

Study points to potential monitoring approach for personalized treatment of spinal cord injuries

December 8 2016, by Emil Venere

Researchers have developed a urine test revealing the presence of a neurotoxin that likely worsens the severity and pain of spinal cord injuries, suggesting a new tool to treat the injuries.

The neurotoxin, called [acrolein](#), is produced within the body after nerve cells are damaged, increasing pain and triggering a cascade of biochemical events thought to worsen the injury's severity. The new test detected the toxin's presence in dogs that had naturally sustained [spinal cord injuries](#). The injuries were acute, meaning they were suffered within a few weeks of the study, when treatment to reduce acrolein might help prevent further damage.

The researchers studied the presence of a chemical compound called 3-hydroxypropyl mercapturic acid (3-HPMA), which is a metabolic product of acrolein.

"This has implications for a potential treatment to hinder further damage and reduce pain in people 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. "Urine 3-HPMA could be used as a biomarker in future clinical trials to non-invasively measure the effect of therapeutic intervention by reducing acrolein after acute spinal cord

injury."

Findings are detailed in a research paper published online in December in *The Veterinary Journal*.

The concentration of acrolein can be reduced using the drug hydralazine, which has been approved by the U.S. Food and Drug Administration for hypertension. The drug has been shown to reduce acrolein and pain following spinal cord injury in laboratory rats and mice.

In the new study, urine was studied from 10 dogs with acute spinal cord injuries, and 10 without injuries as a control. Findings showed the median urine 3-HPMA concentration was significantly higher in dogs with the injuries compared to the control dogs.

"Urine 3-HPMA is the first assay to indirectly assess acrolein concentration by measuring a metabolite of acrolein in dogs," Shi said.

The median urinary 3-HPMA concentration in the dogs with acute spinal cord injuries was 5.76 micromoles per gram of creatinine, a compound found in urine, compared to 3.10 micromoles of 3-HPMA per gram of creatinine in control dogs.

The paper was co-authored by Shi; veterinarian Andrea Sangster; former Purdue doctoral student Lingxing Zheng; veterinarian R. Timothy Bentley, an associate professor of neurology and neurosurgery in Purdue's Department of Basic Medical Sciences and Department of Veterinary Clinical Sciences; and former Purdue associate professor Rebecca Packer, who is now an associate professor of neurology and neurosurgery at Colorado State University.

While previous research focused on rats and mice, progressing to dogs takes the research a step closer to research with humans. At the same

time, because the dogs suffered their injuries naturally and they are much closer to humans in size, they represent a truer comparison to people with spinal cord injuries, Shi said.

Together, these factors increase the likelihood of translating the findings to eventual application to humans, he said.

"It's important to acknowledge the critical role played by Purdue's College of Veterinary Medicine," Shi said. "Because we have an excellent veterinary hospital, we have ready access to facilities and expertise not available to most research institutions."

Ideally, the monitoring approach might be used in personalized medicine to reduce side effects by precisely tailoring drug dosage to individual patients based on the concentration of acrolein.

The study, funded by the National Institutes of Health, was approved by the Purdue University Animal Care and Use Committee. The research dovetails with the goals of a recently formed Purdue Institute for Integrative Neuroscience, at the university's Discovery Park. The institute spans 25 departments and includes around 100 faculty engaged in neuroscience-related research.

Future research may include work to treat [dogs](#) with [spinal cord](#) injuries with hydralazine or other drugs that reduce the concentration of acrolein.

More information: Urine 3-HPMA is increased in acute spinal cord injury due to intervertebral disc herniation in dogs. *The Veterinary Journal*

Provided by Purdue University

Citation: Study points to potential monitoring approach for personalized treatment of spinal cord injuries (2016, December 8) retrieved 24 April 2024 from <https://phys.org/news/2016-12-potential-approach-personalized-treatment-spinal.html>

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