CBV-Based Resting-State fMRI: Detecting Intrinsic Brain Activity Using Whole Brain 3D-VASO Imaging

Xinyuan Miao[1], Hong Gu[2], Lirong Yan[3], Hanzhang Lu[4], Danny JJ Wang[3], Xiaohong Joe Zhou[5], Yan Zhuo[1], and Yihong Yang[2]

[1]*Institute of Biophysics, Chinese Academy of Sciences, Beijing, Beijing, China,* [2]*National Institutes of Health, National Institute on Drug Abuse, MD, United States,* [3]*Department of Neurology, UCLA, Los Angeles, CA, United States,* [4]*University of Texas Southwestern Medical Center, Dallas, TX, United States,* [5]*Center for Magnetic Resonance Research and Department of Radiology, University of Illinois at Chicago, Chicago, IL, United States*

Introduction

Intrinsic brain activities have been implicated in various brain functions, and alterations of these activities may result in neurological and psychiatric disorders[1, 2]. The majority of current knowledge about intrinsic brain activities has been acquired from resting-state BOLD imaging studies, although BOLD signal represents the combined effects of cerebral blood volume, flow and metabolism (CBV, CBF and $CMRO_2$) and therefore is difficult to interpret[3]. Furthermore, BOLD signal has relatively poor spatial localization, compared to CBV and CBF[4, 5]. As such, imaging methods based on a CBV or CBF contrast may overcome the drawbacks of BOLD. In this study, we demonstrate that intrinsic brain activity can be reliably detected by spontaneous fluctuations of CBV-weighted signal using whole-brain gradient and spin echo (GRASE) based vascular space occupancy (VASO) imaging. We further investigated frequency characteristics and susceptibility artifacts of VASO signal, compared to BOLD.

Methods

Image acquisition. VASO and BOLD resting-state data of 18 healthy participants (9 males; mean age 22.8±1.8 yrs) were collected. The acquisition parameters of the 3D-GRASE VASO sequence were: matrix size = 64×64×22 with 2 additional slices for oversampling, FOV = 220×220×110 mm^3, TR/TE/TI=2500/14.6/742 ms, GRAPPA factor along ky = 3, partial Fourier along kz = 6/8, and total acquisition time was 8 min and 30 s. For comparison, a gradient-echo EPI sequence was used for BOLD imaging acquisition, with most acquisition parameters the same as the VASO.

Image processing/analysis. The preprocessing included slice-timing correction, realignment, spatial normalization, spatial smoothing (FWHM = 6 mm), quadratic detrending, and grand-mean scaling. To identify resting functional networks, a group independent component analysis (gICA) was applied to both VASO and BOLD resting data, using the MELODIC in the FSL. The number of components was set at 30. All ICA maps were converted to z maps and thresholded at $z > 3.0$.

Frequency analysis. Frequency spectra of the posterior cingulate cortex were obtained from the BOLD and VASO data respectively. The amplitudes of low-frequency fluctuations (ALFF)[6], which quantifies the strength of fluctuations, of the VASO and BOLD signals were analyzed in three different frequency bands: B1 (0.001-0.01 Hz), B2 (0.01-0.08 Hz) and B3 (0.08-0.15 Hz). A one-way ANOVA analysis was used to identify the main effects of the frequency bands in the ALFF maps of VASO and BOLD, respectively.

Susceptibility analysis. The 3D-GRASE VASO sequence is intrinsically spin-echo weighted with a short TE, rather than T_2* weighted, so that it is expected to suffer less of susceptibility artifacts than gradient-echo EPI. We investigated the functional connectivity of superior and inferior ventral striatum (VSs and VSi), which are known to have connections to the orbital frontal cortex (OFC), a region suffering severe signal voiding.

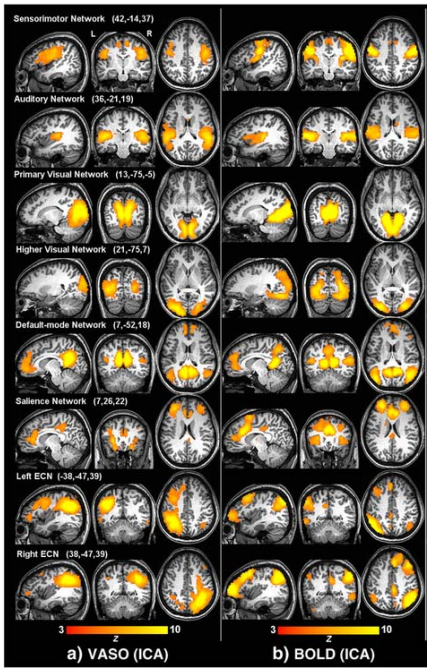

Fig.1 Brain networks detected by the independent component analysis of the VASO (a) and BOLD (b) data.

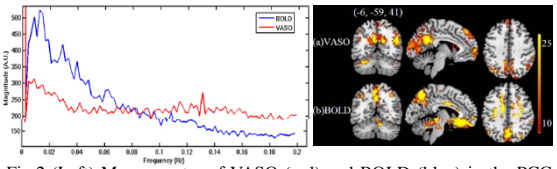

Fig.2 (Left) Mean spectra of VASO (red) and BOLD (blue) in the PCC averaged across 18 subjects; (Right) ANOVA main effects ($F > 10$) of different frequency bands (B1, B2 and B3) in the ALFF maps of VASO and BOLD.

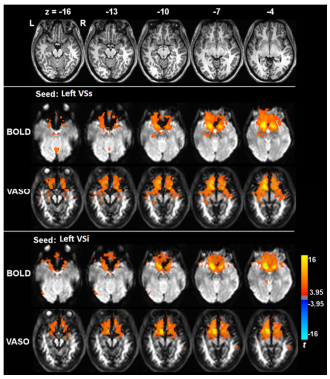

Fig.3 Functional connectivity maps with the seed ROI placed in left VSs -or VSi. ($P_{corrected} < 0.05$)

Results

The gICA identified eight meaningful resting functional networks of VASO and BOLD: sensorimotor, auditory, primary visual, higher visual, default-mode (DMN), salience (SN), left executive-control (ECN), and right ECN network, as shown in Fig.1. Spatial correlation between the VASO- and BOLD-based functional networks revealed a high degree of similarity (mean correlation of 0.45). The spectra of VASO (red) and BOLD (blue) in the PCC are shown in Fig.2 (left). The amplitude of VASO spectra decayed slowly than that of BOLD, crossing the BOLD signal at about 0.08 Hz. In the ANOVA F-maps (Fig.2, right), the main effects of the frequency bands in VASO were mostly in PCC, lateral parietal cortex, and middle and superior frontal cortex; while the main effects in BOLD were mainly in the superior PCC and orbitofrontal cortex. In the connectivity maps (Fig.3), BOLD-based connectivity maps showed little/no connectivity to the medial OFC and parahippocampal gyrus/hippocampus, while VASO-based maps still exhibited connections to these regions.

Discussion and Conclusion

We developed a noninvasive, whole-brain VASO technique for detecting intrinsic CBV-based brain activities with the spatial and temporal resolution comparable to BOLD. Initial results demonstrated that brain networks can be detected reliably by the VASO technique, including DMN, SN, ECN, visual, auditory and sensorimotor networks, similar to those often observed in BOLD. Frequency analyses showed that the VASO signal appeared to contain more high-frequency oscillations, compared to BOLD, although the underlying mechanics of the difference are unknown but warrant further investigation. Susceptibility artifacts in the OFC were substantially alleviated in the 3D-GRASE VASO, compared to the gradient-echo EPI BOLD. Functional connectivity between striatum and OFC was detected robustly by the VASO but not the BOLD. These results suggest that 3D-GRASE VASO imaging may become an attractive technique for assessing brain functions, particularly in regions that have been precluded by traditional BOLD techniques.

References: 1. Buckner RL, et al. Ann. N. Y. Acad. Sci. 1124, 1–38 (2008). **2**. Menon V. Trends Cogn. Sci., 15, 483–506 (2011). **3**. Davis TL, et al. Proc. Natl. Acad. Sci. U. S. A., 95, 1834–1839 (1998). **4**. Duong TQ, et al. Proc. Natl. Acad. Sci. U. S. A., 98, 10904–10909 (2001). **5**. Jin T and Kim SG, et al. NeuroImage, 40, 59–67 (2008). **6**. Zang YF, et al. Brain Dev 29, 83–91 (2007).**Acknowledgements**: This work was supported in part by the Ministry of Science and Technology of China grant (2012CB825500), the National Nature Science Foundation of China grant (91132302), the Chinese Academy of Sciences grants (XDB02010001, XDB02050001), and the Intramural Research Program of the National Institute on Drug Abuse (NIDA), NIH.