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Thursday, September 12, 2019

**Brief Oral Presentations:**
Epilepsy, Functional Mapping, Other modalities, Connectivity & Brain Networks

**Chair:** Ben Dunkley

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Estimating Directional Information Flow During MEG Interictal Spike Recordings
Stephen Robinson
Clinical Utility of High-Density EEG with MEG for Epilepsy Surgery

Will Woods
Swinburne University of Technology

Co-Author(s)
Chris Plummer – Department of Neurology, St Vincents Hospital
Simon J. Vogrin – Department of Neurology, St Vincents Hospital
Michael A. Murphy – Department of Neurology, St Vincents Hospital
Mark J. Cook – Department of Neurology, St Vincents Hospital
David Liley – School of Health Sciences, Swinburne University of Technology

Abstract Theme: Epilepsy

Background and Purpose/Objectives:
Surgery is under-used for drug-resistant focal epilepsy. Better non-invasive methods of identifying the surgical target are needed when MRI shows no lesion or an extensive lesion. Simultaneously-acquired high-density electroencephalography (HDEEG) - magnetoencephalography (MEG) for source localization (EMSL) is one such method but prospective studies are lacking.

Methods
96 consecutive patients underwent simultaneous 60 minute-scalp HDEEG (74-96 electrode cap, ANT waveguard®) MEG (Elekta Neuromag TRIUX® 306 sensors) (1-5 kHz). Electrodes were digitized (Polhemus®) for MRI co-registration. Impact of source localisation (standardized Low-Resolution-Tomographic-Analysis with MRI-individualized Boundary Element Method) on the final surgical plan was noted.

Results
58/96 (60%) patients (39 non-lesional, 19 complex-lesional) returned a clear EMSL result (24/58 seizures plus spikes, 34/58 spikes only). 25/58 have had surgery with at least one-year follow-up (Engel I/II 19/25 Engel III 6/25). 15/58 await surgery, 18/58 yet to complete standard work-up. The treating team indicated that EMSL was a key factor in the surgical plan in 48/58 cases (83%), while 21/48 (44%) became surgical candidates (from being unlikely candidates) when the treating team was exposed to the EMSL result. Of the remaining patients (38/96), EMSL confirmed non-surgical status in 14/38 (multiple independent foci in 12, generalised discharges in 2), EMSL failed to localise recorded activity in 5/38 (insufficient well-defined discharges), and EMSL could not be performed in 19 patients (no spikes or seizures recorded).

Conclusion
Simultaneous HDEEG-MEG for source localization has high clinical utility in the pre-surgical work-up of patients with non-lesional and complex-lesional drug-resistant focal epilepsy.
Utility of Ictal MEG in the Presurgical Evaluation of Patients Undergoing Epilepsy Surgery

Submitter: Alexandra Koptelova – Center of Neurocognitive Research (MEG-centre) of MSUPE

Author: Tatiana Stroganova
Principal researcher
Center for Neurocognitive Research (MEG-centre) of MSUPE

Co-Author(s)
Alexandra Koptelova – Researcher, Center for Neurocognitive Research (MEG-centre), Moscow State University of Psychology and Education
Anna Kruychkova – junior researcher, Center for Neurocognitive Research (MEG-centre), Moscow State University of Psychology and Education
Viktor Chadaev – Neurologist, Russian Children's Clinical Hospital
Pavel Vlasov – Neurologist, 2nd department of Children Neurosurgery, N. N. Burdenko National Scientific and Practical Center for Neurosurgery
Armen Melikyan – Chief Neurosurgeon, 2nd department of Children Neurosurgery, N. N. Burdenko National Scientific and Practical Center for Neurosurgery

Abstract Theme: Epilepsy

Background and Purpose/Objectives:
Although the goal of presurgical MEG evaluation is accepted to be localization of the ictal-onset zone, the reports on ictal MEG recordings are extremely rare in the literature. Here, we investigated seizure-onset patterns recorded by MEG with regard to its prognostic value for favorable surgical outcome.

Methods
We analyzed seizure onset patterns in presurgical MEG recordings of twelve patients within a broad age range 0.5–40 years with temporal and extratemporal intractable partial seizures who subsequently underwent resective surgery with favorable outcomes (Engel I, II). For all patients the site of seizure onset could not be confidently predicted from the long-term video-EEG or other evidence (MR imaging, seizure semiology), and their further examination with interictal and ictal MEG contributed to a planning of the resective surgery. The MEG preictal patterns were defined according to the criteria accepted for intracranial recordings. The sources localization was applied using multi-dipole modeling. Source localization results were retrospectively compared with the site of the resected cortical area.

Results
The concordance of the MEG-defined putative seizure-onset zone (SOZ) with the cortical area, whose resection led to favorable outcomes was observed in nine out of 12 patients. In two patients with mistakenly identified SOZ, it was located in temporal lobe, in third preictal pattern wasn't identified.

Conclusion
The source localization for preictal MEG pattern proved to be a useful tool for presurgical evaluation of SOZ, although temporal sources may be underestimated. The results provide an argument in favour of incorporating ictal MEG into the process of presurgical evaluation.
Abstract # 39 Submission ID 680653

Spike Onset Zone on Magnetoencephalography in Various Epileptogenic Lesions

Hiroshi Shirozu
National Hospital Organization, Nishiniigata Chuo Hospital

Co-Author(s)
Akira Hashizume – Neurosurgery, Takanobashi Central Hospital
Hiroshi Masuda – Functional Neurosurgery, National Hospital Organization, Nishiniigata Chuo Hospital
Masafumi Fukuda – Functional Neurosurgery, National Hospital Organization, Nishiniigata Chuo Hospital
Shigeki Kameyama – National Hospital Organization, Nishiniigata Chuo Hospital
Hiroshi Otsubo – Neurology, The Hospital for Sick Children

Abstract Theme: Epilepsy

Background and Purpose/Objectives:
The spike onset zone (Sp-OZ) is a newly developed concept which indicates the area where interictal spikes originate. Analysis of magnetoencephalography (MEG) using Gradient magnetic-field topography (GMFT) has an advantage in spatiotemporal resolution which is suitable to detect the Sp-OZ.

Methods
This study involved the patients with neocortical epilepsy due to focal cortical dysplasia (FCD) in 41 (type I, 17; type IIa, 13; type IIb, 11), tumor in 4, and tuberous sclerosis (TS) in 7. Preoperative MEGs were analyzed using GMFT for Sp-OZ and equivalent current dipole analysis for spike peak zone (Sp-PZ). The distributions of the Sp-OZ and its correlation with Sp-PZ were retrospectively compared among each lesion group.

Results
The mean distributions (±SD) of Sp-OZ were significantly larger (P=0.004) in TS (4.2±3.0, range 210) than other pathology (FCD type I, 2.2±0.3, range 14; type IIa, 2.7±0.4, range 15; type IIb, 1.8±0.4, range 13; tumor, 2.0±0.5, range, 13). FCD type IIb were likely to show complete concordance between Sp-OZ and Sp-PZ (7/11, 63.3%), while FCD type IIa (9/13, 69.2%) and tumor (5/6, 83.3%) showed more partially concordance. FCD type I (6/17, 35.3%) and TS (2/7, 28.6%) had more discordance between Sp-OZ and Sp-PZ (P=0.013).

Conclusion
The distributions of Sp-OZ and its correlation with Sp-PZ were related to the epileptogenic pathology. FCD type IIb and tumor are considered to have a restricted epileptogenic zone, whereas FCD type I, IIa and TS to have an extensive epileptogenic zone and a complex epileptic network.
Abstract # 41 Submission ID 674045

Preoperative Evaluation for Indication of Total Corpus Callosotomy Using Gradient Magnetic Field Topography (GMFT) in Patients with Intractable Generalized Epilepsy and Drop Attacks

Kota Kagawa, Ph.D
Hiroshima University

Co-Author(s)
Akira Hashizume – Hiroshima University
Koji Iida – Hiroshima University
Masaya Katagiri – Hiroshima University
Kaoru Kurisu – Professor, Hiroshima University
Hiroshi Otsubo – Professor, Neurology, The Hospital for Sick Children

Abstract Theme: Epilepsy

Background and Purpose/Objectives:
Gradient magnetic field topography (GMFT) for magnetoencephalography (MEG) has been developed to demonstrate magnetic-field gradients of interictal epileptic spikes on a volume-rendered brain surface. We evaluated preoperative GMFT for the efficiency of total corpus callosotomy (TCC) in patients with intractable generalized epilepsy.

Methods
Seven patients (age: 2-12 years) were enrolled. All had intractable symptomatic generalized epilepsy with drop attacks. We selected interictal MEG spikes from 30-min recording corresponding to generalized spikes or polyspikes on simultaneous EEG. We generated GMFT from the MEG data band-pass filtered at 14-50 Hz. We defined activated zone (AZ) as a gradient > 400fT/cm on GMFT. Based on the spatiotemporal changes of AZ within 200ms from the MEG spike onset, we divided the spikes as follows: 1) anteriorly- or posteriorlyoriginating, and 2) interhemispheric or intrahemispheric-spreading at 200ms. We compared the proportion of the MEG spikes between good and poor outcome groups.

Results
After TCC, 4 patients (Group A) achieved no more drop attacks and 3 patients (Group B) had residual drop attacks. We analyzed mean of 112.1 (range: 70-173) MEG spikes per patient. The proportion of anterior originating spikes showed no difference between group A (79.4±16.9%) and group B (55.5±31.2%). The proportion of interhemispheric spreading spikes (85.9±8.77%) was significantly higher in group A than in group B (44.1±25.1%) in group B (p=0.025).

Conclusion
Good control of drop attacks following TCC correlated with the preoperative higher proportion of interhemispheric spreading of MEG spikes on GMFT. The interhemispheric connectivity of corpus callosum provoking drop attacks could be stopped by disconnection of TCC.
Abstract Theme: Functional mapping, neurosurgical applications

Background and Purpose/Objectives:
Children undergoing neurosurgery for medically intractable epilepsy are at risk for developing post-operative deficits, including aphasia. Morbidity is minimized through careful mapping of eloquent and epileptogenic cortex. Increasingly, noninvasive neuroimaging is used to lateralize and provide gross localization of language, prior to resective surgery. However, conventional neuroimaging approaches (i.e., fMRI and MEG active-baseline contrasts) fail to distinguish critical language sites in distributed networks, or delineate eloquent margins unambiguously.

Methods
Hubs are nodes or brain regions that are of high importance, either because they are highly connected, or possess integral positioning within a network. We will review findings from our recent publications on language hub mapping, and compare maps with localizations obtained through repetitive TMS (healthy children, 5 to 18 years), and extraoperative stimulation mapping (ESM; children undergoing evaluations for epilepsy surgery candidacy).

Results
Connectivity patterns are frequency-specific; as such, connectivity- and network-based mapping should be tailored to the relevant spectra, or should involve integration across frequencies (i.e., in a multivariate framework). Our initial findings suggest that connectivity- and network-based approaches yield functional maps that are consistent with those obtained from conventional neuroimaging, and concordant with findings from moderately-invasive and invasive findings.

Conclusion
Connectivity and network-based mapping can be used to identify critical sites within distributed network. The approaches are domain-agnostic, and could potentially be used for mapping other cognitive functions, such as memory.
Abstract # 60 Submission ID 679614
Magnetoencephalography and Magnetic Resonance Imaging: MRI Safety and Artifact Predictability Between Two Magnetically Associated Modalities

Stephanie A. Holowka, M.R.T.(R), M.R.T.(MR), MRSO (MRSC)
Lead Technologist, MEG and 3-Dimensional Imaging
The Hospital for Sick Children

Co-Author(s)
Hiroshi Otsubo, MD – Director Neurophysiology Lab, Neurology, The Hospital for Sick Children
Rohit Sharma, RET, REPT – Clinical Manager Neurophysiology Lab/Senior Neurodiagnostic Technologist, Neurology, The Hospital for Sick Children
Amrita Viljoen, BSc, RET, REPT – Senior Registered Neurodiagnostic Technologist, Neurology, The Hospital for Sick Children
Pradeep Krishnan, MD, Assistant Professor, University of Toronto – Staff NeuroRadiologist, Paediatric Neuroradiology, The Hospital for Sick Children

Abstract Theme: Other methodologies and modalities, including TMS

Background and Purpose/Objectives:
For Magnetoencephalography (MEG), metallic objects within or extraneous to the patient pose an artifact risk for data collection. For Magnetic Resonance Imaging (MRI) such metallic objects pose not only risks for artifact but also patient safety.

Methods
In the past nineteen years, the Clinical MEG lab at Sicksks Hospital has collected data on over 1500 paediatric patients for localization related epilepsy. In some patients, dental work, clothing and other items created artifacts significant enough to negate studies using single event dipole mapping. For MRI studies the same items in MEG do cause artifact but may also create a significant safety risk for patients (migration and/or heating). Several case studies will be presented showing artifacts and how they affected data/images in either machine. Best practices for both modalities will be shared. Artifacts from patient apparel, implants and other extraneous items will be shown within both modalities.

Results
Artifacts seen in patients undergoing MEG may be a predictor of artifacts and safety concerns in MRI. Likewise MRI may also predict the likelihood of metal artifacts in MEG.

Conclusion
MEG and MRI are imaging modalities where their sensitivities can predict potential of artifacts and/or risk for either study. Careful screening and changing of patients is required for both modalities. MEG could possibly one day quantify the risk of harm for MRI patients by intentional or unintentional implants.
Abstract # 48 Submission ID 695621

Measuring Brain Activity from Paediatric to Elderly with Two Helmets in One Dewar Cooled by Continuous Reliquefaction: LifeSpan MEG

Yong-Ho Lee
Principal Research Scientist
Korea Research Institute of Standards and Science

Co-Author(s)
Sang-Kil Lee – KRISS
Jin-Mok Kim – KRISS
Hyukchan Kwon – KRISS
Kwon-Kyu Yu – KRISS

Abstract Theme: Other methodologies and modalities, including TMS

Background and Purpose/Objectives:
Present MEG has single helmet that either adult or paediatric population can be measured properly. To measure brain activity from paediatric to elderly using single dewar, we developed a new type of MEG system having dual helmets in one dewar. In addition, present MEG needs regular refill of liquid helium. We aim to develop dual helmet MEG system, cooled by continuous reliquefaction of the evaporated helium gas from the MEG dewar.

Methods
The dewar has horizontal shape for supine measurement, with adult helmet and paediatric helmet on each side of the dewar horizontal axis. Each helmet is optimized for the corresponding population, adult and paediatric of 5-year old, respectively. For measuring the MEG, the dewar can be rotated horizontally to position the corresponding helmet toward the bed. The pickup coils are first-order axial gradiometers of 50 mm baseline, and are installed in the vacuum space to eliminate vibration from the boiling liquid helium. The numbers of pickup coils are 186 and 138 for the adult and paediatric, respectively, with 6 additional reference channels for each helmet. For refill-less operation, the dewar is cooled by a continuously operating reliquefier.

Results
The developed dual helmet MEG is very effective approach to cover wide age range from paediatric to elderly using one helmet and one magnetically shielded room.

Conclusion
Integrated with the continuous re-liquefaction using low-noise and reliable cryogenic technology, the developed MEG system is an economic and sensitive system.
Abstract # 37 Submission ID 676456

Estimating Directional Information Flow During MEG Interictal Spike Recordings

Stephen E. Robinson
Staff Scientist
MEG Core Group

Co-Author(s)
Nugent C. Allison – Director, MEG Core Group, NIH/NIMH
Sara K. Inati, MD – Electroencephalography Section, NIH/NINDS

Abstract Theme: Connectivity and brain networks

Background and Purpose/Objectives:
Understanding the underlying brain network supporting propagation of interictal and ictal activity is of importance for pharmacological and surgical treatment of epilepsy. Although functional imaging of excess kurtosis ($g_2$) may reveal multiple candidate spike locations, it may be difficult to resolve small timing differences between sites. Instead of relying on time offset between spike peaks, we estimate the direction and magnitude of information transport between pairs of regions, using transfer entropy (TE).

Methods
TE is a statistical measure of directional information flow between pairs of time series. Our proposed method is an extension of excess kurtosis imaging. First, a beamformer (SAM) is used to generate weights for estimating the time-course of source activity on a suitable grid of voxels. Next, $g_2$ is computed for each voxel by averaging over multiple overlapping segments of source activity. The presence of spikes yields positive $g_2$ values. The resulting volumetric image reveals candidate regions for interictal activity. We find the coordinates of local maxima in the $g_2$ image and then apply temporo-dynamic symbolic transfer entropy (tdSTE) to all possible time-series pairs. This variant of TE yields that magnitude and direction of information flow along with the stationarity between each pair.

Results
Three examples of clinical MEG recordings analyzed by tdSTE results will be presented). We observe greater information transfer magnitude and increased stationarity from sites having interictal spikes to other brain regions.

Conclusion
It is expected that this new information will help delineate the dynamics of the epileptogenic network.
Thursday, September 12, 2019

Parallel Symposium #1: Epilepsy

Chair: Masayuki Hirata

1400 Abstract # 40 Submission ID 660188
Detection of interictal epileptiform discharges: A comparison of on-scalp and conventional MEG measurements
Karin Westin

1420 Abstract #53 Submission ID 677473
Noninvasive Localization of High-Frequency Oscillations in Children with Epilepsy: Validation against Intracranial Gold-Standard
Christos Papadelis

1440 Abstract #54 Submission ID 660123
Magnetoencephalography as a prognostic tool in patients with medically intractable temporal lobe epilepsy
Myung-Ji Kim

1500 Abstract # 55 Submission ID 676521
Overnight ictal magnetoencephalography in children with drug-resistant epilepsy
Jeremy Moreau
Detection of Interictal Epileptiform Discharges: A Comparison of On-scalp and Conventional MEG Measurements

Karin Westin
Graduate student, MD
Karolinska Institutet, Stockholm

Co-Author(s)
Daniel Lundqvist – Karolinska Institutet

Abstract Theme: Epilepsy

Background and Purpose/Objectives: Magnetoencephalography (MEG) plays an important role in pre-surgical epilepsy evaluation. However, the accuracy of localization of epileptogenic zones is inferior to intracranial measurements. Since these are associated with serious adverse effects, improvement in non-invasive methods is necessary. Newly developed on-scalp MEG sensors (high-temperature SQUIDs) provide better spatial and temporal resolution of spontaneous and evoked brain activity, compared to conventional MEG. This technique could improve noninvasive epileptogenic foci localization. Here, we present the first-ever clinical on-scalp htc-MEG recording from a patient with temporal lobe epilepsy.

Methods
Interictal measurements was performed using conventional and on-scalp MEG in two different sessions. EEG was recorded simultaneously in order to validate findings of interictal epileptiform discharges (IEDs). Source localization of IEDs found in the conventional MEG recording was performed. On-scalp MEG was recorded from the peak positive and negative magnetic field of this source. The raw on-scalp MEG sensor signal is unsuited for visual inspection why a machine learning (ML)-based algorithm was developed for automatic detection of IEDs. The method was validated on conventional MEG recordings.

Results
Visual inspection of EEG co-registered with on-scalp MEG revealed 15 IEDs. Out of these, 11 were found in the on-scalp MEG data using our ML-based algorithm. In addition, 31 possible IEDs were located. Validation of the method on conventional MEG recordings found no IEDs not identified by a trained physician.

Conclusion
We present the first-ever on-scalp MEG recording in a focal epilepsy patient. This technique could possibly render a more precise pre-surgical localization of epileptogenic foci than existing non-invasive techniques.
Abstract #53 Submission ID 677473

Noninvasive Localization of High-Frequency Oscillations in Children with Epilepsy: Validation Against Intracranial Gold-Standard

Christos Papadelis
Director, Clinical MEG Program
Boston Children's Hospital

Co-Author(s)
Eleonora Tamilia – Newborn Medicine, Boston Children's Hospital
Joseph R. Madsen – Boston Children's Hospital
P Ellen Grant – Boston Children’s Hospital
Steven M. Stufflebeam – Athinoula Martinos Center, Massachusetts General Hospital
Phillip L. Pearl – Boston Children's Hospital

Abstract Theme: Epilepsy

Background and Purpose/Objectives:
Patients with medically refractory epilepsy (MRE) need surgical resection of the epileptogenic zone (EZ) to gain seizure-freedom. High-frequency oscillations (HFOs, > 80 Hz) are promising biomarkers of the EZ that are typically localized using intracranial electroencephalography (icEEG). The goal of this study was to localize the cortical generators of HFOs non-invasively using high-density (HD) EEG and magnetoencephalography (MEG) and validate the localization against the gold-standard given by the icEEG defined HFO-zone.

Methods
We analyzed simultaneous HD-EEG and MEG data recorded with Neuromag® and BabyMEG from ten children with MRE who underwent icEEG and surgery. We detected interictal HFOs on HD-EEG and MEG separately, using an inhouse detector followed by human review, and distinguished between HFOs with and without spikes. We localized the cortical generators of each HFO on HD-EEG or MEG using the wavelet Maximum Entropy on the Mean (wMEM). For the HFOs localized in the brain area covered by icEEG, we estimated the localization error (Eloc) with respect to the gold-standard, and classified them as either concordant or not.

Results
We found that: (i) HD-EEG presented a higher rate of HFOs than MEG (1 vs 0.5 HFOs/min, p=0.031); (ii) HFOs without spikes were more likely to be localized outside regions of interest (i.e. covered by icEEG) than HFOs with spikes; and (iii) both HD-EEG and MEG showed high precision to gold-standard (92% and 96%).

Conclusion
We report quantitative evidence that HD-EEG and MEG can localize the HFO generators with high precision to the icEEG gold-standard in children with MRE.
Magnetoencephalography as a Prognostic Tool in Patients with Medically Intractable Temporal Lobe Epilepsy

Myung-Ji Kim
Yonsei Severance Hospital

Co-Author(s)
Jin Woo Chang – Yonsei Severance Hospital
Won-Seok Chang – Yonsei Severance Hospital
Hyun-Ho Jung – Yonsei Severance Hospital
Na-Young Jung – Ulsan University Hospital
Chang-Kyu Park – Kyung-Hee University Hospital

Abstract Theme: Epilepsy

Background and Purpose/Objectives:
Most surgical treatments for medically intractable temporal lobe epilepsy are helpful. When a patient has persistent symptoms after surgery, there are no tests that accurately predict whether a patient will have remnant epileptic foci. The aim of this study was to evaluate the usefulness of magnetoencephalography (MEG) as a prognostic tool in patients with temporal lobe epilepsy.

Methods
From July 2012 to July 2016, 21 patients underwent preoperative and postoperative MEG at our center. Postoperative MEG was performed within 2 weeks after surgery. We analyzed MEG by estimating the time frequency component of the signal to define gamma oscillations (GOs), which are an indicator of epileptogenic foci. We analyzed the relationship between GOs on MEG and surgical outcomes.

Results
Mean follow-up period was 28.3 months (range, 13e44 months). At the last follow-up visit, patients were divided into 2 groups according to surgical outcome. All patients showed spike waves and GOs on preoperative electroencephalography and MEG. In the seizure control group (16 patients), spike waves (2 patients) and GOs (2 patients) were seen postoperatively despite absence of symptoms. In the recurrent seizure group (5 patients), 6 of 123 whereas 3 patients showed spike waves, all 5 patients showed GOs on MEG postoperatively. There was a significant association between presence of GOs on postoperative MEG and surgical outcome (p=0.01).

Conclusion
MEG can provide valuable postsurgical information on epileptic foci in patients with recurrent symptoms; GOs on postoperative MEG were especially correlated with epileptic recurrence. Our data show that GOs on postoperative MEG may have prognostic value.
Abstract Theme: Epilepsy

Background and Purpose/Objectives:
Ictal events are uncommonly captured in routine magnetoencephalography (MEG) recordings due to the typically short duration of such recordings. However, recorded seizures could be of considerable value for outlining the seizure onset zone non-invasively.

Methods
We recorded MEG in 56 children (age range 3-18 y.o.) with drug-resistant epilepsy who underwent presurgical evaluation at the Montreal Children's Hospital from 2015 to 2019. Simultaneous EEG and video were recorded together with the MEG. No sedation was used. Recording duration ranged from 45 minutes to 7 hours (two patients were recorded overnight sleeping in the MEG). Magnetic source imaging of MEG data and windowed time-frequency analyses of the ictal onset contrasted to baseline recordings were performed to localise the seizure onset zone.

Results
Seizures were recorded in 13/56 (23%) of patients, including both patients recorded overnight. A total of 37 seizures, 34 clinical and 3 purely electrographic were obtained (range: 1-14; median: 1). In 2/13 patients, localisation of ictal activity was not possible due to movement. Seizure onset was missed in 1 patient. Amongst the remaining 10 patients, preictal spiking was observed in 5/10, and focal paroxysmal fast activity (PFA) in 7/10.

Conclusion
Ictal MEG in unsedated children is feasible and could contribute to the localisation of the seizure onset zone as part of the presurgical evaluation. Windowed time-frequency analyses of the ictal onset is shown to be a useful way to assess the temporal spread of seizures. Overnight MEG recordings are proposed as a way to increase the yield of the technique.
Thursday, September 12, 2019

Parallel Symposium #2: Psychiatric conditions including PTSD

Chair: Sam Doesburg

1400  Abstract #50 Submission ID 680367
      Machine learning for mental illness diagnoses: use of the MEG connectome as a biomarker for PTSD
      Benjamin Dunkley

1420  Abstract # 51 Submission ID 680558
      Quantifying temporal dysconnectivity among schizophrenia patients: A resting-state MEG study
      Golioush Alamian

1440  Abstract #62 Submission ID 676811
      MEG in Minimally Verbal / Non-verbal Children with Autism Spectrum Disorder
      Timothy Roberts

1500  Abstract #49 Submission ID 677752
      Magnetoencephalographic Correlates of Suicidal Ideation in Major Depression
      Jessica Gilbert
Machine Learning for Mental Illness Diagnoses: Use of the MEG Connectome as a Biomarker for PTSD

Benjamin T. Dunkley
The Hospital for Sick Children

Co-Author(s)
Jing Zhang – Hospital for Sick Children

Abstract Theme: Psychiatric conditions including PTSD

Background and Purpose/Objectives:
PTSD is a psychiatric condition brought about by exposure to a traumatic episode. It is a devastating disorder amongst the general population, and the military in particular. It impairs quality of life and is associated with increased mortality. Current diagnostic methods are subjective, burdensome on the patient and time consuming for clinicians - a biomarker-based diagnosis platform is desirable. MEG presents an ideal tool due to its sensitivity and accuracy in measuring functional circuitry.

Methods
We used the phase lag index from the gamma range and a machine learning-centric strategy to build a predictive model using a support vector machine (SVM) with nested internal cross-validation (CV), along with recursive random forest feature selection. External CV was conducted on the SVM model to evaluate the classification performance. Partial least squares discriminant analysis (PLS-DA) was used to independently verify the effectiveness of PTSD classification with the selected connections.

Results
Nineteen connections were identified that separated PTSD patients (N = 23) from trauma-exposed controls (N = 21), including right inferior frontal gyrus-right paracentral lobule, right Rolandic operculum-right inferior parietal lobule, right cingulum-left parahippocampal gyrus, and left inferior frontal gyrus-left amygdala. The SVM model showed AUC at 0.90, suggesting an excellent classification performance, consistent with the results from PLS-DA.

Conclusion
MEG presents a potent tool to measure the functional connectome for use as a biomarker for PTSD diagnoses and prognostics. We will discuss the general applicability of using a machine learning-based MEG biomarker framework for other mental health and neurological disorders, including anxiety, depression and traumatic brain injury.
Quantifying Temporal Dysconnectivity Among Schizophrenia Patients: A Resting-state MEG Study

Golnoush Alamian, MSc
PhD Candidate: Cognitive Neuroscience
Université de Montréal

Abstract Theme: Psychiatric conditions including PTSD

Background and Purpose/Objectives: Biological systems tend to display complex behaviour with a power-law (1/f-like) distribution. In the brain, this translates into neural activity that exhibits scale-free, temporal or spatial, properties. Beyond previously used features, recent electrophysiology studies have shown the presence of long-range temporal correlations (LRTCs) in the amplitude dynamics of alpha and beta oscillations. Disease, such as psychosis, can alter the temporal properties of neuronal activity and potentially affect information integration.

Methods
In this study, we measured LRTCs in the resting-state MEG signal of 25 schizophrenia (SZ) patients and 25 controls, using Detrended Fluctuation Analysis (DFA). Source-level analysis of LRTCs and amplitude were computed for 5 frequency bands across the cortex and deep structures, and correlated with patients symptom severities. Support vector machine (SVM) was applied to evaluate the discriminative power of LRTCs.

Results
We found an overall attenuation of LRTC exponent values among SZ patients in alpha and beta, specifically. SVM significantly decoded certain brain areas with up to 87% accuracy in these bands. Significant correlations were observed between patients LRTC values in the beta-band and their negative symptoms in the left lateral fronto-orbital gyrus, and also between the amplitude of low-frequency bands and negative symptoms in the inferior parietal lobule.

Conclusion
LRTCs were found to be attenuated in patients in regions that appear highly relevant to the symptomology of SZ. Further exploration of this metric could enhance our understanding of SZ and potentially lead to a new path for early clinical diagnosis.
Abstract #62 Submission ID 676811
MEG in Minimally Verbal / Non-verbal Children with Autism Spectrum Disorder

Timothy Roberts
Professor / Vice-Chair
Children’s Hospital of Philadelphia

Co-Author(s)
Junko Matsuzaki – Children’s Hospital of Philadelphia
Emily Kuschner – Children’s Hospital of Philadelphia
Lisa Blaskey – Children’s Hospital of Philadelphia
David Embick – Linguistics, University of Pennsylvania
James C. Edgar – Children’s Hospital of Philadelphia

Abstract Theme: Psychiatric conditions including PTSD

Background and Purpose/Objectives:
MEG studies of auditory processing show characteristic signatures in ASD (e.g. delayed M50, M100, MMF); most studies are conducted in less-impaired children, who tolerate the challenging environments of MEG/MRI. Using the MEG-PLAN approach (combined behavioral/technical strategy), this study brings MEG measures to the severely-impaired minimally-verbal/non-verbal (MVNV) population, not well-served by the research community.

Methods
MEG-PLAN employs a "parents as partners in research" tailored behavioral desensitization and personalized reward experience in conjunction with technical facilities (passive paradigms, obligate responses, motion tracking and template-source analysis). We studied cohorts of 35 neurotypical, 64 children with ASD without cognitive impairment and 30 MVNV children with ASD. Paradigms included tones for M50/M100 components and oddball paradigms for the MMF. Correlation with neuropsychological assessments/reports of communication and general cognitive ability was performed using the Vineland Communication Domain (obtainable across all cohorts) and NVIQ (WISC-IV/Leiter).

Results
Paradigms could be successfully completed yielding evaluable data in a substantial fraction of MVNV children (M50/M100: 17/30, MMF: 9/30). M50/M100 latencies were prolonged in ASD; delays were exacerbated in MVNV-ASD (M50: TD=78.6+/-.6ms; ASD=82.5+/-.4ms; MVNV: 86.6+/-.7ms; p < 0.05. M100: TD=131.5+/-.7ms; ASD=152.2+/-.6ms; MVNV=170.7+/-.6ms; p < 0.01). MMF latencies were also delayed in ASD and these delays were also exacerbated in MVNV (TD=170.1+/-.4ms; ASD=224.5+/-.2ms; MVNV=270.7+/-.45ms; p < 0.01). M50, M100 and MMF latencies exhibited correlation with both communication and general cognitive ability in hierarchical regression (p < 0.05).

Conclusion
With MEG-PLAN, it is possible to extend MEG research to more-impaired children with ASD. Previous findings in higher-functioning children with ASD were replicated and prolonged in MVNV; the extent of delay correlated with clinical communication impairment.
Magnetoencephalographic Correlates of Suicidal Ideation in Major Depression

Jessica Gilbert
National Institute of Mental Health, NIH

Co-Author(s)
Elizabeth Ballard – National Institute of Mental Health, NIH
Christina Galiano – National Institute of Mental Health, NIH
Allison Nugent – National Institute of Mental Health, NIH
Carlos Zarate – National Institute of Mental Health, NIH

Abstract Theme: Psychiatric conditions including PTSD

Background and Purpose/Objectives:
Defining the neurobiological underpinnings of suicidal ideation (SI) is crucial to improving our understanding of suicide. This study used magnetoencephalographic (MEG) changes in gamma power as a surrogate marker for excitation/inhibition balance to examine the underlying neurobiology of SI. In addition, effects of pharmacological intervention with ketamine were assessed.

Methods
Data were obtained from 29 drug-free patients with major depression and corresponding SI who participated in a double-blind, placebo-controlled experiment comparing a subanesthetic dose of ketamine to a placebo saline infusion. MEG recordings were collected at baseline and 6-9 hours after ketamine and placebo infusions. During scanning, patients rested with their eyes closed. SI and depression were assessed across timepoints. A linear mixed-effects model was used to identify brain regions showing associations between gamma and SI and depression. Two regions of the salience network (anterior insula - AI, anterior cingulate - ACC) were subsequently probed using dynamic causal modeling to model ketamine effects.

Results
Clinically, patients showed significantly reduced SI and depression following ketamine. In addition, distinct regions in AI were found to be associated with SI compared with depression. When modeling AI-ACC connectivity, ketamine was found to lower the membrane capacitance of superficial pyramidal cells. Finally, AMPA-mediated connectivity between AI and ACC was associated with improvements in depression symptoms, but not SI.

Conclusion
These findings suggest that AI plays a key role in SI, perhaps via its role in salience detection. In addition, these findings suggest transient changes in superficial pyramidal cell membrane capacitance might be one mechanism via which ketamine improves SI.
Friday, September 13, 2019

**Brief Oral Presentations:** Neurological conditions, cognition, computational approaches

**Chair:** Tim Bardouille

1300  Abstract #2 Submission ID 680930  
Evaluating Visual Evoked Cortical Magnetic Responses in Youth with Demyelination  
Laura Kim

1307  Abstract # 21 Submission ID 675798  
Reorganization of Functional Language Networks Following Neonatal Arterial Ischemic Stroke Supports Language Outcome  
Zahra Emami

1314  Abstract #47 Submission ID 692928  
Reduction of spontaneous beta bursts in Parkinson’s disease is correlated with motor symptom severity  
Mikkel Vinding

1321  Abstract #45 Submission ID 694591  
Concussion during adolescence disrupts local and large-scale neurophysiological circuits  
Benjamin Dunkley

1328  Abstract #46 Submission ID 694754  
Nonpharmacological Treatment changes resting-state brain activity in patients with dementia  
Yoshihito Shigihara

1335  Abstract #33 Submission ID 676722  
Interbrain coupling during turn-taking verbal interactions between mothers and children  
Jo-Fu Lotus Lin

1342  Abstract #34 Submission ID 678643  
Enhanced beta modulations in primary sensorymotor and visual cortices reflect visuomotor control: A precursor to neurofeedback  
Chungmin Han

1349  Abstract #35 Submission ID 677295  
Limitations of Magnetoencephalography for detecting high frequency activity  
Naohiro Tsuyuguchi
Abstract #2 Submission ID 680930

Evaluating Visual Evoked Cortical Magnetic Responses in Youth with Demyelination

Laura Kim
Hospital for Sick Children

Co-Author(s)
Cecilia Jobst – Hospital for Sick Children
Donald Mabbott – Hospital for Sick Children
E.Ann Yeh – Hospital for Sick Children

Abstract Theme: Neurological conditions (excluding epilepsy)

Background and Purpose/Objectives:
Most youth with acquired demyelinating disorders (ADS) suffer from subclinical visual pathway injury. We evaluated differences in latency (P100) and distinct patterns in cortical magnetic responses (visual evoked potentials, VEP) using magnetoencephalography (MEG) in youth with ADS compared to a healthy control (HC) population.

Methods
This cross-sectional study evaluated latency and source localization from VEP responses to a reversing checkerboard stimulus in each hemifield1,2,3 in youth with ADS (n=26, Multiple Sclerosis (MS)=11, Neuromyelitis Optica Spectrum Disorder (NMOSD)=4 and Myelin Oligodendrocyte Glycoprotein antibody related disorders (MOG)=11) and 21 age/sex-matched HC. Clinical data were obtained using standardized CRF. Informed consent was obtained.

Results
Average participant age was similar (HC=15.55±1.94; ADS=14.47±2.80; MS=16.58±0.96; NMOSD =15.05±1.19, and MOG=12.15±2.66 years). Mean age of disease onset was higher in MS vs MOG (14.05±1.87yrs, MS vs. 12.1±1.12, NMOSD vs. 9.92±3.42, MOG(p < 0.05)). The p100 latency in the MOG (118.80±1.80ms) and MS (116.54±2.11ms) groups were significantly longer than HC (114.33±1.02ms) (p=0.001 and p=0.004, respectively); NMOSD and HC did not differ (110.93±1.02ms). We found no significant differences in source localization between HC and patient groups.

Conclusion
We found delayed p100 in the MS and MOG groups, but not in youth with NMOSD. Reasons for this finding are unclear, but may include early clinical recognition of NMOSD and the use of highly effective therapies for NMOSD early in the disease course. Our findings will be of utility in future clinical trials targeting the visual system in demyelinating disorders.
Abstract # 21 Submission ID 675798

Reorganization of Functional Language Networks Following Neonatal Arterial Ischemic Stroke Supports Language Outcome

Zahra Emami
Hospital for Sick Children

Co-Author(s)
Benjamin T. Dunkley – Hospital for Sick Children
Robyn Westmacott – Hospital for Sick Children
Pradeep Krishnan – Hospital for Sick Children
Nomazulu Dlamini – Hospital for Sick Children

Abstract Theme:  Neurological conditions (excluding epilepsy)

Background and Purpose/Objectives:
Neonatal arterial ischemic stroke (NAIS) is the most common form of childhood stroke, often occurring in brain regions underlying language function. The aim of the study is to use MEG task-based functional connectivity to identify how language re-organization due to neonatal stroke correlates with language outcomes.

Methods
Eight children with unilateral MCA-NAIS (5F; mean 12.3±3.3 years) and seven neurotypical children (2F; mean 13.4±2.7 years) listened to syntactically correct and incorrect sentences while MEG was recorded. Task-related functional connectivity was calculated using the phase lag index as a measure of phase synchronization between brain regions. Language networks were derived from the mean connectivity in time windows and frequency bands of interest. Language outcomes were assessed using a battery of neuropsychological tests.

Results
Patients exhibit a disconnected functional subnetwork involving language areas, including bilateral inferior frontal areas, bilateral middle temporal poles, and the right superior temporal pole (theta band, 1.2-1.4s, pcorr=0.025). While a left-lateralized language network is positively correlated with language skill in controls, involvement of left temporal brain areas is correlated with poorer language skill in patients (p=0.02). Conversely, good outcome in patients is correlated with atypical right frontal connectivity in the language network (p=0.003).

Conclusion
These findings suggest that the reorganization of patients language networks outside of typical language areas is a possible compensatory mechanism to account for impairments in the frontal-temporal language subnetwork. MEG allows investigation of functional brain networks in a clinical context, ultimately guiding precision medicine and improving long-term outcomes in early childhood stroke.
Abstract #47 Submission ID 692928

Reduction of Spontaneous Beta Bursts in Parkinson's Disease Is Correlated with Motor Symptom Severity

Mikkel C. Vinding
Karolinska Institutet

Co-Author(s)
Panagiota Tsi – Karolinska Institutet
Josefine Waldthaler – Karolinska Institutet
Robet Oostenveld – Radboud University Nijmegen
Per Svenningsson – Karolinska Institutet
Daniel Lundqvist – Karolinska Institutet

Abstract Theme: Neurological conditions (excluding epilepsy)

Background and Purpose/Objectives:
Parkinsons disease (PD) is a common neurodegenerative disease characterized by the death of dopaminergic neurons and loss of dopamine. The loss of dopamine is associated with changes in neuronal synchronization in the beta-band (13-30 Hz) which is linked to motor symptoms in PD. Beta-band activity is not steady oscillations but appears as transient bursts.

Methods
We investigated whether beta burst activity in the sensory-motor areas differed between PD patients ON/OFF medication and healthy controls (HC) from three minutes of resting-state MEG data.

Results
PD OFF medication contained 11% (CI: 17-6%) fewer bursts compared to HC. Between the sessions OFF and ON medication, the number of bursts increased only by 2% (CI: -2%-5%) in PD patients. Finally, the results also show a link between burst occurrence and symptom severity in PD: burst occurrence was negatively correlated with the clinical scores (MDS-UPDRS) for motor symptoms bradykinesia and rest tremor severity. All the above differences were related to the occurrence of the burst. Neither bursts duration nor burst amplitude differed between groups or medication state.

Conclusion
Disease and medication-related changes in the beta-band in PD appear primarily due to changes in the occurrence rate of beta bursts, and not by changes in burst amplitude, duration or in sustained oscillatory activity. The link between MEG-based burst occurrence during resting state and clinical symptom severity scores may be useful for the clinical assessment of PD and might be a potential neuromarker for assessing the effectiveness of therapies targeting motor symptoms in PD.
Concussion During Adolescence Disrupts Local and Large-scale Neurophysiological Circuits

Benjamin T. Dunkley
The Hospital for Sick Children

Co-Author(s)
Zahra Emami – The Hospital for Sick Children

Abstract Theme: Neurological conditions (excluding epilepsy)

Background and Purpose/Objectives:
Concussion is a serious public health concern as lingering, chronic symptoms bring about functional impairment that is difficult to treat. Moreover, concussion disproportionately affects youth, as the typical maturational arcs of brain development are perturbed by injury. Diagnosis is difficult given the lack of markers on standard radiological scans, therefore, a reliable and objective biomarker is desirable and magnetoencephalography (MEG) presents an ideal solution due to its sensitivity at measuring disruption to local and large-scale neurophysiological circuits.

Methods
Using MEG, we recorded 5 minutes of eyes-open resting state in 5 adolescents with a concussion, and 4 without. A linearly-constrained minimum variance beamformer was used to recover time course from 90 Automated Anatomical Labelling atlas regions. To quantify local circuits, power spectrum density estimates were calculated for each region. For large-scale circuits, orthogonalised amplitude envelope correlations were computed for all seed pairs.

Results
We identified significant posterior increases in delta and theta oscillatory power in concussion, in contrast to reduced beta power, principally in occipito-parietal regions. Measures of large-scale circuits revealed elevated alpha coupling, predominantly in the visual cortex.

Conclusion
Consistent with previous adult literature positing injury-related perturbation to local excitatory:inhibitory tone, we observed a shift from the dominant alpha frequency to slower rhythms, consistent with the idea of changes in e:i balance. Moreover, since beta is known to carry excitatory efferent signals, the reductions we observed suggest injury selectively disrupts excitatory tone. Finally, the elevated alpha coupling suggests deeper disruption consistent with thalamocortical dysrhythmia.
Nonpharmacological Treatment Changes Resting-state Brain Activity in Patients with Dementia

Yoshihito Shigihara
Director
Hokuto Hospital

Co-Author(s)
Hideyuki Hoshi – Hokuto Hospital
Keita Shinada – Geriatric health facility Kakehashi
Toyoji Okada – Hokuto Hospital
Hajime kamada – Hokuto Hospital

Abstract Theme: Neurological conditions (excluding epilepsy)

Background and Purpose/Objectives:
Dementia is one of the major health problems in elderly individuals. Although nonpharmacological treatment (NPT) is considered as an effective treatment to improve their symptoms, it is not clear how NPT changes their brain conditions especially in case of non early stage. In this study, we measured resting-state brain activity from patients with moderate to severe dementia using magnetoencephalography (MEG) and compared the source-level data between pre- and post-NTP scans.

Methods
Nineteen patients with moderate to severe dementia were enrolled in this study. They were admitted in our geriatric health facility to receive NPT for 3 months. The levels of cognitive impairment and behavioural disturbances were measured using Mini-Mental Scale Examination Japanese version (MMSE-J) and Dementia Behaviour Scale 13 (DBD-13) respectively, at the beginning and the end of the NPT period. Resting-state brain activity was also recorded using MEG. Source intensities were estimated by COH source inversion algorithms for each frequency band. The scores of MMSE-J, DBD-13 and MEG source intensity were compared between at the beginning and the end of the NPT period at each frequency band separately.

Results
The scores of MMSE-J was significantly improved after NPT period, although the improvement of the score of DBD-13 was not statistically significant. Right temporal source intensity was decreased in the alpha-band, and right parietal intensity was increased in the low-gamma-band.

Conclusion
The NPT improved cognitive score and changed resting-state brain activities in patients with moderate to severe dementia.
Interbrain Coupling During Turn-taking Verbal Interactions Between Mothers and Children

Jo-Fu Lotus Lin
Institute for Learning & Brain Sciences (I-LABS), University of Washington

Co-Author(s)
Toshiaki Imada – Institute for Learning & Brain Sciences (I-LABS), University of Washington
Takashi Ikeda – Research Center for Child Mental Development, Graduate School of Medical Science, Kanazawa University
Chiaki Hasegawa – Research Center for Child Mental Development, Graduate School of Medical Science, Kanazawa University
Masayuki Hirata – Endowed Research Department of Clinical Neuroengineering, Global Center for Medical Engineering and Informatics, Osaka University
Patricia K. Kuhl – Institute for Learning & Brain Sciences (I-LABS), University of Washington

Abstract Theme: Cognition, language, memory

Background and Purpose/Objectives:
Turn-taking is important for verbal communication as well as language learning. Recent hyperscanning studies have shown inter-brain synchronization during alternating speech tasks [1, 2] and live dialogs [3-5] in healthy adults. However, less is known about how turn-taking imitation modulates neural activity in the brains of two interacting individuals during language learning. Our study investigated inter-brain coupling in mother-child pairs during a turn-taking paradigm of verbal imitation.

Methods
Simultaneous MEG recordings were collected from ten mother-child pairs using two MEG systems (160-channel and 151-channel system; Yokogawa Ltd., Japan) housed in a single magnetically-shielded room [6]. A turn-taking verbal imitation paradigm was used, in which children imitated their mothers phrases in Japanese. T1-weighted MRIs were obtained from each subject with a 1.5T MRI scanner (Signa Excite, GE Medical Systems, USA). Epochs were defined separately at the onset of the mothers and the childrens utterances. After attenuating EOG, ECG, and muscle artifacts with SSP and ICA, source activity was calculated using minimum-norm estimates. Inter-brain synchronization was calculated using partial coherence to remove the effect of brain-to-speech synchronization.

Results
Inter-brain coupling was observed in the theta band in the mother-child pairs during turn-taking tasks. Specifically, brain-to-brain coherence was observed between the speakers frontal, precentral, and temporal areas and the listeners frontal and temporal areas.

Conclusion
Using a naturalistic turn-taking paradigm, our study shows that reciprocal social interaction could enhance brain-to-brain synchronization in a verbal imitation task, suggesting social interaction might enhance verbal learning. This study has implications for individuals with social communication deficits.
Enhanced Beta Modulations in Primary Sensory motor and Visual Cortices Reflect Visuomotor Control: A Precursor to Neurofeedback

Chungmin Han
Graduate research assistant
University of Texas at Austin

Co-Author(s)
Larry Abraham – Kinesiology, University of Texas at Austin
Mark M. McManis – Dell Children's Medical Center of Central Texas
David Schnyer – Psychology, University of Texas at Austin
James S. Sulzer – Mechanical engineering, University of Texas at Austin
Paul Ferrari – Psychology, University of Texas at Austin

Abstract Theme: Cognition, language, memory

Background and Purpose/Objectives:
Alpha- and beta-band oscillations in addition to reflecting movement parameters also index executive functions involved in motor control, such as attention, and may provide a substrate for inter-areal binding. However, how these cortical oscillations are manifest across distant sensorimotor regions to effect visuomotor control is not well known. We aimed to find the large-scale neural signatures of fine-motor control that can be utilized in a neurofeedback intervention for cognitive-motor rehabilitation in neuromuscular disorders.

Methods
We recorded neuromagnetic signals (Triux, By MEGIN), electromyography (EMG) and index and thumb forces from 16 subjects, they controlled the position of an on-screen cursor with a custom-made pinch-force sensor. In 6-sec trials subjects tracked a target moving diagonally, in two conditions that varied visuomotor feedback. We used a beamformer to reconstruct sources event-related desynchrony (ERD) and synchrony (ERS) as a function of task phase and condition. Morlet-wavelet provided time-frequency maps of source-level oscillatory dynamics. Behavior was assessed via trial root-mean-square-error and EMG. Significance was tested using non-parametric statistics.

Results
We found significant within trial alpha and beta dynamic modulation as a function of task behavior in bilateral sensorimotor and visual cortices. With no overall task-based differences in movement statistics, we find visuomotor feedback-control- results in enhanced ERD and ERS beta oscillations in both sensorimotor and visual cortices.

Conclusion
Task-dependent oscillations in sensory and motor cortices may reflect the degree of top-down mediated visuomotor integration. This simplified ROI network may provide robust, yet complex, features for targeting neurofeedback-based rehabilitation.
Limitations of Magnetoencephalography for Detecting High Frequency Activity

Naohiro Tsuyuguchi
Kindai University Faculty of Medicine, Department of Neurosurgery

Co-Author(s)
Yoshiaki Adachi – Kanazawa Institute of Technology
Masanori Higuchi – Kanazawa Institute of Technology
Daisuke Oyama – Kanazawa Institute of Technology
Takehiro Uda – Osaka City University Graduate School of Medicine

Abstract Theme: Computational and analytical approaches

Background and Purpose/Objectives:
It is well known that high frequency activity (HFA) is increases with human brain activity. This HFA is difficult to detect from the scalp, and is evaluated by the signals from subdural electrodes on the brain surface. However, a few researches on HFA by MEG have been recently reported. Therefore, in experiments using phantoms, it was confirmed that the intensity of the HFA could be detected.

Methods
A stimulation electrode as a signal source was placed into the container on a plastic ball, and measurement electrodes imitating subdural electrodes was placed on the surface of the ball. The balls were filled with agar. The stimulation electrode was adjusted so that the signal at the measurement electrode was 0.5V to 50V. The virtual HFA was measured at 50-330 Hz. Furthermore, we confirmed the detection of high gamma activity (HGA) using Corti Q system from gtec, which is used for awake surgery.

Results
Although HFA cannot be recognized in the original waveform of MEG, it is possible to detect HFA in FFT analysis. However, the signal at 1V or less is at the same level as noise, and it is difficult to distinguish between signal and noise in FFT analysis. Significant detection of HGA in Corti Q had a magnitude of several V or more.

Conclusion
In this study, HFA detection was possible regardless of the frequency. However, in order to detect HFA with various frequencies in the clinical situation by MEG, the signal strength at the brain surface needs several V or more.
Parallel Symposium #3: Neurological conditions (excluding epilepsy)

Chair: Seppo Ahlfors

1400  Abstract #43 Submission ID 677118
The effect of normal-appearing white matter changes on visual-gamma in paediatric acquired demyelinating syndromes
Sonya Bells

1420  Abstract # 57 Submission ID 674683
Communication study: Hyperscanning using dual-MEG
Kazuyori Yagyu

1440  Abstract # 58 Submission ID 673882
Marked Increases in Resting-State MEG Gamma-Band Activity in Combat-related Mild Traumatic Brain Injury: a Novel Imaging Marker
Mingxiong Huang

1500  Abstract # 44 Submission ID 680695
The distinct impact of age on occipital neural dynamics in HIV-infected adults with and without cognitive impairment
Alex Wiesman
Abstract #43 Submission ID 677118
The Effect of Normal-appearing White Matter Changes on Visual-gamma in Peadiatric Acquired Demyelinating Syndromes

Sonya Bells
Research Fellow
The Hospital for Sick Children

Co-Author(s)
Giulia Longoni – The Hospital for Sick Children
Donald Mabbott – The Hospital for Sick Children
E. Ann Yeh – The Hospital for Sick Children

Abstract Theme: Neurological conditions (excluding epilepsy)

Background and Purpose/Objectives:
Normal-appearing white matter (NAWM) microstructural changes have been demonstrated in youth with either monophasic or recurrent acquired demyelinating syndromes (ADS). In this study, we aimed 1) to confirm NAWM microstructural abnormalities using a novel diffusion MRI model, and 2) to demonstrate a direct effect of NAWM microstructural changes on neural synchronization (visual-gamma) in this population.

Methods
We evaluated group differences in the WM tract integrity (WMTI) model within the optic radiation (OR); and visual-gamma between 28 typically developing children (17F; 15.4±2.6yrs) and 25 children with ADS (19F; 14.5±3.2yrs). Neuromagnetic activity during a monochrome checkerboard task was recorded using a 151-CTF system. Beamformer analysis localized cortical gamma activity (40-120Hz) +/-1000ms with respect to checkerboard pattern switch (300ms). Time-frequency plots of visual cortex (V1)-gamma power were computed using a Morlet wavelet transform. A multi-shell diffusion-weighted dataset was acquired with echo planar imaging on a 3T-Siemans system and was processed using DESIGNER. Tract-based spatial statistics was performed on the WMTI parameters to test group differences. Path modelling tested the impact of ADS on visual gamma via their effects on OR NAWM microstructure.

Results
Children and adolescents with ADS showed evidence of myelin and axon compromise (p < 0.007) and reduced visual gamma power (F(2,51)=15.2,p=0.0003). Differences in WMTI metrics within the OR between patients and typically developing children predict peak gamma within V1 (=0.33,p=0.03).

Conclusion
Our findings show a fundamental connection between NAWM microstructure and neural synchronization. Future studies will investigate how the interplay between NAWM abnormalities and abnormal neural synchronization affects cognition within this population.
Abstract # 57 Submission ID 674683

**Communication Study: Hyperscanning Using Dual-MEG**

**Kazuyori Yagyu**  
Assistant Professor  
Funded Research Division of Child and Adolescent Psychiatry, Hokkaido University Hospital

**Co-Author(s)**  
Hayato Watanabe – Hokkaido University  
Atsushi Shimojo – Department of Pediatrics, Hokkaido University, Graduate School of Medicine  
Tsuyoshi Sonehara – Hitachi Corporation  
Koichi Yokosawa – Faculty of Health Sciences, Hokkaido University  
Takuya Saito – Professor, Funded Research Division of Child and Adolescent Psychiatry, Hokkaido University Hospital

**Abstract Theme:** Neurological conditions (excluding epilepsy)

**Background and Purpose/Objectives:** Mental and neurodevelopmental diseases often accompany communication disability. Neurological assessments of communication were usually conducted in an inspector style like face-expression judgements, but original communication studies should be conducted in inter-personal style. We connected two MEG with fiber optic cables and enabled to measure two simultaneous brain activities. In this study, we sought to establish natural face-to-face and time-sensitive communication system and tried to measure both brain activities simultaneously.

**Methods**  
In both sites, video-cameras, projectors, microphones and speakers were prepared at the end of optical fibers with converters. Latency and jitter visual signals were measured beforehand. For more natural face-to-face settings, half-mirrors were equipped in front of subjects to set video-camera and projector at right in front of subjects face. In preliminary study, the two types of image were projected pseudo-randomly: one was real person and the other one was video playback. Video playback images were drawn from a delayed playback system. Subjects were asked to answer whether the image was real person or fake video playback.

**Results**  
The transmission latency for visual signals was evaluated at 80.13 ms (SD ± 5.94 ms). In addition, the halfmirror apparatuses allowed subjects to communicate using direct eye contact in the preliminary study.

**Conclusion**  
In our dual-MEG system, the latency of visual signals was sufficiently least and it provided satisfactory environment for natural communication in the preliminary study.
Marked Increases in Resting-State MEG Gamma-Band Activity in Combat-related Mild Traumatic Brain Injury: A Novel Imaging Marker

MINGXIONG HUANG, PhD
University of California, San Diego

Co-Author(s)
Charles W. Huang – Bioengineering, Stanford University
Deborah L. Harrington, PhD – Professor, Radiology, University of California San Diego
Sharon Nichols, PhD – Neurosciences, University of California San Diego
Roland R. Lee, MD – Professor, Radiology, University of California San Diego
Dewleen G. Baker, MD – Professor, Psychiatry, University of California San Diego

Abstract Theme: Neurological conditions (excluding epilepsy)

Background and Purpose/Objectives:
Combat-related mild traumatic brain injury (mTBI) is a leading cause of sustained impairments in military service members and Veterans. Conventional MRI and CT images are generally negative even in patients with persistent post-concussive symptoms. For years, scientists have focused on developing diffusion-based MRI techniques to identify abnormalities in white-matter tracts with limited sensitivity, owing to the assumed major role of diffuse axonal injury in mTBI. However, recent animal studies show that GABA-ergic parvalbumin-positive interneurons in gray matter are highly susceptible to brain injury, with damage causing abnormal increases in spontaneous gamma-band (30-80 Hz) activity.

Methods
We investigated spontaneous gamma activity in individuals with mTBI using high-resolution resting-state magnetoencephalography (rs-MEG) source imaging. Participants included 25 symptomatic individuals with chronic combat-related blast mTBI, and 35 healthy controls with similar combat experiences.

Results
Compared with controls, gamma activity was markedly elevated in mTBI participants throughout frontal, parietal, temporal, and occipital cortices, whereas gamma activity was reduced in ventromedial prefrontal cortex. Across groups, greater gamma activity correlated with poorer performances on tests of executive functioning and visuospatial processing. Many neurocognitive associations, however, were partly driven by the higher incidence of mTBI participants with both higher gamma activity and poorer cognition, suggesting that expansive upregulation of gamma has negative repercussions for cognition particularly in mTBI. This is the first human study to demonstrate abnormal resting-state gamma activity in mTBI.

Conclusion
These novel findings suggest the possibility that abnormal gamma activities may be a proxy for GABA-ergic interneuron dysfunction and a promising neuroimaging marker of insidious mild head injuries.
The Distinct Impact of Age on Occipital Neural Dynamics in HIV-infected Adults with and Without Cognitive Impairment

Alex I. Wiesman, B.S.
Graduate Research Assistant
University of Nebraska Medical Center

Co-Author(s)
Boman R. Groff – University of Nebraska Medical Center
Kevin R. Robertson – University of North Carolina School of Medicine
Howard S. Fox – University of Nebraska Medical Center
Susan Swindells – University of Nebraska Medical Center
Tony W. Wilson – University of Nebraska Medical Center

Abstract Theme: Neurological conditions (excluding epilepsy)

Background and Purpose/Objectives:
Previous research has established a neural basis for HIV-related declines in visuospatial function, particularly in regard to HIV-associated neurocognitive disorders (HAND). However, little is known about the age-related trajectory of these neural dynamics, and how this trajectory might be altered as a function of HIV-infection and cognitive status. In this study, we investigate whether aging differentially affects neural activity serving visuospatial processing in the largest functional neuroimaging study of HIV-infected participants to date (n = 251).

Methods
All participants underwent neuropsychological assessment followed by performance of an established visuospatial discrimination paradigm during neuroimaging with magnetoencephalography (MEG). These data were analyzed in the time-frequency domain across all groups to identify significant oscillatory responses of interest, which were then imaged using a beamformer. Whole-brain linear models were used to examine frequency-specific interactions between age, HIV-infection, and cognitive status.

Results
We found that cognitively-impaired HIV-infected adults were distinguished from unimpaired HIV-infected and control participants by their negative association between age and parieto-occipital gamma responses, as well as by their unique positive relationship between superior parietal alpha oscillations and age. Interestingly, the relationship between gamma oscillations and age was fully mediated by duration of HIV-infection in the cognitively-impaired, but not the unimpaired, participants.

Conclusion
Participants with HAND exhibited markedly different relationships between age and oscillatory neural responses in the parieto-occipital cortices relative to their peers. This finding implies a differential effect of chronological aging on the neural bases of visuospatial processing in a cognitively-impaired subset of HIV infected adults.
Friday, September 13, 2019

Symposium #4:
Connectivity, Computational Approaches, Perception & Sensation, Other Methodologies

Chair: Sylvain Baillet

1400  Abstract # 38 Submission ID 678997
Characterizing Transient Spectral Events in Big Data
Timothy Bardouille

1420  Abstract #59 Submission ID 666935
Resting state MEG for rational planning of neurostimulation treatment in stroke and dementia
Jed Meltzer

1440  Abstract #61 Submission ID 679283
The respiratory cycle modulates pain processing: an experimental study
Isamu Ozaki

1500  Abstract #36 Submission ID 666061
Simple and concise operation makes the most of MEG
Yoshihito Shigihara
Abstract # 38 Submission ID 678997
Characterizing Transient Spectral Events in Big Data

Tim Bardouille, PhD
Assistant Professor
Dalhousie University

Abstract Theme: Connectivity and brain networks

Background and Purpose/Objectives:
Cortical rhythms are linked to healthy function and dysfunction, and synchrony between brain areas may be indicative of long-range communication. The peaks in a spectrogram that indicate cortical rhythmic activity are caused by short bursts of oscillatory activity, which are sometimes termed transient spectral events. MEG provides a favourable combination of spatial and temporal resolution for observing transient spectral events. Large open-access MEG datasets are now available, which can generalize our understanding of transient spectral events. This has potential value for detecting changes in neurophysiology due to learning, ageing, or brain dysfunction.

Methods
This study used MEG and MRI data collected by the Cambridge Center for Ageing and Neuroscience in 650 healthy adults with balanced representation of males and females, and uniform distribution of age. MEG data were analysed to detect the onset of transient spectral events in each participant. Each events temporal and spectral characteristics were tabulated, and events were localized on the individuals MRI using the beamformer spatial filter.

Results
We showed that transient spectral events can be reliably detected in this population, and that the spatiotemporal characteristics match with previous reports in smaller populations. Beamformer localization of transient spectral events matches localization of the related cortical oscillation. We also showed that the characteristics of transient spectral events change between a cued movement and rest, and evolve with age.

Conclusion
Characterizing transient spectral events offers an alternate window to study neurophysiology, which takes advantage of the unique strengths of MEG and the push to create large open-access datasets.
Abstract #59 Submission ID 666935

Resting State MEG for Rational Planning of Neurostimulation Treatment in Stroke and Dementia

Jed A. Meltzer, Ph.D.
Scientist
Baycrest, Rotman Research Institute

Co-Author(s)
Aneta Kielar, Ph.D. – Assistant Professor, University of Arizona
Priyanka Shah-Basak, Ph.D. – Scientific Associate, Baycrest, Rotman Research Institute

Abstract Theme: Other methodologies and modalities, including TMS

Background and Purpose/Objectives:
Noninvasive brain stimulation shows promise for symptomatic treatment of stroke and dementia, but important questions remain about where and how to stimulate. Measurements of resting state abnormalities with fMRI have mostly focused on connectivity changes, which are sensitive measures but do not uniquely identify local regions of abnormal cortical activity that might be remediated by stimulation. Using resting-state MEG, we identified focal abnormalities (slowed power spectra and reduced entropy) in stroke patients adjacent to structural lesions, which correspond to reduced blood flow but not altered BOLD dynamics. Similar abnormalities in dementia predict slowed neural responses to cognitive stimuli and reduced cognitive function, beyond that accounted for by structural atrophy.

Methods
We investigated the use of resting state MEG abnormalities to target high-definition transcranial direct current stimulation (HD-TDCS) to brain regions that might especially benefit from it.

Results
In 10 patients with aphasia caused by left-hemisphere stroke, a single session of targeted HD-TDCS improved fluency, partially restored resting state activity towards normal levels, and surprisingly, also increased the engagement of the right hemisphere in language processing. In 7 patients with primary progressive aphasia (a form of dementia), one week of HD-TDCS improved picture naming in some patients, with accompanying restoration of normal activity.

Conclusion
These findings point to the expanded use of MEG to map both function and dysfunction in brains affected by neurological disorders, and to use those maps to target therapeutic stimulation to the appropriate areas.
Abstract #61 Submission ID 679283
The Respiratory Cycle Modulates Pain Processing: An Experimental Study

Isamu Ozaki, MD, PhD
Professor
Aomori University of Health and Welfare

Co-Author(s)
Tatsuya Iwabe – Department of Physical Therapy, School of Rehabilitation Sciences, Health Sciences University of Hokkaido
Akira Hashizume – Department of Neurosurgery, Faculty of Medicine, Hiroshima University

Abstract Theme: Perception, sensation, pain

Background and Purpose/Objectives:
There is growing evidence that pain can be relieved by slow deep breathing such as Zen meditation. However, it is not clear whether the analgesic effect changes between inspiratory phase (IP) and expiratory phase (EP). We hypothesize that pain processing is modulated by a respiratory cycle and that pain will be decreased during EP compared to IP in slow breathing as well as normal breath.

Methods
Ten healthy volunteers participated. Intraepidermal electrical stimulation (IES) with a concentric bipolar needle electrode was applied to the hand dorsum at pain perceptual threshold or four times the threshold to produce first pain during EP or IP either of which was determined by the abrupt change in an exhaled CO2 level during normal breathing. IES-evoked brain potentials (IESEPs), sympathetic skin response (SSR), digital plethysmogram (DPG), and subjective pain intensity rating scale were simultaneously recorded.

Results
With either stimulus intensity, IES during expiration produced weaker pain feeling compared to IES during inspiration. The mean amplitude of N200/P400 in IESEPs and that of SSR were smaller when IES was applied during expiration. The magnitude of DPG wave gradually decreased after IES, but a decrease in the magnitude of DPG wave was less evident when IES was delivered during expiration. Regardless of stimulus timing or stimulus intensity, pain perception was always concomitant with appearance of IESEPs and SSR, and changes in DPG.

Conclusion
Our findings suggest that pain processing fluctuates during normal breathing and that pain is gated within the central nervous system during expiration.
Abstract Theme: Computational and analytical approaches

Background and Purpose/Objectives:
MEG has been used in clinical medicine since 1990's. Around 9,000 papers posted in Pubmed proved that MEG is useful in clinical medicine. However, MEG is not popular: its clinical use is limited and a lot of scientific achievements are wasted. Too complicated MEG analyses and the clinical reports prevent non-expert clinicians and researchers from using MEG. They prefer simple and concise conclusions, although we prioritise the accuracy. We should change our mind to make the most of MEG. Scanning and analysis should be (1) objective and (2) easy. Results should be based on (3) statistical analysis. Here, we propose a new operating policy to make MEG more practical in clinical medicine.

Methods
To make MEG analyses (1) 'objective', reference data are required. We scanned 102 healthy volunteers following the protocols of the Normative Database Project in the UK. Our data is open to the public as a reference. To analyse MEG data (2) 'easily', we developed a plug-in to the SPM toolbox. Once MEG data is selected using the GUI, they are processed in a fully-automated manner, which provides (3) statistical results based on the reference data.

Results
In our hospital group, introduction of the new operation policy increased the number of MEG scans five times than before, because (1) non-expert clinicians get interested in MEG and (2) they start using MEG scans for patients with various diseases other than epilepsy.

Conclusion
(1) Objective, (2) easy and (3) statistical-based analysis are three cornerstones to make the most of MEG in clinical medicine.
Thursday & Friday, September 12 & 13, 2019

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MEG head movement compensation in difficult-to-test populations
Seppo Ahlfors

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Detection of auditory evoked response under the magnetic field noise caused by a cochlear implant device
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Ji Hee Kim

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Hideaki Shiraishi
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Changes of stimulus-induced 20-Hz activity for the tongue and hard palate during tongue movement using MEG
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MEG-based dynamic functional coupling is associated with pain interference on cognitive task performance
Junseok Kim

Abstract #29  Submission ID 675116
Cortical oscillations and phase-amplitude coupling during motor processing in young children with autism spectrum disorders
Kyung-min An

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Long-term effects of interictal epileptiform discharge on cognitive development and sociality in preschool children with autism spectrum disorders
Tetsu Hirosawa

Abstract #31  Submission ID 670557
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Abstract #32  Submission ID 677013
Abnormal Auditory Mismatch Fields in Children and Adolescents with 47, XYY syndrome
Junko Matsuzaki
Abstract Theme: Cognition, language, memory

Background and Purpose/Objectives:
Knowledge regarding the brains regions affected by mild cognitive impairment (MCI) is still limited. However, it is known that working memory function is affected by MCI. One element that is potentially sensitive to working memory function is the primacy effect, where sequential memory performance is better for items that occur at the beginning compared to the middle of a sequence. Here, we used a visual sequential memory task and magnetoencephalography (MEG) to identify brain regions relevant to working memory function and MCI.

Methods
We administered the Montreal Cognitive Assessment (MoCA) test, a screening tool for MCI, to 20 elderly participants (mean age, 67.5 years). In the sequential memory task, each participant memorized the directions (up, down, right, or left) of seven sequentially presented arrow images. MEG were recorded during the task, and source-level alpha-band rhythms (8-13 Hz) were estimated.

Results
MoCA score had a significantly positive linear relationship with recall accuracy for memorized items at the beginning of the sequence, indicating that the primacy effect, and thereby working memory function was weaker for lower MoCA scorers. MoCA score furthermore had a significantly negative linear relationship with the amplitude of alpha-band rhythm bilaterally in the precuneus (PCu) during the beginning of sequential memory, indicating poorer working memory function to be associated with less desynchronization of PCu alpha-band rhythm.

Conclusion
The significant relationships between MoCA score, memory performance and alpha-band activity in the PCu suggests that the PCu is a region involved in working memory function and affected by MCI.
MEG Head Movement Compensation in Difficult-to-test Populations

Seppo P. Ahlfors
Athinoula A. Martinos Center, Massachusetts General Hospital

Co-Author(s)
Christopher Wreh – Athinoula A. Martinos Center, Massachusetts General Hospital
Maria Mody – Athinoula A. Martinos Center, Massachusetts General Hospital

Abstract Theme: Computational and analytical approaches

Background and Purpose/Objectives:
Head movements during MEG data acquisition can severely distort the MEG data. For some patient populations, such as autism spectrum disorder, ADHD, Fragile X Syndrome (FXS), staying still during the recording is very difficult. Therefore, methods for detecting head movements and compensating for their effects towards the goal of identifying and salvaging usable MEG data are of critical importance.

Methods
We examined the head movements of patients with FXS during MEG sessions, and developed and evaluated signal processing procedures to optimize the quality of event-related and resting state MEG data in these patients. The Neuromag MaxFilter and the MNE Python software were used, in combination with continuous head position indicator (HPI) measurements. The signal-to-noise ratio of somatomotor activity associated with self-paced button presses was evaluated using different parameter values for the MaxFilter algorithm.

Results
The choices for both the spherical expansion origin and the target head position transformation notably affected the quality of the event-related data. Excluding trials during which prominent changes in the head position occurred was necessary. Large head movements during the MEG recording also complicated the estimation of the noise covariance information for the inverse operator.

Conclusion
Efficient head movement detection and compensation procedures can substantially improve the quality of MEG results in certain patient populations that in general are difficult to test with MEG.
Abstract #5  Submission ID 679683
Detection of Auditory Evoked Response Under the Magnetic Field Noise Caused by a Cochlear Implant Device

Yasuhiro Haruta
Professor
Applied Electronics Laboratory, Kanazawa Institute of Technology, Japan

Co-Author(s)
Masanori Higuchi – Professor, Applied Electronics Laboratory, Kanazawa Institute of Technology, Japan
Gen Uehara – Professor, Applied Electronics Laboratory, Kanazawa Institute of Technology, Japan

Abstract Theme: Computational and analytical approaches

Background and Purpose/Objectives:
Cochlear implants (CIs) are useful to people who no longer benefit from hearing aids; however, they generate strong magnetic and electromagnetic artifacts, limiting the use of MEG and EEG in these recipients. We aimed to detect an auditory evoked response under the noise of a CI magnet.

Methods
We used a 32-channel second-order gradiometer MEG system, newly designed for this study. The lengths of two baselines were optimized to minimize the sensitivity for the CI magnet. We developed a two-step artifact suppression algorithm. First, virtual reference sensors were employed near the CI magnet. Second, the noise component in each MEG channel was estimated as the weighted average of the virtual reference sensor data. A 54-year-old, right-handed, normal-hearing male subject participated in this study. The CI magnet was attached behind his left ear; MEG sensors were placed over his right hemisphere. Tone bursts of 1 kHz, superimposed on continuous white noise, were presented into his left ear at ISI of 1s-2s. A total of 100 epochs were recorded at a sampling rate of 1 kHz, with 0.3-200 Hz bandpass filter.

Results
A clear N1m response was observed at latency of 97 ms. The isofield contour map at N1m peak showed a single-dipole pattern. The estimated equivalent current dipole was localized at the temporal area, with goodness of fit of 87.7%.

Conclusion
We successfully detected an auditory evoked response under the noise of a CI magnet. This result introduces the possibility of applying MEG in patients with CIs.
Automated Detection of Interictal Spikes: Choice of a Computational Framework

Tommaso Fedele
Higher School of Economics

Co-Author(s)
Valerii Chirkov – Moscow State University
Alexandra Kuznetsova – HSE
Alexei Ossadtchi – HSE

Abstract Theme:
Computational and analytical approaches

Background and Purpose/Objectives:
The reliable identification of the irritative zone is a prerequisite for the correct clinical evaluation of medically refractory patients affected by epilepsy. Given the complexity of MEG data, visual analysis is highly time consuming and might leave clinically relevant information undetected.

Methods
Methods: We recorded and analyzed the interictal activity of a patient affected by multifocal epilepsy characterized by low-amplitude spatially distributed spikes (306 channel Vectorview Neuromag). We compared three automated spike detection methods: 1) ICA-based: identification of spiky ICA components [1]; 2) SPLINE-based: fitting to a library of mixed splines; 3) TEMPLATE-based: data-driven spatio-temporal template matching previously applied to neuronal spike sorting [2]. We adjusted detection threshold to obtain approximately equal number of automatically detected spikes across methods and compared their sensitivity towards visually marked events.

Results
The ICA-based detection had a sensitivity of 93% with the fewest total events count, SPLINE-based 85% but required spline scale adjustment, TEMPLATE-based 75%. The specificity was not considered in this analysis as we visually identified only a subset of spikes. All approaches performed best when considering the combination of gradiometers and magnetometers. Computational time on a commercial laptop for a dataset of 10 minutes, 306-sensors, 1000 Hz sampling rate of data was below 5 minutes.

Conclusion
We quantified here the performance of different algorithmic approaches for the automated detection of interictal spikes, to contribute delineating the irritative zone in a complex multifocal case. This computational framework provides the basis for a fast, reproducible, bias-free identification of irritative zone in MEG recordings.
Resting State Connectivity in Fragile X Syndrome

Maria Mody, PhD
Assistant Professor of Radiology
MGH Athinoula A. Martinos Center for Biomedical Imaging & Harvard Medical School

Co-Author(s)
Seppo P. Ahlfors, PhD – MGH Athinoula A. Martinos Center for Biomedical Imaging & Harvard Medical School
Christopher Wreh – MGH Athinoula A. Martinos Center for Biomedical Imaging
Jin-Chen Yang – MGH Athinoula A. Martinos Center for Biomedical Imaging
Anna-Liisa Brownell – MGH Gordon Center for Medical Imaging & Harvard Medical School

Abstract Theme: Connectivity and brain networks

Background and Purpose/Objectives:
The motor system is increasingly implicated in developmental disabilities like autism spectrum disorder (ASD). Fragile X Syndrome (FXS) is the most common known cause of autistic-like symptoms. We propose to examine functional connectivity between the motor system and the rest of the brain in FXS towards an improved understanding of the deficits characterizing these disorders.

Methods
Adult males with and without FXS, matched on age and handedness, participated in a five-minute eyes-open resting state experiment while whole head MEG was recorded using a 306-channel system. Pre-processed raw data was filtered (8 Hz-13 Hz) to obtain alpha band activity and analyzed using MNE Python software. Head movements were monitored throughout the recording and compensated for in the analysis. MEG data was co-registered with anatomical MRI in each subject.

Results
We found significant group differences in functional connectivity in the alpha band between key motor areas (M1, S1, SMA) and frontal areas (middle frontal and inferior frontal gyri).

Conclusion
Language and cognitive deficits in fragile X syndrome may be related to frontal connectivity issues mediated by the motor system.
Adults with Autism Spectrum Disorder Demonstrate Atypical Brain Connectivity During a Response Inhibition Task

Veronica Yuk
Hospital for Sick Children

Co-Author(s)
Kristina Safar – Hospital for Sick Children
Evdokia Anagnostou – Holland Bloorview Kids Rehabilitation Hospital
Margot Taylor – Hospital for Sick Children

Abstract Theme: Connectivity and brain networks

Background and Purpose/Objectives:
Adults with autism spectrum disorder (ASD) often show behavioural difficulties with inhibitory control, as well as atypical connectivity among brain regions during inhibition, although the temporal and spectral differences have not been elaborated. Here we contrasted the temporal, spatial, and spectral aspects of brain connectivity between adults with and without ASD during a response inhibition task using MEG.

Methods
We included 40 adults with ASD (27 M; 26.9±6.1 years old) and 39 controls (27 M; 27.3±5.9 years old), who performed a go/no-go task involving two blocks with different proportions of no-go trials: inhibition (25% no-go) and vigilance (75% no-go). We performed seed-based analyses, examining connectivity between 14 nodes of the inhibition network and the rest of the brain, as well as a whole-brain approach to explore other areas that may be differentially connected in ASD during inhibition. We compared connectivity during correct no-go trials in the inhibition vs. vigilance blocks between 100-400ms and 600-800ms. Results are reported at a FWEcorrected p < 0.05.

Results
While the two groups performed similarly on the go/no-go task, adults with ASD showed increased connectivity in a network containing the bilateral inferior frontal gyri and right supplementary motor area between 600-800ms in the beta band. Our whole-brain analyses further revealed that adults with ASD had decreased connectivity in a similar network in the earlier 100-400ms time window in the alpha band.

Conclusion
Our findings suggest that adults with ASD show delayed recruitment of an inhibitory control brain network compared to controls, and that they may utilize different inhibitory mechanisms.
Developmental Trajectories of Functional Connectivity in Infant Follow-up Study

Chiaki Hasegawa
Kanazawa University

Co-Author(s)
Yuko Yoshimura – Institute of Human and Social Sciences, Kanazawa University
Mitsuru Kikuchi – Research Center for Child Mental Development, Kanazawa University

Abstract Theme: Connectivity and brain networks

Background and Purpose/Objectives:
Infancy is a period of remarkable neural development in the brain that is reflected by increasing cognitive and behavioral capacities for external circumstances or internal changes in later life. We characterized the trajectory of brain signal functional connectivity of typically developing an infant, aged 3 to 36 months, using graph theory applied to magnetoencephalography (MEG).

Methods
We acquired MEG data from five infants from 3 months old to 36 months old under awake conditions (watching preferring video program). We calculated averages among links that connect to the remaining brain regions as node degree (ND), which is the most fundamental network measure.

Results
The analysis revealed frequency-dependent developmental trajectories of ND values. Specifically, we found increases of ND value for delta (2-4Hz) and beta (13-30Hz) band, whereas there were decreases for theta (4-8Hz) and gamma (30-60Hz) band. ND in the alpha band (8-13Hz) showed inversed U-shape development.

Conclusion
Despite a small sample size limiting this study's power, this is the first report of a longitudinal investigation of changes in functional connectivity during early infancy and is unique in its application of graph analysis of longitudinal MEG data during infancy. The results of this pilot study may serve to further our understanding of the longitudinal changes in the neural dynamics of the developing infant brain.
Abstract #10   Submission ID 676725
Equivalent Current Dipole Analysis of Epileptic Spikes Between Spike Peak and Onset

Hiroyuki Yamamoto, MD
Nagoya University Graduate School of Medicine

Co-Author(s)
Hideaki Shiraishi – Pediatrics, Hokkaido University Hospital
Masaharu Tanaka – Pediatrics, Nagoya University Graduate School of Medicine
Jun Natsume – Pediatrics, Nagoya University Graduate School of Medicine

Abstract Theme: Epilepsy

Background and Purpose/Objectives:
Equivalent current dipole (ECD) analysis by magnetoencephalography (MEG) has been used to investigate seizure onset zone. However, ECDs were often estimated in inaccurate area. In this study we investigated the differences of ECD between spike peak and onset.

Methods
We investigated two patients with epilepsy their ECDs showed in the different area from the seizure onset zone. We determined spike peak and analytical onset (at one third from onset to peak). Then we estimated ECDs every 0.001 second between the two points.

Results
Case-1 showed abnormal enlargement of the left amygdala on MRI. FDG-PET showed a decrement in metabolism in the left temporal lobe. We investigated 28 spikes. MEG showed no cluster of ECD at both of peak and analytical onset. The ECD showed highest GOF was substantially middle of two points. Case-2, with no constructive lesion on MRI, showed a decrement in perfusion on Arterial Sin Labeling (ASL) and positive Blood oxygenation level-dependent (BOLD) on EEG-fMRI in the left orbitofrontal cortex. We investigated 57 spikes. ECDs were clustered in the left parietal lobe. The ECD showed highest GOF was substantially middle of two points. However, source distribution analysis of MEG revealed a significant magnetic-field change in the left orbitofrontal cortex.

Conclusion
MEG have the information of seizure onset zone, but ECDs often show the inaccurate area even though choose the most suitable time point.
Abstract Theme: Epilepsy

Background and Purpose/Objectives:
Somatosensory evoked magnetic fields (SEFs) evoked by stimulation of the median nerve are useful to objectively evaluate cortical function of the primary somatosensory area (SI). We measured SEFs for the posterior tibial nerve (PTN) in patients with sensorimotor seizures of the lower limbs.

Methods
This study included 7 consecutive patients with sensorimotor seizures of the lower limbs evaluated in our comprehensive epilepsy monitoring unit from 2011 to 2018. Magnetic resonance (MR) imaging showed that one patient had focal cortical dysplasia (FCD) in the right parietal lobe, one patient had FCD in the left frontal lobe, and the other 5 patients had no lesion. PTN-SEFs were measured in all patients using a 200-channel whole-head magnetoencephalography system (RICOH, Japan). Equivalent current dipoles (ECDs) of the first components (P38m) were compared between left and right sides.

Results
In the patient with right parietal FCD, the ECD moment of P38m of the left PTN-SEF was decreased (18%) compared to the right. In the patient with left frontal FCD, the ECD moment of the right PTN-SEF was almost equal (79%) to the left. In the other patients, the ECD moments of PTN-SEFs for the symptomatic side were decreased in three cases (35%, 55%, and 59%) compared to the asymptomatic side and almost equal in two cases (82% and 89%).

Conclusion
Generally, differentiation of parietal and frontal lobe epilepsy is difficult based on only sensorimotor symptoms of the lower limbs. Measurement of the P38m amplitude of the PTN-SEF may be useful for the differential diagnosis in some such cases.
Estimation of Postoperative Visual Field Defect Using Visual Evoked Field

Takehiro Uda
Lecturer
Osaka City University Graduate School of Medicine

Co-Author(s)
Naohiro Tsuyuguchi – Neurosurgery, Kinki University
Kosuke Nakajo – Neurosurgery, Osaka City University Graduate School of Medicine
Hiroshi Uda – Neurosurgery, Osaka City University Graduate School of Medicine
Yuta Tanoue – Neurosurgery, Osaka City University Graduate School of Medicine
Kenji Ohata – Neurosurgery, Osaka City University Graduate School of Medicine

Abstract Theme: Epilepsy

Background and Purpose/Objectives:
As a presurgical evaluation for the epilepsy associated with occipital lobe, it is important to confirm whether the visual function (VF) is preserved in the affected hemisphere or not. Goldmann kinetic perimetry (GP) is a standard VF test. However, in some pediatric patients or patients with mental retardation, GP is difficult to perform. Here, we present the representative cases with confirming it by visual evoked magnetic field (VEF).

Methods
As visual stimuli, checkerboard was inverted every 500 ms on the screen. MEG data of three sessions (bilateral, left-side and right-side stimulus) were recorded for 3 min. After averaging each data, VEF was estimated with equivalent current dipole method around 100 ms after the stimulus.

Results
In the case of 19-year-old post-traumatic left side epilepsy, VEF by the right-side stimulus was estimated on the left occipital lobe and GP showed right upper quadrantic anopsia. That suggested the right-side VF was preserved in the left occipital lobe. Although we could estimate the postoperative right homonymous hemianopsia, we performed left hemispherotomy for complete seizure relief. In the case of 10-year-old posttraumatic left side epilepsy, VEFs by all three stimuli were estimated on the right occipital lobe. That suggested the VF had been lost from the left occipital lobe. GP could not be performed because of the mental retardation. We performed left-side occipital lobectomy without hesitation.

Conclusion
VEF offers objective preoperative information to estimate the postoperative VF defect. That might be useful especially for the patients with difficulty to perform GP.
Abstract #13 Submission ID 677180

**Correlation Between Fusion EEG-MEG Source Localizations with Hemodynamic Responses and Relation to Surgical Outcome**

Chifaou Abdallah, Postdoctoral Fellow
McGill University, Montreal, Canada

**Co-Author(s)**
Rasheda Chowdhury – CHU Sainte-Justine Research Centre, Montreal, Canada
Giovanni Pellegrino – Neurology and Neurosurgery Department, Montreal Neurological Institute, McGill University
Jean Gotman – Neurology and Neurosurgery Department, Montreal Neurological Institute, McGill University
Elaine Kobayashi – Neurology and Neurosurgery Department, Montreal Neurological Institute, McGill University
Christophe Grova – Multimodal Functional Imaging Lab, Biomedical Engineering Department, McGill University; Multimodal Functional Imaging Lab, Department of Physics and PERFORM Centre, Montreal, Canada

**Abstract Theme: Epilepsy**

**Background and Purpose/Objectives:**
Reliability of source localization of interictal epileptic discharges (IED) using EEG-MEG fusion within the Maximum Entropy on the Mean framework was demonstrated in Chowdhury et al., 2018. In simultaneous EEG-fMRI recordings, the BOLD response to IED with most significant t-value (primary cluster) can highly predict the seizure onset zone (Khoo et al., 2017). Our objective was to evaluate concordance between IED source localization using EEG/MEG fusion with the location of EEG-fMRI primary cluster. We aimed to assess their localizing value (sublobar focal versus extended) and associated surgical outcome.

**Methods:** 13 consecutive neocortical epilepsy patients who underwent simultaneous EEG-MEG and simultaneous EEG fMRI recordings, were retrospectively included. For each patient, similar IEDs were selected for both EEG-MEG and EEG-fMRI analyses. Applying EEG/MEG fusion to every single IED, we computed a fusion consensus map representing the most reliable localization result (Chowdhury et al., 2015) and compared it with the fMRI primary cluster.

**Results**
Fusion-consensus maps were found concordant with the fMRI primary clusters in 7/13 patients. Three situations occurred: a) the fusion-consensus map was concordant with the fMRI primary cluster and both were localizing, 3 underwent surgery and 2 are seizure-free; b) the fusion-consensus map was concordant with fMRI and either fMRI primary cluster or fusion-consensus map was localizing, 3 underwent surgery and none are seizure-free; c) both modalities were discordant, 5 underwent surgery and only 1 is seizure-free.

**Conclusion**
Concordance between fusion EEG-MEG IED source localization consensus map and BOLD response primary cluster was associated with a good post-surgical outcome when both modalities had clinical localizing value.
A Novel Method for Extracting Interictal Epileptiform Discharges in Multi-channel MEG: Use of Fractional Type of Blind Source Separation

Teppei Matsubara
Department of Clinical Neurophysiology, Kyushu University

Co-Author(s)
Naruhito Hironaga – Clinical Neurophysiology, Kyushu University
Taira Uehara – Clinical Neurophysiology, Kyushu University
Hiroshi Chatani – Clinical Neurophysiology, Kyushu University
Shozo Tobimatsu – Clinical Neurophysiology, Kyushu University
Kuniharu Kishida – Professor Emeritus, Gifu University

Abstract Theme: Epilepsy

Background and Purpose/Objectives:
Visual inspection of interictal epileptiform discharges (IEDs) in multi-channel MEG requires a time-consuming evaluation process and often leads to inconsistent results due to variability of IED waveforms. Here, we propose a novel extraction method for IEDs using a T/k type of blind source separation (BSST/k).

Methods
We applied BSST/k with seven patients to test the accuracy of identification of IEDs for various types of epileptic syndrome. We conducted comparisons of the results of BSS components with those obtained by visual inspection in sensor-space analysis.

Results
BSST/k provided better signal estimation of IEDs compared with sensor-space analysis. Importantly, BSST/k was able to uncover IEDs that could not be detected by visual inspection. Furthermore, IED components were clearly extracted while preserving spike and wave morphology. Variable IED waveforms were decomposed into one dominant component.

Conclusion
BSST/k was able to visualize the spreading signals over multiple channels into single component from single epileptogenic zone. BSST/k can be adapted to various types of epilepsy with a simple parameter setting. Our novel method was able to highlight IEDs with high accuracy for diagnosis of epilepsy from multi-channel MEG data.
Monaural Auditory Stimulation Can Be Useful for Identifying Epileptic Focus in Patients with Mesial Temporal Lobe Epilepsy

Tepppei Matsubara
Department of Clinical Neurophysiology, Kyushu University

Co-Author(s)
Katsuya Ogata – Clinical Neurophysiology, Kyushu University
Naruhito Hironaga – Clinical Neurophysiology, Kyushu University
Taira Uehara – Clinical Neurophysiology, Kyushu University
Toshihiko Maekawa – Neuropsychiatry, Amekudai Hospital
Shozo Tobimatsu – Clinical Neurophysiology, Kyushu University

Abstract Theme: Epilepsy

Background and Purpose/Objectives:
Mesial temporal lobe epilepsy (mTLE) patients often exhibit central auditory processing (CAP) dysfunction. Monaural pure tone (auditory evoked field, AEF) and 40-Hz auditory steady-state magnetic (ASSR) were recorded to explore the relationship between CAP and lateralization.

Methods
(1) AEF: Twenty-five left, 14 right mTLE and 32 healthy controls (HCs) were recorded. Auditory stimuli of 500-Hz tone bursts were monaurally presented. M100 amplitude, phase-locking factor (PLF) within bilateral Heschls gyri and phase-locking value (PLV) were evaluated. (2) ASSR: Eighteen left, 11 right mTLE and 16 HCs were examined. Monaural clicks were presented at a rate of 40 Hz. PLF were analyzed within bilateral Heschls gyri.

Results
(1) PLF was more sensitive, than M100 amplitude, to differentiate the mTLE groups, with decreased PLFs in the alpha band observed in right mTLE patients compared with those in left mTLE patients. PLV was reduced in both right and left mTLE patients compared with that of HCs. (2) Symmetrical hemispheric contralaterality was revealed in HCs. However, predominant contralaterality was absent in mTLE patients. Right mTLE patients exhibited a lack of contralaterality in response to left ear stimulation but not right ear stimulation, and vice versa in left mTLE patients.

Conclusion
CAP dysfunction associated with 500-Hz pure tone stimulation was more pronounced in right mTLE patients compared with that in left mTLE patients as well as HCs, while CAP dysfunction associated with 40-Hz ASSR was characterized by a lack of contralaterality corresponding to epileptic focus. Our simple paradigms can provide useful information for localizing epileptic focus in mTLE patients.
Interictal Epilepsy Spike Detection from MEG Signal Using Machine Learning

Simone Liu
Simon Fraser University

Co-Author(s)
Hiroshi Otsubo – The Hospital for Sick Children
Midori Nakajima – The Hospital for Sick Children
Till Nickle – Simon Fraser University
Teresa Cheung – Simon Fraser University
Ash Parameswaran – Simon Fraser University

Abstract Theme: Epilepsy

Background and Purpose/Objectives:
Magnetoencephalography (MEG) brain data is used for presurgical assessment of the localization of the epileptic focus. The most common approach for the detection of epileptic spikes from MEG, is the visual scanning of MEG recordings by a trained neurophysiologist to recognize the signal morphologies associated with epilepsy. The process is somewhat subjective and labor-intensive. This study aims to develop an automatic epileptic spike detection pipeline to aid neurophysiologists to mark MEG signals.

Methods
We first trained and tested machine learning algorithm using eye blink data from the Cam-CAN database of resting MEG on 72 subjects. An eye blink morphology is within the same MEG signal amplitude range as epileptic spike and exhibit dipolar patterns. The eye blinks were marked by automatic threshold detection using the EOG channel. We then tested the pre-trained model with Epilepsy data. LeNet-5 Architecture was employed. The output layer of the neural network can output binary class classification (normal vs epileptic spike or eye blink).

Results
With LeNet-5 architecture, we got 90.3% classification accuracy for the eye blink testing set, with 94.7% of the non-eye blink signals correctly classified and 83.3% of the eye blink signals correctly classified. Test on a small subset of the epilepsy data shows similar trends but lower classification accuracy.

Conclusion
Machine Learning can detect dipolar pattern and then be applied to MEG signal for automatic epileptic spike detection and assist presurgical assessment. Further work includes applying the proposed algorithm on larger datasets of epilepsy data, and the evaluation of different neural network architecture.
MEG Measures of Altered Somatosensory and Motor Function in Children Following Basal Ganglia Stroke

Cecilia Jobst, MSc
The Hospital for Sick Children

Co-Author(s)
Nomazulu Dlamini – The Hospital for Sick Children
Gabrielle DeVeber – The Hospital for Sick Children
Douglas Cheyne – The Hospital for Sick Children

Abstract Theme: Functional mapping, neurosurgical applications

Background and Purpose/Objectives:
Background: Dystonia is a common post-stroke disorder in children involving disabling and painful muscle activity, as well as diminished sensation thought to involve maladaptive neuroplasticity leading to altered cortical inhibition. Purpose/Objectives: We assessed the ability of MEG combined with structural MRI to detect altered somatosensory stimulation and motor function in children following stroke, using protocols optimized for use in children.

Methods
MEG was collected in four children (2 female, mean age 15.25±1.71 y.o.) with unilateral BG stroke and hemi-dystonia. Sensory and motor tasks were performed on both affected and unaffected hands. Somatosensory processing was measured with a paired pulse stimulus (350ms between pulses every 2s) and motor processing using passive index finger movements. Data were analyzed with an event-related beamformer (ERB) to localize evoked responses and their corresponding time courses using the BrainWave toolbox and SPM12.

Results
In all four children, sensory responses showed attenuated waveform amplitudes (1-30 Hz) and lack of gating to the second pulse in the affected hemisphere only, suggesting altered intracortical inhibition of sensory input consistent findings to children with cerebral palsy. Motor beta band rebound (15-30 Hz) was also reduced in the affected hemisphere as shown in previous studies in post-stroke adults without dystonia, indicating the presence of altered excitability in the motor cortex.

Conclusion
Conclusions: These preliminary findings confirm altered responses are present in the affected hemisphere of children following stroke with hemidystonia and suggest such measures could be ideal for assessments in children with similar maladies in future studies.
Use of Magnetoencephalography to Examine Cortical Responses to Deep Brain Stimulation

Irene E. Harmsen
University of Toronto

Co-Author(s)
Nathan C. Rowland – Medical University of South Carolina
Luis G. Dominguez – University of Toronto
Andres M. Lozano – University of Toronto

Abstract Theme: Functional mapping, neurosurgical applications

Background and Purpose/Objectives:
Deep brain stimulation (DBS) is a form of neuromodulation that is being applied to motor circuit disorders such as Parkinson’s disease and dystonia, to mood circuits to treat depression, and to cognitive circuits to treat Alzheimer’s disease. Brain regions that are activated by the focal delivery of electrical stimulation in the brain are not well understood. This project will examine the relationship between implant location, stimulation dosage, current frequency, and brain activation.

Methods
Magnetoencephalography (MEG) is a non-invasive technique for mapping brain activity by recording magnetic fields produced by electrical currents in the brain. MEG was used in DBS patients to obtain spatial and temporal measures of neuronal activity in response to various stimuli.

Results
DBS patients have been recorded from a wide spectrum of neurological and psychiatric disorders. The data provides evidence that MEG in DBS patients is safe, feasible, and can demonstrate specific and logical activation of brain regions.

Conclusion
This is an extremely novel project in a diverse set of patients involving a wide variety of disorders and brain targets. This project will provide valuable insight into the effects of DBS by comparing brain activation across various pathological states and determining the consequences of stimulating different neuronal circuits.
Investigation of Neuromagnetic Auditory Response in Patients with Hemifacial Spasm

Bong Soo Kim
Korea Research Institute of Standards and Science

Co-Author(s)
Won Seok Chang – Yonsei University College of Medicine
Kiwoong Kim – Korea Research Institute of Standards and Science

Abstract Theme: Functional mapping, neurosurgical applications

Background and Purpose/Objectives:
Tinnitus accompanied by hemifacial spasm has been considered a type of hyperactive neurovascular compression syndrome that is similar to hemifacial spasm alone because of the anatomically close relationship between the facial nerve and cochlear nerve as well as the hyperactive clinical nature. To investigate the pathophysiology of tinnitus accompanied by HFS, we used magnetoencephalography (MEG) to study patients and analyzed the relationship between the presence of tinnitus and the MEG results.

Methods
Participants were 29 subjects who presented with hemifacial spasm and neuroradiological evidence of vascular compression of the cranial (facial/cochlear) nerve. We used MEG to estimate the activity of the cochlear nerve in patients with and without tinnitus on the ipsilateral side. We compared the difference in the latency and the ratio of the equivalent current dipole (ECD) strength between the ipsilateral and contralateral sides of the spasm and tinnitus.

Results
Cochlear nerve activity in patients with tinnitus was increased with a shorter latency (p = 0.016) and stronger ECD strength (p = 0.028) compared with patients without tinnitus.

Conclusion
The MEG results from normal-hearing patients who had tinnitus accompanied by hemifacial spasm suggest that the hyperactivity of the auditory central nervous system may be a crucial pathophysiological factor in the generation of tinnitus in these patients. The neurovascular compression that causes sensory input from the pathologic facial nerve activity may contribute to this hyperactivity of the central auditory nervous system.
Abstract Theme: Neurological conditions (excluding epilepsy)

Background and Purpose/Objectives:
Children born low birth weight have a high prevalence of neuropsychological deficits such as attention deficit hyper activity disorder (ADHD), autism spectrum disorder (ASD) and learning difficulties (LD). However, the functional correlates of such impairments in low birth weight children are still unknown. In this study, based on our previous results in children with ASD, the relationship between auditory magnetic mismatch field (MMF) by change in voice intonation and language performance was investigated in preschool children.

Methods
Low birth weight infants were recruited from Kanazawa University hospital in Japan. 13 preterm born children (1 female and 12 male, 68.6±4.6 month) participated in this study. MEG data were recorded using a 151-channel superconducting quantum interference device (SQUID), whole-head coaxial gradiometer MEG system for children (PQ 1151R; Yokogawa/KIT, Kanazawa, Japan). In the present study, we used the oddball paradigm consisting of two types of /ne/ (i.e. Japanese syllable). As an index of language performance, we used riddle which is a subtask of K-ABC.

Results
There were significant correlation between MMF in the left supramarginal and language performance (N = 12, r = 0.758, P = 0.009).

Conclusion
The main result of this study is that children with larger MMF response in the language related area in the left hemisphere to voice intonation change showed higher language performance at preschool age. It is necessary to clarify the brain function involved in the development of low birth weight infants by comparing with groups such as TD and ASD.
Symptom-associated Change of Motor-related Neuromagnetic Fields in a Patient with Multiple Sclerosis: A Case Report

Ji Hee Kim
Hallym university sacred heart hospital

Co-Author(s)
Won Seok Chang – Yonsei university college of medicine
Bong Soo Kim – Korean Research Institute of Standard and Science (KRISS)

Abstract Theme: Neurological conditions (excluding epilepsy)

Background and Purpose/Objectives:
The objective of this study was to investigate functional abnormalities of the brain in a patient with multiple sclerosis (MS) by using magnetoencephalography (MEG) and a finger-tapping task.

Methods
A 46-year-old woman that presented with motor weakness of left hand and was diagnosed with MS. Conventional magnetic resonance imaging (MRI) demonstrated a white matter lesion with hyperintensity on T2-weighted images in the right motor area. MEG recordings were performed during the period of motor weakness and after clinical improvement. Neuromagnetic brain activation was elicited by a simple, visually cued finger movement.

Results
The readiness field, the motor field (MF), and the movement-evoked field (MEF) were analyzed. The Equivalent current dipole (ECD) strength of the MEF in the affected hemisphere was significantly decreased relative to the unaffected hemisphere. After improvement in motor weakness, we found that the lower amplitude of the readiness field and decreased ECD strength of the MEF observed in affected hemisphere during motor weakness had recovered. Analysis of motor-related neuromagnetic fields revealed that MEG may be used to detect diffuse changes in the brain that are not observable by conventional imaging of white matter regions in MS.

Conclusion
The results of the present study have demonstrated that a patient with MS with motor impairment displayed decreased neuromagnetic activation and a lower amplitude of the readiness field in the affected hemisphere during a finger-tapping task.
Detecting Differences with Magnetoencephalography (MEG)-urodynamics Study of Somatosensory Processing Normal Desire to Void and Maximum Desire to Void Sensation

Hideaki Shiraishi
Lecturer
Department of Pediatrics, Hokkaido University Hospital

Co-Author(s)
Kiyoshi Egawa – Department of Pediatrics, Hokkaido University Hospital
Atsushi Shimojo – Department of Pediatrics, Hokkaido University Hospital
Nobuo Shinohara – Department of Urology, Hokkaido University Hospital
Kazuyori Yagyu – Department of Pediatrics, Hokkaido University Hospital
Takeya Kitta – Department of Urology, Hokkaido University Hospital

Abstract Theme: Neurological conditions (excluding epilepsy)

Background and Purpose/Objectives:
Fully understanding and defining how the normal brain responds to bladder filling is essential for identifying central abnormalities in patients with voiding dysfunction. The aim of our study is to clarify changes in brain activity at switching from sensation of normal desire to maximum desire sensation during bladder filling using MEG-urodynamics study.

Methods
We performed real-time MEG-urodynamics in 6 healthy male aged from 30 to 46 years (mean 38). The present study applied MEG to measure the brain responses switching from sensation of normal desire to maximum desire sensation. A urethral catheter was placed and intravesical pressure was monitored throughout the procedure. MEG signals obtained by 204ch gradiometers and 102ch magnetometers (VectorView system). ERD at the vicinity of maximum desire to void for 35 seconds (-30 to 5 seconds) was calculated by Hilbert transform using Brainstorm software. We measured the event related desynchronization (ERD) at the switching point by MEG may be more suitable to localize the source position and define the change of brain activity.

Results
Mean bladder capacity was 360ml (270-480). Detrusor overactivity was never noted throughout the study. Compared with the normal desire to void sensation and maximum desire sensation, real-time change of ERD on cerebral cortex was defined at the right parietal lobe around primary somatosensory cortex.

Conclusion
In this preliminary study, with consideration for the somatosensory processing of micturition reflex, we succeeded in visualizing brain activities at switching from sensation of normal desire to maximum desire sensation.
Abstract #25  Submission ID 677225
Effects of Theta Burst Stimulation on Cortical Dynamics and Sensorimotor Coordination

Josephine Ferrandino
Graduate Student
The University of Texas at Austin

Co-Author(s)
Jody L. Jensen – The University of Texas at Austin
Paul Ferrari – Research Director, Dell Children’s Medical Center

Abstract Theme: Other methodologies and modalities, including TMS

Background and Purpose/Objectives:
Transcranial magnetic theta burst stimulation (TMS-TBS) has been shown to modulate neural activity and improve performance on motor and working memory tasks, leading to investigations of the use of TMS as an adjunct for rehabilitation. However, evidence regarding the neural mechanisms linking TMS-TBS to specific behavioral change is lacking. In an effort to test the potential of TMS-TBS as a useful adjunct in the remediation of coordination disorders, we employed a pre- post-TMS magnetoencephalography (MEG) study to investigate the effects of TMS-TBS of the auditory dorsal stream on cortical dynamics and cognitive-motor performance during sensorimotor coordination tasks.

Methods
Eight neurotypical adults underwent two MEG (MEGIN Neuromag® TRIUXTM) sessions while performing index finger tapping with an auditory metronome, either on-the-beat (synchronization) or off-the-beat (syncopation), as well as self-paced movements and rest. Between sessions, subjects underwent TMS-TBS (Nexstim, Ltd) of the right temporal-parietal-junction. Non-parametric and circular statistics evaluated the imaging and behavioral data respectfully.

Results
TMS was associated with an increase (p < 0.05) in resting state source level theta power in ipsilateral temporal and bilateral frontal and parietal regions. Subjects accuracy increased and coordination variance (relative phase standard deviation) during syncopation decreased by 0.27 radians p < 0.001. No significant differences were observed for the synchronization conditions.

Conclusion
Based on preliminary analysis, TMS-TBS was associated with behavioral change only during syncopation, a task known to engage executive/cognitive-motor resources compared to synchronization. Modulation of theta band activity suggests that TMS-TBS modulated a distributed cortical network. Further analysis will determine specific neural mechanisms correlated with behavioral change.
Abstract #26 Submission ID 676746

Neuromagnetic Brain Responses to Vibrotactile Stimulations of Dominant and Non-dominant Hand

Min-Young Kim
Korea Research Institute of Standards and Science

Co-Author(s)
Hyukchan Kwon – Korea Research Institute of Standards and Science
Tae-Heon Yang – Korea National University of Transportation
Kiwoong Kim – Korea Research Institute of Standards and Science

Abstract Theme: Perception, sensation, pain

Background and Purpose/Objectives:
Vibrotactile perception has received growing attention as the tactile feedback technology is widely used in the mobile electronics. However, relatively little is known about the cortical responses to vibrotactile stimulations of dominant and non-dominant hand. This study aims to investigate the neuromagnetic brain responses for left-hand and right-hand vibrotactile stimulations.

Methods
Whole-head MEG was recorded in thirty healthy right-handed subjects (15 males/15 females) while vibrotactile stimulations at 150 Hz were presented to their right or left index finger for 300 times using a polymer-based actuator. The interstimulus interval was randomly distributed between 1.6 and 2.4 s with a constant stimulus of 200 ms duration. Participants were asked to perform the task by using their left or their right hand, respectively, in two counterbalanced sessions. Time-frequency analysis method was applied to the preprocessed MEG data to evaluate changes in spectral powers (5-50 Hz) over time compared with baseline. Non-parametric permutation tests were applied to assess statistical significance of the time-frequency data.

Results
Prominent vibrotactile induced spectral power changes after stimulation were observed in the somatosensory area contralateral to the unilaterally stimulated finger for both hands. Prolonged suppression of the alpha band activity (between 0.1 and 0.6 s) was observed in the contralateral somatosensory area, while the beta band activity was suppressed initially (0.2-0.4 s) then rebounded (0.5-0.8 s).

Conclusion
Vibrotactile stimuli delivered to the index finger induced modulations of neuronal oscillations in alpha-band and beta band responses in the contralateral somatosensory area for both dominant and non-dominant hand.
Abstract #27 Submission ID 674081

Changes of Stimulus-induced 20-Hz Activity for the Tongue and Hard Palate During Tongue Movement Using MEG

Hitoshi Maezawa
Graduate School of Medicine, Osaka University

Co-Author(s)
Kazuyori Yagyu – Graduate School of Medicine, Hokkaido University
Hideaki Shiraishi – Graduate School of Medicine, Hokkaido University
Hiroaki Hashimoto – Graduate School of Medicine, Osaka University
Masayuki Hirata – Graduate School of Medicine, Osaka University

Abstract Theme: Perception, sensation, pain

Background and Purpose/Objectives:
Changes of 20-Hz rhythmic activity in the primary sensorimotor cortex (SM1) is important for sensorimotor functions in the upper limbs. However, little is known regarding the changes of stimulus-induced 20-Hz activity related to oral sensorimotor function. The objective of this study was to first identify whether 20-Hz cortical activity can be induced by stimulating the tongue and hard palate, and then examining how stimulus-induced 20-Hz activity for tongue and palate is modulated during tongue movement.

Methods
20-Hz cortical activity was recorded following right-sided tongue stimulation during rest (Rest condition) and self-paced repetitive tongue movement (Move condition) using whole-head MEG. To exclude proprioception effects, 20-Hz activity induced by right-sided hard palate stimulation was also recorded in the two conditions. The 20-Hz activity in the two conditions was compared via temporal spectral evolution analyses.

Results
Stimulus-induced 20-Hz activity was detected over bilateral temporoparietal areas in the Rest condition for tongue and hard palate. Moreover, stimulus-induced 20-Hz activity was significantly suppressed in the Move condition for both regions.

Conclusion
Detection of stimulus-induced 20-Hz activity during the Rest condition for both regions suggests that the SM1 functional state may be modulated by oral stimulation. Moreover, the suppression of stimulus-induced 20-Hz activity for the hard palate during the Move condition suggests that the stimulation-induced functional state of SM1 may have been modulated by the movement, even though the movement and stimulation areas were different in the oral regions. In conclusion, sensorimotor function of the oral region may be finely coordinated through 20-Hz cortical activity.
MEG-based Dynamic Functional Coupling Is Associated with Pain Interference on Cognitive Task Performance

Junseok Kim
PhD candidate
Krembil Research Institute

Co-Author(s)
Rachael L. Bosma – Krembil Research Institute
Kasey S. Hemington – Krembil Research Institute
Natalie R. Osborne – Krembil Research Institute
Anton Rogachov – Krembil Research Institute
Joshua C. Cheng – Krembil Research Institute
Benjamin T. Dunkley – The Hospital for Sick Children
Karen D. Davis – Krembil Research Institute

Abstract Theme: Perception, sensation, pain

Background and Purpose/Objectives:
fMRI-based dynamic functional connectivity within and between networks of the dynamic pain connectome (DPC; salience and default mode networks (SN, DMN), ascending nociceptive pathway (Asc)), is associated with pain interference on cognitive task performance. In this MEG study we tested whether individual- and sex-differences in pain interference on cognitive performance is related to DPC dynamic functional coupling (dFCp) within specific frequency bands.

Methods
We acquired 5min resting state MEG data in healthy individuals. Pain interference was based on reaction times in an attention to pain task. MEG data was preprocessed using Fieldtrip. Linearly constrained minimum variance was used for the beamforming on regions of interest (ROIs). We calculated weighted phase lag index (wPLI) and amplitude coupling across each pair of ROI nodes and dFCp as the standard deviation of FCp values across 10s epochs.

Results
Individuals with less pain interference had higher dFCp between theta Asc-DMN, beta Asc-SN, and within the SN (gamma), but reduced alpha Asc-DMN dFCp. In women, less pain interference was associated with higher gamma within Asc dFCp but lower theta Asc-DMN dFCp. However, in men less pain interference was associated with lower beta Asc-DMN dFCp.

Conclusion
The interference effect of pain on cognitive performance is mostly associated with increased dFCp within the DPC. Dynamic communications between areas of the DPC may allow individuals to be more nimble to retain cognitive performance in the face of pain. However, future studies are needed to disentangle sex differences and the importance of specific frequency bands.
Cortical Oscillations and Phase-amplitude Coupling During Motor Processing in Young Children with Autism Spectrum Disorders

Kyung-Min An
Kanazawa University

Co-Author(s)
Yuko Yoshimura – Kanazawa University
Chiaki Hasegawa – Kanazawa University
Tetsu Hirosawa – Kanazawa University
Mitsuru Kikuchi – Kanazawa University

Abstract Theme: Psychiatric conditions including PTSD

Background and Purpose/Objectives:
Autism spectrum disorders (ASD) are neurodevelopmental disorder characterized by restricted interests, repetitive behaviors, impaired social interaction, and disordered communication. In parallel to the core characteristics, the motor deficits have been widely reported in ASD. Individuals with ASD have shown the altered brain oscillations associated with cortical excitatory and inhibitory (E/I) functions. In the present study, we investigated the brain oscillations and phase-amplitude coupling during the motor task in children with ASD using magnetoencephalography (MEG).

Methods
Right-handed 14 preschool age children with ASD and 15 typically developing (TD) children performed a videogame-like task involving the 100 button-press using their right index finger during MEG recording. We calculated time-frequency representations and phase-amplitude coupling in the bilateral primary motor cortex (M1).

Results
Response time was significantly later for children with ASD than for TD children (t(27) = -2.999, p = 0.004). The ASD group showed a reduced gamma band power in the contralateral (t(27) = 2.165, p = 0.02) and ipsilateral M1 (t(27) = 3.158, p = 0.002). The ASD group showed a reduced beta band power in the contralateral M1 (t(27) = 2.265, p = 0.032). In addition, we found the altered phase-amplitude coupling in ASD group.

Conclusion
A prolonged button response time in the ASD group might reflect their motor disruptions. The altered motorrelated oscillations and phase-amplitude coupling in the ASD group might be related to the altered excitatory and inhibitory functions. Our findings provide an important clue into the behavioral and neurophysiological alterations in ASD and a potential biomarker for ASD.
Long-term Effects of Interictal Epileptiform Discharge on Cognitive Development and Sociality in Preschool Children with Autism Spectrum Disorders

Tetsu Hirosawa
Kanazawa university

Co-Author(s)
Kyung-Min An – Kanazawa University
Chiaki Hasegawa – Kanazawa University
Mitsuru Kikuchi – Kanazawa University

Abstract Theme: Psychiatric conditions including PTSD

Background and Purpose/Objectives:
Background: The majority of individuals with Autism Spectrum Disorder (ASD) have co-occurring intellectual disability. A large part of patients with ASD have interictal epileptiform discharges (IEDs) in their electroencephalogram. In typically developing (TD) children, the existence of IEDs implies lower cognitive function. However, in children with ASD, this association remains unclear. Furthermore, the association between IEDs and social impairment has not been studied.

Methods
We recruited 40 TD children (29 male, 11 female, aged 3272 months) and 26 children with ASD (21 male, 5 female, aged 4092 months). At the first visit, we assessed their cognitive function using the Kaufman Assessment Battery for Children (K-ABC) for both groups. For children with ASD, we assessed their social impairment using the Social Responsiveness Scale (SRS). Then, 10 minutes of MEG was recorded for each participant. Participants completed a second evaluation of K-ABC and SRS after at least 300 days.

We assessed the relationship between the frequency of IEDs at baseline and the change over time in cognitive function. For children with ASD, we assessed the relationship between the frequency of IEDs at baseline and the change over time in social impairment.

Results
Higher frequency of IEDs at the first measurement corresponds to higher sociality in this population. The higher frequency of IEDs at the first measurement corresponds to the better development of crystallized and fluid intelligence in this population.

Conclusion
This report provides evidence that the effect of IEDs on cognitive development and sociality in children is favourable in children with ASD.
Abstract Theme: Psychiatric conditions including PTSD

Background and Purpose/Objectives:
Autism Spectrum Disorder (ASD) can be seriously disabling, with symptoms including impaired social communication and interactions and restricted and repetitive behaviours. Despite decades of work, mainly using fMRI, attempting to isolate the brain dysfunction underlying ASD, we are no closer to identifying a biomarker. However, ASD likely involves disrupted functional connectivity among regions, meaning an approach using MEG, given its greater temporal resolution, may succeed where fMRI has failed.

Methods
A total of 294 TD and 192 ASD participants were included in our analyses. All subjects completed a five minute resting state scan with a static fixation cross followed by a structural MRI. Data were coregistered on the AAL atlas and an LCMV beamformer used to enter source space at the centre-of-mass of each AAL region. Data were then frequency filtered into canonical frequency bands and functional connectivity assessed by computing Amplitude Envelope Connectivity (AEC).

Results
We found ASD subjects to differ significantly from TD in all frequency bands. Theta, alpha, and beta were characterised by greater connectivity in TD subjects compared to ASD, predominantly localised to the occipital and parietal lobes. Gamma-band differences were in the opposite direction, with ASD subjects having greater connectivity than TD subjects between the frontal, temporal and subcortical parcels. This may be related to the reported interneuron abnormalities in ASD.

Conclusion
Our first-pass analysis of this dataset is encouraging, with significant effects despite coarse statistical approaches. Given the known links between AEC and brain structure, we plan to investigate the relations between these results and DTI metrics.
Abnormal Auditory Mismatch Fields in Children and Adolescents with 47, XYY Syndrome

Junko Matsuzaki
Children’s Hospital of Philadelphia

Co-Author(s)
Luke Bloy – Children’s Hospital of Philadelphia
Lisa Blaskey – Children’s Hospital of Philadelphia
Judith Miller – Children’s Hospital of Philadelphia
Emily S. Kuschner - Children’s Hospital of Philadelphia
Matthew Ku - Children’s Hospital of Philadelphia
Marissa Dipiero - Children’s Hospital of Philadelphia
Megan Airey - Children's Hospital of Philadelphia
J. Christopher Edgar - Children's Hospital of Philadelphia
David Embick - Children's Hospital of Philadelphia
Judith Ross – Thomas Jefferson University / Nemours A.I. DuPont Hospital
Timothy P. Roberts – Children’s Hospital of Philadelphia

Abstract Theme: Psychiatric conditions including PTSD

Background and Purpose/Objectives:
47, XYY syndrome (XYY) is one of the common forms of sex chromosome aneuploidy in males and tend to have tall stature, developmental delays, language impairment and ASD. Although many mismatch field (MMF) studies have been conducted on ASD populations, investigations of the neural correlates of language abnormality in individuals with XYY have not been explored. This study investigated whether similar findings are observed in XYY-associated ASD and whether delayed processing is also present in individuals with XYY without ASD.

Methods
MEG measured MMFs arising from superior temporal gyrus during an auditory oddball paradigm with vowel stimuli (/a/ and /u/) in children/adolescents with XYY both with/without ASD, as well as idiopathic-ASD (ASD-I) and typically developing (TD). Ninety male participants (6-17 years) were included into final analyses (TD, n=38, 11.50±2.88 years; ASD-I; n=21, 13.83±3.25 years; XYY without ASD, n=15, 12.65±3.91 years; XYY with ASD, n=16, 12.62±3.19 years).

Results
Delayed MMF latencies were found in participants with 47, XYY syndrome with/without an ASD diagnosis, as well as in the ASD-I group compared to the TD group (ps < .001). Additionally, participants in both 47, XYY groups showed a longer MMF latency compared to the ASD-I group (ps < .001). However, there was no significant difference in MMF latency between individuals with 47, XYY with/without ASD. Furthermore, delayed MMF latencies were associated with severity of language impairment.

Conclusion
Findings suggest that auditory MMF latency delays are pronounced in this specific Y chromosome aneuploidy disorder, with or without ASD and may implicate the Y chromosome in mediating atypical MMF activity.