Traumatic brain injury impairs hormone production, disrupting sleep, cognition, memory

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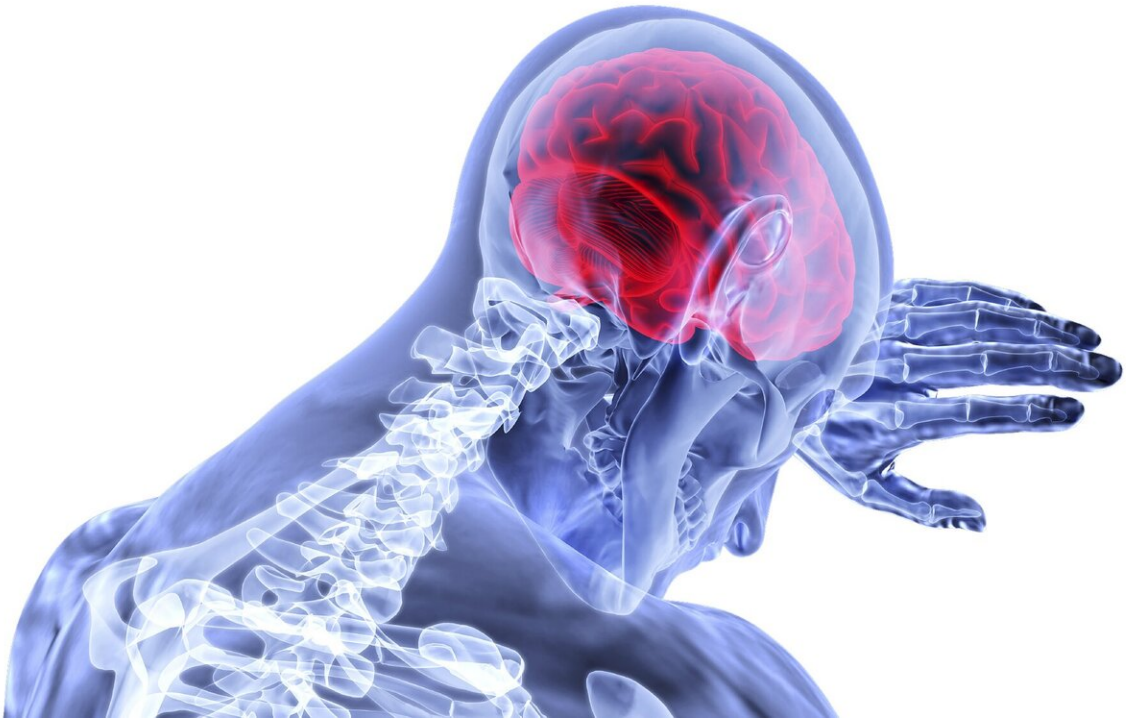

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More than 2.5 million people in the United States alone experience a traumatic brain injury, or TBI, each year. Some of these people are plagued by a seemingly unrelated cascade of health issues for years after

their head injury, including fatigue, depression, anxiety, memory issues, and sleep disturbances.

A collaborative team, led by Dr. Randall Urban, The University of Texas Medical Branch at Galveston's Chief Research Officer and Professor of Endocrinology, has spent the past 20 years investigating this post-TBI syndrome. The team has learned more about how a TBI triggers a reduction in growth hormone secretion and why most TBI patients improve after growth hormone replacement treatment.

The studies led to the definition of the syndrome as brain injury associated fatigue and altered cognition, or BIAFAC, as recently described in a commentary published by Drs Urban and Brent Masel, UTMB Professor of Neurology, in the *Journal of Neurotrauma*. Detailed information on the team's two most recent advances also in the *Journal of Neurotrauma*.

The team's work on brain injuries began in the late 1990's when Galveston philanthropist Robert Moody asked the team whether TBI caused dysfunction of the hormones made by the brain's pituitary gland and funded research for the study. His son, Russell, had suffered a serious TBI during a car accident and was seeking ways to improve the life of his son and others living with brain injuries.

The team has been building on the discovery that TBI triggers a long-term reduction in growth hormone, or GH, secretion that is linked with BIAFAC. Most TBI patients experience dramatic symptom relief with GH replacement therapy, but the symptoms return if the treatment stops. The researchers are trying to better understand BIAFAC and exactly how and why GH replacement works so well in order to develop new interventions.

"We already knew that even mild TBI triggers both short- and long-term

changes to functional connections in the brain," said Urban. "GH administration has been extensively linked with both protection and repair of the brain following damage or disease, however we didn't know much about the particular mechanisms and pathways involved."

They examined 18 people with a history of mild TBI and inadequate GH secretion. The subjects received GH replacement in a year-long, double-blind, placebo-controlled study and were assessed for changes in physical performance, resting metabolic rate, fatigue, sleep quality, and mood. Functional magnetic resonance imaging was also used throughout the year to assess changes in brain structure and functional connections.

The study showed that GH replacement was linked with increased lean body mass and decreased fat mass as well as reduced fatigue, anxiety, depression and sleep disturbance. It was also found, for the first time, that these improvements were associated with better communications among brain networks that have been previously associated with GH deficiency. They also noted increases in both grey and white matter in frontal brain regions, the "core communications center of the brain," that could be related to cognitive improvements.

"We noticed that TBI patients had altered amino acid and hormonal profiles suggesting chronic intestinal inflammation, so we recently completed a trial to investigate the role of the gut-brain axis in the long-lasting effects of TBI," said Urban. "We compared the fecal microbes of 22 moderate/severe TBI patients residing in a long-term care facility with 18 healthy age-matched control subjects, identifying disruptions of intestinal metabolism and changes in nutrient utilization in TBI patients that could explain the reduced growth hormone function."

The results suggest that the people with TBI-related fatigue and altered cognition also have different fecal bacterial communities than the control group. Urban said that the findings suggest that supplementing or

replacing the dysbiotic intestinal communities may help to ease the symptoms experienced after TBI.

"These two studies further characterize BIAFAC and act as a springboard for new treatment options," said Urban. "We hope that the publications will focus the collective wisdom of the research community to better understand and treat this syndrome, providing hope for many. Because these symptoms can manifest months to years after the initial injury and as this cluster of symptoms hasn't been previously grouped together, it often goes unidentified in the medical community."

Provided by University of Texas Medical Branch at Galveston

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