Drug may reduce chronic pain for spinal cord injuries

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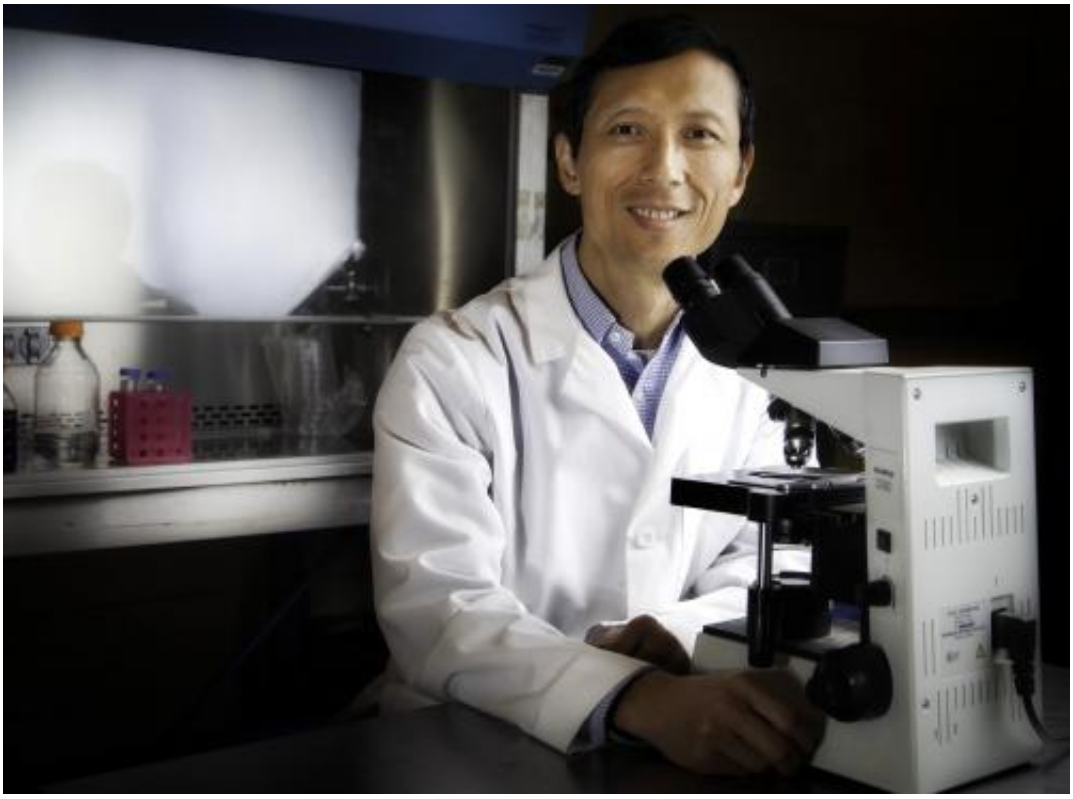

Purdue researcher Riyi Shi is leading work to study the role of a known neurotoxin in chronic pain for people who suffer from paralysis. A drug that has been shown to remove the toxin might be used to treat the pain. Credit: Purdue University photo/Michel Schweinsberg

(Medical Xpress)—Researchers have discovered that a known neurotoxin may cause chronic pain in people who suffer from paralysis,

and a drug that has been shown to remove the toxin might be used to treat the pain.

The toxin, called acrolein, is produced in the body after nerve cells are injured, triggering a cascade of biochemical events thought to worsen the injury's severity. The drug hydralazine, which has been approved by the U.S. Food and Drug Administration for hypertension, has been shown to be effective in reducing acrolein levels in the body.

New research shows hydralazine is effective in reducing chronic pain in laboratory animals and potentially in people who have suffered neurotrauma resulting in paralysis, said Riyi Shi (pronounced Ree Shee), a professor of neuroscience and biomedical engineering in Purdue's Department of Basic Medical Sciences, School of Veterinary Medicine, and Weldon School of Biomedical Engineering.

"Beyond paralysis, chronic neuropathic pain drastically impairs the quality of life for spinal cord injury victims. " he said. "Pain can persist for decades post-injury, which could contribute to depression and suicide."

The research is a collaboration between Purdue and the Indiana University School of Medicine. New findings are detailed in a research paper appearing this month in the *Journal of Neurochemistry*.

Researchers studied the role acrolein plays in hypersensitivity to pain in laboratory rats and the effectiveness of hydralazine in reducing the pain.

"It turns out that acrolein is a very important compound behind neuropathic pain," Shi said. "In a chronic pain situation, a stimulus that ordinarily might feel pleasant, even just a little touch, could cause pain."

Findings show the quantity of acrolein increases after a spinal cord

injury and may activate pain receptors - protein channels called TRPA1 - contained in pain-sensory nerve fibers of dorsal root ganglia located alongside the spine. Following spinal cord injury, the dorsal root ganglia could be affected biochemically or directly through physical trauma.

"The amplification of pain can be exacerbated in spinal cord injury due to acrolein's direct activation of pain receptors, as well as acrolein-induced inflammation that further intensifies pain sensation," Shi said. "Sometimes you have pain even without stimulation. You can have excruciating pain just sitting there."

Findings also indicate that injury causes a three-fold increase in the number of TRPA1 channels, which could further amplify pain caused by acrolein. The research showed hydralazine significantly reduces pain in experiments that measure a rat's reaction to stimulation.

"Even if we delay administration of hydralazine we can still reduce the pain, meaning not only acute but chronic pain might be reduced by acrolein-scavenging treatment," Shi said. "This could be promising news for millions of spinal cord injury victims who may suffer from debilitating pain."

More information: Acrolein involvement in sensory and behavioral hypersensitivity following spinal cord injury in the rat, Michael R. Due, Jonghyuck Park, Lingxing Zheng, Michael Walls, Yohance M. Allette, Fletcher A. White, and Riyi Shi, *Journal of Neurochemistry*, 2013.

ABSTRACT
Growing evidence suggests that oxidative stress, as associated with spinal cord injury (SCI), may play a critical role in both neuroinflammation and neuropathic pain conditions. The production of the endogenous aldehyde acrolein, following lipid peroxidation during the inflammatory response, may contribute to peripheral sensitization and hyperreflexia

following SCI via the TRPA1-dependent mechanism. Here we report that there are enhanced levels of acrolein and increased neuronal sensitivity to the aldehyde for at least 14 days after SCI. Concurrent with injury-induced increases in acrolein concentration, is an increased expression of TRPA1 in the lumbar (L3-L6) sensory ganglia. As proof of the potential pronociceptive role for acrolein, intrathecal injections of acrolein revealed enhanced sensitivity to both tactile and thermal stimuli for up to 10 days, supporting the compound's pro-nociceptive functionality. Treatment of SCI animals with the acrolein scavenger, hydralazine, produced moderate improvement in tactile responses as well as robust changes in thermal sensitivity for up to 49 days. Taken together, these data suggests that acrolein directly modulates SCI-associated pain behavior, making it a novel vietherapeutic target for preclinical and clinical SCI as an analgesic.

Provided by Purdue University