Layer-Dependent Calibrated BOLD Response in Human M1

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Target Audience: Researchers interested in layer-dependent fMRI, calibrated BOLD, hypercapnia and high field fMRI.

Purpose: Increasing interest towards the distribution of neural activity across cortical layers has motivated a number of human and animal multimodal studies but did not yet provide univocal interpretations. The presence of a stronger blood-oxygenation level dependent (BOLD) response arising specifically from neural activity in middle layers remains elusive[1-3]. Due to the complex nature of the BOLD response and, hence, inherent difficulty to derive a quantitative interpretation, additional contrasts and increased spatial resolution are required to obtain reliable information about metabolic activity across cortical layers. The purpose of this study is to apply and evaluate quantitative fMRI of BOLD signal and cerebral blood volume (CBV) at high resolution for layer-dependent estimations of cerebral metabolic rate of oxygen ($CMRO_2$) changes at 7T.

Methods: The experiments were performed in $n = 8$ (one excluded due to suboptimal slice orientation) healthy volunteers. BOLD and vascular space occupancy (VASO) data were acquired in an interleaved fashion using SS-SI-VASO[4] with nominal in-plane resolution of 0.8×0.8mm^2 (0.8 being roughly 20% of the total M1 thickness[5]) and 1.2 to 1.5mm slice thickness (matrix 64×64, 5 to 7 slices) on a Siemens MAGNETOM 7T scanner (Siemens Healthcare, Erlangen, Germany). The functional paradigm consisted of a combination of alternated 30sec periods of finger tapping and rest and a 5%-CO2 gas challenge. The gas was administered during two 3min periods, separated by intervals of normal air breathing, for an overall scan time of 15min. A region of interest in primary motor cortex (M1)[6] was defined using FSL FEAT (FMRI Expert Analysis Tool, http://www.fmrib.ox.ac.uk/fsl) with Z>2.3; p<0.05, cluster level. NIfTI images were resized to 256×256 and the cortex was divided into 20 laminae using an equidistant approach (**Figs. 1c** and **d**, top) starting from the gray matter (GM)-cerebrospinal fluid (CSF) interface.

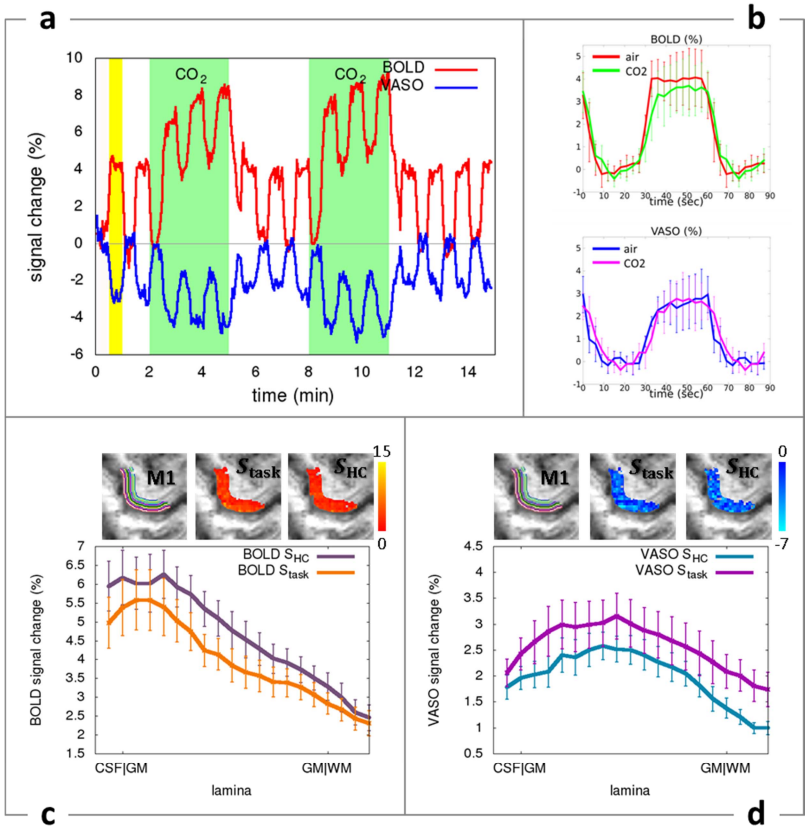
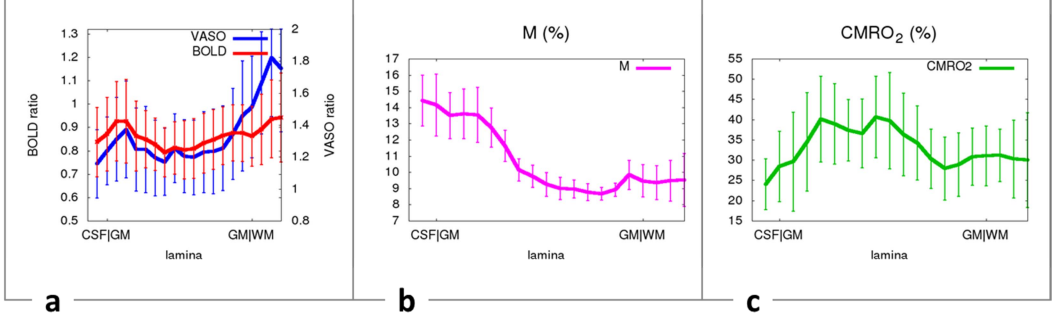


Fig. 1

Results & Discussion: Averaged gradient echo (GE) BOLD and VASO time courses are shown in **Fig 1a**. Green shades indicate the intervals of hypercapnia, while the yellow shade indicates the first episode of tapping. Mean BOLD and VASO responses are depicted in **Fig. 1b** for the conditions 'hypercapnia' and 'task'; activation profiles are shown in **Figs. 1c** and **d**. Scaled profiles were obtained dividing S_{task} by S_{HC} separately for BOLD and VASO signals (**Fig. 2a**). Finally, profiles for the calibration parameter, M, and $CMRO_2$ changes across laminae were calculated according to the Davis model[7] assuming $\alpha_{tot} = 0.38$, $\alpha_{vein} = 0.2$, $\beta = 1$ (**Figs. 2b** and **c**, respectively). Hypercapnia- and task-induced activations generate similar profiles[8]. The average BOLD profile (**Fig. 1c**) shows a peak at the surface, as expected from its sensitivity to pial veins, while VASO peaks in deeper layers (**Fig. 1d**). Unlike BOLD, the scaled VASO profile (**Fig. 2a**) has values above 1 all over the gray matter, consistent with the fact that it is insensitive to $CMRO_2$ changes during the stimulation task. No pronounced increase is visible in middle layers. The parameter M in the Davis model shows a distinct variation with depth (**Fig. 2b**), specifically a graded decrease from the pial surface down to the white matter interface. Finally, the estimated $CMRO_2$ profile (**Fig. 2c**) shows high noise and variability, with a tendency for lower values at the cortical surface. This suggests reduced sensitivity to pial vasculature response and higher specificity to neural activity in middle cortical layers.

Conclusion: Layer-dependent scaled BOLD and VASO signals, compared to the estimation of the parameter M and $CMRO_2$ changes, show puzzling profiles. The distribution of M suggests that the assumption of a constant value for such parameter across the cortex could be prone to errors[9], while the variability of the $CMRO_2$ profile may reflect SNR issues or the limits of applicability of the underlying model. However, the results of this study suggest that quantitative fMRI at 7T can enable layer-dependent calibrated BOLD responses non-invasively in the human brain. Calibrated BOLD fMRI could help to map neural activity with laminar specificity independently of large vascular responses at the cortical surface.

Fig. 2



References: [1] Koopmans PJ, et al. Hum Brain Mapp. 2010;31:1297-1304. [2] Zhao F, et al. NeuroImage. 2006;30:1149-1160. [3] Goense JBM, Logothetis NK. Magn Reson Imaging 2006;24:381-392. [4] Huber L, et al. Magn Reson Med. 2013;72:137-148. [5] Fischl B, Dale AM. Proc Natl Acad Sci USA. 2000;97:11050-11055. [6] Trampel R, et al. Proc ISMRM, 2012;20:663. [7] Davis TL, et al. Proc Natl Acad Sci USA. 1998;95:1834-1839. [8] Yen CC, et al. Proc ISMRM, 2012;20:2834. [9] Herman P, et al. Proc Natl Acad Sci USA. 2013;110:15115-15120.

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