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Program Chair: Dr. Charles Deacon

1. Phase–Amplitude Coupling (PAC) during sleep in patients with focal epilepsy—M. Amiri, B. Frauscher, J. Gotman (Montreal Neurological Institute, McGill University, Canada)

Rationale: The relations between amplitude and phase across different EEG frequency bands have been widely investigated. It has been shown that the amplitude of EEG higher frequency oscillations is often modulated by the phase of lower frequency activities. During sleep, this modulation facilitates the communication among specific brain regions. In this study we investigate the variation of PAC during different sleep stages, and also in epileptic, and normal regions.

Methods: We studied interictal data of 25 patients with focal epilepsy. Sleep was scored manually according to AASM 2.0 criteria. There was no generalized seizure at least 6 h before sleep and 2 h after sleep. During the first sleep cycle, the first 4 minutes of each stage (stage N1, N2, N3 and REM) was selected. The signal was band-pass filtered into low (delta, theta, alpha, and beta) and high (gamma and ripple) frequency bands. Then the envelope amplitude and phase of the filtered signals were obtained using Hilbert transform. The Modulation Index was calculated for each epoch, and each pair of low and high frequencies. Higher values of this index represent stronger coupling between two frequency bands. Sharp transients were discarded allowing the comparison of sections free of epileptic discharges.

Results: The average modulation index in all bands except beta was higher in N3 and N2 compared to REM ($p < 0.05$). The average coupling in delta, theta and alpha band in all stages was significantly higher in the seizure onset zone (SOZ) compared to normal channels ($p < 0.05$). The coupling of delta and theta in all stages was higher in SOZ compared to spiking channels outside SOZ.

Discussion: Considerable differences were seen between the SOZ and normal channels. Stronger coupling in the epileptic regions, and during deep sleep may be explained by increased neuronal synchrony. PAC may lead to an index for localizing epileptic brain regions.

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2. Periictal activity in cooled asphyxiated neonates with seizures—Philippe Major [1], Anne Lortie [1], Mathieu Dehaes, Gregory Anton Lodygensky, Anne Gallagher, Lionel Carmant, Ala Birca (CHU Sainte Justine and University of Montreal, Montreal, Canada)

Seizures are common and worsen the outcome in critically ill neonates. Predicting seizure recurrence could allow individualizing antiepileptic treatment and improving the outcome. To identify EEG signatures of seizure recurrence, we investigated periictal spectral power and electrographic characteristics of seizures in five consecutive asphyxiated neonates under continuous EEG monitoring. All patients had high seizure burden while undergoing hypothermic neuroprotection. Two neonates had recurrence of seizures on rewarming. Spectral power analysis of fifteen artifact-free consecutive ictal events demonstrated, in all neonates, a significant increase in overall spectral power from the interictal to preictal and ictal periods ($p < 0.01$). Delta frequency power increase was consistently observed in all patients. Alpha power increase was more pronounced in the two patients with recurrence of seizures on rewarming and significant when comparing both interictal-to-preictal and interictal-to-ictal periods. In these two patients, preictal and ictal alpha activity displayed a regional, hemispheric or even diffuse distribution contrasting with the focal seizure onset. This distinct alpha activity preceding ictal onset could represent a biomarker of propensity for seizure recurrence. Future studies should be performed to confirm whether quantitative periictal characteristics and electrographic features allow predicting the risks of seizure recurrence in asphyxiated hypothermic neonates and other critically ill patients.

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3. Daily dynamics of states of vigilance in mice—O. Bukhtiyarova, S. Soltani, S. Chauvette, I. Timofeev (Université Laval, Dept. of Psychiatry and Neuroscience, le Centre de recherche de l'Institut universitaire en santé mentale de Québec (CRIUSMQ), 2601 de la Canardière, Québec, Qc G1J 2G3, Canada)

Previous studies demonstrated that (a) mice preferentially sleep during light hours and they are preferentially awake during dark hours; (b) mice have fragmented sleep. Despite multiple investigations involving sleep-wake transitions in mice, the exact patterns of sleep-wake alternations are not known. Here we studied sleep-wake pattern distribution in 5 young adult C57BL/6 mice over 5 days using continuous LFP and EMG recordings with a resolution of 5 s. The states were automatically detected based on LFP delta power, theta power and EMG power.

[1] These authors contributed equally to this work.

We found that daily distribution of states of vigilance in mice was: 12 h of wake, 10.2 h of slow-wave sleep and 1.8 h of REM and it was characterized by several hundred of transitions between different states of vigilance. The majority of detected states lasted less than 40 s. The fragmentation of states of vigilance was higher in the light part of the day and lower in first several hours of the dark part of the day when wake episodes were longer and REM sleep was almost absent. The most stable state of vigilance (longest stable segments) in mice was slow-wave sleep. The main EEG events that contribute to the delta power are slow waves. The existing methods of automatic slow wave detection were not sufficiently robust for their effective automatic recognition in non-anaesthetized mice. We developed a new method for slow wave detection based on neural network pattern recognition and classification, which allowed to retrieve various features of the slow waves in large amounts of data. As expected, we found many slow waves during slow-wave sleep. Surprisingly, isolated slow waves were also present during wake and occasionally during REM sleep. Both delta power and number of slow waves per second were the highest at the beginning of the light cycle, then gradually decreased to the end of the light cycle and reached their minimum in first 3–4 h of the dark cycle. Even though the slow-wave sleep episodes were shorter and occurred less often during dark part of the day, they had higher density in comparison to slow-wave sleep during the light part of the day. We conclude that the results of studies of normal sleep-wake cycle in C57BL/6 mice cannot be directly translated to human research or clinic.

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4. Gamma knife surgery for hypothalamic hamartomas causing refractory epilepsy: Long-term outcomes – A prospective observational study—Véronique Martel, David Mathieu, Catherine-Andrée Pinard, Pascale Bourgeois, Julie Duval, Charles Deacon (Divisions of Neurology and Neurosurgery, Université de Sherbrooke, Centre Hospitalier Universitaire de Sherbrooke (CHUS), Quebec, Canada)

Object: This prospective observational study, conducted at the CHUS between 2005 and 2016, aims to examine the outcomes of patients who underwent radiosurgery for hypothalamic hamartomas (HHs).

Method: Patients were included in the study if they were diagnosed with an HH and refractory epilepsy, without any other suspected seizure focus. After radiosurgery, seizure status was assessed periodically using the Engel Classification. Neuropsychological and quality of life evaluations were performed at baseline and thereafter. A follow-up evaluation was completed ten years after the first Gamma-knife treatment.

Results: Thirteen patients, refractory to medical treatment, were included in the study, ranging in age from 12–57 years. Using the Régis Classification, ten patients had smaller hamartomas (Grade I-III) and underwent treatment of the entire lesion. Radiosurgical disconnection was attempted in three patients with larger lesions (Grade IV-VI). One patient was lost to follow-up, and one died from seizure complications following an open surgery for HH. Disconnection was ineffective. Gamma-knife treatment was repeated in three patients in which the first intervention had failed to reduce the seizure burden. Seven patients (58%) had a good outcome (Engel I-II), including five patients who were seizure-free after a mean time of 6.4 months. Five patients (42%) had Engel classification of III or IV. Treatment adverse events included psychotic depression (1) and radiation necrosis (1).

Conclusion: Radiosurgery seems to offer a better control of epilepsy secondary to HHs, principally in cases where the entire lesion can be targeted. The authors consider that radiosurgery should be attempted as a first-line surgical therapy for these patients.

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5. Sleep deprivation in the activation of interictal spikes and epileptic seizures—Ángela Milán-Tomás[a], Estefania Conde-Blanco[b], Antonio Moreno-Rojas[c], Paul Hwang[d] ([a]Toronto Western Hospital, University of Toronto, Youthdale Child and Adolescent Sleep Center, Toronto, ON, Canada, [b]Neurology Resident at Son Espases Hospital, Mallorca, Illes Balears, Spain, [c]Epilepsy Unit, Son Espases Hospital, Illes Balears, Spain, [d]UTERP, EpLink-OBI, University of Toronto, UHN, Toronto, ON, Canada)

Objective: To describe and review the use of sleep deprived EEG in the activation of interictal spikes and epileptic seizures.

Background: Sleep deprivation (SD) has been used to enhance EEG sensitivity in the diagnosis of epilepsy. However, standardized guidelines for the use of SD-EEGs are lacking. Here, we provide an update in the literature of sleep SD-EEG and epilepsy as well as presenting data from a retrospective study.

Design/methods: A literature search using PubMed was carried out to identify papers focusing on sleep deprivation EEG and interictal discharges. A total of 39 abstracts were obtained, 13 were screened and included in this review. We also present data from a retrospective study of 156 patients that were assessed with a short and long-monitoring EEG as well as SD-EEG at Son Espases Hospital (Spain) and evaluated their sensitivity in the diagnosis of interictal discharges in patients with suspected epilepsy.

Results: Further studies are needed to evaluate the role of SD-EEG in patients with suspected epilepsy. In our retrospective study 21% of patients with a previous normal awake EEG showed interictal discharges in the SD-EEG.

Conclusions: Some studies have shown that SD-EEG increases sensitivity and specificity diagnosing interictal activity. However, the duration of sleep deprivation and length of the test varies according to the different studies. The role of SD-EEG should be further evaluated. The use of subtemporal electrodes may contribute to the diagnosis of temporal lobe epileptiform focus.

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6. The involvement of subcortical inhibitory structures in complex partial seizures—Jabir Mohamed, McIntyre Burnham (University of Toronto, Canada)

The network mechanisms underlying loss of consciousness during temporal lobe complex partial seizures (CPS) are not well understood. The Blumenfeld hypothesis states that unconsciousness results not from epileptic hyper-excitation of the neocortex — which was the traditional view — but from secondary inhibition of the cortex due to the suppression of subcortical arousal systems. To investigate this hypothesis – and more specifically, to characterize the major inhibitory structures involved – we have performed local stimulation experiments and hippocampal kindling studies in rats. We have found that 10 Hz stimulation of the lateral septal nuclei and the nucleus accumbens shell causes behavioural arrest and slow waves in the cortex. Preliminary hippocampal kindling studies have also revealed that the occurrence of propagated discharge in the lateral septum and the nucleus accumbens shell is highly correlated with the presence of neocortical slow waves but not the onset of behavioural arrest. These findings identify the lateral septum and nucleus accumbens shell as key subcortical structures underlying

seizure-related neocortical deactivation. Future studies will be needed to determine the role of other possible candidates.

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7. Thalamic mechanisms in the generation and modulation of the cortical slow oscillation in mice—A. Ozur, S. Chauvette, I. Timofeev (Université Laval, Dept. of Psychiatry and Neuroscience, le Centre de recherche de l'Institut universitaire en santé mentale de Québec (CRIUSMQ), 2601 de la Canardière, Québec, Qc G1J 2G3, Canada)

It is well established that thalamus plays a crucial role in the generation of the synchronous slow oscillation in the cortex during non-REM sleep. The slow/delta power (0.2–4 Hz) is the main measured factor of the quality of sleep. However, the contribution of different thalamic nuclei to the inception of the slow wave activities and its synchronization is not known. We hypothesized that the first-order (specific) thalamic nuclei provide a control of slow waves in primary cortical areas, while higher-order (non-specific) thalamic nuclei may synchronize the slow-wave activities across wide cortical regions. We analyzed local field potentials and spiking activities from different cortical and thalamic areas of anesthetized mice while a thalamic nucleus was inactivated by the GABA-agonist muscimol. Extracellular multiunit recordings in first-order (VPM, VL) and higher-order (PO, CL) thalamic nuclei show dramatically decreased spiking activity and strongly reduced burst firing after inactivation. We conclude that the injection of muscimol strongly reduced the spiking activity and does not potentiate the generation of low-threshold spike mediated bursts. Inactivation of specific thalamic nuclei with muscimol decreased the slow/delta power in the corresponding primary cortical area. The inactivation of a non-specific nucleus with muscimol significantly reduced the delta power in all investigated cortical. Our experiments demonstrate that the thalamus is required for the fine tuning of the cortical slow oscillation. Supported by CIHR and NSERC.

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8. Source localization of the seizure onset zone from ictal EEG and MEG data—G. Pellegrino[a,b], T. Hedrich[a], R.A. Chowdhury[a], J. Hall[b], J-M. Lina[c], F. Dubeau[b], E Kobayashi[b], C. Grova[a,b,d] ([a] Multimodal Functional Imaging Lab, Biomedical Eng Dpt, McGill University, Montreal, QC, Canada, [b] Neurology and Neurosurgery Dpt, Montreal Neurological Institute, McGill University, Montreal, QC, Canada, [c] École de Technologie Supérieure, Département de Génie Electrique, Montreal, QC, Canada, [d] Concordia University, Physics Dpt and PERFORM Centre, Montreal, QC, Canada)

Introduction: Surgical treatment of drug-resistant epilepsy relies on the identification of the seizure onset zone (SOZ) and often requires intracranial EEG (iEEG). We have developed a new approach for non-invasive electric and magnetic source imaging of the SOZ from ictal electroencephalography (EEG) and magnetoencephalography (MEG) recordings, using the wavelet-based Maximum Entropy on the Mean (wMEM) method. Taking as reference the clinical localization of the SOZ defined on the basis of iEEG or lesion topography and considering seizures recorded during simultaneous EEG-MEG scans, we compared: (1) ictal EEG source imaging vs ictal MEG source imaging; (2) Ictal source imaging vs interictal source imaging.

Methods: Among the patients undergoing simultaneous EEG-MEG (56 EEG channels and 275 MEG sensors), 13 had at least one seizure. A total of 46 MEG or EEG seizures were analyzed. wMEM was applied around seizure onset, centered on the frequency band showing the strongest power change. Principal component analysis applied to spatio-temporal reconstructed wMEM sources (0.4–1 s around seizure onset) identified the main spatial pattern of ictal oscillations. Qualitative sublobar concordance and quantitative measures of distance and spatial overlaps were estimated to compare EEG and MEG, ictal and interictal source imaging.

Results: Both ictal EEG and ictal MEG source imaging showed a good concordance with the clinical Seizure Onset Zone, ranging between 64% for EEG to 90% for MEG. Ictal MEG performed slightly better than ictal EEG, localizing sources closer to the clinical-SOZ ($p = 0.012$) and to interictal MEG source imaging ($p = 0.040$). The concordance and distance from the clinical-SOZ was not significantly different between interictal and ictal source imaging.

Conclusions: wMEM allows non-invasive localization of the SOZ from ictal EEG and MEG. EEG ictal source imaging might be sufficient in the daily clinical practice, but for the most challenging cases ictal MEG can provide more accurate results. Ictal source imaging can be a useful tool during presurgical evaluation of drug-resistant epilepsy patients and can guide iEEG implantation and brain surgery.

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9. Drop attacks in Lennox–Gastaut Syndrome: Is Rufinamide the answer?—Boris Yakubov, Janet Shaw, Jose Embuido, Paul Hwang (Windsor University School of Medicine, North York General Hospital, University of Toronto Epilepsy Research Program, Canada)

Introduction: The purpose of this study is to determine whether Banzel (Rufinamide) improves the control of drop attacks in patients with Lennox–Gastaut Syndrome, and whether it controls other seizure types in LGS.

Case report: There are 10 patients with Lennox–Gastaut Syndrome who were candidates for participating in the Rufinamide retrospective cohort-controlled study. Presently, four of five patients are prescribed the drug Rufinamide. They are compared with the control group of LGS 4/5 subjects not on Rufinamide.

Rufinamide dosage was started at 100–400 mg daily dose, while other anti-epileptic drugs (AEDs) were continued in the treated group. The control group continued on original AEDs without the addition of Rufinamide. The most common AEDs were Valproic acid, Clobazam, Lamotrigine, and Topiramate.

Results: After a minimal period of six months of Rufinamide, the treated group had fewer drop attacks than the control group. Approximately 80% of patients (4/5) responded positively to Rufinamide. The treated group was more alert by caregiver observation, and had less drug interactions with other AEDs. Overall an improved quality of life was found with the Rufinamide treatment, leading to continuation of the new drug past the study period. One patient dropped out from the study due to severe side effects to Rufinamide: (1/5 or 20%).

Discussion: Rufinamide at therapeutic doses reduced the frequency of drop attacks or tonic seizures more than other AEDs. There may also be some improvement in control of atypical absences and/or myoclonic seizures in LGS. A subjective presentation of compared quality of life care from Rufinamide for LGS needs to be confirmed in a larger controlled study by quantitative age – specific assessment.

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