The power of context: reconceptualizing the placebo effect

Franklin G Miller[1] • Ted J Kaptchuk[2]

[1] Department of Clinical Bioethics, National Institutes of Health,

[2] Osher Institute, Harvard Medical School,

Correspondence to: Dr FG Miller. E-mail: fmiller@nih.gov

DECLARATIONS

Competing interests
None declared

Funding
None

Ethical approval
Not applicable

Guarantor
FGM

Contributorship
Both authors contributed equally

Acknowledgements
The opinions expressed are those of the authors and do not reflect the position or policy of the National Institutes of Health, the Public Health Service or the Department of Health and Human Services

The placebo effect has received increasing scientific attention in recent years. Progress in translating knowledge about this phenomenon into improved outcomes for patients, however, is hampered by conceptual confusion and misleading terminology. In this article we diagnose what is wrong with the placebo concept and suggest 'contextual healing' as a fruitful alternative way of conceiving the placebo effect.

History

Scientific interest in the placebo effect has grown dramatically over the past thirty years. For the three decades from 1977 to 2006, the number of citations listed on PubMed for 'the placebo effect' has increased from 214 to 651 to 1675. Writing in 1984, Jay Katz noted that 'Physicians and patients may gradually learn that the placebo effect is an integral and inevitable component of the practice of medicine, that it constitutes its art and augments its science.'[1] Despite increasing scientific attention to the placebo effect, including extensive experimentation aimed at understanding the mechanisms underlying this phenomenon, Katz's prediction has yet to be realized. Apart from purely scientific interest in the neurobiology of the placebo effect, the leading rationale for research on this phenomenon is to harness the presumed power of the placebo effect to enhance therapeutic outcomes in clinical practice. A major barrier to clinical translation of the substantial investment in laboratory experimentation on the placebo effect is the confusing and misleading way in which this phenomenon is conceived.

What is wrong with the placebo concept

The term 'placebo' has currency in two different activities, which both contribute to its unsatisfactory conceptualization. First, there is the traditional (and continuing) practice of physicians administering or prescribing 'inert' interventions, or 'active' interventions believed not to have specific efficacy for the patient's condition, with the aim of promoting beneficial outcomes or satisfying the patient's wish to receive treatment.[2,3] The etymology of 'placebo' – 'I will please' – derives from this practice. Second, with the advent of the randomized controlled trial as the canonical method for evaluating treatment interventions, comparison with a placebo control, administered under double-blind conditions, has become the preferred means of rigorously determining treatment efficacy.

In both these contexts the placebo effect has been simultaneously overvalued and dismissed or denigrated. Within clinical medicine there has been an inveterate tendency to attribute therapeutic power to the medications or procedures prescribed or administered by physicians. Improvement in the patient's condition that occurs subsequent to medical treatment is attributed to the physician's intervention. Likewise, Henry Beecher's classic article 'The Powerful Placebo' established the tendency to equate the placebo effect with the average aggregate response of patients receiving placebo controls in randomized trials.[4] In both clinical medicine and clinical research, the attribution of power to the placebo effect has been inflated by failing to attend to the fallacy of *post hoc ergo propter hoc* (after the fact, therefore because of the fact).[5] Just as responses following drug treatment do not necessarily indicate true drug effects, so responses to placebo do not necessarily constitute placebo effects.[6] Patients receiving placebos either in clinical practice or in clinical trials may have improved, or appeared to have improved, for a variety of reasons other than any causal connection (via some psychological or neurobiological mechanism) between the placebo and the outcome. These may include spontaneous

remission, the natural course of waxing and waning of symptoms, regression to the mean in repeated measurements, and biased patient reports that do not reflect real improvement.

On the other hand, the placebo effect has been deflated within the ideology of scientific medicine. The traditional use of placebos and placebogenic treatments in clinical practice has been criticized from an ethical perspective as deceptive, thus infringing patient autonomy and compromising informed consent.[7] Although we do not address here ethical issues relating to placebo treatments, it is noteworthy that there has been relatively little attention devoted to whether and how treatments tapping the placebo effect, deriving from patient expectations or conditioning, can be administered without deception. More importantly, the art of medicine, as reflected in the therapeutic potential of the clinical encounter, has been marginalized in the wake of tremendous advances in the science and technology of medicine.[8] Healing by means of technological intervention has eclipsed healing through the clinician–patient relationship. Similarly, the technique and prevailing understanding of the placebo-controlled trial devalues the placebo effect. Novel treatments are validated by demonstrating that they are superior to placebo controls. Those interventions that fail to pass this test are valueless, as they are no better than 'no treatment'. Yet treatments that are no better than placebo controls may be dramatically superior to no-treatment (wait list) interventions and even standard medical care, as demonstrated by an impressive series of three-arm trials in Germany of acupuncture versus placebo acupuncture versus no treatment or usual care for relief of pain in a range of conditions.[9–13]

The language associated with the placebo phenomenon reflects this twin process of devaluation. The placebo is 'inert', 'inactive' or 'non-specific.' A placebo control is otherwise described as a 'dummy' or a 'sham'. The placebo effect is 'noise' or 'bias', which must be controlled in order to discriminate a valid signal of specific treatment efficacy. The first trio of descriptors reflects the fact that the placebo effect is defined negatively, by what it *is not*, rather than by positive terms that indicate what it *is*. Moreover, these negative descriptors are confusing. Most commonly used placebos are not absolutely inert or inactive. For example, sugar pills and saline solutions have physiological properties.[14] These placebo interventions are considered inert or inactive in relation to specific clinical outcomes. It is presumed that sugar or saline used in placebo analgesics do not have pain-relieving properties. While the ingredients of placebo interventions may be relatively inert in this sense, the placebo intervention as a whole logically cannot be inert or inactive when it produces a real placebo effect. Indeed, if a placebo were an absolutely inactive substance, it would make no sense to describe certain interventions as 'active' placebos. For example, a sedating drug not thought to have any effects on depression might be employed as a control to evaluate an antidepressant.

The common description of the placebo effect as 'non-specific' is also unsatisfactory. There is a valid contrast between interventions that have specific efficacy – they contain specific properties causally associated with particular outcomes – and placebo interventions that do not. However, rigorous laboratory experiments have detected a variety of specific mechanisms underlying the reported effects connected with placebo interventions presented (deceptively) to research subjects as real treatments. These include activation of endogenous opioids and dopamine release.[15] Thus, a medication that works to relieve pain via the placebo effect is non-specific – the specific pharmacological properties of this intervention do not cause pain relief – in contrast to a proven effective analgesic medication that has specific efficacy. But by virtue of causing a real change in a specified outcome, treatments that work only by means of the placebo effect must work by some specific mechanism. Just as placebo treatments with real effects are not absolutely inert, so they are not absolutely non-specific. The confusion is compounded by use of the definite article in describing *the* placebo effect. From a biological perspective, there are multiple placebo effects. It remains an open question whether there is any common psychological mechanism that explains such effects.

Finally, the placebo effect is a misnomer because there is no need to use a placebo intervention to evoke the placebo effect. It has long been recognized that the observed response of patients following drug treatment may include a placebo effect component. In clinical trials, the difference between the aggregate response of patients randomized to drug and that of patients randomized to placebo constitutes the true (specific) drug effect. For example, if the mean reduction of symptoms of depression is 40% in patients receiving an antidepressant drug versus 30% in patients randomized to placebo, then the true drug effect is interpreted to be a reduction in symptoms of 10%. It is presumed that part of the apparent drug effect

may have been due to the placebo effect of receiving an intervention believed to be effective, rather than to the specific antidepressant properties of the study drug. A more direct and accurate demonstration of short-term placebo effects without the use of placebos comes from a series of experiments by Benedetti and colleagues comparing open and hidden administration of analgesic drugs.[16] The therapeutic power of various analgesic drugs is markedly reduced when administered by a computer-controlled infusion pump without the patient knowing that drug is being given, as compared with open administration of the drug by a clinician, described to the patient as a pain-relieving intervention. The difference in clinical outcomes between the open and hidden administration of drug illustrates the placebo effect without the use of a placebo intervention.

Contextual healing

To promote a more accurate understanding of the elusive and confusing phenomenon known as the placebo effect, we suggest that it should be reconceptualized as 'contextual healing'. Healing resulting from the clinical encounter consists of a causal connection between clinician–patient interaction (or a particular component of the interaction) and improvement in the condition of the patient. That aspect of healing that is produced, activated or enhanced by the context of the clinical encounter, as distinct from the specific efficacy of treatment interventions, is contextual healing. Factors that may play a role in contextual healing include the environment of the clinical setting, cognitive and affective communication of clinicians, and the ritual of administering treatment.[17] Contextual healing is precisely what has been off the radar screen of scientific medicine, which has focused on therapeutic benefit produced by medical technology. Fixation on the specific efficacy of treatment interventions obscures the fact that the technological tools of medicine are always applied in some context, which itself may contribute significantly to therapeutic benefit.

Instead of focusing exclusively on the therapeutic power of medical technology and thereby ignoring or dismissing context, we should see the context of the clinical encounter as a potential enhancer, and in some cases the primary vehicle, of therapeutic benefit.[18] Contextual healing may be especially important in chronic conditions for which existing treatments are only partially effective in relieving symptoms. Attention to contextual healing signifies that there is more to medicine than diagnosing disease and administering proven effective treatments. This has long been recognized under the rubric of 'the art of medicine.' However, biomedical science, animated by the search for specific therapeutic efficacy, has left the art of medicine shrouded in mystery. The promise of research on contextual healing is to use scientific experimentation to pull back the veil surrounding the art of medicine, by elucidating the way in which specific contextual factors in the clinical encounter contribute to therapeutic outcomes.

The experiments comparing open and hidden administration of analgesic medication demonstrate that, at least with respect to relief of pain, a substantial part of the therapeutic benefit associated with medication derives from the taken-for-granted ritual of the clinical encounter. Moreover, they illustrate that placebo interventions are unnecessary to produce the placebo effect. The placebo is a methodological tool for understanding contextual healing but is not itself responsible for clinical effects that emanate from the clinician–patient relationship. Conceptualizing the placebo effect as contextual healing suggests that theoretical understanding and scientific experimentation related to this phenomenon should aim at isolating and elucidating those factors in the clinician-patient encounter that contribute causally to improvement in outcomes for patients. It is hoped that in the next 30 years we will translate scientific understanding of contextual healing into enhanced patient care.

References

1 Katz J. *The Silent World of Doctor and Patient.* New York: The Free Press; 1984. p. 194
2 Shapiro AK, Shapiro E. *The Powerful Placebo: From Ancient Priest to Modern Physician.* Baltimore: The Johns Hopkins University Press; 1997
3 Sherman R, Hickner J. Academic physicians use placebos in clinical practice and believe in the mind-body connection. *J Gen Intern Med* 2008;**23**:7–10
4 Beecher HK. The powerful placebo. *JAMA* 1955;**159**:1602–6
5 Miller FG, Rosenstein DL. The nature and power of the placebo effect. *J Clin Epidemiol* 2006;**59**:331–5
6 Ernst E, Resch KL. Concept of true and perceived placebo effects. *BMJ* 1995;**311**:551–3
7 Brody H. The lie that heals: the ethics of giving placebos. *Ann Intern Med* 1982;**97**:112–8
8 Reiser SJ. *Medicine and the Reign of Technology.* New York: Cambridge University Press; 1978
9 Haake M, Muller HH, Schade-Brittinger C, *et al.* German acupuncture trials (GERAC) for chronic low back pain: randomized, multicenter, blinded, parallel-group trial with three groups. *Arch Intern Med* 2007;**167**:1892–8
10 Linde K, Streng A, Jurgens S, *et al.* Acupuncture for patients with migraine. A randomized controlled trial. *JAMA* 2005;**293**:2118–25

11 Melchart D, Streng A, Hoppe A, *et al.* Acupuncture in patients with tension-type headache: randomized trial. *BMJ* 2005;**331**:376–9

12 Brinkhaus B, Witt C, Jena S, *et al.* Acupuncture in patients with chronic low back pain – a randomized controlled trial. *Arch Intern Med* 2006;**166**:450–7

13 Witt C, Brinkhaus B, Jena S, *et al.* Acupuncture in patients with osteoarthritis of the knee: a randomized trial. *Lancet* 2005;**366**:136–43

14 Sievenpiper JL, Ezatagha A, Dascalu A, Vuksan V. When a placebo is not a 'placebo': a placebo effect on postprandial glycaemia. *Br J Clin Pharmacol* 2007;**64**:546–9

15 Benedetti F, Mayberg HS, Wager TD, Stohler CS, Zubieta JK. Neurobiological mechanisms of the placebo effect. *J Neurosci* 2005;**25**:10390–402

16 Colloca L, Lopiano L, Lanotte M, Benedetti F. Overt versus covert treatment for pain, anxiety, and Parkinson's disease. *Lancet Neurology* 2004;**3**:679–84

17 Kaptchuk TJ. The placebo effect in alternative medicine: can the performance of a healing ritual have clinical significance? *Ann Intern Med* 2002;**136**:817–25

18 Di Blazi Z, Kleijnen J. Context effects. Powerful therapies or methodological bias? *Eval Health Prof* 2003;**26**:166–79