathetic and parasympathetic system in both syncope and seizure suggest that these conditions in which cardiac arrhythmia may play a role at the beginning or at the end of the event share an identic pathophysiology through this direction.

065

BETTER UNDERSTANDING OF EPILEPSY-RELATED MORTALITY: THE ACTIONS OF THE FRENCH SENTINEL NETWORK

Picot M-C[1,2], Faucanié M[1], Andrès J[1], Larquier B[2], Jaussent A[1], Valton L[2,3], Hirsch E[4], Derambure P[2,5], Marchal C[2,6], Martin B[7], Ryvlin P[2,8], Tourniaire D[9], Trottier S[2], Allonneau-Roubertie E[10], Arzimanoglou A[2,8], Biraben A[2,11]

[1]CHU Montpellier, Montpellier, France, [2]French League against Epilepsy [LFCE], Tain l'Hermitage, France, [3]CHU Toulouse, Toulouse, France, [4]CHU Strasbourg, Strasbourg, France, [5]CHU Lille, Lille, France, [6]CHU Bordeaux, Bordeaux, France, [7]Université de Rennes, Rennes, France, [8]HC Lyon, Lyon, France, [9]Etablissement la Teppe, Tain l'Hermitage, France, [10]French foundation for Epilepsy Research [FFRE], Paris, France, [11]CHU Rennes, Rennes, France

Purpose: Mortality is three to five times higher in epileptic patients than in the general population, with a particularly high risk of sudden unexpected death (SUDEP) among young adults. In 2010, the French League against epilepsy (LFCE) founded the French sentinel network on epilepsy-related mortality. It aims to inventory epilepsy-related deaths to describe their causes and circumstances, improve communication and collect needs and expectations of bereaved families.

Method: Death cases are mainly reported by physicians (100 epileptologists and neuro-pediatricians) of the network in the French areas, with family agreement. Death circumstances, epilepsy characteristics, medication, compliance, medical history and recent life events are collected. In case of SUDEP, bereaved families are interviewed by a psychologist to identify risk factors. The protocol has been approved by the Ethics committee of Lyon, France.

Results: Since January 2010, 94 deaths have been recorded (SUDEP: 78%, accidents: 7%, drowning: 4%). Mean age of patients who died from SUDEP was 30 years and 80% of them were drug resistant. Forty-three interviews were conducted with families. A network of bereaved families was established in 2011 to support them. A website (www.mortalite-epilepsie.fr) provides information to epileptic patients and their families about the network activities and mortality risk.

Conclusion: Increasing communication about risk of SUDEP would improve patient involvement, particularly compliance, and would strengthen confidence in health professionals. The collected information provides valuable insights to understand early mortality in epileptic patients.

Acknowledgements: Supported by grants from LFCE and French Foundation for Epilepsy Research (FFRE)

066

TELE-EPILEPSY: DEVELOPING A MULTI-MODAL DEVICE FOR NONEEG, EXTRAMURAL, NOCTURNAL SEIZURE MONITORING

Andel J. M. van[1,2,3,4], Tele-Epilepsy Consortium

[1]University Medical Centre Utrecht, Utrecht University, Utrecht, Netherlands, [2]Rudolf Magnus Institute of Neuroscience, Utrecht, Netherlands, [3]Kempenhaeghe – Epilepsy Institue in the Netherlands, Heeze, Netherlands, [4]SEIN – Epilepsy Institute in the Netherlands, Zwolle, Netherlands

Purpose: In epilepsy, 25% of patients have regular, intractable seizures, especially children with epilepsy syndromes and patients with gross brain abnormality and cognitive impairments. About half of seizures will be at

night, posing problems in these vulnerable patient groups who depend on caregivers not sleeping in the same bed. A reliable seizure detection and alert system will provide a major step in patient safety, care, quality of life and disease management, however presently this is lacking. In this project a new multimodal device using an optimized combination of nonEEG sensors is developed. Based on preliminary studies 4 modalities were selected: audio, automated video frame analysis, ECG and 3D-accelerometry.

Method: A diagnostic study design is used to define optimal combinations of algorithms analyzing the 4 modalities in the target population: children under 18 years of age, and mentally impaired adolescents and adults with major nocturnal seizures. The multimodal device is tested in an in-hospital setting in 100 patients, simultaneously with the gold standard of clinical video-EEG.

Modern methods of classification and regression analysis are applied to define optimal sets of joint thresholds for the modalities. The aim is to achieve a high detection rate for seizures, with a minimum of false alarms in seizure free periods. Patient factors are taken into account, potentially allowing for tuning thresholds to invidual patients.

Results: In 2012 data was collected in 49 patients, in 11 patients major nocturnal seizures were recorded. An interim-analysis of results of 50 patients will be presented in June 2013.

Conclusion: In this study, the performance of a newly developed device for home detection of epileptic seizures during sleep in children and mentally impaired adults with major nocturnal seizures is tested.

Platform Session: Neuropsychology
Tuesday, 25th June
14:30–16:00

067
SOCIAL COGNITION DISORDERS IN TEMPORAL LOBE EPILEPSY PATIENTS

Hennion S[1,2], Delbeuck X[1], Lopes R[1], Tyvaert L[1,2], Derambure P[1,2], Szurhaj W[1,2]

[1]University Medical Center, Lille, France, [2]Laboratory of Functional Neurosciences and Pathologies (EA 4559), Lille, France

Purpose: In temporal lobe epilepsy patients (TLE), recent behavioral studies have demonstrated impaired social cognition. Social cognition abilities are necessary to establish adequate and appropriate social interactions. We studied the social cognition disturbances in TLE patients, aiming to further characterize them.

Method: An evaluation protocol of social cognition abilities was used in 45 TLE patients and 45 matched healthy controls. We analyzed several parameters:

(1) the emotional identification ability,

(2) the ability to feel emotional content during the presentation of emotional scenes and,

(3) the theory of mind ability (inferences about the other's mental states) during tasks testing the detection and the interpretation of verbal blunders (Faux Pas task) and of sarcasms during social interactions.

Results: Compared with matched healthy controls, patients TLE showed:

1) difficulties identifying emotional multimodal specifically affecting the recognition of fear and anger; however, the recognition of joy was preserved;

2) modification of emotional experience during emotional scenes;

3) Faux Pas and sarcasms still detected but associated with reduced interpretation accuracy.

The effect of the epileptic focus side (left or right) and of a lesion (with or without hippocampus sclerosis) has been also analyzed.

Conclusion: These results support the hypothesis of a specific cognitive profile in TLE patients partly characterized by an impairment of social cognition. These disorders may disturb communication and interpersonal interaction. Thus, they could be involved in the emergence of psychoaffective disorders, such as anxiety or depression, common in TLE patients. However, this interaction remains to be further explored.

068
THE IMPACT OF INTERVENTION ON WORKING MEMORY IN CHILDREN WITH INTRACTABLE EPILEPSY: PRELIMINARY RESULTS FROM A REPEATED MEASURE STUDY

Kerr EN[1,2], Alavie N[1], Blackwell M[1]

[1]Department of Psychology, The Hospital for Sick Children, Toronto, ON, Canada, [2]Department of Paediatrics, The University of Toronto, Toronto, ON, Canada

Purpose: Difficulties with attention and working memory (WM) are among the most common cognitive deficits associated with epilepsy and have significant implications for life outcomes. Research documenting the efficacy of interventions aimed at improving these skills for those with epilepsy is virtually non-existent. We examine the effectiveness of a commercially available, computer-based, WM intervention (Cogmed™) in improving attention and WM in children with intractable epilepsy.

Method: Nineteen children (6–15 years, 12 females) with intractable epilepsy from an Epilepsy Clinic with intelligence (IQ) falling above the 2nd percentile participated. Performance changes on cognitive assessment (IQ, attention span, WM, sustained attention, learning) pre (T1) to post (T2) five weeks of 25 self-adjusting computer sessions was completed. Twelve children were waitlisted (W). The influences of seizure variables, age, IQ, and co-morbid diagnoses were evaluated.

Results: Significant T1–T2 standard scores improvements were documented in visual sustained attention reaction time ($p < 0.05$) and in auditory and visual WM; namely, listening recall ($p < 0.05$), backward digit span ($p < 0.01$), central executive ($p < 0.05$), spatial span forward ($p < 0.05$) and backward ($p < 0.01$). Effect sizes (n^2_p) were small to medium. No significant differences were documented from W to T1. Children on monotherapy ($n = 9$) performed significantly better than those on polytherapy at T2 on auditory attention span ($p < 0.01$), rote learning ($p < 0.01$), and retention ($p < 0.05$). T2 WM reaction time and T2 central executive were significantly correlated with IQ ($p < 0.05$). Neither age nor presence of co-morbidities ($n = 12$; ADHD, PDD, Anxiety, Oppositional behaviour) was significantly related to cognitive indices.

Conclusion: Significant improvements in age-adjusted scores and lack of change without intervention indicate that Cogmed™ is promising for improving attention, WM, and learning in some children with intractable epilepsy. A larger cohort will increase power and aid in determining which seizure and demographic variables influence outcome.

069
THE NATURE & EXTENT OF COGNITIVE DISRUPTION IN MESIAL TEMPORAL LOBE EPILEPSY RELATIVE TO UNAFFECTED SIBLINGS AND HEALTHY CONTROLS

Maher H[1,2], Pender N[2], Delanty N[3], Doherty C[4], Burke T[1]

[1]School of Psychology, University College Dublin, Dublin, Ireland, [2]Department of Psychology, Beaumont Hospital, Dublin, Ireland, [3]Department of Neurology, Beaumont Hospital,

Dublin, Ireland, [4]Department of Neurology, St. James's Hospital, Dublin, Ireland

Purpose: Despite extensive research on mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE+HS), many questions regarding neuropsychological status remain unanswered. Through a range of research studies, we aimed to clarify both the nature and extent of neuropsychological disturbance in this patient cohort. In order to investigate factors beyond the direct and indirect effects of seizures that might influence cognitive performance, a pre-operative MTLE+HS sample was compared to their unaffected siblings and to standardised norms. Unaffected siblings were further compared to a meticulously matched control sample.

Method: Thirty four patients with unilateral MTLE+HS (21 female; 13 male), 34 unaffected same-sex siblings and 34 matched controls were evaluated on an extensive test battery.

Results: As a group, the MTLE+HS cohort exhibited poorer performance on a range of tests relative to both published norms and relative to unaffected siblings. However, two distinct cognitive phenotypes ('intact' and 'impaired' on IQ) were identified by cluster analysis, with both patient clusters performing more poorly than their unaffected siblings on selected tests. Additionally, results revealed that siblings of 'impaired' patients showed subtle cognitive disruption on some test measures relative to carefully matched control participants.

Conclusion: In line with current literature, our results indicate that cognitive disruption in the patient cohort extends beyond the domain of memory. Furthermore, results point to possible vulnerability in families with MTLE+HS and we conclude that at least some portion of cognitive difficulty seen in MTLE+HS may be attributable to factors other than the direct and indirect effects of epilepsy and its treatment.

070
ACCELERATED LONG-TERM FORGETTING IN CHILDREN WITH TEMPORAL LOBE EPILEPSY

Gascoigne M[1], Webster R[2], Barton B[3], Gill D[2], Smith ML[4,5], Lah S[1]

[1]School of Psychology, The University of Sydney, Sydney, NSW, Australia, [2]Department of Neurology, The Children's Hospital at Westmead, Sydney, NSW, Australia, [3]Children's Hospital Education Research Institute, The Children's Hospital at Westmead, Sydney, NSW, Australia, [4]University of Toronto Mississauga, Toronto, ON, Canada, [5]Hospital for Sick Children, Toronto, ON, Canada

Purpose: Accelerated long-term forgetting (ALTF) involves difficulties in recall following long delays despite normal recall after short delays. Previous ALTF studies have focussed on adults with temporal lobe epilepsy (TLE), with little focus on children. Furthermore, in children with TLE, deficits in short-term recall have been shown to emerge during development. It is unclear whether long-term recall deficits develop in a similar fashion. This study examined the presence and potential development of ALTF in children with TLE.

Method: The study included 23 children with TLE and 58 healthy control children (NC), matched on sex distribution, age and SES, but not IQ (TLE < NC). Participants completed a battery of neuropsychological tests, including a list-learning task that required recall of information after short (2- and 30-min) and long delays (7 days) and 7-day recognition.

Results: A two-way analysis of covariance (group x time, controlling for IQ) on list-learning found a significant interaction ($p < 0.05$) and main effect of delay ($p < .001$), but not group. Planned contrasts revealed that, compared to the NC group, TLE participants displayed a significant reduction in the proportion of words recalled from 30-mins to 7-days ($p < 0.05$), but not from 2-mins to 30-mins and had poorer 7-day recognition ($p < 0.01$). Within the TLE, but not NC group, age was negatively correlated (*ps* < 0.05) with recall after short (2- and 30-mins: $r = -0.49$ and $r = -0.50$) and long delays ($r = -0.62$) and recognition ($r = -0.43$), but not with the decrease in recall from 30-mins to 7 days.

Conclusion: To our knowledge, this is the first study to find evidence of ALTF in children with TLE. Furthermore, our findings suggest that difficulties with long-term recall and recognition are likely to be found in older children with TLE.

071
DEVELOPMENT OF A HOME-BASED INTERVENTION TO ADDRESS COGNITIVE DYSFUNCTION IN EPILEPSY

Caller TA[1], Secore K[1], Ferguson RJ[2], Roth R[3], Kleen J[1], Scott R[1], Alexandre FP[1], Jobst BC[1]

[1]Department of Neurology, Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA, [2]Department of Psychology, Eastern Maine Medical Center, Bangor, ME, USA, [3]Department of Psychology, Geisel School of Medicine at Dartmouth, Hanover, NH, USA

Purpose: Psychosocial comorbidities such as depression and cognitive dysfunction are often neglected in the process of delivering epilepsy care. Limited treatment options and resources with which to intervene represent a major barrier. Our objective was to ascertain the degree of self-reported cognitive symptoms in our epilepsy population and determine if an intervention could be developed to address cognitive symptoms.

Methods: To ascertain the degree of subjective cognitive dysfunction in an outpatient epilepsy population, the six questions comprising the cognitive subset of the validated Quality of Life in Epilepsy (QOLIE-31) scale were administered to all patients at every clinic encounter over a four month period. Based on the findings, an intervention was developed to address cognitive dysfunction.

Results: One hundred and fifteen patients seen in the epilepsy clinic yielded an average cognitive score of 49 on a scale of 0–100 (with zero indicating very poor cognitive function). A documented seizure within the past month increased the likelihood of a cognitive score below 50 ($p = 0.01$). Based on the high prevalence of cognitive symptoms and the impact these symptoms have on quality of life, we developed a self-management program called HOBSCOTCH (HOme Based Self-management and Cognitive Training CHanges lives). HOBSCOTCH utilizes problem solving therapy, which is widely used in treating depression. Compensatory strategies for enhancing memory in day-to-day life are taught primarily over the phone. Working memory training via a commercially available device (Nintendo, Inc. Brainage®) will be delivered to a subset of patients.

Conclusion: There is a high prevalence of cognitive dysfunction in epilepsy, supporting a clear need for a cost-effective intervention. The feasibility and effectiveness of HOBSCOTCH is currently being evaluated. Our primary outcome is to improve quality of life, with secondary outcomes of mood, subjective memory symptoms, objective memory, executive function and depression.

This work is supported by the CDC 3U48DP001935-04S3.

072
UNILATERAL MESIAL TEMPORAL EPILEPSY IMPAIRS REMOTE BRAIN ACTIVATION AND SOCIAL COGNITION

Toller G[1], Broicher SD[1], Grunwald T[1], Huber D[2], Krämer G[1], Kurthen M[1], Jokeit H[1]
[1]Swiss Epilepsy Center, Zürich, Switzerland, [2]MRI Institute Dominik Huber, Zürich, Switzerland

Purpose: Unilateral mesial temporal lobe epilepsy (MTLE) has been associated with impaired social cognition and ipsilateral amygdala dysfunction. Due to the high prevalence of functional alterations in structures remote from the mesial temporal lobe, deficits in social cognition may not merely be attributable to amygdalar dysfunction. Whether a dysfunctional amygdala causes functional changes in remote regions underlying social cognition has yet to be thoroughly investigated. Therefore, in this multiple case study, the frequencies and topographic distributions of cortical and subcortical BOLD-responses to animated fearful faces were described in patients with unilateral MTLE.

Method: A previously validated fearful face paradigm with proven reliability to evoke amydala activation in single cases (Schacher, 2006a) was used in 50 patients with unilateral MTLE (24 right-sided) and 25 healthy controls. Single-subject fMRI analyses were applied. At the behavioral level, both affective and cognitive aspects of self-reported empathy and theory of mind (ToM) were assessed.

Results: Right and left MTLE was associated with functional alterations in remote frontal and limbic-paralimbic regions. Notably, these functional modulations were more prominent in patients with right- than left-sided seizure onset. Consistent with these findings, both affective and cognitive aspects of self-reported empathy and TOM were more severely impaired in patients with right than left MTLE.

Conclusion: These results indicate that impaired social cognition in MTLE is associated with predominantly right frontal lobe dysfunctions attributable to remote influences of the primary epileptogenic zone. These findings shed further light on the etiopathogenesis of impaired social cognition in patients with unilateral MTLE.