Visual and Retinal Correlates of Traumatic Brain Injury (TBI): Biology and Behavior

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PUBLIC ABSTRACT

There is rapidly growing awareness among the medical community and federal government -- including and especially the military -- of the risks of traumatic brain injury (TBI). Notably, given the lifestyles of many armed service personnel prior to their enlistment, it is likely that a larger proportion of them have suffered TBI (of "domestic" origin) than the general population. After adding the common head injuries suffered in accidents in training and deployment, and of course, in combat, service personnel are clearly at dramatically heightened risk of TBI. Given the demands of deployment, such as the need to make well-reasoned snap judgments in extraordinary and unpredictable circumstances, the cognitive and mood impairments that characterize TBI -- whether domestic or military in origin -- become of vital importance to the mission. The data collected in the present study will provide a basis for readily detecting TBI and will provide a basis for understanding the relationship between the eye, the brain, and behavior in TBI.

Chronic traumatic encephalopathy (CTE), a form of TBI, is a progressive tauopathy resultant to mild, repeated brain injury. Cognitive and emotional impairment consequent to TBI/CTE is frequently progressive and, obviously, impacts mission readiness; therefore, it is important to predict, not just diagnose, TBI/CTE-induced disability. Our team of collaborators has strong expertise in TBI, having recently reported evidence of CTE in the young brains of high school, collegiate, and semipro athletes. We identified biomarkers, in brain, that include perivascular neurofibrillary tauopathy in hypothalamus, mammillary bodies, brainstem, basal ganglia, and white matter tracts. Distressingly, we found that CTE has almost identical manifestations in those brains as in the injured brains of veterans of Iraq and Afghanistan exposed to blasts from improvised explosive devices.

TBI is also associated with vision loss. We don't fully understand what mechanisms lead to visual difficulties consequent to TBI. To facilitate further study of TBI-based neurotrauma, we developed a blast neurotrauma mouse model that is the only one, to our knowledge, fully validated to recapitulate CTE-linked neuropathology in wild-type mice; it does so in as little as 2 weeks following exposure to a single blast. We have also developed a mouse impact-injury model that is unique in that it does not crush the brain and eyes as other impact models do but as head injury in humans typically does not. Just as in human TBI, our TBI mice have hippocampal-dependent learning and memory deficits. These deficits are concomitant with impaired axonal conduction and defective, activity-dependent, long-term potentiation of synaptic transmission in hippocampus. We need to quantify the effects of TBI on the visual system of these mice, as well. There are many benefits to understanding the effect of TBI on the eye, including TBI detection, identifying targets for clinical intervention, and diagnosing and perhaps eventually treating vision loss in pharmaceutical trials.

In the current project, our multidisciplinary (ophthalmologists, electrophysiologists, psychiatrist, optical physicists), multi-institutional (Boston Children's Hospital, BCH; Boston University, BU; Physical Sciences, Inc., PSI) team proposes to compare and contrast the
eyes, brains, and behaviors of singly and multiply blasted and impacted TBI mice with controls. Our main goal is to identify new biomarkers for TBI and effective-yet-economical means to detect them in armed services personnel and recruits (and, eventually, in the general population). We believe that the retina, as the most accessible part of the brain, is uniquely positioned to provide important new knowledge about the acute and chronic sequelae of TBI. And, as noted, once such easily accessible biomarkers are successfully identified, they can readily provide a reference for therapeutic interventions in preclinical trials.

In our pilot data, we found structural and functional correlates to brain injury in traumatically injured eyes. Changes in retinal structure and pronounced changes in the response of the retina and the pupil to light are very likely to associate with visual dysfunction. We do not yet know if and how well retinal biomarkers correlate with vision loss or with TBI/CTE disease in other parts of the brain, but it is vital that we learn.