Detection of Human Neuronal Currents with Phase MRI

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Introduction: Brain activity-associated neuronal currents produce weak transient magnetic fields that would affect both magnitude and phase of the local MRI signal. A recent simulation study investigated these effects using a realistic neuronal currents MRI (ncMRI) model specifically for human cerebral cortex [1]. The modeling results indicate that the effects are too weak to be detected (magnitude/phase change ≤ -1.4×10^{-6}/0.02°), but the phase signal induced by spontaneous activity may reach a detectable level (up to 0.2°) in favorable conditions. Our recent study demonstrates that the present magnitude ncMRI technique is not sensitive enough to reliably detect the neuronal current-induced signal attenuation in human visual cortex [4], consistent with the modeling prediction. In this study we investigate whether phase ncMRI techniques have the sensitivity to detect the neuronal current-induced phase signal changes in human visual cortex.

Theory: Cell recording studies of macaque monkeys show that a brief visual stimulation evokes transient neuronal responses in the early visual areas (Fig. 1A and 1B), and it takes the neurons in these areas an average of about 70 ms to respond to the stimulus [2,3]. The precise timing of this stimulus-evoked response provides a means of detecting and testing the neuronal current-induced phase signal changes in ncMRI. As illustrated in Fig. 1C, detection depends on the temporal position of the MR data acquisition window and whether the stimulus-evoked neuronal currents induce any phase signal change. When the MR data are acquired before the onset-response (the red arrow in Fig. 1B), there should be no phase signal change because the stimulus-evoked neuronal currents have not yet arisen. The maximum phase signal change should be expected when the acquisition window is placed right at the center of the largest response. Accordingly, placing a series of acquisition windows to fully cover the whole response duration (the solid color lines in the "On" period in Fig. 1C) should yield a different phase signal change for each acquisition window. For the "Off" period, there should be no phase signal change for any acquisition window due to the absence of neuronal currents, providing a reference for contrasting the neuronal current-induced phase signal changes. For each run as illustrated in Fig. 1C, the two signals acquired during each on/off cycle form a paired signal; the former signal has the phase signal change and the latter does not. The difference of this paired signal, i.e., $\Delta\Phi=\Phi_{on}-\Phi_{off}$, provides a measure to quantify the phase signal change in each acquisition window, and the standard deviation (SD) of ΔΦ determines the sensitivity level of the ncMRI technique to detect the neuronal current-induced phase signal change.

Methods and Materials: Three healthy subjects (2 male and 1 female, ages from 46 to 53) participated in the study, and each subject had two studies in different days for testing the reproducibility. Functional brain images were acquired on a GE 3.0 T scanner with a quadrature single-channel head coil using a GE-EPI pulse sequence (TE/TR = 50/300 ms, FA 36°, FOV 23 cm, matrix 64×64, slice thickness 4.0 mm, and spacing 1.0 mm). A functional localizer scan was implemented to identify activated visual cortex during scanning, and then an oblique slice parallel to calcarine sulcus was placed within the activated visual cortex for the ncMRI scan. Each subject had a visual cortical activation paradigm to determine the activated voxels within the visual cortex that form a region-of-interest (ROI) for ROI analysis. The paradigm consists of an 18 s visual stimulation followed by a blank period of 18 s, and the whole event is then repeated six times. During each 18 s visual stimulation, a black-and-white striped pattern is presented for 117 ms followed by a blank of 483 ms (Fig. 1A), and the whole event is then repeated 30 times. The visual stimulation paradigm for ncMRI consists of a total of 600 same stimulation cycles as depicted in Fig. 1A, and phase images were acquired. The ncMRI session was comprised of six runs, as illustrated in Fig. 1C, and the time difference between any two adjacent runs was 50 ms, enabling a full coverage of the 300 ms on-period. Image processing and data analysis were performed with in-house developed software, and any phase wraparounds were detected and corrected.

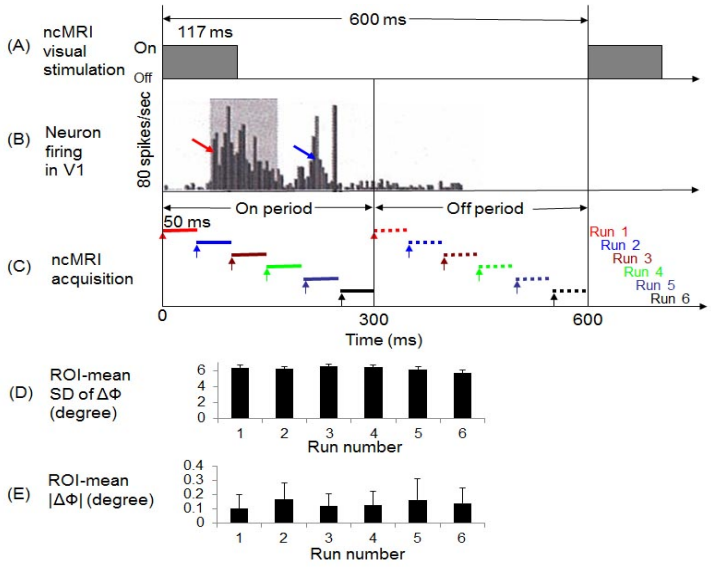

Fig. 1. Illustrations of the ncMRI study design (A-C). D: the ROI-mean SD of ΔΦ, and E: the ROI-mean of |ΔΦ| for a representative subject, respectively.

Results and Discussion: The correlation coefficient (CC) between the signal intensity time course of the functional images from the activation scan and an ideal hemodynamic response function was computed voxel-by-voxel, and activated voxels were determined as those with CC>0.16 ($p<1.0\times10^{-5}$). As expected, similar activation patterns in the visual cortex were observed in each subject and each study. The cluster of the activated voxels in the vicinity of V1 formed the ROI. For each ncMRI run, the difference of the paired signal (ΔΦ) was computed for each of the 600 paired signals. To determine the sensitivity level of the ncMRI technique for detecting the neuronal current-induced phase signal change, we first computed the SD of ΔΦ and then its mean value over the ROI (ROI-mean) for each run. Fig. 1D plots the ROI-mean SD of ΔΦ vs. run number for a representative subject. These values are almost the same across all of the six independent runs, showing that the level of noise of the phase signal change remains unchanged for all runs. This consistent noise level across all runs demonstrates our experimental design provides a reliable measure for detecting neuronal current-induced phase signal change. These results were found to be consistent across all subjects with all studies. To detect any significant neuronal current-induced phase signal change, we first computed the paired t-test value ($t = \sqrt{N}\cdot\overline{\Delta\Phi}/SD$, where $\overline{\Delta\Phi}$ is the mean of ΔΦ and N=600), and then thresholded it with t_{TH} >1.97 (two-tailed paired t-test, p<0.05) for each ncMRI run. Comparing these t maps among the six runs shows no sign of any significant neuronal current-induced phase signal changes in the visual cortex, and this result is consistent with all other subjects and studies. Fig. 1E shows the ROI-mean of the absolute value of ΔΦ of the representative subject for the six runs that also demonstrates the lack of any significant neuronal current-induced phase signal changes. These results show that the visual stimulus-evoked neuronal currents in the visual cortex do not induce phase signal change that is significantly large enough to be detected with the presented phase MRI technique. It also implies that this technique is not sensitive enough to reliably detect neuronal currents associated with brain activity. With the mean SD=6.21°, t_{TH} =1.97, and N=600, we calculated that the maximum neuronal current-induced phase signal change was less than 0.5° ($t_{TH}\cdot SD/\sqrt{N}$), consistent with the maximum 0.2° phase signal change predicted by Luo's model [1]. To detect the 0.2° phase signal change, it requires more than a 2.5-fold reduction to the temporal phase noise level.

References: 1. Luo, Q, *et al*, Magn Reson Med 65: 1680-89, 2011. 2. Macknik, SL & Martinez-Conde, S, Neurocomputing 58-60: 775-82, 2004. 3. Schmolesky, MT, *et al*, J Neurophysiol 79: 3272-8, 1998. 4. Huang, J, Magn Reson Med, DOI 10.1002/mrm.24720, 2013.