VASO ACDC with Applications to BOLD Calibration

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Introduction: The goal of the *Va*scular *S*pace *O*ccupancy (VASO) imaging technique is to use selective nulling of the blood signal to infer relative changes in cerebral blood volume (CBV) [1]. Recent work has shown that changes in the local CSF fraction (x_c) with activation can significantly impact the VASO signal, thereby limiting our ability to infer ΔCBV from ΔVASO alone [2]. Here we present a method of incorporating both resting CSF fraction, $x_{c,rest}$, and the change in CSF fraction with activation, Δx_c, into VASO-based calculations of relative CBV change. This technique of *Ac*counting for *D*ynamic *C*SF (ACDC) is applied across the whole brain during a breath-holding task, providing results consistent with gold-standard PET data obtained during hypercapnia. CBV measurements obtained using VASO ACDC are used for calibration of the BOLD signal across the whole brain, offering a promising alternative to calibration using CBF data, the latter of which is limited by complexities associated with the implementation of multi-slice ASL.

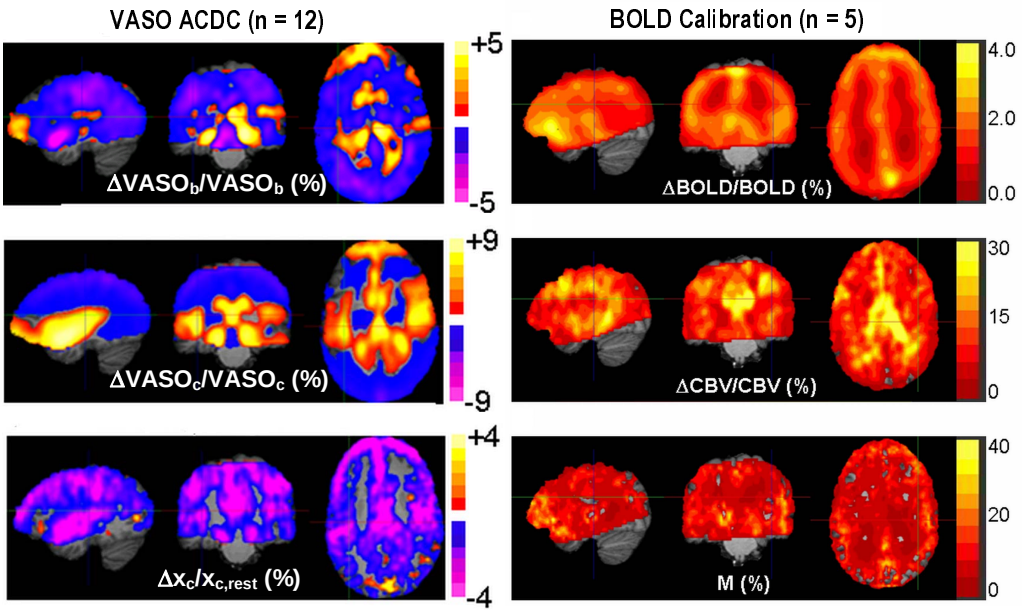
Methods:

Theory: We have previously shown that a VASO acquisition in which CSF is nulled instead of blood may provide additional information about local changes in x_c with activation [2]. Let us define $VASO_b$ and $VASO_c$ respectively as the blood-nulled and CSF-nulled VASO signals. $\Delta VASO_{b,c}$ depends on Δx_c, ΔCBV, $x_{c,rest}$, CBV_{rest}, and $M_{b,c}(TI_{b,c})/M_t(TI_{b,c})$ where $M_{b,c}$ is the longitudinal magnetization of blood or CSF relative to that of tissue (M_t) at the time of acquisition, TI (which differs for $VASO_b$ and $VASO_c$ acquisitions). For MAGIC (*M*ultiple *A*cquisitions with *G*lobal *I*nversion *C*ycling) [3], the $M_{b,c}/M_t$ ratios are determined for each slice from simulations, while tissue type (t = GM or WM) is assigned by segmentation of a high resolution anatomic image. $x_{c,rest}$ can be calculated from a normalized T_2-weighted TSE acquisition [4], and local CBV_{rest} values may be taken from the literature. Acquisition of $\Delta VASO_b$ and $\Delta VASO_c$ will produce 2 equations and 2 unknowns, allowing the calculation of $\Delta x_c/x_{c,rest}$ and $\Delta CBV/CBV_{rest}$ for each voxel [5]. BOLD signal calibration can be achieved by manipulating blood flow independently of $CMRO_2$, for example via hypercapnia, and using the measured vascular and BOLD responses to calculate a calibration factor, M, which may then be used in subsequent functional experiments to calculate $\Delta CMRO_2$ [6, 7]. The vascular response is generally gauged by CBF measurements obtained from *A*rterial *S*pin *L*abeling (ASL), while assuming a constant relationship between changes in CBV and CBF [8], but alternatively could be done using CBV data acquired from VASO ACDC.

Experiment: Hypercapnia was induced using a paradigm consisting of 21 s blocks of breath-holding following inspiration, alternating with 27 s blocks of self-paced breathing, repeated 5 times per run. All acquisitions were performed on a Siemens 3.0 Tesla Trio Scanner with the following parameters for MAGIC $VASO_{b,c}$: 21 axial slices (3 per global inversion) with 3.5 x 3.5 x 4 mm^3 voxels, TE = 8.8 ms, TR = 3 s, TI_b = 752 ms and TI_c = 973 ms. TSE (TE = 116 ms) and 3D-MPRAGE acquisitions were performed for each subject to obtain $x_{c,rest}$, and GM/WM segmentation, respectively. A map of CBV_{rest} was taken from previously acquired PET data [9]. ΔCBV and Δx_c were calculated on a voxel-wise basis using VASO ACDC in 12 subjects. In addition, GE-EPI BOLD images with TE = 47 ms were acquired in a subset of 5 subjects with identical slice positioning, resolution, and TR as MAGIC VASO. BOLD calibration was performed separately for each of these subjects using the co-registered BOLD and CBV data.

Results: The $VASO_b$ and $VASO_c$ equations were solved simultaneously for ΔCBV and Δx_c using a least squares optimization. The mean percent signal change maps are shown below for $VASO_b$, $VASO_c$, Δx_c. By incorporating the seemingly small changes in CSF into our calculations, CBV changes are found to be in much better agreement with the literature than VASO-based calculations which do not account for CSF change. For example, by including the impact of the 2.7% decrease in CSF fraction in the superior cortical region, we obtain $\Delta CBV/CBV_{rest}$ = 10.4%, in contrast to the value of 0.7% calculated when assuming $\Delta x_c = 0$. These CBV changes are consistent with those reported previously using PET [10, 11]. The results of the BOLD calibration using hypercapnia are also in good agreement with the literature. A comparison of M across different VOIs located in the motor, visual, and auditory cortices indicates similar calibration factors, ranging from M = 9 – 13%, which is consistent with previous results in the visual cortex [12, 13] and motor cortex [12, 14].

Discussion and Conclusion: Given the proximity of CSF to the cortical surface and its similar viscosity to water, it is highly likely that CSF will redistribute in response to local blood vessel dilatation. When using VASO solution methods that employ the constraint $\Delta x_c = 0$, the mean $\Delta CBV/CBV_{rest}$ values are significantly lower than those for which the CSF fraction is permitted to change with activation and they do not compare as well to the previous literature. These findings suggest that $VASO_b$ imaging alone is not sufficient to infer ΔCBV; Δx_c must also be considered. BOLD calibration using VASO ACDC rather than ASL may be advantageous since it does not require slice-specific corrections for transit delay times. This remains a limitation of calibrations reliant upon multi-slice ASL, which has generally been implemented using ≤5 slices, which is insufficient for whole-brain coverage [6, 7].



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