

Scientists examine how neuropathic pain responds to Metformin

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UT Dallas doctoral student Stephanie Shiers led a recent study with Dr. Sven Kroener (left) and Dr. Ted Price, both of the School of Behavioral and Brain Sciences, that examined how metformin, gabapentin and clonidine affected neuropathic pain-induced impairments. Credit: University of Texas at Dallas

Scientists seeking an effective treatment for one type of chronic pain

believe a ubiquitous, generic diabetes medication might solve both the discomfort and the mental deficits that go with the pain.

"People who are in constant pain have problems thinking straight sometimes. The longer you're in pain, the more entrenched the impairment becomes," said Stephanie Shiers, a fourth-year cognition and neuroscience doctoral student at The University of Texas at Dallas and lead author of a study recently published in the *Journal of Neuroscience*. "These impairments aren't addressed by existing therapeutics."

In the study, UT Dallas researchers show how a type of [chronic pain](#) called neuropathic pain responds to metformin, one of the most prescribed medications worldwide, as well as to pain relievers gabapentin and clonidine.

Neuropathic pain is caused by damage to nerve cells, as opposed to other body tissue. Examples include phantom limb syndrome, pain resulting from a stroke and the "pins and needles" sensations associated with diabetes.

Dr. Sven Kroener, associate professor in the School of Behavioral and Brain Sciences (BBS), and Dr. Ted Price, a Eugene McDermott Professor in BBS, are co-senior authors of the paper. Price, who is head of neuroscience, explained that pain affects a wide variety of regions of the brain.

"The sensory input that drives pain sends electrochemical signals almost everywhere in your brain, including the prefrontal cortex," he said. "When neuropathic pain occurs and certain nerves become active all the time, a huge swath of your brain is now receiving this constant sensory input, and it has to adapt. It makes it go haywire."

The study, which was conducted on mice, used a task that gauges

attention and mental flexibility to measure how each drug helped or harmed the cognitive abilities of the rodents.

"When we talk about flexibility, we mean being able to recognize and react to new stimuli in the environment," Kroener said. "The task that we used has been well studied in rodents, and we know what brain structures are involved."

While clonidine did not change task performance and gabapentin affected it negatively, metformin reversed pain-induced impairments.

"We chose clonidine because it has a very robust effect on pain if injected into the spinal canal and gabapentin because that's the most widely prescribed nonnarcotic pain drug," Shiers said.

Previous studies have established that [neuropathic pain](#) patients' cognitive deficits can persist even when the pain has been treated.

"That suggested to us that there was a long-lasting type of structural change at work in the [brain](#)," Shiers said. "In this regard, metformin outperformed both clonidine and gabapentin."

The research also turned up a significant difference in performance for male and female mice—a trend that has become prominent in recent pain work.

"Since we began doing studies on both sexes, we see a sex difference in almost everything we do involving [pain](#)," Price said. "I'm no longer surprised by it, but I can't explain it in most cases."

Kroener, whose research focuses on the function of the prefrontal cortex in animal models of schizophrenia and addiction, said the next step is to gain a better understanding of why metformin is effective in these cases.

"It's great if a drug works. It's even better if we know how it works," Kroener said. "We observe the results, but we don't know how they are achieved. That's what we should pursue next: determining the pathways in which [metformin](#) works to correct these defects and how the physiology changes."

More information: Stephanie Shiers et al. Neuropathic Pain Creates an Enduring Prefrontal Cortex Dysfunction Corrected by the Type II Diabetic Drug Metformin But Not by Gabapentin, *The Journal of Neuroscience* (2018). [DOI: 10.1523/JNEUROSCI.0713-18.2018](https://doi.org/10.1523/JNEUROSCI.0713-18.2018)

Provided by University of Texas at Dallas

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