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## The placebo effect: A new study underscores its remarkable power

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Research suggests a placebo's therapeutic impact can be so strong that even patients who know they're taking a sugar pill may start feeling better

In the not too distant future, your family doctor's first line of treatment for minor illnesses such as migraine and irritable bowel syndrome may well be snake oil. Prescribing a placebo, or sugar pill, is a stealthy way to raise a patient's expectations of getting better.

But according to new research, the therapeutic effects of a placebo are so powerful that an inert pill has a good chance of reducing symptoms – even if patients know they are taking a dummy pill.

Harvard researcher Dr. Ted Kaptchuk made this counterintuitive conclusion in a study published last week in Science Translational Medicine. Kaptchuk and colleagues found that the placebo effect greatly enhanced pain relief in migraine sufferers who had the expectation they were getting an effective drug, compared to when they took the active drug with the incorrect label "placebo." More surprising, however, is that the patients reported significant pain relief, compared to an untreated migraine attack, even when they knew they had swallowed nothing more than a sugar pill.

Kaptchuk is director of the Program in Placebo Studies and the Therapeutic Encounter at Harvard, and his findings suggest new ways of harnessing the placebo effect. But in practice, giving an unwitting patient a sugar pill is widely regarded as unscrupulous. Bioethicists have cautioned that the placebo effect is unreliable, and that the use of placebos violates patient trust, since it normally involves tricking a patient into receiving a sham drug or treatment.

The American Medical Association considers the use of placebos without a patient's consent unethical. In a 2010 report, the British Parliament's Science and Technology Committee called the practice "bad medicine." (The Canadian Medical Association has no guidelines on placebos.) Considering its therapeutic potential, however, can a placebo play a role in good medicine?

Kaptchuk's study suggests a possible alternative to deceptive placebos, said Dr. Howard Brody, a bioethicist at the University of Texas who has written volumes on the placebo effect. Using techniques used in the study as a model, doctors could explain to a patient how he or she may benefit from the placebo effect and then prescribe a correctly labelled sugar pill with a clear conscience, he said.

That being said, ethical qualms haven't stopped a surprising number of doctors from duping their patients. In a 2008 study published in BMJ, more than half of American doctors said they had given their patients placebos ranging from vitamins and sedatives to unnecessary antibiotics, which are hardly benign.

In Canada, a 2011 study conducted by Dr. Amir Raz at McGill University found that 20 per cent of psychiatrists as well as non-psychiatrists routinely prescribed placebos in their practices.

In Europe, the German Medical Association sparked international debate with the release of a 2011 report encouraging doctors to keep a few sugar pills handy for patients with minor conditions.

Despite the ethical controversy, there is good evidence that the placebo effect "helps stimulate the healing response," Brody said.

He cited neuroimaging studies conducted by Italian neuroscientist Dr. Fabrizio Benedetti, who found that placebos may change the circuitry and chemistry of the brain using the same mechanisms activated by certain medications.

Ethical use of "open-label" placebos, as Kaptchuk calls them, cannot be put into practice until Kaptchuk's findings are replicated by other researchers, Brody said. Nevertheless, he praised Kaptchuk's study designs for "getting rid of the noise" of confounding variables that have bogged down placebo research.

In his newest study, Kaptchuk used the same 66 migraine patients for each study parameter instead of giving one set of patients a placebo and comparing them with a control group. Effectively, "patients were their own controls," Kaptchuk said.

Each suffered a migraine attack without treatment. In six subsequent attacks, each patient was given either the migraine drug Maxalt, or a placebo.

To minimize variations in doctor-patient interactions, patients did not see a doctor except for a pre-screening visit when they received instructions to take pills in a specific order for subsequent attacks. The pills were in envelopes marked "Maxalt," "placebo" or "Maxalt or placebo," but the patients did not know which labels were correct.

The surprising effectiveness of open-label placebos in the study "definitely deserves more attention," said Dr. Mark Sinyor, a psychiatrist at Sunnybrook Health Sciences Centre in Toronto.

But prescribing a sugar pill is not the only way to leverage the placebo effect, said Sinyor, who has studied how patients' expectations of getting well may combine with drug therapies in a synergistic healing process.

Previous research has shown that patients who see a warm and caring practitioner tend to recover sooner from conditions such as strep throat and the common cold, he pointed out.

Many patients have turned to alternative therapists simply because they are more empathic, Sinyor said. But he added that doctors, too, can help trigger a patient's internal resilience by expressing genuine warmth and concern.

The ultimate goal should be to combine evidence-based medicine with a good bedside manner, Sinyor said: "Part of the job of a healer is, where possible, to help people have hope."

Researchers are not entirely sure how the placebo effect works, but studies showing the release of pain-relieving opioids in the brains of patients treated with placebos suggest it is a true biological phenomenon.

## Some theories on how placebos work

**It's in your head:** One theory is that patients' expectations that a given treatment will help may activate a physiological response that promotes healing.

**It's in your body:** Another theory involves embodied cognition, in which the body remembers feeling better after taking previous pills and releases neurotransmitters that set the healing process into motion, in a kind of Pavlovian response.

**Or maybe it's both:** A third hypothesis melds the theories of expectation and conditioning with the notion that the patient's degree of motivation in a therapeutic ritual determines how strong their placebo response – and healing – will be.

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