Comparison of GE and SE BOLD fMRI techniques in temporal-encoding iso-orientation maps.

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[Introduction] Orientation column-like functional structures can be mapped using GE BOLD fMRI with high reproducibility when large orientation-nonspecific signals including draining artifacts are reduced [1]; for this, the continuous stimulation is essential and Fourier analysis is effective to extract the temporally-encoded orientation-specific signal [2,3]. However, iso-orientation maps obtained from GE BOLD fMRI may be distorted by stimulation-related draining signals because GE BOLD signals are extremely sensitive to large draining veins [4-9]. To address this issue, SE BOLD fMRI, which is less sensitive to large vessels and improves spatial specificity to the parenchyma [10], was performed to compare GE BOLD fMRI during exactly the same continuous stimulation paradigm.

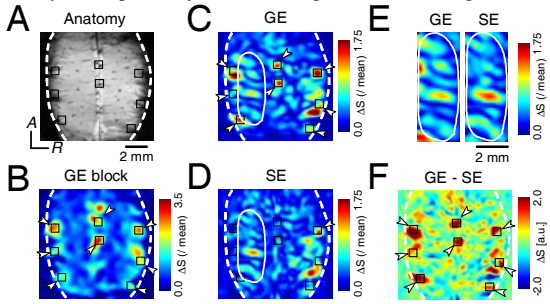

Figure 1. Comparison of large surface vessel's artifacts between GE and SE BOLD fMRI. (*A*) A 1-mm-thick T_2*-weighted MR anatomic image. Large surface veins marked by black boxes are overlaid on subsequent functional images. (*B*) GE BOLD single-condition activation map; mean magnitude is 1.26%. (*C-D*) GE and SE BOLD orientation-specific magnitude maps. Mean orientation-specific magnitudes in active tissue region are 0.40% and 0.24%, respectively. (*E*) Magnified GE and SE BOLD maps in internal cortical region (white contours in *C* and *D*). (*F*) Differential map obtained by subtracting SE from GE BOLD map. For ease of comparison, each map is normalized by its average signal change in tissue activation area.

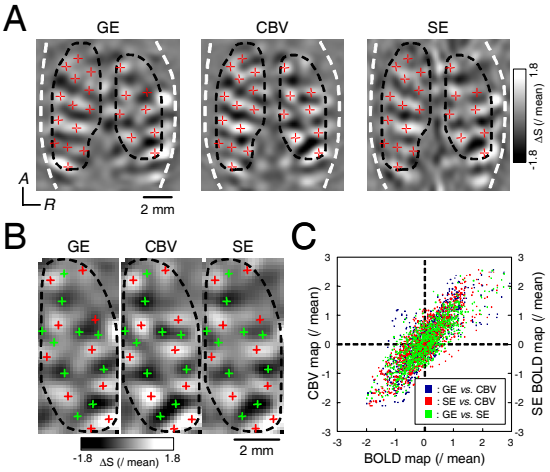

Figure 2. Comparison of iso-orientation maps of GE BOLD, CBV, and SE BOLD fMRI. Data obtained from the same cat shown in Fig. 1. (*A*) Iso-orientation maps of 0° stimulation with GE BOLD, CBV, and SE BOLD fMRI. Note that all the values of CBV map are reversed for ease of comparison. Red plus signs indicating the increase of CBV response for 0° stimulus orientation are overlaid on the GE and SE BOLD orientation maps. Mean orientation-specific signals of CBV, GE and SE BOLD are 0.68%, 0.20%, and 0.13% in ROIs (black-dashed contours), respectively. (*B*) Regions including the black-dashed ROIs in right hemisphere on the images A are enlarged for detailed comparison. Red and green plus signs indicating an increase and a decrease in CBV for 0° orientation stimulation, respectively, are overlaid on the GE and SE BOLD orientation maps. (*C*) Scatter plots within the active ROI for GE BOLD *vs*. CBV, SE *vs*. CBV and GE *vs*. SE BOLD 0° iso-orientation maps. All correlation coefficients of the comparisons were significantly high (0.78, 0.86, and 0.80, $P < 0.001$, respectively).

[Methods] All MR imaging was performed on a 9.4 T magnet (Varian Inc., CA) using a surface RF coil positioned over the cat primary visual cortex. The position of the functional imaging slice was determined based on a 3-D venogram (TR = 20 ms; TE = 50 ms, matrix = 512 × 256 × 256, FOV = 3.5 × 2.2 × 2.2 cm^3, resolution = 68 × 86 × 86 μm^3) [11]. Using venographic images, a single 1-mm thick imaging slice was selected based on two criteria: *i*) avoiding large surface veins which induce a large susceptibility artifact in EPI, and *ii*) including a flat dorsal surface area tangential to the marginal gyrus, as large as possible. For fMRI studies, three different fMRI images were obtained using EPI techniques with data matrix = 64 × 64 and FOV = 2 × 2 cm^2; *i*) GE BOLD EPI with TR = 0.5 s and TE = 18 ms, *ii*) SE BOLD EPI with TR = 2 s and TE = 40 ms, and *iii*) CBV-weighted EPI with TR = 1 s and TE = 10 ms following an intravascular bolus injection of dextran-coated MION contrast agent (10 - 20 mg Fe/kg body weight). Average repetitions of runs were 3.2 for GE BOLD, 5.3 for SE BOLD and 2.7 for CBV-weighted fMRI studies. Visual responses were induced by presenting 100% contrast square-wave gratings binocularly (0.15 cycle/°, 2 cycles/s, moving direction reversal per 0.5 s). For continuous stimulation, eight consecutive orientations (0° to 157.5°, 22.5° steps, 10 s each) were presented eleven times without any rest between orientations; total 880-s stimulation. The block-design stimulation (20 s[on] - 50 s[off]) was presented before the 880-s continuous stimulation, which was used to obtain a single-condition map. Orientation-specific signals were extracted with Fourier analysis at a frequency of 1/80 Hz. Orientation-nonspecific signals were obtained by subtracting the orientation-specific signal from the single-condition signal in the block-design stimulation. Magnitude and orientation column maps were used to compare GE BOLD and SE BOLD to CBV fMRI maps; BOLD contribution was corrected from CBV-weighted fMRI map. Cross-correlation (R) was calculated to quantify the similarity of BOLD maps to CBV maps.

[Results and Conclusion] In the single-condition GE BOLD map (Fig. 1B), large signal changes (yellow and orange) were observed at the edges and midline of the brain where large draining vessels exist (black boxes in Fig. 1A). In continuous stimulation data (Fig. 1C and D) large vessel areas still have high signal intensity in the GE BOLD orientation-specific magnitude map (Fig. 1C), but not in the SE BOLD map (Fig. 1D). However, high signal intensity regions in the internal cortical region excluding the edges and midline (white contours in Figs. 1C and D) look similar between the GE and SE BOLD maps (see Fig. 1E). The difference between the GE and SE BOLD maps can be easily seen in a subtraction map (Fig. 1F). Besides large signals at the edges and midline for the GE BOLD signal, orientation-specific signal changes in the internal cortical regions for GE BOLD (0.31 ± 0.10%, n = 10) was significantly ($P < 0.001$) higher than that for SE BOLD (0.20 ± 0.06%, n = 10) and thus CNR of orientation-specific signal for GE BOLD (6.47 ± 2.18, n = 10) was significantly higher ($P < 0.001$) than that for SE BOLD (2.84 ± 0.84, n = 10). However, the spatial specificity (i.e. ratio of orientation-specific to –nonspecific signal) of GE BOLD (0.21 ± 0.09, n = 10 hemispheres) was significantly lower ($P = 0.0097$) than that of SE BOLD (0.37 ± 0.18, n = 10), suggesting that GE BOLD signal point spread function is wider than SE BOLD possibly due to draining artifact even in the intracortical small vessel region. Although draining artifacts present, GE BOLD orientation maps are well matched with SE BOLD orientation maps and both BOLD maps are well correlated with the CBV fMRI map if the large draining vessel regions at the edges and midline of the brain are excluded (see Fig. 2A and B). Pixel-wise scatter plots within the active ROI (dotted line in Fig. 2B) show that all three orientation maps are highly correlated with each other (Fig. 2C). Average pixel-wise correlation coefficients within an active ROI for 10 hemispheres are statistically not different (one-way ANOVA; $F(2,29) = 2.154$, $P = 0.136$) across GE BOLD *vs*. CBV (0.74 ± 0.07), SE BOLD *vs*. CBV (0.73 ± 0.09), and GE BOLD *vs*. SE BOLD (0.65 ± 0.14) fMRI maps. These results suggest that higher orientation-specific BOLD signals located at larger orientation-specific CBV response regions and are likely to mark the sites of increased neural activity.

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