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Why Placebos Really Work: The Latest Science

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Illustration: Jason Schneider for The Wall Street Journal

By
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Scientists are finding a growing number of ways placebos appear to bring about real health benefits in patients.

The research could someday lead to increased use of placebos—substances that have no apparent pharmaceutical effect—in treatments for common diseases.

Studies have shown that administering placebos reduces pain and symptoms in patients with irritable bowel syndrome and migraines, even when patients know they are taking a placebo. Scientists are exploring if they can get the same result in chronic back pain and cancer-related fatigue.

Parkinson's-disease researchers discovered that stopping patients' real medication and substituting a placebo continues to ease their symptoms, likely because the body is preconditioned to trigger the same response.

Numerous studies have documented neurobiological effects that placebos have in the brain, resulting in the release of neuromodulators that can help reduce pain and symptoms of illness. New evidence suggests the fake drugs may also affect the body, in particular the immune system, according to an animal study published online in July in the journal Nature Medicine.

"This is not just making it up in your mind. The placebo effect has a biology," says Ted J. Kaptchuk, director of the Program in Placebo Studies and Therapeutic Encounter at Beth Israel Deaconess Medical Center in Boston and a professor at Harvard Medical School. "The pathways that we know the placebo effects use are the pathways many significant drugs use."

Placebos are most commonly used in clinical drug trials, paired off against a new drug being developed. A surprisingly large number of doctors—studies and surveys suggest at least half—prescribe placebos to their patients. This is usually when there isn't a suitable remedy on the market for a patient's symptoms or the symptoms don't seem to be a serious threat, such as fatigue or minor aches.

The placebos doctors most often prescribe are active drugs but in such low doses that there is no apparent therapeutic benefit, says Walter Brown, a clinical professor of psychiatry at Brown University who wrote "The Placebo Effect in Clinical Practice," a book published in 2013. Physicians also prescribe vitamins, antibiotics or over-the-counter analgesics, like aspirin. Doctors rarely will prescribe an outright sugar pill.

Guidelines from the American Medical Association from 2006 tell doctors it is unethical to

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‘This is not just making it up in your mind. The placebo effect has a biology,’ says Ted J. Kaptchuk, director of the Program in Placebo Studies and Therapeutic Encounter at Beth Israel Deaconess Medical Center in Boston. *Photo: Beth Israel Deaconess Medical Center*

give patients a placebo without disclosing it to them. But few doctors are believed to actually do this, experts say.

Dozens of studies have shown that the power of placebos goes beyond patients’ imaginations, says Prof. Kaptchuk, of Beth Israel Deaconess. This was first demonstrated in 1979 when patients in a dental-pain experiment were given a placebo they thought was a painkiller, he says. About one-third of them reported less pain. Subsequent drugs to block the action of painkillers removed the placebo effect.

The study showed placebos cause the brain to release endogenous opioids, or endorphins, that reduce pain, Prof. Kaptchuk says. Subsequent research has found that other substances are also activated by placebos, including endocannabinoids and dopamine, part of the brain’s reward system.

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Asya Rolls, an assistant professor at the Technion, Israel Institute of Technology, found in a new animal study that placebos not only activate the reward system in the brain, they also affect the body's physiology, in particular the immune system. *Photo: Haim Magiura*

Even when patients are told a medication they are getting is a placebo, it still can ease symptoms and pain. Prof. Kaptchuk says he found this to be true in a randomized controlled trial of 80 patients with irritable bowel syndrome published in the journal PLOS One in 2010, and in a 2014 study in Science Translational Medicine involving 66 migraine patients. There were similar results among patients with chronic back pain in a study Prof. Kaptchuk plans to publish. Genetic differences in people may make some more likely to respond to a placebo, he says.

"Brain-imaging studies have shown that during placebo, people have an activation of the reward system" in the brain, says Asya Rolls, an assistant professor at the Technion, Israel Institute of Technology, and senior researcher on the study in Nature Medicine. "We wanted to see whether activation of the reward system can do anything on the physiology and we focused on the immune system," she says.

To do that, the researchers infected mice with E. coli bacteria and used technology to

activate the neurons in the reward circuit of the brain.

They found that the immune system was more responsive—killing bacteria twice as efficiently—than it was in mice whose reward system wasn't activated. The mice also produced more antibodies to the bacteria --- a month later when injected with E. coli again they had a stronger immune response.

Although the human brain-reward system has much in common with mice, it isn't known if people would show the same immune response. Activation of the brain's reward system likely also affects other aspects of the body's physiology, Dr. Rolls says.

Luana Colloca, an associate professor at the University of Maryland, Baltimore, has studied the placebo effect in Parkinson's patients. After the patients several times use the drug apomorphine, a common treatment that activates dopamine, it can be substituted with a placebo, she says.

"When we use a placebo after an active treatment, the placebo mimics the same action of the active treatment through a mechanism we call pharmacological conditioning," says Dr. Colloca, who is currently focusing on the placebo effect in acute and chronic pain. "A current goal is to reduce opioids to optimize pain management," she says.

In previous published research, Dr. Colloca says she and colleagues detected differences in neurons in the brains of Parkinson's patients given a placebo. The patients reported fewer tremors and less muscle rigidity even when receiving a placebo treatment, she says. Other research groups are exploring similar phenomena in patients with asthma and sleep disorders, she says.

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