Understanding the Vascular Effect on Resting-State fMRI: a Multi-Modality Approach

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TARGET AUDIENCE: fMRI researchers

PURPOSE: In the last few years, the application of resting-state fMRI (1) has gained great momentum because it provides the potential to understand the intrinsic functional connectivity between brain regions and the disruption of functional connectivity at diseased states. However, the potential vascular effect on resting-state fMRI is still not well understood. In this work, using a multi-modality approach, we demonstrated the presence of high-level coupling between the vascular signal fluctuations driven by cardiac activity (2) and the fluctuations of resting-state fMRI and near-infrared BOLD signals. Given the current and potential impact of rest-state fMRI, it is essential to have an in-depth understanding of the vascular effect on BOLD signal.

METHODS: Twelve healthy older adults (65±6 years old, 4 females) participated in this study. Beat-by-beat changes in mean arterial blood pressure (MABP) using photoplethysmography, cerebral blood flow velocity (CBFV) from the middle cerebral artery using transcranial Doppler (TCD) ultrasonography, cerebral tissue oxygenation index (CTOI) from the frontal brain region using near-infrared (NIR) spectroscopy were simultaneously measured. Resting-state fMRI data was collected on a Philips Achieva 3T scanner at an "eye-closed" condition with the following parameters: EPI, 29 contiguous 5-mm axial slices, 30-ms TE, 1500-ms TR, 60° flip angle, 24-cm field of view, 80×80 matrix size and 200 time points. High-resolution T_1-weighted MPRAGE 3D images were also collected.

The power spectrums of CBFV, CTOI and MABP, as well as the coherence functions between each pair of these measurements, were estimated. The fMRI signal was first pre-processed with motion correction, detrending and baseline removal. Six anatomical regions of interests (ROIs) (right and left isthmuses of cingulate cortex (ICCs), hippocampi, and lateral occipital cortices (LOCs)) were defined with the FreeSurfer software. The mean signal time courses were generated at each ROI as well as at CSF, white-matter and global brain regions. The power spectrums of all these time courses, as well as the coherence functions between each pair of time courses, were estimated. The same procedure was applied again after the additional common pre-processing steps (removal of brain global, white-matter and CSF mean signals, and band-pass filtered within the 0.009-0.08 Hz range). Post-hoc comparisons of signal coherence were also carried at the frequency range of 0.016-0.078 Hz, in which the signal power is concentrated.

RESULTS: The power spectrums of MABP, CBFV, CTOI, global brain, white-matter, CSF and at the above six ROIs all show the concentrated signal power at about the same frequency range of < 0.1 Hz (Fig. 1). The coherence functions between the brain global mean signal and the signal at each ROI, and between CBFV and CTOI also show high level of coherence at < 0.1 Hz (Fig. 2). This frequency range totally overlaps and coincides with the range due to spontaneous neuronal activity assumed in the current resting-state fMRI technology (1). As expected, there is an overall reduction of coherence between each pairs of ROIs after the application of the common pre-processing steps. The coherences between homologous ROI pairs were higher than other pairs both before and after the pre-processing steps.

DISCUSSION AND CONCLUSION: These results suggest the presence of high-level coupling between vascular fluctuations and the BOLD signals (both MRI and NIR). Of note, due to MRI compatibility limitations, BOLD fMRI was not measured simultaneously with TCD CBFV; however, NIR BIOLD signal was measured simultaneously with CBFV. Thus, the high level of coupling between vascular and BOLD signal fluctuations raises an important question of whether the fMRI BOLD signal used to assess brain functional connectivity is primarily due to the vascular effects produced from the upstream cardiac activity. Many studies of functional connectivity have gained support from neuroanatomy and DTI-based structure connectivity despite the vascular inference on BOLD signal (3-4). In this aspect, the findings of the present study demonstrates the importance and necessity to develop new methods to uncover the BOLD signal due to spontaneous neuronal activity from the strong vascular contamination.

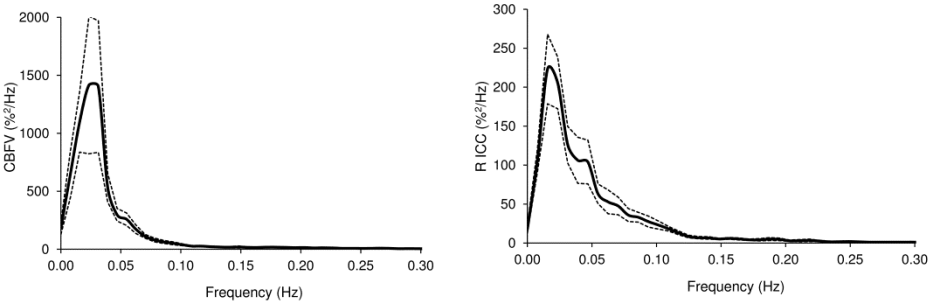

Fig. 1. Power spectrums (n =12) of (a) CBFV and (b) BOLD signal at the right isthmus of cingulate cortex (R ICC). Solid line: mean; dotted lines: standard error.

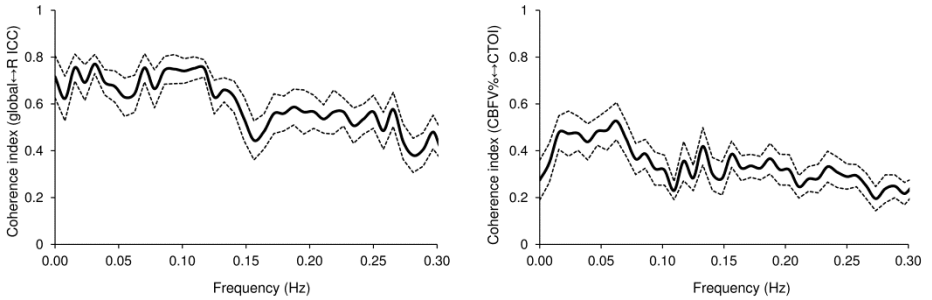

Fig. 2. Coherence functions (n =12) between (a) global and right isthmuscingulate cortex (R ICC) mean BOLD signals, and (b) CBFV and CTOI. Solid line: mean; dotted lines: standard error.

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