Placebo effect explained? Study shows the brain’s own endorphins may be responsible

By thinking the pain away, patients can prompt their own brains to release natural pain-relievers, according to a study conducted at the University of Michigan. Published in the August 24th issue of the Journal of Neuroscience by a team from the UM Molecular and Behavioral Neurosciences Institute (MBNI), the study provides the first direct evidence that the brain’s own pain-relieving chemicals - called endorphins - play a role in the placebo effect.

The placebo effect is one in which a patient’s symptoms are alleviated by an otherwise ineffective treatment because of his or her mere expectation that the treatment will help fight the disease. The results of UM study are the first to show a specific brain chemistry mechanism behind the placebo effect.

"This deals another serious blow to the idea that the placebo effect is a purely psychological, not physical, phenomenon," says Jon-Kar Zubieta, lead author on the paper and an associate professor of psychiatry and radiology at the UM Medical School. "We were able to see that the endorphin system was activated in pain-related areas of the brain, and that activity increased when someone was told they were receiving a medicine to ease their pain. They then reported feeling less pain. The mind-body connection is quite clear."

The study’s findings are based on data collected from the brain scans of 14 young, healthy men, who agreed to let researchers inject their jaw muscles with a concentrated salt water solution, causing pain. During the scans, the participants were told that they would be given a drug (in fact, a placebo) that may relieve their pain. Researchers monitored the brain chemistry of the participants using a positron emission tomography (PET) scanner while each injection was given, paying especially close attention to activity of the brain’s natural pain-relieving endorphins, called opioids.

Endogenous opioids relieve pain by binding to brain cell receptors called mu-opioid receptors, which stops the transmission of pain signals from one nerve to the next. Researchers monitored the activity of these receptors through the use of an imaging method in which tiny doses of a medicine called carfentanil are attached to a short-lived radioactive form of carbon, which releases subatomic particles known as positrons. The PET scanner detects these positrons, acting like a photographic camera, and determines where they originated from and how many are coming from each region. Because carfentanil also binds to mu-opioid receptors, competing with opioids for space, the PET scans can be used to see how active the opioid system and mu-opioid receptors are.

As the researchers alerted the participants that the placebo was coming, and injected the placebo dose (a small amount of hydrating solution), the level of activation in their mu-opioid endorphin system increased, indicating that more of the opioids were binding to the mu-opioid receptors, and relieving pain. The most pronounced activation occurred in four areas of the brain known to be involved in complex pain processing and response.
Because the study was only conducted on young men, the UM researchers were quick to point out that further studies will be needed to determine whether the effect occurs in women and in people with various illnesses.

In addition to Dr. Zubieta, the research team included MBNI members Joshua Bueller, Lisa Jackson, David Scott and Janyun Xu; radiology professor Robert Koeppe, Ph.D.; Thomas Nichols, Ph.D., an assistant professor of biostatistics in the U-M School of Public Health; and Christian Stohler, formerly of the U-M School of Dentistry and now at the University of Maryland School of Dentistry.