Hypercapnia-Induced and Stimulus-Induced Changes in Cerebral Blood Volume (CBV) in Human at 7T

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Introduction: Hypercapnia is believed to induce changes of cerebral blood supply without significant alterations in metabolism. A large number of studies have investigated the relationship between cerebral blood flow (CBF) and blood oxygen level dependent (BOLD) signal. However, the dynamics of CBV during hypercapnia and its connection to BOLD have not been fully investigated. The understanding of the CBV-BOLD relationship during hypercapnia and during stimulation has important implications on calibrated BOLD methods [1]. A novel slab-selective, BOLD-corrected VAscular Space Occupancy (VASO) [2] variant with partial inversion has been developed to compare changes in CBV in humans induced by visual stimulation and hypercapnia. The slab-selective, BOLD-corrected VASO [3] uses a slab-selective gradient to increase SNR [4], but without contamination of CBF and BOLD. With this high SNR sequence unprecedented VASO 1.5mm isotropic resolution can be achieved. Due to relatively long blood T_1 at high field strengths, the blood-nulling-time can become larger than the time the blood needs to flow from the neck (outside of the head coil) into the micro vessels of the cortex. The tremendous decrease of arterial arrival time during hypercapnia [5] can therefore result in the inflow of fresh (not-inverted) blood into the microvessels during the blood-nulling-time TI. In order to decrease the blood-nulling-time we developed a novel VASO variant with partial adiabatic inversion. Here we present results using this VASO variant in human brain at 7T during hypercapnia and a visual task.

Fig. 1 Sequence diagram and corresponding steady-state z-magnetization in the slab-selective, BOLD-corrected VASO sequence with partial inversion

Methods: The slab-selective, BOLD-corrected pulse sequence with partial inversion was implemented on a Siemens 7T MRI scanner. Sequence diagram and corresponding magnetization are depicted in Fig. 1. Scan parameters were: nominal voxel size = 1.5mm isotropic, TE/TR=19/1500ms, inversion efficiencies were 75%, 86% and 100% with corresponding blood-nulling-times TI=1328/1123/765ms. Functional data were acquired with 2D multi-slice single-shot GRE EPI without slice gaps. A tr-FOCI pulse [6] was implemented to achieve proper slab-selective inversion despite B_1 inhomogeneities and SAR constraints. The pulse was adapted in order to achieve an inversion efficiency of 100%, 86% and 75% in a B_1 independent way. A phase skip of B_1 was introduced during the inversion at the time when the frequency of the adiabatic pulse was exactly on resonance. This opens the "cone of precession" of the magnetization that precesses around the effective magnetic field during inversion. A 10 min. flashing checkerboard (30s rest vs. 30s stimulation) was used to activate the visual cortex of four subjects. The hypercapnia task consisted of 2min/5min/5min breathing air/5%CO_2/air. The heart rate and respiratory gas composition were recorded with a BIOPAC MP150 unit (BIOPAC Systems Inc, USA). Activated visual areas were defined by a statistical analysis with a z-threshold of 2.3 and a cluster significance threshold of p=0.05 (FEAT ver. 5.98) without spatial smoothing. A grey matter map was generated, to account for voxels only
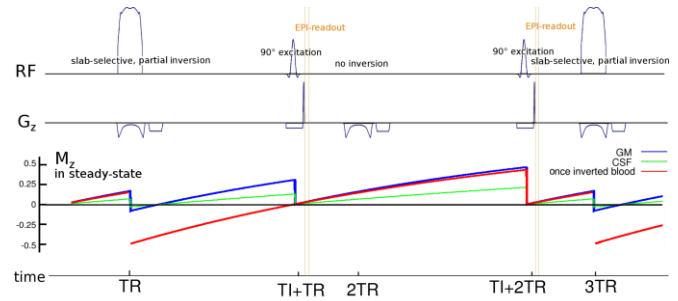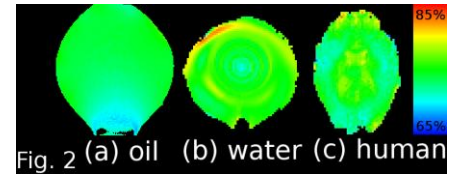

Fig. 2 (a) oil (b) water (c) human

GM map

Fig. 3

0% — 60% ΔCBV vis. stim.

0% — 7% ΔBOLD vis. stim.

0% — 5% ΔVASO hypercap.

0% — 10% ΔBOLD hypercap.

Fig. 4 BOLD and VASO time courses

5% CO_2

partially filled with grey matter. To compute ΔCBV from ΔVASO, CBV_{rest}=5.5 vol% blood within the GM portion [7] was assumed.

Results and Discussion: Fig. 2 depicts inversion efficiency maps for a desired inversion efficiency of 75%. Even in the water phantom, the partial inversion efficiency is insensitive to B_1, despite the fact that B_1 varies between 8µT and 50µT. Subtle remaining variations in inversion efficiency might result from B_0 dependency. Fig. 3 summarizes the spatial distributions of VASO and BOLD signal changes in one subject with TI=765 ms where no fresh blood has yet entered into the microvessels. CBV changes during visual stimulation are localized in the grey matter. Large VASO signal changes during hypercapnia can be found throughout grey mater. Dark regions in this map are associated with signal increase during hypercapnia and might correspond to large vessels with inflow of fresh (not-inverted) blood during the TI. White matter shows small but significant VASO signal decrease. The CNR for VASO is approximately half of the CNR for BOLD. Fig. 4 shows time-courses of BOLD and VASO for different blood-nulling-times. Due to inflow of not-inverted blood into the microvessels, VASO signal decrease during hypercapnia appears smaller (blue and red line). Here we circumvent this effect with partial inversion that is associated with shorter blood-nulling-times. Different temporal evolution might result from varying blood partial pressure of $CO_2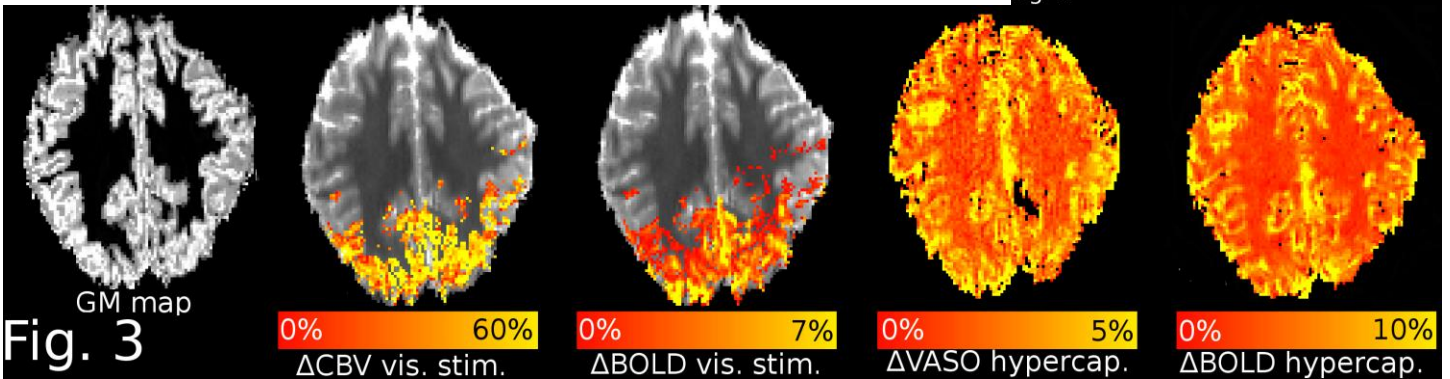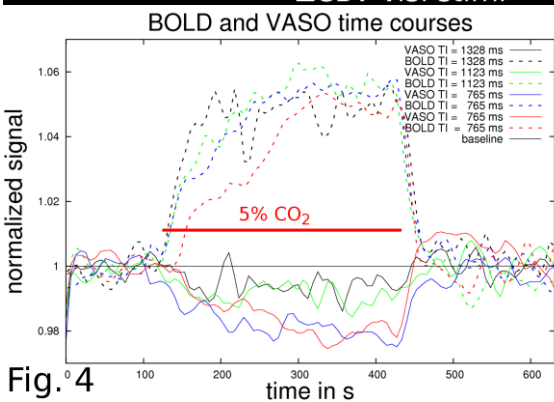$ due to the specific breathing patterns of the subjects. Tab. 1 shows the relative changes of CBV and BOLD signal during hypercapnia and during stimulation in the visual areas. BOLD signal increase is significantly larger during hypercapnia compared to visual stimulation in contrast to ΔCBV. This indicates that the larger ΔBOLD during hypercapnia compared to visual stimulation results from smaller $CMRO_2$ during hypercapnia [8]. The amount of ΔCBV during stimulation is consistent with previous VASO studies [2,9], but is higher than microscopy studies suggest [10]. In the slab-selective approach the grey matter signal is smaller compared to CSF (see Fig.1). This attenuates partial volume effects of CSF regardless of the vasodilatation mechanism [11] that can be a problem in VASO [12].

Conclusion: The decrease in arterial arrival time during hypercapnia can hamper VASO at high field strengths. ΔCBV maps of high sensitivity can be achieved without the effect of inflowing fresh blood by using shorter blood-nulling times. Slab-selective, BOLD-corrected VASO with partial inversion efficiency might be a useful tool to investigate the precise relationship of ΔCBV and ΔBOLD with high resolution during hypercapnia.

Tab. 1

ΔCBV hypercap.	ΔBOLD hypercap.	ΔCBVstim.	ΔBOLD stim.
49±4%	3.6±0.2%	44±4%	2.2±0.2%

References: [1] Davis, TL., et al, 1998, PNAS; [2] Lu, H, et al., 2003, MRM; [3] Huber, L, et al., Proc. ESMRMB; [4] Jin, T, et al., 2008 NeuroImage; [5] Ho, YL., et al., 2011, JCBFM; [6] Hurley, AC., et al., 2010, MRM; [7] Lu, H, et al., 2005, MRM; [8] Hoge, RD., et al., 1999, MRM; [9] Yan, L., et al., 2011, MRM; [10] Tian, P., et al., 2010, PNAS; [11] Piechnik, SK., et al., 2009, MRM; [12] Donahue, MJ., et al., 2006, MRM