Chronic pain affects approximately 20% of the United States population
and 30% of the global population. Along with sensory manifestations, chronic pain conditions also are associated with high rates of comorbid depression and substance abuse. Unfortunately, the complex and variable clinical presentations of chronic pain and affective comorbidities, as well as the multifaceted regional and molecular underpinnings of the disease, make it difficult to comprehensively treat all symptoms.

A new study by researchers at Boston University Chobanian & Avedisian School of Medicine has found that prolonged nerve injury (in an experimental model of chronic pain) reduces the expression of the transcription factor, Myocyte Enhancer Factor 2C (MEF2C) in the nucleus accumbens, a brain region that regulates emotion, reward and pain processing. The research is published in the journal *Pain*.

Transcription factors manage gene expression and their dysregulation under nerve injury states can lead to increased expression of genes that enhance pain transmission or perception, or silencing of those that counteract pain-related symptoms.

"By increasing the level of this transcription factor to counteract the effects of injury, we were able to alleviate pain-like and anxiety-like behaviors, while also correcting neuronal dysfunction and altered neurotransmission in the brain mesolimbic system," explains corresponding author Venetia Zachariou, Ph.D., Edward Avedisian Professor and chair of pharmacology, physiology & biophysics at the school.

According to first author Randal Serafini, Ph.D., postdoctoral fellow in Zachariou's lab, one of the reasons that a reliable treatment for chronic pain does not currently exist is that neuronal networks are uniquely altered in response to a persistent injury. Serafini says, "There are specific brain regions that directly regulate pain and many of these comorbidities, the nucleus accumbens being one of them."
"By better understanding the mechanisms that contribute to pain in these regions, we can get one step closer to identifying treatments that are more effective," adds Zachariou.

The researchers believe that the next steps include looking through pharmacology databases to identify approved drugs that have strong safety profiles and either activate MEF2C or similarly regulate the downstream targets of MEF2C. This would allow them to move their findings to the clinic more quickly.


Provided by Boston University School of Medicine


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