Simultaneous Measurement of BOLD and Magnetic Source Functional MRI Signals

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Introduction: functional MRI (fMRI) based on the blood oxygenation level dependent (BOLD) contrast mechanism detects signal changes in regional oxygenation environment associated with neural activation. Therefore, BOLD signal inherently suffers from hemodynamic delay in the order of a few seconds. Recently, magnetic source MRI (msMRI) has been proposed to detect the changes in local magnetic fields directly associated with neuronal activation [1]. A msMRI requires multiple scan sessions with the introduction of discrete/differential time-delays in regard to the stimulation events. During this process, a small inter-stimulus-interval (ISI) of 2 seconds is used to allow BOLD signal to be remain in a steady state [2]. By adjusting the time delay between stimulus and data acquisition, the signal reduction accompanying the neuronal activation can be detected in subsecond range. We were motivated to combine conventional block-based fMRI methodology with msMRI whereby task blocks are used as the msMRI data acquisition scheme to measure both BOLD and msMRI signals simultaneously.

Methods: Three healthy volunteers (a male and two females, aged 24-26) participated in the experiment. All subjects provided informed consent. A visuomotor task was used to investigate neural activation of the human motor cortex [1]. Subjects tapped the left hand cued by brief (100 msec) visual stimulus of a checkered wedge. The response time was measured using MR-compatible button press.

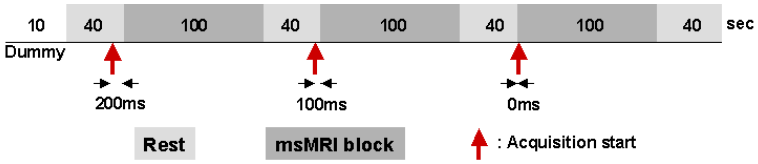

Fig. 1 Block-msMRI protocol of the proposed method

Protocol and Data acquisition: Proposed method can be regarded as a hybrid between block-based fMRI and msMRI protocol (see Fig.1 for the illustration). The method consisted of three blocks of task sessions, which served as msMRI data acquisition sessions. Subjects were presented stimuli in three, 100-sec blocks consisting of 100msec visual stimulation presented at 2sec ISI. Each stimulation block was followed by 40sec of rest to fixate on center point. Total scan time was 470 sec including dummy scans to allow for T1 equilibration. MRI data were acquired at 3 Tesla MRI scanner (ISOL Tech. Korea) using a gradient-echo echo-planar-imaging (EPI) pulse sequence with following parameters: TR=1000msec, TE=50msec, a flip angle of 80 degrees, 64x64 matrices, 240mm x 240mm Field-of-View (FOV), 5mm slice thickness with no gap. Five contiguous axial slices were acquired with ascending order to image the hand motor area. Data acquisitions for three blocks started at -200, -100, 0 msec relative to stimulation onset, respectively (Fig. 1). These onset delays were determined from the experiment of Xiong *et al* [1] to capture neuronal events from -200 to 800ms with respect to the timing of the stimulus onset. Each block consisted of 50 ON/OFF cycles, with pairs of five-slice images for each cycle. If neuronal activation exists, the signal recorded at ON cycle is reduced compared to the signal recorded at OFF because the former experiences the magnetic field perturbation by neural firing,

Data analysis: The MRI images were processed in MATLAB environment. All data were smoothed to reduce spatial noise using 2-D spatial Gaussian filter with full-width at half-maximum of 7mm. The data was analyzed using two different methods. For BOLD fMRI, we used traditional *t*-tests to compare task blocks (which contained the data for msMRI) and rest blocks. The time course of the BOLD signal change and activation map was generated. For msMRI, a total of 300 volumes, 100 from each of three blocks were sampled. After the first 20 volumes of each block were discarded to avoid transient period hemodynamics, we applied *t*-tests to detect the regions with significant (P<0.02) signal reduction during the neuronal activation.

Results: Based on the analysis of block-based BOLD signals, a functional map, typical to the given motor task, was obtained with activation observed in the primary motor cortex (M1) and the supplementary motor area (SMA) as shown in Fig. 2A. msMRI analysis revealed that regional signal decrease was observed in the activated regions identified from the BOLD fMRI results (Fig. 2B). The msMRI data generated functional map of a classical sensorimotor circuitry in terms of activation locations, and as well as in its temporal latency (300 msec to 500 msec later from visual cue) as measured by the response time.

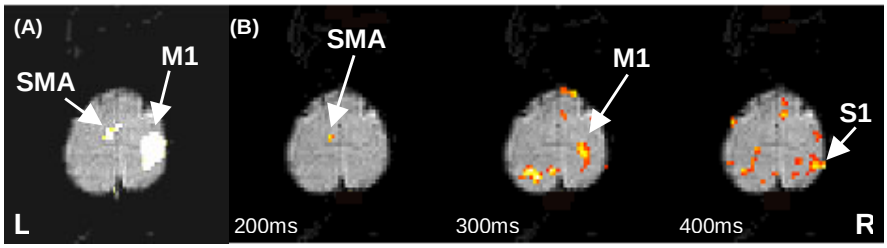

Fig. 2 (A) BOLD fMRI activation map and (B) time-resolved neuronal activities detected by msMRI

Discussion: We have shown that simultaneous measurement of BOLD and msMRI signals were possible. msMRI is advantageous compared to BOLD fMRI in term of temporal resolution (also independent from hemodynamic delay) and enhanced detection sensitivity toward the site of neuronal firing. In spite of these advantages, limitations of the current approach include; (1) multiple fMRI sessions with variable time-delays would be necessary to measure the activation-related signal changes and (2) examination time-window is limited by the slice location, slice order (due to the 'slice-timing'), and the number of stimulation blocks. Application of randomized and variable ISIs to the protocol along with correction of the slice timing issues are being evaluated to overcome these limitations.

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References: [1] J. Xiong *et al.* Human Brain Mapping, 2003
[2] C. Janz *et al.* Magnetic Resonance in Medicine, 2001