Exploring the Invisible Wound: Interface Astroglial Scarring, a Pattern of Brain Damage Unique to Blast Exposed Service Members with Prominent Persistent Behavioral/Neurologic Symptomatology

Daniel P. Perl. MD[1,2]

1 Department of Pathology and 2Neurology, Uniformed Services University of the Health Sciences, F. Edward Hébert School of Medicine, Bethesda, MD, 20814

2 Center for Neuroscience and Regenerative Medicine, Brain Tissue Registry and Neuropathology Core, Bethesda, MD, 20814

Since 2001 approximately 2.6 million U.S. service members have been deployed to the Middle East in the war on terror. Almost daily, allied forces encountered attacks with high explosives that often resulted in mild traumatic brain injuries (mild TBIs, concussions). For current military conflicts, these blast TBIs have been called the “invisible wound” since numerous service members suffer from debilitating persistent neurologic and behavioral symptoms in the absence of detectable abnormalities on routine neuroimaging and lack of medical knowledge about underlying pathophysiology. Despite innumerable deaths from high explosives, especially in the military since the early 20th century, the medical literature offers few studies characterizing acute or chronic neuropathologic sequelae in the human brain after blast exposure.

At the Uniformed Service University (USU), we have developed the Center for Neuroscience and Regenerative Medicine (CNRM) Brain Tissue Repository, the only such facility in the world specifically dedicated to the study of military TBI. Within this facility, we have identified a distinct and previously undetected pattern of damage to the human brain in blast-exposed cases (see *Lancet Neurol.* 2016 15:944-953). We found astroglial scarring, indicative of neuroanatomical areas with damage, in a distinctive pattern occurring at the interfaces of tissues with differing densities, for example, between cerebrospinal fluid and brain parenchyma (subpial) and between the gray and white matter within brain parenchyma. This neuroanatomical lesion distribution at tissue interfaces complements known biophysics of the blast wave impinging on the human body. We have not found interface astroglial scarring (IAS) in postmortem brain tissues of patients with histories of impact TBIs (in the absence of blast exposure). Furthermore, most cases identified with IAS following blast TBI failed to show evidence of significant pathologic *tau* accumulation, indicative of chronic traumatic encephalopathy (CTE), a disorder mostly encountered following repeated impact TBI. These data suggest that the clinical phenotype of persistent neurologic/behavioral symptoms, particularly as seen after blast exposure, may be due to specific neuropathophysiology, and significantly differs from what is seen in non-blast forms of impact TBI.

In this talk, these findings will be illustrated and their pathophysiology and implications for diagnosis, prevention and treatment will be discussed.

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