MedicalXpress

Researchers find long-term consequences for those suffering traumatic brain injury

January 4 2013

Researchers from the University of South Florida and colleagues at the James A. Haley Veterans' Hospital studying the long-term consequences of traumatic brain injury (TBI) using rat models, have found that, overtime, TBI results in progressive brain deterioration characterized by elevated inflammation and suppressed cell regeneration. However, therapeutic intervention, even in the chronic stage of TBI, may still help prevent cell death.

Their study is published in the current issue of the journal PLOS ONE.

"In the U.S., an estimated 1.7 million people suffer from traumatic brain injury," said Dr. Cesar V. Borlongan, professor and vice chair of the department of Neurosurgery and Brain Repair at the University of South Florida (USF). "In addition, TBI is responsible for 52,000 early deaths, accounts for 30 percent of all injury-related deaths, and costs approximately $52 billion yearly to treat."

While TBI is generally considered an acute injury, secondary cell death caused by neuroinflammation and an impaired repair mechanism accompany the injury over time, said the authors. Long-term neurological deficits from TBI related to inflammation may cause more severe secondary injuries and predispose long-term survivors to age-related neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease and post-traumatic dementia.

Since the U.S. military has been involved in conflicts in Iraq and

Afghanistan, the incidence of traumatic brain injury suffered by troops has increased dramatically, primarily from improvised explosive devices (IEDs), according to Martin Steele, Lieutenant General, U.S. Marine Corps (retired), USF associate vice president for veterans research, and executive director of Military Partnerships. In response, the U.S. Veterans Administration has increasingly focused on TBI research and treatment.

"Progressive injury to hippocampal, cortical and thalamic regions contributes to long-term cognitive damage post-TBI," said study co-author Dr. Paul R. Sanberg, USF senior vice president for research and innovation. "Both military and civilian patients have shown functional and cognitive deficits resulting from TBI."

Because TBI involves both acute and chronic stages, the researchers noted that animal model research on the chronic stages of TBI could provide insight into identifying therapeutic targets for treatment in the post-acute stage.

"Using animal models of TBI, our study investigated the prolonged pathological outcomes of TBI in different parts of the brain, such as the dorsal striatum, thalamus, corpus callosum white matter, hippocampus and cerebral peduncle," explained Borlongan, the study's lead author. "We found that a massive neuroinflammation after TBI causes a second wave of cell death that impairs cell proliferation and impedes the brain's regenerative capabilities."

Upon examining the rat brains eight weeks post-trauma, the researchers found "a significant up-regulation of activated microglia cells, not only in the area of direct trauma, but also in adjacent as well as distant areas." The location of inflammation correlated with the cell loss and impaired cell proliferation researchers observed.

Microglia cells act as the first and main form of immune defense in the central nervous system and make up 20 percent of the total glial cell population within the brain. They are distributed across large regions throughout the brain and spinal cord.

"Our study found that cell proliferation was significantly affected by a cascade of neuroinflammatory events in chronic TBI and we identified the susceptibility of newly formed cells within neurologic niches and suppression of neurological repair," wrote the authors.

The researchers concluded that, while the progressive deterioration of the TBI-affected brain over time suppressed efforts of repair, intervention, even in the chronic stage of TBI injury, could help further deterioration.

More information: Acosta SA, Tajiri N, Shinozuka K, Ishikawa H, Grimmig B, et al. (2013) Long-Term Upregulation of Inflammation and Suppression of Cell Proliferation in the Brain of Adult Rats Exposed to Traumatic Brain Injury Using the Controlled Cortical Impact Model. PLOS ONE 8(1): e53376. doi:10.1371/journal.pone.0053376

Provided by University of South Florida