BOLD fMRI with Magnetization Transfer Effects: Determination of Arterial Blood Volume Change during Neural Stimulation

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Introduction

Magnetization transfer (MT) effects selectively reduce signals originating from tissue, but have little effect on signals arising from blood (1). Thus, the MT effect can be used to separate extravascular and intravascular contributions to BOLD fMRI. Recently, Zhou et al. found that during hypercapnia the intravascular contribution to overall BOLD effects was increased with the addition of MT pulses and proposed using the finding to image total CBV (2). In our current study, the contribution of intravascular signal to BOLD with graded magnetization transfer ratios (MTR) was investigated during neural stimulation. Since the intravascular venous blood contribution to SE BOLD with long TE values is minimal at 9.4 T, the remaining intravascular component represents arterial blood volume change (ΔCBV_a). ΔCBV_a can also be calculated in arterial spin labeling (ASL) experiments with graded MTR (3). Here we compare ΔCBV_a quantification by both methods in the same animals; BOLD with graded MTR and previously-presented ASL data with graded MTR (4).

Theory

It is assumed that signals from an imaging voxel consist of three compartments; tissue/capillary, arterial blood, and venous blood. Since venous blood T_2 is 5-7 ms at 9.4 T, the venous blood contribution will be minimal when TE > 30 ms. Only tissue and arterial blood signals will be detectable. During stimulation, volume fractions will change in both arterial blood and tissue pools, while T_2 only changes in the tissue compartment. The signal change originating from the tissue pool is linearly dependent on MTR, which is quantitatively, $1-(S_{MT}/S_0)$, where S_{MT} and S_0 are the equilibrium signal in the presence and absence of MT saturation, respectively. However, the signal change induced by an arterial blood volume increase will be independent of MTR. The stimulation-induced signal change with MT normalized by the signal without MT ($\Delta S_{MT}/S_0$) can be approximately expressed as

$$\Delta S_{MT} / S_0 \approx [(1 - v_a - v_v - \Delta v_a - \Delta v_v)(-\Delta R_{2,t} \cdot TE) - (\Delta v_a + \Delta v_v)] \cdot (1 - MTR) + \Delta v_a \cdot \exp(-(R_{2,a} - R_{2,t}) \cdot TE) \approx A \cdot (1 - MTR) + \Delta v_a$$

where subscript *a*, *v* and *t* represent arterial, venous and tissue compartments, v is the fraction of spins, and R_2 is the transverse relaxation rate; at 9.4T, $R_{2,a} \cong R_{2,t} \cong 25\ s^{-1}$. Thus, when $\Delta S_{MT} / S_0$ vs. (1–*MTR*) is fit by a linear function, the intercept $\times \lambda$ represents ΔCBV_a (in units of mL/ 100 g), where λ is the tissue-to-blood partition coefficient of 0.9 mL/ g, and the slope represents tissue compartment changes, including volume fractions and susceptibility effects.

Methods

Forepaw stimulation of 15-s duration was performed in thirteen male Sprague-Dawley rats weighing 350-450 g under isoflurane-anesthesia (1.3-1.5%). Surface-coil experiments were implemented at 9.4 T. Spin-echo EPI images were acquired using an adiabatic single-shot sequence; parameters were slice thickness = 2 mm, matrix size = 64 × 32, FOV = 3.0 × 1.5 cm^2, TR = 2.5 s and TE = 30 or 40 ms. The targeted MTR values 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, 0.3 and 0.5. Functional maps and percentage changes were calculated for each MTR. ΔCBV_a was determined by choosing a 9-pixel ROI in the contralateral forelimb area. Then, normalized ΔS_{MT} signals for each of the MT levels ($\Delta S_{MT}/S_0$) were linearly fit against (1-MTR), and ΔCBV_a was obtained from the intercept in each animal. ΔCBV_a values were compared with values previously reported for ASL with graded MTR in the same ROI (4).

Results and Discussion

As MTR increased, signals in baseline EPI images decreased (Fig. A). For all three MTR values, significant signal changes were observed in the contralateral somatosensory area, with the percentage signal changes increasing with MTR (Fig. A); average ΔR_2 values in the somatosensory ROI were -0.43 ± 0.04, -0.52 ± 0.04 and -0.61 ± 0.06 s^{-1} for MTR = 0, 0.29 ± 0.03 and 0.56 ± 0.01 (n = 13), respectively. When $\Delta S_{MT} / S_0$ vs. baseline (1-*MTR*) was linearly fit (Fig. B), the intercept of averaged data was 0.51%, which represents the MT-independent arterial blood signal. ΔCBV_a values determined for individual animals by BOLD with graded MTR vs. ASL with graded MTR agree very well (R^2 = 0.72, n = 13) (Fig. C). This indicates that quantification of ΔCBV_a during neural stimulation can be determined without ASL. The implementation of BOLD with graded MTR is simple, but it can only provide ΔCBV_a, while ASL with graded MTR provides both baseline CBV_a and ΔCBV_a values. At low magnetic fields, BOLD with graded MTR will have higher remaining intravascular venous contributions to the intercept values, causing greater errors in ΔCBV_a quantification relative to ASL with graded MTR. In conclusion, we measured significant arterial blood volume changes in BOLD experiments with graded MTR.

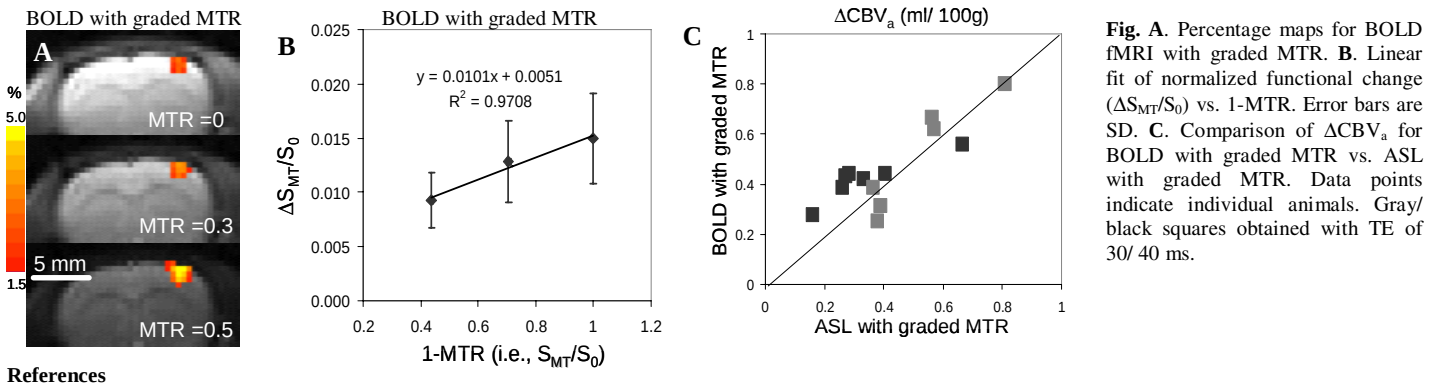

Fig. A. Percentage maps for BOLD fMRI with graded MTR. **B**. Linear fit of normalized functional change ($\Delta S_{MT}/S_0$) vs. 1-MTR. Error bars are SD. **C**. Comparison of ΔCBV_a for BOLD with graded MTR vs. ASL with graded MTR. Data points indicate individual animals. Gray/ black squares obtained with TE of 30/ 40 ms.

References
1. Balaban et al., Radiology 180:671-5,1991. 2. Zhou et al., MRM 53:356-66,2005. 3. Kim and Kim, MRM 54:333-42,2005. 4. Kim et al., JCBFM 27:1235-47,2007
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