Cortical Layer-dependent BOLD and Arterial Blood Volume Responses Measured by MT-varied BOLD fMRI

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Introduction

Cerebral blood volume (CBV) responses induced by visual stimulation were the highest at the middle of the cortex and at active cortical columns (1,2), indicating that CBV is reasonably specific to neural activity areas. Since increased CBV during neural activation originates mainly from arterial (CBV_a) rather than venous CBV changes (3), functional CBV_a change is expected to improve spatial specificity relative to BOLD fMRI. Recently, we proposed to measure functional CBV_a changes (ΔCBV_a) using BOLD fMRI with graded magnetization transfer (MT) (4), which is technically simple and also provides higher temporal resolution than arterial spin labeling-based techniques (3). This MT-varied BOLD method relies on the separation of the intravascular contribution from BOLD signals; the intravascular signal change is dominated by ΔCBV_a, since venous intravascular contribution is minimal at high magnetic fields (4). In this study, we applied the MT-varied BOLD technique to investigate spatial specificity of ΔCBV_a across cortical layers. If fMRI is specific to neural activity and metabolism, middle cortical layer (layer 4) should have the highest responses. Thus, cortical depth profiles of BOLD and ΔCBV_a responses were compared.

Methods

Three female adolescent cats weighing 1.0 - 1.5 kg were performed on a 9.4T MRI (Varian) system under 0.9-1.1% isoflurane-anesthesia with air supplemented with O_2 to attain a total O_2 level of ~30% throughout the experiments. Binocular full-field visual stimuli were presented with square-wave high-contrast moving gratings (two cycles/sec) with 0.15 cycles/degree of spatial frequency during 40-s stimulation. Animals were maintained within normal physiological ranges. Gradient-echo (GE) EPI images were acquired using a surface-coil; parameters were slice thickness = 2 mm, matrix size = 64 × 64, FOV = 2.0 × 2.0 cm^2, flip angle = ~ 20°, TR = 1 s and TE = 20 ms. The targeted MT rates (MTR) in tissue were achieved by adjusting the power level of MT-inducing RF pulses with +8500 Hz off-resonance frequency. In each animal, fMRI studies were performed in a randomized order for target MTR = 0, 0.4 and 0.6. For normalization purpose, images (S_0) were also acquired with the same parameters, but TR = 6 s. BOLD percentage maps were generated by stimulation-induced signal changes divided by baseline signal ($\Delta S_{MT}/S_{MT}$) in each MT level. Normalized stimulation-induced signal changes with MT ($\Delta S_{MT}/S_0$) were linearly fit against normalized baseline signal with MT (S_{MT}/S_0), and CBV_a was obtained from the intercept. Cortical depth profile analysis was performed in area 18 within the visual cortex (see Fig. 2C red ROIs).

Results and Discussion

Percentage BOLD signal changes increase with MT levels (Fig. 1), as seen in our previous report (4); average ΔR_2^* values were -0.65 ± 0.29, -0.80 ± 0.27 and -0.92 ± 0.19 s^{-1} (n = 3). Average ΔCBV_a values were 0.26 ± 0.14 % (n=3), which can convert to 0.24 ml/ 100g by multiplying by the tissue-to-blood partition coefficient of 0.9 ml/g. Time courses were generated from middle cortical ROIs; thus the ΔCBV_a temporal response was similar with that of BOLD (Fig. 1).

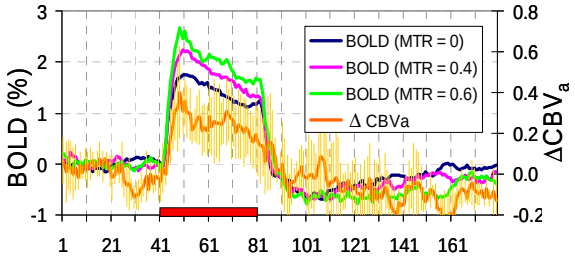

Fig. 1. Time courses of varied-MT BOLD fMRI and ΔCBV_a. Red color bar shows 40-s stimulation period. Error bars: SD

Figure 2 shows functional maps and cortical depth profiles of BOLD fMRI and ΔCBV_a. In conventional GE BOLD fMRI, the highest percentage signal changes were observed at surface areas, where large draining veins locate (yellow pixels outside green contours in Fig. 2a). This agrees well with previous observations (1). In ΔCBV_a fMRI, the highest signal changes were detected at the middle of cortex within the cortex and at the cortical surface area (Fig. 2b and 2d), suggesting that both small parenchymal and upstream pial arterial vessels dilate during stimulation. ΔCBV_a response at the cortical surface was varied possibly due to inter-subject variation of pial arterial vessel location (Fig. 2d). Within the cortex, the highest CBV_a response was observed at the middle layer (indicated by pink box in Fig. 2d), which is consistent with total CBV changes observed previously (1). This suggests that functional ΔCBV_a can improve spatial specificity relative to BOLD fMRI.

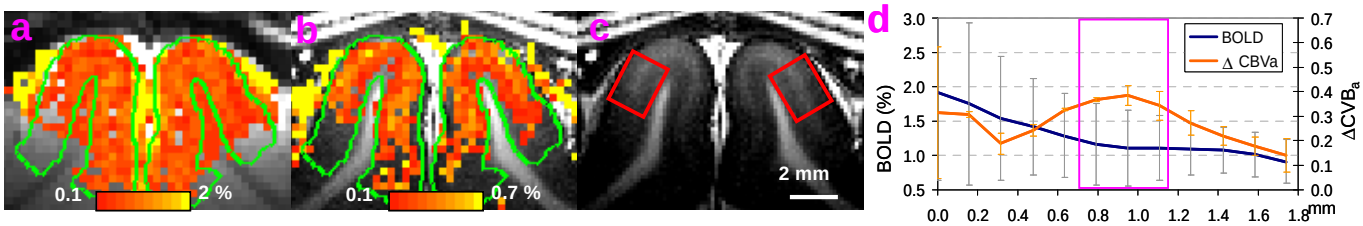

Fig. 2. (a) Percentage map of BOLD fMRI with no MT effect. (b) ΔCBV_a map. Green contours indicate gray matter. (c) T_1-weighted anatomical image with two red quadrangular ROIs for cortical depth analysis. (d) Average cortical depth profiles of BOLD and ΔCBV_a. Layer 4 is marked as a pink box. Error bars: SD

References

1. Zhao et al., NeuroImage 30: 1149-60, 2006. 2. Zhao et al., Neuroimage 27:416-424, 2005. 3. Kim et al., JCBFM 27:1235-47, 2007.4. Kim et al., Proc. ISMRM 2008, p2390.

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