Mapping of $CMRO_2$ changes in visual cortex during a visual motion paradigm at 7T

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Introduction: Regional changes in the cerebral metabolic rate of oxygen ($CMRO_2$) associated with neural activation can be estimated with MRI from cerebral blood flow (CBF) and blood oxygenation level dependent (BOLD) responses using the deoxyhaemoglobin (dHb) dilution model [1, 2]. The latter also requires the calibration of resting-state BOLD signal against an iso-metabolic change in the local dHb concentration. This change has been achieved using hypercapnia [1-3] or hyperoxia [4, 5], and recently the combination of the two using inhaled carbogen [6]. Carbogen breathing induces large changes in dHb concentration and thus allows more precise evaluation of the calibration constant M, which defines the largest possible BOLD signal change. Despite such and other recent advances [7] the calibrated BOLD approach has not yet found widespread use in cognitive fMRI experiments, perhaps due to the low signal-to-noise ratio (SNR) of arterial spin labeling (ASL) techniques even at 3T. The benefit of high magnetic fields, such as 7T, for ASL is twofold: the increase in SNR and the increase in T_1, both in blood and brain tissue. The utility of ASL for $CMRO_2$ mapping at 7T may be limited by RF transmit field (B_1+) inhomogeneity, and the larger SAR. To establish the feasibility of the calibrated BOLD technique at 7T, we used a visual motion paradigm with a calibration step combining carbogen breathing and intense visual stimulation, following Gauthier et al [6]. This approach enables quantitative comparison of brain work across the cortical regions V1 and V5.

Materials and Methods: All experiments were performed on a 7T whole-body MR scanner (MAGNETOM 7T, Siemens, Erlangen, Germany) using an 8-channel phased-array coil (RAPID Biomedical, Rimpar, Germany). The study was approved by the local ethics committee and all subjects gave informed consent. A multi-slice single-echo pulsed arterial spin labelling (PASL) sequence with GRE EPI readout was used for simultaneous CBF and BOLD measurements. The PASL sequence was based on flow-sensitive alternating inversion recovery (FAIR) labelling scheme [8] with quantitative imaging of perfusion using a single subtraction (QUIPSS II) technique [9] and inversion times TI1/TI2 = 1000/1700 ms. Preliminary tests ensured that B_1+ was sufficient for proper adiabatic inversion of the vascular territories supplying the visual cortex for all subjects. Eleven oblique slices through the occipital lobe were acquired in 6 healthy volunteers (3 male) with TR=3 s, TE=14 ms, and 3x3x3 mm^3 resolution. The subjects underwent a gaseous challenge scan for BOLD calibration, during which they wore a nose clip, and air or a mixture of 5% CO_2 with 95% O_2 (carbogen) was administered through a mouthpiece connected to a non-rebreathing gas delivery circuit. The calibration scan began with 2 minutes air breathing, followed by 5 minutes carbogen administration, finishing with 3 minutes of air breathing. During the calibration scan subjects had to attend to a block-design visual task projected on a screen positioned at the back of the scanner. The paradigm consisted of 1 minute black and white checkerboard flickering at 8 Hz alternating with 1 minute isoluminant grey screen. The visual motion paradigm covered the same portion of the visual field and consisted of 30 s moving star-field, 30 s static star-field, both of high contrast, and 30 s blank screen with fixation dot repeated 12 times, totalling 18 minutes. Motion correction was performed in SPM8 for all data, and areas of statistically significant activation in CBF for each contrast were determined using a combined perfusion and BOLD model in FSL FEAT. CBF and BOLD time-courses were calculated from the PASL time-series using sequential image subtraction and addition, respectively, and used for estimating voxel-wise the stimulus-induced signal changes. Voxels within the activated clusters that were computed to have physiologically improbable changes of CBF (negative or over 300%) were confirmed to be outliers and excluded from further analysis. The M values were estimated as the difference in the mean BOLD signal during 48 s of the checkerboard stimulus accompanying carbogen breathing and 48 s of grey screen stimulus during initial air breathing. Voxels with M higher than 0.2 (20%) were identified as contaminated by veins and excluded from further analysis. For computation of the $CMRO_2$ the dHb dilution model was used with $\alpha = 0.2$ [10] and $\beta = 1.3$ [5]. T_1 maps of the imaged region for anatomical reference were calculated from inversion recovery GRE EPI scans with 4 inversion times: 41 ms, 80 ms, 160 ms and 1000 ms.

Results and Discussion: Figure 1 shows a slice of the normalized maps of $CMRO_2$ increase for the three functional contrasts, in a representative subject. The maps show areas with statistically significant activation in CBF, thresholded at Z = 2.3 and cluster significance with $p<0.05$ (corrected for multiple comparisons), overlaid on the T_1 map. Figure 1a depicts the contrast 'moving star-field vs blank screen'; 1b 'static star-field vs blank screen'; and 1c 'moving vs static star-field'. Table 1 summarizes the percentage $CMRO_2$ changes, contrasting pairwise the visual motion conditions for each subject, and the mean across subjects. The regions of interest (ROIs) were: primary visual cortex V1, and motion sensitive visual area V5. V5 showed a statistically significantly smaller $CMRO_2$ increase than V1 ($p<0.001$) in the moving vs blank condition. By comparison, V1 showed the same mean $CMRO_2$ increase between the blank screen and moving or static star-field conditions.

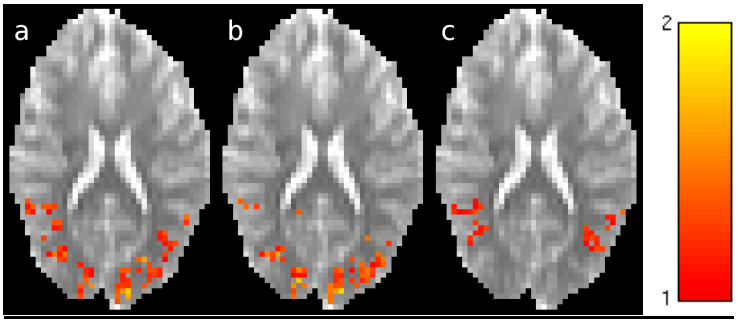

Figure 1: Normalized unsmoothed maps of $CMRO_2$ increase for a representative subject overlaid on the T_1 map: a) moving starfield vs blank screen; b) static starfield vs blank screen; c) moving vs static starfield

	contrast	S1	S2	S3	S4	S5	S6	Mean ± SD
V1	moving-blank	41	22	27	30	22	23	28 ± 7
	moving-static	5	1	3	1	-1	3	2 ± 2
	static-blank	36	26	26	34	30	23	29 ± 5
V5	moving-blank	19	14	12	17	17	16	16 ± 2
	moving-static	12	22	12	13	0	13	12 ± 7

Table 1: $CMRO_2$ changes in percent in the V1 and V5 regions for each of the contrasts and each of the subjects as well as the mean and standard deviation

The 8-channel coil was used, rather than the 24-channel NOVA coil also available, because the latter delivered insufficient B_1+ to fully label the blood supply to visual cortex for every subject. Although SAR limits restricted the number of slices to 11, these were sufficient to cover the whole occipital lobe. This approach for M-value determination seeks to measure the maximum possible BOLD signal change directly, and does not rely on measurements of CBF changes due to induced hypercapnia. It was used because PASL acquisitions with the long inversion times used here are unsuitable for estimating the global CBF changes found during CO_2 breathing [11]. Although this calibration method may not reach the ultimate maximum BOLD signal change, it provides robust and reasonable lower bounds for the M-value without using intolerable levels of CO_2. In conclusion, we have shown that calibrated BOLD at 7T can measure relative changes in $CMRO_2$ across cortical areas with good accuracy and small ROIs, using a simple and robust calibration method.

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