It's not all in your head: Descending neural mechanisms of placebo-induced pain control

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A new study reveals that when it comes to pain control, the "placebo effect" involves evolutionarily old pain control pathways in the human brainstem, the part of the brain that is continuous with the spinal cord. The research, published by Cell Press in the August 27th issue of the journal *Neuron,* provides fascinating mechanistic insight into how and why simply expecting that a treatment will reduce pain can act as an effective analgesic.

Placebo analgesia refers to an individual's relief from pain following administration of a chemically inert substance and is thought to be due to a person's belief that a potent pain medication was administered. Endogenous opioids, which are naturally produced by the brain in small amounts and play a key role in the relief of pain and anxiety, have been implicated in placebo analgesia. Brain imaging studies have shown that placebo analgesia stimulates release of endogenous opioids from higher brain regions associated with pain modulation and is associated with a decrease in signals from pain-sensitive areas.

"It has been hypothesized that placebo analgesia also recruits the opioidergic descending pain control system, which inhibits pain processing in the spinal cord and, therefore, subsequently reduces pain-related responses in the brain, leading to a decreased pain experience," explains lead study author Falk Eippert from the University Medical Center Hamburg-Eppendorf in Germany. However, thus far this has not been demonstrated experimentally.

Eippert and colleagues employed sophisticated brain imaging techniques to examine both higher cortical and lower brainstem responses in two groups of subjects: one receiving a drug called naloxone, which blocks opioid signaling, and one group with a natural opioid state. Expectations of pain relief were induced in both groups using an established placebo analgesia paradigm.

The researchers found that naloxone reduced behavioral placebo effects as well as placebo-induced decreases in pain-related brain responses. Most importantly, they also observed that, under placebo, cortical areas interacted with brainstem structures implicated in pain control and that these interactions were dependent on endogenous opioids and were related to the strength of experienced placebo effects.

"Taken together, our findings show that opioid signaling in pain-modulating areas and the projections to downstream effectors of the descending pain control system are crucially important for placebo analgesia," concludes Eippert. "It will be interesting to see whether opioid-dependent activation of the descending pain control system is a common feature of different forms of pain modulation, such as hypnosis and attentional distraction, which share some common neuroanatomical features."

Source: Cell Press (news : web)