What Is the Nocebo Effect?

For some patients, the mere suggestion of side effects is enough to bring on negative symptoms



(Photo by Tom Varco)

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What if taking an absolutely harmless substance could make you sick? What if a sugar pill caused you to feel nausea, or a fake dose of lactose triggered unwelcome stomach symptoms in patients who are lactose intolerant?

The strange truth about medicine and the brain is that they often interact in completely unpredictable and counterintuitive ways. Nowhere is this more true than with the bewildering phenomenon known as the nocebo effect.

Most of us already know about the placebo effect. As part of medical studies, a control group is typically given an inert substance (usually a sugar pill) that provides a baseline to which researchers can compare the effectiveness of the new medicine being tested. The members of this group are told that the placebo is real—and surprisingly, they sometimes experience an actual improvement in their symptoms, simply because they expect that the medicine will make them feel better.

An opposite tendency—and one that has been largely overlooked by the research community—is the nocebo effect. Put simply, it is the phenomenon in which inert substances or mere suggestions of substances actually bring about *negative* effects in a patient or research participant. For some, being informed of a pill or procedure's potential side effects is enough to bring on real-life symptoms. Like the placebo effect, it is still poorly understood and thought to be brought about by a combination of Pavlovian conditioning and a reaction to expectations.

Last week, researchers from the Technical University of Munich in Germany published one of the most thorough reviews to date on the nocebo effect. Breaking down 31 empirical studies that involved the phenomenon, they examined the underlying biological mechanisms and the problems it causes for doctors and researchers in

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clinical practice. Their conclusion: although perplexing, the nocebo effect is surprisingly common and ought to be taken into consideration by medical professionals on an everyday basis.

In many of the experiments they analyzed, the suggestion or expectation of pain brought about significant increases in the amount of negative side effects experienced by participants. For example, in one study, 50 people who suffered from chronic back pain were given a flexibility test. Half were told beforehand that the test might cause some pain, while the others were not. Afterward, the first group reported a significantly higher amount of pain, despite enduring the exact same procedure.

In another experiment, the drug finasteride was administered to help relieve symptoms of prostate disease, and half the participants were told that it could cause erectile dysfunction, while the other half was kept in the dark. Forty-four percent of the first group reported that they'd experienced ED, compared with just 15 percent of the uninformed group.

The nocebo effect might even be powerful enough to kill. In one case study, researchers noted an individual who attempted to commit suicide by swallowing 26 pills. Although they were merely placebo tablets without a biological mechanism to harm the patient even at such a high dose, he experienced dangerously low blood pressure and required injections of fluids to be stabilized, based solely on the belief that the overdose of tablets would be deadly. After it was revealed that they were sugar pills, the symptoms went away quickly.

The researchers suggest that doctors reconsider conventional beliefs about pain management to avoid magnifying painful side effects. It's commonly thought that properly preparing a patient for pain—for example, "this might hurt quite a bit"—is the best way to minimize anxiety, so the patient knows what to expect. But one experiment analyzed showed that the very words used by a doctor before injecting radiographic substances affected the amount of pain experienced. The more frequently the words "sting," "burn," "hurt," "bad" and "pain" were said, the more discomfort felt by patients.

Of course, trying to avoid this sort of scenario puts a doctor in an ethical dilemma—limiting the patient's discomfort could be at odds with keeping them informed about the procedure. To navigate this tension, the study's authors advise doctors to emphasize positives (re-framing warnings into phrases such as "the majority of patients tolerate this well") and, in some cases, actually getting permission from patients to keep them in the dark about certain mild side effects.

Figuring out how to handle patients' fears and anxieties, it turns out, can be just as difficult as fighting real diseases and infections. The surprising conclusion you might come to after learning about the nocebo effect? What you don't know can't hurt you.

About Joseph Stromberg



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