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Friday, February 16, 2018 - Abstracts

1. The development of propagated discharge and behavioural arrest in hippocampal and amygdala kindled seizures—J. Mohamed [1], B.W. Scott [2], O. David [3], W.M. Burnham [1,2] ([1] Institute of Medical Science, University of Toronto, Toronto, Canada , [2] Department of Pharmacology & Toxicology, University of Toronto, Canada , [3] Grenoble Institut des Neurosciences, Université Grenoble Alpes, Grenoble, France)

Patients with focal temporal lobe seizures often experience transient episodes of impaired awareness with behavioural arrest, but the precise mechanism remains unknown. The Blumenfeld hypothesis attributes these deficits to a loss of cholinergic input to the cortex. This is presumed to result from increased activation of inhibitory regions that suppress subcortical arousal, giving rise to slow wave activity. To investigate this hypothesis – and more specifically, to characterize the relationship between propagated discharge, cortical slow waves and behavioural arrest – we performed kindling studies in rats. We found that seizure discharge took longer to spread from the amygdala than the hippocampus, and took more kindling stimulations to elicit behavioural arrest. In addition, the onset of propagated discharge in subcortical and cortical sites did not always match with the onset of behavioural arrest. Importantly, the activity seen in the cortex did not resemble the slow waves seen in deep sleep. Together, these findings suggest an additional mechanism – other than the Blumenfeld hypothesis – to explain how temporal lobe seizures may produce behavioural arrest and impair awareness.

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2. The anticonvulsant effects of intravenous 5a-dihydroprogesterone on amygdala-kindled seizures in rats—Yinhao V. Wu, W. McIntyre Burnham (Department of Pharmacology and Toxicology, University of Toronto, Toronto, Ontario, Canada)

Background: 5a-dihydroprogesterone (DHP), the first metabolite of progesterone and the precursor of allopregnanolone, has anticonvulsant properties. Past studies have reported the suppression of amygdala-kindled seizures by DHP administered via the subcutaneous route. We now demonstrate strong anticonvulsant effects of DHP administered intravenously (IV) via the jugular vein.

Methods: Female Wistar rats were implanted with an electrode in the right basolateral amygdala. They were kindled to 15 stage 5 seizures, stability tested, and cannulated in the jugular vein. The dose-response and time-response effects of IV DHP were then tested against focal electrographic seizures and secondarily generalized convulsions.

Results: Dose-Response Study - At 5 min post-injection, a dose-dependent suppression of both generalized and focal seizures was seen, with ED50s of 1.69 mg/kg for the generalized convulsive seizures and of 3.48 mg/kg for the focal electrographic seizures. Ataxia, as rated by the Löscher ataxia scale, was also seen, with a TD50 of 3.57 mg/kg.

Time-Response Study - The time-response study, done with the ED75 for focal seizure suppression, showed suppression of both generalized and focal seizures from immediately after injection to about 60 min post-injection.

Significance: DHP has demonstrated anticonvulsant effects in a drug-resistant model of human complex-partial seizures. Its analogs might be developed as new anticonvulsants.

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3. The effect of environmental enrichment on GBL-induced Infantile Spasm-like seizures in Ts65Dn mice—Chun Kit Li [1,2], Brian W. Scott [2,3], Miguel A. Cortez [2] ([1] Department of Human Biology, University of Toronto, Toronto, Canada , [2] Neuroscience and Mental Health, Hospital for Sick Children, Toronto, Canada , [3] Department of Pharmacology & Toxicology, University of Toronto, Canada)

Infantile spasms (IS) is the most common and severe form of epilepsy that occurs in infants between four and twelve months of age. Symptoms of IS include sporadic flexion and/or extension in all limbs and torso, multifocal spike discharges and manifestation of cognitive and psychomotor impairments later on in development. A strong correlation between Down Syndrome (DS) and IS was reported in recent research. It has also been shown that environmental enrichment was able to reduce the severity of atypical absence epilepsy, which is observed after IS in some patients, in a

rat model. We therefore used the Down Syndrome mouse model (Ts65Dn) to test the hypothesis that environmental enrichment would reduce the number of γ-butyrolactone (GBL)-induced spasms in Ts65Dn mice. There was a significant decrease in the number of four-limb extensions 10-min-post-injection in Ts65Dn mice housed in an enriched environment compared to those in standard caging. The effect of environmental enrichment was non-significant 20- and 30-min-post-injection. The number of four-limb extensions, however, was significantly reduced at all three time points in the control mice in enriched housing relative to standard condition. Here, we also report GBL-induced flexion phenotypes that were not seen in previous studies using the Ts65Dn model. Our results suggest that the protective effects of environmental enrichment might only be applicable to non-DS infants. It also provides a potential model to study for the mechanism behind IS flexions in the future.

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4. Suppression of hippocampal kindling seizures by lorazepam and levetiracetam—Hongmei Song [1,3], Mark Ma [1,4], Chiping Wu [1], Liang Zhang [1,2] ([1] Krembil Research Institute, University Health Network, Toronto, Canada, [2] Department of Medicine (Neurology), University of Toronto, Toronto, Canada, [3] Departments of Neurosurgery, The First Hospital of Jilin University, Changchun, China , [4] Departments of Pediatrics, The First Hospital of Jilin University, Changchun, China)

Introduction: Benzodiazepine GABA enhancers and levetiracetam are known to be effective in suppression of kindling seizures, but the effects of these antiepileptic drugs on regional after discharges adjacent to the kindling sits are largely unknown. We explored this issue in a mouse model of hippocampal kindling and compared the effects of lorazepam and levetiracetam on hippocampal and piriform after discharges as the piriform cortex is thought to play a critical role in genesis of kindling seizures.

Methods: C57 black mice received electrode implantations in unilateral hippocampal CA3 and piriform cortical areas and then underwent twice daily hippocampal stimulation for a few weeks. The effects of antiepileptic drugs were tested in fully kindled mice. Lorazepam (1.5 mg/kg) or levetiracetam (100 mg/kg) was applied by an intra-peritoneal injection 15 or 60 min before hippocampal stimulation. The effects observed following similar saline injections were taken as baseline controls.

Results: Evoked motor seizures and associated piriform after discharges were abolished by lorazepam whereas the durations of corresponding hippocampal afterdischarges were unchanged from baseline controls (n = 6 mice). Evoked motor seizures and corresponding hippocampal and piriform afterdischarges were significantly decreased by levetiracetam, but shortened afterdischarges were more pronounced in the piriform than in the hippocampal area (n = 6 mice).

Summary: Lorazepam may suppress motor seizures by inhibiting seizure spread from the stimulated hippocampal focus to the piriform cortex and other brain areas, and levetiracetam may inhibit both focal/hippocampal seizures and seizure spread in our model.

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Saturday, February 17, 2018 - Abstracts

5. Prospective pre-emptive EEG study prior to west syndrome—Elana F Pinchefsky [1], Diane Wilson [1], Torin Glass [1], Vann Chau [1], Jason Boulet, Vera Nenadovic, Roy Sharma, Ying Wu, Paula Melendres, Justine Staley, Ann Richards, Amrita Viljoen, Sherida Somaru, Lee Robles, Chantal O'Neil, Saber Jan, Robyn Whitney, Emily Tam, Nadia Kabir, Miguel A. Cortez (The Hospital for Sick Children (SickKids), Division of Neurology, Canada , Department of Paediatrics, University of Toronto, Toronto, Ontario, Canada)

Since the original description of hypsarrhythmia by visual inspection as a "chaotic" and disorganized pattern in 1954, we have continued this clinical practice of EEG interpretation with solely visual inspection until the present day. The description of hypsarrhythmia as "chaotic" [Gibbs EL, Fleming MM, Gibbs FA. Pediatrics 1954;13 (1):66–73], was challenged by van Putten and Stam 17 years ago [IEEE Eng Med Biol Mag. 2001;20(5):72–9]. We are now conducting the first prospective study in newborn babies with risk factors for infantile spasms. Our rational is that 40 out of the 200 known risk factors can be detected during the neonatal period. After consent, we conduct the longitudinal EEG protocol every 2 months until 1 year of age. Phase synchrony and variability analyses are performed to detect the earliest EEG changes before hypsarrhythmia onset. The EEG analyses from the dynamics perspective opens a new examination of hypsarrhythmia and electrodecremental events (EDEs) in infantile spasms, beyond the sole visual inspection of the EEG. We will present cases to illustrate the value of the phase synchronization index and the temporal variability of the index. Preliminary data suggest that both abnormal EEG patterns, hypsarrhythmia and EDEs are associated with high phase synchronization. These preliminary findings question the prevailing notion that hysparrhythmia is a disorganized pattern and may account for the observed developmental stagnation in these children. The visual inspection of hypsarrhythmia does not appear sufficient to appreciate the highly synchronized EEG pattern in patients with infantile spasms.

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6. Continuous spike-waves of slow-wave sleep in 20 year old woman with epilepsy and autism—Soumia Djirar, Colin Shapiro, Alina Chu, Janet Shaw, Paul Hwang (Sunnybrook Hospital, Youthdale Child & Adolescent Sleep Centre, EEG Lab, NYGH & UTERP, Toronto, Canada)

A 20 yo RH woman, followed for 16 years by the same neurologist (PAH), had seizure onset at 1.5 years: afebrile CPSz secondarily generalised with automatisms, duration 5 min, recurrent every 2–4 weeks. Initial treatment consisted of PHT 5 mg/kg/day, then CBZ 30 mg/kg + VPA 18 mg/kg/day with improvement. PMHx: SGA 2.7 kg at birth, 7–8 h labour, "R. leg bent" at birth, in India. FHx negative Szs. Initial development "normal": walked 12 months, words at 18 months (Gujerati), ESL at 4 years (JK, Can.).

EEG #1 (1.5 y): Generalised SWD, L > R, DX. POSZ, not SFC. EEG #2: (4y): Generalised irregular SED2–3 Hz, DBA: secondary generalised epilepsy. EEG #3: (6 y): Epileptic encephalopathy with multiple independent spike foci;

PSG c video-EEG (19 y): DIMS, OSA c CPAP; EEG:ESES or CSWSWS pattern >65% sleep.

Seizures: staring spells, likely atypical absences; LD due to cognitive developmental assessment, IEP. Headaches 2–3/week, x 1–2 h, relieved by sleep. Behaviour: autistic self-stimulatory, asocial.

[1] First author contribution. Supported by EpLink - The Epilepsy Research Program of the Ontario Brain Institute.

Conclusion: An unusual prolonged evolution of epileptic encephalopathy of childhood extending into early adulthood with refractory secondarily generalised epilepsy and a pattern of EEG from irregular generalised spike-wave discharge to ESES or continuous spike-waves of slow-wave sleep pattern. The impact of CSWSWS on cognitive development in childhood should be considered in treatment long-term.

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7. Frequency and etiology of status epilepticus in pediatric patient of KAUH, Kingdom of Saudi Arabia—Reem Alyoubi, Maria Bakry, Nojoud Ben hli, Ghaidaa Sindi, Maha Alhainiah, Maram Alateeq (King Abdulaziz University Hospital, Department of Pediatric, Saudi Arabia)

Background: Status epilepticus (SE) is a condition of continuous seizure which persists more than 30 min or two or more seizures without full recovery. Any seizure that lasts more than 5 min needs to be considered as a case of SE for successful management of the condition. SE poses serious threat to life in children and requires immediate medical attention because continuous seizures not only damage the brain but also hinders the development of brain in later stages.

Purpose and relevance: The purpose of this study was to evaluate etiology and frequency of SE among children in Jeddah region of Kingdom of Saudi Arabia. Moreover, there is paucity of data on SE among infants and children in this region. Hence, this study will be helpful to assess the factors associated with SE.

Participants and methods: In this retrospective study, the data for 88 patients were collected from King Abdul Aziz University Hospital (KAUH) from 2006 to 2017. Patients were either infants (age $\geqslant$ 28 days) or children (age $\leqslant$ 14 years) and only those patients were selected who showed the symptoms of SE. Data collection sheet was used to record the required information.

Analysis: Data was recorded as mean value with its standard deviation. Statistical analysis was conducted by using SPSS, version 23 (IBM, Armonk, NY, USA). Statistical significance was set at $p < 0.05$.

Results: We found that the major causative factors behind SE were febrile seizure (30.5%), electrolytes imbalance (11.9%), hydrocephalus (8.5%), CNS infections (6.8%) and neoplasm (6.8%). SE cases originated due to other factors such as trauma, hemorrhagic stroke, intractable seizures, cerebro-vascular accidents etc. were also reported. However, the etiologies of 8 cases were not clearly established. SE was more prevalent in boys (67.8%) as compared to girls (32.2) and the majority of patients (64.3%) were non-Saudi. This study also elaborate that the majority of epilepsy types were generalized 56 (91.8%), and that 34 (58.6%) of the participants showed compliance to their epilepsy medications.

Conclusion: The author found that the most common causes of SE was febrile seizure, electrolytes imbalance and hydrocephalus, respectively. The frequency of SE is high in KSA. However, a nation-wide study is needed to detect other major causes in Kingdom of Saudi Arabia for effective management and prevention. The compliance to AEDs is also requiring more attention and prompt family and patient education.

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8. The impact of comorbidity on seizure severity in elderly patients—Madihah Alhubayshi [1], Salah Al Baz [2] ([1] MOH, Department of Neurology, king Abdulaziz Hospital, Makkah, Saudi Arabia, [2] Epilepsy Monitoring Unit, Department of Neurology, King Faisal specialist hospital, Riyadh, Saudi Arabia)

Objective: To evaluate the effect of the presence of comorbidities on the severity of seizures among elderly patients in Saudi Arabia KFSH&RC.

Methods: We retrospectively reviewed the medical records of patients who are 60 years old and above at KFSH&RC, in Riyadh, KSA between 1990 and 2014 with epilepsy and systemic illness (diabetes, hypertensive, metabolic disease and CVD).

Results: 78 epilepsy patients were studied where in 22.4% (17) patients of our population have mild form of epilepsy and 13.1% (10) patients have a moderate severity of epilepsy, while half of them 51% (39) classified as severe epilepsy, this ratio probably due to selection bias. There was a significant correlation found between the severity of seizures and a presence of comorbidities in the majority of our population. Those with severe epilepsy, around 88% (33), complained of comorbid diseases, and 66% (24) suffer from vascular comorbidities.

Conclusion: There was significant influence of comorbidities on severity of epilepsy and epilepsy control in the elderly. This indicates a positive correlation between vascular comorbidities and severity of epilepsy, which indicate the importance of controlling risk factors (HTN, dyslipidemia, DM, CVD). This may have a significant role in reducing the severity of epilepsy in our population.

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9. Epileptogenic high-frequency oscillations skip the motor area in children with multilobar drug-resistant epilepsy—Yasushi Iimura, Hiroshi Otsubo (Division of Neurology, Hospital for Sick Children, Toronto, Ontario, Canada)

Objective: Subtotal hemispherectomy involves the resection of multiple lobes in children with drug-resistant epilepsy, skipping the motor area (MA). We determined epileptogenicity using the occurrence rate (OR) of high-frequency oscillations (HFOs) and the modulation index (MI), demonstrating strength of coupling between HFO and slow wave. We hypothesized that epileptogenicity increased over the multiple lobes but skipped the MA.

Methods: We analyzed 23 children (14 subtotal hemispherectomy; 9 multilobar resections). Scalp video-EEG and magnetoencephalography were performed before surgery. We analyzed the OR(HFO) and MI(5 phases = 0.5–8 Hz) on electrodes of total area, resection areas, and MA. We compared the data between good [International League Against Epilepsy (ILAE) class I–II] and poor (III–VI) seizure outcome groups.

Results: ILAE class Ia outcome was achieved in 18 children. Among the MI(5 phases) in the resection areas, MI(3–4 Hz) was the highest. The OR(HFO) and MI(3–4 Hz) in both total area and resection areas were significantly higher in the good seizure outcome group than in the poor outcome group. The OR(HFO) and MI (3–4 Hz) in resection areas were significantly higher than in the MA.

Conclusions: Our patients with multilobar drug-resistant epilepsy showed evidence of multifocal epileptogenicity that specifically skipped the MA.

Significance: This is the first study demonstrating that the electrophysiological phenotype of multifocal epilepsy specifically skips the MA using OR(HFO) and MI(3–4 Hz).

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