Skeptic: Extraordinary Claims, Revolutionary Ideas, and the Promotion of Science

In this week’s eSkeptic:

- feature article: The Placebo Effect
- Skepticality: The Great Psychic Detective Challenge
- upcoming lecture: Thank God for Evolution, with Michael Dowd
- SkepticBlog: Thinking Digital — The TED of the UK

So much has been written and said about the placebo effect that we thought we should put our SkepDoc on the trail of finding out what is fact and what is myth about placebos and their effects. You will be surprised by some of Dr. Hall’s findings. Be sure to check out the relevant books and the Skeptic back issue that we’ve highlighted in the article which are available at Shop skeptic.

The Placebo Effect

by Harriet Hall, MD
JANE D. WAS A REGULAR VISITOR TO OUR ER, usually showing up late at night demanding an injection of the narcotic Demerol, the only thing that worked for her severe headaches. One night the staff psychiatrist had the nurse give her an injection of saline instead. It worked! He told Jane she had responded to a placebo, discussed the implications, and thought he’d helped her understand that her problem was psychological. But as he was leaving the room, Jane asked, "Can I get that new medicine again next time instead of the Demerol? It really worked great!"

What’s going on here? What is the placebo effect and how does it work?

The term “placebo effect” is unfortunate; it leads to misunderstandings. Placebos themselves don’t have any effect. They are inert: that’s what placebo means. The word placebo comes from the Latin for “I please.” You can think of it as the opposite of “I benefit.” What we really mean by “the placebo effect” is not some mysterious effect from giving an inert treatment, but the complex web of psychosocial effects surrounding medical treatment. Those effects occur with effective treatments too, not just with inert treatments.

Mark Crislip, MD, thinks the placebo effect is a myth. "I think that the placebo effect with pain is a mild example of cognitive behavioral therapy; the pain stays the same, it is the emotional response that is altered ... Ain’t no such thing as a placebo effect, only a change in perception."\(^1\) He’s correct in saying that the placebo effect does nothing to change the pain signals in the nerves. But most people think the change in
perception is the placebo effect and is worth pursuing.

There is a big difference between pain and suffering. A woman’s labor pains hurt, but with a joyful end in sight she may not suffer as much as a man who has milder pain sensations but is worried that his injured leg may need to be amputated. Some people say that morphine doesn’t relieve pain so much as make you not care about it. The experience of pain and the meaning of pain for the patient matter as much as the strength of the pain stimulus. If the placebo effect can do anything to divert the patient’s attention or help him reframe the meaning of his pain, his altered perception can reduce his experience of suffering.

Beecher Says Placebos Are Powerful

In 1955, Dr. Henry Beecher published a seminal paper entitled “The Powerful Placebo” in the Journal of the American Medical Association. He reviewed studies that compared an active treatment to a placebo, and found that on average 35% of patients improved with the placebo. So any study that doesn’t have a placebo group for comparison is likely to give a false positive result. The placebo-controlled trial is now one of the cornerstones of medical science. It’s not enough to show that Miracle-mycin works; we have to show that it works better than a dummy pill that looks like Miracle-mycin but only contains sugar.

Beecher’s paper has been widely cited as evidence that 35% of patients respond to placebos, but that’s not really what it showed. He wasn’t measuring the placebo effect in isolation — he was actually measuring a combination of the placebo effect, the natural course of disease, and other factors. The patients who apparently responded to placebo included patients who showed improvement for other reasons. Reasons like spontaneous improvement, fluctuation of symptoms, regression to the mean, answers of politeness, experimental subordination, conditioned answers, misjudgment, etc.

Hrobjartsson Says Placebos Are Powerless

To tease out how much of that 35% should be attributable to placebo, we need to know how many patients might have reported improvement without any treatment. In 2001 two Danish researchers, Ashjorn Hrobjartsson and Peter Gotzsche, published a paper entitled “Is the Placebo Powerless?” in the New England Journal of Medicine. They reviewed studies that included a no-treatment group, and they compared the improvement with placebos to the improvement with no treatment. They “found little evidence in general that placebos had powerful clinical effects.”

For studies with a binary outcome (improved versus not improved) there was no significant difference between the placebo and no treatment groups. For studies with continuous outcomes, there was some apparent effect of placebo; but not so for objective outcomes that could be measured by someone else, such as blood pressure, but only for subjective outcomes that depended on self-reports, such as pain. They weren’t even sure about that, however, because the effect was greater in smaller trials, indicating possible bias.
But Placebos Do Work, Don’t They?

It’s hard to reconcile a study like this with what we know about placebos from experiences like the case of Jane D. They do seem to work, and they seem to work very dramatically at times.

In a study of pain after dental surgery, patients were given either intravenous morphine or a saline placebo. If they were told that the saline was a powerful new painkiller, they got just as much relief as the patients who received morphine. In another study, all patients were given morphine for post-op pain, but only half were told they were getting it. The patients who didn’t know they were getting it only experienced half as much pain relief. In a study of acupuncture for post-op dental pain, there was no difference between the “real” acupuncture and placebo “sham” acupuncture groups, but when they asked patients which group they thought they were in, they discovered that those who believed they were in the “real” group reported significantly more pain relief than those who believed they were in the “sham” group — regardless of which group they were actually in!

We not only know placebos “work,” we know there is a hierarchy of effectiveness:

- Placebo surgery works better than placebo injections
- Placebo injections work better than placebo pills
- Sham acupuncture treatment works better than a placebo pill
- Capsules work better than tablets
- Big pills work better than small
- The more doses a day, the better
- The more expensive, the better
- The color of the pill makes a difference
- Telling the patient, “This will relieve your pain” works better than saying “This might help.”

In one study patients were given the same aspirin in either a brand name bottle or an unlabelled bottle; it worked better if it was labeled as a brand they recognized. Our pharmacy used to stock two different
brands of allergy pills that were made in the same factory and were identical except that one was green and the other was blue. When a patient said it wasn’t working any more, we’d switch him to the other brand and it would start working again.

Along with placebo effects, there are nocebo (“I harm”) effects. People getting inert treatments often report new symptoms. A friend of mine stopped taking her homeopathic sleep remedy because she thought it was causing side effects. (Homeopathy is the ultimate placebo because its remedies usually contain nothing but water.) In the Women’s Health Initiative study of postmenopausal hormone treatment, when the treatment was stopped, 63% of the women taking hormones reported withdrawal symptoms, but so did 40% of the women taking a placebo. If we tell patients a treatment may cause nausea, they are far more likely to report nausea than if we don’t mention that possibility.

The placebo effect is mainly subjective. Placebos don’t work on patients who are asleep or unconscious. You have to know you’re being treated. Placebos don’t keep women from getting pregnant. They don’t cure cancer, heal broken bones, or do anything you can measure objectively. They work for more elusive complaints like headache, depression, itching, shortness of breath, tension, indigestion, and other symptoms that require us to accept the patient’s self-report of what he is experiencing.

That doesn’t imply that those symptoms are not real. Some misguided doctors have tried to use placebo response as a test to diagnose whether a patient is really sick or not. That test doesn’t work, and even if it did it would be unethical.

Some researchers believe that placebos can have objective effects. When doctors painted warts with an inert dye and told patients the wart would disappear when the color wore off, the warts disappeared. Patients with newly implanted pacemakers improved even before the pacemakers were turned on. Asthmatics’ airways dilated when they were told they were getting a bronchodilator. Colitis patients treated with placebo not only reported feeling better but actually had less inflammation of the intestines visible on sigmoidoscopy. Patients with ulcers healed faster when given two placebo pills instead of one.

Harvard University medical researcher Herbert Benson believes that the placebo effect yields clinical improvement for 60–90% of diseases, including angina, asthma, herpes simplex, and ulcers. Studies that have not been replicated have suggested that the placebo effect can influence things like swelling, movement disorders, temperature, pulse, blood pressure, cholesterol, blood sugar, and exercise tolerance.

So far the evidence for objective placebo effects is weak. Another hypothesis is that the placebo effect is only subjective, but that these subjective effects can indirectly lead to objectively measurable effects. For example, if you are in pain and the placebo effect decreases your perception of that pain, you might expect your pulse and blood pressure to drop. If you are asthmatic and are wheezing, any psychological factor that reduces your anxiety level or helps you relax might indirectly ease your breathing symptoms and even allow your constricted bronchi to dilate. In this view, the placebo effect doesn’t really cause objective effects, it allows you to have a different experience of your symptoms and it is that different experience that indirectly affects your physiology. Semantic quibbling, perhaps.

Placebo surgery is another controversial subject. Forty years ago, a young Seattle cardiologist named Leonard Cobb conducted a unique trial of a procedure then commonly used for angina, in which doctors made small incisions in the chest and tied knots in two arteries to try to increase blood flow to the heart. It was a popular technique — 90% of patients reported that it helped — but when Cobb compared it with placebo surgery in which he made incisions but did not tie off the arteries, the sham operations proved just as successful. The procedure, known as internal mammary ligation, was soon abandoned.4
In a more recent study, sham arthroscopic surgery was compared to real arthroscopic surgery for knee osteoarthritis. The patients who had only a skin incision got just as good results. One patient who was told he had the sham procedure still refers to it as the surgery that cured him.

Some people question whether studies like these really show that surgery has a placebo effect. Maybe the surgery was unnecessary and patients would have improved anyway.

How Could It Work?

If the placebo effect is real, what might the mechanism be? We can’t just write it off as delusions of hyper-suggestible patients. There’s evidence that several things might be going on. The main hypotheses are: expectancy, motivation, conditioning, and endogenous opiates.

1. Expectancy is an established psychological phenomenon. It even affects vision: we are more likely to see what we expect to see. Wine tastes better if the price is higher. Kids like fast food better if it comes in a McDonald’s wrapper. If we expect to feel pain we are more likely to feel pain. If we are told to expect a strong painkiller, we’re more likely to get pain relief.

2. Motivation, the need or desire to improve health or get relief, has been shown to contribute independently to the placebo response. Patients who are strongly motivated to get well are more compliant and follow health advice more conscientiously. And patients who are more compliant about taking their placebo pills regularly get a stronger placebo response.

3. Conditioning is what Pavlov did to his dogs. People learn to associate pills and medical treatments with relief of symptoms. The body even learns physiologic responses: dogs salivate when injected with morphine; after they become conditioned, injecting a placebo makes them salivate, although not as much.

4. Endogenous opiates are pain-relieving chemicals produced in the brain that mimic the effects of opium-like drugs (morphine, etc.). There is some evidence that when patients respond to placebos, their brains produce more of these chemicals. Imaging studies have shown activation of opioid
receptors in the brain when people are told that a placebo is a painkiller. And there is evidence that giving a drug that blocks the effect of narcotics can also block the placebo effect.

Dopamine levels increased in the brains of Parkinson’s patients after taking a placebo; and patients who said they felt better released higher levels of dopamine. In another brain imaging study, researchers had patients play a game and estimate their chances of winning. The same reward areas in the brain lit up in subjects who thought they would win as in patients who were most convinced that the placebo painkiller would work. Another study of patients who preferred either Coca Cola or Pepsi found that brand information was processed in a different part of the brain than taste from blind taste tests. We may be seeing clues about how the brain handles anticipation, expectation, optimism, previous experience, or who knows what. There may be genetic differences or differences in dopamine receptor responsiveness. Brain imaging is a blunt tool, and it’s too soon to know what these studies mean, but it’s a promising avenue of research.

Can Animals Respond to Placebos?

Believers in homeopathy and acupuncture tell us that animals respond to those treatments and animals can’t respond to placebos, so that must mean those treatments are effective. But the veterinary literature accepts the reality of placebo response in animals, and there are plausible explanations:

1. They can develop a learned physiologic response to a drug and then respond similarly when a placebo is substituted.
2. They respond to attention and care from humans.
3. Human owners can experience the placebo effect for their pets by perceiving a response where there really is none.
4. Since animals can’t talk, we have to interpret an animal’s behavior as indicating relief of pain; this may not always be accurate.

What About Ethics?

Some people don’t even want to know whether a treatment is a placebo or not. If they feel better, that’s all that matters to them. In Snake Oil Science: The Truth About Complementary and Alternative Medicine, R. Barker Bausell argues that the primary benefit of alternative therapies is a placebo effect, often enhanced by ritual and impressive pseudoscientific jargon.

If we can give patients a placebo and relieve their pain, what’s wrong with that? If a little white lie benefits the patient, why not lie? The answer is that it’s unethical for doctors to lie to patients or prescribe ineffective treatments, and because deception undermines the doctor-patient relationship in the long run. Also, as Bob Carroll of The Skeptic’s Dictionary points out, “the placebo can be an open door to quackery.”75
In a recent study in Denmark, 48% of doctors reported prescribing a placebo at least 10 times in the last year, including antibiotics for viral infections and vitamins for fatigue. Specialists and hospital-based physicians were less likely to prescribe them. A 2004 study of physicians in Israel found that 60% reported using placebos for reasons like “fending off” requests for unjustified medications or calming a patient.

What if doctors were honest? If they told patients a treatment was a placebo, would that destroy the placebo effect? Maybe not. After clinical trials, patients who were told they’d been taking the placebo have asked if they could keep taking it. In one study patients were told one pill was inert and would only serve as a “dose extender” (i.e., a placebo that would allow a lower dose of the effective pill); patients accepted it and were able to lower their dose. What if a doctor tells a patient a treatment is not supported by any scientific evidence but some people believe it has helped them? Placebos raise ethical dilemmas on which doctors do not agree.

In a recent court case, the proponents of a particular form of quackery known as Q-rays admitted their device was bogus, but argued that since the placebo effect was effective they were justified in selling it. The court disagreed.

Is there any ethical way doctors can use the placebo effect to help their patients? Yes, of course. They already do. The placebo effect is an integral part of every doctor-patient interaction. Good doctors have always gained their patients’ trust and given them hope and reassurance.

What’s effective is not the placebo, but the meaning of the treatment. We enter into a human relationship with a caring person who offers to help us. We may be given a token of that caring in the form of a prescription. We may have a conditioned response to expect improvement because we have been helped in the past. We get a story, a narrative that explains why we feel sick and what we can do to get better. We get hope, support, human warmth, touch. All these factors might lead to an actual physiological response in which our pulse rate drops, we relax, our stress hormones decrease, and other changes facilitate healing, or at least comfort. One study supposedly showed that patients recovered faster if their window looked out on trees rather than a brick wall; even if they didn’t recover faster, wasn’t it nice to give them a view? Even if we can’t document a quantifiable effect on patient outcome, the quality of life is important.

Effective treatments have placebo effects too. A substantial percentage of the effects from antidepressants may be placebo effects. Morphine works even better if your doctor tells you it’s strong.
We can’t isolate placebo effect from conventional medicine — it gets us thinking the wrong way. As the neurologist Robert Burton says, "Even given our advanced state of medical knowledge, much of routine medical care — from treating backaches to the common cold — relies primarily upon reassurance and hope, not disease-specific treatments … we need to reconsider how to facilitate the placebo effect with minimal risk and cost, and without deception."6

References


The Great Psychic Detective Challenge


This week, Derek talks with paranormal investigator Benjamin Radford. Recently, the host of the pro-paranormal Skeptiko podcast challenged Ben to look into a "best case" psychic detective claim — supposedly a "slam dunk" that proves that paranormal detectives are real.
The idea of a placebo effect—a therapeutic outcome derived from an inert treatment—was discussed in 18th century psychology[13] but became more prominent in the 20th century. An influential 1955 study entitled The Powerful Placebo firmly established the idea that placebo effects were clinically important,[14] and were a result of the brain's role in physical health. A 1997 reassessment found no evidence of any placebo effect in the source data, as the study had not accounted for regression to the mean.[15][16]. Contents. The medical and scientific community has recognized the placebo effect for many years. For a person that is not involved with science, the phrase might be somewhat familiar too. Regular people, however, might not believe in the true power of what is the placebo effect. Until they experience it themselves. It doesn’t have to be some sort of groundbreaking cure of cancer or dementia. The placebo effect has many examples in everyday life. Of course, nobody documents them but they do happen quite regularly. Accordingly, the placebo effect (also referred to as the placebo response) is a phenomenon where people experience a beneficial effect as a result of a placebo treatment, which cannot be attributed to the physical properties of the placebo, and which is therefore attributed to people’s psychological reaction to it. Understanding placebos and the mechanisms behind them can allow you to take advantage of their beneficial effect in a variety of contexts. As such, in the