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Immune response may cause harm in brain injuries, disorders

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Could the body's own immune system play a role in memory impairment and cognitive dysfunction associated with conditions like chronic epilepsy, Alzheimer's dementia and concussions? Cleveland Clinic researchers believe so, based on a study published online by *PLOS ONE*.

The study focuses on the role of a protein known as S100B, which serves as a biomarker for brain damage. Normally, S100B is found only in the brain and spinal column. However, following a brain injury, it can leak through the blood-brain barrier into the blood.

Once S100B enters the bloodstream, it is identified as an intruder by the immune system, which releases antibodies to attack the protein.

"Our results show an unexpected role for S100B in the regulation of a neuro-immune response, connecting the function of the brain to the immune system," said Damir Janigro, Ph.D., senior author and molecular medicine researcher at Cleveland Clinic's Lerner Research Institute. "Uptake of S100B was prominent in cells that are known to be involved in regulating immune responses. Repeated increases of S100B – whether due to epileptic seizures, Alzheimer's disease, or repeated hits to the head in sporting events – may thus become boosters of an autoimmune response against the brain, which may slowly but inexorably result in chronic neurological disease."

These findings are the first to report a connection between a brain-derived protein and an immune response in the context of normal

immunological function.

"Prior to this research, S100B autoantibodies have been described in a variety of diseases, primarily in Alzheimer's dementia and chronic epilepsy. More recently, repeated subconcussive episodes in football players included a post-game increase of S100B, followed by an autoimmune response against the protein," Janigro said. "Therefore, it appears that autoimmunity against brain proteins may be one of the initial steps in the progression towards posttraumatic cognitive decline."

The study tested the hypothesis that the presence of S100B in extracranial tissue is due to the production of antigen-presenting cells in the blood, which may induce the production of auto-antibodies against S100B. To test this hypothesis, researchers used animal models of seizures, enrolled patients undergoing repeated disruption of the blood-brain barrier, and collected blood samples from epileptic patients.

If further research confirms the study's findings, treatments for brain injury may include anti-inflammatory therapy or immunomodulators to decrease the autoimmune response, as has been done in the treatment of multiple sclerosis and myasthenia gravis.

Provided by Cleveland Clinic