Measurement of Parenchymal T2* Changes During Visual Stimulation Using Grey Matter Nulled and VASO fMRI

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Introduction

High-resolution T_2 data from visual cortex has been used to determine venous oxygen saturation (Y_v) directly in draining veins for estimation of oxygen extraction fraction (OEF) by MRI [1]. More recently, Lu et al [2] used vascular space occupancy (VASO) fMRI [3] to measure extravascular T_2^* changes during visual stimulation in the human visual cortex and derived Y_v from these data to obtain a change in OEF due to stimulation. The BOLD signal has contributions from both intravascular blood and extravascular tissue at low and intermediate magnetic field strengths. We hypothesised that grey matter nulled (GMN) fMRI [4] technique by virtue of probing MR signal changes mainly in blood may provide transverse relaxation data from intravascular blood. VASO fMRI was used to obtain T_2^* changes from extravascular parenchyma for the comparison with relaxation data by GMN fMRI.

Methods and Materials

T_2^* of respective parenchymal compartments at rest and during stimulation can be determined from the dual echoes in GRE-EPI images of GMN and VASO data respectively by

$$T^{*rest}_{2,par(blood)} = (TE_2 - TE_1)/\ln\left(S^{rest}_{GMN,1} / S^{rest}_{GMN,2}\right)$$

$$T^{*act}_{2,par(blood)} = (TE_2 - TE_1)/\ln\left(S^{act}_{GMN,1} / S^{act}_{GMN,2}\right)$$

$$T^{*rest}_{2,par(tissue)} = (TE_2 - TE_1)/\ln\left(S^{rest}_{VASO,1} / S^{rest}_{VASO,2}\right)$$

$$T^{*act}_{2,par(tissue)} = (TE_2 - TE_1)/\ln\left(S^{act}_{VASO,1} / S^{act}_{VASO,2}\right)$$

where TE_1 and TE_2 are the echo times, $S_{GMN,1}$ and $S_{GMN,2}$ ($S_{VASO,1}$ and $S_{VASO,2}$) are the respective signal intensities of GMN (VASO) data at these two echoes, and superscripts '*rest*' and '*act*' represents the state in resting and activated conditions. With measured T_2^* change from extravascular parenchyma by VASO fMRI, Y_v and OEF can be derived [2] respectively by

$$\Delta R^*_{2t,Hb} = f_v \cdot \gamma \cdot B_0 \cdot \frac{4}{3}\pi \cdot \Delta\chi \cdot Hct\left[CBV_{act}\left(1-Y_v^{act}\right) - CBV_{rest}\left(1-Y_v^{rest}\right)\right]$$

$$\left(1-Y_v\right) = 1 - Y_a + OEF \cdot Y_a$$

where f_v = 0.7, γ is the gyromagnetic ratio, B_0 is the field strength, $\Delta\chi$ = 0.31 ppm, Hct = 0.357, Y_a = 0.98, Y_v^{rest} = 0.61 and CBV_{rest} = 0.047 mL blood/mL grey matter. CBV_{act} is calculated by [2]

$$CBV_{act} = -\frac{S^{act}_{vaso} - S^{rest}_{vaso}}{S^{rest}_{vaso}} \cdot \left(C_{par} - CBV_{rest} \cdot C_{blood}\right)/C_{blood} + CBV_{rest}$$

where C_{par} = 0.89, C_{blood} = 0.87, and S_{vaso}^{rest} and S_{vaso}^{act} are VASO signals at baseline and during stimulation at TE = 0.

Table 1. Measured intravascular blood and extravascular tissue T_2^* at 3.0 T

	Subject 1	Subject 2	Subject 3	Subject 4	Subject 5	Subject 6	Mean±SD
GMN fMRI $T^*_{2,rest}$ (ms)	51.6	55.6	48.8	57.3	60.0	46.6	53.3±5.2
GMN fMRI $T^*_{2,act}$ (ms)	53.1	58.4	49.9	60.0	61.6	47.5	55.1±5.8
GMN fMRI ΔT^*_2 (ms)	1.5	2.8	1.1	2.7	1.6	0.9	1.8±0.8
VASO fMRI $T^*_{2,rest}$ (ms)	36.7	40.3	37.5	37.5	39.9	35.7	37.9±1.8
VASO fMRI $T^*_{2,act}$ (ms)	37.8	40.9	37.9	37.9	40.8	36.1	38.5±1.9
VASO fMRI ΔT^*_2 (ms)	1.1	0.6	0.4	0.4	0.9	0.4	0.6±0.3

Table 2. Calculated Y_v during activation and OEF from VASO data

	Subject 1	Subject 2	Subject 3	Subject 4	Subject 5	Subject 6	Mean±SD
Y_v^{act}	0.80	0.75	0.75	0.76	0.79	0.76	0.77±0.02
OEF	0.18	0.23	0.24	0.23	0.19	0.22	0.22±0.02

Six healthy male volunteers (aged between 24 and 52) were recruited, each providing with a signed informed consent before taking part in the study. A Philips Achieva 3.0T MR system (Philips Medical Systems, Best, The Netherlands) was used for fMRI. A single oblique axial slice (5 mm) along the calcarine sulcus was manually selected. The GMN and VASO fMRI scans were acquired with following parameters: single shot GRE-EPI, TR = 3000 ms, FA = 90°, FOV = 224x224 mm, matrix = 112x112, SENSE factor = 2, TE_1 = 10 ms, TE_2 = 76 ms, and TI = 703 ms for GMN and 889 ms for VASO. Visual stimulation consisted of 30 s OFF and 30 s ON in five cycles with B/W checkerboard flashing at 8 Hz. 110 dynamic images were acquired for each fMRI scan in 330 s. T_1 values were determined at baseline with acquisition of a series of inversion recovery data with TI = 200, 400, 600, 800, 1000, 2000, 3000 and 4000 ms. TE = 10 ms and TR = 10 s were used at the same spatial resolution from the same slice as for fMRI. Four repeats were averaged in T_1 measurements to improve SNR. T_1s were determined by fitting the multiple TI data to a three-parameter model. Activation maps were obtained using FEAT (FMRI Expert Analysis Tool), part of FSL package (http://www.fmrib.ox.ac.uk/fsl). Routines under IDL 6.0 (Research Systems Inc., Boulder, CO) were used to determine the T_1 value at each activated voxel, the T_2^* at baseline and during activation as well as the Y_v and OEF.

Results and Discussion

Table 1 shows T_2^* results from individual subjects, the mean T_2^* values from GMN and VASO fMRI and their changes associated with brain activation. T_2^* values obtained with GMN fMRI for baseline and activation were 53.3 ± 5.2 ms and 55.1 ± 5.8 ms, respectively. In contrast, the T_2^* values from active pixels in VASO fMRI, that are thought to be representative for extravascular grey matter (GM) [2], were 37.9 ± 1.8 ms for baseline and 38.5 ± 1.9 ms for activation. GM T_2^* values we determined at baseline (37.9 ms) agree with published results for pure GM (41.6 ms) at 3T [5]. The change in T_2^* to visual stimulation quantified by GMN fMRI was three-times larger than that by VASO fMRI (1.8 ± 0.8 ms vs 0.6 ± 0.3 ms, paired t-test, $p < 0.025$). Table 2 shows the calculated Y_v and OEF results from each subject determined from VASO data. The computed Y_v during activation (0.77 ± 0.02) and the derived OEF (0.22 ± 0.02) are consistent with those derived by Lu et al [2]. The T_1 values (averaged for six subjects) for GMN and VASO fMRI activated voxels were 1608 ± 283 ms and 1247 ± 214 ms, respectively (t-test, $p < 0.0001$). These values are close to the typical T_1 values of blood (1627 ms) [6] and GM (1283 ms) [5] at 3T.

The data above strongly support the idea that activated voxels in GMN fMRI gain chief contribution from blood. Vascular compartments (arterioles, capillaries and veins) contribute approximately by 21%, 33% and 46%, respectively [7] to the microvascular blood volume. T_2^* in these compartments depends on Y and hematocrit (Hct) value. In the bovine blood at 3T, typical T_2^* values for arteriole, capillary and venous blood are 72.5, 32 and 21.2 ms [8], respectively (using Y_a = 1.0, Y_c = 0.79 and Y_v = 0.62 at Hct = 0.44 in large vessels, which corresponds to Hct = 0.37 in microvessels). The GMN fMRI T_2^* at baseline (53.3 ms) is within the range of these vascular T_2^*s, but much longer than that averaged from all types of blood (72.5x0.21 + 32x0.33 + 21.2x0.46 = 35.5 ms). This difference may be due to partial volume effects of CSF as CSF T_2^* is much longer than that of blood. Nevertheless, prolonged T_2^* in GMN fMRI is likely to reflect change in venous blood, because the T_2^* of CSF will not change during brain activation.

Conclusion

Parenchymal T_2^* values were measured using GMN and VASO fMRI methods. The change in T_2^* by GMN fMRI during visual stimulation was three-times greater than that by VASO fMRI. These fMRI data allow to assessing OEF responses in the human brain.

References

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