Group non-negative matrix factorization reveals functional connectivity changes in mTBI
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Background: Mild traumatic brain injury (mTBI) is a sub-type of traumatic brain injury when loss of consciousness and disorientation is shorter than 30 minutes. Though brain imaging with MR and CT often appear normal, the patient may sustain long-term cognitive difficulties such as headache, blurry vision, memory problems, attention deficits, mood swings and frustration. In this paper, we report multiple network disconnections with the right cerebellum in mild TBI that is associated with symptoms.

Methods: After obtaining informed consent, rs-fMRI was recorded from 78 patients at four time points (3 days, 7 days, 3 weeks and 3 months) after mTBI and 26 healthy controls (2 sessions, 1 week apart). After eliminating missing and noisy data, we analyzed 184 time points in total. Using GE 3T MRI scanner, multi-band (acceleration factor 3) 2D-EPI, TR/TE = 900/30 ms was acquired for 6 minutes (395 volumes), with 1.875 mm² in-plane resolution and 3 mm slice thickness to cover the whole brain. T1-weighted scan was acquired at each time point. All participants filled a neuropsychological self-assessment questionnaire that was used to calculate symptom severity scores (SSS). rs-fMRI data were motion corrected, rigid registered to T1-weighted image, non-rigid registered to MNI atlas, nuisance (physiological noise) removed using aCompCor, spatial smoothed using Gaussian filter (FWHM 4mm) and temporally filtered to pass 0.01 to 0.1 Hz using custom built software. Group non-negative matrix factorization by temporal concatenation was performed to derive 30 components using custom built software. Neuro-physiologically relevant components were manually selected using spatial spread and frequency distribution of the component time courses. Voxel-wise associations of functional networks with SSS were investigated using general linear model. Cluster-level FDR was used to control multiple comparison confounds.

Results: Twenty-two neuro-physiologically relevant networks were identified. Several functional networks revealed functional connectivity to brain regions significantly associated SSS. Interestingly, several networks’ (including primary visual, higher order visual, auditory, language, dorsal and ventral visual streams) connection to different regions in the right cerebellum was significantly positively associated with SSS. Several other networks’ (including subcortical networks, primary and higher order visual, default mode network) connection to different regions in the left temporal lobe showed positive correlation with SSS. Inferior parietal lobule’s connection to visual stream and premotor networks was also significantly correlated with SSS. The dorsal attention system’s connection to the left intra-parietal sulcus was also significantly correlated with SSS.

Conclusions: Functional networks derived using Group NMF had spatial distribution in agreement with typical functional networks. NMF has been able to extract functional connectivity associated with SSS. The right cerebellum’s connectivity to several networks appeared to be higher in mTBI patients with higher SSS. Cerebellar connectivity dysfunction has been reported previously in mTBI. The left temporal lobe also showed hyper-connectivity to several networks in patients with higher symptoms, pointing to a possibility of the temporal lobe also being vulnerable in mTBI.