Connectome-scale Assessment of Structural and Functional Connectivity in Mild Traumatic Brain Injury at the Acute Stage

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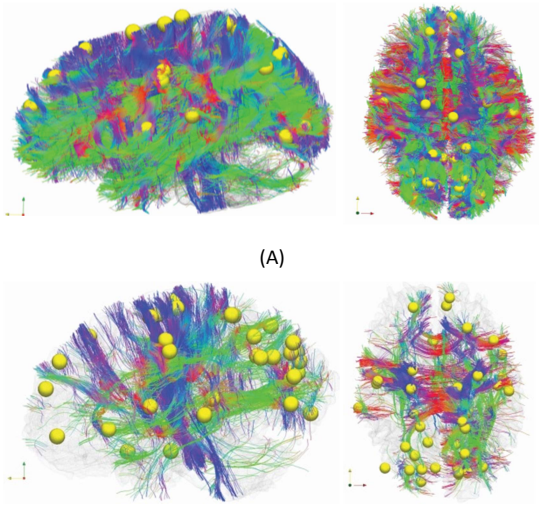
INTRODUCTION: Mild traumatic brain injury (mTBI) accounts for over one million emergency visits each year in the United States. Most mTBI patients have normal findings in clinical neuroimaging. Several functional network alternations have been reported after mTBI [1]; however, the network alternations at the large scale, particularly at connectome scale, is still unknown. Advanced magnetic resonance imaging (MRI) has detected microstructural damage in major white matter tracts by diffusion tensor imaging (DTI) [2]. We hypothesize that mTBI results in large-scale network connectivity changes, particularly at the connectome scale. In this study, we adopted a novel approach to analyze both structural and functional network changes at connectome level in mTBI patients.

MATERIALS AND METHODS: Forty (40) mTBI patients (age: 38.03±13.69 years) and 50 demographically matched healthy controls (age: 29.88±10.75 years) were recruited from the emergency department of a Level-1 Trauma Centre and scanned. The patients were scanned at the acute setting before their discharge. Both diffusion magnetic resonance imaging (dMRI) and resting state functional magnetic resonance imaging (rsfMRI) data were acquired. Data analysis was applied at connectome level using a novel approach called DICCCOL (dense individualized and common connectivity-based cortical landmarks) [3]. Each DICCCOL node is a functional landmark with consistent white matter (WM) fiber connection profile across individuals and thus preserves the same functional role across individuals. For each DICCCOL node, the optimized location was obtained by using our trace-map searching algorithm to minimize dissimilarity of fibers passing from the node on a subject and templates. Both common and discrepant (i.e. structurally disrupted) DICCCOL nodes were identified by comparing patients and controls. The common DICCCOL nodes were used as the regions of interests for functional connectivity analysis in resting state fMRI data.

RESULTS: Despite the negative findings on the mTBI patient's structural MRI, the patient's white matter structure shows significant differences in the 41 nodes among 358 nodes in comparison with controls using DICCCOL analysis (p-value < 0.01). These DICCCOLs are called discrepant DICCCOLs. Since the structural connectivity is disrupted in discrepant DICCCOLs, we can observe significant difference in white matter tracts that are connected in discrepant DICCCOLs between controls and patients (see Fig 1). Among all discrepant nodes (see Fig 2), the precuneus (Brodmann Area 7, Somatosensory Association Cortex) has the greatest number of discrepant DICCCOLs. The structural pathways associated with these discrepant networks include the corpus callosum, superior and inferior longitudinal fasciculi, cingulum, arcuate fasciculus, and dorsolateral frontal white matter. Functional connectivity analysis of the 317 common DICCCOLs showed 60 functional connectivities as the most distinctive and discriminative features of our data to differentiate healthy control subjects and patients, labeled as connectomic signatures (see Fig 3). These connectomic signatures gave 93.75% sensitivity and 100% specificity. Using meta-analysis, connectomic signature DICCCOLs were classified into five major categories, which showed decreased intra-network connectivity within the emotion network and among emotion-cognition interactions, and increased interactions among action-emotion and action-cognition as well as within perception networks (see Fig 4).

CONCLUSION: This work suggests that mTBI may result in changes in structural and functional connectivity on a large or connectome scale at the acute stage. It shows that multiple fiber tracts and multiple functional networks are affected in mTBI patients in the acute stage.



(A)

(B)

Fig 1. White matter fiber tractography of a randomly chosen control subject (A) and a randomly chosen mTBI patient (B) by using the 41 discrepant DICCCOLs (yellow spheres) as seed points. Despite the negative findings on the mTBI patient's structural MRI, the patient's white matter structure shows significant differences in the 41 discrepant networks in comparison with controls. Of particular note, the difference in the major white matter tracts between controls and patients is not because of the loss of white matter tracts in the patient; instead, it is the injury at these discrepant DICCCOLs fail the fiber tractography algorithm when using the discrepant DICCCOLs.

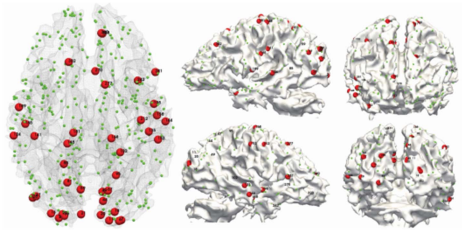


Fig 2. Visualization of the location of discrepant DICCCOLs (red sphere) and the common DICCCOLs (green sphere) on cortical surface. IDs of discrepant DICCCOLs are labeled. The fiber connection patterns of the DICCCOLs are available online at: http://dicccol.cs.uga.edu.

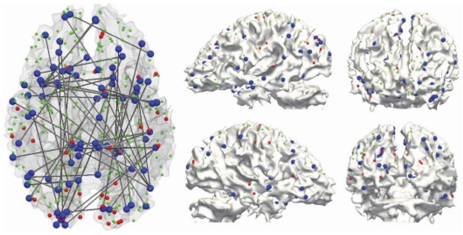


Fig 3. Visualization of discriminative functional connectivities (gray lines) between mTBI patients and healthy subjects and the location of related DICCCOLs. DICCCOLs were represented by color-coded spheres (blue: DICCCOLs related to discriminative functional connectivities, red: discrepant DICCCOLs, green: rest common DICCCOLs).

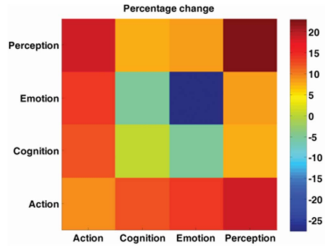


Fig 4. Visualization of the location of discrepant DICCCOLs (red sphere) and the common DICCCOLs (green sphere) on cortical surface. IDs of discrepant DICCCOLs are labeled.

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