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IN VIVO DETECTION OF PATHOLOGY AT THE DEPTHS OF CORTICAL SULCI IN SPORTS REPETITIVE HEAD IMPACTS

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Abstract:
Purpose: Post-mortem evidence suggests the depths of sulci (DoS) are vulnerable to repetitive head impacts (RHI). Diffusion MRI (dMRI) has identified microstructural features of brain injury but has largely overlooked the juxtacortical white matter (jWM). We assessed the relationship of RHI due to heading in soccer players with dMRI in DoS jWM. RHI has been associated with worse verbal learning; we assessed the mediating role of dMRI in this relationship.
Methods and Materials: Healthy amateur adult soccer players (*n*=380; 18-53 years old; 30% female) and healthy non-collision athlete controls (82; 18-50; 61%) were included. We assessed the cross-sectional relations among estimated 12-month RHI (HeadCount) represented in quartiles (medians: 43, 300, 782, 2,607) and verbal learning (International Shopping List).
3T dMRI (2mm^3, 109 directions, b=300, 800, 2000) was processed to extract DTI (fractional anisotropy, FA; axial diffusivity, AD; radial diffusivity, RD; mean diffusivity, MD) and NODDI (orientation dispersion index, ODI; neurite density index, NDI; isotropic water fraction, ISO) metrics from jWM subjacent to the DoS, jWM subjacent to the crests of gyri (CoG), and deep WM (dWM: corticospinal tract, corpus collosum, fornix, and uncinate fasciculus). dMRI metrics at each region for each RHI quartile were compared to non-collision athletes, using linear models adjusted for age, sex, and concussion history. Significant associations underwent causal mediation analysis using bootstrapping to test the significance the mediating effect of a dMRI metric on the relationship of RHI with verbal learning. Bonferroni correction was applied.
Results: dMRI metrics in DoS jWM differed from controls in an RHI dependent fashion. The highest RHI quartile exhibited (corrected $P<0.001$) lower FA in the frontal lobe (FL), orbitofrontal cortex (OFC), parietal lobe (PL), temporal lobe (TL), and occipital lobe (OL); lower AD in OFC, PL, TL, and OL; higher RD in FL, OFC, PL, TL, and OL; higher ODI in FL, OFC, PL, TL, and OL; and lower NDI in OFC. DoS effect sizes were larger than CoG or dWM. jWM ODI in OFC partially mediated the association of greater RHI with worse verbal learning ($P=0.008$); other white matter regions had no mediation effect.
Conclusions: Microstructural injury related to RHI in young healthy individuals is most prominent in DoS jWM. The adverse association of RHI with verbal learning is partially mediated by OFC DoS jWM, consistent with measurable functional effects of subclinical axonal injury, demyelination, and/or inflammation.
Clinical Relevance/Application: Our findings suggest DoS jWM holds potential for identifying clinically significant injury pathology in RHI, which can be applied to expand and improve the use of imaging in assessment of traumatic brain injury.