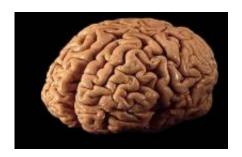


Placebo response, pain experience occur at nonconscious level: study

September 10 2012



With the discovery that the unconscious mind plays a key role in the placebo effect, researchers have identified a novel mechanism that helps explain the power of placebos and nocebos.

Described in the September 10 on-line issue of the <u>Proceedings of the National Academy of Sciences</u> (*PNAS*), the new findings demonstrate that the <u>placebo effect</u> can be activated outside of <u>conscious awareness</u>, and provide an explanation for how patients can show clinical improvement even when they receive treatments devoid of active ingredients or of known <u>therapeutic efficacy</u>.

"In this study, we used a novel experimental design and found that <u>placebo</u> and nocebo [negative placebo] effects rely on brain mechanisms that are not dependent on cognitive awareness," explains first author



Karin Jensen, PhD, of the Department of Psychiatry and the Martinos Center for Biomedical Imaging at Massachusetts General Hospital (MGH) and the Program in Placebo Studies (PiPS) at Beth Israel Deaconess Medical Center/Harvard Medical School. "A person can have a placebo or nocebo response even if he or she is unaware of any suggestion of improvement or anticipation of getting worse."

It has long been believed that placebo responses are related to conscious beliefs or thoughts and that when given an inert pill or therapy, patients get better because they have the expectation that they will get better, or in the case of nocebos, get worse because they anticipate that they will get worse.

However, more recently, scientists have recognized that humans learn to expect either reward or threat quickly and automatically without needing to consciously register the idea in their brains. As the authors write, neuroimaging studies of the human brain have suggested that certain structures, such as the striatum and the amygdala, can process incoming stimuli before they reach conscious awareness, and, as a result, may mediate non-conscious effects on human cognition and behavior.

The scientists set out to determine whether placebo and nocebo responses might be activated outside of a person's conscious awareness, even if he or she has no expectation of either improving or declining.

Jensen, together with the study's senior author Jian Kong, MD, also of MGH and the PiPS, studied 40 healthy volunteers (24 female; 16 male, median age 23). Two experiments were conducted: In the first, researchers administered heat stimulation to participants' arms while simultaneously showing them images of male human faces on a computer screen. The first face was associated with low pain stimulations and the second image with high pain. Patients were then asked to rate their experience of pain on a scale of 0 to 100, 0 being no



pain and 100 being the worst imaginable pain, but without the patient's knowledge that all heat stimulations would have the same moderate heat intensity. As predicted, the pain ratings correlated with the previously learned associations, with a pain rating of 19 when the subjects saw the low pain face while the high pain face resulted in subjects' mean reports of 53 on the pain scale (nocebo effect).

Then, in the second experiment, the participants were administered the same levels of thermal heat stimulation. Once again, the facial images were projected on the computer screen – but this time, they flashed by so quickly that subjects could not consciously recognize them. The participants once again rated their pain, and despite a lack of consciously recognizable cues, the participants reported a mean pain rating of 25 in response to the low pain face (placebo effect) and a mean pain rating of 44 in response to the high pain face (nocebo response) even though they did not consciously recognize the faces on the screen.

"Such a mechanism would generally be expected to be more automatic and fundamental to our behavior compared to deliberate judgments and expectations," explains Kong. "Most important, this study provides a unique model that allows us to further investigate placebo and nocebo mechanisms by using tools such as neuroimaging."

As PiPS Director and study coauthor Ted Kaptchuk notes, "It's not what patients think will happen [that influences outcomes] it's what the nonconscious mind anticipates despite any conscious thoughts. This mechanism is automatic, fast and powerful, and does not depend on deliberation and judgment. These findings open an entirely new door towards understanding placebos and the ritual of medicine."

Provided by Beth Israel Deaconess Medical Center



Citation: Placebo response, pain experience occur at nonconscious level: study (2012, September 10) retrieved 26 April 2024 from https://medicalxpress.com/news/2012-09-placebo-response-pain-nonconscious.html

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