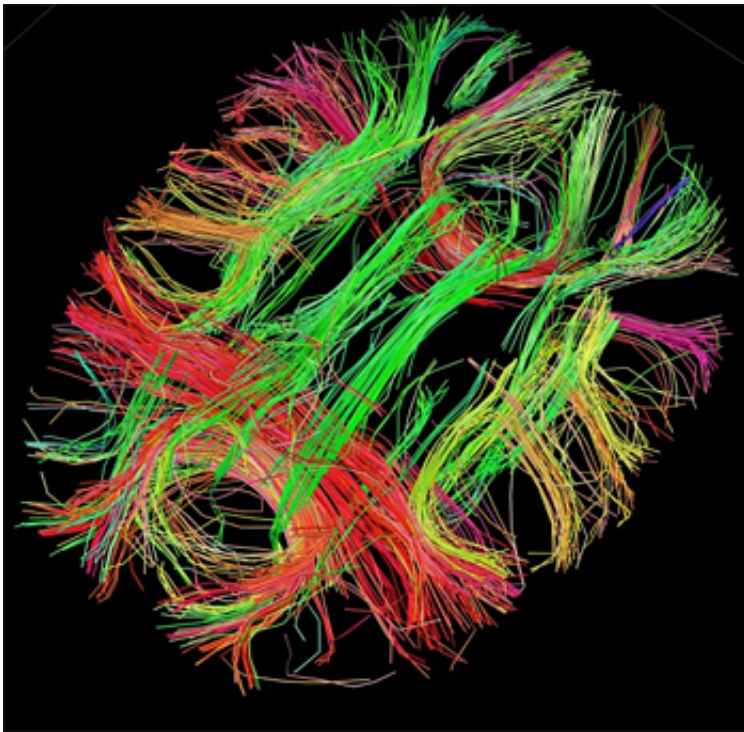


What causes brain problems after traumatic brain injury? Studies have a surprising answer

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White matter fiber architecture of the brain. Credit: Human Connectome Project.

A new paper by researchers at the University of Maryland School of Medicine (UM SOM) argues that there is a widespread misunderstanding about the true nature of traumatic brain injury and how it causes chronic degenerative problems.

In a perspective article published in the latest issue of *Neurotherapeutics*, the two authors - Alan Faden, MD, a neurologist and professor of anesthesiology, and David Loane, PhD, an assistant professor of anesthesiology, propose that chronic brain damage and neuropsychiatric problems after trauma are to a large degree caused by long-term inflammation in the brain. In their view, this inflammation is a key culprit behind the myriad symptoms that have been linked with [traumatic brain injury](#) and mild traumatic [brain injury](#), including brain atrophy, depression and cognitive decline.

Dr. Faden and Dr. Loane also say that there has been too much emphasis on a specific diagnosis known as [chronic traumatic encephalopathy](#) (CTE), the set of symptoms and pathology that has been found in some former professional football players. They argue that this may deflect focus from other mechanisms, which may be more important and treatable. They say that although chronic traumatic encephalopathy is a serious problem, relatively few people have been diagnosed with this condition. Instead, they contend, researchers and journalists should focus more on the fact that even repeated concussive impacts or mild traumatic brain injury may trigger chronic [brain inflammation](#) that can persist for years and cause lasting damage.

"Brain inflammation is a key issue, and it has been under-emphasized," says Dr. Faden. "Recent brain imaging studies, including those in former [professional football players](#), indicate that persistent brain inflammation after a single moderate head injury or repeated milder traumatic brain injury may be very common, and may contribute to cognitive problems. In addition, larger studies indicate that brain inflammation persists for many months or years in many people with traumatic brain injury."

The paper also points out that chronic brain inflammation related to traumatic brain injury may be treatable. Dr. Faden and Dr. Loane say recent research shows that some experimental drugs, as well as carefully

controlled exercise programs, can block brain inflammation caused by traumatic brain injury. They maintain that these avenues should be pursued vigorously.

The paper follows two recent groundbreaking publications by Dr. Faden, which appeared several months ago. The papers, which looked at animal models of traumatic brain injury, examined the mechanisms by which even mild brain injuries can cause sustained cognitive and psychiatric problems. This work elucidated how this process occurs, and appeared in of the *Journal of Neuroscience* and the *Journal of Cerebral Blood Flow and Metabolism*.

"These studies show how repeated mild injuries can lead to the same kinds of injuries that occur after a single moderate or severe traumatic brain injury," said Dr. Faden. "The brain inflammation and loss of brain cells look remarkably similar in both cases. Now that we understand more about the mechanism behind the damage, we can develop strategies to prevent or minimize the problems."

For the paper in the *Journal of Cerebral Blood Flow and Metabolism*, Dr. Faden and his colleagues found that the brains of animals with mild traumatic brain injury showed substantial loss of neurons, as well as increases in microglia, a kind of inflammatory immune cell active in the brain. These changes lasted for several weeks after the injury. The researchers also found that repeated mild traumatic brain injury, and the resulting inflammation, were associated with decreased function in a part of the brain called the hippocampus, which is crucial for memory.

In the other paper, in the *Journal of Neuropathology and Experimental Neurology*, which included Dr. Loane as the lead author, the scientists found that traumatic brain injury triggers specific long-term molecular changes that causes increased inflammation lasting up to a year and leads to the death of brain neurons and cognitive loss. "Traumatic brain injury

is a major social problem, in athletics, the military and elsewhere," said Dean E. Albert Reece, MD, PhD, MBA, who is vice president for Medical Affairs, University of Maryland, and the John Z. and Akiko K. Bowers Distinguished Professor and Dean of the School of Medicine. "This work by Dr. Faden and his colleagues helps illuminate more about the causes of traumatic brain injury, and possible treatments."

More information: Downregulation of miR-23a and miR-27a following experimental traumatic brain injury induces neuronal cell death through activation of proapoptotic Bcl-2 proteins. *Journal of Neuroscience*, July 23, 2014; [link.springer.com/article/10.1...07/s13311-014-0319-5](https://doi.org/10.1523/JNEUROSCI.07/s13311-014-0319-5)

Repeated mild traumatic brain injury causes chronic neuroinflammation, changes in hippocampal synaptic plasticity, and associated cognitive deficits. *Journal of Cerebral Blood Flow and Metabolism*, July 2014

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