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

Maital Neta¹, Jennifer Mize Nelson¹, Matthew Garlinghouse², Arthur Maerlander¹, Steven E. Petersen³, and Cary R. Savage¹
¹University of Nebraska-Lincoln, Lincoln, NE; ²University of Nebraska Medical Center, Omaha, NE; ³Washington University in St. Louis, St. Louis, MO

PURPOSE
Each year, thousands of adolescents and young adults experience sports-related 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 critical need 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, associated with neurocognitive dysfunction and poor functional outcomes.
- Decreased white matter integrity
- Imbalance and inefficiency within and between functional networks

Brain lesion location outweighs lesion size in predicting functional outcome.

AIMS
Aim 1: Characterize baseline (pre-season) 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 changes in brain connectivity pre- and post-injury, and post-recovery.

Prediction: 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.

Prediction: 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.

APPROACH
Participants (N=110 football players) will complete the study within the 3T Siemens Skyra.
- At baseline (pre-season)
- Follow-up in the event of SRC injury:
  - 24-48 hours post-injury
  - At return to play

These data will be used to determine the extent to which brain connectivity is associated with individual differences in functional outcome.
- Neuropsychological testing is considered a gold standard of functional outcome in clinical work and neuroimaging studies.

Structural brain connectivity (brain wiring):
- DTI (single-shot echo planar)

Fig. 1: FSL TBSS white matter tracts displayed on a template brain.

Functional brain connectivity:
- rsfMRI (multiband echo-planar)
- Graph theory for characterizing complex brain connectivity patterns

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

Identification of structural connectome will be paired with rsfMRI to assist with identification of hubs and predicting functional outcome.

These data will be used to determine the extent to which brain connectivity is associated with individual differences in functional outcome.
- Neuropsychological testing is considered a gold standard of functional outcome in clinical work and neuroimaging studies.

Structural brain connectivity (brain wiring):
- DTI (single-shot echo planar)

Fig. 1: FSL TBSS white matter tracts displayed on a template brain.

Functional brain connectivity:
- rsfMRI (multiband echo-planar)
- Graph theory for characterizing complex brain connectivity patterns

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

Identification of structural connectome will be paired with rsfMRI to assist with identification of hubs and predicting functional outcome.

These data will be used to determine the extent to which brain connectivity is associated with individual differences in functional outcome.
- Neuropsychological testing is considered a gold standard of functional outcome in clinical work and neuroimaging studies.

Structural brain connectivity (brain wiring):
- DTI (single-shot echo planar)

Fig. 1: FSL TBSS white matter tracts displayed on a template brain.

Functional brain connectivity:
- rsfMRI (multiband echo-planar)
- Graph theory for characterizing complex brain connectivity patterns

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

Identification of structural connectome will be paired with rsfMRI to assist with identification of hubs and predicting functional outcome.

These data will be used to determine the extent to which brain connectivity is associated with individual differences in functional outcome.
- Neuropsychological testing is considered a gold standard of functional outcome in clinical work and neuroimaging studies.

Structural brain connectivity (brain wiring):
- DTI (single-shot echo planar)

Fig. 1: FSL TBSS white matter tracts displayed on a template brain.

Functional brain connectivity:
- rsfMRI (multiband echo-planar)
- Graph theory for characterizing complex brain connectivity patterns

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

Identification of structural connectome will be paired with rsfMRI to assist with identification of hubs and predicting functional outcome.

These data will be used to determine the extent to which brain connectivity is associated with individual differences in functional outcome.
- Neuropsychological testing is considered a gold standard of functional outcome in clinical work and neuroimaging studies.

Structural brain connectivity (brain wiring):
- DTI (single-shot echo planar)

Fig. 1: FSL TBSS white matter tracts displayed on a template brain.

Functional brain connectivity:
- rsfMRI (multiband echo-planar)
- Graph theory for characterizing complex brain connectivity patterns

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

Identification of structural connectome will be paired with rsfMRI to assist with identification of hubs and predicting functional outcome.

These data will be used to determine the extent to which brain connectivity is associated with individual differences in functional outcome.
- Neuropsychological testing is considered a gold standard of functional outcome in clinical work and neuroimaging studies.

Structural brain connectivity (brain wiring):
- DTI (single-shot echo planar)

Fig. 1: FSL TBSS white matter tracts displayed on a template brain.

Functional brain connectivity:
- rsfMRI (multiband echo-planar)
- Graph theory for characterizing complex brain connectivity patterns

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

Identification of structural connectome will be paired with rsfMRI to assist with identification of hubs and predicting functional outcome.