# Ending chronic pain with new drug therapy

December 21 2015

Credit: Human Brain Project

A brain region controlling whether we feel happy or sad, as well as addiction, is remodeled by chronic pain, reports a new Northwestern Medicine study.

And in a significant breakthrough for the millions of Americans suffering from chronic pain, scientists have developed a new treatment

strategy that restores this region and dramatically lessens pain symptoms in an animal model.

The new treatment combines two FDA-approved drugs: a Parkinson's drug, L-dopa, and a non-steroidal anti-inflammatory drug. The combined drugs target brain circuits in the nucleus accumbens and completely eliminate chronic pain behavior when administered to rodents with chronic pain. The key is administering the drugs together and shortly after an injury.

As a result of the study's findings, the scientists are pursuing a clinical trial. The treatment has the potential to prevent chronic pain if used early enough after injury, the scientists said.

The study will be published December 21 in *Nature Neuroscience*.

"It was surprising to us that chronic pain actually rewires the part of the brain controlling whether you feel happy or sad," said corresponding author D. James Surmeier, chair of physiology at Northwestern University Feinberg School of Medicine. "By understanding what was causing these changes, we were able to design a corrective therapy that worked remarkably well in the models. The question now is whether it will work in humans."

"The study shows you can think of chronic pain as the brain getting addicted to pain," said A. Vania Apkarian, also a corresponding author and a professor of physiology at Feinberg. "The brain circuit that has to do with addiction has gotten involved in the pain process itself."

A group of neurons thought to be responsible for negative emotions became hyper-excitable and more strongly connected with other regions of the brain linked to feeling bad within days after an injury that triggers chronic pain behavior, the study showed. It went on to show this change

was triggered by a drop in dopamine, a critical neurotransmitter.

When scientists administered the non-steroidal anti-inflammatory drug and L-dopa, which raises dopamine levels, the changes in the brain were reversed and the animals' chronic pain behavior stopped.

"These results establish chronic pain cannot be viewed as a purely sensory phenomenon but instead is closely related to emotions," Apkarian said.

In addition, Northwestern scientists treated rats experiencing chronic pain with another Parkinson's drug, pramipexole, that activated dopamine receptors, mimicking dopamine's effect. This drug also decreased the animals' pain-like behavior.

"It is remarkable that by changing the activity of a single cell type in an emotional area of the brain, we can prevent the pain behavior," said Marco Martina, associate professor of physiology at Feinberg and also a corresponding author.

Currently, the most common treatment for chronic pain is a non-steroidal anti-inflammatory type of drug, which has limited effectiveness.

"The treatments for chronic pain we currently have are very limited," said Surmeier, also the Nathan Smith Davis Professor of Physiology.

The results of the study suggest supplementing anti-inflammatories with a medication that activates dopamine receptors or raises dopamine levels might be more effective in treating chronic pain and/or preventing a transition to chronic pain.

Chronic pain is an intractable problem for millions of Americans. It's the

number one cause of disability in the U.S. and costs more than $600 billion per year in in health care.

An estimated 20 percent of the U.S. and world population suffers from chronic pain, reports the World Health Organization and the National Academy of Sciences.

**More information:** The indirect pathway of the nucleus accumbens shell amplifies neuropathic pain, *Nature Neuroscience*, DOI: 10.1038/nn.4199

Provided by Northwestern University