Cerebral Blood Volume Decreases Demonstrated during Breath Hold with Vascular Space Occupancy (VASO) and VASO-FLAIR fMRI

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Introduction. Sustained negative functional MRI (fMRI) responses in selected brain regions surrounding areas of increased fMRI signal have been observed in both CBF (1) and blood-oxygenation-level-dependent (BOLD) studies (2). While much work has focused on understanding positive relationships between CBF, BOLD and neuronal activity, negative responses remain poorly characterized. Negative responses could represent a "steal" phenomenon where blood is redistributed to the more CBF-demanding regions in the brain (3), possibly related to a suppression of neuronal activity (4). Here, using vascular space occupancy (VASO)-fMRI (5), we provide experimental evidence for a possible steal phenomenon by demonstrating robust decreases in CBV surrounding regions of increased CBV during a breath hold task.

Methods. VASO is a recently developed inversion recovery blood nulling technique which is sensitivite to changes in CBV (5). In addition, VASO-FLAIR (6), which utilizes a second inversion pulse to null blood and CSF signal, has recently been proposed as a method for measuring CBV changes independent of CSF. Since CBV changes are often localized to parenchyma in border regions with CSF, VASO-FLAIR is helpful in discriminating CBV changes from minor CSF fluctuations. Here, VASO and VASO-FLAIR-fMRI consisting of four blocks of 52s normal breathing, 4s exhalation, and 14s breath hold were performed on healthy volunteers (n=10) at 3T. Data were corrected for motion and baseline drift, after which voxels meeting activation criteria for vasodilation (cc<-0.15) and vasoconstriction (cc>+0.15) were analyzed. Additional criteria: cluster size>5 and SNR>20. Imaging parameters were FOV=240 mm, imaging matrix=80x80, slice thickness=3 mm, SENSE=2.5, gradient echo, single-shot EPI (TE=15 ms).

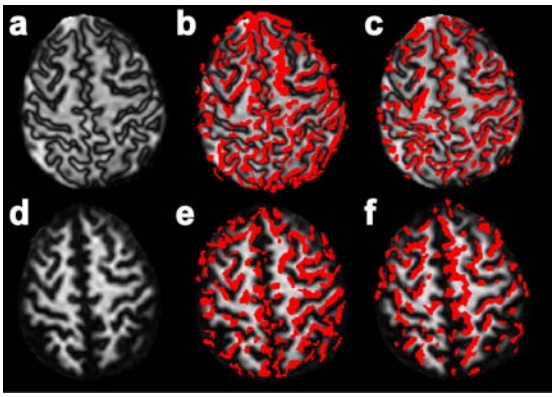
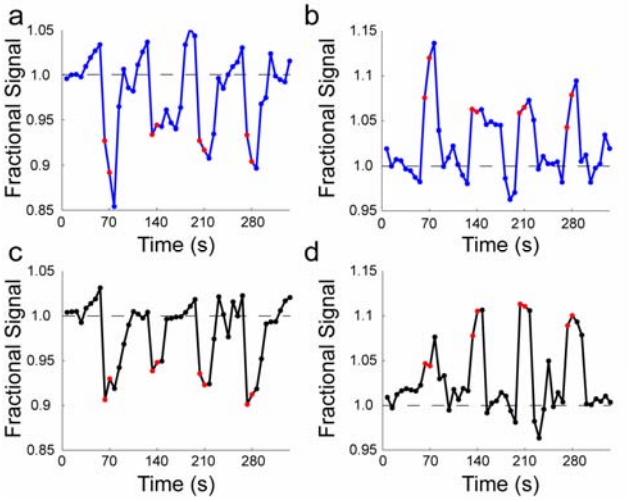


Fig. 1. VASO image (a) with overlaid vasodilating (b) and vasoconstricting (c) voxels from breath hold paradigm. VASO-FLAIR image (d) with overlaid vasodilating (e) and vasoconstricting voxels (f). Notice the robust regions of surrounding vasoconstriction in both scans. Gradient echo, SS-EPI, FOV=240, imaging matrix=80x80, TR/TE=7/0.015s.

Results. Fig. 1 shows the VASO image (a) as well as overlaid voxels corresponding to vasodilation (b) and vasoconstriction (c) for a typical subject. In addition, the VASO-FLAIR image (d) shows a clear nulling of CSF signal with similar activation maps for vasodilation (e) and vasoconstriction (f) as was found in VASO. There were substantial areas of vasoconstriction surrounding the regions of vasodilation in both VASO and VASO-FLAIR. The corresponding hemodynamic time courses are shown in Fig. 2.

Discussion. While vasodilation is a well characterized correlate of gray matter activation in VASO and VASO-FLAIR scans, it is clear that vasoconstriction occurs in large areas of peri-activation tissue. The corresponding hemodynamic time courses also tend to have comparable absolute magnitude and similar slope. The physiological interpretation of this robust effect is not obvious, but several hypotheses are possible. For instance, using combined electrophysiological and BOLD data on monkeys, Logothetis et al. have recently demonstrated that a negative BOLD response, which surrounds regions of increased BOLD response, correlates temporally and spatially with decreases in neuronal activity. A decreased BOLD response could reflect changes in $CMRO_2$ which outweigh changes in CBF, as has been shown to be the case in some functional studies (7). Moreover, it has recently been demonstrated by Mulligan et al. (8) that vasoconstriction of arterioles can be regulated locally by Ca^{2+} which propagates into the endfeet of astrocytes. Therefore, it is possible that blood flow is redirected through constriction of an arterial branch away from regions of decreased neuronal activity into regions of increased neuronal activity. This occurrence has already been suggested in rodents (9) and would indicate that hemodynamic regulation is locally very intricate. In summary, using CBV-sensitive VASO and VASO-FLAIR-fMRI, we provide experimental evidence for CBV reduction surrounding areas of activation. Based on these initial results, we believe that VASO may help elucidate cerebral blood flow redistributive phenomena in health and disease.



References. **1.** Shulman, et al. J. Cogn. Neurosci. 9,648-663(1997). **2.** Logothetis, et al. Phil. Trans. R. Soc. Lond. B 357, 1003-1037(2002). **3.** Harel et al. JCBFM. 22,908-917 (2002). **4.** Shmuel et al. Nature Neuroscience. 9,569-577 (2006). **5.** Lu et al. MRM. 2003Aug;50(2):263-74. **6.** Donahue et al. MRM. 2006 Oct 30; [Epub]. **7.** Lu et al. JCBFM. 2004 Jul;24(7):764-70; **8.** Mulligan et al. Nature 431;195-199 (2004). **9.** Woolsey T. et al. Cereb Cortex 6:647-660 (1996). Funding: NCRR RR15241, NIBIB EB004130, Philips Medical systems.

Fig. 2. Negative signal changes (a) corresponding to vasodilation and positive signal changes (b) corresponding to vasoconstriction for VASO activation maps (Fig. 1b,1c). Negative (c) and positive (d) signal changes for VASO-FLAIR activation maps (Fig. 1e,1f) are shown below in black. Red=breath hold period.