

Soccer Heading Over 2 Years is Associated with Change in Frontal White Matter Microstructure That Varies by Exposure Magnitude

PURPOSE

Repetitive head impacts (RHI) in soccer have been associated with adverse cognitive and neuroimaging outcomes in cross-sectional studies. However, few have reported on the longitudinal effects of soccer RHI on neuroimaging and cognitive performance. The objective of this study was to assess the association of soccer heading over two years with change in brain microstructure and cognitive performance in adult amateur players (n=148, mean age 26.7 years, 25.6% female).

METHODS AND MATERIALS

Two-year heading exposure was categorized as low (0-556 total headers), moderate (564-1,512 total headers), or high (1,538-23,462 total headers) using the HeadCount-12m questionnaire. Diffusion tensor imaging (3T, 32 encoding directions, b=800 s/mm, 2mm isotropic resolution), neurite orientation dispersion and density imaging (same parameters as above except three shells instead of one: 6 directions at b = 300 s/mm, 32 at b = 800 s/mm, and 60 at b = 2,000 s/mm, and the Cogstate battery were acquired at the initial study visit and two years later. Mixed-effects models accounted for age, concussion history, sex, and education. Significant findings survived false discovery rate of 0.05 (actual p-values 0.001-0.004).

RESULTS

The high heading exposure group, over two years, demonstrated an increase of mean diffusivity (MD), radial diffusivity (RD), and axial diffusivity (AD) in frontal WM regions, and a decrease of orientation-dispersion index (ODI) in the right superior frontal white matter and superior corona radiata. Low and moderate heading was associated with a decrease of MD, RD, and AD, and increase of ODI over the same period. High heading was associated with decline of verbal learning performance over two years, whereas low and moderate heading exposure was associated with improvement in verbal learning, but these findings did not reach statistical significance.

CONCLUSIONS

These results suggest greater heading exposure over two years is associated with adverse effects on white matter microstructure in young adult amateur soccer players. Our results are suggestive of a subclinical effect, given the sub-significant pattern of verbal learning changes. Larger longitudinal studies in diverse cohorts are needed to determine the potential for adverse microstructural and functional change over the longer term to better guide intervention and policy.

CLINICAL RELEVANCE/APPLICATIONS

Decline of brain microstructure over 2 years in soccer players who head at high levels, with trends toward decline of cognitive performance, suggests potential subclinical injury, which could affect long-term brain health.

Adverse Association of Soccer Heading with Verbal Learning is Mediated by Microstructure of the Orbitofrontal Gray Matter-White Matter Interface

PURPOSE

Repetitive head impacts (RHI) from soccer heading are an integral part of the sport. High RHI exposure is associated with worse verbal learning (VL). Adverse associations of RHI with white matter (WM) microstructure have also been identified using diffusion tensor MRI (DTI). The orbitofrontal region and the gray matter (GM) - WM interface (GWI) are known predilection sites for head impact shear force trauma, but DTI investigations have been restricted to deeper WM regions. Moreover, studies have not yet tested the causal role of imaging findings in the pathway from RHI exposure to worse cognitive function. We tested the mediating role of orbitofrontal GWI microstructure in a known association of RHI with worse VL. We hypothesized the natural sharp transition from high WM fractional anisotropy (FA) to low GM FA is attenuated as a function of RHI and this attenuation mediates the association of RHI with VL.

METHODS AND MATERIALS

We analyzed RHI (12-month heading from HeadCount, a validated instrument), DTI (3.0T; 32 directions; $b=800$; voxel size 2mm) and VL (International Shopping List) from 353 amateur soccer players (18-53, 27% female). To overcome limitations (e.g., misregistration and partial volume effects) we interrogated the transition from low GM FA to high WM FA by computing the slope of FA orthogonal to the GWI (defined by FreeSurfer) over the entire orbitofrontal region, as follows: we binned all orbitofrontal voxels by distance to the GWI and computed average FA within each bin. Average FA was plotted vs. distance to the GWI and fit to a 7th order polynomial. FA slope across the GWI is defined as the maximum slope magnitude of the polynomial fit. To test mediation by GWI microstructure, we fitted linear models to test the associations of (1) RHI with VL, (2) RHI with FA slope and (3) RHI and FA slope with VL, with age and sex as covariates. Mediation by FA slope was calculated as the product of RHI effect size in model (2) and FA slope effect size in model (3). Mediation significance was tested using the Sobel test.

RESULTS

We confirmed an association of higher RHI with worse VL ($p=0.0305$). High RHI was associated with lower orbitofrontal GWI FA slope ($p=0.00745$). The orbitofrontal GWI FA slope was a significant mediator ($p=0.0186$) of the association of higher RHI with worse VL.

CONCLUSIONS

GWI microstructure integrity in the orbitofrontal region, as quantified by FA slope, mediates the association of RHI with VL. These results support a mechanistic role for juxtacortical white matter in adverse associations of soccer RHI with worse cognitive performance.

CLINICAL RELEVANCE/APPLICATIONS

GWI microstructure findings support a causal role in the adverse association of RHI with cognitive performance and may serve as a complementary biomarker of trauma-related brain pathology.