Deficits in Visual System Functional Connectivity after Blast-Related Mild TBI are Associated with Injury Severity and Executive Dysfunction

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Background

Traumatic Brain Injury (TBI) is known as the "signature wound" of recent military operations. Approximately 15–25% of American service members deployed to Iraq or Afghanistan reported mild TBI (mTBI), with 75% of these incidents involving an explosive blast. Visual processing problems and cognitive dysfunction are common complaints following mTBI. Little is known, however, about the relationship between these complaints. A better understanding of the effects of blast mTBI on functional relationships between visual pathways and higher order regions of the brain associating vision and cognition could serve as a foundation for understanding and treating visual and cognitive symptoms associated with mTBI.

Methods

Participants were 131 veterans of Operations Enduring Freedom and Iraqi Freedom (Age: M=32.9±8.2 years). Symptoms of blast-related mTBI were assessed using the Minnesota Blast Exposure Screening Tool (MN-BEST). All participants underwent a 6-min eyes-closed resting-state fMRI scan (Siemens TIM Trio 3T scanner). We examined functional connectivity (FC) of four seeds within the visual system: lateral geniculate nucleus (LGN), primary visual cortex (V1), lateral occipital gyrus (LO), and fusiform gyrus (FG). *Individual-Level Analysis.* A multiple regression analysis between the extracted average time-series from each seed and all voxels in the brain generated a map with a correlation coefficient for each voxel, for each individual, for each seed. Correlation coefficients were transformed to standardized *z*-values, which showed degree of correlations with corresponding seed. *Group-Level Analysis:* Linear regression analyses were conducted to regress scores from the MN-BEST representing blast TBI severity on the standardized z-maps (for each seed separately). Resulting *F*-statistic maps were used to identify brain regions in which individual FC variability was related to individual severity of blast TBI. A threshold/cluster method derived from Monte Carlo simulations was applied to control for false positive findings. Clusters that survived correction for multiple comparison were identified. Correlations between FC and performance on the Stroop Color-Word and Trail-Making B tasks, visual cognitive tasks requiring executive and inhibitory functioning, were performed across those participants with available behavioral data (n=95).

Results

Linear Regression results showed that severity of blast TBI was negatively correlated to FC between: (A) LGN seed and (i) medial frontal gyrus, (ii) lingual gyrus, and (iii) right thalamus; (B) V1 seed and precuneus; (C) LO seed and middle frontal gyrus; (D) FG seed and (i) superior and medial frontal gyrus, and (ii) left middle frontal gyrus. Further, higher FC between visual network regions and frontal cortical regions was significantly correlated with better performance on the Stroop Color-Word and Trail-Making B tasks.

Conclusions

This is the first study to investigate visual system resting state FC in blast-related mTBI. The severity of veterans' blast-related mTBI was associated with the magnitude of resting FC between visual network regions and regions in occipital, parietal, and frontal cortex. In addition, these are the first results that directly illustrate the relationship between blast TBI, alterations in visual-frontal neural networks, and executive dysfunction. The identification of deficits in specific visual-frontal neural networks associated with severity of blast-TBI highlights the detrimental relationship between TBI and integration of visual sensory input and executive processes.