

# Frontal Lobe Interhemispheric Connectivity Changes Associated with a Season of High School Football

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## Purpose

The goal of this study is to determine if cumulative head impacts over a season of high school football has an effect on frontal lobe interhemispheric connectivity.

## Materials

Thirty football players without history of prior concussion (age: 14-18, gender: male) from a local high school team participated in the study. For each subject, biomechanical data was acquired using the head impact telemetry (HIT) system during practices and games. The HIT system records kinematic data from head impacts using sensors embedded in the helmet. All subjects participated in structural and resting-state functional magnetic resonance imaging (fMRI) data acquisition including pre and post-season sessions. Images were obtained using a Siemens Trio 3 Tesla scanner. 6 minutes of resting-state fMRI was acquired in each subject (echo planar imaging acquisition, TE = 5 ms, TR = 20 ms, flip angle =40°, matrix = 64×64).

## Methods

The biomechanical metric utilized to capture each player's head impact exposure was the risk weighted cumulative exposure (RWE<sub>CP</sub>)<sup>1</sup>. This metric is defined as the combined risk of concussion calculated from the peak resultant linear and rotational acceleration for each impact. fMRI data preprocessing was performed using SPM8. For each subject, fMRI data was motion corrected, normalized to MNI space and band-pass filtered at 0.01 - 0.1 Hz. The 6 rigid-body motion parameters, as well as parameters for the white matter signal, global mean signal, and cerebrospinal fluid signal were regressed from the time series. Interhemispheric connectivity between regions was determined using frontal lobe regions defined in the AAL atlas, including: frontal superior, frontal superior orbital, frontal midline, frontal middle orbital, frontal inferior operculum, frontal inferior triangularis, and frontal inferior orbital. For each subject, connectivity differences between post and pre-season for each ROI were computed.

In order to investigate the relationship between functional connectivity changes and RWE<sub>CP</sub> a multiple regression analysis was performed using a linear model of RWE<sub>CP</sub> vs. pre-post difference in functional connectivity. Body mass index (BMI), time between scans, and participant age were included in the model as confounders. Significance was determined using a bootstrap analysis with 1000 resamplings. None of the players included in the study experienced clinical concussion during the season.

## Results

Two regions including the frontal mid and the frontal inferior triangular areas were identified as significant ( $p < 0.05$ ). There were several other areas that were close to achieving statistical significance (frontal superior orbital and frontal middle orbital). These areas all demonstrated decreases in connectivity. Table 1 shows the results obtained using multivariate linear regression analysis and the bootstrapping multiple linear regression analysis for RWE<sub>CP</sub> vs. pre-post season difference of functional connectivity in frontal lobe structures.

Table 1. Statistical results of univariate and multivariate linear regression analysis for RWE<sub>CP</sub> vs. pre-post season difference of functional connectivity in frontal lobe structures significant relationships are identified by bolded text.

Interhemispheric connectivities	T-stat and P-value without bootstrapping				P-value with bootstrapping
	Univariate Model	Multivariate Model			
Frontal superior	-0.81	0.4225	-1.07	0.2970	0.292
Frontal superior orbital	-1.75	0.0906	-2.00	0.0568	0.075
<b>Frontal midline</b>	<b>-1.88</b>	<b>0.0712</b>	<b>-2.28</b>	<b>0.0315</b>	<b>0.033</b>
Frontal middle orbital	-2.01	0.0545	-1.77	0.0897	0.063
Frontal inferior operculum	0.41	0.6821	0.15	0.8818	0.861
<b>Frontal inferior triangularis</b>	<b>-2.02</b>	<b>0.0528</b>	<b>-2.68</b>	<b>0.0129</b>	<b>0.014</b>
Frontal inferior orbital	-0.90	0.3768	-0.94	0.3560	0.374

## Discussion and Conclusion:

These results indicate changes in connectivity of frontal structures in non-concussed subjects during a single season of football. This is in accordance with several studies which have shown significant changes in frontal lobe interhemispheric connectivities<sup>2,3</sup> associated with mTBI. These findings add to a growing body of literature that cumulative subconcussive sports-related impacts may have an effect of the brain and brain function.

## References

1. Urban JE, Davenport EM, Golman AJ, Maldjian JA, Whitlow CT, Powers AK, Stitzel JD, et al. Head impact exposure in youth football: high school ages 14 to 18 years and cumulative impact analysis. *Annals of Biomedical Engineering*. 2013; 41 (12): 2474–2487.
2. Slobounov SM, Gay M, Zhang K, Johnson B, Pennell D, Sebastianelli W, Horovitz S, Hallett M, et al. Alteration of brain functional network at rest and in response to YMCA physical stress test in concussed athletes: RsfMRI study. *NeuroImage*. 2011; 55: 1716–1727.
3. Johnson B, Zhang K, Gay M, Horovitz S, Hallett M, Sebastianelli W, Slobounov S, et al. Alteration of brain default network in subacute phase of injury in concussed individuals: Resting-state fMRI study. *NeuroImage*. 2012; 59: 511–518.