MEASURING CHANGES IN ARTERIAL AND VENOUS CEREBRAL BLOOD VOLUME IN HUMAN BRAIN AT 7T

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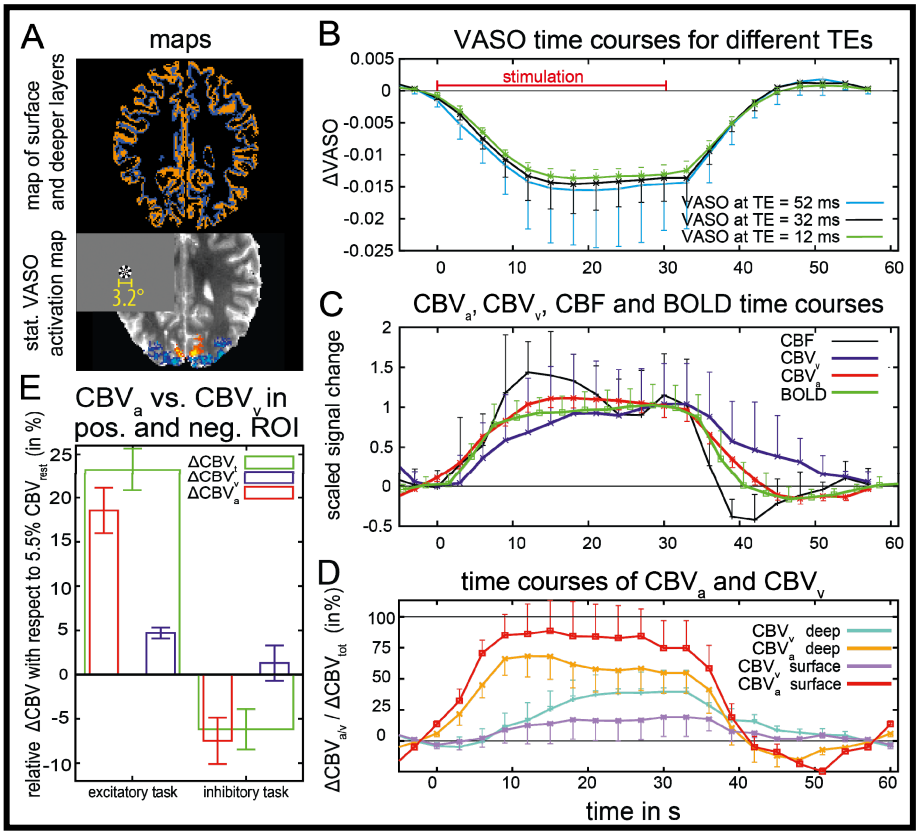
Target audience: neuro-vascular coupling researchers, fMRI researchers (preclinical and human applications), researchers interested in brain physiology and hemodynamics. Developers of fMRI pulse sequences.

Purpose: The interplay of functional changes in cerebral blood flow (CBF), cerebral blood volume (CBV), and blood oxygenation level dependent (BOLD) signal and their underlying neurovascular origin is an important focus of current research. Of particular interest are phenomena such as negative BOLD signal, BOLD sensitivity across cortical profile, and temporal features (e.g. the post-stimulus undershoot). The purpose of this study was to develop a method that can simultaneously and non-invasively elucidate the functional dynamics of the arterial and venous vasculature in human brain. Furthermore, comparisons of arterial and venous CBV with CBF and BOLD responses were used to shed new light on the various phenomena mentioned above.

Methods: A multi-echo slice-saturation, slab-inversion VASO sequence [1] was used to obtain interleaved measurements acquired with blood nulling (bn) and without blood nulling (wbn) at three echo times (TE = 12, 32 and 52 ms). Further experimental parameters were: TR/TI1/TI2 = 3/1/2.5 s, nominal resolution (1.3 mm)^3, 12 blocks of 30s rest and 30 s stimulation with a small flickering checkerboard (Fig. A), N = 17 subjects. T_1 maps, acquired with the same read-out, were used to distinguish between surface vessels and tissue vessels (Fig. A). CBF measurements were acquired with FAIR-QUIPSSII, a nominal resolution of (3 mm)^3 and the same stimulation paradigm (N = 7). BOLD correction of VASO images was done with dynamic division of consecutive time steps with and without blood nulling. The division of these two contrasts is sensitive to the CBV that is nulled in the bn-VASO-images but not nulled in wbn-BOLD-images [1]. At the shortest TE, this method measures both arterial and venous CBV changes. At longer TE, the signal intensity of arterial and venous blood is weighted differently, depending on its oxygenation and the corresponding T_2^*. Fig. B depicts how the time course of BOLD-corrected VASO signal depends on the relative contribution of arterial and venous CBV and their slightly different dynamics (e.g. green line is slightly delayed). Using literature values of arterial and venous T_2^* [2] in a three-compartment model, the measured TE-dependence allowed the isolation of venous and arterial CBV contributions.



Results: Timecourses of CBF, BOLD signal and arterial and venous CBV of regions with positive BOLD response are shown in Fig. C. Venous CBV change is delayed and slower than the arterial CBV change. The relative contributions between arterial and venous CBV changes are 78% and 22%, respectively. The CBF time course is noisier and crosses the baseline even earlier than arterial CBV. Figure D illustrates that the reactive vessels are filled with more oxygenated blood in voxels containing upper layers and pial vasculature, compared to deeper voxels. This is consistent with the fact that the vessels release oxygen as they penetrate the cortex from surface to deeper layers. Vasoconstriction in ROIs of NBR occurs in arterial vessels only (Fig. E). This is consistent with the faster response (post-stimulus baseline crossing) in inhibited ROIs compared to positive ROIs as previously reported [3].

Discussion: Neurovascular features previously accessible only in animals can now be investigated in humans. The relative contributions and functional dynamics of arterial and venous vessels can be accounted for using functional principles relating to actively- and passively-controlled vascular compartments, respectively, that have been established in animal studies (review in [4]).

Conclusion: We have shown that the method proposed can be used to simultaneously and noninvasively investigate arterial and venous responses individually. The data suggest that the relationship between vascular responses (CBV_a, CBV_v, CBF) and BOLD signal differs between excited and inhibited regions, as well as between voxels containing superficial and deeper cortical layers, thus resulting in variable temporal dynamics.

References: **1**. Huber, et al., MRM, 2013. **2**. Ivanov, et al., Proc. ISMRM, 2013. **3**. Goense et al., Neuron 2012. **4**. Kim et al., JCBFM 2012.