Source of phase change in BOLD and CBV-weighted fMRI

F. Zhao[1,2], P. Wang[2], T. Jin[2], T. Nagaoka[3], N. Harel[3], X. Hu[1], S-G. Kim[2]

[1]Biomedical Engineering Department, Emory / Georgia Tech University, Atlanta, GA, United States, [2]Neurobiology Department, Pittsburgh University, Pittsburgh, PA, United States, [3]CMRR, University of Minnesota, Minneapolis, MN, United States

INTRODUCTION

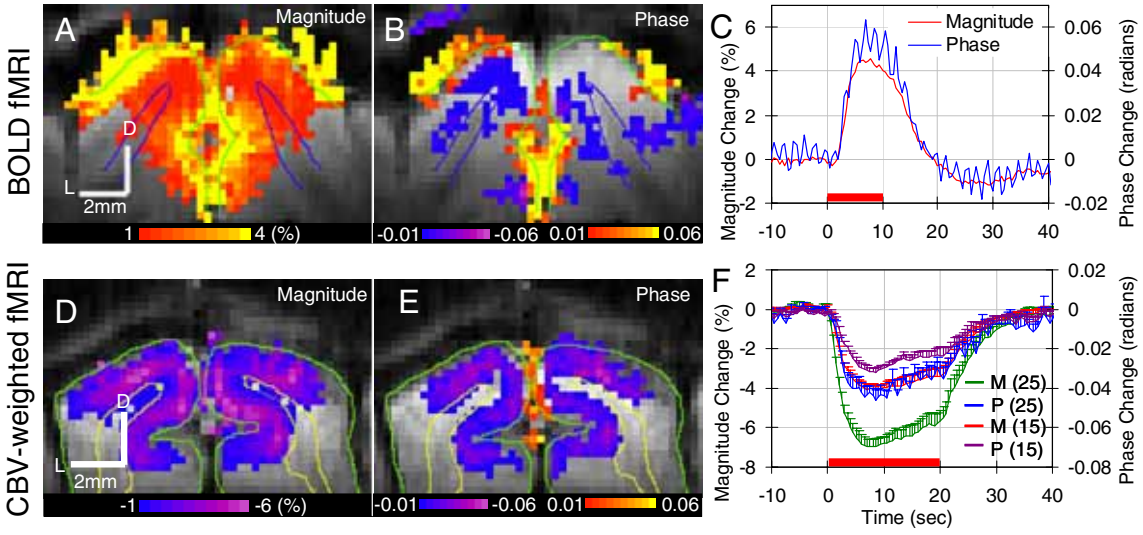
High magnetic susceptibility perturbators in blood vessels induce field inhomogeneities within and around vessels (1). During neural stimulation, a change in deoxyhemoglobin concentration in blood and/or a change in blood volume can modulate the field inhomogeneity, consequently spin dephasing effect. This induces the change in the MRI signal intensity, which has commonly used for fMRI studies. However, in the cylindrical blood vessel model (6), the sum of phases around vessels will be zero. Since the voxel size is much larger than a single vessel, we do not expect the phase change in tissue induced by a change in blood susceptibility effect. However, the phase change was observed in human BOLD fMRI studies (2-4). This is attributed to the intravascular (IV) signal in large draining vein regions (3), or temperature change by the mismatch between the generation of heat in tissue by increased metabolism and the removal of heat by increased blood flow (4). In order to investigate the source of phase change in fMRI, we performed the BOLD and CBV-weighted fMRI studies in the cat visual cortex at 9.4T. Since the injection of MION removes contribution of IV signals to fMRI, we can evaluate whether the IV contribution is the major source of the phase change. Similarly, the temperature hypothesis is also tested by evaluating whether the phase change is identical in fMRI before and after the injection of MION.

METHODS

Cats (n = 10) were intubated and maintained under ~1.3% isoflurane. Blood pressure level, arterial blood gases, end-tidal CO_2 and temperature were maintained under a normal condition (5). The binocular visual stimuli consisted of drifting square-wave gratings (0.2 cycle/degree, 2 cycles/s). All NMR measurements were performed on a 9.4T/31cm (4.7T/40 cm) scanner (Varian) with a 1.6-cm diameter surface coil. Single 2-mm thick imaging slice was selected perpendicular to the surface of the cortex in area 18. Images with 64x64 matrix size and FOV of 2x2 cm^2 were obtained using the gradient-echo (GE) EPI technique with TR of 0.5s. Typically, each fMRI run consisted of 20 control – 20 stimulation – 20 control images. Generally 10-15 runs were repeated and averaged. Three experiments were performed; single-echo BOLD with TE of 20 ms, four-echo BOLD, and two-echo CBV-weighted fMRI. For four-echo BOLD studies, TEs of 10, 15, 20, and 25ms.were used, while TEs with 15 and 25ms were used for CBV weighted fMRI. Different TE values were interleaved in the same scan for minimizing scan-by-scan variations. The phase of k-space data was first eddy-current compensated and then transformed by 2DFT. Magnitude and phase images were obtained. In order to calculate phase change during the stimulation period, phase at some pixels was unwrapped if necessary. The magnitude and phase images from all fMRI runs under the same conditions were averaged to improve contrast-to-noise ratio. Cross-correlation (CC) maps were obtained using a boxcar cross-correlation method with a typical CC threshold of 0.3. A minimal cluster size for an active region of 4 pixels was further imposed. Then, relative changes in magnitude and phase were calculated on the activated pixels. The time courses were generated by averaging the signals from the activated phase maps.

RESULTS and DISCUSSION

Magnitude and phase maps and the corresponding time courses of single-echo BOLD fMRI using 10-s stimulation (Figs. A, B, C) at 9.4 T and CBV-weighted fMRI using 20-s stimulation (Figs. D, E, F) at 4.7T were shown in figure. Green contours indicate the cortical surface, and white matter boundaries are delineated by blue/yellow contours. L: Lateral; D: Dorsal. The y-axis in figure C and F is percentage signal change of magnitude and phase change in radians. M: magnitude; P: phase. The numbers in parenthesis are TE with ms. The red bars in C and F indicate the period of visual stimulation. For the BOLD magnitude map (A), MRI signal intensities increase during stimulation with the highest changes (yellow pixels) near the cortical surface where the large veins are located. These magnitude results are consistent with previous BOLD observations (5) and theoretical predictions (6). BOLD phase changes (B) show unexpected characteristics; the positive phase change is mainly located at the cortical surface where the large veins are located, while in the surrounding tissue and even in the scalp, the negative phase change was detected. In CBV-weighted fMRI with TE of 15 ms, a decrease in signal magnitude was detected (D). CBV-weighted phase change (E) is negative at the middle of the cortex, and positive at the surface of the cortex. This observation is almost opposite to the BOLD phase change. By combining BOLD and CBV-weighted phase changes, we can conclude that (i) the IV contribution does not cause phase changes in our data, and (ii) temperature change is not the major source either. According to previous reports, the phase change induced by temperature should be delayed compared to the magnitude change. We did not observe this either (C), and further eliminating the possibility of the temperature hypothesis. For multiple-TE BOLD fMRI, the activation maps and the time courses of magnitude and phase are similar as Figs. A, B and C (data not shown), irrespective of the TE value. Based on the time courses, quantitative analysis was conducted. The BOLD magnitude change is linearly dependent on TE: $\Delta S/S = 0.87 \times TE\ (s) + 0.0086$ (n=5, R2 = 0.99). The BOLD phase change is also linearly dependent on TE: $\Delta p\ (radian) = 1.6 \times TE\ (s)$ (n=5, R2 = 0.97), which can not be determined by the IV signal contribution (8). Similar observations were found in CBV-weighted fMRI; $\Delta S/S = -2.55 \times TE\ (s)$ (n=5, R2=0.997) and $\Delta p = -1.6 \times TE\ (s)$, (n=5, R2=0.868). Both the magnitude and the phase changes are linearly dependent on the TE. To explain TE-dependent phase change in BOLD and CBV-weighted fMRI, we need to have an alternative explanation. One possible explanation is that the volume-averaged magnetization change during the stimulation due to 'Lorentz Sphere' effect (7). Simulation studies are needed.



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