By shutting down inflammation, agent reverses damage from spinal cord injury in preclinical studies

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Researchers at Georgetown University Medical Center (GUMC) have been able to speed recovery and substantially reduce damage resulting from spinal cord injury in preclinical studies.

Their research, published online in *Annals of Neurology* and led by Kimberly Byrnes, PhD, shows that inflammation following injury causes the neurotoxicity that leads to lasting nerve cell damage, and that an experimental agent is able to block this inflammatory reaction.

"The findings we have made in this study may potentially be applicable to other neurological disorders, including stroke, head injury, Alzheimer's disease and Parkinson's disease," says senior investigator Alan I. Faden, MD, a professor of neuroscience and director of the Laboratory for the Study of Central Nervous System Injury at GUMC.

Faden says that the experimental agent they tested (CHPG), an activator of a type of glutamate receptor, is not ideal for human use because it cannot easily penetrate the blood-brain barrier. But he adds, "now that we know the biological target, a new drug could be designed that is better suited for clinical treatment of these neurodegenerative disorders."

CHPG shuts down activation of key immune cells in the brain known as microglia, which sense pathogens or damage in the spinal cord and brain. They helpfully foster the destruction of microbial invaders and clean up

biological detritus that occurs after an injury, but researchers say they have a dark side as well - they can worsen the damage by releasing toxic inflammatory factors.

"Under certain conditions, like spinal cord injury and brain trauma, microglia become activated," Faden says. "They release toxic chemicals that can kill healthy adjacent tissue, and this process can continue for months.

"We have found that six months after an injury, the expression of certain inflammatory factors in the spinal cord is 4-5 times normal levels," he says, adding that it has been shown that after human trauma, brain tissue can continue to be lost even more than a year after the injury. "Microglial related toxicity may contribute to this progressive loss," says Faden.

The study is a continuation of a long line of research by this investigative group that aims to stop that persistent damage. The team had previously found that microglial cells express a certain receptor, the group I metabotropic glutamate receptor 5 (mGluR5), on their surface. Further work showed that if these receptors were specifically activated on microglia, these immune cells would not produce the neurotoxins that led to cell death near the site of injury. CHPG serves to selectively activate the receptor, reducing microglial toxicity.

Source: Georgetown University Medical Center