Disrupted Anatomical Brain Connectivity in Retired Professional Football Players

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Introduction: An emerging body of evidence suggests that recurrent concussions in contact sports, e.g., wrestling, football, and soccer, may cause delayed brain damages that affect retired athletes [1]. Memory impairments, sleeplessness, and headaches, as well as increased risk of clinical depression and dementia [2][3] were found to be increasing common in retired National Football League (NFL) players. However, the important question of how brain circuitry changes in relation to these functional deficits is still not sufficiently addressed. In this abstract, by taking a graph-theoretic approach that has been shown to be successful in quantifying brain connectivity changes, we report results which will shed light on this matter. We hypothesize that, in retired football players, the brain network is disrupted in association with the functional deficits. We tested this hypothesis by investigating brain networks constructed from brain images of a cohort of players, and compared their network properties with those derived from age- and gender-matched healthy controls.

Methods: For this study, we recruited 34 retired NFL players based on a general health questionnaire and telephone interview of cognitive status (TICS) suggestive of mild to moderate memory impairment over the past year. 20 age- and gender-matched healthy controls were also recruited for comparison. The demographic information is summarized in Table 1. Both T1- and 54-direction diffusion-weighted MR brain images were collected using a 3T Siemens scanner. The graph-based network analysis approach we take models the brain as a complex network, which is composed of a collection of nodes and edges. The nodes represent the anatomical regions of interest (ROIs), and the edges characterize the between-node interaction. The nodes were defined in the diffusion image space by employing the AAL template [4] to parcellate the brain into 78 regions (39 for each hemisphere; ROIs for subcortical regions and cerebellum were omitted). Once ROIs were determined, the edges were defined as the number of fibers passing through each pair of ROIs. To achieve this, diffusion tensor was reconstructed for each subject. A whole-brain streamline fiber tractography was then performed with minimal seed point FA of 0.25, minimal allowed FA of 0.20, minimal fiber length of 20mm and maximal fiber length of 400mm. The resulting fiber tracts were manually examined to ensure the correctness. Finally, a 78x78 connectivity map was constructed for each subject. Since we are only interested in the underlying common connectivity pattern, we averaged the connectivity maps for all subjects in each group to obtain a backbone connectivity map [5].

Table 1. Demographics of Participants.

	Gender	Age* (years)
Retired NFL Players	34 males	64.4±5.8
Healthy Adults	20 males	62.2±5.9

*No significant difference between two groups

Graph-theoretic techniques were used to study the topographical characteristics of brain networks derived from their connectivity matrices. Specifically, we focused on studying network efficiency, normalized clustering coefficient, and normalized path length in relation to network sparsity. Network sparsity was measured as the percentage of the number of existing edge with respect to all possible connections. In this study, network sparsity values used were from 6% to 20%. Network efficiency describes the efficiency of parallel information transfer from each brain region to all other brain regions. Clustering coefficient is the average node degree, while the shortest absolute path length is the average of the shortest absolute path length between each pair of nodes. Random network was generated by rewiring each edge of the existing brain network with 50% probability. Measures derived from the random network were used to normalize the clustering coefficient and path length for verifying the small-world topology. Statistical analysis regarding impaired connections was performed on the fiber count maps of two populations. The fiber number of each pair of regions was compared through two sample t-test and thus only significant connections were retained. To correct for multiple comparison, false discovery rate (FDR) was employed.

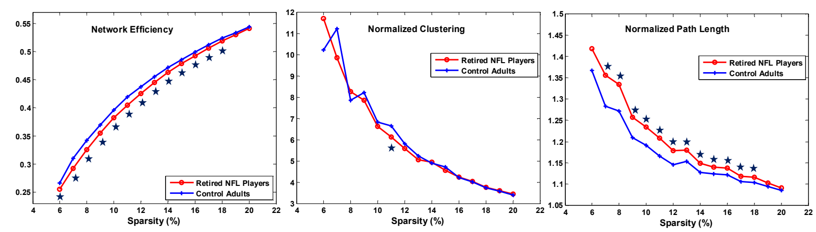

Fig. 1. Network efficiency (A), normalized clustering coefficient (B), and normalized path length (C) as a function of brain network sparsity. Data points marked with a star indicate significant differences (p<0.05) between two groups.

Results: Fig. 1 shows the network efficiency, normalized clustering coefficient, and normalized path length as a function of network sparsity. Network efficiency is significantly reduced in the retired NFL players. The maximum decrease of efficiency is 6% when network sparsity is 7%. Both retired NFL players and control subjects were found to demonstrate small-world topologies. Particularly, both groups demonstrated significant larger clustering coefficient (3.5 in players and 3.4 in controls when sparsity is 20%) after divided with comparable random networks. Similarly, the normalized path length is only marginally longer than that of random networks (both 1.4 in players and controls when sparsity was 6%). Thus, the small-world topologies were conserved in both groups. Meanwhile, significant longer path length was found in players over most network sparsities, suggesting a less economic architecture. Clustering coefficient, however, has no difference between the two populations for most network sparsities.

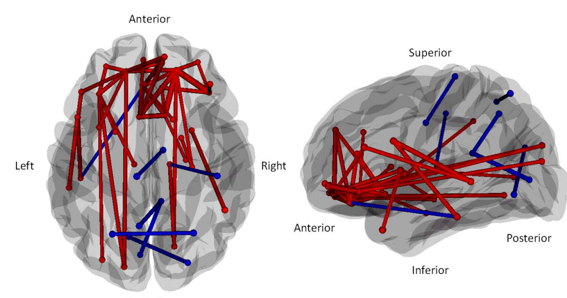

Fig. 2. Inter-regional connections with significantly (p<0.05, FDR corrected) higher number of fibers in controls (red) or in retired NFL players (blue).

Fiber connection for each pair of ROIs was investigated. Connections are shown in Fig. 2 if significant they are at p<0.05 with FDR corrected. A red edge means a lower number of fibers were found in players and a blue edge means otherwise. It can be observed that players show reduced fiber connections in the prefrontal regions, and frontal to temporal, parietal, and occipital regions. Frontal regions demonstrate severe fewer connections with other regions in players. This is in agreement with previous findings that FA decreases in the frontal-occipital fasciculus, genu, sagittal stratum, posterior corona radiate, corticospinal tract, and splenium [3]. Only a few blue edges were found; most are distributed sparsely in parietal and occipital regions.

Discussion: This study yields two findings: 1) Although the brain network of retired football players shows small-world topology, they have significantly lower network efficiency and longer path length. This suggests that their brains are less economically organized for information transfer and processing; 2) Fiber connections involved in the frontal regions are severely affected, suggesting damage of frontal region related fibers and functions. These findings validated our hypothesis that there is some form of disruption in the brain connectivity of retired football players.

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