Advanced MRI Detection of Blast-Related Traumatic Brain Injury in US Military Personnel: Early Prediction of Post Traumatic Stress Disorder Severity

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Introduction: In the current conflicts in Iraq and Afghanistan, the number of blast-related TBIs may be as high as 320,000.[1] Most are categorized as uncomplicated "mild" or "concussive" TBI based on clinical criteria and absence of intracranial pathology on CT or conventional MRI. Little is known about these "mild" injuries and the relationship between TBI and PTSD remains controversial.[2, 3] Computer simulations of the effects of blast-induced pressure waves on the brain suggest that specific regions, especially the orbitofrontal regions and the posterior fossa (cerebellum and brainstem), would likely sustain the most intense mechanical strains, independently of the subject's head orientation relative to the blast.[4] A recent Positron Emission Tomography study demonstrated reduced cerebellar basal glucose metabolism[5] and a case report documented a cerebellar white matter lesion on MRI following blast injury.[6] In a swine model of experimental blast injury, axonal injury in several regions including cerebellar tracts was demonstrated.[7]

Methods: Active-duty service members were scanned on a 1.5T Avanto MRI scanner (Siemens, Erlangen, Germany). Following the methods of Shimony et al, (Cereb Cortex, 2006), patients were scanned with 25 direction DTI (TR=10200ms, TE=102ms, 2.5 x 2.5 x 2.5 mm voxels). Standard anatomical scans (MPRAGE, T2-weighted fast spin echo, and FLAIR) were also employed. All service members were male, ages 19-49 yrs (median 25 yrs), ranging 1-90 days post injury (median 17 days). Post-processing was preformed to align each set of scans into standardized Talairach coordinate system using cross modal affine transformations. DTI parameters (relative anisotropy-RA, axial diffusivity-AD, and radial diffusivity-RD, and apparent diffusion coefficient -ADC) were analyzed in 12 regions across multiples slices encompassing the entire white matter tract of interest for each subject and compared to controls. These regions included the genu, body and splenium of the corpus callosum, bilateral anterior as well as posterior internal capsule, bilateral cingulum, bilateral uncinate fasciculus, bilateral middle cerebellar and cerebral peduncles and bilateral orbitofrontal white matter. Patients were followed for 6-12 months and then re-scanned with an identical imaging protocol on a second 1.5T Avanto MRI scanner. At the time of follow up, patients also completed a battery of neurological, neuropsychological and psychiatric assessments.

Results: DTI revealed abnormalities consistent with traumatic axonal injury in 18/63 TBI subjects. None had detectible intracranial injury on CT or conventional MRI. DTI abnormalities were observed in the orbitofrontal and cerebellar regions uncommonly injured in civilian TBI but predicted to be vulnerable to blast. Neurological function and neuropsychological performance were generally intact. However, post-traumatic stress disorder (PTSD) was more common (29/47 vs. 5/18, p=0.014) and more severe (Clinician-Administered PTSD Scale 62±27 vs. 40±26, p=0.004) in TBI subjects than controls. In multivariate modeling, early clinical factors and specific DTI abnormalities significantly predicted later PTSD severity (r=0.55, p=0.0002; added contribution of DTI: p=0.016).

Discussion: Blast-related traumatic axonal injury in specific brain regions may contribute to PTSD symptoms. Early DTI-based detection of axonal injury could aid triage and proactive PTSD treatment planning following blast-related TBI.

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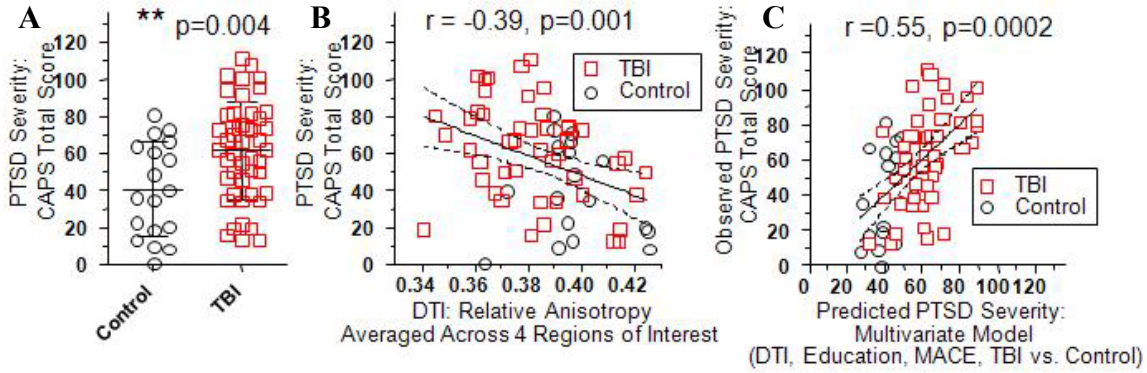

A. Severity of PTSD (CAPS total score, 0-136, higher scores worse). **B.** PTSD severity 6-12 months post injury vs. RA 1-90 days post injury. RA averaged across 4 ROIs: right orbitofrontal white matter, right cingulum, right and left posterior limb of internal capsule. **C.** Multivariate predictive model of PTSD severity based on early DTI and clinical data. DTI data significantly added to the correlation strength (β_{DTI}= -0.28, p=0.016).

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