

# Changes in low frequency fluctuations in patients with mild traumatic brain injury: a resting state fMRI study

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## Purpose

Resting-state fMRI (rfMRI) is a powerful tool for investigating spontaneous neural activity [1]. The purpose of this study was to utilize rfMRI to investigate changes in low-frequency fluctuations related to mild traumatic brain injury (mTBI). Traumatic brain injury is a serious public health problem, and the neurobiological correlates of mTBI have been difficult to study [2]. While there are several ways to examine regional spontaneous activity in resting state fMRI, in this study we used fractional amplitude of low-frequency fluctuations (fALFF), which is a fraction of ALFF in a given frequency band to the ALFF over the entire frequency range detectable in a given signal [3]. To date, most rfMRI studies have examined spontaneous activity at a frequency band of 0.01-0.1 Hz. However, some studies suggest that the pattern of brain activity is sensitive to specific frequency bands [3]. Therefore, we examined the changes in fALFF in mTBI using two different frequency bands as a means of identifying functional changes in this disorder.

## Methods

Resting state functional images were collected on a 3T scanner for 50 subjects with mTBI and 20 healthy controls (HC). Data processing was done using the DPARSFA toolbox [4] in Matlab. First, the data were motion corrected and normalized to MNI space, followed by spatial smoothing with a 4mm FWHM Gaussian kernel. No temporal filtering was implemented. For each subject, the fALFF maps were calculated for two frequency bands: Slow4: 0.027-0.073 and Slow5: 0.01-0.027. To determine the effects of group and frequency on fALFF, we performed a full factorial second-level analysis in SPM8 on a voxel-by-voxel basis with groups and bands as factors. For those clusters showing significant main effects for group and frequency band, post-hoc and two-sample t-tests were performed. All statistical maps were thresholded using FWE<0.05 with cluster size>20 voxels.

## Results

The main effects for the frequency band and for the group of subjects are shown in Figs. 1 and 2. The brain regions showing a significant main effect for frequency were identified for Slow4>Slow5 in frontal superior and middle cortex, supplementary motor area, cingulate gyrus, caudate, thalamus, putamen, insula, hippocampus, and cerebellum, and for Slow5>Slow4 in superior medial frontal, orbital cortex, anterior cingulate, parietal and occipital cortex, rectus and cuneus. No significant interaction was seen between frequency and group; however, main effects were found for HC>mTBI. Brain regions showing a significant group effect for HC>mTBI include medial superior frontal, middle frontal, medial orbital cortex, and anterior cingulate. For mTBI>HC no clusters survived the height and extent thresholds.

## Discussion and Conclusion

The fALFF indicates the relative contribution of low frequency fluctuations within a specific frequency band to the whole detectable range. There are differences in fALFF between the two bands in many brain regions, specifically in regions associated with motor functions. The significant differences between HC and mTBI patients show that spontaneous activity in frequency bands located in frontal regions, particularly in medial frontal and anterior cingulate areas, are reduced in mTBI. These differences are important, as they demonstrate focal functional differences in the absence of task demands. Moreover, this technique may be useful as an index of treatment response.

## References

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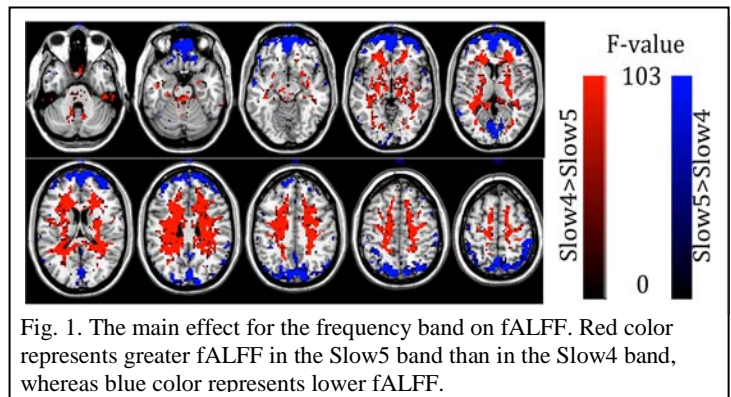


Fig. 1. The main effect for the frequency band on fALFF. Red color represents greater fALFF in the Slow5 band than in the Slow4 band, whereas blue color represents lower fALFF.

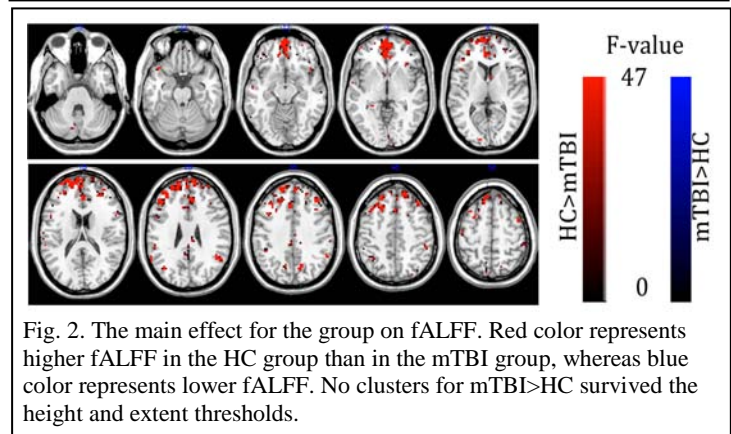


Fig. 2. The main effect for the group on fALFF. Red color represents higher fALFF in the HC group than in the mTBI group, whereas blue color represents lower fALFF. No clusters for mTBI>HC survived the height and extent thresholds.