

# Microstructure Analysis of Repetitive Traumatic Brain Injury in National Football League Players: A Data-driven White Matter Parcellation Study

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**Background:** Repetitive head impacts, particularly in competitive contact sports such as professional football, can lead to microstructural changes in the brain. Previous research shows that corpus callosum (CC) is frequently damaged in traumatic brain injury. In this study we examined later-life CC microstructure alteration in retired National Football League (NFL) players. Data-driven white matter parcellation was used to discover anatomical structures based on group spectral clustering of tractography. We applied this technique in the current study to Diffusion Tensor Imaging (DTI) obtained from retired NFL players. By comparing former NFL players to an age-matched control group of former elite non-contact sport athletes, we explored the microstructure alteration of CC in retired NFL players.

**Methods:** Seventy-six retired NFL players (56.7 +/- 6.7 years) and a control group of 27 males (57.6 +/- 7.3 years) were investigated on a 3T MR scanner. A data-driven study-specific fiber cluster atlas was created to parcellate the white matter using groupwise fiber tract registration and spectral clustering. Six hundred and fifty fiber clusters were generated from each participant according to the atlas, of which 58 clusters were extracted as CC. T-tests were performed to investigate differences in mean Fractional Anisotropy (FA) of CC between NFL players and athlete controls.

**Results:** In this preliminary data-driven study, we focused on the assessment of the corpus callosum. Through visual inspection, we confirmed that fiber tracts of similar locations and shapes clustered together and that we obtained fiber cluster correspondence across participants. Compared to athlete controls, NFL players demonstrated lower FA in 19 tracts out of 58 extracted CC tracts ( $p < 0.05$ ). These 19 tracts were located in posterior CC, comprised of splenium and isthmus.

**Conclusions:** Data-driven white matter parcellation is a promising method for investigating the microstructure alteration of repetitive brain trauma. NFL players showed decreased white matter diffusion anisotropy in posterior CC, which is one of the CC regions known to experience the greatest shear strain due to head impacts. This finding is in concordance with other studies showing altered diffusivity, brain structure, and connectivity following exposure to repetitive brain trauma.