DTI abnormalities following blast-related TBI across 4 Independent Cohorts: Regional specificity for the middle cerebellar peduncle

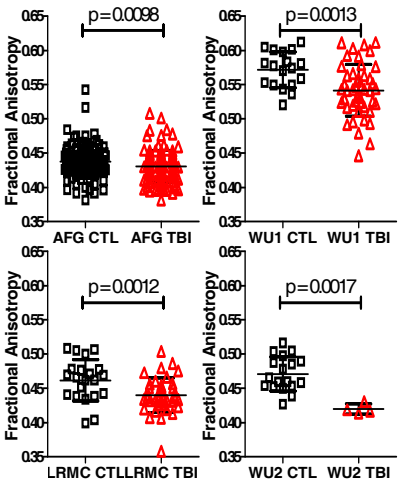
Christine MacDonald[1], Ann Johnson[1], Octavian Adam[2], Dennis Rivet[2], James Sorrell[1], Brian Sammons[1], Dana Cooper[1], Linda Wierzechowski[3], Yolanda Barnes[3], John Ritter[4], Todd May[5], Maria Barefield[2], Josh Duckworth[2], Don Labarge[2], Dean Asher[2], Benjamin Drinkwine[2], Joshua Shimony[6], Matthew Parsons[7], Abraham Snyder[6], Michael Russell[8], John Witherow[3], Raymond Fang[3], Stephen Flaherty[3], and David Brody[1]

[1]Neurology, Washington University, Saint Louis, MO, United States, [2]NATO Role 3 Kandahar Air Field, Kandahar, Afghanistan, [3]Landstuhl Regional Medical Center, Landstuhl, Germany, [4]Bastion Hospital, Helmond Province, Afghanistan, [5]Camp Leatherneck, Helmond Province, Afghanistan, [6]Radiology, Washington University, Saint Louis, MO, United States, [7]Radiology, Washington University, Saint Louis, Missouri, United States, [8]US Army, San Antonio, TX, United States

Introduction: Blast-related traumatic brain injury (TBI) has been called the 'signature injury' of the wars in Iraq and Afghanistan. Simulation studies have suggested that there may be a specific vulnerability of the brain to blast exposure unrelated to other mechanisms of TBI (*1*). This vulnerability has been investigated in only a single case report (*2*), but not in larger cohorts of patients. In the current study, 4 independent cohorts of individuals exposed to blast were studied. These cohorts consisted of blast-exposed patients who were either scanned acutely in Afghanistan (AFG), medically evacuated and scanned at Landstuhl Regional Medical Center (LRMC) in Landstuhl Germany, scanned chronically at Washington University in St. Louis (WU 1), and a rare, small cohort of patients who only experienced a single, primary blast exposure and had no previous history of TBI or other neurological disorders also scanned at Washington University (WU2). These cohorts provided a unique opportunity to compare and contrast imaging findings across patients following blast exposure at varying time points post injury; potentially documenting the temporal evolution of this injury.

Methods: Patients were recruited and scanned in three different forums. For each cohort a group of controls without a history of blast-related TBI were enrolled and scanned for comparison. Controls were also US military personnel deployed to Iraq or Afghanistan during the same time frame as the patients. All scanners were 1.5T and either Siemens' Avanto (LRMC, WU) or Phillip's Achieva (AFG). All subjects were 18- 49 y/o, both male and female, and from all branches of the military, with no prior history of a neurological disorder. The time since injury varied for TBI subjects by cohort: 0-7 days (AFG) 0-30 days (LRMC), 6- 12 months (WU1), and 2-4 years (WU2). Group size also varied across cohort: AFG 108 TBI: 98 CTL, LRMC 40 TBI: CTL 21, WU1 47 TBI: 18 CTL, and WU2 4 primary-blast TBI: 18 CTL. The same control group was used to compare both independent groups of blast TBI patients at WU. AFG subjects scanned in theatre were enrolled under a study conducted by Dr. Adam and colleagues at Kandahar air field and Camp Leatherneck. LRMC subjects were scanned in Germany and enrolled under a study conducted by Dr. Brody and colleagues at Landstuhl. WU subjects were scanned in St. Louis and enrolled under a study conducted also by Dr. Brody and colleagues (WU1) in collaboration with Dr. Russell (WU2). All scanning protocols consisted of a T1 and T2-weighted 1x1x1 mm isotropic image for atlas registration as well as 2 DTI acquisitions b-1000, 2.5 x 2.5 x 2.5 mm isotropic voxels with 15 directions (AFG), or 25 directions (LRMC, WU). Post-processing was performed to align each set of scans into standardized Talairach coordinate system using cross modal affine transformations(*3*). DTIstudio software was then utilized to perform a whole brain white-matter analysis (*4, 5*). FA values were compared between control and TBI cohorts for each site. No attempt was made to combined data sets across sites as cross-scanner comparisons could not be validated. In the WU1 cohort, hand-drawn regions of interest were utilized (*6*) to test whether the specific analysis approach could possibly bias the results.

Results and Discussion: Although each cohort identified regions of reduced anisotropy indicative of white matter injury, only the left middle cerebellar peduncle was found to be abnormal across all 4 cohorts. AFG (p=0.0098), LRMC (p=0.0012), WU1 (p=0.0013), WU2 (p=0.0017). 1-sided Mann Whitney U, uncorrected p-values. Conventional images acquired at the same time did not reveal abnormalities in this region as reported by a board-certified radiologist. The identification of such a region lends support to the notion that there may be specific regions of vulnerability following a blast. However, it remains to be determined if this is truly from the blast or from additional insults endured during the exposure as 3 of the 4 cohorts experienced 'blast plus' events at the time of their head injuries. It is possible that the middle cerebellar peduncle is universally vulnerable to injury. Direct comparison to identically assessed us military personnel with non-blast related TBIs is ongoing.



References:

1. P. A. Taylor, C. C. Ford, Simulation of blast-induced early-time intracranial wave physics leading to traumatic brain injury. *Journal of biomechanical engineering* **131**, 061007 (Jun, 2009).
2. D. L. Warden *et al.*, Case report of a soldier with primary blast brain injury. *NeuroImage* **47 Suppl 2**, T152 (Aug, 2009).
3. J. S. Shimony *et al.*, Diffusion tensor imaging reveals white matter reorganization in early blind humans. *Cereb Cortex* **16**, 1653 (Nov, 2006).
4. S. Mori, K. Oishi, A. V. Faria, White matter atlases based on diffusion tensor imaging. *Current opinion in neurology* **22**, 362 (Aug, 2009).
5. K. Oishi *et al.*, Atlas-based whole brain white matter analysis using large deformation diffeomorphic metric mapping: application to normal elderly and Alzheimer's disease participants. *NeuroImage* **46**, 486 (Jun, 2009).
6. C. L. Mac Donald *et al.*, Detection of blast-related traumatic brain injury in U.S. military personnel. *The New England journal of medicine* **364**, 2091 (Jun 2, 2011).