T2* Responses in Grey Matter Nulled and VASO fMRI Images during Visual Stimulation in Hypoxic Hypoxia

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Introduction

Grey matter nulled (GMN) [1] and vascular space occupancy (VASO)-dependent [2] fMRI methods are used to probe cerebral blood volume (CBV) changes in brain parenchyma during activation. While the VASO method is probing pure tissue signal in parenchyma due to CBV change, the GMN method is more sensitive to the blood signal in parenchyma due to increase in CBV during brain activation. In this study, we explored not only the CBV change but also T_2^* change in these different parenchymal compartments in the presence of hypoxia using GMN and VASO fMRI methods in combination. Two echoes were acquired by both GMN and VASO fMRI for quantification of T_2^*.

Methods and Materials

T_2^* was calculated from dual echoes in gradient-echo echo-planer imaging (GRE-EPI) images of GMN and VASO data by $T_2^* = (TE_2 - TE_1)/\ln(S_1 / S_2)$ where TE_1 and TE_2 are the echo times, and S_1 and S_2 are the corresponding signal intensities at these two echoes. Seven healthy subjects (4 males, 3 females, aged between 24 and 52) were recruited, each provided with a signed informed consent before taking part in the study. A Philips Achieva 3T MR system (Philips Medical Systems, Best, The Netherlands) was used for fMRI data acquisition. A single oblique axial slice (5 mm) along the calcarine sulcus was manually selected for fMRI scans. The GMN and VASO fMRI scans were performed as follows: single shot GRE-EPI, TR = 3000 ms, FA = 90°, FOV = 224x224 mm, matrix = 112x112, SENSE factor = 2.5, TE_1 = 10 ms, TE_2 = 56 ms, and TI = 703 ms for GMN and 889 ms for VASO. 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 within a period of 225 s. Inspired oxygen tension (FIO_2) was either 21% (room air) in normoxia or 12% (O_2 balanced with N_2 in a non-rebreathing circuitry) in hypoxia. Arterial oxygen saturation levels (Y) and pulse rates were monitored from a finger on the left hand with a Pulse Oximeter (System 4500 MRI, In Vivo Research Inc., USA). Activation maps were obtained from the short echo GMN and VASO data 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 GMN and VASO signal changes from short echo data (TE = 10 ms) and their corresponding T_2^* changes from dual echo data. Two types of active voxels were analysed within each fMRI technique, one for all activated voxels determined individually in normoxia and hypoxia, and the other the overlapping voxels common to both oxygenation states.

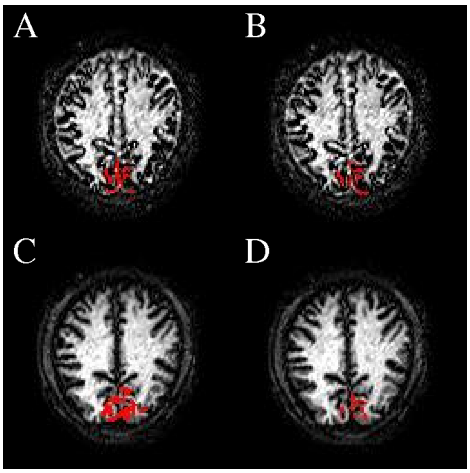

Figure 1. GMN (top) and VASO (bottom) activation maps overlaid on respective GMN and VASO raw data in normoxia (left) and hypoxia (right).

Results

Hypoxic hypoxia increased heart rate from 62±9 to 74±11 ($p < 0.05$) and decreased oxygen saturation from 0.99±0.01 to 0.86±0.05 ($p < 0.001$). Activated brain areas reduced by 72±22% in GMN and 66±23% in VASO during hypoxia (See Fig. 1 for a typical volunteer). Figure 2 shows the GMN and VASO signal time courses averaged for 7 subjects (top) and T_2^* time courses (bottom) in normoxia and hypoxia for all activated voxels. GMN signal changes from all activated voxels were 5.9±1.8% in normoxia and 6.3±1.7% in hypoxia (not significant =ns). The corresponding VASO signal changes were -2.90±0.57% and -3.21±0.64% (ns). Similar signal changes were also found for overlapping voxels, i.e., for GMN, 8.3±2.8% in normoxia and 8.0±1.4% in hypoxia (ns), and for VASO, -3.3±1.1% in normoxia and -3.9±0.9% in hypoxia (ns). VASO signal time courses were of similar shape both in normoxia and hypoxia. However, the shapes of GMN signal time courses were slightly different, with an initial stimulus overshoot in normoxia but not in hypoxia. T_2^* time courses for extravascular tissue (T_2^*-VASO signal) from all activated voxels showed that T_2^* increase during activation was larger in normoxia (3.6±1.2%) than in hypoxia (2.4±1.3%) ($p < 0.05$). Extravascular tissue T_2^* signals showed initial stimulus overshoot, but no post-stimulus undershoot. Blood T_2^* (T_2^* in GMN activated pixels) in normoxia and hypoxia show significant differences, with a positive T_2^* signal change to visual stimulation in normoxia (2.6±0.8%), but a negative T_2^* change in hypoxia (-2.9±2.9%) ($p < 0.001$). Consistent results were found for T_2* in overlapping voxels (+6.32±3.16% in normoxia and -0.77±3.01% in hypoxia ($p < 0.001$)). Initial overshoot and post-stimulus undershoot were evident in blood T_2^* signal in normoxia, but not in hypoxia.

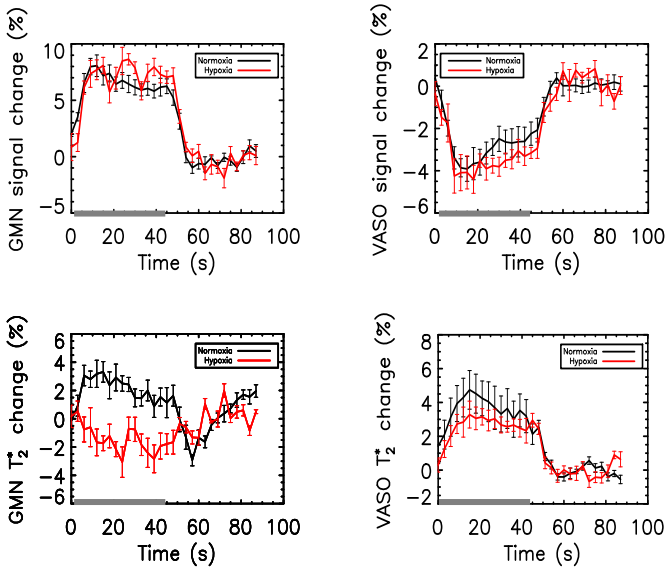

Figure 2. GMN and VASO averaged signal (top) and averaged T_2^* (bottom) time courses in normoxia and hypoxia from all activated voxels. The grey horizontal bars indicate stimulation duration (45 seconds).

Discussion and Conclusions

The current results show that while the CBV response as probed by both VASO and GMN fMRI behaves similarly in activated visual cortex in normoxia and hypoxia, T_2^* in GMN activated region change very differently. The former observation agrees with a previous study in VASO showing that vascular reactivity is not influenced by moderate hypoxia [3]. It is intriguing to see that T_2* in GMN active pixels shortens in hypoxia, a change that is opposite in sign to that detected in normoxia by GMN fMRI or by VASO under both oxygenation conditions. VASO and GMN active pixels overlap only by about 7% [1] possibly due to differing extravascular and intravascular contributions. We speculate that in a sub-volume of the visual cortex showing CBV increase to visual stimulation during hypoxia compromised oxygen availability leads to high oxygen extraction that shortens T_2*. This hypothesis is supported by previous evidence for heterogeneous oxygen extraction in the visual cortex during stimulation [4].

References

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