Looking for a link between seizures and migraine after traumatic brain injury in soldiers

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Traumatic brain injury (TBI) affects many Americans: high school athletes, drivers and passengers in motor vehicle accidents, and victims of domestic violence, to name a few. Some of the most striking effects of brain injury are seen in our soldiers and veterans returning from Iraq and Afghanistan. Two University of Utah researchers are teaming up with the Department of Defense to investigate the long-term effects of TBI in these returning soldiers. K.C. Brennan, M.D., assistant professor in the Department of Neurology, and Edward Dudek, Ph.D., professor and chair of the Department of Physiology, are collaborating on the study.

"Because of advances in protective equipment and armor, more and more of our service personnel are surviving their initial injuries," says Brennan, the study's lead investigator. "However, the long-term consequences of TBI can leave our returning servicemen and women completely incapacitated. Post-traumatic epilepsy (PTE) and post-traumatic headache (PTH) are two of these consequences, and they are probably related: both likely result from increased excitation in the brain."

In PTE, the excitation of the brain results in a seizure, while in PTH, it can cause cortical spreading depression (CSD), an event that can trigger a severe migraine-like headache, according to Dudek. "The fact that many service personnel suffer from both of these conditions at the same

time offers a clue that both PTE and PTH may have a common origin in TBI," he says. "Evidence from intensive care units suggests that this is the case: patients after TBI suffer from both seizures and CSD, and these two events seem to interact with one another."

The study funded by the Department of Defense will provide $725,000 over three years to investigate seizures and CSD together to better understand how TBI can set PTE and PTH in motion. The Utah researchers hope understanding this will allow them to develop better treatments for service personnel and veterans, as well as others with TBI. The study will attempt to define the time period when patients are most at risk in order to determine when seizures and CSD occur, and how they interact with each other so that treatment can be delivered when needed. The researchers predict that they will occur together in clusters, during the first few days following injury.

"We will also look into what generates seizures and CSD after brain injury," continues Dudek. "To answer this we will use a variety of imaging and electrical recording tools to dissect the underlying mechanisms within the brain. Only by understanding these mechanisms will we be able to anticipate what damage is likely to occur, and thus prevent it. Our suspicion is that the same mechanisms that lead to repair in the brain also leave the brain in a more excitable state, and we plan to test this possibility."

The ultimate goal, according to Brennan, is to see whether the changes that lead to PTE and PTH after traumatic brain injury can be prevented. "Using the information gained in the first two portions of the study, we will try to prevent these changes with memantine, a medication we identified as a headache preventive, which also prevents CSD and shows promise in enhancing recovery from brain injury," he says. "Our hope is that medications like memantine could be used after TBI, to improve recovery, and to prevent PTE and PTH."

"We owe a great deal to our men and women in uniform," Brennan says. "We hope this work will make a difference in their lives, by improving the care they receive when injured."

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