CEREBRAL BLOOD VOLUME CHANGES IN NEGATIVE BOLD REGIONS DURING VISUAL STIMULATION IN HUMANS AT 7T

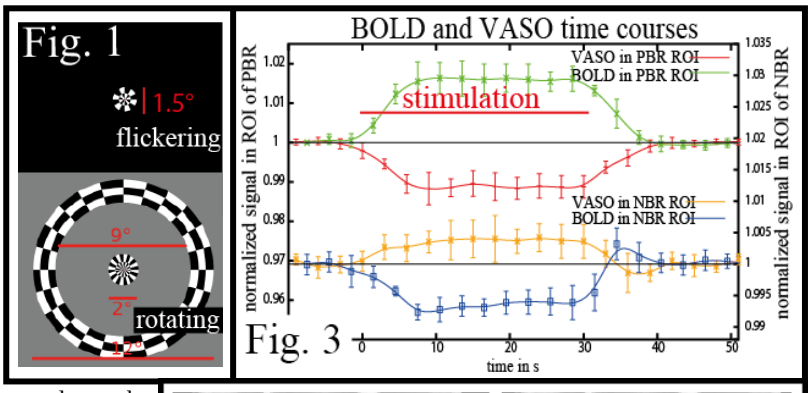
Laurentius Huber[1], Jozien Goense[2], Dimo Ivanov[3,4], Steffen N. Krieger[3], Robert Turner[3], and Harald E. Moeller[1]

[1]*NMR-Unit, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany,* [2]*Physiology of Cognitive Processes, Max Planck Institute for Biological Cybernetics, Tübingen, Germany,* [3]*Neurophysics, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany,* [4]*Cognitive and Clinical Neuroscience, Maastricht University, Maastricht, Netherlands*

Target audience: sequence developers, neuro-vascular-coupling researchers, fMRI researchers (preclinical and human applications), researchers interested in brain physiology and hemodynamics

Purpose: The negative blood oxygenation level dependent (BOLD) response (NBR) is less studied than the positive BOLD response (PBR), and little is known about the underlying mechanisms. Studying non-human primates, Goense et al.[1] have recently shown cerebral blood volume (CBV) increases in the deeper cortical layers of areas with decreased BOLD signal, neural activity and blood flow. At first glance, these results seem to contradict the universal validity of the Grubb relationship, and disagree with earlier studies of NBR in cats and rats, suggesting that more research is necessary. This study aims to clarify the role of CBV changes in the NBR regions for the first time in humans at high resolution, and to investigate additional features such as temporal dynamics, oxygenation and spatial characteristics.

Methods: A recently developed, slab-selective, BOLD-corrected, CBV-sensitive Vascular Space Occupancy (VASO) variant[2] was implemented on a Siemens 7T MRI scanner. This method utilized the different steady-state behavior of the magnetization of stationary tissue and flowing blood to increase VASO SNR. Interleaved BOLD images were used both to define regions of NBR and to correct the BOLD contamination in VASO. To enable determination of T_2*, a multi-echo EPI readout was implemented. Parenchymal T_2* was compared during stimulation and rest while blood is nulled and while blood is not nulled. This was used to estimate the T_2* and corresponding oxygenation level of the blood compartment that changes its volume. To circumvent inflow of fresh (non-inverted) blood magnetization into the microvasculature of the imaging slice, which can be problematic in VASO at 7T, we reduced the inversion efficiency of the inversion pulse so that the blood nulling time of the VASO sequence was shorter than the arterial arrival time. In order to achieve proper inversion despite B_1-inhomogeneities and SAR constraints, an adiabatic partial inversion pulse was designed and implemented. Sequence parameters were: TE1/TE2/TE3/TI/TR=12/32/52/1000/1500 ms, nominal voxel size =1.5mm isotropic. A 12-min visual paradigm (alternating 30s rest vs. 30s stimulation) was used to obtain positive and negative BOLD response in the visual cortex of six volunteers. It consisted of a flickering or rotating checkerboard pattern (Fig. 1). Anatomical reference T_1-maps were obtained using measurements using multiple TI with the same EPI scan.



Results: Significant positive and negative VASO signal change was detected in all subjects for both stimulation paradigms used (images of two subjects with a flickering stimulus are shown in Fig. 2a after smoothing with a 1mm kernel). Signal time courses averaged over all subjects of all voxels in ROIs of PBR show strong VASO signal decrease, corresponding to CBV increase of 18%±4%. Signal time courses of voxels in ROIs of NBR show a smaller VASO signal increase, corresponding to a CBV decrease of 7%±4% (Fig. 3). The temporal characteristics of positive and negative VASO signal changes are comparable in ROIs with PBR and NBR. The relatively high resolution enables distinction of cortical surface voxels from voxels within deeper layers, based on the partial volume fraction of CSF (Fig. 2b). Surface voxels in ROIs with NBR show a strong CBV decrease, while deeper layers contain also many voxels with a small CBV increase. In NBR ROIs, the average partial volume of CSF was 22%±5% and 1%±4% for voxels with CBV decreases and increases, respectively. Based on the multi-echo readout, the CBV increase in PBR ROIs was estimated to arise mainly from a blood compartment with T_2* > 20ms, suggesting that it contains blood with a mean oxygenation level above 80%[3].

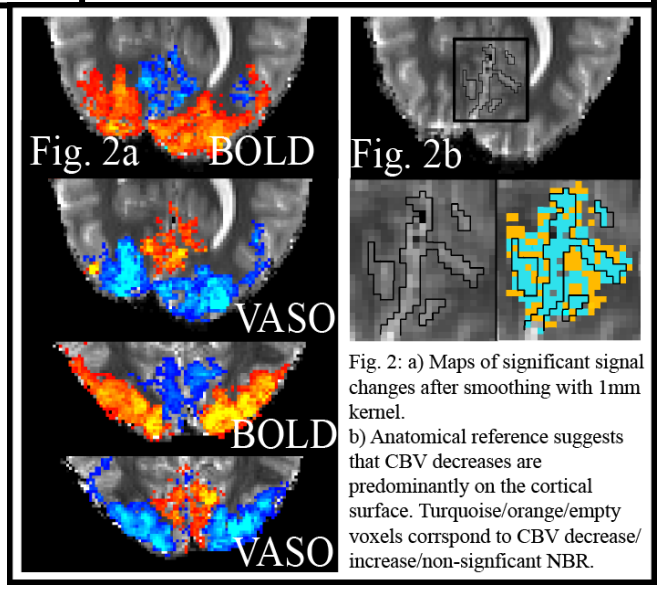


Fig. 2: a) Maps of significant signal changes after smoothing with 1mm kernel.
b) Anatomical reference suggests that CBV decreases are predominantly on the cortical surface. Turquoise/orange/empty voxels corrspond to CBV decrease/ increase/non-signficant NBR.

Discussion: Our results suggests that the CBV increase in areas with NBR occurs predominantly in surface voxels, while in PBR ROIs, CBV increases mostly occur in voxels deeper in the cortex[2]. This seems consistent with results from Goense et al.[1], which show that the CBV increase in ROIs of NBR occurs mainly in deeper layers of the cortex, while surface layers tended to have a CBV decrease. However, CBV studies using iron-based contrast agents are most sensitive to smaller vessels, since the magnetization in and near large superficial vessels is lost due to dephasing, while VASO captures CBV changes in both vessel types. Hence, the two methods might report on changes in different vascular compartments.

Conclusion: Slab-selective, BOLD-corrected VASO with partial inversion provides sufficient tSNR to investigate the vasculature dynamics in ROIs of NBR. CBV decreases in surface layers dominated the total ROIs and are larger than CBV increases in deeper layers of the cortex.

References:

1. Goense J, et al., High-resolution fMRI reveals laminar differences in neurovascular coupling between positive and negative BOLD responses. Neuron, in press

2. Huber L, et al., Slab-Selective, BOLD-Corrected VASO (SS-VASO) in Human Brain at 7T. Proc. ISMRM, 2012:331

3. Ivanov D, et al., In vivo estimation of T_2* dependence of blood on oxygenation at 7T. Proc. OHBM, 2012:987