Vascular Autocalibration of fMRI (VasA fMRI) Improves Sensitivity of Population Studies

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TARGET AUDIENCE: Those interested in functional MRI group studies.

PURPOSE: The BOLD signal is widely used for fMRI of brain function in health and disease. Statistical power of fMRI group studies is significantly hampered by high inter-subject variance, which arises from differences in baseline physiology (such as blood volume). Several methods have been proposed to account for physiological vascularization differences between subjects and hence improve the sensitivity in group studies. However, those methods require the acquisition of lengthy reference scans (such as resting-state fMRI). We present a novel vascular autocalibration (VasA) method which reduces inter-individual variation and does not require any additional reference scans. VasA fMRI is based on the observation that slow oscillations (< 0.1 Hz) in arterial blood CO_2 levels occur naturally due to changes in respiration patterns. These oscillations yield fMRI signal changes whose amplitudes reflect blood oxygenation levels and underlying local vascularization (such as the blood volume). VasA uses the amplitude of these CO_2-driven oscillations to normalize the amplitude of task-related fMRI responses, in order to account for vascular differences between subjects. VasA extracts the CO_2-driven fluctuations directly from task-related fMRI data instead of separate reference scans. VasA fMRI is validated successfully using two databases containing a wide variety of tasks with a total of 138 subjects.

METHODS: We used data from two different databases to assess the performance of VasA fMRI. The Human Connectome Project (HCP) pre-processed dataset included resting-state and task-based fMRI (rsfMRI/tfMRI) datasets for each participant (n=80; details in [1]). The Predicting Language Outcome and Recovery After Stroke (PLORAS) dataset (details in [2]) included tfMRI data only (n=58). Statistical analyses of the functional images were performed in two steps in SPM12b. Each subject's pre-processed tfMRI time-series was fitted voxel-wise using the respective GLM describing the task. Regressors were convolved with a canonical hemodynamic response function. We used the residuals of the model fit, i.e., the differences between the spatially unsmoothed tfMRI time series data and the GLM prediction to estimate the VasA low frequency fluctuation maps in an analogous way to ALFF estimation [3]. The averaged square root of the power of the residuals within the frequency band of 0.01-0.08 Hz was calculated for each voxel. The resulting low frequency fluctuation maps were smoothed with a Gaussian kernel with 4 mm FWHM. At the single-subject (first) level a contrast image describing the activation in each task was created and smoothed using 4 mm FWHM. The contrast image was then either not calibrated (standard approach) or calibrated, i.e., the voxel-wise contrast estimate was divided by the low frequency fluctuation maps. The standard or calibrated contrasts were then entered into a second-level analysis to enable inferences at the group level, resulting in statistical t-score maps at the group level ($p < 0.05$, FWE for multiple comparisons). The t-scores (for the positive contrast) from VasA fMRI were plotted against the t-scores from standard analysis for all activated voxels. The percentage change in t-score was computed as the slope in the linear regression between the t-scores from VasA fMRI and those from the standard analysis for all activated voxels.

RESULTS: VasA fMRI increased the functional sensitivity substantially for different experiments and data acquisition schemes (examples shown in Figs.1-2). On average the mean t-score increase across all activated brain areas was approximately 10% but it reached up to 21% for particular brain regions. Fig. 1 shows an example of a group-level t-score map (n=80) for a relational processing task from the HCP data analysed with the standard and with the VasA approach. In general, VasA fMRI increased the spatial extent of activations and t-score values across the entire brain. In some areas the increases relative to the standard analysis exceeded 30%, such as in the visual cortex (Fig. 2). Those increases were achieved for different types of datasets, i.e. the increased sensitivity afforded by VasA fMRI was independent of task and data acquisition.

CONCLUSIONS: VasA increased t-scores by up to 30% in specific brain areas and on average by 10% areas across the brain while still controlling the nominal false positive rate. VasA fMRI can be readily applied to any task-related fMRI dataset, even retrospectively irrespective of task or acquisition protocol. It does not require time-consuming reference scans or complicated procedures. The principled correction method is derived from basic BOLD physiology models. It, therefore, can be used to improve sensitivity and reduce scanning time and stress for patients/participants.

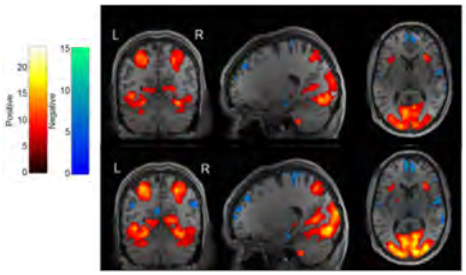

Fig. 1: Group level activation maps ($p < 0.05$, family-wise error corrected for multiple comparisons [FWE]) for a relational processing task (contrast: relational processing task versus baseline) using the standard analysis (a) and VasA fMRI (b).

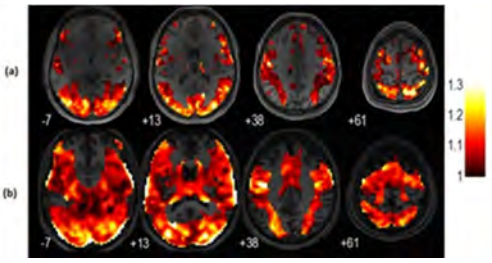

Fig. 2: Average functional sensitivity improvement factor using VasA for all brain areas that were tested using all available tfMRI data from the HCP (19 contrasts) (a) and PLORAS data (14 contrasts) (b). Sensitivity increases exceeded 30% in several brain areas and were consistent across the different datasets.

REFERENCES:

1. Barch, D. M. *et al.* NeuroImage **80**, 169-189, 2013.
2. Hope, T. M. H. *et al* Frontiers in human neuroscience ***8***, 2014.
3. Zang, Y. F. *et al.* Brain & development **29**, 83-91, 2007.

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