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Functional Decline 5 Years After Blast Traumatic Brain Injury: Sounding the Alarm for a Wave of Disability?

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The long-term outcomes associated with wartime traumatic brain injury (TBI) and general combat exposure remain poorly understood as they relate to service members from recent military conflicts. Most of the research on mild TBI (mTBI) has been conducted on athletes and civilians; these studies suggest that a majority of individuals experience complete recovery within a few weeks or months after injury. The effects of combat on long-term health and aging have been studied among individuals who served during World War II or in the Korean and Vietnam War eras, and the results are somewhat mixed. Some studies report poorer overall health with aging among veterans compared with nonveterans,^{1,2} particularly for those who experienced combat.^{3,4} However, other studies seem to support what has been called the “healthy soldier effect,”⁵ suggesting that service members continue to be healthier than their nonveteran peers for decades after military service.^{5,6} Research on blast mTBI has been growing since mTBI was labeled one of the signature injuries of the recent wars. Studies examining military breachers, who conduct dynamic entry into buildings often using planned explosive blasts, have shown that chronic exposure to low-level blasts can lead to clinical sequelae.⁷ A recently published study revealed the presence of astroglial scarring on the surface of the brain after blast TBI, suggesting that blast mTBI is different from routine sports concussion and also may explain some of the clinical sequelae seen after blast mTBI.⁸

In this issue of *JAMA Neurology*, Mac Donald et al⁹ reveal functional changes during early midlife in military service members who were deployed to Afghanistan and Iraq and suggest that widely held expectations for stable recovery after uncomplicated sports mTBI may not generalize to those injured in the recent conflicts. They compared data collected at 3- and 3-

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year follow-up points from a unique cohort of military service members who were diagnosed with blast mTBI in the combat theater and medically evacuated to Germany with data from a comparison control sample consisting of combat-deployed service members with no history of mTBI. This extraordinary cohort of individuals with well-characterized, medically documented, clinician-confirmed mTBI and extensive prospective follow-up evaluations provides an exceptional opportunity to evaluate the course of recovery after blast mTBI immediately through short- (3-year) and long-term (3-year) follow-up. Their data indicate that individuals in the blast mTBI group had worse functional outcomes relative to noninjured control individuals at the 3-year follow-up and, surprisingly, that most individuals with blast mTBI actually demonstrated deterioration from the 3- to 3-year postinjury period. Also concerning is the finding that a small but notable proportion of deployed controls with no known TBI also experienced deterioration during that same interval.

The prospect that young, otherwise healthy military service members would experience any deterioration in functional status after uncomplicated blast mTBI, much less after deployment that did not result in mTBI, has consequential and wide-ranging implications. If individuals with deployment-related blast mTBI continue to have psychiatric and behavioral problems, poor life satisfaction, and global disability 3 years after injury (long after the expected window of recovery), the general medical and mental health needs of this group will be extensive and may exceed the services available, especially for the Department of Veterans Affairs health care system. Moreover, the evidence presented by Mac Donald et al⁹ indicating deterioration in functional status from 3 to 3 years after exposure suggests that, for some individuals, concussive blast injury may be associated with a progressive, evolving disease process. The authors also have a parallel article examining changes on magnetic resonance imaging scans in a subset of this cohort wherein they report that 33% of the cohort with blast mTBI had reductions in fractional anisotropy indicative of chronic brain changes.¹⁰ Finally, the finding that 3 of 33 combat deployed controls (33%) also experienced deterioration suggests that military exposure may, in and of itself, carry long-term health risks. Together, the results of this important study suggest that military service members may require proactive interventions to facilitate community reintegration and mental health optimization after deployment, in addition to a long-term investment in medical management to maximize health and life quality.

To some extent these findings are consistent with a growing body of literature that suggests TBI is most appropriately conceptualized not as an isolated event but as a disease process that may cause and/or accelerate medical and mental health morbidity long after the initial injury.¹¹ Of importance, much of the empirical literature supporting this conceptualization comes from survivors of moderate or severe TBI, which has been associated with higher rates of disease across multiple body systems¹¹ and reduced life expectancy compared with the general population.¹² The study by Mac Donald et al⁹ provides evidence of deterioration or disease progression but in relatively young individuals exposed to a clinically defined mTBI.

Replication of these findings in other larger cohorts and investigation of the associations between military service and blast mTBI on a wider range of functional and clinical

outcomes, including performance validity tests not included in the study by Mac Donald et al⁹ will be important. More frequent follow-up evaluations during the first 3 years after exposure might help to elucidate the mechanisms underlying functional and neurodegenerative decline after mTBI. Advancing this knowledge will require prospective studies in well-characterized military and civilian cohorts. Some ongoing efforts may be well positioned to contribute to this knowledge, including the Defense and Veterans Brain Injury Center 33-Year Study, a longitudinal study conducted by the Chronic Effects of Neurotrauma Consortium (CENC) in military and veteran samples,¹³ and the Transforming Research and Clinical Knowledge of TBI (TRACK TBI)¹⁴ and TBI Model Systems¹⁵ in civilian samples.

We need to identify risk and protective factors for clinical deterioration after mTBI to identify novel treatment targets and inform the development of tailored interventions. Estimates from the Iraq and Afghanistan conflicts suggest that as many as 33% of service members had at least 3 mTBI; many sustained multiple TBIs.¹⁶ Results of the study by Mac Donald et al⁹ suggest that functional deterioration may begin well in advance of older adulthood for some individuals with deployment-related blast mTBI, raising important questions about how these exposures will interact with the aging process. Because Mac Donald and colleagues intend to continue following up this cohort, future results are likely to further elucidate the long-term consequences of blast mTBI. Only by concentrating efforts and supporting research in this high-priority area can the nation best serve those service members and veterans who have sacrificed for our country.

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