Detecting Neuronal Currents with MRI: A Human Study

Jie Huang[1]

[1]*Department of Radiology, Michigan State University, East Lansing, MI, United States*

Introduction: It is an open question as to whether present magnetic resonance imaging (MRI) techniques are sensitive enough to reliably detect neuronal currents associated with brain activity. Although there is no dispute that local neuronal currents produce weak transient magnetic fields that would attenuate local MR signal intensity, there is not yet consensus as to whether the magnitude of this attenuation is detectable using current MRI techniques. Some groups have reported a successful detection of neuronal currents using MRI (ncMRI) [1-4], but other groups failed to detect this activity [5-8]. More studies are required to test whether present ncMRI techniques have the sensitivity to reliably detect neuronal currents in human brain. This study investigates the magnitude of neuronal current-induced signal attenuation using a temporally well-controlled visual stimulation paradigm with a known neuronal firing pattern in 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 B), and it takes the neurons in these areas an average of ~70 ms to respond to the stimulus [9,10]. The precise timing of this stimulus-evoked response provides a means of detecting and testing the magnitude of the neuronal current-induced signal attenuation 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 signal attenuation. When the MR data are acquired before the onset-response (the red arrow in Fig. 1B), there should be no signal attenuation because that the stimulus-evoked neuronal currents have not yet arisen. Maximum attenuation 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 varied signal attenuation for each acquisition window as illustrated in Fig. 1D (the solid color bars). For the off period, there should be no signal attenuation for any acquisition window due to the absence of neuronal currents (the dashed color lines in the off period in Fig. 1C and the corresponding dashed color bars in Fig. 1D), providing a reference for contrasting the neuronal current-induced signal attenuation. 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 attenuation and the latter does not. The relative difference of this paired signal, i.e., $\Delta I=2(I_{on} - I_{off})/ (I_{on} + I_{off})$, provides a measure to quantify the magnitude of the neuronal current-induced signal attenuation. The comparison of these measurements for the whole response duration enables testing the likelihood of the signal attenuation due to the stimulus-evoked neuronal currents.

Methods and Materials: Four healthy subjects (2 male and 2 female, ages from 22 to 52) participated in the study. Functional brain images were acquired on a GE 3.0 T clinical scanner using a GE-EPI pulse sequence (TE/TR = 70/300 ms, FA 36°, FOV 23 cm, matrix 64×64, slice thickness 4.0 mm, and spacing 1.0 mm). Three oblique slices parallel to calcarine sulcus (CS) with the first slice placed right below CS were scanned. Each subject had an event-related (ER) visual cortical activation paradigm to determine the activated voxels within the visual cortex and form a region-of-interest (ROI) for ROI analysis. The ER paradigm consists of a 3 s visual stimulation followed by a blank period of 18 s, and the whole event is then repeated ten times. During the 3 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 five times. The visual stimulation paradigm for ncMRI consists of a total of 600 same stimulation cycles as depicted in Fig. 1A. 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.

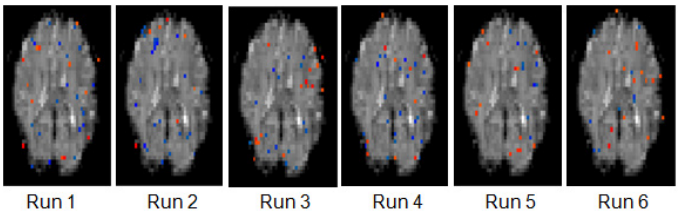

Fig. 2. t maps for the six ncMRI runs from a representative subject. The colored voxels represent significant ΔI: red for positive and blue for negative.

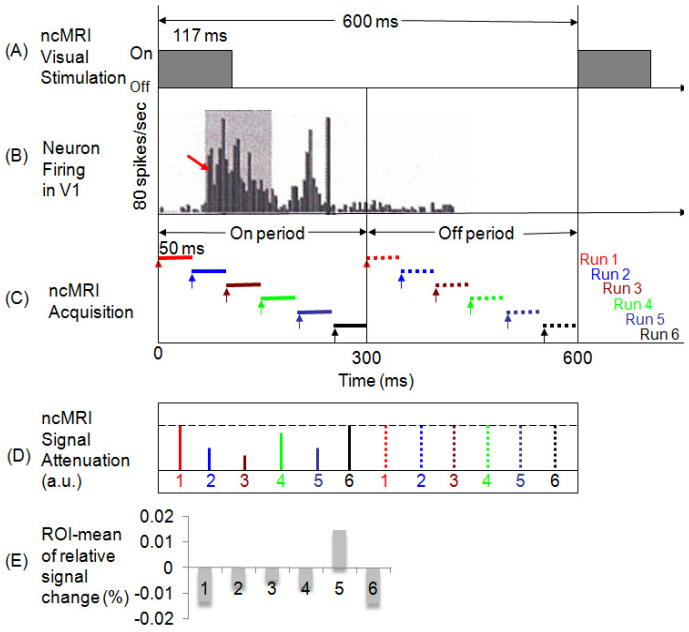

Fig. 1. Illustrations of the ncMRI study design (A-C), the anticipated neuronal current-induced signal attenuation (D), and the measured relative signal change (E). a.u.: arbitrary unit.

Results and Discussion: The correlation coefficient (CC) between the signal intensity time course of the functional images from the ER scan and an ideal hemodynamic response function was computed voxel-by-voxel, and activated voxels were determined as those with CC>0.20 ($p<1.0\times10^{-7}$). As expected, similar activation patterns in the visual cortex were observed in each subject. The cluster of the activated voxels in the vicinity of V1 formed the ROI. For each ncMRI run, the relative difference of the paired signal (ΔI) was computed for each of the 600 paired signals. The mean value and its standard error for these 600 differences were further computed, yielding the corresponding paired t-test value (the ratio of the former to the latter). A t map was thresholded with t>1.97 (two-tailed paired t-test, $p<0.05$) for each ncMRI run, and Fig. 2 shows the t maps of a representative subject for the six runs. Comparing these t maps among the six runs shows no sign of any significant neuronal current-induced signal attenuation in the visual cortex, and this result is consistent with all other subjects. Fig. 1E shows the ROI-mean of ΔI of the representative subject for the six runs that also demonstrates the lack of any neuronal current-induced signal attenuation as compared to Fig. 1D. These results show that the visual stimulus-evoked neuronal currents in the visual cortex do not induce detectable signal attenuation with the current MRI technique, and improved techniques are required for such detections. In conclusion, the current MRI technique is not sensitive enough to reliably detect neuronal currents associated with brain activity.

References: 1. Xiong, J, *et al*, Hum Brain Mapp 20: 41-9, 2003. 2. Chow, LS, *et al*, Magn Reson Imaging 24: 681-91, 2006. 3. Chow, LS, *et al*, Magn Reson Med 60: 1147-54, 2008. 4. Xue, Y, *et al*, Magn Reson Med 61: 1073-82, 2009. 5. Chu, R, *et al*, Neuroimage 23: 1059-67, 2004. 6. Parkes, LM, *et al*, Magn Reson Med 57: 411-6, 2007. 7. Tang, L, *et al*, Magn Reson Imaging 26: 484-9, 2008. 8. Luo, Q, *et al*, Magn Reson Med 66: 492-7, 2011. 9. Macknik, SL & Martinez-Conde, S, Neurocomputing 58-60: 775-82, 2004. 10. Schmolesky, MT, *et al*, J Neurophysiol 79: 3272-8, 1998.