Researchers see promise in treatment to reduce incidence of dementia after TBI

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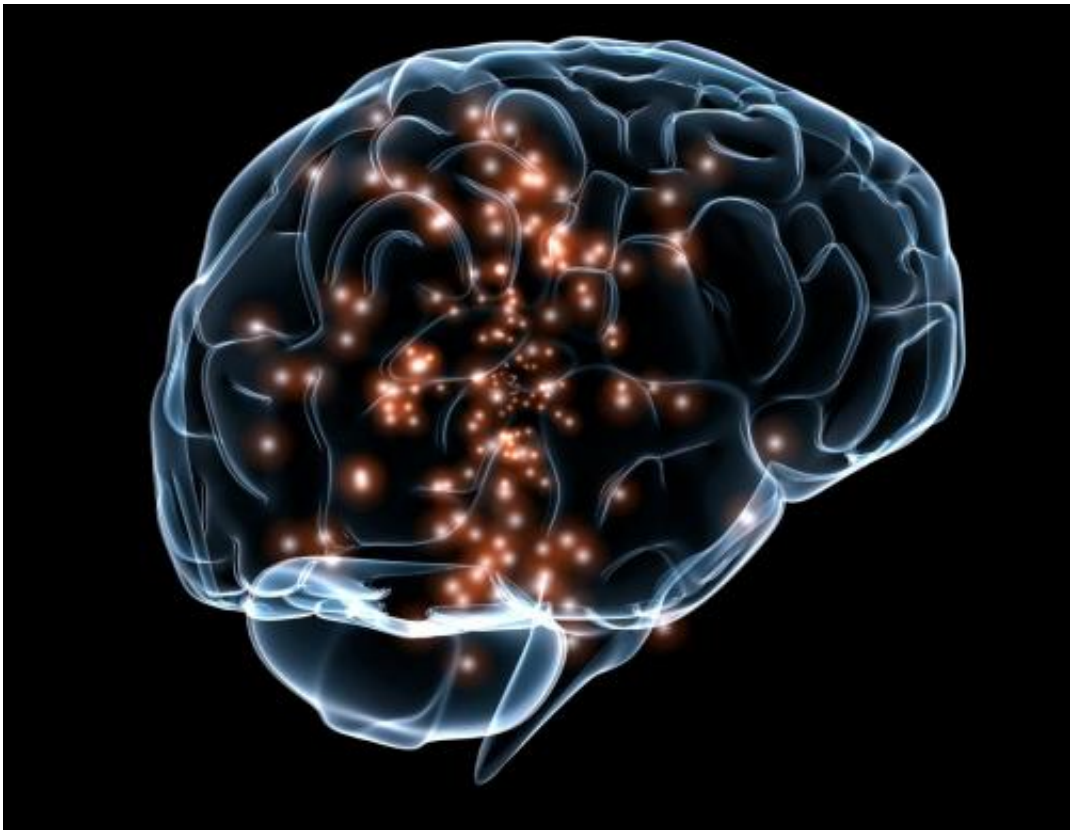

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It was once thought that effects of a mild head injury—dizziness, headaches, memory problems—were only temporary, and the brain would heal over time. However, while the long-term consequences of head trauma are not fully known, growing evidence suggests that even a

mild head injury can increase the risk for later-in-life development of dementias such as Alzheimer's disease.

Researchers at the University of Kentucky's Sanders-Brown Center on Aging have been attempting to understand the cascade of events following mild head injury that may lead to an increased risk for developing a progressive degenerative brain disease, and their new study, which was published in the current issue of the *Journal of Neuroscience*, shows initial promise for a treatment that might interrupt the process that links the two conditions.

"By defining the cascade of events that occurs after a mild brain injury, we ultimately hope to discover ways to disrupt that process," said Adam Bachstetter, PhD, of the Sanders-Brown Center on Aging. "Our goal is to uncover the biology that underlies the link between head injury and dementia, and in our latest research, we think we have found evidence that an altered inflammatory response from cells in the brain called glia may be at least part of the link."

To explore the chain of events that link TBI to increased risk for dementia, Bachstetter and co-author Scott Webster, PhD, of the Sanders-Brown Center on Aging, used a mouse that has been genetically altered to make a human protein called amyloid beta, which is a key player in Alzheimer's disease. The researchers also developed a surgical procedure to mimic the most common form of traumatic brain injury.

"We wanted to know if we could accelerate the onset of memory problems in these mice, similar to what is believed to occur in humans," said Webster. "It gave us a way to ask the important mechanistic questions that might one day lead to a better treatment for head injury patients."

Bachstetter and Webster used a small molecule drug known as MW151

which blocks overproduction of the molecules that cause inflammation in the brain following TBI. MW151 was developed by Linda Van Eldik, PhD, director of the Sanders-Brown Center on Aging, and D. Martin Watterson, PhD, of Northwestern University's Feinberg School of Medicine. The drug was given to the mice starting a week after TBI. After three weeks of treatment, mice that received MW151 no longer showed learning and memory problems, while the mice that didn't receive the drug showed profound learning and memory problems.

"MW151 was able to rescue the memory impairments in mice even when treatment was started a week after the injury," said Webster. "The potential implications are compounded when you factor in that many people who suffer a mild brain injury don't seek treatment right away."

In addition to the human suffering caused by Alzheimer's disease, there is an enormous strain on the health care system and families, consuming about $20 billion in direct costs alone. As the Baby Boomer generation continues to age, that figure is expected to rise exponentially.

"As the signature injury of the Iraq and Afganistan wars, and with approximately 1.5 million people in the United States each year seeking medical treatment for a traumatic brain injury, the impact of earlier onset of dementia in such a large number of people is simply unthinkable, Van Eldik said. "Adam and Scott's work could have a large impact both socially and economically."

Provided by University of Kentucky