

# The Relationship Between the Functional Connectivity of the Dorsal Amygdala and Cognitive Control Centers and Cognitive Functioning in Traumatic Brain Injury

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## Introduction

- Resting state functional magnetic resonance imaging (rsfMRI) is a commonly used tool to study changes in task-independent brain activity following traumatic brain injury (TBI).
- Functional connectivity (FC) is measured using rsfMRI by correlating the blood oxygen level dependent (BOLD) timeseries within and between anatomically distinct brain regions.
- rsfMRI FC has been used to identify biomarkers that may predict outcomes following brain injury.
- Given the long-lasting and debilitating cognitive dysfunction experienced by many individuals following TBI, we evaluated the relationship between the FC of brain regions associated with cognitive control and cognitive functioning in individuals with TBI and healthy controls (HCs).

## Methodology

### Sample

- N= 32 individuals with subacute mild to severe TBI and N=20 HCs
  - N=2 subjects (1 TBI, 1 HC) were excluded for failing to meet QA checks

### Measures

- rsfMRI Seed-to-Voxel FC with dorsal amygdala (dAmy) defined as the seed of interest
- Automated Neuropsychological Assessment Metrics (ANAM) Total Score and Subtests
  - Neural Processing (SR1, SR2)
  - Working Memory (MATH)
  - Associative Memory (CS)
  - Visual Spatial Memory (MTS)
  - Processing Speed (PRT)
  - Delayed Memory (CSD)

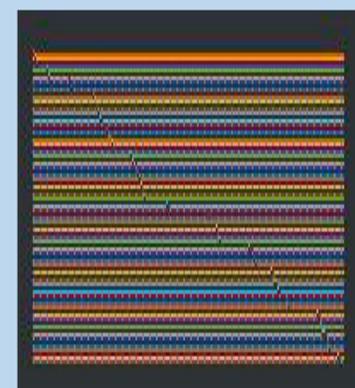
### Data Analysis

- Independent sample t-tests or Mann-Whitney U tests, as appropriate, and Chi-Squared tests were conducted to assess group differences.
- Pearson correlations were calculated to test relationships between the FCs between brain regions that were significantly different between groups and cognitive functioning as measured by the ANAM.

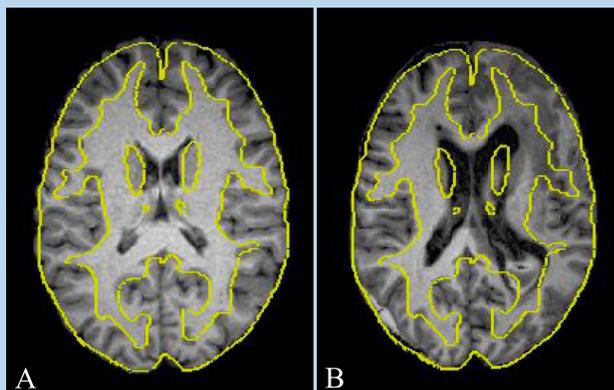
### Imaging Quality Analysis

- Exclude subjects with > 15% invalid scan volumes
- Exclude subjects with > 1.00 mm of mean motion
- Characterize fit of Montreal Neurological Institute (MNI) template on structural and functional MRIs
- Characterize brain structure (e.g. lesions, atrophy, mass effect, etc.)

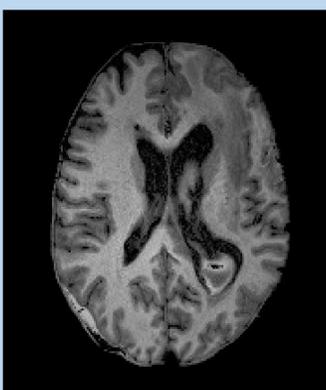
**Figure 1.** Excluded subject with 52 (30.41%) scrubbed fMRI volumes.



**Figure 2.** A. Subject with good MNI fit. B. Subject with poor MNI fit.



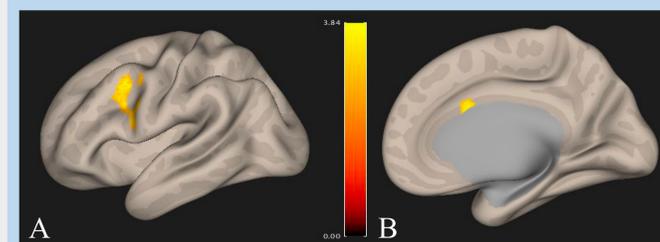
**Figure 3.** T1 Brain MRI from TBI subject with a R frontoparietal lesion and R ventricular enlargement



## Results

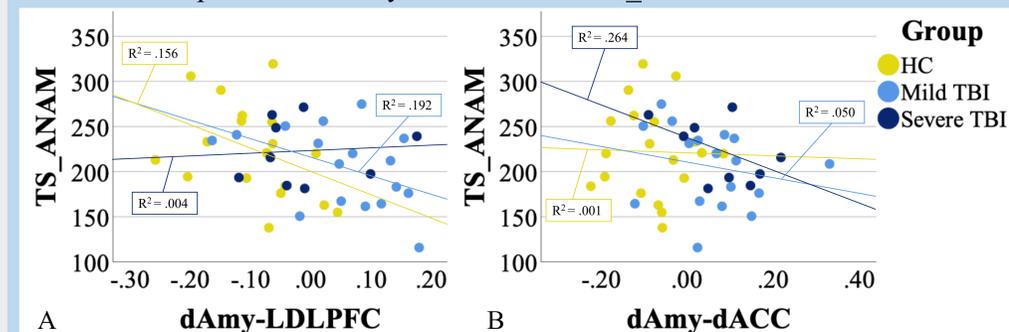
**Table 1. Group Differences**

	TBI (N=31)	HC (N=19)	p-value
Mean Age (SD)	34.42 (14.86)	36.53 (18.97)	.880
Sex	8F, 23M	8F, 11M	.349
Median Glasgow Coma Score (Range)	13.5 (3-15)	---	---
Mean Days Post-Injury	33 (6-107)	---	---
Glasgow Outcome Scale Extended (GOSE)	8 (2-8)	---	---
Code Substitution (CS)	48.51 (12.90)	52.78 (14.92)	.310
Code Substitution Delayed (CSD)	41.19 (18.24)	48.53 (20.35)	.223
Matching to Sample (MTS)	32.43 (9.93)	33.93 (11.91)	.647
Mathematical Processing (MATH)	22.45 (10.36)	22.42 (8.46)	.485
Procedural Reaction Time (PRT)	102.03 (16.83)	101.91 (18.64)	.894
Simple Reaction Time 1 (SR1)	214.36 (45.50)	225.52 (49.12)	.268
Simple Reaction Time 2 (SR2)	219.17 (47.85)	226.34 (36.06)	.535
Total ANAM Score (TS_ANAM)	210.76 (41.07)	222.62 (50.34)	.389
dAmy-LDLPFC FC	.05 (.10)	-.08 (.08)	< .0005
dAmy-dACC FC	.05 (.10)	-.09 (.08)	< .0005



**Figure 4.** A. FC between the dAmy seed and left dorsolateral prefrontal cortex (LDLPFC) voxel cluster was significantly greater in individuals with TBI than HCs. B. Greater FC between the dAmy seed and dorsal anterior cingulate cortex (ACC) voxel cluster in individuals with TBI compared to HCs was trending towards significance.

**Figure 5.** A. Relationship between dAmy-LDLPFC FC and TS\_ANAM. B. Relationship between dAmy-dACC FC and TS\_ANAM.



**Note.** Significant correlation between the TS\_ANAM and dAmy-LDLPFC FC was driven by ANAM subtests SR1, measuring processing and efficiency, MATH, measuring working memory, and CS, measuring associative learning and efficiency.

## Conclusion

- The present study found greater FC between the dAmy-LDLPFC and dAmy-dACC in individuals with TBI compared to HCs, suggesting an effect of TBI on between network connectivity in these regions.
- These data support the amygdala hijacking model of cognitive dysfunction, with hyperconnectivity between these regions associated with worse performance on cognitive assessment, particularly measures of cognitive control.