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# New research provides hope for people living with chronic pain

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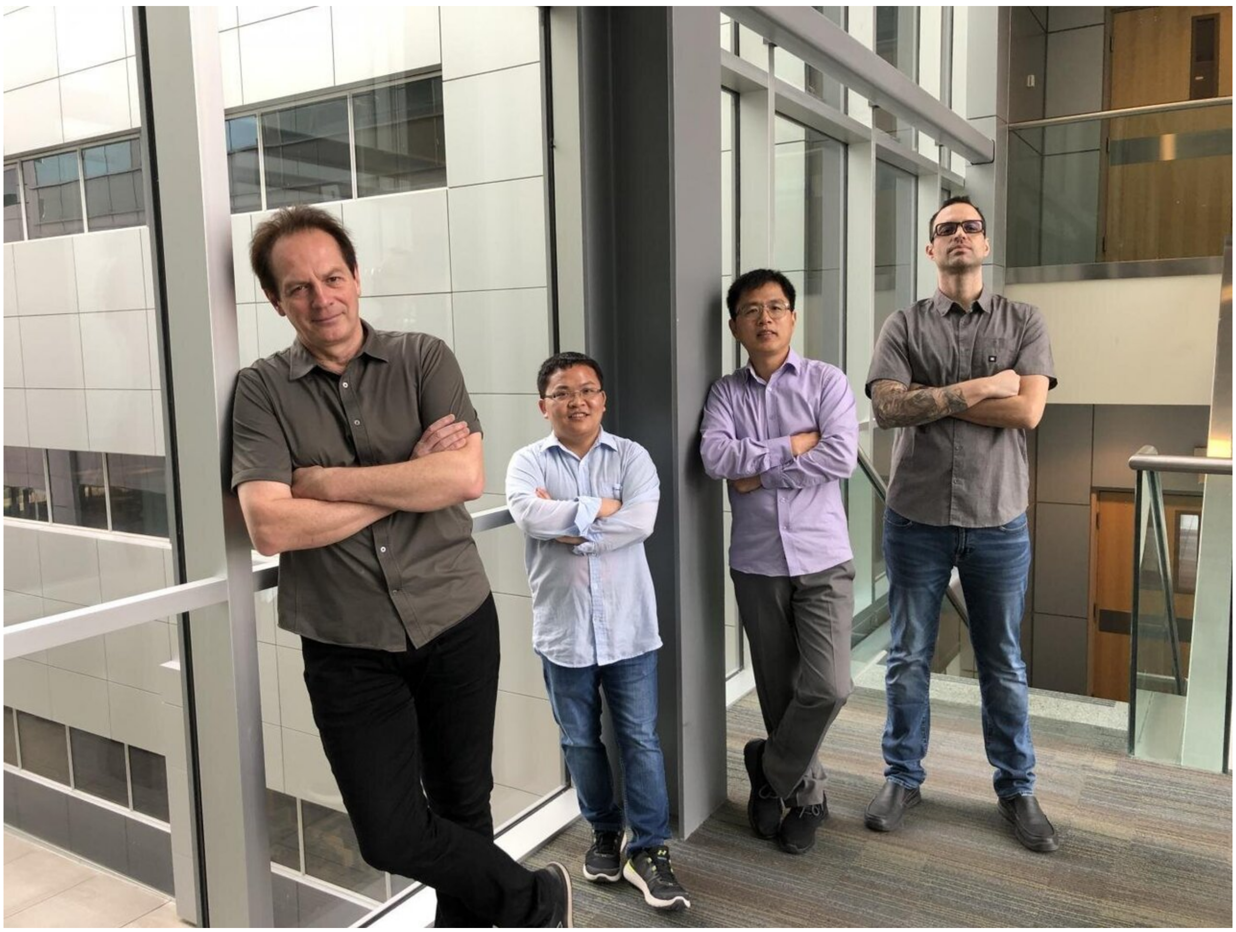

UCalgary team included (from left), Gerald Zamponi, Junting Huang, Zizhen Zhang, Vinicius Gadotti. Credit: Kelly Johnston, Cumming School of Medicine

When you experience severe pain, like breaking or shattering a bone, the pain isn't just felt at the sight of the injury. There is an entire network of receptors in your body running from the site of the injury, through your nervous system, along the spine and into the brain that reacts to tell you how much pain you are feeling. This system goes into high alert when the injury occurs, and then usually resets as you heal. However, sometimes, the system doesn't reset, and even though the injury has mended, nerve damage has caused your brain to be permanently altered. It means you still feel the pain, even though the injury has fully healed.

Dr. Gerald Zamponi, Ph.D., and a team with the Cumming School of Medicine's Hotchkiss Brain Institute (HBI) and researchers at Stanford University, California, have been investigating which brain circuits are changed by injury, in order to develop targeted therapies to reset the brain to stop chronic pain.

"It's a terrible situation for many people living with chronic pain, because there is often very little that works for them to control their pain," says Zamponi, senior associate dean (research) and a professor in the departments of Physiology & Pharmacology and Cell Biology & Anatomy at the CSM. "This doesn't just impact people who have experienced peripheral nerve damage. There are cases of people having a stroke and are experiencing severe pain afterward in another part of their body. It may also explain why some people who have lost a limb can still feel pain in the limb even though it's no longer there."

Working closely with Dr. Junting Huang, Ph.D., and Dr. Vinicius Gadotti, Ph.D., co-first authors on the study, along with Dr. Zizhen Zhang, Ph.D., the team utilized optogenetics to study the neuron connections in the brains of mice. Optogenetics allow scientists to use light to target and control individual neurons in the brain. With this tool, researchers are able to map a pathway showing which neurons are communicating with each other to process a pain signal and then communicate this information all the way back through the spine where painful stimuli are first processed.

"We've known that certain parts of the brain are important for pain, but now we've been able to identify a long range circuit in the brain that carries the message and we've been able to show how it is altered during chronic pain states," says Zamponi who is also a member of the CSM's Alberta Children's Hospital Research Institute.

Much of the research for chronic pain has been focused on the spinal cord and targeting nerve fibres where the pain response is processed. Treatment with current pain relief medications is often ineffective and can have serious side effects. This new understanding of the pain signaling circuit may allow scientists to develop new drug therapies and targeted brain stimulation treatments to address chronic nerve pain, and hopefully provide relief for pain sufferers. Working with mice, Zamponi's lab has proven that targeting certain pathways in the brain can interfere with the pain signal and stop pain sensation.

"If you understand how the brain rewires itself, you can interfere with that and you can restore it. That's important," says Zamponi. "If you think about it, there are some drugs you don't want to give to kids who have chronic pain. What if you could non-invasively stimulate certain brain regions or inhibit them, and bring pain relief that way? I think it would be a tremendous, alternative approach to taking drugs."

Zamponi expects the results the lab has seen in mice will be comparable in humans. While the human brain is very complex, the communication network is similar in the animal brain. Findings are published in *Nature Neuroscience*.

The Zamponi lab is already applying this research to investigate how this brain circuit interacts with other parts of the brain involved in more complex behaviours like the interaction between pain pathways and addiction, depression, and anxiety.

**More information:** A neuronal circuit for activating descending modulation of neuropathic pain, *Nature Neuroscience* (2019). DOI: 10.1038/s41593-019-0481-5 , nature.com/articles/s41593-019-0481-5

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