Study identifies signs of repeated blast-related brain injury in active-duty United States Special Operations Forces

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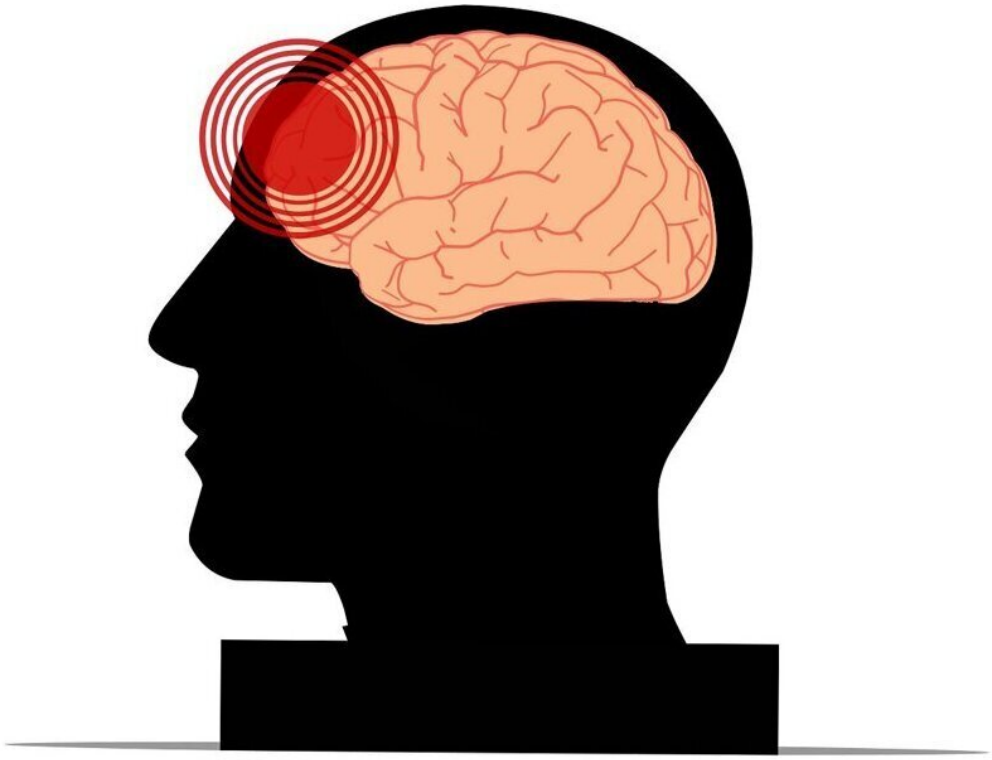

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Repeated exposure to explosive blasts has the potential to cause brain injuries, but there is currently no diagnostic test for these injuries. In a

study of 30 active-duty United States SOF personnel, researchers found that increased blast exposure was associated with structural, functional, and neuroimmune changes to the brain and a decline in health-related quality of life. The researchers are now designing a larger study to develop a diagnostic test for repeated blast brain injury

United States (US) Special Operations Forces (SOF) personnel are frequently exposed to explosive blasts during training and combat. However, the effects of repeated blast exposure on the brain health of SOF personnel are unclear, and there is currently no diagnostic test that can detect brain injury caused by the cumulative effects of subconcussive blast exposure.

As a result, SOF personnel may experience cognitive, psychological and physical symptoms for which the cause is never identified, and they may return to training or combat when their brains are vulnerable.

US Special Operations Command (USSOCOM) recognizes that the health and well-being of its elite SOF members is a critical element to develop and employ the world's finest warfighters. Because brain health is a key element to fielding a healthy force, USSOCOM willingly participated in this pilot study to help both the US Military and the medical community understand and identify signs related to repeated blast effects. Collectively, USSOCOM hopes that the impact of this study will benefit all US Military members with repeated blast exposure in the future.

To understand the effects of repeated blast exposure on SOF brain health and inform the development of a diagnostic test for repeated blast brain injury, a team at Massachusetts General Hospital, a founding member of the Mass General Brigham health care system, conducted the ReBlast study, a comprehensive, multimodal investigation of 30 active-duty US SOF. The University of South Florida, Institute of Applied

Engineering coordinated and managed the study, which was supported by USSOCOM.

In a publication titled "Impact of Repeated Blast Exposure on Active-Duty United States Special Operations Forces," published in *Proceedings of the National Academy of Sciences*, the team reports that higher blast exposure was associated with structural, functional, and neuroimmune brain alterations and lower health-related quality of life.

The magnetic resonance imaging (MRI) and positron emission tomography (PET) findings converged at a region of the frontal lobe called the rostral anterior cingulate cortex (rACC), which is known to be a widely connected brain network hub that modulates cognition and emotion.

Three lines of evidence—structural MRI, functional MRI, and translocator protein PET—showed an association between cumulative blast exposure and changes in the rACC. Among all the findings, the association between cumulative blast exposure and structural MRI changes in the rACC was the most significant. These results suggest that the rACC may be particularly sensitive to blast waves that penetrate the openings in the skull behind the eyes.

Higher cumulative blast exposure was also associated with decreased health-related quality of life on self-reported questionnaires. However, blast exposure was not associated with changes in cognitive performance, post-traumatic stress disorder symptoms, or blood proteomics. No signs of blast-related brain injury were identified by conventional MRI scans.

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Characteristics of study participants

SOF study participants represented all branches of the military and included both enlisted personnel and officers. On average, participants were 37 years old and had 17 years of military service. All participants had extensive combat exposure and reported levels of cumulative blast exposure at which individuals are likely to experience cognitive, physical or psychological symptoms. They also reported high levels of blunt impacts to the head, with half the cohort having more blows to the head than they could recall.

These blunt head impacts, as well as age and amount of combat exposure, were accounted for in statistical analyses that tested for associations between blast exposure and a broad spectrum of cognitive, physical symptom, psychological, neuroimaging and blood-based biomarkers.

"A key limitation of the study is that we were unable to measure the many additional exposures that SOF personnel experience during training and combat, such as inhalation of heavy metals, lack of oxygen during high-altitude jumping or deep-sea diving, and acceleration g-forces when flying in aircraft or traveling over waves at high speeds," explains Brian L. Edlow, MD, principal investigator of the study.

"As a result, the associations we observed between cumulative blast exposure and brain network disruption do not prove causation."

Dr. Edlow is co-director of Mass General Neuroscience, associate director of the Center for Neurotechnology and Neurorecovery (CNTR)

at Mass General, an associate professor of Neurology at Harvard Medical School and a Chen Institute MGH Research Scholar 2023-2028.

"Future studies with more comprehensive and objective exposure measurements, larger sample sizes, and a longitudinal design are needed to definitively link blast exposure to the imaging biomarkers that we observed," adds Natalie Gilmore, Ph.D., first author of the study and a research fellow in the CNTR.

The researchers are now designing such a longitudinal study with the goal of developing a reliable diagnostic test for repeated blast brain injury. Although no specific blood-based biomarkers for brain injury were detected during the study, the researchers did find higher than expected levels of tau in the blood of study participants, a finding that could help in developing a portable diagnostic test.

"The availability of a reliable diagnostic test could improve Operators' quality of life by ensuring that they receive timely, targeted medical care for symptoms related to repeated blast brain injury," explains Yelena G. Bodien, Ph.D., co-senior author of the paper and an investigator in the CNTR.

"A diagnostic test could also be used to inform decisions by Commanders about the combat readiness of individual Operators."

"Ultimately, the goal of this research is to enhance the combat readiness, career longevity, and quality of life of the United States' most elite forces," Edlow says.

"These are American heroes who answered the call to serve after the terrorist attacks of September 11, 2001 and fought the most dangerous missions of the Global War on Terror for two decades. They deserve the best medical care, and while more research is needed, our results suggest

that a diagnostic test for repeated blast brain injury is within reach."

More information: Edlow, Brian L., Impact of repeated blast exposure on active-duty United States Special Operations Forces, *Proceedings of the National Academy of Sciences* (2024). DOI: 10.1073/pnas.2313568121. doi.org/10.1073/pnas.2313568121

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