

Section Editors

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The placebo effect

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WHAT IS A CLINICAL RESEARCH TRIAL? In the medical world, a clinical research trial or clinical research study is usually done to prove whether a new medication or therapy is effective, before it becomes an approved and widely used treatment. Patients with the target disease are often asked to take part in clinical research trials. To show that the new treatment is truly effective, it is often compared to a placebo.

WHAT IS A PLACEBO? Placebos are usually thought of as “sugar pills.” They are important “sham” or phony treatments that are used to keep doctors and patients honest in testing new drugs or procedures. To prove that a drug works, it is generally tested against a placebo: a “dummy” medication that should have no effect on the condition.

Placebos are not only drugs. Sometimes patients get sham or phony surgery, sham radiation, or some other “pretend” treatment. Many patients and many doctors are unaware of the strength of “mind over matter.” I often tell my patients about a person who was in a study where the drug did not work. He insisted that the drug did work, and that he should be given the drug after the study ended. It turned out that he was not receiving the drug and that he wanted more of the placebo!

WHY ARE PLACEBOS IMPORTANT IN RESEARCH? Doctors and patients both want to see benefit from a new treatment. To prove that a therapy “really” works, some of the patients are given the sugar pill, and some get the drug. Who receives active drug and who receives placebo is often decided by a “coin toss” or a process called randomization. This process makes sure that patients are fairly divided between the two treatments. The change with the real drug is compared to the change with the placebo. The patient and doctors are not told until after the study is over who got the active drug and who got the placebo.

Some people wonder whether it is fair or ethical to give a placebo treatment to a patient with a disease and not tell the patient. Many research studies are designed so that all patients eventually are able to use the study medication, even if they do not receive it at first. Studies are carefully reviewed to be sure that use

of a placebo treatment does not create a dangerous situation for a patient. In the end, all patients benefit from studies that are carefully done using a placebo, so that the true effect of the treatment can be fully understood.

HOW DO PLACEBOS WORK? How placebos work is still a mystery. It is important to understand that not all placebo effects are good. Just as some patients improve with the power of positive thinking, some get worse and drop out of research studies because of the side effects caused by the placebo. In a recent, well-publicized and fascinating study of Parkinson disease (PD), it was discovered that the patients who improved with placebo had changes in their brain that were identical to the changes caused by the actual medication (called levodopa).¹ Levodopa causes an increase in brain dopamine, and the placebo should not. However, the patients who got better with placebo had a similar increase in dopamine, identical to what happened in those who were given the drug. Talk about mind over matter! That is like convincing yourself you can run a 40-yard dash in 4 seconds and then doing it. Similar effects of changes in brain chemistry have been found in studies of pain and of depression. However, this does not work in secret. When patients in a study of treatment for pain were given pain medications without their knowledge, the benefit was far less than when they were given placebo and they were able to expect a benefit.

WHAT DID THE AUTHORS OF THIS STUDY DISCOVER ABOUT PLACEBOS?

Diederich and Goetz² brought together some placebo studies in the areas of PD, depression, and pain, and they tried to develop a theory as to why the placebo effect is so large, and how it occurs. They reviewed studies designed to investigate how a placebo produces benefit. The patients with PD who thought that they were receiving the real treatment but who really received a placebo had the same changes in their brains on PET scans as those who received the medication. It was the *expectation* of the benefit that led to the same chemical response in the placebo group. Similar chemical changes on brain imaging tests were seen with placebo in studies of pain and in studies of de-

pression. In the studies of PD and of pain, the more severe the disease symptoms and the more dramatic the treatment (surgery, injection that the patient can see rather than by a pump), the more likely the subjects were to experience benefit with placebo treatment.

Why should brain chemistry change when patients are convinced they are receiving a treatment and their physicians expect them to improve? It seems that the expectation of benefit activates the same natural pathways in the brain as medications. If we could harness these same mechanisms in the clinic, patients could help themselves without the side effects of medications.

WHY ARE THESE STUDIES IMPORTANT? WHAT DOES THE FUTURE HOLD? The authors point out that placebo effects make the study of new treatments very difficult. This is because the effect of a new treatment has to be much greater than the placebo effect, which can be quite large.

If the placebo effect is strong, it is harder to prove that a drug or treatment is effective. This means that most research trials have to use many more people than they would if the placebo effect was very small or did not exist at all. This makes the studies cost more and take longer to accomplish. Better understanding of the placebo effect will help us to design faster, more effective studies to better combat disease. Perhaps one day we will also learn how to better harness the positive parts of the placebo effect to use as part of medical therapy.

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