

Volumetric analysis of cingulum in retired NFL players: Its relationship with NFL experience and subjects' cognitive and functional performance

Hardik Doshi¹, Ira Casson², David Viano^{3,4}, John Woodard⁵, E Mark Haacke³, and Zhifeng Kou³

¹Biomedical Engineering, Wayne State University School, Detroit, mi, United States, ²Department of Neurology, Long Island Jewish Medical Center, New Hyde Park, NY, United States, ³Biomedical Engineering and Radiology, Wayne State University School of Medicine, Detroit, MI, United States, ⁴ProBiomechanics LLC, Bloomfield Hills, MI, United States, ⁵Department of Psychology, Wayne State University School, Detroit, MI, United States

Introduction: There are 1.6-3.8 million sports concussions recorded in United States each year. Especially athletes of American football, Hockey, wrestling and boxing are more prone to concussion. After concussion or mild traumatic brain injury (mTBI), subjects may present a constellation of post concussion symptoms (PCS). Further, chronic traumatic encephalopathy (CTE) has been also reported related with sports concussion. It has been reported that cingulum cortex has been reported as susceptible to injury after trauma ^[1,2]. Cingulum Cortex is an important hub for emotional, memory and attentional processing. The main motivation behind this study is to investigate the effects of multiple traumas on the volumes of anterior and posterior cingulum cortex (ACC & PCC) and determine its effects on Neuropsych and functional test scores.

Data Acquisition and Neuropsych scores: 45 retired National Football League (NFL) players were scanned. The average age of the players was 45.6 ± 9.30 years. Data from each player's playing career including duration of professional, college and high school football career and number of concussions and dings each player had suffered were recorded. The MRI data was acquired on Siemens 1.5 T magnet. The parameters of the T1 sequence were as following: $T_R/T_E = 2000/4.84$ ms, Flip angle = 8 degrees, Bandwidth = 160 Hz/Px, Field of view was 512x512, Slice thickness of 2 mm and resolution was 0.5x0.5x2 mm³. Beck Depression Inventory (BDI_II) and Mini Mental State Examination (MMSE) scores were recorded. BDI_II scores were 9.6 ± 9.25 and MMSE scores were 28.35 ± 1.27 for the group.

Analysis Method: An automatic approach similar to Voxel Based Morphometry (VBM) was adopted as shown in figure 1. All the subjects' images were non-linearly registered to JHU Talairach T1 template using SPM8 ^[5]. A set of predefined ROIs for JHU Talairach T1 template from ROIEditor (Version 1.6, mristudio.org) was used. Once all the subjects are in the standard template space, an inverse transform matrix was applied to all the subjects. Along with that, same matrix was applied to the predefined ROIs in template space. As a result all the subjects as well as ROIs are back into the native space. All the ROIs in native space were compared with respective segmented tissue type to avoid any type of bad registration. IBM analytical tool SPSS 21.0 (SPSS, Inc., Chicago IL) was used for the statistical analysis. Bivariate correlations between volumes of ACC & PCC were checked for any correlation with Neuropsych test scores. In the second part, mediation analysis using "PROCESS" by Dr. Hayes (model 4) was performed to see any mediation effect of volumes of ACC and PCC on the relationship between players' career data and neuropsych scores ^[3].

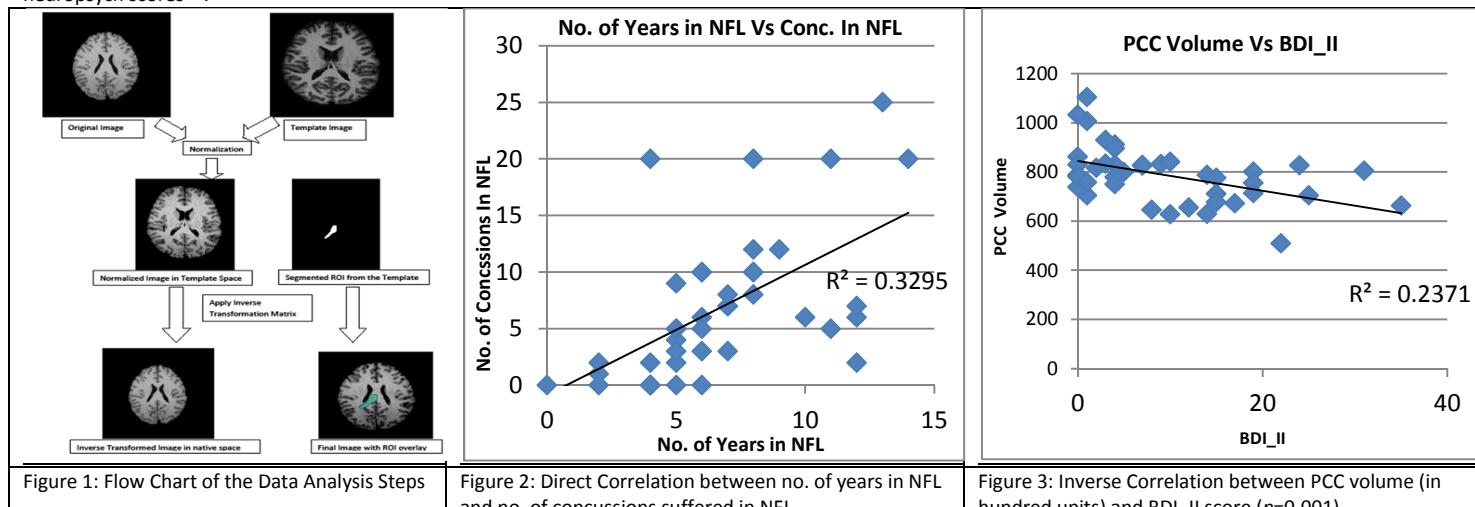


Figure 1: Flow Chart of the Data Analysis Steps

Figure 2: Direct Correlation between no. of years in NFL and no. of concussions suffered in NFL

Figure 3: Inverse Correlation between PCC volume (in hundred units) and BDI_II score ($p=0.001$)

Results: We tested whether PCC volume mediated the effects of duration in NFL on BDI_II scores using bootstrapping, which is appropriate for testing mediation in smaller sample sizes ^[4]. Volume of PCC partially mediates the relationship between number of years played in NFL and BDI_II score (Table 1, Total effect significance $p=0.003$). Volume of ACC did not mediate any correlation significantly. In bivariate correlation analysis, Volume of PCC is negatively correlated with the BDI_II score ($p=0.001$, Figure 3). Volume of ACC shows tendency in inverse correlation with BDI_II score ($p=0.023$). Number of years played in NFL is directly correlated with number of concussions suffered in NFL ($p=0.00001$, Figure 2).

Discussions and Conclusion: Players are susceptible to more concussion when they play for longer duration. Mediation model explains that number of years in NFL has some effects on PCC volume, which in turn affects on depression score. Possible mechanism could be loss of neurons due initial concussion. This would be aggravated by more concussions, ultimately leading to change in volume. Cingulum cortex is emotional hub. So changes in PCC volume may reflect on depression score. Also ACC and PCC volumes have inverse correlation with BDI_II score. This also strengthens the hypothesis. This is in line with few earlier studies suggesting that more detailed research is required to look into the role of cingulum cortex in CTE.

	Effect Size	Standard Error	p Value
Total Effect	1.27	0.41	0.003
Direct Effect	0.93	0.4	0.026
Indirect Effect	0.34	0.18	

Table 1: Output of the mediation analysis model including No. of years in NFL (input), PCC volume (Mediator) and BDI_II score (Output)

References: [1] C. L. MacDonald et al., *N. Engl. J. Med.*, 2011, 364, 2091. [2] S. N. Niogi, et al, *AJR Am. J. Neuroradiol.*, 2008, 29, 967. [3]<http://www.afhayes.com/introduction-to-mediation-moderation-and-conditional-process-analysis.html>. [4] Shrout, P. E., & Bolger, N. (2002). *Psychological Methods*, 7(4), 422-445. [5] <http://www.fil.ion.ucl.ac.uk/spm/software/spm8>.