Morphology of the eMRI Magnitude Response to Interictal Spikes: Timing, Amplitude and the Dip

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Introduction: We recently developed a functional neuroimaging technique, encephalographic MRI (eMRI) [1], designed to acquire rapid gradient-echo EPI and measure an MR signal more directly linked to neuronal electromagnetic activity than BOLD-fMRI. For reliable detection of such an MR signal, we imaged fast (20-200 ms), high amplitude cortical discharges in a cohort of focal epilepsy patients. In our earlier work, we reported easily detectable MR magnitude signal changes concurrent with interictal spikes seen on scalp electroencephalography (EEG). In this study, we investigate the morphology of the spike-related MR magnitude response. Specifically, we report amplitudes and durations across multiple patients and multiple spikes, for the following signals: EEG interictal spikes, concurrently measured eMRI magnitude responses, and the prolonged post-spike MR signal undershoot. We also investigated the spike-related BOLD response.

Methods: All imaging for this IRB-approved study was performed at 3T (Signa, General Electric, Milkwaukee, WI, USA). We imaged 7 patients (4 female, 3 male; ages 20-57 years) with focal epilepsy and frequent, high amplitude interictal discharges on EEG. One patient was imaged twice, with the two scans one year apart. Subjects were instructed to relax and lie still during the scan. In each case, we acquired concurrent MRI and EEG. The MR data were single-slice gradient-echo EPI axial scans with the following scan parameters: TR 47 ms, TE 22 ms, flip angle 20°, 64 x 64 matrix, 28 cm FOV, slice thickness 5 mm. An 8-channel phased-array head coil was used. We repeated the single slice acquisition at multiple axial locations to image the entire brain. Each acquisition block consisted of 512 consecutive images. We obtained 10-15 such data blocks for each axial slice. We recorded 32-channel EEG using an MR-compatible EEG system (BrainProducts, Munich, Germany). Two epileptologists reviewed each subject's EEG and identified a total of 51 interictal epileptiform spikes. Temporal alignment of the MR voxel time courses and the concurrent EEG recording was done using in-house software and based solely on the TTL pulses sent to the EEG system by the MR scanner at each TR. We inspected the MR magnitude voxel time courses corresponding to all 51 spikes. We measured time durations and amplitudes for each EEG spike and the corresponding eMRI response as defined in Fig 1. The morphological parameters were measured using in-house software [2]. For each parameter, we computed the mean, minimum and maximum values, and the corresponding standard deviations. These measurements were performed on the time course of the particular EEG electrode selected by the epileptologist and on the MR magnitude time course showing the largest response to the spike. For each spike, we also looked for BOLD signal changes by computing for each voxel, the correlation between the corresponding detrended MR magnitude time course and a canonical hemodynamic response function (HRF). The interictal spike was modeled as an impulse located at the spike peak. The HRF was positioned with t=0 corresponding to the spike peak and a positive lobe at 6 seconds. For these correlations, we also computed Bonferroni-corrected statistical significance.

Results: For all spikes, we observed large MR magnitude changes concurrent with the EEG interictal spike. Following this change, we observed a prolonged MR signal undershoot that lasted several seconds. We call this undershoot a *dip*, after similar observations in optical imaging [3,4]. Morphological measurements on the EEG spikes and the MR magnitude responses are summarized in Table 1. We found no correlation between EEG spike amplitudes the main eMRI magnitude response (r=0.2). However, the amplitude of the eMRI magnitude response appeared to be correlated with the amplitude of the prolonged post-spike eMRI undershoot (r=0.6, p<7e-5). The duration of the dip was uncorrelated with the EEG spike amplitude (r=0.01), the dip amplitude (r=0.04), and the eMRI response amplitude (r=0.2). We observed a BOLD response (Fig 2) corresponding to the spikes.

Discussion: Interictal epileptiform spikes are often used as a marker for epileptic cortex and represent a population of hypersynchronous neurons. The prolonged dip following the spike-related eMRI response may be due to supranormal metabolic demands associated with these spikes. A similar phenomenon has been observed in optical imaging as a several seconds-long dip in hemoglobin oxygenation [3,4]. The area associated with the dip appears to correlate with the regions where BOLD changes were seen 6-7 seconds after the spike. Further work is required to better elucidate these events.

References: (1). P. Sundaram et al. MRM, In Press 2010 (2) J. Fernandes et al. Journal of Clinical Neurophysiology, 22(1) 2005 (3) S. Bahar et al. NeuroReport, 17(5) 2006 (4) M. Suh et al. Journal of Neuroscience, 25(1) 2005

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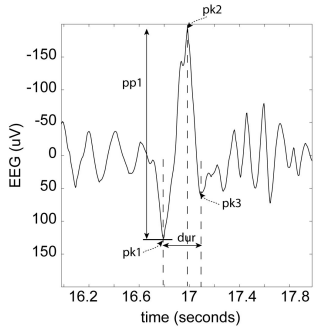

Fig 1a. Interictal EEG spike waveform. Timing-related and amplitude-related parameters are defined.

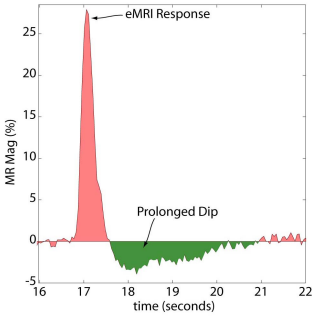

Fig 1b. eMRI magnitude response to the interictal spike in (a) is highlighted in pink. This is concurrent with the spike and is followed by a prolonged dip that is several seconds long. Time course shown is an average over a 2x2 voxel ROI.

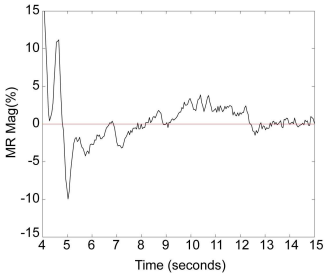

Fig 2a. MR magnitude (%) for a small ROI (arrow). A small signal increase is seen 6-7 seconds after spike.

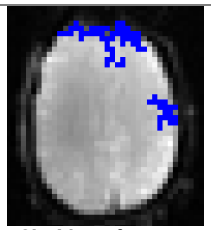

Fig 2b. Map of area under the prolonged dip.

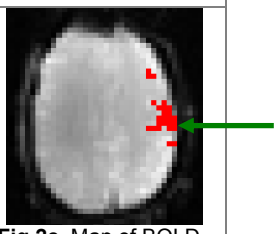

Fig 2c. Map of BOLD activation. Red pixels, $p < 10^{-8}$

Parameter	Mean	Min	Max	Stddev
EEG Spike – amplitude	353.3 uV	88.2 uV	1191 uV	198.4 uV
EEG Spike – duration	353.5 ms	143.8 ms	1409.4 ms	228.6 ms
Main MR Mag - amplitude	23.6%	4%	64%	13.8%
Main MR Mag – duration	677.7 ms	199.5 ms	1485 ms	324.2 ms
Epileptic Dip – amplitude	7.9 %	2%	20.6%	4.6%
Epileptic Dip – duration	4.2 sec	1.1 sec	12.3 sec	2.2 sec

Table 1: Descriptive Statistics: EEG spikes and MR Mag Responses