Hunting for Neuronal Currents: Absense of Rapid MRI Signal Changes During Visual Evoked Response

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Introduction

Recently, the use of MRI to detect changes in neuronal currents during human brain activation has been suggested (1-4). Neuronal current based fMRI could have tremendous impact in the field of neuroscience, complementing existing measurement methods of microscopic (e.g. single cell recordings) and macroscopic (EEG/MEG) electrical activity. However, it has not been demonstrated convincingly that: 1) MRI can separate neuronal current effects from other (e.g. BOLD) effects; 2) MRI has adequate sensitivity to detect neuronal currents *in vivo*. Here we introduce a method that can separate rapid (e.g. neuronal current) from slow (e.g. BOLD) processes, and apply this method to investigate whether MRI allows detection of neuronal current response to visual stimulus.

Materials and Methods

To improve sensitivity, we combined an efficient fMRI stimulus, based on the binary m-sequence probe method (5), with a highly sensitive MRI detector. To allow detection of rapid events, the stimulus was run at high frequency (20 bins of 100 ms). This fast sequence was used to modulate the bits of a slow one (150 bins of 2 s), used to obtain a separable BOLD reference signal (Fig. 1). M-sequence 1's corresponded to a 50 ms display of a checkerboard (15-20 degree visual angle), followed by 50 ms darkness (0's = 100 ms darkness). The stimulus was back-projected using a DLP projector with a computer-controlled, MRI synchronized, liquid-crystal shutter. Per subject (n=5) 4 runs were performed, 2 of which incorporated a 50 ms delay between stimulus and MRI acquisition.

Single shot EPI MRI was performed on a General Electric 3 T in an oblique slice centered on the calcarine fissure using a 16-channel detector built by Nova Medical, Inc. (6) (81 ms TE; 100 ms TR; 25^{o} flip angle; 4x4x5 mm^3 nominal resolution). Baseline image SNR averaged ~100 in visual cortex, temporal SNR ~50. Phase images were derived from complex data corrected using navigator echoes.

MEG was performed with the same stimulus on the same subjects using a 275-channel system (CTF Inc.). MEG data were acquired at 600 Hz and down-sampled to 50 Hz. MRI and MEG data were analyzed in identical fashion using correlation analysis (5). MRI data were analyzed for signal intensity (magnitude) and phase effects. The BOLD signal was extracted by correlation with a zero-filled slow m-sequence. Subsequent correlation of the 0-2 s lag bins in the correlogram with the rapid m-sequence resulted in a BOLD-free signal sensitive to rapid processes such as neuronal current effects.

Results and Discussion

All subjects showed highly significant BOLD fMRI and MEG activation signals but no significant neuronal current (rapid fMRI) activation in magnitude (example in Figs 2-3) or phase. Averaged over 2 runs and across the activated region (Fig. 2), BOLD reached t-values > 6 (Fig. 3, top). The average rapid response, expected to show a transient similar to the MEG response, did not exceed t=0.5 (red line in Fig. 3 top and bottom), and was insignificant. The MEG response (2 run average) from a single occipital channel (Fig. 3, bottom) showed a significant rapid signal with t-values exceeding 20.

Despite the sensitive methodology used in these experiments, previous results (1,4) could not be reproduced. Under the conditions described above, the sensitivity of MRI to detect evoked responses through neuronal currents is at least an order of magnitude below that BOLD-based fMRI or MEG.

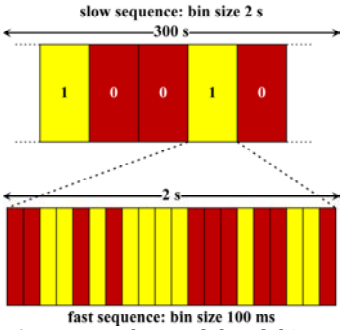

Figure 1: *The modulated binary m-sequence used to simultaneously map slow (BOLD) and rapid (neuronal) effects.*

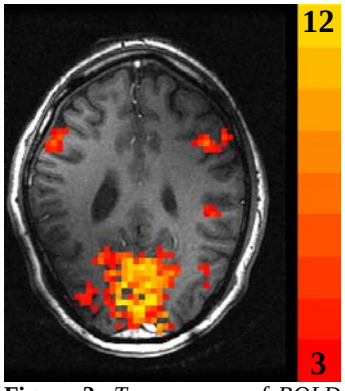

Figure 2: *T-score map of BOLD activation.*

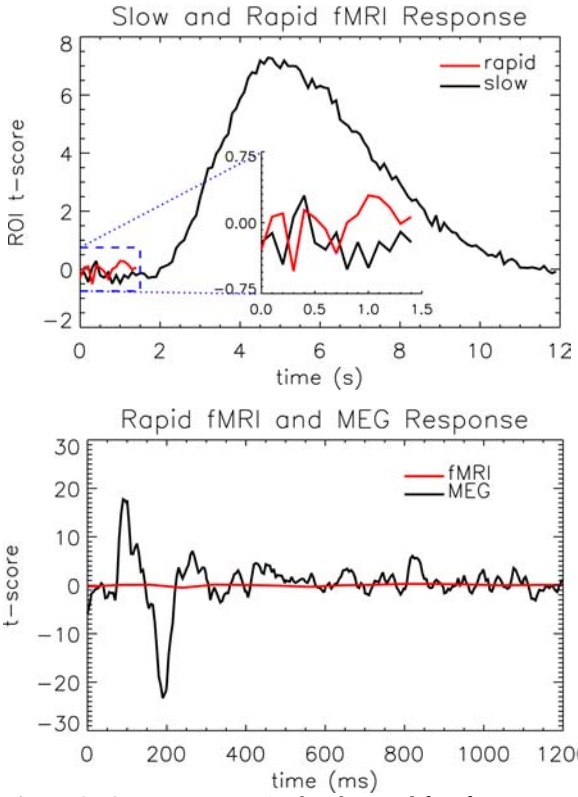

Figure 3: *Average t-score in the slow and fast fMRI response (top). The bottom plot shows a comparison of the fast fMRI response with the response of an occipital MEG channel.*

References

1) Kamei, IEEE Trans Magn. 1999; 2) Bodurka, MRM 2002; 3) Konn, MRM 2003; 4) Xiong, HBM 2003; 5) Kellman, Neuroimage 2003; 6) de Zwart, MRM 2004 [in press]