Investigating Longitudinal Continuity of Persistent White Matter Alterations in Sport-related Concussion Using Individualized Analyses

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Background: Sport-related concussion (SRC) has been shown to lead to acute and long-term alterations in white matter (WM) organization. The Centers for Disease Control estimates around 283,000 children each year seek medical attention for SRC/recreation-related traumatic brain injury. However, literature on subject-specific longitudinal WM abnormalities in SRC is limited.

Purpose: Given the heterogeneous nature of SRC on WM microstructure, the goal of this study is to investigate the longitudinal continuity of persistent white matter alterations using a subject-specific approach.

Methods: MRI is a non-invasive imaging modality suitable for detecting neuropathophysiological changes after SRC. Compared to conventional anatomical MRI, using diffusion MRI to probe WM microarchitecture may provide additional sensitivity.

The diffusion MRI data from 50 participants were obtained from the CARE consortium, a prospective multisite study examining the natural history of concussion. Each concussed athlete underwent MRI scan at three time points: (1) 24-48 hours after concussion, (2) asymptomatic state, and (3) 7-days after returned to play. Diffusion tensor imaging (DTI) and neurite orientation dispersion and density imaging (NODDI) metrics were computed and Z-scored based on a normal distribution template created from non-contact sport controls. Potential WM alterations indicated by extreme deviations of Z-score maps were calculated for all diffusion metrics in each concussed participant and time point.

Results: WM alterations persistent across all three timepoints manifested in 76%, 62%, and 82% of the participants as quantified by increases of mean, axial, and radial diffusivity, respectively. 58% of the participants had fractional anisotropy decreases. For NODDI metrics, 82% and 86% of the participants showed increases of isotropic volume fraction and orientation dispersion index, respectively.

Conclusion: This study demonstrated that by applying subject-specific analysis, extreme Z-score voxels can be identified across time in the same or spatially proximal brain regions suggesting persistent WM abnormalities beyond apparent clinical recovery.