Brain injury to soldiers can arise from exposure to a single explosion: study

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A team of investigators have shown evidence of chronic traumatic encephalopathy (CTE) in brain tissue from blast-exposed military service personnel.

Laboratory experiments conducted at Boston University, New York Medical College (NYMC) and the Veterans Affairs Boston Healthcare System demonstrated that exposure to a single blast equivalent to a typical improvised explosive device (IED) results in CTE and long-term brain impairments that accompany the disease. They also found that the blast wind, not the shock wave, from the IED blast leads to traumatic brain injury (TBI) and long-term consequences, including CTE.

This research, which represents the first case series of postmortem brains from U.S. military personnel who were exposed to a blast and/or a concussive injury, will be published online May 16 by *Science Translational Medicine*.

This extensive multi-disciplinary study, led by Lee Goldstein, M.D., Ph.D., associate professor at Boston University School of Medicine (BUSM) and Boston University College of Engineering, and Ann McKee, M.D., professor at BUSM and director of the Neuropathology Service for VA New England Healthcare System, included key experimental findings from the laboratories of Patric K. Stanton, Ph.D., and Libor Velisek, M.D., Ph.D., both professors at NYMC.

CTE, which can only be diagnosed postmortem, is a progressive

neurodegenerative brain disorder that has been reported in athletes with multiple concussions or subconcussive injuries. In early stages, CTE is characterized by the presence of abnormal deposits of a protein called tau in the form of neurofibrillary tangles, glial tangles and neuropil threads throughout the brain. These tau lesions eventually lead to brain cell death. CTE has clinical features in common with TBI, including psychiatric symptoms and long-term cognitive disability involving memory and learning deficits. TBI can impact military personnel exposed to an explosive blast and may affect approximately 20 percent of the 2.3 million servicemen and women deployed since 2001.

In this study, investigators performed comprehensive neuropathological analyses on brain tissue from four military service personnel with known blast exposure and/or concussive injury. They compared these results with brain tissue samples from three young amateur American football players and a professional wrestler, all of whom had a history of repetitive concussive injury, and four samples from comparably-aged normal controls with no history of blast exposure, concussive injury or neurological disease.

The investigators found that CTE neuropathology in the brains of blast-exposed military veterans was similar to that found in young athletes with repetitive concussion and consistent with what has been observed in brain samples from other athletes with a history of repetitive concussive injury.

"Our results showed that the neuropathology from blast exposure, concussive injury, or both were virtually indistinguishable from those with a history of repeat concussive injury," said McKee, who is the director of the Brain Banks for BU's Alzheimer's Disease Center and the Center for the Study of Traumatic Encephalopathy, which are based at the Bedford VA Medical Center. McKee said that these findings indicate that TBI caused by different factors may trigger similar disease

pathways in the brain.

"The neuropsychiatric symptoms of CTE that have previously been associated with athletes diagnosed with CTE could also be attributed to military personnel who were exposed to blast," said Goldstein, who also is affiliated with the BU Photonics Center and served as the study's lead author.

To examine the impact of a single blast exposure, the investigators collaborated with leading experts in blast physics, experimental pathology and neurophysiology at Boston University, VA Boston Healthcare System, White River Junction VA Medical Center, New York Medical College, Fraunhofer Center for Manufacturing Innovation, University of Massachusetts Lowell, Lawrence Livermore National Laboratory, Massachusetts General Hospital and the University of Oxford. The team's experimental data showed that one blast comparable to that experienced by military service personnel in the field resulted in both neuropathological and behavioral evidence of CTE. Surprisingly, the long-term impairments in brain function, including impaired learning and memory, were observed just two weeks after exposure to a single blast.

"Our laboratory experiments show that blast exposure can produce both structural and functional damage that may be long-lasting and is likely to underlie the profound cognitive, memory, and perhaps mood and post-traumatic stress disorders, experienced by many soldiers," said Stanton, who is director of the Neural Systems Laboratory at NYMC. "We must now move to identify the neurochemical events that produce this damage, and initiate a rational search for treatments to ameliorate the devastating effects of CTE on the lives of our veterans."

Libor Velisek, M.D., Ph.D., professor and director of the NYMC Developmental Epilepsy Laboratory and Behavioral Phenotyping Core

Facility, added: "Our finding of clear impairments in the ability to both learn and remember one month after a blast exposure leads us to wonder just how long-lasting these impairments are, and whether they can be prevented or rescued."

The blast wind from an IED can reach a velocity of up to 330 miles per hour, which is greater than the largest wind gust ever recorded on earth. "The force of the blast wind causes the head to move so forcefully that it can result in damage to the brain," said Goldstein.

Based on the results, the investigators went a step further and explored how they could prevent the brain injury. They demonstrated that immobilizing the head during a blast exposure prevented the learning and memory deficits associated with CTE that occurred when the head was not immobilized.

"Our study provides compelling evidence that blast TBI and CTE are structural brain disorders that can emerge as a result of brain injury on the battlefield or playing field" added Goldstein. "Now that we have identified the mechanism responsible for CTE, we can work on developing ways to prevent it so that we can protect athletes and our military service personnel."

The study results provide a pathway for the development of novel diagnostic strategies for blast-related brain trauma, as well as to treat and rehabilitate those who have been exposed to blast and/or a concussive injury.

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