MRI detection of short-duration "epileptiform" discharges in an ionic-current phantom

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Introduction: Fast MRI changes accompanying interictal spikes (high-amplitude electromagnetic discharges that occur in between seizures in the brains of epilepsy patients) have been demonstrated in a previous study [1]. However, the exact conditions under which these brief (20-200ms) events can be reliably detected with MRI are still not well understood—the spatiotemporal characteristics of the discharges, the MRI acquisition parameters and the post-processing methods employed can all affect the detection of these events. Here, we investigate these conditions by rapidly imaging a custom-built phantom through which we passed ionic currents of various amplitudes and durations, including those designed to approximate interictal spikes. These results allow us to estimate the limits of detecting short-duration currents with our existing experimental paradigm. Although our particular focus is on epilepsy, the general ability to reliably image neuronal currents in patients and in healthy individuals would provide an important and novel contrast mechanism for fMRI.

Methods: The ionic-current phantom was constructed by embedding three glass capillary tubes (75mm length, 1.2mm inner diameter, 1.6mm outer diameter) inside a plastic bottle. The tubes were joined at right angles, such that the central capillary tube was oriented in the left-right direction in the scanner, orthogonal to the main magnetic field $\mathbf{B}_0$, with the other two tubes running parallel to $\mathbf{B}_0$ (i.e., the tubes formed three sides of a square). The bottle and the capillary tubes were filled with a solution of 1L saline (0.9%) and 1mL of gadopentetate dimeglumine (Magnevist, Berlex Laboratories). Chloridized silver electrodes, non-polarizing and thus advantageous for the application of direct currents, were inserted into the two outer capillary tubes, in the section of these tubes that extended outside the bottle. The two electrodes were connected to a twisted-pair cable leading to a signal generator (Rigol DG1022) and a 10kΩ resistor, connected in series, in the scanner console room. The potential difference across the resistor was measured with an oscilloscope (Rigol DS1052E), allowing us to calculate the current running through the circuit. This setup allowed us to pass ionic direct currents of various amplitudes (ranging from 12 to 60μA) and durations (100 to 4000ms) through the capillary tubes, with only currents in the central tube producing magnetic fields with a component along $\mathbf{B}_0$. All experiments were performed on a Siemens 3T Trio scanner equipped with a 12-channel receive array coil. Single-slice gradient-echo EPI scans were acquired with the following parameters: TR 48ms, TE 22ms, BW 2298 Hz/pixel, flip angle 20^o, 64x64 matrix, 200x200mm FOV and 5mm slice thickness; these closely match the parameters used in our previous study of adult epilepsy patients [1]. The sagittal slice was positioned such that it was perpendicular to and approximately halfway along the central capillary tube. Each EPI run lasted approximately 50 seconds, consisting of magnitude and phase images at 1024 time points. In addition, a 1mm isotropic 3D MPRAGE scan was acquired with the following parameters: TR 2300ms, TE 2.98ms, TI 200ms, flip angle 9^o, FOV 256x240x176mm and R=2 GRAPPA acceleration. Linear trends were removed from the EPI time series for each voxel in order to remove any scanner drift and the (Pearson) correlation coefficient between the time course of the applied current and the time series for each voxel was computed, resulting in a magnitude- and phase-correlation image for each EPI run.

Results: Fig. 1a shows an MPRAGE sagittal slice at approximately the same location as the EPI slices through the phantom, with the cross-section of the central capillary tube faintly visible near the image center (red arrow). Ionic current flowing through this capillary tube produces a magnetic field whose z-component changes the phase of the net magnetization vector in each voxel. The spatial pattern of these phase shifts, derived from Ampère's law for a thin, infinitely-long capillary tube, is shown in Fig. 1b. The phase-correlation image corresponding to an EPI run during which a 60μA square wave current (4s ON, 4s OFF) was applied is shown in Fig. 1c, and demonstrates a high degree of similarity to the spatial pattern shown in Fig. 1b. For this 50% duty-cycle current, the time course of the detrended phase for a central voxel is shown in Fig. 1d. The phase-correlation image resulting from lowering the current amplitude to 12μA (while maintaining the duty cycle at 50%) is shown in Fig. 1e. The phase-correlation image resulting from lowering the duty cycle to 2.5% (corresponding to a 200ms ON time) is shown in Fig. 1f (current amplitude: 60μA). Note that although the correlation images in Fig. 1e and Fig. 1f are significantly noisier than the correlation image in Fig. 1c, the underlying spatial pattern can still be readily discerned. However, when the duty cycle was lowered to 1.25% (100ms ON time), this pattern was no longer apparent. In all cases, correlations with the EPI magnitude time series were substantially weaker than the corresponding phase correlations.

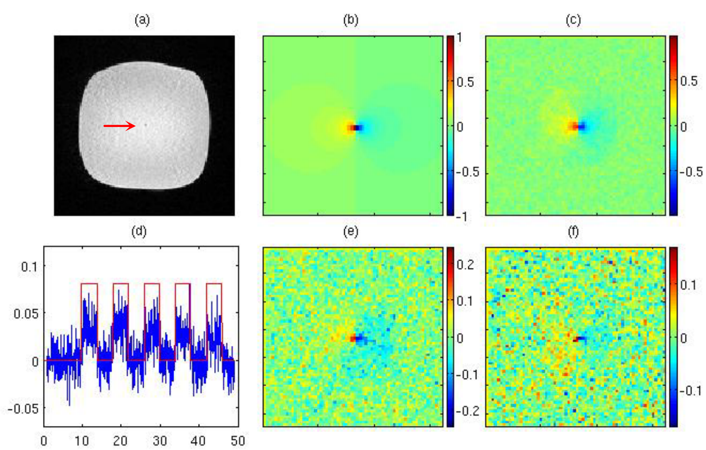

Fig. 1: (a) MPRAGE sagittal slice of phantom (red arrow indicates the location of the central capillary tube). (b) Predicted phase change image for an infinitely long capillary tube. (c) Correlation image for 60μA, 50% duty-cycle current (8s period). (d) Applied current (red, in arbitrary units) and phase (blue, in radians) versus time (in seconds) for a central voxel of (c). (e) Correlation image for 12μA, 50% duty-cycle current (8s period). (f) Correlation image for 60μA, 2.5% duty-cycle current (8s period).

Discussion: Although previous studies have demonstrated the detection of 50% duty-cycle currents (carried by metal wires or in solution) in phantoms with gradient-echo phase images [2,3], there has not to date been a systematic investigation of this topic in the context of short-duration events such as interictal spikes, where brief electromagnetic discharges are separated by long, quiet intervals. Our results demonstrate the feasibility of detecting 60μA currents of 200ms duration occurring every 8s (corresponding to approximately one interictal spike per page of clinical EEG), with our threshold of detection lying between 100 and 200ms. A current amplitude of 60μA is a reasonable approximation for epileptiform discharges [4] and is probably conservative for pediatric epilepsy, where the amplitude of the observed electromagnetic activity is typically higher than in adult epilepsy. The long, straight currents used here are, however, far from realistic for the brain—an issue that will be addressed in the future through the use of more biologically plausible phantoms.

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Acknowledgements: This work was supported by grants from the National Institutes of Health (NIH R21 NS076859, NIH P41 RR019703, NIH P41 RR13218), an ISMRM/ASNR Seed Grant and a CHB-MIT Collaborative Research Fellowship Grant. We also thank Larry Wald, Thomas Witzel, Azma Mareyam, Alyssa Wilson and Cameron Trenor for help with the construction of the phantom, Christina Triantafyllou for help with EPI phase image reconstruction and Arnie Cyr for help with data acquisition.