



US DEPARTMENT OF DEFENSE

## BLAST INJURY RESEARCH PROGRAM COORDINATING OFFICE

# Neurobehavioral and Psychological Health Outcomes Characterization of Interface Astroglial Scarring in Human Brain after Blast Exposure: A Postmortem Case Series

No evidence-based guidelines are available for the definitive diagnosis or directed treatment of most blast-associated traumatic brain injury (TBI), partly because the underlying pathology is unknown. Moreover, few neuropathological studies have addressed whether blast exposure produces unique lesions in the human brain, and if those lesions are comparable with impact-induced TBI. Researchers at the Uniformed Services University of the Health Sciences (USUHS) hypothesize that blast exposure produces unique patterns of damage, differing from that associated with impact-induced, non-blast TBIs. In this postmortem case series, the study team investigated several features of TBIs, using clinical histopathology techniques and markers, using brain specimens from male Service Members with chronic blast exposures and from those who had died shortly after severe blast exposures.<sup>1</sup> They compared these results with those from brain specimens from male civilian (e.g., non-military) cases with no history of blast exposure, including cases with and without chronic impact TBIs and cases with chronic exposure to opiates, and analyzed the limited associated clinical histories of all cases. Brain specimens from five cases with chronic blast exposure, three cases with acute blast exposure, five cases with chronic impact TBI, five cases with exposure to opiates, and three control cases with no known neurological disorders were analyzed. All five cases with chronic blast exposure showed prominent astroglial scarring that involved the subpial glial plate, penetrating cortical blood vessels, grey-white matter junctions, and structures lining the ventricles; all cases of acute blast exposure showed early astroglial scarring in the same brain regions. All cases of chronic blast exposure had an antemortem diagnosis of posttraumatic stress disorder (PTSD). The civilian cases, with or without a history of impact TBI or a history of opiate use, did not have any astroglial scarring in the brain regions analyzed.

An important component of TBI occurring among Service Members on the battlefield relates to exposure to blasts produced by high explosives, primarily through the use of improvised explosive devices (IEDs) and suicide bombs by the enemy. Identification of this unique and characteristic pattern of brain damage related to blast exposure, as discovered and described in this publication, may begin to explain why large numbers of Service Members exposed to such weapons return from deployment with persistent and troublesome neurologic and behavioral symptoms, such as chronic headaches, sleep disorders, problems with concentration and memory loss, depression, irritability, and abrupt mood swings ranging from agitation to despair, sometimes leading to suicide. It is hoped that these findings will lead to better and more targeted approaches to diagnosis, treatment, and prevention of these serious sequelae following participation in modern warfare.

1 Shively, S. B., Horkayne-Szakaly, I., Jones, R. V., Kelly, J. P., Armstrong, R. C., & Perl, D. P. (2016). Characterisation of interface astroglial scarring in the human brain after blast exposure: a post-mortem case series. *The Lancet. Neurology*, 15(9), 944–953. [https://doi.org/10.1016/S1474-4422\(16\)30057-6](https://doi.org/10.1016/S1474-4422(16)30057-6)





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## CLINICAL PRESENTATION OF CASE 1

Case 1 was a 45 year old male veteran who died from a self-inflicted gunshot wound. During his 25 year military career he received numerous commendations, and colleagues considered him highly competent, reliable, and emotionally stable.

According to members of his team, they routinely experienced blast exposures during training exercises and combat missions with bombs landing or improvised explosive devices (e.g., those made and deployed not according to standard military procedure) detonating in close proximity. With blast exposure, team members described a jolting sensation and noted that these incidents commonly resulted in post-concussive like symptoms. After retirement, the patient admitted to multiple mTBIs during his military service, but had chosen not to report his symptoms at the time for fear of being deemed unfit for duty. He complained of headache and memory problems and described trouble maintaining mental focus, which he attributed to severe sleep disturbance. He often lost coherence of thought and jumbled his speech. His wife reported that he experienced cognitive and behavioural changes. For example, she described his abnormally slow hand movements over the car steering wheel, ignition and gear shift, as if confused about their functions. Formerly superior in spatial concepts, he struggled to pack the car for holiday travel. He failed to remember family plans. On several occasions, he became uncharacteristically angry with her. Clinicians described poor eye contact, flat affect, and low voice tone, and treated him for PTSD, depression, and anxiety. One month before he died, conventional MRI (1.5 T) showed no brain abnormalities. No formal report of TBI could be found in his medical records. His wife recounted that he had wrestled and boxed during his school years and experienced three motor vehicle accidents throughout his life. There was no indication of substance abuse by medical history or post-mortem toxicology screening.

