MEG Coherence Analysis of PLEDS

David Burdette[1,2], Susan Bowyer[1,2,3], John E Moran[1], Karen Mason[1], Norman Tepley[1], Gabor Zoltay[1]

[1] Henry Ford Hospital, Detroit, MI, USA; [2] Wayne State University, Detroit, MI, USA; [3] Oakland University, Rochester, MI, USA

drsusan@umich.edu

Abstract

Introduction: This study utilized MEG to evaluate the magnetic fields associated with periodic lateralized epileptiform discharges (PLEDs). PLEDs are focal electroencephalographic findings believed to represent focal irritability or hyperexcitability. They are most commonly seen in the setting of acute, destructive cortical brain lesions and in the setting of prolonged status epilepticus. Although they are associated with increased risk of acute, epileptic seizures, it is controversial whether they are ictal phenomena or the accompaniment of "injury currents".

Methods: We recruited 12 epilepsy patients who were experiencing PLEDS. Each of these patients were experiencing changes in mental status. Some were in clinical status epilepticus prior to EEG determination of PLEDs. When clinical stability and cessation of overt seizure activity was obtained, the MEG studies were performed. Spontaneous cortical brain activity was recorded with 148-channel MEG for 10 minutes. Data were sampled at 508Hz, DC-100Hz, filtered from 1-40 Hz and imaged with MR-FOCUSS. Coherence analysis was then performed and compared to the location of cortical activity from the PLEDs and to lesions seen on the MRI (8 patients) or CT (4 patients).

Results: PLED waveforms were similar between EEG and MEG. In those patients with lesions, coherence analysis revealed a tendency for PLEDs to arise from the interface between the lesion and the surrounding, normal cortex rather than from the lesion itself.

Conclusions: This study confirmed that MEG can non-invasively detect and localize PLEDS arising from damaged cortex. Coherence imaging may provide physicians with MEG markers to identify those networks that are producing the PLEDs and a means to determine when treatment with antiepileptic drugs has been adequate to prevent overt seizures and status epilepticus. These studies may also further the basic science of underlying neural networks involved in the generation of PLEDs.

Introduction

Periodic lateralized epileptiform discharges (PLEDs), as the name implies, arise from one hemisphere and typically from one location in the brain. They consist of spike or sharp wave complexes that occur every 1-2 seconds and are followed by a slow wave [6]. They are associated with increased risk of seizures arising from that hemisphere and have been described in a number of clinical settings. In the broadest of terms, PLEDs will arise from the region surrounding a cerebral lesion although they may also be seen in the setting of prolonged, focal status epilepticus. Clinical EEG has revealed a strong association between focal seizures/focal status epilepticus and PLEDs, and controversies have arisen regarding the correct interpretation of PLEDs. Are they epiphenomenal versus the cause or versus the result of seizures. Most clinicians believe that PLEDs are either ictal (seizures) or interictal (injury currents).

In 2000, Hisada, et al [5] reported a case of a patient with PLEDs associated with a right parietal metastasis. They use MEG and the equivalent current dipole (ECD) technique to localize the primary components of the PLED waveforms to the peri-lesional cortex.

In this study we used MEG coherence imaging to determine where PLED waveforms arose. Recently, techniques have been investigated that calculate coherence between sources of MEG imaged brain activity. These techniques vary in analysis methods applied to MEG data, the number of sources for which paired coherence can be calculated, and the use of phase synchrony in place of coherence. MR-FOCUSS is capable of imaging both focal and extended cortical activation [3]. We have combined MR-FOCUSS with Independent Component Analysis (ICA) that enhances the imaging of brain electric activity [4]. We investigated the utility of MEG for detecting neuronal activity underlying PLED activity.

Methods

- 12 epilepsy patients who were experiencing PLEDS
- The study population included 4 men and 8 women.
- A 148-channel MEG system: Magnetometers (4D Neuroimaging Magnes WH2500) recorded spontaneous brain activity while each subject lay still.
- Data were sampled at 508Hz, DC-100Hz.
- Data were bandpass filtered 1-40 Hz.
- MEG data was imaged using MR-FOCUSS [2] and ICA [3] source separation techniques.
- For active brain sources, average coherence with all other active sites was calculated [4]. Epochs of 7.5 seconds were used to calculate coherence. These epochs were then averaged together. Total analysis included 600 seconds of data per patient. Filtering of data to exclude major artifacts (ECG) was done in selected cases.
- MEG results were co-registered to the patient's MRI scan.
- MEG-TOOLS is a freeware package that is available at: **www.megimaging.com**

Results: PLEDs Patients

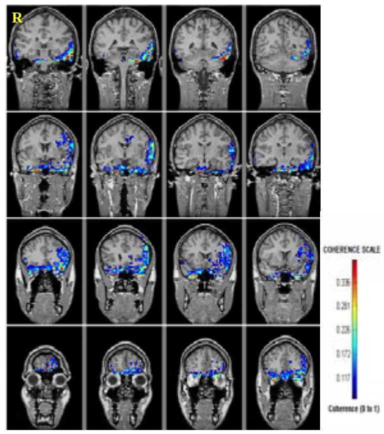

Figure 1. MEG coherence results for a non-lesional patient who presented with partial status epilepticus. MEG ECD localizations are seen in the left frontocentral region, but the coherence analysis revealed greater coherence with inferior left temporal structures.

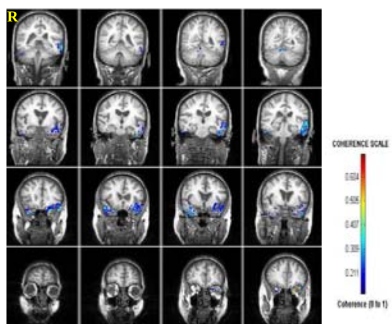

Figure 2 shows the coherence images from a non-lesional patient who presented with partial status epilepticus in the setting of sepsis. MEG coherence analysis revealed greater coherence with temporal structures on the left.

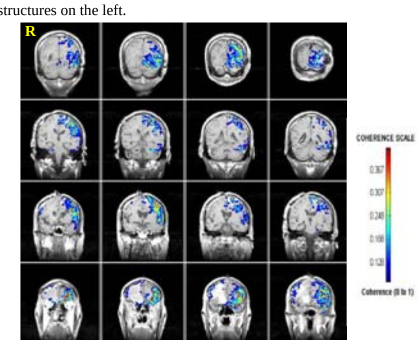

Figure 3 shows the coherence images from a lesional patient with multiple metastatic lesions (lung primary) including left frontoparietal and left occipital (resected). MEG coherence analysis revealed increased coherence adjacent to both lesions in the left hemisphere.

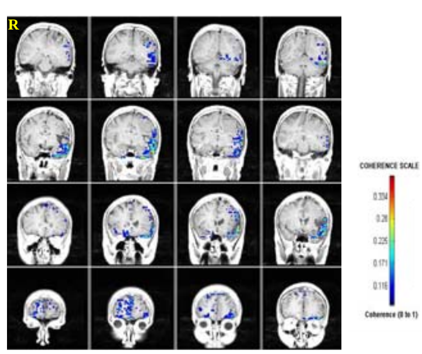

Figure 4 shows the coherence images from a lesional patient status post resection of a left parietal arteriovenous malformation. MEG coherence analysis revealed increased coherence adjacent to the lesion.

Results

- PLED waveforms activity was seen in all patients.
- 7 Patients had lesions seen on MRI (6 focal, 1 diffuse).
- 2 patients had focal lesions seen on CT.
- 3 patients had no focal lesions and had recently treated focal (partial) status epilepticus
- PLED waveforms seen on EEG and MEG had similar morphology.
- In those patients with lesions, coherence analysis revealed a tendency for PLEDs to arise from the interface between the lesion and the surrounding, normal cortex rather than from the lesion itself.
- Figure 1 shows the coherence images from a non-lesional patient who presented with partial status epilepticus in the setting of medication non-compliance. EEG and MEG localizations were similar (left frontocentral), but the coherence analysis revealed greater coherence with inferior temporal structures on the left, potentially representing propagation of the PLEDs associated with the patient's highly epileptogenic state.
- Figure 2 shows the coherence images from a non-lesional patient who presented with partial status epilepticus in the setting of sepsis. EEG and MEG localizations were dissimilar (EEG – right frontotemporal, MEG - bitemporal), and the coherence analysis revealed greater coherence with temporal structures on the left, again potentially representing propagation of the PLEDs associated with the patient's highly epileptogenic state.
- Figure 3 shows the coherence images from a lesional patient with multiple metastatic lesions (lung primary) including left frontoparietal and left occipital (resected). EEG and MEG localizations were similar (left central), but coherence analysis revealed increased coherence adjacent to both lesions in the left hemisphere.
- Figure 4 shows the coherence images from a lesional patient status post resection of a left parietal arteriovenous malformation. EEG and MEG localizations were similar (left parietotemporal), and coherence analysis revealed increased coherence adjacent to the lesion.

Conclusions

- This study confirmed that MEG can non-invasively detect and localize PLEDS arising from damaged cortex.
- MEG localization confirms the previous findings of Hisada et al [5] that the PLEDs in lesional patients arise from the perilesional cortex.
- Coherence imaging suggests that epileptogenic networks in lesional patients are driven predominantly by perilesional cortex whereas the epileptogenic networks in non-lesional patients with PLEDs and recent status epilepticus are more likely to involve temporal lobe structures and may not reflect findings on the EEG and/or MEG.
- Coherence imaging may provide physicians with MEG markers to identify those networks that are producing the PLEDs and a means to determine when treatment with antiepileptic drugs has been adequate to prevent overt seizures and status epilepticus.
- The benefits of MEG neuroimaging include a better understanding of the underlying neural networks involved in the generation of PLEDs.
- This study provides further evidence that differences in distinctive neuronal activation from epileptic activity can be detected.

References and Acknowledgment

1. Salmelin R and Kujala J Neural representation of language: activation versus long-range connectivity. TRENDS in Cognitive Sciences 2006, 10(11):519-525.
2. Moran JE, Bowyer SM, and Tepley N. Multi-Resolution FOCUSS: A source imaging technique applied to MEG data. Brain Topography, 2005. 18: p. 1-17.
3. Moran JE, Drake CL, Tepley N. ICA Methods for MEG Imaging, In Biomag 2004: 13th International Conference on Biomagnetism, E. Halgren, Ahlfors, S., Hamalainen, M, Cohen, D., Editor. 2004: Boston. p. 573-574.
4. MEG-TOOLS available at megimaging.com
5. Hisada K, et al. Magnetoencephalographic analysis of periodic lateralized epileptiform discharges (PLEDs). Clinical Neurophysiology 2000, 111:122-127.
6. Chartrain GE, Shaw CM, Leffman H. The significance of periodic lateralized epileptiform discharges in EEG. A electrographic, clinical and pathological study. Electroenceph clin neurophysiol. 196417: 177-193.

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