Resting-State Functional Connectivity Measured by VASO and BOLD

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Introduction

Functional connectivity in the brain can be investigated using low-frequency fluctuations in resting-state fMRI data that are temporally correlated between functionally related brain areas (1). Recent reports have shown applications of resting-state fMRI in the study of Alzheimer's disease (2), antidepressant effects (3), and "default mode" of brain networks (4). Almost all resting-state fMRI studies used BOLD contrast, primarily due to its high sensitivity, fine temporal resolution, and ease to implement. However, since BOLD signal reflects the combined effects of cerebral blood flow (CBF), cerebral blood volume (CBV), and cerebral metabolic rate of oxygen (CMRO2), it is not straightforward to interpret resting-state data without understanding the relationship between the signal and each of these physiological parameters. Recently, VASO (vascular space occupancy) imaging was proposed as a CBV-based contrast for detecting brain activation (5). Further development allows simultaneous measurements of VASO and other fMRI signals (BOLD and CBF) (6). In this study, we used simultaneous VASO and BOLD imaging to investigate the resting-state functional connectivity in visual cortex.

Methods

VASO and BOLD Resting-State Data Acquisitions. VASO imaging uses an inversion recovery (IR) sequence to acquire data when blood signal is zero (5,6). Simultaneous VASO and BOLD measurements were realized using an IR sequence with two excitations, one at the blood nulling point for VASO and another at a later time with appropriate T_2^* weighting for BOLD (6). Experiments were performed on 5 healthy volunteers on a 3T Siemens Allegra scanner. Three oblique axial slices (5mm in thickness) encompassing the primary visual cortex were chosen for resting-state imaging. An adiabatic inversion pulse was utilized for non-selective inversion, and echo-planar imaging (EPI) was used for data acquisition with TE of 7.6ms for VASO and 27ms for BOLD, and TR of 2s. A total of 180 VASO and BOLD volumes were collected in 6 min, during which subjects were instructed to close their eyes and not to think of anything in particular. For comparison, a 4 min block-design fMRI experiment with an alternated visual flashing checkerboard (8 Hz) and control cross was performed in the same brain location, using a conventional T_2^* weighted sequence (TE/TR =27ms/2s). To address potential effects of cardiac pulsation on resting-state data, a short TR BOLD resting-state data was also collected with TE/TR/FA =27ms/0.4s/44degrees and a repetition of 900.

Data Processing and Analysis. For the resting-state fMRI data, a low-pass digital filter was used to suppress high-frequency components (>0.1 Hz). Cross correlation was used to evaluate temporal correlation between brain areas. Seed voxels were identified based on the task-induced activation maps. A threshold of 0.4 for correlation coefficient was used to obtain functional connectivity maps. To address the potential effects of cardiac pulsations on the functional connectivity, temporal resolution of the short TR (0.4s) resting-state data was down-scaled to TR of 0.8, 1.2, and 2 s, respectively, and functional connectivity maps were generated from these data sets.

Results

Typical task-related activation maps and resting-state functional connectivity maps obtained from the simultaneously measured BOLD and VASO data are illustrated in Fig.1. As expected, both BOLD and VASO activation maps show increased activity in the primary visual cortex (Fig.1a and 1c). With a voxel in the activation map as a seed point, functional connectivity in the primary visual cortex is shown in both BOLD and VASO resting-state data (Fig.1b and 1d).

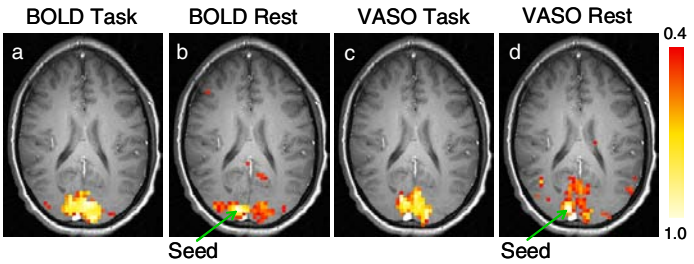

Fig.1 BOLD (a) and VASO (c) activation maps obtained from the visual task. BOLD (b) and VASO (d) functional connectivity maps obtained from resting-state experiment.

Fig.2 shows functional connectivity maps obtained from the short TR (0.4s) resting-state data, and down-scaled to effective TR of 0.8, 1.2, and 2 s, respectively. The connectivity maps at different effective TR show consistent pattern in the visual cortex, although the size of the connectivity area decreases with the increase of effective TR due to reduced sensitivity at longer TR (more data points were discarded in the down-scale process). However, there are no global effects potentially induced by cardiac pulsations.

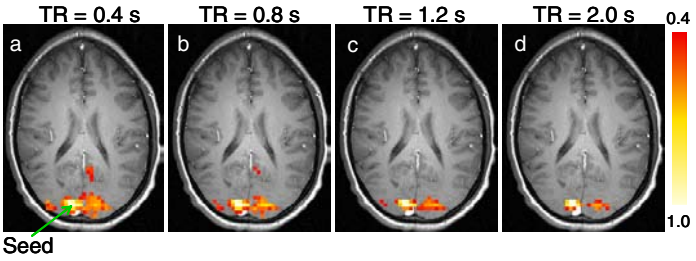

Fig.2 Functional connectivity maps obtained from BOLD resting-state data with various effective TR.

Discussions

In this study, we showed for the first time that resting-state VASO imaging can be used to achieve functional connectivity maps in the brain. This indicates that low-frequency fluctuations that are temporally correlated between functionally related brain areas can be reflected by a more specific physiological parameter (CBV). Previous animal studies using laser Doppler flowmetry demonstrated that blood flow waves are associated with patterns of electro-cortical activity (7). A study using blood flow to assess brain connectivity in humans has also been reported (8). The observed synchronized low-frequency CBV fluctuations in this study may come from similar sources of synchronous neuronal activities as observed in the CBF studies.

VASO signal reflects changes primarily in the microvasculature, and therefore has better spatial specificity than BOLD (5,6). Functional connectivity maps obtained from VASO resting-state data could provide more accurate spatial localization, less sensitive to large veins that are remote from actual neuronal activity sites. A possible confound in VASO imaging is the potential contamination of BOLD signal. In this study, however, we used minimal TE (7.6ms) with partial (75%) k-space acquisition, making the contamination of BOLD signal negligible. An advantage of using very short TE in VASO is its reduced sensitivity to susceptibility artifacts, which makes it possible for VASO resting-state fMRI to study brain areas (e.g. inferior prefrontal lobe) affected by susceptibility-induced signal loss.

In summary, we have demonstrated that VASO resting-state fMRI is able to detect functional connectivity in human visual cortex. The connectivity maps obtained from a single physiological parameter may help understand the source of the resting-state signal. VASO resting-state fMRI has additional advantages of better spatial localization and reduced sensitivity to image artifacts.

References

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