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Assessing Functional and Structural Connectivity in ex-Professional Athletes

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Synopsis

Recently there has been considerable attention directed towards the increased risk for head injuries that athletes face while participating in high impact sports. Furthermore, there is also heightened interest in asymptomatic sub-concussive blows that possibly lead to long term neurological deficits. The goal of this study was to investigate retired professional athletes, who played at least 4 seasons of Canadian football, using functional connectivity mapping and DTI techniques. When compared to an age matched control population, differences were observed both in functional and structural connectivity, suggesting that even years after retiring the brain still exhibits signs of damage.

Introduction

Mild traumatic brain injury (mTBI), also known as concussion, affects upwards of 1.7 million people each year[1]. A concussive injury often comes with a host of post-concussive symptoms, ranging from fatigue, dizziness and headaches, to depression, irritability, deficits in memory and executive function[2]. In addition to these symptomatic concussive injuries, athletes participating in high impact contact sports (such as Canadian football and ice hockey) are prone to less symptomatic sub-concussive injuries, which may occur in large numbers throughout their career[3]. There is evidence which indicates that these repetitive sub-concussive blows place the athlete at higher risk for developing persistent post-concussive symptoms, structural alterations in the brain as well as neurodegenerative disease such as chronic traumatic encephalopathy (CTE)[4,5]. By applying advanced neuroimaging techniques on a population of retired professional athletes from the Canadian Football League (CFL) who had not been recently diagnosed for a mTBI, we sought to identify the presence of microstructural and functional alterations that may be the result of their high impact professional careers.

Methods

Retired CFL players (n=10, mean age=56±6yrs) having played at least 4 seasons of professional football, and not having recently suffered a mTBI, were recruited for the study. Healthy subjects to serve as controls were sourced from online data repositories (Milwaukee, n=43, age=54±6yrs, ICBM, n=48, age=50±8yrs)[6,7]. A GE MR750 Discovery 3T MRI scanner and 32-channel RF receiver coil was used for scanning the retired athlete group. To assess functional connectivity, resting state functional BOLD data was acquired using an echo planar imaging (EPI) sequence (FOV=22cm, 64x64 matrix, flip angle=90^{o}, TE/TR=35/2000ms, slice thickness=3mm and 175 temporal points). Axial diffusion tensor imaging (DTI) data was acquired using a dual echo EPI sequence (60 non-coplanar directions, TE/TR=87/8800ms, b=1000s/mm2, 122x122 matrix, 70 slices, 2mm thickness, FOV=244mm, ASSET=2, i.e. 2mm isotropic voxels). fMRI data was processed using the MELODIC toolbox within the FMRIB Software package[8]. Thirteen different activation networks were identified using probabilistic ICA. With the FMRIB Diffusion Toolbox (FDT) and Tract-Based Spatial Statistics (TBSS), diffusion tensors were reconstructed, a common registration target was created and each subjects aligned fractional anisotropy (FA) image was projected onto this target. Voxel wise statistics were performed, in addition to ROI analysis of 20 individual structures according to the JHU DTI-based white-matter atlas[9]. For fMRI and DTI data, group differences were probed through permutation testing methods (FSL randomise)[10]. This included the design of a simple general linear model, and application of Threshold-Free Cluster Enhancement (TFCE)[11].

Results

Interrupted functional connectivity within several different networks was observed. More specifically, decreases, relative to controls, were observed within the frontal lobe network, default mode network (DMN), cingulate network and executive control networks ($p<0.05$). Increased functional connectivity versus controls was also found in the DMN ($p<0.05$). DTI TBSS analysis identified deficits in FA in the corticospinal tracts, superior longitudinal fasciculi, thalamic nuclei, forceps minor and uncinate fasciculus ($p<0.05$) (Fig.1). ROI analysis of 22 white matter structures confirmed the visual results of TBSS, with significant decreases in FA (as well as increases in mean diffusivity, MD, and radial diffusivity, RD) observed in the anterior thalamic nuclei, corticospinal tracts, forceps minor, superior and inferior longitudinal fasciculus and uncinate fasciculus ($p<0.05$). Larger differences were observed in right brain white matter structures.

Discussion

Our results suggest that even decades after retiring from participating in professional football, deficits in both structural and functional connectivity appear to remain within the brain. The anomalies we observed appear to have similar characteristics to those noted weeks to months after a mTBI[12]. Decreased FA was observed through TBSS across several white matter structures, whereas general ROI analysis provided similar results (also increased MD and RD), and identified increased deficits on the right side of the brain. Hyper-connectivity of the DMN pathway and recruitment of surrounding structures could be interpreted as compensation for the loss of core white matter microstructural integrity.

Conclusion

There are significant deficits in both resting state functional network connectivity and core microstructural integrity present in retired professional football athletes, even decades after professional play.

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Figures

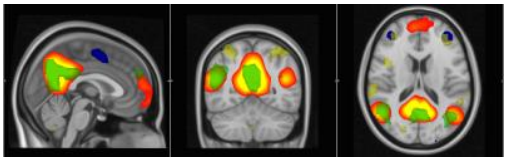

Figure 1. DMN extracted through probabilistic ICA (mean activation map shown in red-yellow and blue-light blue) and overlaid on the MNI space. The player population (n=10, age=55±6yrs) was compared to the Milwaukee control population (n=43, age=54±6yrs). Regions of increased activation in players compared to controls appear in green, and regions of decreased activation appear in yellow ($p<0.05$). Interestingly, the player group demonstrated higher DMN connectivity within the core of the DMN (precuneus cortex and angular gyrus) than the controls, and exhibited decreased DMN connectivity in the frontal poles.

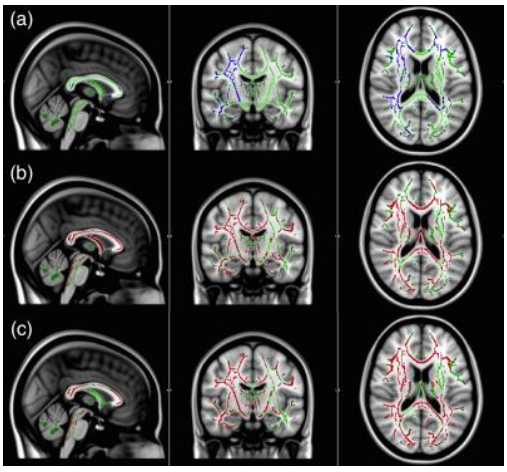

Figure 2. DTI TBSS results shown on a standard MNI 1mm overlay. The green underlay for all images is the mean FA skeleton across all players (n=10, age=55±6yrs) and healthy controls (UCLA DTI, n=48, age=50±8yrs). (a) Blue regions indicate FA values where controls>players ($p<0.05$); (b) Red indicates RD values where players>controls ($p<0.05$); (c) Red shows regions where MD in players>controls ($p<0.05$).

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