



Society Proceedings

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1. Alternating hemiplegia of childhood into adulthood (AHCA): Case series and literature update—Reem Alyoubi, Ingrid Park, Joe Embuido, Paul Hwang (Departments of Paediatrics & Medicine, Univerisy of Toronto, UTERP, EpLink-OBI, King Abdulaziz University, Jeddah, Saudi Arabia, North York General Hospital, Toronto, Canada)

Objective: To describe the clinical and electrophysiological characteristics of 3 cases of AHC, including novel treatment (off-label use).

Study design: We report three patients with AHCA. The clinical phenotype comprises of episodes of hemiplegia that moves from one side of the body to the other. The onset of the weakness usually occurs in the first few months of life. Movement disorder such as dystonia can also accompany the hemiplegic attacks in 2/3 cases. Intellectual impairment and epilepsy have been reported in these patients. However, the onset of seizures is usually in the age range between 3 and 4 years. Half the children with AHC have epilepsy, and these seizures are usually quite distinct from AHC attacks in their manifestations, although they may occur simultaneously. If an EEG is recorded during the seizure it usually shows an appropriate abnormality, but between seizures the EEG is normal. Seizures may be prolonged in two forms: epilepsy partialis continua or a more generalized convulsive status epilepticus. There is no agreed specific drug for seizure prevention in AHCA, and indeed, the epilepsy is often resistant to treatment. It is usual to give antiepilepsy drugs (AEDs) if the child has epilepsy, but one should monitor their effect and not continue in the face of side effects and poor efficacy. The management of these cases is challenging. The only drug with some efficacy is flunarizine and AEDs for seizure control. A trial of gamma-hydroxy butyrate (GHB) in $N = 1$ study had some efficacy and lateralised EEG changes contralateral to the side of hemiplegia, reversing with GHB.

Results: The diagnosis of AHCA was confirmed by the finding of ATP1A3 gene mutation in all 3 patients. In 2/3 cases the disorder extended into adulthood necessitating a name change: AHCA for the same genotype.

Discussion: The mutation found to be associated with AHCA is the ATP1A3 gene in 3/3 cases, reported in a majority of AHCA patients, with some familial cases.

Conclusion: AHCA is very uncommon, likely underdiagnosed clinically but with a high index of suspicion for early diagnosis and appropriate therapy, may ameliorate outcome and long-term prognosis in a larger RCT study.

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2. Characterization of the tuberous sclerosis complex population in the province of Quebec: Healthcare services utilization and long term outcome—A. Bernier^a, J.S. Landry^b, A.S. Kristof^b, L. Carmant^a, P. Major^a (^aUniversity of Montreal, Canada, ^bMcGill University, Canada)

Background: Tuberous sclerosis complex (TSC) is a neurocutaneous syndrome that can present with many disabling neurological disorders, the most common being epilepsy. Although it is a chronic multi-system disease, healthcare utilization and long-term outcome of subjects with TSC are not yet well defined. The goal of this study was to evaluate the direct cost and long-term outcome of TSC in the province of Quebec, compared to other forms of epilepsy and healthy controls.

Methods: Our provincial health care database was interrogated to determine use of medical services by patients with TSC, epilepsy and healthy controls from 1996 to 2011. Data on demographics, outcomes and health care utilization were analyzed.

Results: 1004 TSC, 41,934 with epilepsy and 41,934 controls were identified. The prevalence of TSC was 1/7872 compared to 1/189 for epilepsy. TSC experienced more hospitalizations, medical visits and prescription drug use. Their most common admission diagnosis was seizures and age at death was significantly lower: 61.3 years old for TSC vs 69.6 and 76.6 years old for epilepsy and controls ($p < 0.001$).

Conclusions: TSC subjects have a significantly higher burden of disease than other subjects with epilepsy. These results stress the need for specialized services in this population through the lifespan.

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3. Polarized and lens color effects on photoparoxysmal response—Erik J. Kobylarz, Stanley Rydjeski, Richard P. Morse (Dartmouth-Hitchcock Medical Center, Lebanon, NH, United States)

Introduction: Approximately 5% of epilepsy patients' photosensitivity can be detected on EEG recordings. This photoparoxysmal response (PPR) may prevent patients from performing their daily activities and also can result in seizures and anxiety. The objective of this study is to optimize the use of Z1 and other polarized and colored lenses for reducing PPR in epileptics.

Purpose: We propose that by covering central and temporal visual fields with either Z1 lenses plus side guards or elongated polarized lenses may suppress the PPR by altering the luminance and/or wavelength.

Methods: 22 pediatric patients with Type 4 PPR (Waltz et al.) were tested with and without Z1 lenses using photic stimulation from 1 to 21 Hz. 19 patients had primary generalized epilepsy (5 JME & 14 Absence), 2 had reflex epilepsy and 2 had Dravet's Syndrome.

Results: Responses were classified into 3 groups: PPR disappearance, persistence or attenuation. 14 patients had reduced PPR (64%) and in 5 patients PPR disappeared (23%). 3 patients (13%) demonstrated persistence of the PPR with Z1 lenses. Several patients tested with side guards plus cobalt blue tint polarized lens sunglasses showed marked PPR reduction. Several patients tested with elongated polarized sunglasses covering the temporal visual field showed PPR attenuation. Placing a red lens over the photic stimulation lamp augmented the PPR from 1 to 19 Hz stimulation in several patients. A blue lens over the photic lamp resulted in attenuation or disappearance of the PPR at several photic stimulation frequencies in several patients.

Conclusions: Z1 and other blue lenses reduced the PPR in nearly all patients. Possible mechanisms include polarization, reduction of luminance, and filtering of red light. Further testing of photosensitive patients will be performed. Comparisons will be made between Z1, elongated polarized, cobalt blue, red and green lenses.

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4. Temporal lobe atrophy: Frequent in elderly with epilepsy of unknown etiology—Emmanuelle Lapointe, Charles Deacon, Christian Bocti, Louis Royer-Perron, Stephen Cunnane, Alexandre Castellano (Université de Sherbrooke, Sherbrooke, Que, Canada)

Objective: To evaluate the degree of temporal lobe atrophy (TLA) in elderly patients with new-onset epilepsy, and its relation to temporal epileptiform discharges.

Background: No etiology can be identified in as much as 30% to 50% of cases of new-onset epilepsy in the elderly, despite adequate investigation. Degenerative diseases, notably Alzheimer's disease (AD), increase the risk of epilepsy, and are often underdiagnosed in routine clinical practice. Abnormal activity on electroencephalography (EEG) of demented epileptic individuals is most often found focally in temporal regions.

Design/methods: We retrospectively reviewed neuroimaging and EEG results of a consecutive cohort of 322 elders with new-onset epilepsy. The > 65 year-old patients were evaluated at the Centre Hospitalier Universitaire de Sherbrooke (CHUS) between January 2001 and October 2010. On imaging, TLA was assessed visually on axial images and graded on a 0–3 scale estimating sulcal widening and temporal horn ventricular enlargement. Measurement of the temporal horn radial width (THRW) was also acquired as a quantitative estimate of TLA. TLA was compared between subjects with epilepsy of unknown etiology ($n = 127$) and demented epileptic individuals of the same cohort ($n = 10$), as well as a healthy elderly control group ($n = 31$) and non-epileptic AD patients ($n = 10$). EEG interpretations were also analyzed, looking for correlation between temporal lobe atrophy and temporal epileptiform discharges, in the whole epileptic cohort.

Results: MRI (46%) or CT (93%) was available for 112 patients with epilepsy of unknown etiology. Thirty-eight percent of elderly with new-onset epilepsy of unknown cause had significant temporal atrophy, using the dichotomized 0–3 scale (0–1 vs 2–3) or THRW. This was significantly more than the healthy control group (0%) after adjustment for age and sex ($p = 0.000$). As expected, individuals of the same cohort with epilepsy attributed to dementia had higher prevalence of significant TLA using both THRW and the visual scale (70.4%, $p = 0.026$ and 76.9% $p = 0.021$) as did patients with established AD (70% $p = 0.040$ and 60% $p = 0.077$). EEG results were available for 297 of the 322 patients (92.2%), including 125 of the 127 subjects with epilepsy of unknown etiology. Epileptiform discharges were present in 111/297 (37.3%) and 45/125 (36%) individuals respectively, of which 68.5% and 55.5% were found in temporal leads. No correlation was found between the presence of temporal lobe atrophy, using either dichotomized THRW or the visual scale, and temporal epileptiform activity ($p = 0.312$ and 0.469).

Conclusions: A considerable proportion of elderly with new-onset epilepsy of unknown cause exhibit temporal lobe atrophy on brain imaging, which suggests that a degenerative disease such as AD could be underrecognized as a possible etiology. However, it appears there is no correlation between this atrophy and the temporal localization of epileptiform activity.

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5. Visual evoked potentials, contrast sensitivity and foveal optical coherence tomography in Parkinson's disease patients—Shahnaz Miri^a, Priyanka Chopra^b, Sofya Glazman^a, Lee Mylin^a, Ivan Bodis-Wollner^{a,c} (^aDepartment of Neurology, SUNY Downstate Medical Center, United States, ^bSchool of Medicine, SUNY Downstate Medical Center, United States, ^cDepartment of Ophthalmology, SUNY Downstate Medical Center, United States)

Background and objective: Impaired vision and remodeled foveal pit are demonstrated in Parkinson's disease (PD) patients. Visual evoked potentials (VEPs) reflect abnormality anywhere in the retina to cortex pathways. We evaluated the correlation between the VEP, contrast sensitivity (CS) and foveal thickness in PD and assessed diagnostic yield of their combination.

Methods: Ten PD (20 eyes) and eight HC subjects (16 eyes) were enrolled in the study. The two groups were matched for age, gender and ethnicity ($P > 0.05$). All subjects underwent standard neurological and ophthalmological examination to exclude any pathology. CS

was evaluated using Pelli-Robson chart. Two-channel VEP was recorded on each subject with two different stimuli (pattern reversal, frequency of 2.3 cpd; and on/off pattern frequency of 4.6 cpd). N70 and P100 were recorded. Macular optical coherence tomography (OCT) scans were obtained using Zeiss-HD OCT and macular thickness, volume and ganglion cell layer-inner plexiform layer (GCL-IPL) thickness were extracted. Statistical analysis was performed using SPSS software (version 21.0).

Results: PD patients had a significantly longer N70 (reversal pattern) and P100 (on/off pattern) latency (86.7 ± 10.2 and 132.9 ± 8.7 ms, respectively) compared to healthy controls (78.8 ± 6.6 and 125.5 ± 11.5 ms, respectively) ($P = 0.01$ and $P = 0.03$). CS score was significantly lower in PD patients (1.66 ± 0.21 vs. 1.89 ± 0.15 ; $P = 0.001$). PD patients had decreased thickness at the distance of 1.5–2.5 mm from the foveola (perifovea) ($255.0 \pm 6.5 \mu$ vs. $264.9 \pm 18.7 \mu$; $P = 0.03$). N70 latency was negatively correlated with CS ($R = -0.419$, $P = 0.01$) and average GCL-IPL thickness ($R = -0.529$, $P = 0.001$). CS was positively correlated with parafoveal thickness ($R = 0.490$, $P = 0.002$). A combination of parafoveal thickness and CS score yielded an AUC of 0.784, which increased to 0.844 when combined with N70 and P100 measures.

Conclusion: Visual function is correlated with foveal morphology. A combination of VEP parameters, CS score, and foveal thickness has a high diagnostic yield for PD.

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6. Frontopolar sharp potentials—Umang Modi, Paul Hwang (North York General Hospital, Toronto, Ont., Canada)

Sudden appearance of totally unexpected bisynchronous frontopolar dominant unexpected potential initially embedded in eye blink with progressive recruitment and phase change. At times, it reaches up to 2.5 Hz, with awake background, and virtually minimal or limited spread to fronto-temporal or posterior frontal area on encephalogram. After very close examination and accepting wide variety of opinions, patient is being considered for epilepsy monitoring unit (EMU), so as same potential can be reproduced and evaluated for any fronto-polar epilepsies.

There are few unexpected potentials appears at fronto-polar region in EEG laboratory recording and must not escape, even though the patient has no additional oculographic leads. Potential described here, presented while ambulatory monitoring. The ocular potentials are mostly quite impressive and almost always give rise to marked eye movement artifacts in fronto-polar and anterior temporal leads. The use of polygraphic documentation makes the task much easier, as patient is being considered for EMU. When an REM phase occurs directly at sleep onset, the transition from drowsiness to REM is not very pronounced in the EEG, whereas the change from deep NREM sleep to REM is a very dramatic one (Matsuo, 1981).

During photic stimulation, light from the flash stimulus may produce artifact in the fronto-polar leads (Fp1/Fp2). This artifact can be mistaken for photic driving due to the synchrony with the stimuli. The source maybe the retina (ERG) or from a nonphysiologic source such as a frontopolar electrode with high impedance creating a photo-cell. Covering the eye with a towel will block the input to the retina (ERG) and this should not be confused with the photoelectric effect (Tyner et al., 1983).

The alpha rhythm may occasionally extend slightly into the superior frontal leads (F3, F4). Extension into the fronto-polar region (Fp1, Fp2) is practically unheard of. Apparent alpha rhythm in the fronto-polar leads may be very prominent in referential (unipolar) montages if the referential ear electrode picks up the posterior alpha rhythm. This is particularly common when the mastoid region is used instead of the ear lobe (the mastoid being a preferred place with paste technique) (Niedermeyer's Electroencephalography).

Fronto-polar or orbito-frontal onset of seizures may be recorded from fronto-polar electrodes, and better resolved by supra-orbital or infra-orbital electrodes, sometimes it's been referenced to midline electrodes like electrode on nose/chin, Fz, Cz or Pz. It is not uncommon for bilateral synchrony to occur in frontal lobe epilepsy (Atlas of EEG, 2013). Subtle lateralization may be present with bilateral synchronous activity, mainly during sleep. This lateralization could be misleading. Absence of any ictal or immediate post ictal slowing has been reported in patient with mesial frontal lobe epilepsy (Bautista et al., 1998).

Behavioral manifestations with normal interictal EEG encountered in frontal lobe epilepsy may be misdiagnosed as psychogenic nonepileptic seizures. It emphasizes the need for early video-EEG



monitoring in ambiguous cases before starting or modifying AED treatment.

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7. Identifying the pathological substrate(s) of complex partial seizures: Blumenfeld's network inhibition hypothesis—Jabir Mohamed, McIntyre Burnham (University of Toronto, Canada)

Complex partial seizures – which often arise in the temporal lobes – are the most common seizures in adults and are often drug resistant. They involve transient episodes of impaired consciousness with behavioural arrest. Identifying the neural substrate for these common and drug-resistant attacks will be valuable not only for understanding epileptogenic networks, but also for evolving new pharmacologic or stimulation paradigms designed for complex partial seizures.

Dr. Hal Blumenfeld at Yale University has offered a testable hypothesis concerning the neural substrate of complex partial seizures. Blumenfeld postulates (2012): (1) that focal discharge arises somewhere in the brain, typically in the temporal lobes; (2) that the focal discharge spreads to subcortical structures that have strong inhibitory outputs, such as the septal nuclei; and (3) that the discharge in these structures suppresses activity in the arousal systems of the upper brain stem and diencephalon. Suppression of the arousal systems leads to unconsciousness, which is signaled by the onset of behavioural arrest and slow waves in the neocortical EEG.

Blumenfeld's hypothesis has not yet been tested in the amygdala-kindling model – the most widely used and drug-validated animal model of complex partial seizures. Tests involving the Blumenfeld hypothesis and amygdala-kindled rats are now underway in our laboratory. We predict that behavioural arrest in kindled animals will correlate with the onset of slow waves in the rat neocortex. We also predict that the behavioural arrest will not be suppressed by anti-epileptic drugs (AEDs), since AEDs do not suppress complex partial seizures in patients or the kindled amygdala focus in rats (Albright and Burnham, 1980).

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8. Evaluation of counselling received by women with epilepsy in their reproductive years and management in pregnancy—Lisa Sabella, Charles Deacon, Nadine Sauvé (Centre Hospitalier Universitaire de Sherbrooke, Canada)

Objective: The primary outcome of the study was to evaluate whether women with epilepsy (WWE) of reproductive age received counselling before conception, including issues such as folate supplementation, antiepileptic drug selection (AED) and their potential teratogenic risks.

Background: WWE of reproductive age should be counselled regarding their condition and the potential complications of pregnancy associated with epilepsy and AEDs, considering that 50% of pregnancies are unplanned.

Design/methods: We retrospectively reviewed 64 consecutive medical charts of WWE between the ages of 13 and 50, who were followed prior to conception, and managed during pregnancy at the Centre Hospitalier Universitaire de Sherbrooke (CHUS) between July 1, 2003 to June 30, 2013. Twenty patients were excluded primarily due to referral to the CHUS only after conception. Forty-two patients, encompassing 62 pregnancies were included. Maternal and neonatal charts were thoroughly reviewed and information was collected on an Excel spreadsheet. The protocol was approved by the Ethics review Board of the CHUS. We described our population regarding pre-conception counselling, dose of folate supplementation taken, type, dose and quantity of AEDs, control of seizure in the year preceding pregnancy as well as throughout pregnancy, maternal and neonatal complications or malformations. We evaluated whether those who received counselling before pregnancy were less likely to be taking Valproic acid (VPA) during pregnancy, have less seizures during pregnancy and less complications during pregnancy and delivery.

Results: Counselling before conception was documented in 45/62 (72.6%) of medical charts. Folate supplementation before pregnancy was prescribed in 44/62 (71%) pregnancies. Risks of complications were formally documented in 27/62 (43%) of charts. There were no statistically significant differences between those receiving counselling and those that did not, in terms of seizure frequency during pregnancy, and VPA use. Interestingly, of the 15 (100%) women on an AED polytherapy, all received counselling compared to those who did not ($p = 0.006$). There were no statistically significant differences regarding maternal and neonatal complications for women on polytherapy, those on VPA or women with seizure during pregnancy, compared to their counterparts. Two cases of malformations were detected and one woman died unexpectedly at 18 weeks of pregnancy. Between 2003 and 2008 there were 11/34 (32%) women on VPA compared to 2/26 (7%) between 2009 and 2013, $p = 0.026$.

Conclusion: This study has shown that the rate of counselling received by WWE at our centre was satisfactory, but remains an area that can be improved. Physicians should more actively be prescribing folate supplementation to this population due to the high rate of unexpected pregnancies. More attention should be placed in formally documenting important discussions about risks of epilepsy and AED. We plan to raise awareness of these issues to the health-care professionals at our center who are involved in the care of WWE during their reproductive years.

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9. The anticonvulsant effects of cannabidiol examined in animal seizure models—Miles D. Thompson, Ruth A. Ross, W. McIntyre Burnham (Department of Pharmacology and Toxicology, University of Toronto, Canada)

Cannabidiol (CBD), a major nonpsychotropic compound of *Cannabis sativa*, is emerging as a treatment for intractable seizures and their comorbid cognitive, behavioral and quality of life sequelae. Basic research studies in animals have started to define the anticonvulsant properties of CBD. Studies of CBD in mice and rats using maximal electroshock (MES) and pentylenetetrazol (PTZ) models of generalized clonus or myoclonus reported ED50 values of CBD as early as the 1970s – however chromatographic analysis of CBD purity was often not reported. The ED50 values for CBDs reported previously may be inaccurate for some botanical derived extracts; although historically, the ED50 values reported for MES in rats

(10 mg/kg) may be an order of magnitude lower than those reported in mice. We will compare recent data derived from in vivo studies with the published data. Testing of CBD in seizure models will be interpreted in this context – including a study of CBD in ventral subiculum kindling. The latter studies provide a useful comparison with the drug-standardized amygdala kindling model – the model in which we evaluate novel drugs that may be effective against complex-partial seizures of temporal lobe origin. The systematic investigation of CBD efficacy, toxicity and pharmacokinetics may be important in view of the tendency to add CBD to other antiepileptic drug regimens for the treatment of treatment-resistant epilepsy. Better evaluation of the ED50 of CBD in animal models will form the basis for more reliable dosing in human epileptic patients.

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