The Dynamically Changing Default-Mode Network Functional Connectivity after Concussion in Sports

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Target audience: Neuroimaging researchers/clinicians in traumatic brain injury.

Purpose: Current diagnosis and monitoring of mild traumatic brain injury (mTBI)/concussion rely on neuropsychological examination. Conventional brain imaging often does not reveal abnormality. Brain alteration and recovery process after mTBI is unclear. Recent work by Johnson et al. demonstrated the alteration of default-mode network (DMN) with resting-state fMRI (rs-fMRI) in the sub-acute phase after mTBI (1). To further understanding the recovery process, in this pilot work, we assessed the dynamic change of DMN with rs-fMRI on days 1, 7 and 30 after concussion.

Methods: Six intercollegiate athletes participated in this study after concussion sustained during athletic competition, which was clinically diagnosed by a team physician or a neurologist. ImPACT (Immediate Post-Concussion Assessment and Cognitive Testing) scores were collected within the first 24 hours and then following days. High-resolution 3D T_1-weighted, T_2*-weighted, diffusion-tensor and rs-fMRI brain images were collected on a GE 3T Signa® HDx MR scanner from each subject within 1 day, on 7 ± 1 days and then 30 ± 1 days after concussion. The rs-fMRI included two 7-min resting-state (relax, eyes closed but staying awake) EPI datasets with the following parameters: 38 contiguous 3-mm axial slices, 27.7-ms TE, 2500-ms TR, 80° flip angle, 22-cm FOV and 64×64 matrix size. For each subject, correlation analyses of rs-fMRI were carried in AFNI (2). Slice-timing and motion corrections were applied. Baseline, linear and quadratic system trends were removed. Brain global, cerebral spinal fluid and white matter mean signals were modeled as nuisance variables and were removed from the time courses. Band-pass filter in the range of 0.009 Hz – 0.08 Hz was applied. Voxel-based correlation was done on every voxel of the brain against the time course from the average signal within a seed region. The right and left isthmi of cingulate cortex (ICCs), which are within the key hub regions of DMN (3), were defined with FreeSurfer (4) as these seed regions. Correlation analysis results from individual subject were warped to Talairach template for group analyses. Since only four subjects completed all image data collection, the group means were used to demonstrate the trend of functional connectivity. The DMN was functionally defined based on the union of the group means of the correlations with both right and left ICCs as seeds and from all three time points with a threshold on correlation > 0.25. The cluster sizes of DMN components connected to ICCs at different time points were estimated for each subject and for the group.

Results: Data collection has been completed on four subjects. Data on Days 1 and 7 have been collected on the fifth subject. Neurologic clinical evaluation and ImPACT sores showed that all subjects returned to normal ranges within 7 days. Table 1 summarized the cluster sizes of the five distant components of DMN connected to the ICCs. Fig. 1 shows the whole-brain mean functional connectivity to the left ICC at three time points. There were general reductions of functional connections from different components of DMN to both right and left ICCs after 7 days and some recovery after 30 days. The strongest connections were seen on the first day after concussion. A consistent reduction of DMN functional connection was observed after 7 days on four subjects, but marginally increase on the fifth subject. We did not see noticeable changes on conventional anatomical images and diffusion-based fiber tracks to the ICCs. The functional connection between left and right lateral occipital cortices (part of the visual network) increased from day 1 to day 7 overall, a trend opposite to DMN.

Discussion and Conclusion: There appeared a dynamically changing functional connectivity within DMN, as well as other networks after concussion. It is still unclear if this implies that a dynamic recovery process is still occurring even after clinical examination and ImPACT testing return to normal. Furthermore, the potential correlation between functional connectivity and the level of physical activity after concussion can be a confounder. More concussed subject as well as normal controls will be recruited. However, our pilot data results clearly demonstrate that rs-fMRI can potentially serve as an important and sensitive tool to monitor the dynamically changing brain function after sports related concussion, and to further our understanding of brain alteration not revealed by neuropsychological and conventional clinical imaging techniques.

References: 1. Johnson B et al. NeuroImage 2012;59:511-518. 2. Cox RW. Comput Biomed Res 1996;29:162-173. **3.** Buckner RL et al. Ann N Y Acad Sci 2008;1124:1-38. 4. Fischl B et al. Neuron 2002;33:241-355.

Table 1. Default-mode network functional connectivity to ICC

		Cluster size (mm^3) at				
Seed Region	Days after concussion	MePFC	Left TPJC	Right TPJC	Left MeTL	Right MeTL
Left ICC	1	46502	13278	9657	3181	989
Left ICC	7	897	1604	1568	24	26
Left ICC	30	25984	9878	6276	672	59
Right ICC	1	41234	10495	11759	2381	1537
Right ICC	7	1309	157	2632	0	1
Right ICC	30	24615	5654	9728	535	284

4 subjects with mean correlation > 0.25.

MePFC = medial prefrontal cortex, TPJC = temporoparietal junction cortices,

MeTL = medial temporal lobe, including hippocampus, parahippocampus and sounding regions.

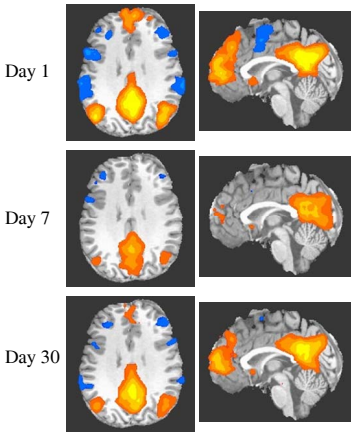

Fig 1. Mean functional connectivity to the left ICC (R > 0.25) of four subjects over time.