Neurotoxin in cigarette smoke worsens pain in spinal cord injuries

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People with spinal cord injuries may suffer “neuropathic pain” in various parts of the body. Credit: Purdue University photo/Michel Schweinsberg

Researchers have identified a key component in cigarette smoke that worsens pain in people with spinal cord injury, suggesting that a critical element within tobacco is responsible for such pain-inducing effects.

"Findings support anecdotal information suggesting that smoking increases pain in patients with spinal cord injuries," said Riyi Shi (pronounced Ree Shee), a professor of neuroscience and biomedical engineering in Purdue University's Department of Basic Medical Sciences, College of Veterinary Medicine and Weldon School of Biomedical Engineering. "This neuropathic pain could be felt in the leg and upper extremities, or in any part of the body."

A toxin from cigarette smoke has been shown to cause pain in animals with spinal cord injuries. The same toxin is known to activate pain sensors in nerve fibers.

The research showed that a neurotoxin called acrolein contained in cigarette smoke intensified neuropathic pain after spinal cord injuries in rats. Acrolein is known to worsen pain by activating and causing a proliferation of pain receptors called TRPA1, or transient receptor potential ankyrin-1, found in nerve fibers.

The findings are detailed in a research paper appearing on Aug. 15 in the Journal of Neurological Sciences. The paper, published online May 22, was co-authored by Shi and graduate students Breanne Butler and Glen Acosta.

"Previously, it was reported that people with spinal cord injury-induced chronic neuropathic pain have experienced heightened pain sensitivity when smoking tobacco cigarettes, and less pain following the termination of smoking," Shi said. "However, the molecular mechanisms of smoke-induced hypersensitivity are not yet clear. We show in the current study not only that the inhalation of cigarette smoke can worsen the pain, but inhaling acrolein alone, apart from cigarette smoke, at a concentration similar to that emitted from cigarettes, can produce significant increases in pain-related behavior after spinal cord injury as well. Furthermore, the intensified pain behavior due to acrolein

inhalation was reduced when an acrolein scavenger, phenelzine, was administered to the animals during acrolein exposure."

The study could open the door to a variety of possible preventive or therapeutic approaches to mitigate pain affecting the quality of life in spinal cord injury victims.

One of the principal impacts of the discovery is the possibility of reducing pain by using acrolein-scavenging drugs such as phenelzine, an anti-depressant approved by the U.S. Food and Drug Administration. Other potential FDA-approved anti-acrolein drugs including hydralazine, a medication for hypertension, and dimercarprol, an acute heavy metal poisoning treatment, have been tested and shown to be effective acrolein scavengers in Shi's lab. The drugs are thought to mitigate pain in active smokers, but also among those with pain caused by second-hand smoke for people with spinal cord injuries.

Acrolein also is produced by the body in response to spinal cord injury, and this natural source of the neurotoxin has been found to increase pain. However, the new research findings are the first showing that both acrolein introduced from an external source and cigarette smoke itself increases pain. A potential mechanism is that acrolein may increase pain by activating the TRPA1 receptors after spinal cord injury, as shown in some of Shi's previous work.

"The pain caused by cigarettes is noticeably more severe than acrolein alone, so there could be other compounds in cigarette smoke that also play a role," he said.

More information: Breanne Butler et al. Exogenous Acrolein intensifies sensory hypersensitivity after spinal cord injury in rat, *Journal of the Neurological Sciences* (2017). DOI: 10.1016/j.jns.2017.05.039

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