Resting state connectivity in mild traumatic brain injury: abnormally increased contributions from orbitofrontal cortex and thalamus

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Purpose

Resting state connectivity analysis [1] has been applied to a number of brain disorders to help characterize disturbances in the functional connectivity [2]. Given the limited sensitivity of standard clinical imaging approaches for detecting neurobiologic changes in mild traumatic brain disorder (mTBI), we examined functional connectivity (FC) based on resting state fMRI measures in individuals with mTBI and a group of healthy comparison subjects (HC). Based on previous models of mTBI injury we hypothesized that functional connectivity (FC) of the orbitofrontal cortex (OFC) and thalamus would differ significantly between patients with mTBI and controls.

Methods

Resting state functional images were collected on a 3T scanner over 8 minutes for 50 subjects with mTBI and 20 healthy controls (HC) (TR=2s, TE=28, number of slices=40, slice thickness=3mm, 245 images per session). Data processing was done using the DPARSFA toolbox [3] 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 FC maps were computed by using a standard seed-based whole brain correlation method [2]. We used the unilateral OFC and thalamus as seed regions and sampled both hemispheres. One sample t-tests within the groups of subjects were performed to generate group resting state network (RSN) maps ($P<0.001$ and cluster size>100 voxels). Two-sample t-tests were also performed to measure the differences between RSNs of mTBI and HC subjects ($P<0.01$ and $k>100$ voxels).

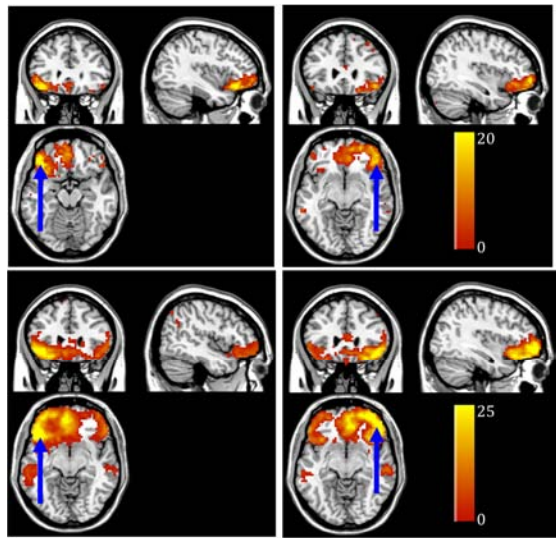

Fig. 1. Orbito-frontal functional RSNs obtained using a one-sample t-test for HC (top row) and mTBI patients (bottom row). Seeds were placed in the left and right OFC, as indicated by arrows.

Results

Figures 1and 2 show functional networks during the resting state for HC and mTBI patients using left and right OFC and thalamus.

Discussion and Conclusion

In healthy volunteers, our results demonstrated a normal pattern of OFC and thalamic functional RSNs. Compared with control subjects, patients with mTBI demonstrated stronger and more widely distributed functional connectivity for both the OFC and the thalamus. Specifically, the lateralized seeds of the OFC region showed predominantly unilateral projections in HC, whereas the same regions showed bilateral projections in mTBI. Based on the two-sample t-tests, the increased functional connectivity in the mTBI group in orbitofrontal RSNs involved regions in temporal gyrus, insula, supramarginal gyrus and parietal lobe. In the thalamic functional RSNs, the increased connectivity was shown in the temporal gyrus, hippocampus, insula, and frontal gyrus. These findings may be caused by the aberrant frequency distribution of low-frequency fluctuations in these regions secondary to injury. We are currently correlating functional resting state networks for OFC, thalamus and other seeds with clinical and neurological traumatic brain injury symptoms.

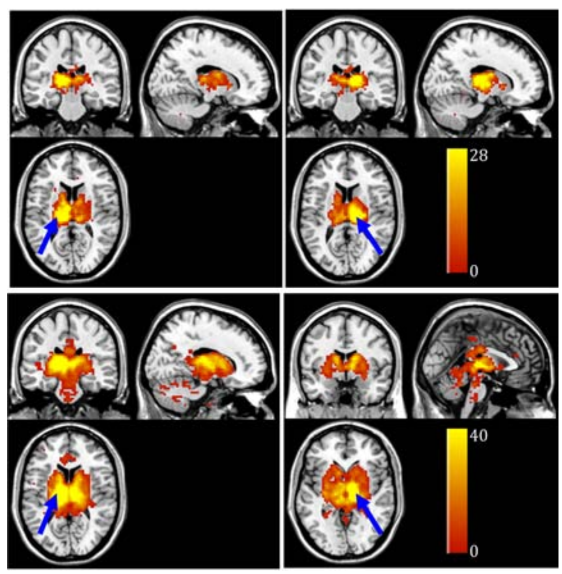

Fig. 2. Thalamic functional RSNs for HC (top row) and mTBI patients (bottom row).

Refereneces

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3. Yan C and Zang Y (2010) Front. Syst. Neurosci. 4:13.
4. Tang L, Ge Y et al (2011) Radiology 260(3):831-840;