

# Placebo Nation: Just Believe

**W**HEN YOU WRITE ABOUT SCIENCE, THERE IS NO SHORTAGE OF topics that incite the wrath of readers. Climate change. Evolution. Racial differences in IQ. But say that dummy pills with no pharmacologically active ingredients—placebos—are about as effective as antidepressants in treating depression, and watch out. People are incensed at the very thought that the (often expensive) meds they rely on might be 21st-century versions



of the magic feather that Dumbo, the flying elephant, was told would make him airborne. It was only when Dumbo dropped the feather he was clutching in his trunk while in free fall, and started flapping his ears, that he grasped that his powers actually came from within, allowing him to fly.

No one is saying “positive thinking” can cure cancer, or that patients should throw out their pills, let alone that illnesses that respond to the placebo effect are “all in your head”—imagined. But there is no denying the drumbeat of studies on the therapeutic power of placebos. Over the years they have been shown to relieve asthma, lower blood pressure, reduce angina and stop gastric reflux. An inert solution injected into the brains of patients with Parkinson’s disease reduced muscle rigidity about as well as standard drugs. In a bizarre finding, sham surgery of the knee, in which patients got sedation and an incision but no actual procedure, relieved the pain of osteoarthritis better than actual arthroscopy—and produced an equal improvement in joint function, scientists reported in 2002. And last month an analysis of clinical trials of a range of antidepressants found that, except in the most severe cases, placebos lifted the black cloud as well as meds did.

To be sure, no study is perfect. In the antidepressant one, the placebo might not have looked as effective if it had been compared with the drug that worked best for each patient, rather than with the one that happened to be chosen for the clinical trial. (Some patients respond better to Paxil, some to Effexor or others, for reasons that remain murky.) But the fact remains that placebos are at least somewhat effective and sometimes very effective for some patients. Rather than railing against that finding or pretending it doesn’t exist, what we should be doing is learning how brain activity that corresponds to the expectation of cure translates into clinical improvement. As Dan Ariely of Duke University says, “It’s not that medicines are crummy, but that the placebo effect is so powerful.”

There have been clues about the source of that power. In Parkinson’s disease, studies find, the expectation of getting better raises brain levels of the neurochemical dopamine, whose shortage underlies Parkinson’s, and normalizes the pattern of firing in a region of the brain where aberrant firing causes the loss of motor control. When the placebo effect relieves pain, it releases natural opioid-like molecules in the brain that have analgesic effects like morphine.

Ariely, a behavioral economist, saw the power of placebos

during the three years he spent in a hospital recovering from a horrific accident that left him with third-degree burns over 70 percent of his body. Night after excruciating night, patients would beg for painkillers. One day, he recalls, “I overheard the doctors telling the nurses not to give a certain patient any more morphine. A few hours later, when the same patient started begging for painkillers I saw the nurse going to her room with an injection,” and soon the patient fell asleep. When Ariely asked the nurse about it, she said the injection was plain saline—a placebo.

Ariely’s curiosity about the power of expectation—which he explores in his new book, “Predictably Irrational”—inspired a study of what affects those expectations. He and colleagues gave 82 volunteers a brochure explaining that they would be testing a new pain drug called Validone that worked like codeine, but faster. (It was actually a placebo.) Each then received a series of electrical shocks on their wrists, rating them from “no pain at all” to “the worst pain imaginable.” Each then took a “Validone.” Half were told it cost \$2.50, the other half that it cost a dime. They then received shocks again. Of those who got the \$2.50 pill, 85 percent felt less pain from the same voltage than before taking it; 61 percent of those taking the cheap pill felt less pain, the scientists reported last week in *The Journal of the American Medical Association*.

**It’s not that medicines are ‘crummy,’ but that placebos are so powerful. It’s time scientists learned why.**

The pricier the drug, the higher the expectation of efficacy, and the stronger the placebo effect. That will not surprise doctors whose arthritis patients screamed bloody murder after Vioxx was withdrawn from the market after studies showed it raised the risk of heart attacks. People insisted that switching to cheap aspirin just did not relieve their pain and suffering. Maybe. But in light of Ariely’s research, you’ve got to wonder: And patients who protest when their insurer makes them switch from a name-brand drug to a cheaper, biologically identical generic? “Many claim the generic is less effective,” says Ariely, “but you have to consider whether that’s an effect of the price. The placebo effect is about expectations, and we expect more-expensive medicines to work better.” Maybe researchers would be interested in figuring out how to harness that effect if only it were patentable.

