

# A Placebo Can Work Even When You Know It's a Dummy Pill

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## STORY AT-A-GLANCE

- › A placebo is an inert substance that has no effect on your body. In medical research, placebos are used as controls against which the effects of drugs are measured
- › The placebo effect taps into your body's own virtual pharmacy. Drugs work because your body has chemical receptors for the drugs, but you also have natural brain chemicals that act on those same receptors, effectively mimicking the results of drugs
- › Body chemicals are released in response to or in accordance with your mental or emotional expectations or beliefs
- › Placebos can work even when the patient is fully aware they're getting a dummy pill. In one study, nearly 60% of patients openly told they were given a placebo pill reported relief from irritable bowel syndrome, compared to just 35% of those who received no treatment
- › The placebo effect accounts for more than half of the therapeutic value of the migraine drug Maxalt, and subjects reported pain relief even when they were informed that they were receiving a placebo, when compared to no treatment at all

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By definition, a placebo is an inert substance that has no effect on your body. In medical research, placebos (such as sugar pills) are used as controls against which the effects of drugs are measured.

However, the placebo effect, in which a patient believes he or she is getting an actual drug and subsequently improves despite receiving no active substance at all, has

become a well-recognized phenomenon.<sup>1</sup> Some studies into the placebo effect have even concluded that many conventional treatments "work" because of the placebo effect and little else.

Indeed, the placebo effect may even be at work in some surgical procedures, as evidenced in studies showing sham knee surgery is as effective as the real thing.<sup>2,3</sup> This, despite the fact that the physical problem is in no way addressed.

## **Placebo Effect Works by Affecting Brain Chemistry, Circuitry**

While we know the placebo effect is real, questions abound as to the mechanisms that makes it work. Writing in the journal *Neuropsychopharmacology*<sup>4</sup> in 2011, the researchers highlighted the following observations:

*"1. First, as the placebo effect is basically a psychosocial context effect, these data indicate that different social stimuli, such as words and rituals of the therapeutic act, may change the chemistry and circuitry of the patient's brain.*

*2. Second, the mechanisms that are activated by placebos are the same as those activated by drugs, which suggests a cognitive/affective interference with drug action.*

*3. Third, if prefrontal functioning is impaired, placebo responses are reduced or totally lacking, as occurs in dementia of the Alzheimer's type."*

As noted by The Washington Post and published studies,<sup>5,6</sup> researchers have also discovered a "hierarchy of effectiveness," with certain types of placebos appearing to have stronger effects than others. For example, injections or creams have stronger placebo effects than pills, and sham injections and sham acupuncture (which also uses needles) being more effective than placebo pills.

Price also matters,<sup>7</sup> with expensive pills or treatments garnering better results than inexpensive ones. Lastly, telling the patient that the treatment will relieve their symptoms produces a greater placebo effect than saying it "might" help.

# **Your Expectations Direct Your Body Chemistry**

Using brain imaging technology during placebo tests, researchers have been able to show that even when a placebo is used, your brain still responds according to expectations.

For example, in trials involving placebos for pain relief, the participant's brains release natural opioids that provide opioid-mediated pain control. So, the placebo effect is tapping into the same pain control centers as opioid drugs. Placebos can also trigger the release of many other natural brain chemicals, such as those involved in making us feel more energized, or those that help us sleep better.

In short, the placebo effect taps into your body's own virtual pharmacy. Drugs work because your body has chemical receptors for the drugs, but you also have natural brain chemicals that act on those same receptors. This is why placebos so often can mimic the effects of the drugs.

This tells us that the placebo effect is not illusory. Rather, it relies on your body's own chemicals, which are released in response to or in accordance with your mental or emotional expectations or beliefs. With that in mind, just how far can a placebo take you? Placebo trials on patients with Parkinson's disease have revealed that even this serious condition can be ameliorated with a dummy pill.

Lack of dopamine is one of the factors producing the symptoms of Parkinson's, and brain scans show that when Parkinson's patients are told they're receiving an active medication, the dopamine levels in their brains increase, even when there's no active ingredient in the pill. Remarkably, a placebo can release as much dopamine as amphetamines in a person with a healthy dopamine system,<sup>8</sup> so the response can be quite dramatic.

## **Placebos Work Nearly as Well as Antidepressants**

Another excellent example of the placebo effect is that of antidepressants. Research<sup>9</sup> published in 2010 suggests antidepressants work no better than a placebo for people with mild to moderate depression.

An earlier meta-analysis<sup>10</sup> also concluded the difference between antidepressants and placebo pills is indeed very slight. According to the authors:

*"Drug-placebo differences in antidepressant efficacy increase as a function of baseline severity, but are relatively small even for severely depressed patients. The relationship between initial severity and antidepressant efficacy is attributable to decreased responsiveness to placebo among very severely depressed patients, rather than to increased responsiveness to medication."*

Considering the long list of side effects associated with antidepressants, including worsening depression, it seems reasonable to conclude that a placebo would be a far preferable option to the real thing.

## **Placebo Effect Growing in Potency Among Americans**

Interestingly, investigations reveal the placebo effect is growing in potency among Americans, and it's having a dramatic real-world impact on the development of new painkillers.

Drug companies are finding it increasingly difficult to get pain-reducing drugs through clinical trials, because as people's responses to placebos are getting stronger, it makes it more difficult to prove that the drug actually works.<sup>11,12</sup>

Equally interesting, research shows placebos can work even when the patient is fully aware of the fact that they're getting a dummy pill.<sup>13</sup> This effect appears to be so reliable that entrepreneurs are now selling placebo pills and creams on Amazon.

## **Placebos Work Even When Patient Knows They're Not Real**

Ted Kaptchuk, professor of medicine at Harvard Medical School, is one of the leading researchers on the placebo effect. Normally, the placebo effect is studied by giving half of the test subjects the real treatment while the other gets a dummy pill, but neither of the groups is aware of what they're getting.

Kaptchuk was curious what might happen if people knew they were receiving a placebo right from the start. So, in 2009, he launched the first open-label placebo trial,<sup>14</sup> enrolling people diagnosed with irritable bowel syndrome (IBS). As reported by Time:<sup>15</sup>

*"The findings were surprising. Nearly twice as many people in the trial who knowingly received placebo pills reported experiencing adequate symptom relief, compared with the people who received no treatment.*

*Not only that but the men and women taking the placebo also doubled their rates of improvement to a point that was about equal to the effects of two IBS medications that were commonly used at the time. 'I was entirely confused,' says Kaptchuk. 'I had hoped it would happen, but it still defies common wisdom.'"*

Overall, nearly 60% of the patients given a placebo pill (and, again, told they were receiving a placebo) reported adequate relief from IBS symptoms, compared to just 35% of those who received no treatment. Even more astonishing, those taking the placebo reported improvements that were virtually the same as those reported from people taking the strongest IBS medications.

## **Mind Over Body, or Is It Body Over Mind? Perhaps Both**

Kaptchuk's team is now working on a replication study with a \$2.5 million grant from the National Institutes of Health. So far, 270 people with IBS have participated in this still-ongoing trial.

While it sounds implausible that you would get results when you're fully aware that you're taking a dummy pill, Time recounts the story of Linda Buonanno, who participated

in Kaptchuk's 2009 IBS study; three weeks after taking a clearly marked placebo twice a day, she was completely free of symptoms.

This, despite the fact she was sorely disappointed when she realized it was an open placebo trial, and that she wouldn't receive any real treatment. "I didn't have a clue what was going on," Buonanno told Time. "I still don't."

After the study ended, her symptoms came back, so Kaptchuk is now treating her in his home clinic — with sugar pills. "All I know is that it works," Buonanno says. "That's all I care about." Kaptchuk admits he doesn't fully understand it either, but he believes your body may have the ability to respond even when your mind knows the factual truth. Time writes:<sup>16</sup>

*"He struggles to find adequate analogies, but likens it to watching Romeo and Juliet when you know what's going to happen. If the performance is evocative enough, even though you know it's fake, 'your body reacts in ways that go beyond the mind,' he says. You might get a lump in your throat or tear up.*

*More important to Kaptchuk than understanding why honest placebos work is figuring out how the gain in scientific knowledge could translate into clinical practice. 'Placebo has generally been denigrated in medicine, but I always wanted to figure out ways to ethically harness it,' he says."*

Writing in Reader's Digest,<sup>17</sup> Robert Anthony Siegel also discusses his own experience with placebo. A longtime friend of John Kelley, psychology professor at Endicott College and deputy director of Harvard's program in placebo studies and therapeutic encounter, Siegel received a specially designed placebo to treat chronic writer's block with accompanying panic attacks and insomnia.

## **Placebo Effect Accounts for Half the Value of Migraine Drug**

Kaptchuk's team has also investigated the placebo effect on migraines, and compared dummy pills against the migraine drug Maxalt (rizatriptan) for recurring migraines.<sup>18</sup> Here, as in Kaptchuk's open-label placebo trial on IBS patients, subjects reported pain

relief even when they were informed that they were receiving a placebo, when compared to no treatment at all.

Overall, the placebo effect was found to account for more than 50% of the therapeutic value of Maxalt. Kaptchuk explained:<sup>19</sup>

*"This study untangled and reassembled the clinical effects of placebo and medication in a unique manner. Very few, if any, experiments have compared the effectiveness of medication under different degrees of information in a naturally recurring disease.*

*Our discovery showing that subjects' reports of pain were nearly identical when they were told that an active drug was a placebo as when they were told that a placebo was an active drug demonstrates that the placebo effect is an unacknowledged partner for powerful medications."*

## **The Future of Medicine — Harnessing the Power of Placebo**

Alia Crum, Ph.D., a placebo researcher at the Stanford Mind & Body Lab, also stresses that "placebo is not magic." Rather, the effect is "the product of your body's ability to heal, which is activated by our mind-sets and expectations ... shaped by medical ritual, branding of drugs and the words doctors say." According to Time:<sup>20</sup>

*"Crum says honest-placebo research is fascinating and important, but she doesn't see doctors prescribing placebo pills anytime soon. Instead, she's interested in how doctors can get their patients into the right mindset for medical care.*

*'We've been pumping billions of dollars into developing new drugs and treatments without making much headway on the chronic-disease crisis,' she says. 'What if we spent that same time, money and effort on achieving a greater understanding of the patients' natural abilities to heal?' ...*

*Crum and a colleague are working with Stanford Primary Care to roll out a curriculum called Medicine Plus, in which medical teams, including everyone from receptionists to physicians, learn how to create an environment that is most conducive for healing.*

*The strategies focus on leveraging patients' mind-sets but build on the power of the placebo with the ultimate goal of helping medical practitioners harness the same forces that contribute to placebo effects alongside active medications and treatments, says Crum.*

*Ideally, she says, one day these types of lessons should be incorporated into care much earlier, when health providers are in medical school."*

While placebo treatments are unlikely to become mainstream anytime soon, discussions and scientific investigations into ways in which the placebo effect may be fruitfully harnessed in clinical practice are underway.

A 2011 special issue of Philosophical Transactions of the Royal Society B (published by the U.K.'s national academy of science) reviewed the available research, concluding that "more rigorously designed studies are needed" to tease out the complexities involved and find ways in which the placebo effect might be adapted for clinical use.<sup>21</sup>

Perhaps one of the simplest ways for a doctor to harness the placebo effect in clinical practice, without taking any ethical risks, is to tap into empathy and raise the patient's expectation of relief. Studies have repeatedly found that patients who feel their doctor is warm and empathetic (have so-called good bedside manner) are more apt to get well.

Describing how a medication or treatment can make a patient better has also been shown to have a positive impact, likely because it heightens the patient's expectations.

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