Hooked on a Feeling

This is your brain on a placebo.

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As far as the body is concerned, a placebo is nothing—a sugar pill, a sham treatment, an inert compound. But try telling that to the brain, as scientists led by Daniel Cherkin of Group Health Center for Health Studies in Seattle recently saw. They assigned 638 adults with chronic lower-back pain to receive either standard acupuncture therapy, customized acupuncture (tailored to the individual, such as by using nonstandard acupuncture points), sham acupuncture (toothpicks in acupuncture-needle guide tubes that mimic the feel of real acupuncture) or standard back-pain care, such as anti-inflammatory drugs and massage. As the scientists reported this month in Archives of Internal Medicine, pain diminished significantly for 60 percent of the people in all three acupuncture groups—but for just 39 percent of patients receiving usual care. On average, both fake and real acupuncture reduced pain more than twice as much as standard care. Weirdly, this is being spun as "acupuncture is better than standard medical care for back pain!" I say "weirdly" because the key finding is that sham acupuncture delivered as much benefit as real acupuncture. And the most parsimonious explanation for that finding is inescapable: it is possible to think yourself out of pain.

In fact, the power of thought to relieve pain has been known since 1978, when neuroscientists began studying placebo responses in earnest. Now they have even mapped the brain processes that underlie it. When people expect their pain to diminish, typically because a doctor tells them that a little pill or other treatment will do so, that mere expectation produces activity in the prefrontal cortex, site of higher mental function, which in turn activates other regions to release the brain's own homemade opioids, says Fabrizio Benedetti of the University of Turin Medical School, a pioneer in placebo research. (A big advance in understanding placebo was showing that a drug that blocks the effects of opioids also blocks the placebo effect on pain, prima facie evidence that the brain's endogenous opioids are in play.) The higher the expectations, the greater the pain relief, too. When scientists led by Dan Ariely of Duke University gave volunteers identical dummy pills before and after an electric shock, and told some of their human guinea pigs that the pills were analgesics costing $2.50 and others that they cost 10 cents, more of those getting the expensive placebo than the cheaper one reported pain relief (85 percent vs. 60 percent).

It's not just pain anymore, either. If neuroscientists have learned anything about placebo, it is that there is not a single placebo effect, but placebo effects, plural, each with different mechanisms and each shedding light on how ethereal, high-level mental functions control the nitty-gritty of lower-level brain processes. For one thing, what Benedetti calls "mind over matter" (matter being the body) turns out to be effective in conditions having nothing to do with pain. Injecting an inert saline solution reduced the symptoms of Parkinson's disease. For instance, when patients were told that they were receiving medication, many of them began to move more fluidly and had less rigidity, scientists at the University of British Columbia found. What seems to happen is that expecting a treatment to be effective releases dopamine, which is both the brain's reward molecule and the precise chemical that is scarce in the brains of Parkinson's patients. That dopamine surge from the striatum calms the chaotic neuronal firing that causes the spasms and rigidity of Parkinson's, as Benedetti showed in the first study of the placebo effect on individual neurons. "Verbal suggestions of clinical improvement changed the activity of neurons in specific brain areas," says Benedetti. It doesn't work on everyone, and the effect typically fades after a while—two of the many remaining mysteries about placebo responses.
Remarkably, placebo effects occur through physiological pathways that have nothing to do with expectations and the release of opiates or dopamine. Instead, they work because the brain has learned that a particular experience is followed by a particular response—Pavlovian conditioning. Morphine, for instance, is notorious for depressing respiration, which is why it can be dangerous. In one 1999 study, after patients had received several doses of a morphinelike drug for post-op pain, a placebo produced the same respiratory depression: the brain had learned, at the neuronal level, that injection equals slow, shallow breathing, and responded that way even to an inert compound. "The response is completely unconscious," says Benedetti. Similarly, when he and colleagues gave volunteers a cortisol-lowering drug twice, and then a placebo, the placebo mimicked the cortisol-decreasing action of the drug, regardless of what patients expected. Pavlovian conditioning also seems to be behind placebo effects on the immune system. When scientists repeatedly gave the powerful immune suppressant cyclosporine (used to prevent rejection of transplanted organs) along with a flavored drink, and then the drink alone, the patients' immune systems were as quiet as when on the drug. It was like finding that Kool-Aid can prevent transplant rejection. Mind over matter had struck again.

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