FUNCTIONAL MRI OF INTERICTAL EEG ACTIVITY

Simultaneous EEG and Functional MRI of Epileptic Activity: A Case Report

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OBJECTIVES: Attempts to localize the source of epileptic activity by linking electroencephalographic (EEG) abnormalities to blood oxygenation level-dependent (BOLD) magnetic resonance imaging (MRI) signal alterations are hampered mainly by EEG distortions during MRI, subject motion, and unknown hemodynamic response characteristics.

METHODS: Using T2*-weighted echo-planar imaging at 2.0 T (2 s temporal resolution, $2 \times 2 \times 4$ mm(3) spatial resolution), this work demonstrates strategies to alleviate some of these problems while studying a patient who had idiopathic generalized epilepsy with poly-spike and slow-wave complexes.

RESULTS: Continuous EEG recordings during dynamic MRI (500 ms scanning, 1500 ms delay) and post-examination derivation of an EEG reference function for MRI analysis revealed positive BOLD MRI responses with temporal characteristics similar to those obtained for functional challenges.

CONCLUSIONS: The ability to map focal epileptic activity and/or associated cognitive processing provides new potential for both epilepsy research and clinical patient management.

Spatio-Temporal Imaging of Focal Interictal Epileptiform Activity Using EEG-Triggered Functional MRI

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EEG-triggered, blood oxygen level-dependent functional MRI (BOLD-fMRI) was used in 24 patients with localization-related epilepsy and frequent interictal epileptiform

discharges (spikes) to identify those brain areas involved in generating the spikes, and to study the evolution of the BOLD signal change over time. The location of the fMRI activation was compared with the scalp EEG spike focus and the structural MR abnormality. Twelve patients (50%) had an fMRI activation concordant with the EEG focus and structural brain abnormalities where present ($n = 7$). In 2 other patients, the fMRI activation was non-concordant with electroclinical findings. The remaining 10 patients (41.7%) showed no significant fMRI activation. These patients had significantly lower mean spike amplitudes compared to those with positive fMRI results ($p = 0.03$). The time course of the BOLD response was studied in 3 patients and this revealed a maximum signal change 1.5 to 7.5 sec after the spike. In conclusion, EEG-triggered fMRI can directly identify the generators of interictal epileptiform activity, with high spatial resolution, in selected patients with frequent spikes. The superior spatial resolution obtainable through EEG-triggered fMRI may provide an additional non-invasive tool in the presurgical evaluation of patients with intractable focal seizures.

COMMENTARY

The authors of the first article imaged the localization of the epileptogenic cortex in a single patient using simultaneous functional magnetic resonance imaging (MRI) and EEG. They used blood oxygenation level-dependent (BOLD) MRI and T2*-weighted echo-planar imaging at 2.0 Tesla. Previous studies were limited by magnetic distortion of the EEG signal and by the time lag between EEG identification and image acquisition. Because BOLD images blood flow, the result of this lag is that the imaged flow might not reflect the site of earlier epileptogenic activity.

A nonferrous head box was used to obtain the EEG. Motion artifact was removed by visual inspection. The MRI signal to be analyzed was time shifted to account for the lag between cortical activity and blood flow response (estimated to be 4 to 6 sec). MRI was continuously acquired, rather than being acquired only when triggered by EEG. The MRI artifact seen on the EEG was useful in synchronizing the two.

This provides a practical approach to simultaneous EEG and MRI acquisition. Continuous acquisition has advantages over triggered acquisition because of the constant environment experienced by the patient. As the authors note, the images obtained do not necessarily have to correspond to the region of epileptogenesis: They could instead represent spread. Also, epileptiform discharges would have to occur often enough to be found within the time of the MRI acquisition session.

Nonetheless, this study helps to show how the superior temporal resolution of EEG and the superior spatial resolution of MRI can be used in ways that could enhance our ability to localize sites of seizure onset.

The second study used ECG channels to enable digital subtraction of ECG artifact. Image acquisition was manually triggered with a 3.5-second delay after spike observation for imaging of activated EEG and after 10 seconds of spike-free EEG for control EEG. Activated and control EEG acquisitions were randomly distributed; it appears that this was done informally and not with a specific randomization paradigm. Nine echo-planar images were obtained beginning 1.5 seconds after a spike or the during the control period. The imaging was such that nine groups of images were obtained over 18 seconds. Images were then processed using statistical parametric mapping, with processing similar to that used for conventional functional MRI (fMRI) and with images spatially normalized, smoothed, and low pass filtered.

In this study, 14 of 24 patients showed focal fMRI activa-

tion. In 12 patients, this activation was concordant with the EEG focus. The activation region was concordant with a structural lesion in 7 patients. The 2 of 14 patients whose fMRI focus was not concordant are interesting. One had left temporal spikes and confirmed left hippocampal sclerosis. There was right temporal neocortical fMRI activation. The second had a left temporal EEG focus. One fMRI study showed left temporal activation. The second showed right parietal activation.

The 10 patients without significant fMRI activation had significantly lower spike amplitudes. There were no differences in age, underlying pathologies, number of sampled spikes, or delay from spike to acquisition. Three patients with restricted lesions had no fMRI changes. Others with more widespread lesions had fMRI changes.

In summary, fMRI appears to be a very promising method for imaging the brain during epileptiform activity. Optimal methods for acquisition remain to be determined. Moreover, it must be kept in mind that the sensitivity and selectivity of the technique for demonstrating spike-related changes remain to be determined. More importantly, we do not know how accurate the technique is for demonstrating an area of epileptogenesis, as opposed to an area activated by epileptiform activity. This will require a correlation of fMRI results with those based on intracranial recordings.

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