Comparison of conventional BOLD and CBV-weighted fMRI iso-orientation column maps in cat visual cortex.

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[Introduction]

It is generally assumed that an increase in BOLD signal is correlated to an increase in neural activity. However, the BOLD signal is due to a mismatch between oxygen consumption and blood flow changes, and thus the spatial profile of the BOLD signal at a sub-millimeter columnar resolution is closely dependent on the distance between neighboring columns and point spread functions of metabolic and blood flow changes [1]. For example, in human visual BOLD fMRI studies, Cheng et al. described that higher BOLD signal changes induced by right eye stimulation may indicate left-eye dominance columns due to this mismatch [2]. Thus, it is conceivable that the region with higher BOLD signal changes may indicate less neural activity at the columnar resolution level. To address this issue, we compared the orientation maps of conventional BOLD, $CMRO_2$-related, and cerebral blood volume (CBV)-weighted fMRI with iron oxides. CBV-weighted fMRI was used as a reference because it can detect cortical columns accurately [3], and the validity of this CBV-weighted fMRI map has confirmed in the separate experiments using conventional 'gold-standard' intrinsic optical imaging (see a companion abstract). In all experiments, we adopted a temporally-encoded stimulation paradigm to improve the sensitivity of orientation-specific responses and Fourier analysis to separate non-specific components, such as draining artifacts, from the orientation-specific response [4].

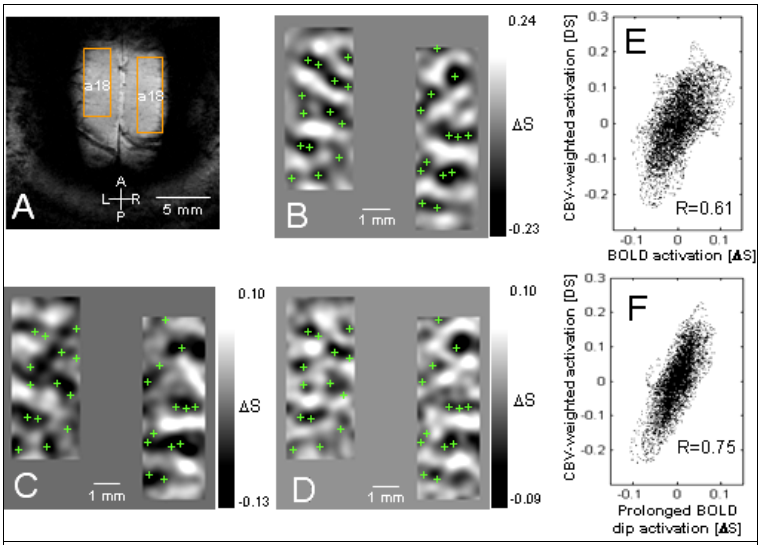

Figure 1. Comparison of iso-orientation maps between CBV-weighted, conventional positive BOLD, and prolonged BOLD dip fMRI. ***A***, Tangential anatomy image. The orange box is the ROI for the comparison of maps. *A*, anterior; *P*, posterior; *M*, medial; *L*, lateral; *D*, dorsal; *V*, ventral; *a18*, area 18.***B***, Activation map of CBV-weighted fMRI in the ROI in A. A spatial band-pass filter (0.25~1.5 kHz (max. spatial frequency, 12.8 kHz (= 1/78 μm)) was applied to improve SNR. Green "+" signs were marked for the 0° orientation sites, and overlaid on Figs. C and D. The intensity scale is arbitrary. ***C***, Activation map of positive BOLD fMRI. ***D***, Activation map of prolonged BOLD dip-based fMRI. ***E***, Scatter plot of positive BOLD vs. CBV-weighted fMRI signal changes.. ***F***, Scatter plot of prolonged BOLD dip-based vs. CBV-weighted fMRI signal changes.

[Methods] Orientation-specific activations in the cat primary visual cortex were measured using conventional BOLD, $CMRO_2$-related and subsequently CBV-weighted fMRI using monocrystalline iron oxide nanoparticles (10 mg/kg) in the same anesthetized animal (n = 4). A $CMRO_2$-related fMRI signal (prolonged BOLD dip) was obtained by suppressing the stimulus-induced CBF and CBV responses with intravenous injection of a vasodilator, sodium nitroprusside [5, 6]. It has been confirmed that neural activity is intact without evoked CBV responses. Visual responses were induced by binocularly presenting high-contrast square-wave moving gratings. A continuous stimulation paradigm was prepared for comparison as follows: eight orientations (10 s each) were presented without any intermittent gaps between stimuli and repeated 10 times (the total presentation time of 800 s). Thus, the orientation specific cycle was 80 s. The orientation of the moving bars increased from 0° to 167.5° in steps of 22.5°. A conventional block design stimulation was also used in a BOLD fMRI experiment as a control of standard method. Four orientations (10 s each) were presented every 20 s and the orientation specific cycle was also 80 s. All three fMRI experiments were performed using a custom-made surface RF coil (2.5cm diameter) placed over the primary visual cortex and a 9.4 T/31 cm horizontal magnet (Varian, CA). A navigator-echo corrected four-segmented GE EPI sequence was used with FOV = 2x2 cm^2, matrix = 128x128, and 1 mm slice thickness (TR/TE = 500/18 ms for the conventional BOLD and prolonged BOLD dip-based fMRI acquisitions, and TR/TE = 500/10 ms for the CBV-weighted fMRI acquisitions). During the 800 s visual stimulation presentation, 400 images were acquired continuously without any interruption. Five sessions for the same stimulation paradigm were repeated to improve SNR by off-line averaging. The visual area selection did not include large surface running vessels based on a 3-D venogram (TR/TE = 20/50 ms, matrix = 512x256x256, FOV = 4.0x2.0x2.0 cm^3, isotropic resolution = 78 μm) [7]. The imaging slice was positioned ~500 μm below the pial mater to avoid artifacts from the large pial vessels and white matter contamination. The ROI was selected within visual area 18 (a18 in Fig. 1A) based on the CBV-weighted activation map. For analysis, the frequency components, magnitude and phase, at the orientation-specific stimulation cycle (1/80 Hz) were extracted from the time series data on a pixel-by-pixel basis to obtain the signal change. The hemo-dynamic response delays were measured experimentally and compensated before comparing different imaging maps.

[Results and Conclusion]

We succeeded in mapping orientation columns by using conventional BOLD fMRI in the anesthetized cat visual cortex using the continuous stimulation paradigm (Fig. 1C). The orientation columns were not clear when the conventional block design stimulation paradigm was used (not shown), suggesting that the sensitivity of the signal could be the major issue to detect orientation-specific responses. Maps of conventional BOLD fMRI were very similar to those of CBV-weighted fMRI with correlation factor, R = 0.51 ± 0.08 (Mean ± SD, n = 4) (Fig. 1 B-C, E). This result strongly suggests that the higher BOLD signal changes occur at the sites of the neural activity to orientation stimulation. Prolonged BOLD dip-based fMRI maps were closer to those of CBV-weighted fMRI maps (R = 0.73 ± 0.06, n = 4) (Fig. 1 B-D, F) compared to conventional BOLD fMRI maps. The detectability of orientation-specific conventional BOLD fMRI (0.24 ± 0.05) and prolonged BOLD dip-based fMRI (0.28 ± 0.10) were not different (p = 0.332, n = 4). Since conventional BOLD fMRI and prolonged BOLD dip-based fMRI signals have similar detectability and similar draining effects, the larger local difference between conventional BOLD fMRI and CBV-weighted fMRI maps compared to prolonged BOLD dip-based fMRI maps is likely due to a broader spatial point spread function for the conventional BOLD signal. Our data demonstrates that the region with higher BOLD signals corresponds well to neural active domains in the cat visual cortex. Thus, extending the assignment of cortical columns to human BOLD functional maps should be possible, where the higher BOLD signal region corresponds to the neural active site.

[Reference]

1. Duong, T.Q. et al., *MRM*, 44, 231-242 (2000). **2**. Cheng K et al., Neuron, 32, 359-374 (2001) **3.** Zhao, F. et al., *Neuroimage* 27, 416-24 (2005). **4**. Engel, S.A. et al., *Cereb Cortex* 7, 181-92 (1997). **5**. Nagaoka, T. et al., *JCBFM* in press, (2005). **6**. Fukuda, H. et al., *Neuroimage* in press, (2005). **7**. Park, S.H. et al., *ISMRM* 1718, (2005).

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