Magnetic Resonance Imaging of Cerebral Electromagnetic Activity in Epilepsy

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Introduction: In this study, we attempt to visualize an MR signal directly linked to neuronal activity. While previous work on direct MR imaging of neuronal activity have demonstrated feasibility in phantoms and in cell cultures [1,2], its use *in vivo* has yielded inconclusive, conflicting results [3]. We hypothesized that reliable detection of an MR signal directly linked to neuronal activity *in vivo*, would be most likely under the following conditions: (i) fast gradient echo EPI, (ii) a cohort of epilepsy subjects, and (iii) concurrent EEG. Our subject cohort frequently experiences high amplitude stereotypical cortical electromagnetic discharges between seizures called *interictal discharges*. These *interictal EEG spikes* are sustained by synchronous paroxysmal membrane depolarization generated by assemblies of hyper-excitable neurons. In this study, we demonstrate that these interictal spikes in the EEG of our subject cohort induce easily detectable MR signal changes. We refer to our technique as *Encephalographic Functional Magnetic Resonance Imaging* (efMRI).

Theory: Neuronal currents generate local electromagnetic fields according to Maxwell's laws. The component ΔB_z of these magnetic fields that lies parallel to the main field B_o of the MR scanner alters the local water proton precession rate, modulating the phase Φ of the MR signal, thus potentially providing a contrast mechanism. The phase change $\Delta\Phi$ caused by ΔB_z the B_o-aligned component of local magnetic flux density change, is given as, $\Delta\Phi \approx \gamma\, TE\, \Delta B_z$, where TE is the echo time and γ is the gyromagnetic ratio.

Methods: All imaging for this IRB-approved study was performed at 3T (Signa, General Electric, Milwaukee, WI, USA). We imaged 9 patients (4 male, 5 female; ages 20-57 years) with medically intractable focal epilepsy and well-characterized surface EEG abnormalities. We also scanned 5 healthy subjects. Subjects were instructed to relax and lie still during the scan. In each case, we acquired concurrent MRI and EEG. We scanned the brain one axial slice at a time using gradient echo EPI with TR 47 ms, TE 22 ms, flip angle 20°, 64 x 64 matrix, 28 cm FOV, slice thickness 5 mm, pixel bandwidth 7.8 MHz. An 8-channel phase array quadrature head coil was used. Single-slice acquisition was repeated multiple times at different axial positions in order to image the entire brain. With a TR of 47 ms, the sampling rate was 21 images per second. Each acquisition block consisted of 512 consecutive images. We obtained 10-15 such data blocks for each axial slice. The mean efMRI scan time per subject was 28.9 minutes. We recorded 32-channel EEG (sample rate 5000 Hz) continuously during imaging using an MR-compatible EEG machine (BrainProducts, Munich, Germany). For 3 epilepsy subjects, we repeated the acquisition without EEG in order to verify that our findings were not affected by the presence of the EEG equipment. We also acquired concurrent EEG and head motion tracking for a single epilepsy patient in order to verify that the interictal spikes were not accompanied by head motion. Our subjects' EEGs were characterized by frequent pathological events. Two epileptologists reviewed each subject's EEG and identified a total of 61 interictal spikes (mean amplitude -254 μV). Temporal alignment of the MR voxel time courses and the concurrent EEG recording was done using software and was based solely on the TTL pulses sent to the EEG system by the MR scanner at each TR; EEG did not trigger the MR acquisition. We inspected the MR magnitude and phase voxel time courses corresponding to all the spikes identified by the epileptologists.

Results: We found that both MR magnitude and phase showed large-amplitude changes concurrent with the EEG epileptiform spike (Fig. 1). These responses were observed in all the identified EEG spike events in all the epilepsy subjects and were absent in all our healthy subjects. We found that the EEG signal was empirically well-modeled by the temporal derivative of the MR phase time course (Fig. 1). The phase changes showed symmetry above and below the mean, with both positive and negative changes in different regions on the same image. With TE = 22 ms, our maximal measured phase change of 0.3714 radians corresponds to a ΔB_z of 63.1 nTesla. This is an order of magnitude larger than similar results reported for evoked responses. We observed similar MR signal changes in the sessions without the EEG apparatus. Interictal spikes had no accompanying head motion that could affect the MR signal (to a precision of 0.33 mm).

Discussion: The temporal derivative relationship between MR phase and EEG strongly suggests that MR phase change may be directly related to local electromagnetic activity. The phase output may be conceived as relating the voxel's position to the local neuronal current, with ΔB_z at that voxel either parallel or anti-parallel to B_o. We found the large MR magnitude changes accompanying the spike event to be surprising. Due to the speed of the responses observed, localized changes in blood flow and hemoglobin oxygenation are unlikely. Bulk head motion could cause saturation effects, but our motion tracking results render this explanation unlikely. Inflow of unsaturated blood into the imaging plane could cause sudden magnitude signal increases, but they do not explain the rapid return to baseline. Additional multi-slice acquisitions with similar results further reduce the likelihood of blood inflow effects (data not shown). Micro-motions of brain tissue during the spike and water shifts due to neuronal cell swelling may also cause signal changes. Our technique, *efMRI,* may potentially serve as a novel functional neuroimaging modality.

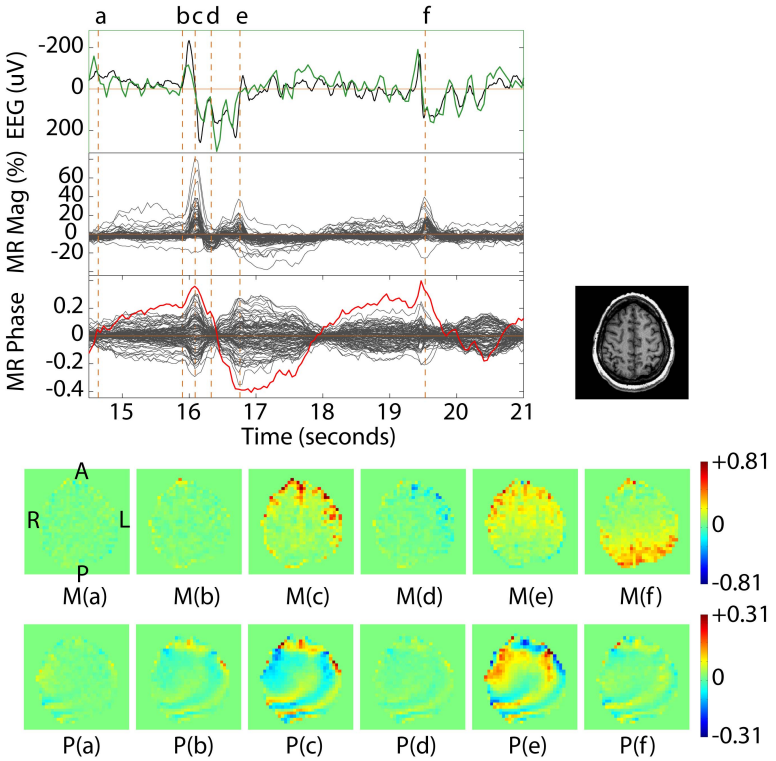

Fig 1. Tight temporal correspondence between the interictal spike seen on EEG (black line, top), percent change in MR magnitude (middle) and demeaned MR phase in radians (bottom). Temporal derivative (green) of the MR phase time course (red) closely follows EEG. M(a-f) and P(a-f) show percent MR magnitude change and demeaned MR phase in radians at times (a-f) respectively. The T1-weighted image corresponding to this slice is shown.

References

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