Partial volume effect has an impact on individual differences of ALFF from resting-state fMRI

Submission Number:

3821

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Introduction:

Amplitude of low frequency fluctuations (ALFF) is a measure for quantifying the low-frequency oscillations of blood-oxygen-level dependent (BOLD) signals, supposedly reflecting the intensity of spontaneous brain activity at rest [1,2]. This measure has been used to describe functional changes in various clinical populations (e.g., ADHD and epilepsy) as compared with controls [1,3], implying a potential role as a bio-marker for brain diseases.
In the original studies [1,3,4], ALFF is typically computed for all voxels across the brain and then further compared between subjects, voxel-by-voxel. Notably, due to the limited spatial resolution of BOLD acquisition, there are a large number of voxels covering different brain tissues (e.g., gray matter/GM, white matter/WM and cerebrospinal fluid/CSF), referred to as partial volume effect (PVE). The computed ALFF value for each voxel is essentially an average of measures from every involved part of brain tissues, which exhibited distinct ranges for ALFF values [2,4]. Therefore, the observed ALFF variation across individuals may come from two sources: 1) the difference of tissue fractions; and 2) the true difference of ALFF. To date, how the variation of tissue composition across individuals in a voxel affects observed ALFF differences remains unexplored. Here, we aim to provide a preliminary examination on this issue by assessing correlations between ALFF and gray matter density (GMD) derived from voxel-based morphology (VBM).

Methods:

Both resting-state fMRI and T1 images were acquired from 161 health young subjects (96 males, all right handed). For each subject, the T1 image was first co-registered to mean BOLD image and segmented into GM, WM and CSF density maps, which were then normalized to the MNI space. The fMRI images were preprocessed with DPARSF [5] by following steps: slice timing, realignment and regressing covariates (12 head-motion parameters, WM and CSF time courses). The ALFF map was calculated [1] and further normalized to the MNI space for each subject.
We compared ALFF values between brain tissue types. The mean ALFF values for each brain tissue type were extracted for each subject and two-sample t-tests were applied to evaluate the difference between tissue pairs. Specifically, GM, WM and CSF masks were defined by thresholding group-mean

density at 0.5 (Fig.1A).
For each voxel, we tested linear correlations between ALFF and GMD. To correct for multiple comparison, FWE-corrected $p<0.05$ (AlphaSim, uncorrected $p<0.001$) was considered as significant.

Results:

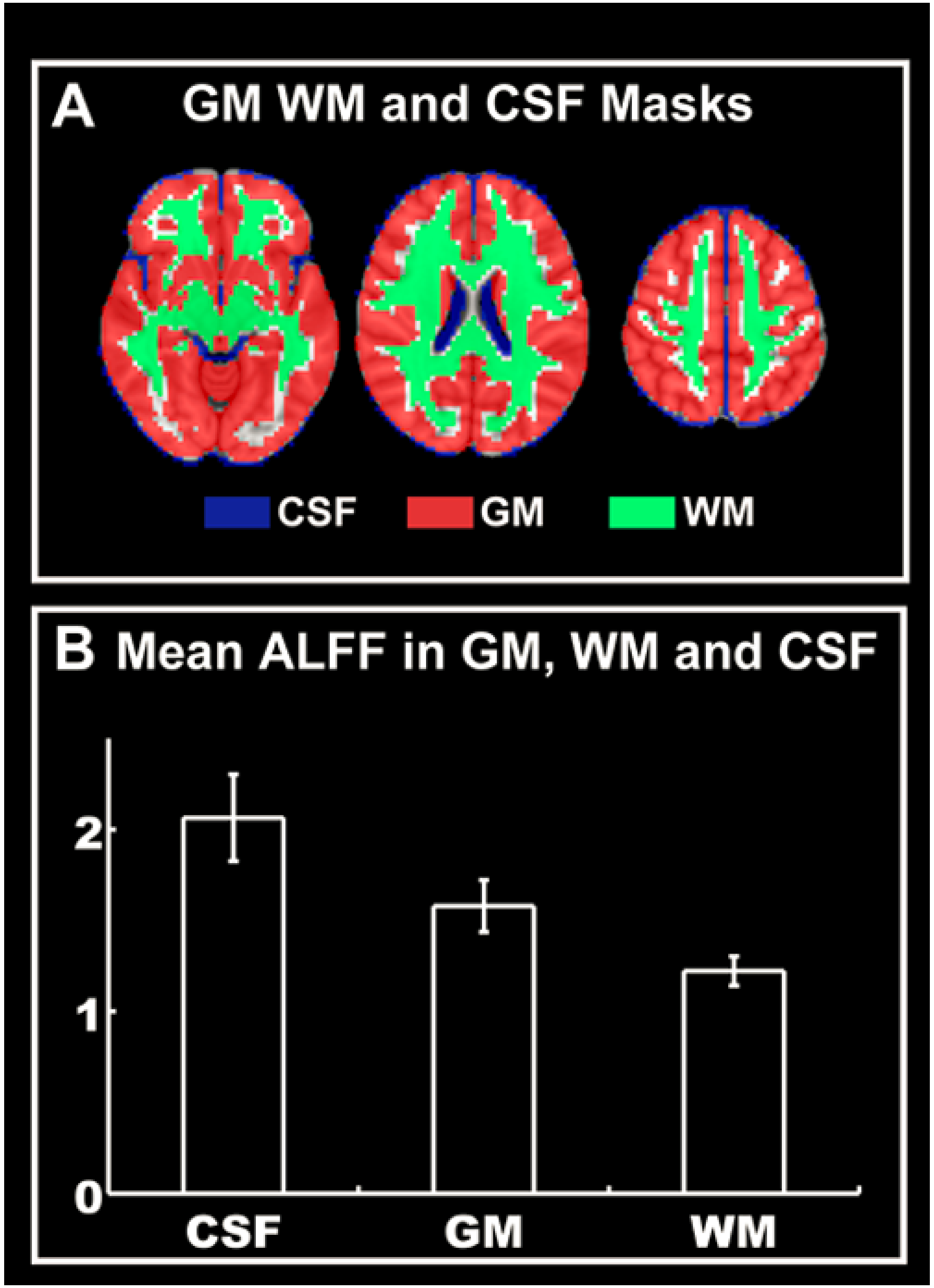
Significant differences of ALFF values were found between any two tissue types ($p<0.001$) (Fig.1B). Specifically, ALFF showed the largest values in CSF and the smallest in WM.
Widespread clusters around GM boundary areas showed significant correlation between ALFF and GMD across subjects (AlphaSim corrected $p<0.05$), as demonstrated in Fig.2. Notably, the ALFF-GMD correlation was positive around the boundary between cortical GM and WM, but negative around the boundary between cortical GM and CSF (Fig.2 & Fig.3). These results indicated a remarkable dependence of ALFF differences on the GMD difference across individuals.

Conclusions:

Our study demonstrated that PVE has a remarkable impact on the ALFF differences across individuals. Therefore, correcting against PVE is recommended when comparing the ALFF between subjects.

Modeling and Analysis Methods:

Exploratory Modeling and Artifact Removal


A GM WM and CSF Masks
CSF
GM
WM
B Mean ALFF in GM, WM and CSF
2
1
0
CSF
GM
WM

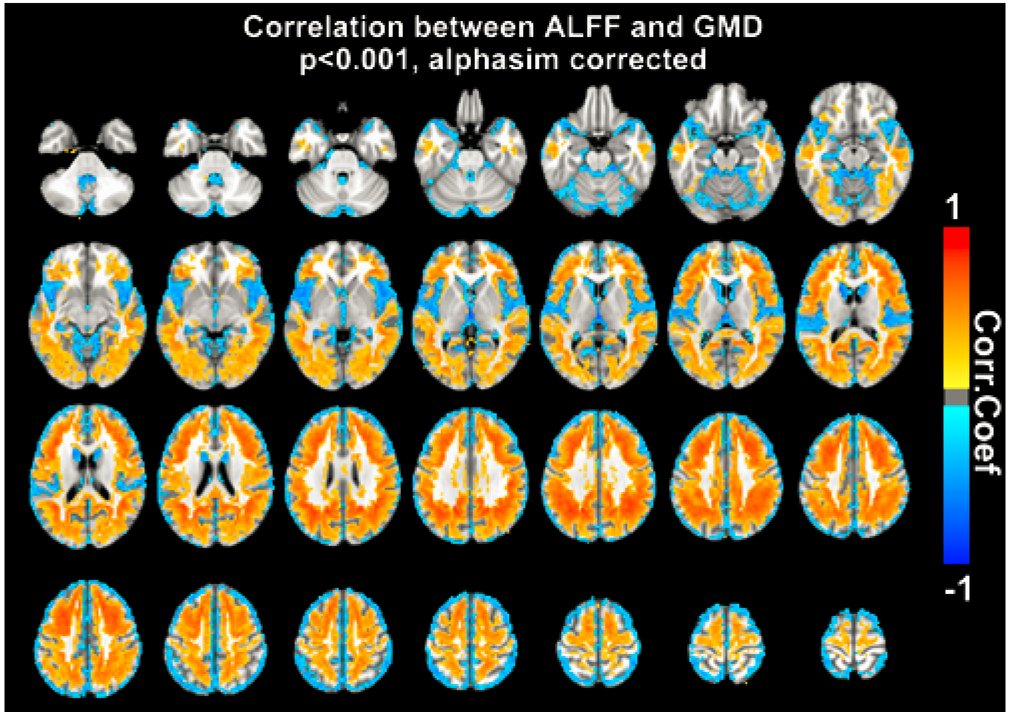


Fig.2. Voxel wise linear correlation between ALFF and GMD. All boundaries between gray matter and white matter show positive correlation and those between gray matter and cerebrospinal fluid show negative correlation.

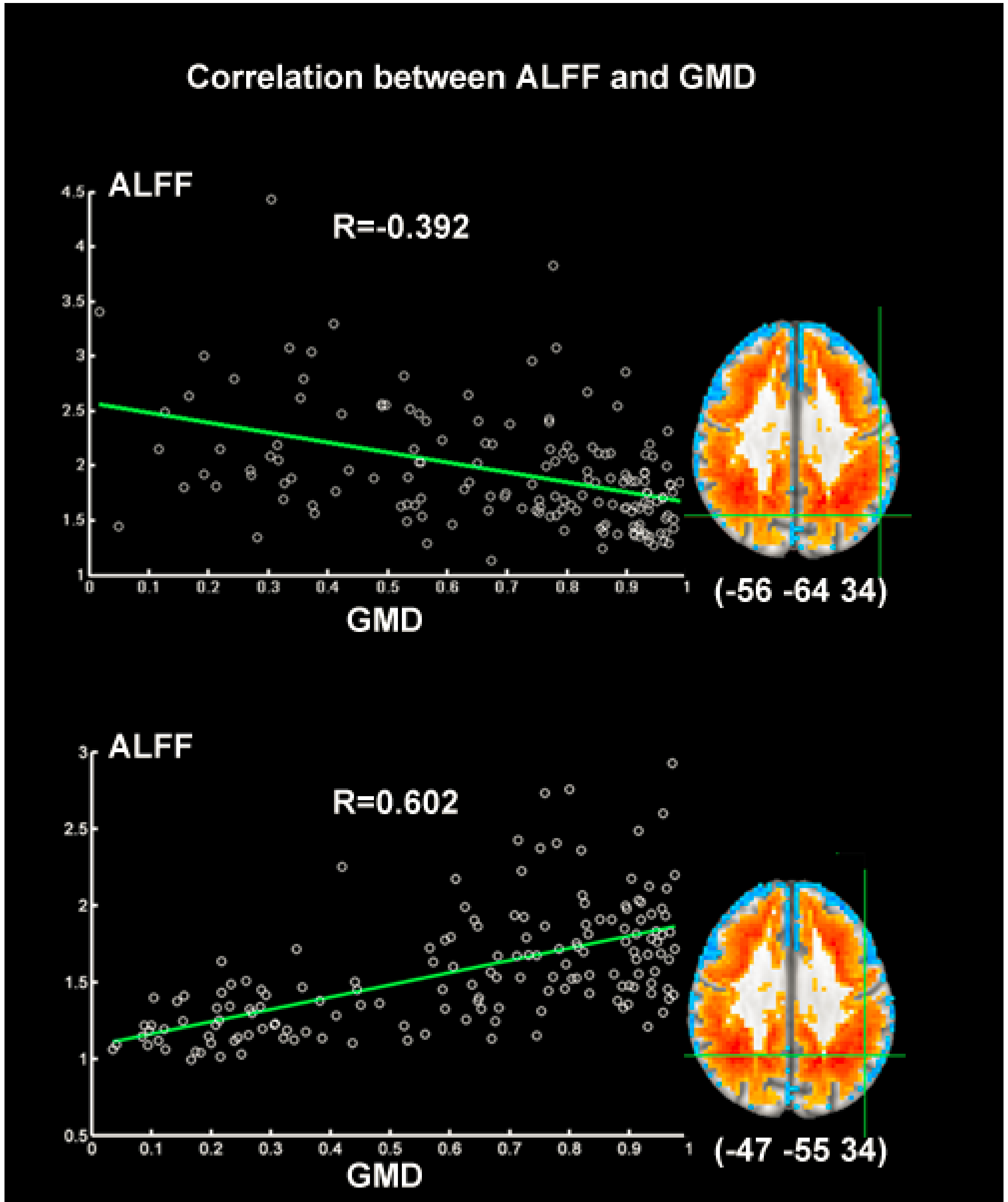


Fig.3. Cross subject correlation between GMD and ALFF in two sample voxels. one is a boundary voxel between GM as CSF (upper), the other is on GM-WM boundary (lower).

Reference

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