Study in teens shows that brain responses to rewards are linked to pain sensitivity

26 January 2017

Patterns of brain responses to rewards are a significant predictor of pain symptoms—a link that is already present by adolescence—and may be influenced by gene variants affecting pain sensitivity, reports a study in *PAIN*, the official publication of the International Association for the Study of Pain (IASP).

"Distributed" feedback patterns to rewards predict heightened pain sensitivity, according to the new research led by Frauke Nees, PhD, Central Institute of Mental Health, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany. The researchers write: "Our results might provide a first step early in life in identifying possible risk factors for future pain complaints."

Reward Responses and Pain Are Linked; Gene Variants May Play a Role

A group of more than 600 European adolescents were studied at two times. At ages 14-15, the teens participated in an experiment in which they could earn rewards—in the form of M&M's candies—for performing a computer task. Functional magnetic resonance imaging (fMRI) scans were performed to examine how the brain processed these rewards. Two years later, the teens were evaluated on a commonly used pain symptom scale.

Patterns of reward processing at age 14-15 were evaluated as predictors of pain complaints at age 16-17. The study also examined the effects of two variants of the mu-opioid receptor gene (OPRM1) that have previously been linked to differences in pain processing. These genetic variants may affect not only responses to opioid drugs (such as morphine) but also the body's natural or "endogenous" opioids (such as endorphins).

The results showed that reward-related feedback responses in a brain area called the dorsal striatum at age 14-15 predicted the magnitude of pain symptoms at age 16-17. Whereas responses in another brain area called the ventral striatum have been linked to reward processes, the dorsal striatum has been implicated in planning, motor (movement) processing, and habit learning.

For one of the two OPRM1 variants studied, pain complaints were predicted by reward feedback-related responses in a more widely distributed brain area, including the ventral striatum. Teens with this genetic variant had a higher magnitude of pain responses.

Pain and rewards are considered "opponent yet interacting processes" involving partly similar brain regions. Identifying brain responses to rewards and their association with pain symptoms may help in understanding the neurological basis of pain-related behaviors and lend new insights into the brain areas involved in the critical transition from acute to chronic pain.

Within the limitations of the experimental study—limited to healthy children without any clinical pain problems—the results suggest that "aversive" outcomes such as pain may be related to "appetitive" reward outcomes. "Distributed brain response patterns during reward processing may be significant predictors for pain complaints, partly depending on an opioidergic genetic predisposition," Dr. Nees and colleagues conclude.

In an accompanying commentary, Dr. David Borsook of Boston Children's Hospital highlights some important questions raised by the new results, including whether an individual's "opioidergic tone" is a real indicator of pain susceptibility and risk of developing chronic pain. While further studies will be needed, he writes, "The door has been opened for an intriguing process that may have a significant influence on improving our approach to evaluating and treating patients with pain."

More information: Frauke Nees et al. Brain substrates of reward processing and the ?-opioid receptor, *PAIN* (2017). DOI: 10.1097/j.pain.0000000000000720

Provided by Wolters Kluwer Health