A Model of Anisotropy and Diffusivity in Chronic Mild Blast-related Brain Injury

Julie C. Chapman, PsyD [1,2]
Patrick M. Sullivan, MA [1]
Massimo S. Fiandaca, MD [2,3]
Christine J. Eickhoff, MA [1]
Melody J. Powers, MA [1]
Jonathan H. Pincus, MD [2,4]
Marshall R. Balish, MD, PhD [2,4]
Marc R. Blackman, MD [5,6,7]

[1] War Related Illness & Injury Study Center, Veterans Affairs Medical Center, Washington, DC
[2] Department of Neurology, Georgetown University School of Medicine, Washington, DC
[3] Department of Neuroscience, Georgetown University School of Medicine, Washington, DC
[4] Neurology Service, Veterans Affairs Medical Center, Washington, DC
[5] Research and Development Service, Veterans Affairs Medical Center, Washington, DC
Departments of [6] Medicine and [7] Rehabilitation Medicine, Georgetown University School of Medicine, Washington, DC

Corresponding Author Mailing Address: Dr. Julie C. Chapman, War Related Illness & Injury Study Center, Veterans Affairs Medical Center, 50 Irving Street, NW, (MS 127), Washington, DC 20422.
Tel. 1+ (202) 745-8249; Fax (202) 518-4666; Email: Julie.Chapman@va.gov

Introduction

The global incidence of traumatic brain injury (TBI) is approximately 10 million cases annually. Among Operation Enduring Freedom (OEF)/Operation Iraqi Freedom (OIF) veterans, incidence rates as high as 23% have been estimated, with mild TBI (mTBI) being the most common. Findings from DTI studies have bolstered objective evidence of brain abnormalities subsequent to mild TBI (mTBI), generally showing differences between those with and without brain injury. However, these results have been inconsistent with respect to tract involvement and type of anomaly, yielding no consistent marker. The heterogeneity of brain injury as well as differences in patient selection/definition, phase of recovery, level of severity, and presence and type of co-morbidities also contribute to the variability of findings.

Methods

To better understand the long-term effects of mild blast-related TBI (mbTBI), we undertook a DTI study with a design focus on internal validity. DTI metrics and psychosocial outcomes were compared between OEF/OIF veterans with mild blast-related TBI (mbTBI) (n=15) and uninjured control veterans (n=15). Cases were at least 1 year post-injury at evaluation. Measures of Fractional Anisotropy (FA), Mean Diffusivity (MD), Axial Diffusivity (AD) and Radial Diffusivity (RD) were assessed for a set of white matter tracts using DTI Studio. To convert images to MNI space, AIR was used to perform an affine trilinear alignment on all images using FA to drive the transformation. Subsequently, Large Deformation Diffeomorphic Metric Mapping was run using FA and Trace. Standard Regions of Interest (ROIs) for each participant were selected from the Johns Hopkins University (JHU) MNI template Type III White Matter Parcellation Map (WMPM).

Results

Due to a significant group difference in age (controls higher) and the known impact of age upon DTI results, ROI comparisons were calculated using Univariate ANCOVAs holding age constant. Numerous group differences in widespread tracts revealed a repeated pattern in measures of anisotropy and diffusivity. Significant FA differences emerged in 14 disparate tracts, 79% of which conformed to the pattern of lower anisotropy for cases versus controls. In all but one (97%) of the significant differences in measures of AD (7 tracts), RD (14 tracts), and MD (12 tracts), case values were higher than controls. Both the number and the distribution of these differences varied substantially from what would be expected by chance. Psychosocial variables did not account for any variance among DTI results.

Conclusions

We demonstrated a consistent pattern of diffusion metrics in our sample comparing veterans with and without mbTBI. Our design focus on internal validity likely increased the accuracy of our results. We propose a physiologic model to explain the observed pattern of data. These results support the presence of lasting structural abnormalities following mbTBI. Although this pattern must be replicated with a larger sample, refinement of a predictable model for mbTBI could assist in diagnosis and monitoring of this injury.

Keywords: Diffusion tensor imaging, blast, traumatic brain injury, anisotropy, diffusivity, veterans