Cerebellar white matter abnormalities following primary blast injury

Christine MacDonald[1], Ann Johnson[1], James Sorrell[1], Thomas Malone[1], Dana Cooper[1], Elliot Nelson[2], Nicole Werner[1], Joshua Shimony[3], Matthew Parsons[3], Abraham Snyder[3], Marcus Raichle[3], Raymond Fang[4], Stephen Flaherty[5], Michael Russell[6], and David Brody[1]

[1]Neurology, Washington University, Saint Louis, MO, United States, [2]Psychiatry, Washington Univeristy, Saint Louis, MO, United States, [3]Radiology, Washington University, Saint Louis, MO, United States, [4]Landstuhl Regional Medical Center, Landstuhl, Germany, [5]Cape Fear Valley Medical Center, Fayetteville, NC, United States, [6]HQ, US MEDCOM, United States

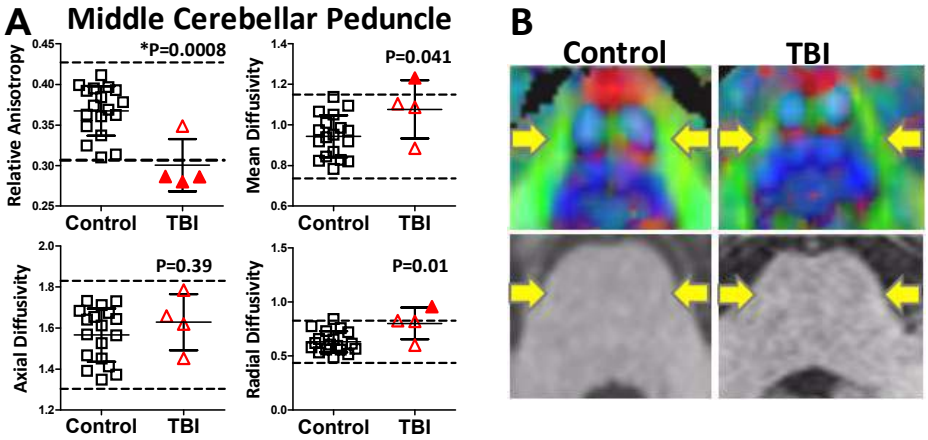
Introduction: Blast-related traumatic brain injury (TBI) has been called the 'signature injury' of the wars in Iraq and Afghanistan. Simulation studies have suggested that there may be a specific vulnerability of the brain to blast exposure unrelated to other mechanisms of TBI (*1, 2*). This vulnerability has been investigated in only a single case report (*3*), but not in a series of individuals with single, primary blast exposure and no previous history of TBI or other neurological disorders. These cases are quite rare but scientifically important to our understanding of blast-related TBI. In the current study we evaluated four such individuals in an attempt to better understand the specific contribution of the primary blast event.

Methods: Primary blast subjects were recruited from the Rehabilitation and Reintegration Division of the US Army by advertisement (M. Russell). Through rigorous screening of military personnel with previous primary blast exposure, we identified four individuals who had only sustained a single event consistent with traumatic brain injury. They had no other history of TBI, no prior change in neurological status, no previous neurological or psychiatric disorders, and no life history of any event that could potentially have caused a concussion. Collateral histories were also obtained to corroborate information. At the time of study evaluation, all primary blast TBI subjects were 2-4 years post exposure and had not been exposed to any additional blasts, had not endured subsequent TBI, were not abusing alcohol or drugs and had not previously done so. A control group was studied for comparison (n=18). Controls consisted of returning military personnel from Iraq or Afghanistan who were clinically evaluated to be free of brain injury with no history of head injury, neurological or psychiatric disorder (*4*). Control subjects were 6-12 months post deployment and denied abuse of drugs and/or alcohol. Following the methods of Mac Donald et al NEJM 2011, the evaluations consisted of an MRI scan with diffusion tensor imaging (DTI) on a 1.5T Siemens Avanto scanner (*4*), as well as in person clinical assessments.

Results: DTI revealed abnormalities in 3 of the 4 primary blast TBI subjects in comparison to controls, specifically in middle cerebellar peduncle (Figure 1A). A significant decrease in relative anisotropy was observed in the primary blast TBI subjects. An example of this reduction in signal intensity is displayed in Figure 1B. Yellow arrows point to the middle cerebellar peduncles (shown in green on the DTI images). This reduction in anisotropy is consistent with white matter injury. No other DTI parameter was found to be significant after Bonferroni correction for multiple comparisons (noted with asterisk in figure). A reduction in anisotropy was not found in any other region in any of the subjects. T1-weighted images that have been coregistered to the DTI images are shown for comparison. There is no indication of abnormality in this region as evidenced by the conventional images acquired at the same time.

Discussion: The cerebellum may be selectively vulnerable to primary blast effects. The cerebellum, brainstem, and orbitofrontal cortex were predicted to have the highest shear stresses during computational modeling of blast in comparison to other brain regions (*1*). Previous studies and case reports have highlighted neuronal and metabolic changes in these same regions (*3-5*). Experimental animal models of blast have also found pathological changes in the cerebellum and brainstem regions suggesting that there may in fact be a selective vulnerability in this area to blast exposure (*6, 7*).

Support: Department of Defense grant PT075299 (D. Brody), WashU NeuroImaging Lab, and the Geneva Foundation.



DTI abnormalities in the middle cerebellar peduncle following primary blast TBI. **A.** Relative anisotropy was significantly reduced in three of the four primary blast TBI subjects. Dashed lines indicate two standard deviations from mean control for each parameter. Diffusivities are in units of 10^{-3} mm^2/sec. **B.** DTI abnormalities are not apparent on conventional MRI in the same region. Arrows indicate regions of abnormally low anisotropy in primary blast TBI subjects. Images are displayed in radiological convention.

1. P. A. Taylor, C. C. Ford, *J Biomech Eng* **131**, 061007 (Jun, 2009).
2. M. S. Chafi, G. Karami, M. Ziejewski, *Ann Biomed Eng* **38**, 490 (Feb).
3. D. L. Warden *et al.*, *Neuroimage* **47 Suppl 2**, T152 (Aug, 2009).
4. C. L. Mac Donald *et al.*, *N Engl J Med* **364**, 2091 (Jun 2, 2011).
5. E. R. Peskind *et al.*, *Neuroimage* **54 Suppl 1**, S76 (Jan, 2011).
6. R. A. Bauman *et al.*, *J Neurotrauma* **26**, 841 (Jun, 2009).
7. R. H. Garman *et al.*, *J Neurotrauma* **28**, 947 (Jun, 2011).