"The Placebo Effect and Depression: Who Is Susceptible and How Does It Work?"

Saisai Chen

Excerpt

These findings on the moderating effects of severity can be extended to explain why placebos are typically less effective among hospitalized inpatients than among outpatients, since inpatients suffer from more-severe depression. Guelfi et al. (1995) randomly assigned 93 severely depressed and hospitalized *inpatients* to either antidepressant or placebo conditions. They found that antidepressant-treated patients showed significantly greater improvement over placebo-treated patients after just four days of treatment. Shea et al. (1992) conducted a similar study but assigned 239 depressed *outpatients* to either antidepressant or placebo treatment conditions. They, on the other hand, found no significant difference between the groups in the proportion of patients who recovered and remained well eight weeks following treatment. These apparently conflicting results can be reconciled by recognizing that inpatients usually suffer from more-severe depression than outpatients (Page & Hooke 2012), and more severely depressed patients are less likely to benefit from placebo treatment. It is worth noting that in the Kirsch et al. (2002) meta-analysis mentioned earlier, 39 of the 47 clinical trials only included outpatient subjects, whereas just 2 of the 47 only included inpatients hospitalized for severe depression. Including more outpatients skews the meta-analysis results in favor of the placebo effect because the placebo response is greater among outpatients, who generally have milder depression.

Despite evidence presented by the Kirsch et al. (2002) meta-analysis claiming an impressive placebo effect in the treatment of depressed patients, the effect is hardly universal. Rather, it is reduced in patients with chronic depression, patients who have not benefited from previous antidepressant medications, and patients with more-severe depression (Khan et al.

1991; Brown et al. 1991; Elkin et al. 1989). Moreover, the placebo effect may be exaggerated in some studies. It is often the case that significantly more patients in the placebo group discontinue the study due to ineffectiveness of treatment than patients in the medication group (Guelfi et al. 1995). Hence, the number of placebo responders at the conclusion of a treatment period tends to be inflated. It should be noted that subject diversity is restricted in some of the studies mentioned above. In particular, participants in the Khan et al. (1991) study were 99% white and those in the Mayberg et al. (2002) study were not only few but also all male. Future research should investigate the potential moderating effects of ethnicity and gender. Cultural factors may affect expectations for improvement, and gender may affect neurobiological responses, which can then influence the patient's response to placebos. Taken together, research suggests that the potential clinical use of placebo pills in treating depressed patients may not be appropriate, especially when the depression is chronic and severe or when previous treatments have been ineffective. Nonetheless, clinicians should still take into account the patient's expectations, past experience with medication, and neuroanatomical features even when prescribing antidepressants. If these factors alone can lead to symptom improvement for certain patients, perhaps combining them with active medication will result in a synergistic effect.

Fellow Commentary

Alaka Halder

We include Saisai Chen's essay because it is an excellent demonstration of accessibility and the elements of a workhorse conclusion. By necessity, science writing is often discipline-specific and difficult to comprehend holistically if one is not a researcher in that specific field. Nevertheless, a good scientific conclusion—like the introduction—should be accessible to a lay reader who hopes to grasp the essay's key arguments, findings, and implications.

Saisai's conclusion is an effective microcosm of her essay. In the penultimate paragraph, she revisits her sources and engages them in one final, convincing discussion that is reminiscent of the notion of "literature review as motive." As this is a conclusion, Saisai goes further by summarizing her findings in light of these sources before laying out original implications and puzzles for future research. Although this is a psychology paper, I feel that the clarity of Saisai's writing and her exclusion of jargon make her work accessible to readers of all disciplines. This is perfect, as I feel that this excerpt contains some of the universal elements of a solid, convincing conclusion. Lastly, I enjoyed her author commentary because it provides an insightful glimpse into how she crafted this masterful piece of writing. It is a great example of "show, don't tell," and we hope that Saisai's journey will provide companionship and inspiration to readers of this anthology when they embark on their own forays into writing.

Author Commentary

Saisai Chen

The conclusion section is often written in the last minutes before a paper is due. But an effective conclusion takes time to develop. It leaves the reader satisfied by helping to resolve the issue that motivated the paper in the first place. This is no easy feat. It requires that the author balance large amounts of information in mind, making connections here and there until a coherent story is crafted. The purpose of the conclusion is to remind the reader of the significance of what he/she has learned from reading your paper, to incite further action, and to elicit that gratifying "Aha!" moment. Here's how I managed it:

The assignment for this paper was very open ended; I was asked to write about anything related to health psychology that interested me. When given such freedom, I like to explore topics that are often overlooked or taken for granted. One such topic is the placebo effect. By using placebos as controls for clinical trials, scientists often discount the effects that a humble sugar pill can have on the human body. From a biological perspective, the idea that sugar pills can cure disease is laughable. Yet, in reality, it happens. But the placebo effect is such a broad topic that I'd never have been able to analyze it as thoroughly as I'd have liked in the space of only a few pages. After doing some preliminary literature searches, I found an abundance of research looking at the placebo effect and depression. However, the research was very conflicted. Some publications showed that placebos are ineffective, whereas others show that up to 80% of the outcomes found in patients taking antidepressants can be replicated in those taking sugar pills. While these contradictory findings may cause some people to furrow their brows and push them aside, they excited me greatly. Why are placebos effective for some

patients but not for others? What are the mechanisms underlying these moderating factors? How can this overwhelming mess of counterintuitive data be sorted out and understood?

One of the more controversial papers I found was a large meta-analysis that concluded that placebos were extraordinarily effective in treating clinically depressed patients. This serves as the primary motivation for my paper. After all, if the claim were true, then pharmaceutical companies should become candy factories! In the main body of my paper, I identify several factors that contribute to variability in the effectiveness of placebos, such as whether the patients were chronically or acutely depressed, the patient's previous experiences in taking antidepressants, and the severity of the depression as determined by neurological impairments. For each factor, I propose a mechanism that can account for how the identified factor contributed to the differential effectiveness of placebos.

As I sifted through enormous amounts of data, I began noticing patterns and connections between different publications. A phenomenon reported in one paper may help explain the results of another paper. For example, one study found that the more severe the patient's depression, the less likely placebos are to cure the illness. Why is that? A separate study showed that the severity of depression is associated with different neurological changes. Yet another study showed that placebos and antidepressants affect different areas of the brain. Putting the studies side by side, I realized with a jolt that the areas related to the severity of depression corresponded to the areas targeted by the treatments. A logical leap in reasoning led me to hypothesize that outpatients, who tend to suffer from less-severe depression, should less likely be able to respond favorably to placebos. A quick literature search confirmed my prediction. This in turn drew me back to the methods section of controversial meta-analysis (a section that is, unfortunately, too often passed over), where I remembered reading that the studies analyzed mainly included only outpatients. A light bulb went off: since the meta-analysis included a disproportionately large number of outpatients who have less-severe depression, and less-severe depression increases the likelihood of patients to respond to placebos, it's really no wonder that the meta-analysis found placebos to be so effective. Aha! It all makes sense now!