

The New MEG Frontier?

Organizer: Jing Xiang

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MEG Detection of Low to High Frequency Neuromagnetic Activity

Recent success in localizing low- (LFBS, 0-14 Hz) and high-frequency brain signals (HFBS, 70-2,884 Hz) opens a new window for the study of epilepsy, migraine and potentially many other disorders using magnetoencephalography (MEG). This topic is very important and interesting because both clinicians and basic researchers can benefit from it. For example: (1) localization of HFBS can increase the effectiveness of epilepsy surgery by approximately 30%. By promoting the applications of HFBS, MEG tests may result in millions of intractable epilepsy patients being seizure free. (2) By using LFBS and HFBS, MEG has revealed that migraine has abnormal cortical excitability and that medications normalizing cortical excitability can reduce the incidence of migraine attacks. (3) A discussion of LFBS and HFBS can advance our understanding of the cerebral mechanisms of multi-frequency brain activity. In addition, MEG hardware and software developers may use LFBS and HFBS to create novel solutions for diagnosis and treatment of many brain disorders.

Speakers:

- **Milena Korostenskaja** (Florida Hospital for Children, USA)
"High Gamma Functional Mapping for epilepsy surgery"

The essential part of epilepsy surgery is localization of eloquent cortex (responsible for motor, sensory, language, and memory functions) that must be maximally preserved while removing pathological epileptogenic substrate from the patients' brain. We have implemented innovative real-time functional mapping (RTFM) methodology based on real time detection and analysis of high gamma oscillations (70 - 110 Hz) for pre-surgical evaluation of epilepsy surgery candidates. We have validated RTFM against other functional mapping modalities, such as magnetoencephalography (MEG), electrical cortical stimulation mapping (ESM), and functional magnetic resonance imaging (fMRI). The results of our studies are highly promising and support clinical application of RTFM methodology for pre-surgical eloquent cortex localization. Moreover, we have demonstrated significant contribution of RTFM to decreasing post-surgical language morbidity. Our performed comparison between RTFM and MEG functional mapping approaches demonstrates a strong promise for the development of highly sophisticated, reliable and safe non-invasive MEG-based functional mapping procedures based on the analysis of different frequency bands, including high gamma. Inclusion the whole spectrum of frequencies (both low and high) in the analysis of functional mapping data may lead to increase in sensitivity and specificity of functional brain mapping results.

- **Kimberly A. Leiken** (Cincinnati Children's Hospital Medical Center, USA)
"Assessment of Cortical Excitability in Migraine with Neuromagnetic High-frequency Signals"

Reports suggest that abnormal cortical excitability may be associated with acute migraines. The present study quantitatively assesses the degree of cortical dysfunction in pediatric migraine subtypes. We investigated 27 children with chronic migraine, 27 acute and 27 controls using magnetoencephalography (MEG), recording at a sampling rate of 6000 Hz. All groups were age- and gender-matched. Neuromagnetic brain activation was elicited by a finger-tapping motor task. The spatiotemporal and spectral signatures of MEG data within a 5-2884 Hz range were analyzed using Morlet wavelet transform and beamformer analyses. Compared with controls, both migraine groups showed (i) prolonged latencies of movement-elicited magnetic fields (MEFs) 5-100 Hz; (ii) increased spectral power 100-200 Hz, and 2200-2800 Hz; and (iii) a higher likelihood of neuromagnetic activation in the ipsilateral sensorimotor cortices, supplementary

motor area, and occipital regions. Though early MEFs (< 100 ms) were identified in all groups, later MEFs (>150 ms) were only apparent in migraine groups. Between the migraine groups, chronic migraine patients showed higher odds than acute of having strong MEFs after 150 ms. Chronic migraine patients also showed higher odds than acute of having neuromagnetic activation from the deep brain areas. Results demonstrated that chronic migraine was not only different from controls, but also from acute. The chronification of migraines may be associated with delayed neural response, as well as aberrant localization of cortical activation.

- **Woorim Jeong** (Seoul Nat'l Univ. Hospital and Seoul Nat'l Univ. College of Natural Science, Korea)
"Usefulness of multiple frequency band source localizations in ictal MEG"

We evaluated the diagnostic value of multiple frequency band MEG source localization within a wide time window during the preictal period. Data for 13 epilepsy patients who showed an ictal event during MEG were analyzed. Several seconds of preictal data were localized in the theta, alpha, beta, and gamma bands by using wavelet transformation and the sLORETA algorithm. The same analysis was performed with narrow time and frequency band. Localization concordances to the surgically resected area were compared. Source localization in the gamma band for a 10s window before ictal onset showed best concordance to the resection cavity. Eight of 13 patients showed sub-lobar concordance in the 10s gamma band localization, whereas 3 showed concordance in the narrow time and frequency analysis. Four of 7 patients with focal cortical dysplasia (FCD) achieved seizure-free outcome, and all 4 showed sub-lobar concordance. A 10s time window gamma source localization method can be used to delineate the epileptogenic zone. The use of a long period during preictal gamma source localization has the potential to become a localizing biomarker of the epileptogenic zone in candidates for surgical intervention, especially in MRI-suspected FCD.

- **Yuping Wang** (Capital Medical Univ., China)
"MEG low frequency activity detection for the localization of temporal lobe epilepsy"

Epileptic discharges are of importance for the diagnosis of epilepsy and localization of epileptogenic zone. However, rhythmic oscillations are the most common electrical manifestation of epilepsy patients. Low frequency activity of cerebral cortex is related with cerebral functional changes. Depth electrode EEG can clearly show such low frequency activity in temporal lobe epilepsy (TLE) patients. Magnetoencephalography (MEG) has been used for the detection of low frequency activity in 14 TLE patients. All of them were seizure-free more than three years after the unilateral temporal resective surgery. Their MEG data were analyzed using beamformer analysis. Beamformer analysis was performed on at least two segments with spike and one segment without spike (resting state). The beamformer analysis showed time-dependent energy fluctuation in low frequency band in 11 patients (11/14, 78.6%), the energy majority was ipsilateral to the surgically treated side, irrespective of the presence or absence of spikes or MRI lesions. Delta band activity had higher lateralizing value than other frequency bands. Low frequency fluctuation in beamformer MEG source imaging was valuable for lateralizing epileptogenic zone.

- **Stefan Rampp** (Univ. Hospital Erlangen, Germany)
"Low frequency activity in patients with focal epilepsy"

In recent years, novel markers for the epileptic network beyond interictal spikes and ictal seizure correlates have been described. Slow activity in theta, delta and lower frequency ranges have been detected using invasive EEG and non-invasive MEG/EEG. While such activity also occurs associated e.g. with large lesions and after intracranial surgery, certain subtypes may be utilized to localize the epileptic network. The presentation will give an overview of MEG slow frequency markers in patients with focal



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epilepsy. Current evidence, clinical applications and putative mechanisms are presented and illustrated with case examples.