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Don't Ask, Don't Tell? Revealing Placebo Responses to Research Participants and Patients

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For centuries, placebos have been used to treat pain. They also represent a pillar of clinical research, wherein the double-blind placebo-controlled study stands as the gold standard for establishing the efficacy of pain treatments. Although legitimate ethical concerns have been voiced regarding the use of placebos in clinical practice (Sullivan, Paice, and Benedetti, 2004), evidence suggests that clinicians continue to use placebos widely to manage both acute and chronic pain syndromes (Chung, et al. 2007).

Despite this widespread use of placebos in both clinical and research settings, their role in the pain experience remains poorly understood and consensus does not yet exist surrounding their appropriate and ethical application. The recently published study by Chung, et al. (2007) is the first paper to directly address an important question: What happens if patients are informed that their pain was alleviated after they received a placebo treatment? Traditionally, pain researchers and clinicians, reticent to inform individuals of their personal placebo response, have maintained an implicit “Don’t ask; don’t tell” policy. This stance is based on the concern that revealing to the patient that he/she received a placebo might engender a sense of mistrust and betrayal, and hence might interfere with future efforts to manage pain (Chung, et al., 2007).

Intriguing, and contrary to expectation, is the Chung et al. (2007) finding that disclosure of an earlier positive response to a placebo does not alter healthy volunteers’ likelihood of responding positively to subsequent placebo treatment (Study 2). Chung, et al. (2007) also demonstrated, in irritable bowel syndrome patients (Study 1), that informing patients that their clinical pain had initially responded to a placebo resulted in slightly increased frustration but had minimal effect on other moods such as anger, fear, anxiety, or depression and on the likeability or trust of the experiment. Taken together, the seminal methods and findings of Chung, et al. (2007) have important implications for understanding, revealing, and harnessing the potential therapeutic effects of placebos in pain research and clinical practice.

Research

Two major features of the research methods used by Chung, et al. (2007) likely contributed to the magnitude and persistence of the placebo response. First, both studies incorporated conditioning trials in which a placebo cream was repeatedly paired with sequentially lower

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levels of pain stimuli, to induce the expectation that pain relief would accompany administration of the placebo cream. Conditioning trials are used in many placebo studies; evidence suggests that placebo effects obtained via conditioning are unusually resistant to extinction (e.g., Colloca and Benedetti, 2006; Voudouris, Peck, and Coleman, 1985). A worthy direction for future research would be to determine whether a threshold number of conditioning trials is needed to ensure that a placebo response persists after an individual learns that he/she responded favorably to a placebo. Second, the instructions used by Chung et al. (2007) differ from those typically used in double-blind, placebo-controlled clinical trials. Specifically, the investigators told placebo-receivers that “the agent that had just been given is known to significantly reduce pain in some people.” This instruction diverges from that typically delivered to patients at the outset of a double-blind placebo-controlled study, where participants are typically informed that they have a 50/50 chance of receiving a real pain medication or a placebo. An important direction for future research would be to examine and compare the impact of different instructional sets on development of the placebo effect, and the placebo effects’ persistence after revealing to the patient his/her positive placebo response.

Participants’ reactions to being told that they responded positively to a placebo are a fruitful area of inquiry. Chung, et al. (2007) provided participants with graphs showing the magnitude of their pain relief when a placebo treatment was administered. How well do participants understand graphic displays of their analgesic response? What is the best way to convey information about placebo response? Most important, what meanings do participants ascribe to a “placebo response,” and do participants and investigators understand its meaning in the same way or differently? Future research should address these and related questions, with the ultimate goal of developing standard research procedures that translate best evidence about conditioning trials, instructional sets, and ways of informing participants of their personal placebo response into routine research practices.

Clinical

Results from the Chung, et al. (2007) study raise an interesting question: Can we actively educate, and even empower, patients by telling them about placebo effects, thereby abandoning the “Don’t ask, don’t tell” posture? The meaning of placebo responses could then be addressed as an active intervention. Prior to using placebos in clinical practice, for example, patients could be provided with an educational rationale for the use of placebo effects, one which underscores the role that positive expectations can play in triggering one’s own pain regulatory systems. Potential positive effects (pain relief) and benefits (reduction of side effects) of placebos could be outlined. Patients could be told that, at times during their treatment course, conditioning trials and instructional sets will be woven into their care so as to increase the likelihood of a positive placebo response. How would such an educational intervention affect the therapeutic relationship? If patients come to view placebo treatment as a means of more actively involving them in their own health care and management, this approach may represent an improvement over current practices. In essence, the traditional “Don’t ask, don’t tell” policy would be replaced by “Ask and tell” – in the context of explicit patient education about placebo response. (Of course, studies investigating the characteristics of patients who do, and do not, respond well to this strategy would be warranted.) This change in practice is not only ethical, but it might actually strengthen the therapeutic relationship and enhance the efficacy of both placebo and active pain treatments. It could also help to mitigate recent ethical concerns about how best to inform patients of the nature of treatments they have received in clinical trials (Wainwright, 2002).

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