Enhancing Relative BOLD Signal Changes Using Magnetization Transfer (MT)

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Introduction: Gradient echo (GE) BOLD fMRI is the most widely used functional brain mapping method. However BOLD often suffers from low image quality as a long TE (30-50ms at 3T) is required to get a reasonable signal change. Magnetization transfer (MT) is known for detecting macromolecules indirectly via the magnetization exchange between the bulk water spins and macromolecular spins (1). The MT effect is much larger in pure tissue than in blood (2,3), and can be used to selectively suppress tissue signal. When applied to BOLD, this can provide information concerning the contribution of intravascular and extravascular signal changes. If intravascular effects contribute to BOLD, the relative BOLD signal change will be greater due to the increased contribution from the blood (4). The extravascular/total signal change contribution ratio can then be calculated by comparing MT-BOLD and BOLD. In this study, we show that both relative signal change and CNR can be enhanced in MT-BOLD fMRI experiments in primary visual cortex of human brains at 3T.

Materials & Methods: Visual stimulation with black/white flashing checkerboard (40s/20s off/on; 4 repetitions) was performed at 3.0T (Philips Medical System). In this first study, 24 experiments were performed on a healthy subject and repeated twice (n=2) to assess reproducibility. 12 of the 24 scans consist of MT-BOLD with varying TR and TE. TR/FA/dynamics/slices=1s/66˚/280/7, 2s/80˚/140/15, 4s/90˚/70/21, each for TE=15ms (halfscan=0.746), 30ms, 45ms, 60ms. Multi-slice sequences were employed to minimize the inflow effect. The slice volume was centered on the visual cortex and only the central slice was analyzed. A five-lobed sinc-gauss MT pre-pulse (frequency offset 1.5kHz) was added before each acquisition (5). The length and amplitude of the pulse was adjusted for each sequence so that the MT ratio (MTR) produced in a 18% cross-linked bovine serum albumin phantom was about 30% and the SAR was 2.8-2.9W/kg, i.e. below the FDA limit. Common scan parameters were: voxel volume = 2x2x5 mm^3, SENSE=2, single-shot GE EPI. 12 BOLD fMRI experiments (without the MT pre-pulse) were also performed with the same acquisition parameters. An SE image was acquired for anatomical reference (TR/TE/FA =7sec/4.9ms/90˚, 2x2x5 mm^3, SENSE=2, multi-shot TSE, TSE factor=4). Requirements for voxel activation were z-score>3, p <0.01, SNR>50, and cluster size ≥ 4. Experiments were conducted in pairs of MT-BOLD and BOLD for each combination of TE and TR; only voxels activated in both experiments were used for analysis.

Results & Discussion: Fig.1 shows the relative signal change between rest and activation for MT-BOLD and BOLD fMRI experiments of three different TRs (1s, 2s, 4s) versus TE (15ms, 30ms, 45ms, 60ms). The enhancement ranges from 30% to 50% of the relative BOLD signal change. The image intensities averaged over the activated voxels in MT-BOLD experiments are 75%±4% of the intensities in the corresponding BOLD experiments (i.e. MTR~25%). Therefore the SNR of MT-BOLD is actually only about 80% of the BOLD SNR. Nevertheless, since the relative signal change elevation surpasses the SNR drop, the CNR is still 10-20% higher in MT-BOLD. This also implies that the same amount of relative signal change can be achieved with MT-BOLD at a shorter TE, which offers an advantage of less image distortion and better image quality. The relative signal changes for both methods demonstrate the well-known linear dependence on TE (6). Notice that there is a residual inflow effect, especially for TR=1s, due to the decreased number of slices (slices=7) acquired here. This inflow effect was corrected by subtracting the vertical intercept of a linear fit to the data points from the measured relative signal changes. For each pair of MT-BOLD and BOLD experiments, a two compartment model (4,7) with parameter values in literature (4,6-9) was employed to calculate the extravascular relaxation rates ($R_{2,ex}^*$) during baseline activity and visual stimulation, based on the assumption that the extravascular and intravascular contribution to the total signal changes are different in these two methods (i.e. 2 equations with 2 measurements and 2 unknowns). As the $R_{2,ex}^*$ values should not be TE and TR dependent, the averaged values (n=12) are shown in Table.1. The total BOLD $R_{2,tot}^*$ values were also fitted from the multiple TE BOLD experiments and the averaged values over the three TRs are shown in Table.1. The extravascular BOLD contribution ($\Delta R_{2,ex}^* / \Delta R_{2,tot}^*$) was then calculated as 65%±8%. All these values are in agreement with previous studies in human brain at 3T (6).

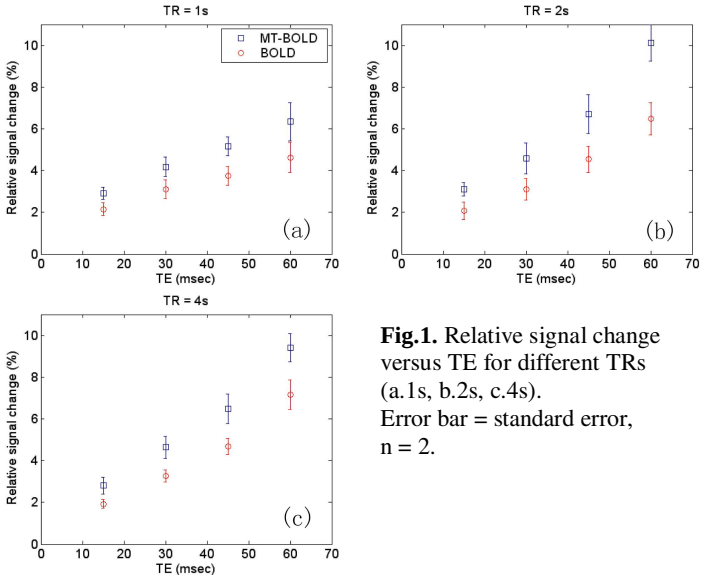

Fig.1. Relative signal change versus TE for different TRs (a.1s, b.2s, c.4s). Error bar = standard error, n = 2.

Table.1	$R_{2,rest}^*$ (s^{-1})	$R_{2,act}^*$ (s^{-1})	ΔR_2^* (s^{-1})
Extravascular (n=12)	21.04±0.97	21.36±1.01	-0.32±0.08
Total (n=3)	23.13±2.01	22.64±1.82	-0.49±0.17

Conclusion: Relative signal change and CNR can be enhanced by adding an MT pre-pulse in BOLD sequence at a reasonable SAR level well below the FDA limit. The extravascular/total BOLD signal ratio can be calculated using combined MT-BOLD and BOLD. Importantly, MT-BOLD can produce the same amplitude of relative signal change at a shorter TE than with conventional BOLD. It is likely that many studies may benefit from the improvement in image quality available with these shorter TE, MT-BOLD fMRI acquisitions.

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