Assessment of Intravascular and Extravascular BOLD Signal with Grey Matter Nulled and VASO fMRI Methods

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Introduction

The BOLD fMRI signal consists of intravascular and extravascular components from both small and large blood vessels [1]. The BOLD signal originating from capillary site and surrounding areas is thought to provide good spatial localisation for neuronal activation. However, at low and intermediate field strengths, the gradient echo (GE) BOLD effects from large draining veins often contaminate the fMR images, causing misplacement of actual neuronal activation site. Recently developed grey matter nulled (GMN) [2] and vascular space occupancy (VASO) [3] fMRI techniques can reveal changes in cerebral blood volume (CBV) associated with brain activation. These fMRI techniques allow also for direct assessment of intravascular and extravascular BOLD signals without contamination from draining veins. In this study, we have used both fMRI methods to explore intravascular and extravascular BOLD signals in parenchyma at 3T.

Method and Material

Eight healthy volunteers (five males, three females, aged between 24 and 51) were recruited with signed informed consent before taking part in the study. The fMRI scanning was performed on a 3T MR system (Philips Medical Systems, Best, The Netherlands). The BOLD, GMN and VASO fMRI scan data were acquired as follows: single shot GE-EPI, TR = 3 s, FA = 90°, FOV = 224 mm, matrix = 112x112, SENSE factor = 2.5, slice thickness = 5 mm, TE = 40 ms for BOLD, TE = 10 ms for both GMN and VASO, and TI = 703 and 889 ms for GMN and VASO, respectively. A single oblique axial slice covering the primary visual cortex was manually selected. Visual stimulation consisted of 45 s OFF and 45 s ON in two cycles with B/W checkerboard flashing at 8 Hz. Seventy five dynamic images were acquired for each fMRI scan in 225 s. Activation maps for GMN, VASO and BOLD fMRI scans were obtained using FEAT (FMRI Expert Analysis Tool), part of FSL package (http://www.fmrib.ox.ac.uk/fsl) for the volunteers. The overlap of either BOLD and GMN or BOLD and VASO activation maps was determined individually. The BOLD signal change from each overlapping area was calculated under the routines of IDL 6.0 (Research Systems Inc., Boulder, CO). Similarly, the BOLD signal from regions showing no activation in either GMN or VASO fMRI was also calculated. The BOLD intravascular signal was taken as the overlapping region of BOLD and GMN activation maps, whereas the BOLD extravascular region was determined from the overlap of BOLD and VASO activation maps.

Results

The number of active voxels in GMN (68±30 voxels) and VASO (66±20 voxels) fMRI from eight subjects were found to be much smaller than that by BOLD (347±47 voxels). This difference is largely attributed to substantial macrovascular venous contribution to the BOLD fMRI [1]. GMN and VASO activation voxels are nearly completely located within the BOLD active regions (spatial overlaps by 85±9% and 78±11% respectively). However, the overlap of active GMN and VASO voxels is very low (6.9±5.2%), indicating that the respective fMRI signals originate from different parenchymal components. Figure 1 shows BOLD signal traces from the activated voxels in the regions that (i) overlap with GMN fMRI (blue trace), (ii) overlap with VASO fMRI (red trace) and (iii) no overlap (black trace). Table 1 shows the percentage of changes for BOLD signals from the three voxel types above for all eight subjects. The BOLD signal change in the GMN overlapping region (3.8±1.2%) is greater than that in VASO overlapping voxels (3.3±1.2%) (paired-t test, $p < 0.01$). The BOLD signal from the non-overlapping voxels is much lower (1.2±0.3%) than that in those overlapping either with GMN or VASO fMRI.

Discussion and Conclusion

The current results indicate that the BOLD signal at 3T with spatial resolution of 2x2x5 mm^3 is 3-fold larger in the brain parenchyma with increased CBV, as revealed by GMN and VASO fMRI methods, than outside of this area. It has been proposed that VASO fMRI measures the signal change from extravascular tissues due to expansion of blood vessels to brain activation and has been considered to be sensitive to microvascular compartment, largely to vessels around ~200 μm in diameter [3]. Since hyperoxygenation due to brain activation is strongest in postcapillary venules and veins in the vicinity of activated brain region, both GMN and VASO signals are likely to arise from these vascular compartments. Recent evidence also points to substantial intravascular contribution to the GMN fMRI signal change [2]. Therefore, it is likely that GMN and VASO are sensitive to signal changes in intravascular and extravascular compartments, respectively. As demonstrated by this study, the intravascular BOLD signal at 3T, as defined in the parenchyma by GMN fMRI, is larger than the extravascular BOLD signal evaluated with VASO fMRI [3]. Non-overlapping BOLD region may represent draining vein contribution, which gives a relatively low BOLD signal due to mixing with blood draining non-activated brain region.

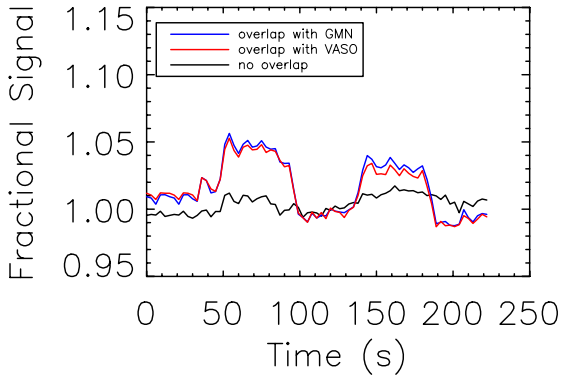

Figure 1. Plots of time course data from the BOLD responses in the regions (i) overlapping with GMN fMRI (blue), (ii) overlapping with VASO fMRI (red) and (iii) non-overlapping (black) for a typical subject.

Reference

[1] Ogawa S, et al; Biophys J 1993; 64:803-812.
[2] Shen Y, et al; Proc. ISMRM 2007; 27.
[3] Lu H, et al; Magn Reson Med 2003; 50:263-274.

Table 1. BOLD signal changes from the voxels (i) overlapping with GMN, (ii) overlapping with VASO and (iii) non-overlapping ones.

BOLD Signal Change (%)	Subject 1	Subject 2	Subject 3	Subject 4	Subject 5	Subject 6	Subject 7	Subject 8	Mean±SD
Overlapping with GMN	2.9	6.2	4.0	3.5	4.5	2.6	3.8	2.6	3.8±1.2
Overlapping with VASO	2.3	5.9	3.6	3.1	3.4	2.5	3.5	2.2	3.3±1.2
Non-overlapping voxels	1.8	1.1	1.0	1.2	1.5	1.0	0.8	0.9	1.2±0.3