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White Matter Integrity in the Brains of Professional Soccer Players Without a Symptomatic Concussion

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To the Editor

Soccer is the most popular sport in the world, with more than 250 million active players. It is the only sport in which the unprotected head is a primary point of contact when heading the ball. In other contact sports, the deleterious long-term effects of repetitive traumatic
brain injury (TBI), such as impaired white matter integrity,\textsuperscript{2} are well recognized.\textsuperscript{3} However, whether frequent subconcussive blows to the head lead to TBI remains controversial,\textsuperscript{4,5} although evidence suggests impaired neuropsychological function in soccer players.\textsuperscript{5} We evaluated concussion-naive soccer players using high-resolution diffusion tensor imaging (DTI), which is highly sensitive for detecting alterations in white matter architecture.

**Methods**

All right-handed male soccer players from 2 training groups of an elite-level soccer club in Germany were approached to participate. All were trained since childhood for a career in professional soccer. A comparison cohort of swimmers, which is a sport with low exposure to repetitive brain trauma, was recruited from competitive clubs to match on age (group-matched), handedness, and sex. Exclusion criteria were history of concussion or any other neuropsychiatric disorder. The local ethics committee approved the study and written informed consent was obtained.

A DTI sequence with 64 diffusion directions was acquired on a 3T magnetic resonance scanner (Verio, Siemens Healthcare) in July and August 2011. Group analyses were performed using automated whole-brain, tract-based spatial statistics\textsuperscript{6} for the following measures of diffusivity: fractional anisotropy, mean diffusivity, radial diffusivity, and axial diffusivity. Fractional anisotropy and mean diffusivity have been shown to be sensitive markers for mild TBI.

Axial diffusivity and radial diffusivity measure axonal and myelin pathology. Voxel-wise statistics were used to investigate group differences at a 2-sided significance level of $P < .05$, corrected for multiple comparisons. Voxels with a significant group difference were merged into a single cluster. Diffusivity measures were obtained for each individual and a linear regression model was applied to test for group differences adjusted for age and years of training. SPSS version 20 (SPSS Inc) was used.

**Results**

Twelve of 40 soccer players (mean [SD] age, 19.7 [1.6] years; mean duration of playing soccer, 13.3 [2.9] years) and 11 of 20 swimmers (mean [SD] age, 21.4 [2.8] years; mean duration of training, 9.3 [2.9] years) met the inclusion criteria. Three swimmers were excluded from the statistical analyses for anatomic or technical problems.

Widespread differences between groups were found, with increased radial diffusivity in soccer players (mean, 0.000444 [95% CI, 0.000427-0.000461] mm$^2$/s vs 0.000368 [95% CI, 0.000356-0.000381] mm$^2$/s in swimmers) in the right orbitofrontal white matter, the genu and anterior portions of the corpus callosum, association fibers involving bilateral inferior fronto-occipital fasciculus, bilateral optic radiation, and bilateral anterior cingulum, right anterior, right superior, and bilateral posterior corona radiata, right anterior limb of the internal capsule, right external capsule, and right superior frontal gyrus (Figure 1A).

Axial diffusivity was higher in the corpus callosum in soccer players (mean, 0.00156 [95% CI, 0.00154-0.00158] mm$^2$/s vs 0.00143 [95% CI, 0.00140-0.00146] mm$^2$/s in swimmers;
No significant differences were found for fractional anisotropy or mean diffusivity. Cluster analysis revealed significantly higher radial and axial diffusivity in soccer players; age and years of training had no significant association with diffusivity values (Figure 2). Structural images as read by a neuroradiologist showed no abnormalities.

**Comment**

This study found differences in white matter integrity in a small sample of soccer players compared with swimmers. Although only participants without previous symptomatic concussion were included, advanced DTI revealed widespread increase in radial diffusivity in soccer players, consistent with findings observed in patients with mild TBI, and suggesting possible demyelination.

The etiology of the findings, however, is not clear. One explanation may be the effect of frequent subconcussive brain trauma, although differences in head injury rates, sudden accelerations, or even lifestyle could contribute. Additionally, soccer players showed increased axial diffusivity in the absence of increased radial diffusivity limited to the corpus callosum, possibly resulting from specialized training or neuroinflammation.

Limitations of the study include small sample size, single cross-sectional evaluation, and lack of information regarding functional outcomes. Future studies are needed to confirm the results and elucidate the etiology and effects of white matter alterations in soccer players.

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References


Figure 1. Results of the Tract-Based Spatial Statistics (TBSS) Analysis
The diffusion tensor for each voxel was estimated by the multivariate linear fitting algorithm, and the tensor matrix was diagonalized to obtain 3 pairs of eigenvalues ($\lambda_1$, $\lambda_2$, $\lambda_3$) and eigenvectors. Voxelwise summary parameters included fractional anisotropy, radial diffusivity ($([\lambda_2 + \lambda_3]/2)$, axial diffusivity ($A_1$), and mean diffusivity ($\lambda_1 + \lambda_2 + \lambda_3$). Group analyses were performed using whole-brain TBSS for the following measures of diffusivity: fractional anisotropy, mean diffusivity, radial diffusivity, and axial diffusivity. For all analyses, threshold-free cluster enhancement was used to obtain significant differences between groups at $P < .05$. After accounting for multiple comparisons using the family-wise error rate, the voxels highlighted in red demonstrate significantly increased radial diffusivity and axial diffusivity values for the soccer group compared with swimmers.
Figure 2. Diffusivity Measures for Each Individual
Voxels with a significant group difference as revealed by Tract-Based Spatial Statistics (Figure 1) were merged to a single cluster. Circles indicate individual values, squares indicate mean values, and error bars indicate 95% confidence intervals. Diffusivity measures were obtained for each individual and plotted for the 2 study groups. Linear regression showed no significant association of age or years of training with radial diffusivity ($P = .13$ and $P = .12$, respectively) or for axial diffusivity values ($P = .22$ and $P = .54$, respectively).