YALE JOURNAL OF BIOLOGY AND MEDICINE 86 (2013), pp.323-331.

FOCUS: RESEARCH AND CLINICAL ETHICS

Deceit and Transparency in Placebo Research

Stewart Justman

Director, Liberal Studies Program, University of Montana, Missoula, Montana

Studies designed to elicit the full strength of the placebo effect differ from those in which the placebo effect represents a nuisance factor to be accounted for in order to establish the efficacy of a treatment. In the latter, informed consent is the rule; in the first, while consent may be informed in some narrow sense of the word, deception is common. However, the trickery of placebo experimentation goes beyond straightforward lies to include the use of crafty ambiguities, half-truths, and deliberate omissions in scripts read to the subjects of these studies. As words come to resemble therapeutic agents in their own right, it is only to be expected that researchers would methodically exploit verbal effects to evoke the responses they are looking for. Even experiments in which placebo is disclosed as placebo have used language in leading and misleading ways. Such studies are conducted in the hope of yielding results that might translate into clinical practice, but it should be noted that good clinical practice has a placebo value of its own — that is, confers a benefit over and beyond the specific effects of treatments — even if nothing like a sugar pill is administered.

CUES, SUGGESTIONS, AMBIGUITIES

In 1955, a paper that has since been cited well over 1,000 times calculated that some 35 percent of the subjects in a sampling of clinical trials responded to placebo as to a medication [1]. While this figure has been challenged in recent years for conceptual sloppiness and other inaccuracies [2], clearly the placebo effect must be accounted for in clinical trials of proposed medications if the results are to mean anything. The author of the paper in question, Henry Beecher, was himself an advocate of the placebo-controlled trial. In another paper — one that has not attracted the notice received by "The Powerful Placebo" — Beecher urged the practice of informed consent in medical studies [3]. A half-century ago, neither the randomized clinical

To whom all correspondence should be addressed: Stewart Justman, Director, Liberal Studies Program, University of Montana, Missoula, MT 59812; Tele: 406-243-5793; Fax: 406-243-5313; Email: stewart.justman@umontana.edu.

†Abbreviations: RCT, randomized clinical trial; IBS, irritable bowel syndrome; HIP, Health Insurance Plan of New York; ADHD, Attention Deficit Hyperactivity Disorder.

Keywords: placebo, deception, suggestion, consent

trial (RCT†) nor informed consent were normative. The two appear to go hand in hand [4].

As a rule, subjects in RCTs are truthfully informed that they will receive either a certain treatment or a placebo — that is, a visibly indistinguishable replica whose effect, if any, derives not from its actual composition but from the expectations it engenders. Because the placebo effect is largely dependent on expectation and subjects who know they have a 50/50 chance of an active treatment can only expect so much, the standard RCT is not an ideal tool for eliciting the power of the placebo, something it was never intended to do in the first place. A considerably stronger therapeutic effect is produced when subjects are told positively that the treatment they are receiving is an active one [5]. However, many studies that follow this practice compromise the informed consent that ought to be in place in any experiment involving human subjects.

While a placebo response of some degree is commonplace in trials using placebo as a control, there cannot be many cases in which placebo produces the same response as drug across a study population. One such rarity is a small study of irritable bowel syndrome (IBS) in which experimenters deliberately led the subjects to believe that two of the inert treatments they received were active. Specifically, in an attempt to determine if verbal suggestions of pain relief contribute to the sensation of relief, the subjects were told, "The agent you have been given is known to significantly reduce pain in some patients," just after a balloon was inserted into their rectum. Bearing out the importance of verbal cues to the experience of pain, the study found that the placebo treatments reduced pain just as effectively as rectal lidocaine [6].

Given that the study hinged on getting the subjects to mistake placebo for a medication, it comes as a surprise to the reader of the study report that "All patients signed informed consent prior to the start of the study." How can this be? Were the participants truthfully informed, in something approaching a Cretan paradox, that they were going to be deceived? There is no indication of that. On the contrary, the study report maintains that the labeling of placebo as an active treatment was truthful, in that a placebo jelly had been shown in a previous study to reduce "evoked rectal pain." Thus, by describing the jelly as "an agent ... known to significantly reduce pain," the experimenters could fool the subject into expecting an actual treatment while technically satisfying informed consent. Though the principle of informed consent was built into clinical trials so that subjects would know they had an equal chance of receiving placebo or drug, in this case an informed consent document served to excuse the presentation of placebo as drug.

It is because placebo can reduce pain in some cases that the experimenters were able to describe it in a way that makes it sound like an active treatment. This double entendre, worthy of a team of lawyers, was compounded by another troubling circumstance: "the doctor who performed the experiment was the doctor that the patients normally consulted in the clinic and with whom the majority of the patients had a good relationship," in the words of the study report. A trusted doctor makes a particularly good confederate in an experiment all the more deceptive because it is technically truthful. (As thoughtful commentators have noted with this study, among others, in mind, "Especially problematic is the use of deception in experiments conducted by clinicians who have a prior clinician-patient relationship with the patients enrolled in the study" [7].) Mentioned incidentally in the study report is that the doctor "took time to talk with each patient before the experiment," although what the doctor said is not reported — a significant gap in a study of the contribution of verbal suggestion to the placebo effect. In this sense, part of the study took place off the record.

Perhaps even more paradoxical than a study that turned on an equivocation but purported to be truthful and employed a standard script except when the doctor performing the experiment "took time to talk

with each patient," was a European study of a few years before comparing the benefits of active and inactive pacemakers. Finding that inactive devices yielded both subjective and objective benefits, the pacemaker study is one of many that have revealed the surprising scope of the placebo effect, although like related studies of sham surgery it leaves the reflective reader puzzled. For according to the study report, "Study protocol was approved by the local ethics committees of all participating hospitals. All patients gave their written informed consent to participate in the study" [8]. Did cardiac patients knowingly consent to the implantation of a pacemaker that would be switched off for 3 months behind their back, as the protocol required? It is reasonably theorized that subjects in clinical trials who suspect they are receiving placebo enjoy less placebo effect because they are haunted with uncertainty [9]. If I suspected the pacemaker in my chest might actually be off, it would not only haunt me with uncertainty, it would send palpitations right through me. But if informed consent can cut into the placebo effect, there may be ways of framing the language of consent forms that reduce that possibility.

A probing commentary published a few years ago found "misleading statements that informed consent was obtained from the research participants" to be endemic in research on the placebo effect [10]. According to the authors, such statements are often no more than boilerplate language employed to give the appearance of good practice. Along with the tactic of leaving the use of deception to be "inferred by the reader" (who may or may not actually infer it), the conversion of the ethical safeguard of informed consent into a stumbling block for the subject and even the reader points to a troubling syndrome in the placebo literature. The authors of the commentary, whom I will designate M and K, proceed to critique three studies, one of which exhibits a "lack of full transparency" from start to finish, with the finish being the published report of the results. As it happens, K contributed to this study; in reproaching the trickery of placebo research, he does not spare himself. The published report in question cites the consent, albeit not the informed consent, of the subjects, thereby equivocating with the reader just as the consent form, which concealed the deceptive component of the experiment, equivocated with the subjects [11]. In fact, the trickery of placebo experimentation goes beyond straightforward lies to include the use of artful ambiguities (as in this case), half-truths, and deliberate omissions in informational scripts and "verbal suggestions" [12].

A leading investigator of the placebo effect, Fabrizio Benedetti, has suggested that "words and drugs may use the very same mechanism and the very same biochemical pathways." (Hence, in patients with Parkinsonism, "verbal suggestions of motor improvement activate the same dopamine receptors in the very same brain areas" as anti-Parkinson agents [13].) As words come to resemble therapeutic agents in their own right, it is only to be expected that researchers would exploit subtle verbal effects and use language in carefully ambiguous ways to elicit the responses they are looking for. In due course, I will cite as an example of this practice a study whose authors include M and K themselves and which was actually designed to avoid the ethical shortcomings of placebo research.

Placebo research is so bound up with deception in one guise or another that the very attempt to manage deception ethically can create further problems. In an intricately constructed experiment on the influence of expectation on drug effects, which employed a balanced placebo design — with some subjects receiving a drug presented as placebo, some a placebo presented as drug, and others either drug or placebo presented without deception — the consent form advised subjects that information presented to them in the course of the study "may be inaccurate." Given that "inaccurate" here really means "deliberately false," the wording introduces an element of euphemism into the act of disclosure. The same document stated: "The drugs that you might receive are commonly prescribed or over-the-counter, non-experimental drugs, and they are given

in doses that are unlikely to cause you any discomfort." Were I to read this in the same form that notified me that I might be receiving inaccurate information, I wouldn't know what to think. Is the information that the drugs are in common use somehow inaccurate itself [14]? Given the sort of binds that deception leads to, it is no wonder that placebo researchers are interested in the possibility of doing away with it altogether. Presenting placebos as placebos eliminates both the ethical problem of deception and the tactical problem of framing consent language that does not give away too much. Moreover, if undisguised placebos were found to yield therapeutic benefits in clinical trials, the results could in principle be translated into the clinic.

OPEN PLACEBOS

It may be a measure of interest in open (that is, undisguised) placebos that a "Nonblind Placebo Trial" of 1965 has been cited as precedent-setting in the placebo literature and is still adduced as a kind of proof of principle, despite such ethical deficiencies as the use of actual patients rather than volunteers and such methodological shortcomings as the lack of a control group. Conducted by Park and Covi, the study in question, involving fifteen "neurotics" recently admitted to a psychiatric clinic, took place in 1963 and ran for just 1 week. Upon entering the study, the subjects were told, according to a "carefully enacted" script,

> "Many different kinds of tranquilizers and similar pills have been used for conditions such as yours, and many of them have helped. Many people with your kind of condition have also been helped by what are sometimes called 'sugar pills,' and we feel that a so-called sugar pill may help you, too. Do you know what a sugar pill is? A sugar pill is a pill with no medicine in it at all. I think this pill will help you as it has helped so many others. Are you willing to try this pill?" ... The statement that the pills had helped many others was usually repeated again, especially if the patient asked questions concerning the treatment, conveying doubtful attitudes about its possible effectiveness [15].

The shift from the statement that the pill "may help you" to the statement that the pill "will help you as it has helped so many others" anticipates what is now a sort of principle in the placebo literature: that definite expectations of benefit from a placebo treatment are more potent than conditional or uncertain ones. Clearly, the subjects were being prompted to accept "a pill with no medicine in it at all" as some sort of therapeutic agent — a suggestion enhanced by the label on the pill bottle, which bore the name of Johns Hopkins Hospital. And it appears the subjects complied.

Of the 14 who completed the short study, all but one reported improvement, with the group as a whole showing a 41 percent decrease in symptoms. The possibility that some simply reported to the experimenters what the latter were looking for — now a recognized risk of open-placebo experimentation — was not considered. It is also notable that, in a converse of the doubts known to haunt those randomized to placebo in a conventional trial, six of the 14 believed the sugar pills *did* contain medication, according to the study report. For whatever reason, six subjects presumed that the psychiatrists who ran the study were lying to them. (In experiments with a balanced placebo design, as above, one group is in fact told it will receive placebo but gets drug instead.) Though wrong about the contents of the pills, the suspicious subjects were onto something.

While the shortcomings of the Park and Covi trial, including but by no means limited to the lack of a control group, were detailed in 2008 by David Jopling [16], no one to my knowledge has commented on the trick that this supposed exercise in openness turned upon. As we know, the script "enacted" for the patients stated twice over —

for some, three times — that many other patients have been helped by sugar pills. But those other patients were helped precisely because they were deceived into believing the pills an active medication. In 1963, doctors still used placebos at their own discretion, and even in randomized clinical trials, which were not yet the norm of medical research, informed consent was not necessary. In the Health Insurance Plan of New York (HIP) trial, also launched in 1963 and considered the first RCT of cancer screening, the control group did not even know it was part of a trial [17].

Inasmuch as the "Nonblind Placebo Trial" was the first of its kind, the "many others" referred to in its script could not in fact have received placebos disclosed as placebos. On the contrary, they received placebos masked as actual medications, presumably expected the benefits of such medications, and, in accordance with the dynamics of the placebo effect, these expectations shaped their experience to one degree or another. Note, too, that if we remove the references to "many others" from the script, what we are left with is a bare sugar pill with no claim on anyone's credence at all. In this way, the script smuggles the fruits of deception into a study purporting to do away with deception. It is therefore as much of an equivocation as the sort of consent language faulted by M and K for its deliberate ambiguity. (Indeed, Jopling takes the sugar-pill script as an informed consent document.) "Are you willing to try this pill?" the script asked.

The principle that we tend to expect the benefits that "many others" appear to derive from a medical treatment is a potent one with a place of importance in the history of placebo research [18]. In the first investigation of the placebo effect in England, John Haygarth and his colleagues tested the efficacy of certain dubious brass devices said to be able to draw pains out of the body ("tractors") by treating a handful of patients at the Bath General Hospital with identical-looking articles fashioned of wood. By and large, the subjects responded to the sham instrument exactly as if it were "real," thereby demonstrating that the tractor itself was a sham. But Haygarth knew it was not enough to simply wave the article over the subjects of his experiment. In order to really recommend the treatment to them, he, like Park and Covi, made sure to refer to the many others who had been helped by tractors. Writes Haygarth:

> If any person would repeat these experiments, it should be done with due solemnity. During the process, the wonderful cures which this remedy is said to have performed ought to be particularly related. Without these indispensable aids, other trials will not prove as successful as those which are reported above. The whole effect undoubtedly depends upon the impression which can be made upon the patient's Imagination [19].

The "due solemnity" of this deceptive experiment bears comparison with Park and Covi's "carefully enacted" script, just as the "wonderful cures" attributed to tractors presage the "many others" helped by sugar pills. An experiment in transparency employed potent conventions of deception.

Moreover, since Park and Covi, the invocation of the many others who have benefited from placebos — albeit not *open* placebos — has continued in nonblind placebo trials. In a recent study involving children diagnosed with Attention Deficit Hyperactivity Disorder (ADHD), subjects as young as 6 were told supposedly openly about the placebo. (Can a 6-year-old comprehend something as paradoxical as an inert pill that is not really inert?) The script used with children from 10 to 12, which is almost identical to that used for younger children, reads in part:

> This little capsule is a placebo. Placebos have been used a lot in treating people. It is called 'Dose Extender.' As you can see, it is different from Adderall. Dose Exten-

> der is something new. It has no drug in it. I can promise you that it won't hurt you at all. It has no real side effects. But it may help you to help yourself. It may work well with your Adderall, kind of like a booster to the dose of Adderall. That's why it's called a Dose Extender. I won't be surprised when I hear from you and your parents and your teachers that you're able to control your ADHD better [20].

Just as the Park and Covi script promoted placebo from something that may help to something that will help, so in this case the script seems designed to encourage a self-fulfilling prophecy, whereby a Dose Extender that "may help" becomes an actual therapeutic agent by the power of expectation. The claim that "Placebos have been used a lot in treating people" similarly echoes the leading or misleading language of the Park and Covi script, though it also brings to mind a line used in the experiment on the power of verbal suggestion that I began with: "The agent you have just been given is known to significantly reduce pain in some [IBS] patients." In another reminder of just how tangled deception and transparency have become, the authors of the IBS study contend that because placebos have been known to reduce pain, verbal suggestions for pain relief in general "need not be deceptive and thereby ethically problematic." Of course the placebos they refer to are not open placebos.

Can a placebo openly disclosed as such reduce pain — say, the pain associated with IBS? Recently, this possibility was put to the test by a team including both M and K. In a widely cited experiment, a group of 37 IBS patients, of whom 31 completed the study, were treated with pills labeled as placebo and described as being "something like sugar pills" of proven therapeutic power. After 3 weeks, 59 percent of patients treated with the placebo reported adequate relief as compared to 35 percent of the control group, a finding qualified by a number of limitations laid out by the authors. For present purposes, though, the important point is that subjects recruited into this study of "placebos without deception" seem to have been told several times "that placebo pills ... have been shown in rigorous clinical testing to produce significant mind-body self-healing processes" [21]. Therefore, while the study does represent the first RCT to compare a group given open placebo to a no-treatment group, in another respect it continues past practice, using a variant of the sales pitch that has been employed in open or semi-open or indeed deceptive placebo experiments since Park and Covi established it half a century ago.

The impressive rhetoric of "rigorous clinical testing" in the study's script makes placebo sound like a medication in its own right, or at least like something of attested efficacy that "will help you as it has helped so many others," in the language of Park and Covi. What of the benefits attributed to the placebo treatment? While placebo produces reports of improvement in countless clinical trials (as when placebo branded as aspirin outperformed its generic counterpart [22]), the claim that such improvement represents the work of "significant mind-body self-healing processes" is arguably both tendentious and inflated. Despite the inspirational rhetoric of "healing," the only sense in which the study subjects treated with open placebo were healed is that many of them felt better. Their IBS itself did not heal in the way ulcers, for example, do — with or without treatment. According to the Oxford English Dictionary, the first meaning of "to heal" is "to make whole or sound in bodily condition; to free from disease or ailment, restore to health or soundness; to cure." Placebo treatments of IBS do none of this. Given that the evidence suggests that placebos do not in fact stimulate the body's capacity for repair, as some champions of the placebo effect maintain, but act on symptoms only [23], given that the IBS experiment accordingly measured improvement of symptoms and that we hear nothing further of "self-healing" after the study subjects are primed to expect it — given all this, we may question just how transparent the presenta-

tion of the placebo actually was in this officially transparent experiment.

A defender of "placebos without deception" might ask what harm there can be in a slight exaggeration that does, in fact, make for a reduction of distress. However, the same defense might be made of some of the studies faulted by M and K for their use of misleading statements and tactical concealments.

THE CARE EFFECT

The Park and Covi experiment had 14 completers; the "placebos without deception" study had 31 completers in the treatment group. The IBS study involving rectal distension, along with deliberately ambiguous "verbal suggestions" deemed truthful by the authors, had 13 subjects. In addition to the ADHD study already mentioned, which enrolled 70 children, a related study reported in 2007 enrolled 26 [24]. Compared to placebo responders in conventional clinical trials, these 154 persons represent a modest grand total, surely. Beecher's paper of 1955 took as its database 15 trials with a total of 1,082 patients. Open placebos do not seem to be much of a practical possibility.

But this is not to deny that research into the placebo effect (as distinguished from trials where placebos serve as controls) has yielded rich results. Among its intriguing findings is that a drug administered in full view of the patient is markedly more effective than the same drug administered covertly; the first engages expectations — as well as the evocative power of ritual, perhaps — while the second does not. (By the same token, saline solution presented to a patient as a drug may trigger an effect but will be less potent than the drug itself openly administered; in the latter case, the placebo effect is supplemented, if you will, by the drug's specific activity.) In contrast to studies that turn upon deceptions and semi-deceptions, findings like these point to the benefits of transparency. If a drug seen to be administered by a doctor or nurse has a greater effect than the same quantity of drug administered secretly, perhaps care in and of itself has a therapeutic effect.

A care effect may have been silently imported into the IBS study involving rectal balloons when the patients' own doctor conferred with them before the pain procedure and, in fact, went on to perform it. By contrast, a care effect is explicitly built into the study of "placebos without deception." A secondary finding of the study, one which has not attracted much attention or comment, is that 35 percent of the subjects who received nothing but supportive care reported adequate relief of IBS, as compared with 59 percent of those who received the active treatment — in this case, a placebo pill. That those in the treatment group received the same care raises the possibility that much or even most of the relief they reported was attributable not to the pill per se (despite its seeming centrality) but the context of sympathetic care in which it was given and received. Moreover, fully 76 percent of those in the care-only group were well enough satisfied with the result that they did not regret being denied the placebo pill as a result of randomization. Evidently, it is possible to deliver care itself in a way that produces a potent placebo effect — in the process, solving the issue of deception by rendering it completely moot. On the other hand, a placebo prescribed to get the patient out the door — as in Denmark, where the most common reported reason for using placebo is to give the appearance of doing something when "the doctor feels there is no time for a detailed explanation or lengthy discussion" — can short-circuit care itself [25].

The Park and Covi study of open placebos contains case notes, many of which suggest the importance of the context of care in which the giving of placebo was embedded. Patient A "wanted to stay with the same doctor," as did Patient C. Patient T, though convinced that his pill contained no active ingredient, "had a strong positive reaction to the therapist;" patient U, though likewise convinced, "was very satisfied with the idea of staying with the same doctor and pills." Patient H reported, "Every time I took a pill I thought of my doctor," and Patient S said, "For people, each time they take a pill it's a symbol ... of

someone caring about you." Perhaps the lesson of the experiment is not that inert pills lend themselves to ethical use but that care itself is such a potent influence that it can endow an inert pill with a semblance of activity.

The theory that care per se contributes importantly to the placebo effect was tested in a study of IBS conducted 2 years prior to the "placebos without deception" trial. Unlike the latter, in which the treatment and no-treatment groups received the same supportive care, in this instance one group received placebo treatment (sham acupuncture) with only minimal care, while the other received the same treatment augmented with care described as "warm and empathetic." (In sharp contrast to the practice of using placebo to get rid of the patient, the care protocol in this case called for an initial visit of 45 minutes with a practitioner.) The proportions of patients reporting "moderate or substantial improvement on the global improvement scale" at 3 weeks were 20 percent for the placebo-treatment-only group and 37 percent for the group that enjoyed empathetic care in addition to the placebo treatment [26].

We may note that this study of separate components of the placebo effect deceived subjects into thinking they received acupuncture (the device used did not actually pierce the skin) and concealed its own purpose. The "informed consent" given by the subjects turns out to have been considerably less than informed:

> All participants gave written informed consent, but the consent disclosure omitted certain descriptors of the trial to protect the study's scientific validity. Thus, participants were told that the trial was a placebo controlled study of acupuncture for irritable bowel syndrome and were completely unaware of the study's primary aim to examine placebo effects.

The study thus falls into the pattern of using the very act of disclosure as a mechanism of deception. However, other aspects of the study point in fruitful directions. Taking its lead from this one, a study could disaggregate placebo and care, such that one group received an open placebo in the context of minimal care and another group attentive care but no placebo. Other studies could tease out the elements of attentive care itself so that clinicians might know which practices best promote good outcomes. Given that "benefits of standard medical treatments have two components, the specific effects of the treatment itself and the perception that the therapy is being given" [27], how best to foster the perception of care? In view of our keen responsiveness to words in a medical setting, how might a doctor or nurse explain a treatment? And how much listening should they ideally do? Open placebos may or may not have much application in clinical medicine, but good practices of care certainly do — by definition. Misleading consent language and suggestive double-entendres jeopardize the ethical framework of medicine, while good practices of care strengthen it. Research into the placebo effect would do well to turn to the investigation of such practices.

REFERENCES

1. Beecher H. The Powerful Placebo. J Am Med Assoc. 1955;159(17):1602-6.
2. Kienle G, Kiene H. The Powerful Placebo Effect: Fact or Fiction. J Clin Epidemiol. 1997;50(12):1311-8.
3. Beecher H. Ethics and Clinical Research. N Engl J Med. 1966; 274(24):1354-60.
4. Kaptchuk T. Powerful Placebo: Dark Side of the Randomised Controlled Trial. Lancet. 1998;351(9117):1722-5.
5. Benedetti F. How the Doctor's Words Affect the Patient's Brain. Eval Health Prof. 2002;25(4):369-86.
6. Vase L, Robinson M, Verne GN, Price D. The Contributions of Suggestion, Desire, and Expectation to Placebo Effects in Irritable Bowel Syndrome Patients: An Empirical Investigation. Pain. 2003;105(1-2):17-25.
7. Miller F, Wendler D, Swartzman L. Deception in Research on the Placebo Effect. PLoS Med. 2005;2(9):e262.
8. Linde C, Gadler F, Kappenberger L, Rydén L. Placebo Effect of Pacemaker Implantation in Obstructive Hypertrophic Cardiomyopathy. Am J Cardiol. 1999;83(6):903-7.
9. Miller F, Rosenstein D. The Nature and Power of the Placebo Effect. J Clin Epidemiol. 2006;59(4):331-5.

10. Miller F, Kaptchuk T. Deception of Subjects in Neuroscience: An Ethical Analysis. J Neurosci. 2008;28(19):4841-3.
11. Kong J, Gollub R, Rosman R, et al. Brain Activity Associated with Expectancy-Enhanced Placebo Analgesia as Measured by Functional Magnetic Resonance Imaging. J Neurosci. 2006;26(2):381-8.
12. Justman S. Placebo: The Lie That Comes True? J Med Ethics. 2013;39(4):243-8.
13. Benedetti F. The Placebo Response: Science Versus Ethics and the Vulnerability of the Patient. World Psychiatry. 2012;11(2):70-2.
14. Mitchell S, Laurent C, de Wit H. Interaction of Expectancy and the Pharmacological Effects of d-Amphetamine: Subjective Effects and Self-Administration. Psychopharmacology (Berl). 1996;125(4):371-8.
15. Park L, Covi L. Nonblind Placebo Trial: An Exploration of Neurotic Patients' Responses to Placebo When Its Inert Content Is Disclosed. Arch Gen Psychiatry. 1965;12:36-45.
16. Jopling D. Talking Cures and Placebo Effects. Oxford: Oxford University Press; 2008.
17. Mukherjee S. The Emperor of All Maladies: A Biography of Cancer. London: Fourth Estate; 2011.
18. Justman S. To Feel What Others Feel: Social Sources of the Placebo Effect. San Francisco: University of California Medical Humanities Press; 2013.
19. Haygarth J. Of the Imagination, as a Cause and as a Cure of Disorders of the Body. Bath: R. Cruttwell; 1800.
20. Sandler A, Glesne C, Geller G. Children's and Parents' Perspectives on Open-Label Use of Placebos in the Treatment of ADHD. Child Care Health Dev. 2008;34(1):111-20.
21. Kaptchuk T, Friedlander E, Kelley J, et al. Placebos without Deception: A Randomized Controlled Trial in Irritable Bowel Syndrome. PLoS One. 2010;5(12):e15591.
22. Branthwaite A, Cooper P. Analgesic Effect of Branding in Treatment of Headaches. Br Med J (Clin Res Ed). 1981;282(6276):1576-8.
23. Miller F, Colloca L, Kaptchuk T. The Placebo Effect: Illness and Interpersonal Healing. Perspect Biol Med. 2009;52(4):518-39.
24. Sandler A, Bodfish J. Open-Label Use of Placebos in the Treatment of ADHD: A Pilot Study. Child Care Health Dev. 2008;34(1):104-10.
25. Hróbjarttson A, Norup M. The Use of Placebo Interventions in Medical Practice—A National Questionnaire Survey of Danish Clinicians. Eval Health Prof. 2003;26(2):153-65.
26. Kaptchuk T, Kelley J, Conboy L, et al. Components of Placebo Effect: Randomised Controlled Trial in Patients with Irritable Bowel Syndrome. BMJ. 2008;336(7651):999-1003.
27. Colloca L, Lopiano L, Lanotte M, et al. Overt versus Covert Treatment for Pain, Anxiety, and Parkinson's Disease. Lancet Neurol. 2004;3(11):679-84.