

Placebo Science: Research You Can Believe In

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Controversial and ethically tenuous, placebos are central to medicine. Scientific reports make it clear, even if strange and counterintuitive, that receiving—unrelated to the actual content of—medical treatment can trigger and propel a healing process. Thus, therapeutic effects can arise from knowledge that therapy is occurring, rather than from the direct physiological effects of a drug or treatment, because expectations can result in physiological responses. Historically, fewer biochemically-viable therapies were available and healing practices involved the widespread use of placebo treatments. This practice fell out of favour, however, as better drugs and knowledge became part of the modern clinical armamentarium, and as a medical revolution shaped new professional codes and as ethics guidelines began to emphasize patient autonomy.

Placebos are a great vehicle to elucidate mind–body regulation. Just a few weeks ago, on May 16th, the Royal Society—the world’s oldest scientific academy—published a volume of its *Philosophical Transactions* devoted to placebos. In this regard, MBR is in good company. We dedicate the present and upcoming issues to placebo effects and placebo responses, and some of the data that bear on these elusive clinical and research themes.

Placebo effects are strongest for disorders that are predominantly mental and subjective. In the case of depression, for example, giving patients placebos can produce nearly the same effect as dosing them with the latest antidepressant drugs. Pain is another area susceptible to placebo treatment: even when giving a placebo, leading patients to think that they are receiving morphine provides more pain relief than if they think that they are getting aspirin. Placebo treatments, moreover, can influence autonomic functions, including heartbeat and blood pressure. The science of placebos poses some difficult questions: Why are placebo injections more effective than placebo pills? And why is sham surgery more effective than both? Why do red placebos stimulate whereas blue placebos calm? Why do more placebos work better than few? And why do more expensive placebos work better than cheaper ones? Symbolic thinking seems central to sketching even the most tentative answers.

Many physicians worry that for placebos to work deception is necessary. And yet, at least in specific clinical contexts, placebos may effectuate strong therapeutic outcomes even if patients know that they are getting placebo treatments.

...IN THE MEDICAL CLINIC

Physicians use placebos. That’s a fact. Some people are comfortable with this fact. Other individuals consider this trend a harmless form of duplicity or a virtuous lie. Still others view it as downright unethical. The American Medical Association (AMA) issued this stern warning in 2006: “Physicians may use [a] placebo for diagnosis or treatment only if the patient is informed of and agrees to its use.” The AMA ruling followed a controversial article published by two Danish scientists in the *New England Journal of Medicine*, which concluded that “outside the setting of clinical trials, there is no justification for the use of placebos.” Although this objectionable report has been widely critiqued and largely dismissed, many a practitioner

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still tacitly endorses its tenor and undercurrents. Whereas the AMA still adheres to the policy which largely frowns on the use of placebos in clinical practice, the German Medical Association recently announced considerable latitude in the clinical administration of placebos. Canada, to date, has no formal policy on the use of placebos in the clinic.

My team as well as other research groups have probed the knowledge, practices, and beliefs of physicians concerning placebos. We have canvassed randomly selected groups of doctors, both in Canada and the United States, who most often deal with conditions, such as depression, that respond well to placebos. Findings from the United States, for example, show that more than half said they prescribed “placebo treatments” from time to time and that they believed the practice was ethical. Some 40% said they used painkillers or vitamins as placebos and 13% acknowledged using antibiotics and sedatives for this purpose. Barely 3% said they use sugar pills. Over two-thirds reported that they described the medicines to patients not as placebos, but euphemistically as “a potentially beneficial medicine or treatment not typically used for their condition.”

A string of recent studies has drawn on imaging of the living human brain to show what areas light up as a result of placebo administration. Though details are still preliminary, the patient’s “positive expectation of a reward” seems to play a major role in placebo effects and placebo responses. The use of placebos often leads to the secretion of dopamine in the brains of people with Parkinson’s disease or to the release of endogenous painkillers in individuals suffering from pain.

Hidden dosing techniques demonstrate the power of the placebo effect. In these open-hidden paradigms, often used to research pain, we often administer morphine secretly, openly, or give a placebo masquerading as a powerful pain reliever. Telling patients that they are receiving a painkiller, even when the injection is actually a saline solution, can be as potent as covertly administering 6–8mg of morphine—a level slightly below the standard post-operative dose of 10–12mg—with the covert dose needing to reach 12mg to surpass the placebo effect. Giving pretend painkillers, therefore, can reduce the amount of pain a patient experiences. On the other hand, patients taking fake opiates after having been prescribed the real thing may experience the shallow breathing that is a side-effect of the real drugs.

Whether a placebo is a way of placating a fretful patient or a legitimate exercise in modern therapeutics, the ethics of placebos is tenuous and the controversy over the use of placebos in the clinic is unlikely to disappear soon.

IN CLINICAL PSYCHOLOGY

The history of psychological curative techniques—from the King’s Touch to the therapeutic spinning chair proposed by Erasmus Darwin and the theories of Sigmund Freud—reeks of placebo effects. Harvard psychologist Saul Rosenzweig noted that all these healers and treatments had a similar way of working on the minds of patients: they used drama and ritual to divine a cure. If that approach worked for thousands of years of human history, said Rosenzweig, why should contemporary mind-based therapies be different? In 1936, Rosenzweig proposed an overarching recipe for any treatment, citing parameters such as the therapeutic alliance—the collaborative bond between the patient and therapist; the provision of a believable framework that placates potential distress; and the buoying hope patients experience once in therapy.

Reporting an extremely strong bond with a therapist is hardly a guarantee to improvement. On the one hand, some practitioners seem to achieve considerably better results than their colleagues. On the other hand, few studies have examined how the skills of a given therapist affect the outcome of treatment. Findings from one such study, for example, suggest that the better therapists weren’t the ones who had more experience but those who would rather talk to their patients than prescribe medication and who expected talk-therapy to take a long time.

We should probably look for simple ways to make therapies work better. Specific factors that have little to do with the theoretical foundation of a treatment could make a substantial difference. For example, the ability to form a strong bond with clients and the manner one communicates with patients would both affect the outcome of many, if not any, intervention. Placebos are tricky, topical, and counterintuitive. They work irrespective of our theoretical perspective and findings suggest that many a treatment could boost in effectiveness by enhancing the placebo impact.

IN COMPLEMENTARY AND ALTERNATIVE MEDICINE

Alternative medicine is big business. Because the field is largely unregulated, reliable statistics are hard to provide. A conservative estimate, however, values the industry around the world at about \$60 billion.

The rigorous study of everything from acupuncture and crystal healing to Reiki channeling and herbal remedies reveals that around 95% of the treatments are statistically indistinguishable from placebo treatments. In only 5% of cases was there either a clear benefit above and beyond a placebo or even just a hint that would warrant further research.

And yet research and education about the science of placebos helps address a serious public-health problem. Research findings need to demonstrate that conventional medicines are both safe and efficacious before they can go on the market. Alternative treatments, on the other hand, largely reassure consumers by appealing to a mixture of tradition and natural products. While most claims are usually harmless, some can become dangerous (e.g., when practitioners, despite a lack of evidence, suggest that treatments, such as homeopathic remedies to cure malaria, work).

Unlike their conventional counterparts, practitioners of alternative medicine often excel at harnessing the placebo effect. Whereas harried modern doctors struggle to find time, less conventional practitioners often offer long, relaxed consultations. And these practitioners often believe passionately in their treatments, which often involve great and reassuring theatrics. These meaningful flairs are enough to do some good, even though the magnets and crystals, by themselves, are likely meaningless.

I hope the information you will find in the present, as well as the upcoming, issue of MBR will pique your curiosity and whet your appetite for placebos.