A study by a UT Dallas researcher has revealed new information about a potential chemical causing pain hypersensitivity in migraines, which is the third most common disease in the world.

A key to the sensitization process, according to Dr. Greg Dussor, associate professor of neuroscience in the School of Behavioral and Brain Sciences, could be related to a protein called brain-derived neurotrophic factor (BDNF). Other studies have shown elevated levels of BDNF in human migraine patients, but its origin and the way it works have not been clear.

Dussor and his colleagues used a drug to, in essence, soak up the BDNF from the brain stem area in rats. The result was that the animals became desensitized to migraines when they were later prompted with stimuli that otherwise would provoke a headache.

"There's something that BDNF has done, and potentially is continuing to do, that is keeping migraine patients sensitized to these later events," he said. "It's exciting that we can influence that sensitization or priming by manipulating BDNF in an animal model."

Dussor's findings will be published in the December issue of the journal *Pain*.

Many scientists believe the pain of migraines originates in the meninges, which are membranes that encase the brain and spinal cord. The theory is that information travels from the meninges through trigeminal neurons into the brain stem, and then into the thalamus and other brain regions where it ultimately is processed as pain.

"There's a large amount of pain signaling that can come in from the meninges during migraines," Dussor said.

In a recent study, researchers in Dussor's lab initially stimulated the meninges in rats with a substance called interleukin 6, which seems to be involved in migraine attacks. Then, 24 hours later, the researchers injected a drug into the brain stem that soaks up the BDNF.

Dussor's team found that the removal of the BDNF desensitized the animals to subsequent migraines.

"There's some critical role for BDNF in the brain stem that allows this plastic state to develop and probably also allows it to maintain itself," Dussor said.

According to the Migraine Research Foundation, migraine is an extremely incapacitating collection of neurological symptoms that usually includes a severe, throbbing, recurring pain on one side of the head. However, in one-third of migraine attacks, both sides are affected. Attacks last between four and 72 hours, and often are accompanied by one..."
or more of the following disabling symptoms: visual disturbances, nausea, vomiting, dizziness, extreme sensitivity to sound, light, touch and smell, and tingling or numbness in the extremities or face.

In the United States, nearly one in four households include someone with migraine. Migraine is three times more common in adult women than it is in men. Dussor said migraine patients often have attacks that are triggered by stimuli that are completely innocuous in non-migraine patients.

"Stress, too much sleep, too little sleep, skipping a meal, certain scents, bright lights—all kinds of things can be triggers. But many people experience those same conditions and don't get migraines," he said.

Dussor said several non-BDNF-based therapeutic medicines are in clinical trials and could prove to be helpful to some migraine patients. But he said their effectiveness likely would vary from person-to-person and for the different types of migraines.

He said his ongoing research will be aimed at determining the root causes of migraine, particularly in regard to the BDNF protein.

"We have a lot of work to do to try to figure out what happens downstream of BDNF, trying to determine how we can target the pain system while not impacting learning and memory, emotion and movement," Dussor said. "We are still working on solving the puzzle."

**More information:** Carolina C. Burgos-Vega et al. Dural stimulation in rats causes brain-derived neurotrophic factor–dependent priming to subthreshold stimuli including a migraine trigger, PAIN (2016). DOI: 10.1097/j.pain.0000000000000692

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