

G R E A T P L A I N S IDeA Clinical and Translational Research

Brain Connectivity for Prediction of Lesion Site in Sports-Related Concussion

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PURPOSE

Each year, thousands of adolescents and young adults experience sportsrelated concussion (SRC), a form of mild traumatic brain injury (mTBI). Although a mild injury by definition, the consequences can be profound if the injury is not identified and managed properly.

There is <u>critical need</u> to identify reliable biomarkers of injury that afford better understanding of injury severity, with the goal of informing more personalized treatment (e.g., return to play decisions) and promoting better outcomes.

BACKGROUND

SRC and mTBI are significant public health problems with well-documented variability in functional outcome.

- Cognitive dysfunction immediately post-injury has not been predictive of outcome.
- Disruption of structural and functional brain networks (resting-state MRI; rsfMRI, and diffusion tensor imaging; DTI) has been shown to be a potential biomarker of promise^{1,2}, associated with neurocognitive dysfunction and poor functional outcomes³⁻⁵.
 - Decreased white matter integrity
 - Imbalance and inefficiency within and between functional networks

Brain lesion location outweighs lesion size in predicting functional outcome.^{6,7}





Lesions in a brain hub (i.e., a brain region that is both strongly intraconnected in its own networks and inter-connected with other networks) are associated with significantly worse functional outcome.⁸

AIMS

Aim 1: Characterize <u>baseline (pre-season)</u> brain connectivity in student-athletes at high risk for SRC.

Prediction: There will be individual differences in brain connectivity at baseline, and these . differences will be useful for predicting cognitive function (speed and memory) at baseline.

Aim 2: Identify <u>changes in brain connectivity</u> pre- and post-injury, and post-recovery. <u>Prediction:</u> Connectivity changes following SRC will be observed relative to baseline (e.g., white matter tract health will decrease acutely, altering structure in functional brain networks), but will improve in the weeks post-injury to baseline-like structure. Further, injury at hubs will be associated with more acute connectivity changes.

Aim 3: Identify changes in brain connectivity and cognitive processing in an effort to predict clinical outcome.

<u>Prediction:</u> We will be able to use brain connectivity to predict cognitive function post-injury and post-recovery, providing neural biomarkers of readiness to return to play. Further, we predict that injury at hubs will be associated with worse functional outcome.

Participants (N=110 football players) will complete • Follow-up in the event of SRC injury:

Shown to be reduced in concussed athletes (see 9 for review of validity studies).



Fig. 2: A graph theory model showing 5 brain regions, their connections, and a matrix representing

Fig. 3: Data from previous work using SVR to predict brain maturity. (A) Functional correlations positively (orange) and negatively (green) correlated with age. (B) Brain regions contributing to these connections.

FUTURE DIRECTIONS

Translational benefit of this project is its potential impact on practice. • There has been no clear biomarker for recovery, which has limited progress in developing tools for identification, management and treatment.

- management across the country.
- concern and debate.
- the basis for a large NIH grant.

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Identifying a sensitive biomarker will provide a criterion against which to validate current and future tools that might be more cost-effective and easily administered, changing the face of concussion evaluation and

Establishing a sensitive protocol will allow for longitudinal monitoring that is necessary for answering questions about the longer-term health and well-being of athletes in contact sports – an area of considerable

This project is consistent with the goals for research set out in the Institute of Medicine's Report on Sports Concussion in Youth and is a high-priority for NIH funding. When completed, these data will serve as

References

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