Inter-Subject Correlations between Resting-State Spontaneous Fluctuations and Fractional Volume of Gray Matter

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Introduction

Low frequency resting-state BOLD fluctuations [1] have been widely used to assess alterations of baseline activities in healthy aging, and neurological and psychiatric disorders. Fractional amplitude of low frequency fluctuations (fALFF) [2, 3] has been proposed to measure the strength of resting-state fluctuations as a reflection of baseline neuronal activities. However, the underlying mechanism of fALFF is not clear yet and the inter-subject variations of fALFF impede the extensive applications of this technique. Since fALFF is thought to reflect neuronal activities, we hypothesized here that fALFF would be higher in regions/subjects with higher fraction of gray matter ($f_{v,GM}$). To test this hypothesis, we performed a voxel-wise analysis at a group level using resting-state fALFF and $f_{v,GM}$ measured by a fast fractional signal mapping from inversion recovery (FRASIER) [4]. We tested whether fALFF was correlated with $f_{v,GM}$ across the subjects, and whether $f_{v,GM}$ could be used as a covariate to reduce inter-subject fALFF variations.

Methods

Data acquisition: Fifty-one healthy subjects (27.7 ± 8.2 years old, 25 females) were scanned on a 3T Siemens MR scanner. Resting-state fMRI data were acquired with a gradient-echo echo-planar imaging (GE-EPI) sequence when the subjects were instructed to keep eyes closed and relax. The parameters for GE-EPI sequence were as follows: TR/TE = 2000/27 ms, FA=77°, slice thickness = 4mm without gap, 33 slices, FOV = 220×220 mm^2 with in-plane resolution = 3.44×3.44 mm^2, scanning duration = 8 minutes. FRASIER were acquired with a single-shot inversion recovery Look-Locker echo-planar-imaging at a steady state (IR LL-EPI SS) sequence [5] with the same parameters as GE-EPI sequence except with TR of 400 ms, FA of 16°, and scanning time of 1 minute.

Data analyses: All data analyses were conducted with FSL [6], AFNI [7] and MATLAB. For resting-state fMRI data, voxel-wise fALFF between 0.01-0.1 Hz was calculated for each subject as described in [3]. Automatic segmentation for intra-voxel tissue fractions ($f_{v,GM}$, $f_{v,WM}$, and $f_{v,CSF}$) was performed for each subject. To facilitate group analysis, individual data (fALFF and $f_{v,GM}$ maps) were spatially normalized to the Talairach space with a resampled resolution of 3×3×3 mm^3 using both linear and nonlinear registration [8]. Pearson correlation between $f_{v,GM}$ and fALFF across the subjects was calculated for each voxel in the brain. We tested whether, and if so, to what extent, $f_{v,GM}$ can be used as a covariate to reduce inter-subject fALFF variations. Voxel-wise standard deviation of fALFF across subjects was calculated with and without using $f_{v,GM}$ as a covariate, and percentage reductions in standard deviation were calculated.

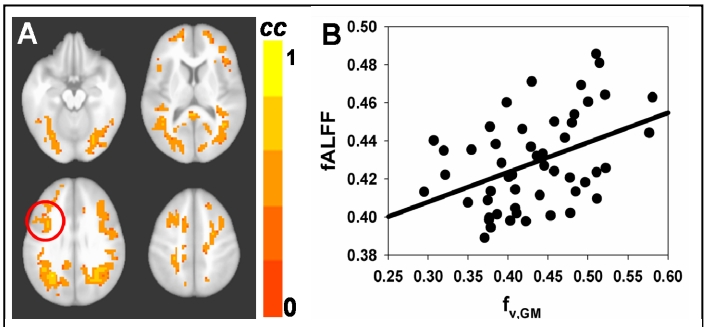

Fig. 1. (A) Pearson correlations between $f_{v,GM}$ and fALFF across fifty-one subjects. (B). $f_{v,GM}$ vs. fALFF correlations at the right dorsolateral prefrontal cortex as indicated in the red circle in panel A.

Results

As shown in Fig. 1A, $f_{v,GM}$ is positively correlated with resting-state fALFF over large parts of the brain including the bilateral fusiform, prefrontal cortex, middle frontal gyrus, superior frontal gyrus, anterior insula, occipital regions, and parietal regions ($p < 0.05$, corrected for multiple comparisons). As a demonstration of these correlations, a scatter plot of fALFF against $f_{v,GM}$ in the right dorsolateral prefrontal cortex (as indicted in the red circle in fig. 1A) is illustrated in Fig. 1B. Fig. 2 shows that inter-subject variations are reduced 10-30 %, when using $f_{v,GM}$ as a covariate, in the similar regions showing significant correlations between $f_{v,GM}$ and fALFF.

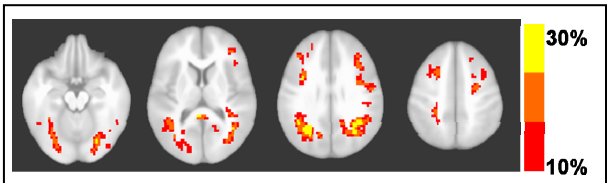

Fig. 2. Reductions in standard deviation of fALFF across subjects using $f_{v,GM}$ as a covariant.

Summary and Discussion

Inter-subject correlations between $f_{v,GM}$ and resting-state fALFF were observed over large parts of the brain mainly in the occipital, frontal and parietal cortices. Further investigations showed that using $f_{v,GM}$ as a covariate remarkably reduced inter-subject fALFF variations in the similar occipital, frontal and parietal regions. These results suggest that it is helpful to consider the variations of inter-subject tissue fraction (such as $f_{v,GM}$) in a group fALFF analysis in these correlation-sensitive regions, which would help to improve statistical power. Moreover, the correlations between $f_{v,GM}$ and fALFF support the notion that the amplitude of spontaneous fluctuations at rest might reflect the level of local neuronal activities. Future studies could investigate the effects of tissue fraction variations on brain activations, especially in the fronto-parietal regions that could be activated by attention and cognitive tasks.

References

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