CHANGES IN RESTING STATE MRI NETWORKS FROM A SINGLE SEASON OF FOOTBALL DISTINGUISHES CONTROLS, LOW, AND HIGH HEAD IMPACT EXPOSURE

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ABSTRACT

Sub-concussive asymptomatic head impacts during contact sports may develop potential neurological changes and may have accumulative effect through repetitive occurrences in contact sports like American football. The effects of sub-concussive head impacts on the functional connectivity of the brain are still unclear with no conclusive results yet presented. Although various studies have been performed on the topic, they have yielded mixed results with some concluding that sub concussive head impacts do not have any effect on functional connectivity, while others concluding that there are acute to chronic effects. The purpose of this study is to determine whether there is an effect on the functional connectivity of the brain from repetitive sub concussive head impacts. First, we applied a model free group ICA based intrinsic network selection to consider the relationship between all voxels while avoiding an arbitrary choice of seed selection. Second, unlike most other studies, we have utilized the default mode network along with other extracted intrinsic networks for classification. Third, we systematically tested multiple supervised machine learning classification algorithms to predict whether a player was a non-contact sports youth player, a contact sports player with low levels of cumulative biomechanical force impacts, or one with high levels of exposure. The 10-fold cross validation results show robust classification between the groups with accuracy up to 78% establishing the potential of data driven approaches coupled with machine learning to study connectivity changes in youth football players. This work adds to the growing body of evidence that there are detectable changes in brain signature from playing a single season of contact sports.

Index Terms**—** machine learning, sub-concussive head impact, resting state networks, youth football

1. INTRODUCTION

Understanding the association between repetitive sub-concussive head impacts in youth (ages 9-13) football players and healthy brain development is arousing growing concern, and yet the association is challenging to understand [9][3]. Although, professional and collegiate football has been the subject of intensive study, players at the youth level have received little to no attention despite constituting the clear majority (70%) of all football players [4]. Recent resting state functional MRI (rs-fMRI) studies revealed that changes in resting state networks can corresponds to pathophysiological changes. Indeed, there is growing evidence in the ability of functional neuroimaging (fMRI, MEG) to detect subtle changes in the functional connectivity due to sub-concussive impacts in youth football [11] [7].

TBI often affects the visual system; players sustaining a concussion frequently complain of sensitivity to visual stimuli. Therefore, we hypothesized that the visual networks would contain discriminatory information. Recently, Zhu David c. et al [13] demonstrated the ability of functional connectivity of the default mode network (DMN) to serve as a potential biomarker to monitor dynamic changes in brain function after sports related concussion. Neurophysiological changes in youth football athletes with exposure to sub-concussive impacts have also been reported with changes in the DMN [1]. There is increasing evidence that the hippocampus, a core region for human memory, should be included in the DMN. Since traumatic brain injury (TBI) often compromises memory we also hypothesized that the DMN would have telltale features that characterize injury level.

Most previous studies use seed based approaches to detect changes in specific resting state network such as the DMN. Such results can critically depend on seed placement precision, while the location of the networks in the brain across subjects is variable. Therefore, we propose to use a data driven, model free approach coupled with the training of a machine learning classifier to characterize the association between cumulative head impact exposure categories (little to no exposure, light exposure, heavy exposure), and functional connectivity measured from resting state network extraction. The accuracy of our classification is an indicator of the level of association and the features used by the classifier reveal the aspects of functional brain connectivity most effected from the exposure.

2. MATERIALS AND METHODS

2.1 Dataset

The data used in this study is a subset of that measured in an ongoing IRB-approved iTAKL study [9] of the effect of repetitive sub-concussive head impacts in youth football players. During all practices and games, the football player is instrumented with the HIT system [6], which uses accelerometers mounted inside the helmet to measure skull

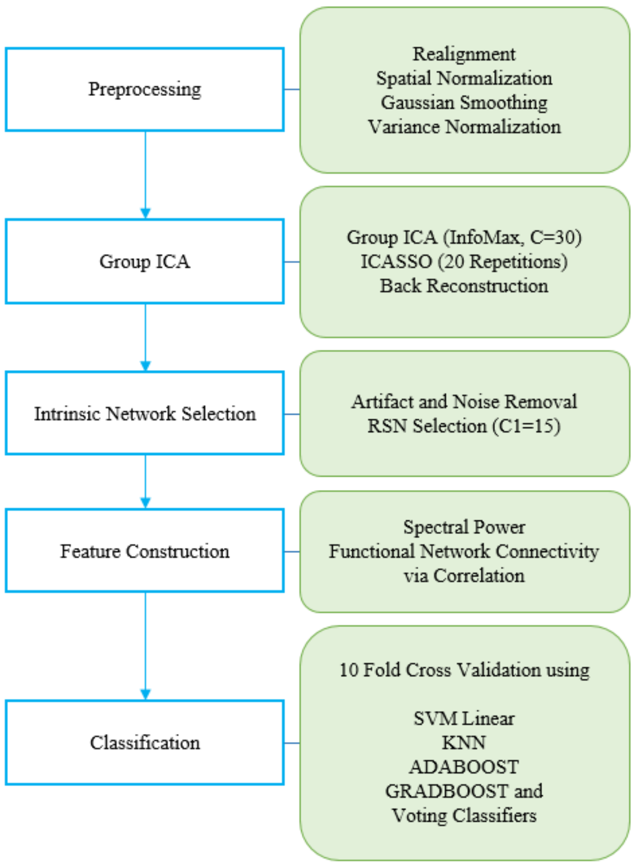

Figure 1 : Schematic of analysis, feature selection and classification

acceleration and infer impact location. The risk of concussion was computed from the combined probability risk function calculated for each impact and summed to compute each football player's risk of concussion-weighted cumulative exposure (RWE_{CP}) for the season [12]. Thirteen players with the highest RWE and 13 players with the lowest RWE were selected as our heavy and light head impact exposure football groups respectively. Thirteen noncontact athlete control are also included to further compare group differences. All players (ages 9-13) including both non-contact sport controls (N=13) and football players (N=26) receive resting-state functional magnetic resonance imaging (rs-fMRI) pre- and post-season to measure brain health. The rs-fMRI measures the BOLD signal from which we can infer neuronal activation patterns, intrinsic functional architecture and overall health of the brain. The MRI data were acquired on a Siemens 3T Scanner. The rs-fMRI scans were acquired with an echo planar sequence covering the entire brain (FOV = 224 x 224, flip angle = 90, TR = 2 sec, TE = 25 msec) over a 6-minute period. The participants are instructed to keep their eyes open fixating at a point. The fMRI data was preprocessed using an in house developed processing pipeline that includes steps for motion correction, spatially smoothing and spatial normalization to a common atlas space(MNI) inorder to facilitate group ICA, Fig. 1.

2.2 Group ICA and intrinsic network selection

After preprocessing the resting state fMRI, thirty (30) independent components were extracted using temporal concatenation group spatial ICA was applied to the pre- and post-season data from all 39 subjects performed for all subjects at once. This entails reshaping all fMRI volumes into a row vector, time concatenating all subject data, and data reduction using PCA. The components, consist of pairs of a group spatial map and a time course, were extracted using InfoMax ICA algorithm. Subject specific spatial maps and time courses are constructed using back-reconstruction with the GIFT toolbox [4][6]. Our overall processing pipeline is shown in Fig. 1. We applied group ICA for consistent ordering of the components for all subjects. We identified the 15 components of neurophysiological origin, and discarded the noise and artifact components. Representative examples including two neurophysiological group components and one noise component are shown in Fig. 2. The neurophysiological components include: the default mode network (DMN), visual medial (VM), visual lateral, fronto-parietal network are identified based on their stability across several runs using ICASSO, power ratio, and by manual inspection. [2] [11].

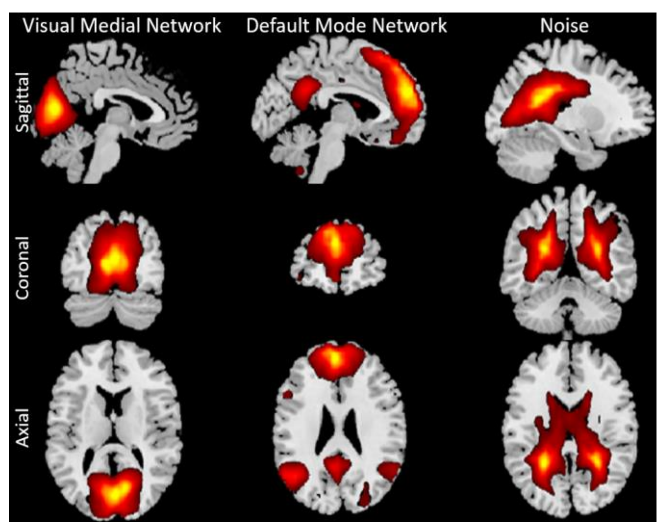

Figure 2: Mean Group Components, Left: Visual medial, Middle: Default Mode Network, Right: Noise (CSF)

2.3 Feature construction and classifier training

We constructed two types of features. For the first type, we converted the subject specific time course of each network (component) into a power spectrum through power spectral decomposition. Such a frequency based feature allows comparisons of time based activity patterns across subjects when there is no inherent temporal alignment. For the second type, we computed the Pearson correlation coefficient between pairs of time courses of the networks extracted for each subject. These pairwise values were used to populate a functional network connectivity (FNC) matrix. Our power spectrum feature vector consisted of the power at 129 frequency bins while our FNC feature vector was comprised of 105 features from the upper triangle values of the FNC correlation matrix. The feature vectors from the pre-season of each subject were calculated and subtracted from the post season features for baseline correction. This allowed us to focus on changes of the intrinsic network due to a single season of football. The power spectra and FNC feature for a single subject is shown in Fig. 3.

Next we systematically trained multiple classifiers to distinguish between the 3 subject groups using each feature type. The classifiers included: linear SVM, K-nearest neighbors, Adaboost, Gradboost and a Voting classifier (that combines all of these) to classify a subject into one three groups: controls, light impact exposure and heavy impact exposure [10]. We use nested 10-fold cross validation and grid search to select the best parameter for each classifier and obtain an unbiased estimate of classifier accuracy.

3. RESULTS

Overall, we observe high prediction accuracy separating pairs of groups. The linear SVM tended to perform well relative to the other classifiers.

3.1 Classification based on power spectrum

The delta power spectrum of the DMN provided a classification accuracy of 78% between control vs high and 75% for low vs high groups, shown in Table 1. Using the ΔPSD features, the low exposure group was not distinguishable from controls; classifier accuracy at near chance 50%. The power spectrum of the visual medial (VM) network showed similar accuracies for control vs high and low vs high: 78% and 68% respectively using linear SVM classifier (Table 1). The accuracy of the DMN and visual medial power spectrum was robust in classifying high exposure players from the other two groups.

3.2 Classification based on FNC

Using single season change in functional network connectivity features (ΔFNC) yielded a somewhat different results. In particular, this enabled discrimination between control versus low exposure players. ΔFNC features enabled a classification accuracy of 75% for control vs high exposure players with Adaboost and 65% for control vs light when using linear SVM classifier. The ΔFNC based classification accuracies between the groups and the various classifiers are shown in Table 1.

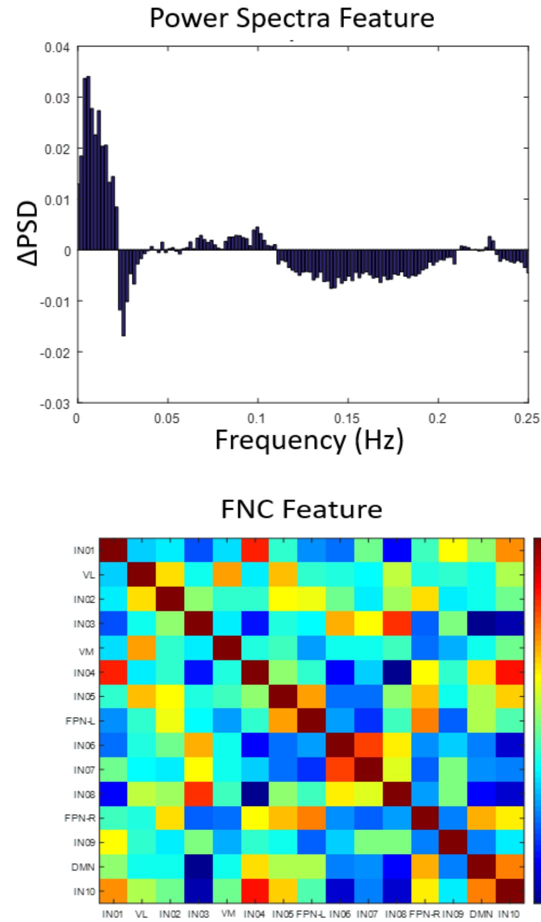

Figure 3: Power spectra (top) and functional network connectivity (bottom) feature for a single subject

Table 1: Classification accuracies for DMN, visual power spectra and functional network connectivity features

Classifiers	DMN Power Spectra			Visual Medial Power Spectra			FNC		
	Control vs HI	Control vs LI	HI vs LI	Control vs HI	Control vs LI	HI vs LI	Control vs HI	Control vs LI	HI vs LI
SVM (%)	**78**	35	**75**	**78**	57	68	65	**65**	15
KNN (%)	65	53	60	50	55	**72**	47	42	35
Adaboost (%)	62	50	72	70	53	70	**75**	57	17
Gradboost(%)	**78**	30	60	65	50	62	68	45	38
Voting (%)	72	35	65	65	53	68	72	60	24

HI -Heavy Impact; LI- Low Impact; Function network connectivity

4. DISCUSSIONS

We hypothesized that there is a discernable difference in the activation time course of the resting state networks and their connectivity between network. The DMN is implicated in memory as it is often found to be tightly correlated with hippocampal activity. Our classification results tend to support our hypotheses that the DMN and visual networks would contain telltale information about brain injury. The high classification accuracy using the DMN and VM power spectra features demonstrates their ability to capture intrinsic network changes of high cumulative head impact exposure players with respect to the other two groups. This suggests that these features capture tangible differences in brain connectivity that uniquely identify high exposure players. We also tested the other networks but they did not yield classification accuracies above chance.

The DMN and VM power spectrum features may contain similar information. This would explain the similar classifier performance obtained using either alone or both together. The FNC features are robust for classifying control subjects against the players regardless of exposure levels. This result shows the ability of the FNC features of resting state networks to capture changes due to playing a contact sport. The FNC feature yields results that show a stronger, difference between the control group (non-contact sport athlete) and the youth football players and a smaller difference between the two groups of football players. The other networks didn't show significant accuracies between the groups.

5. CONCLUSION

We coupled a model-free, data-driven approach with machine learning classification to check for an association between intrinsic network connectivity differences between youth athletes and their cumulative risk of concussion from repeated sub-concussive head impacts. We examined whether resting network based features can discriminate the youth football players with respect to their cumulative sub concussion head impact exposure. Time course power spectrum and FNC between the pairs of components from group ICA were computed and used to train several classifiers using 10-fold cross validation. Power spectra of the default mode network and the visual medial network provided tangible difference in the network changes and thus, robust classification between high exposure and the other groups. This, supports the hypothesis that intrinsic network changes occur as a result of sub-concussive head impacts. Also the improvement of the classification accuracy using the ΔPSD from low RWE to high RWE compared with controls suggested the difference in injury increases as the level of exposure increases which corroborates the increasing white matter integrity loss with increasing RWE as shown in [9].

We have studied the changes in power spectra density of the time courses of the DMN and visual medial networks between control and the players group. We have also, studied the changes in connectivity between all canonical resting state functional networks. The classifier we construct using these features predicts well the categories of cumulative head impact exposure This result establishes the potential use of these features to study changes in the intrinsic network connectivity of players with respect to repeated head impacts.

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