Correlations between cerebral blood flow and amplitude of BOLD fluctuation in the Resting State

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Introduction

Spontaneous fluctuations in resting-state fMRI have been thought to reflect the coherent neuronal activities in specific brain networks, although the underlying mechanism of the fluctuations remains unknown. Among the approaches to characterize resting-state signal, amplitude of low-frequency fluctuations (ALFF) has been proposed to measure the strength of intrinsic resting-state brain activity (1). ALFF quantifies the spectral power of the spontaneous fluctuations, which has been recently demonstrated to have high reliability (2). However, there has been no direct evidence linking ALFF to neuronal activity or cerebral metabolism. In the current study, we investigate the relationship between ALFF and cerebral blood flow (CBF), an index closely related to cerebral metabolism (3). Specifically, CBF in the whole cerebral cortex was measured using a pseudo-continuous arterial spin labeling (pCASL) sequence and ALFF was obtained from BOLD data of the same subjects. Voxel-wise comparisons between ALFF and CBF were made within multiple brain networks including visual, motor, attention and default mode networks.

Materials and Methods

Data acquisition: Twenty healthy subjects (30.3 ± 8.7 years old, 10 females) were scanned with a pCASL and a gradient-echo echo-planar imaging (GE-EPI) sequence on a 3T Siemens MR scanner. The same imaging parameters of the two sequence were: TR/TE = 2750/27 ms, sixteen 6mm slices (20% gap) covering the whole cerebral cortex, and 64×64 in-plane matrix size. For the pCASL sequence, labeling duration = 1.2 s and post-labeling delay = 0.8 s. For both sequences, two runs of seven minutes (156 measurements each) data were acquired for each subject, with randomized order between subjects. During the scanning, subjects were instructed to keep their eyes closed. For registration purpose, a high resolution T1-weighted 3D anatomical image was acquired for each subject.

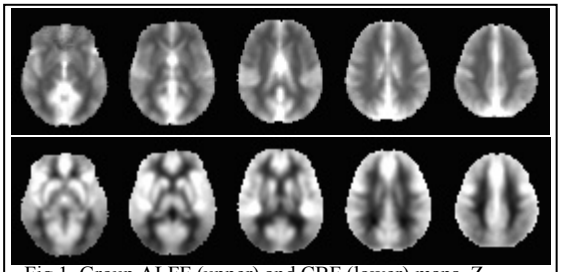

Fig.1. Group ALFF (upper) and CBF (lower) maps. Z coordinates ranges from -1.5 to 35.5 with a step of 9 mm.

Data analyses: 1) For the pCASL data, following head motion correction, label images were sinc-subtracted from control images to correct for temporal offset between the label and control images and to reduce BOLD contamination (4). CBF-weighted images were generated by averaging the control-label difference images, transformed to the Talairach and Tournoux (TT) space, and spatially smoothed with a 6-mm Gaussian kernel. CBF was quantified using a one-compartment model (5). The normalized group CBF map was generated by averaging all subjects' CBF maps and then dividing it by its global mean. 2) For the BOLD data, preprocessing steps included slice-timing correction, head motion correction, linear trend removal, spatial normalization to TT space followed by spatial smoothing with a 6-mm Gaussian kernel. After transforming the time course of each voxel to the frequency domain, ALFF was calculated as the amplitude integral over a frequency range of 0.01-0.08 Hz. ALFF maps of individual subjects were normalized by their corresponding global mean, and a normalized group ALFF map was generated by averaging the normalized ALFF maps across all the subjects. 3) The preprocessed BOLD data of the 20 subjects were decomposed into 20 components using the MELODIC group ICA analysis (6), and a mask for each network was generated by a threshold at Z > 5. 4) Spatial correlations between CBF and ALFF of all the voxels within each network were calculated based on the group CBF and ALFF maps.

Results and Discussion

Figure 1 shows the normalized group ALFF (upper) and CBF (lower) maps from the 20 subjects. Consistent with previous findings (1), ALFF is generally higher in gray matter than white matter. Similar to PET studies (3), CBF is higher in gray matter, particularly in the visual cortices, temporal cortices, and subcortical areas including the basal ganglia and thalamus. Figure 2 (upper) demonstrates six representative networks from group ICA analysis: attention network, anterior cingulate cortex, temporal cortex, motor areas, medial visual cortex and posterior cingulate cortex. Voxel-wise ALFF was plotted against CBF (lower row) within each of these networks. The spatial correlations between ALFF and CBF within these six networks were 0.83, 0.64, 0.57, 0.47, 0.44 and 0.39 respectively. Table 1 shows spatial correlations within each of the 20 networks from the group ICA analysis. Seventeen of the 20 networks showed significant ($p < 0.01$, corrected for multiple comparison) spatial correlations between ALFF and CBF. Among these 17 networks, 16 of them are cortical or subcortical networks and have positive correlations. Only one network, the ventricle component, demonstrated negative correlation.

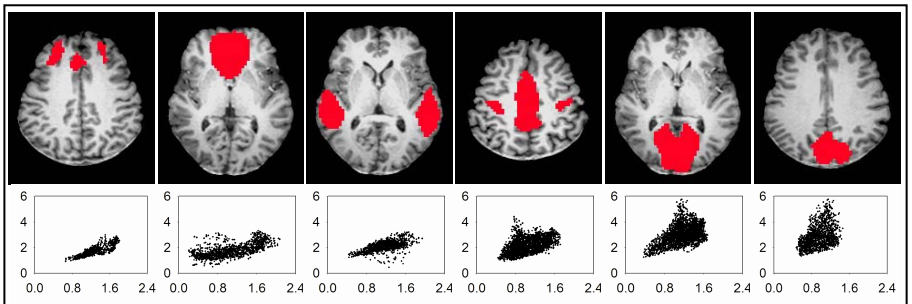

Fig.2. Upper: masks (in red) generated from the group ICA; lower: voxel-wise comparisons of normalized CBF (x-axixs) and ALFF (y-axixs) within the corresponding networks.

These results demonstrated for the first time that the strength of the fluctuations in resting-state BOLD is correlated with baseline CBF in the majority of the brain networks revealed by ICA. Since resting-state CBF is closely related to baseline cerebral metabolism (3), ALFF in these brain networks might be correlated to the basal metabolic demanding, reflecting the level of spontaneous neuronal activities. The relationship between CBF and ALFF (or other resting-state indices) may help understanding the underlying mechanisms of resting-state fMRI signal.

References

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Tab.1. Spatial correlations between CBF and ALFF within specific networks

ICs	Att1	ACC	Temp-Mot	Temp	Mot	Med Vis	Lat Vis1	PCC	Att2	Amy-Hip	WM	Lat Vis2	DMN	BG	Att3	Att4	Lin-Fus	Ceb-CSF	Att5	Vent
cc[a]	0.83	0.64	0.63	0.57	0.47	0.44	0.43	0.39	0.30	0.23	0.20	0.19	0.16	0.15	0.12	0.06	0.00	-0.08	-0.09	-0.53
p[b]	<.01	<.01	<.01	<.01	<.01	<.01	<.01	<.01	<.01	<.01	<.01	<.01	<.01	<.01	<.01	>.01	>.01	>.01	>.01	<.01

[a]Pearson correlation. [b]*p* value was corrected for multiple comparison. Abbreviations: Att, attention network; ACC, anterior cingulate cortex; Temp, temporal cortex; Mot, motor cortex; Med, medial; Vis, visual cortex; PCC, posterior cingulate cortex; Amy, amygdala; Hip, hippocampus; WM, white matter; Lat, lateral; DMN, default mode network; BG, basal ganglia; Lin, lingual gyrus; Fus, fusiform gyrus; Ceb, cerebellum; CSF, cerebrospinal fluid; Vent, ventricle.