

The Placebo Effect: Mental or Physical?

Morton E Tavel*

Professor Emeritus, Indiana University School of Medicine, Indianapolis, Indiana, USA

***Corresponding Author:** Morton E Tavel, Professor Emeritus, Indiana University School of Medicine, Indianapolis, Indiana, USA.

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Abstract

The placebo effect is defined as any improvement of symptoms or signs following a physically inert intervention. Its effects can be profound, especially in relieving subjective symptoms such as pain, fatigue, and depression. Present to a variable extent in all therapeutic encounters, the placebo effect is intensified by hands-on contact with close verbal communication between care-giver and recipient. Thus it may be used to benefit patients but provides a ready avenue for unscrupulous “healers” of all types. Conventional medical practitioners often intervene in some way-by pill or procedure-and, without knowing what caused the improvement, may claim credit for the apparent benefit. Physicians must be skeptical about apparent “responses” to treatments, using the lessons described herein in order to better understand what we are-or not-accomplishing to provide the best possible outcomes for our patients.

Less well studied, the “nocebo effect” defines negative responses to placebo interventions. This latter effect may be quite profound and likely is causative in many maladies believed to have psychic origins.

Keywords: *Placebo Effect; Mental; Physical*

A placebo is characterized as “an inert medication used for its psychological effect, or for purposes of comparison in an experiment”. This generally applies to the standard execution of a controlled, double-blind study to determine the efficacy of a new treatment. But a placebo also includes any treatment that exerts no physical effect on a disease. These “treatments” are often discovered to be ineffective months or even years after administration, and can include virtually any type of intervention-such as simple encounters with medical professionals, physical manipulations, and even surgical procedures.

The placebo effect can thus be defined as any improvement in subjective discomfort or illness not explained by the physical effect of the treatment given. I have deliberately broadened the definition to include unconventional care providers such as faith healers and, for the most part, practitioners of alternative medicine. This effect also plays an important role in the daily practice of medicine for almost all mainstream medical caregivers.

Few people outside of the medical profession understand the power of the placebo effect. It has been aptly characterized as “something to control in clinical research, something to cultivate in clinical practice, and something present in all healing encounters” [1]. Although not well understood, the mechanism of the placebo effect relates to the power of the mind to affect bodily sensations and functions. It is especially effective in relieving pain, anxiety, fatigue, insomnia, and depression, but can go far beyond these even to enhance the effectiveness of medical interventions with acknowledged physical benefit. With this expanded definition we can proceed to review some of the vast experience with this phenomenon, and lessons learned, over the past half century.

Based on a review of medical studies, placebos improve or relieve symptoms in a widely divergent percentage of individuals suffering from numerous maladies. But the cause for such variable responses depends on the type of illness treated, the context of its administration, and how long the subjects are observed [1,2]. For instance, when used to evaluate new drugs, researchers focus solely on the difference between the active drug and the placebo, and so the placebo effect itself is rarely analyzed or compared with an absence of treatment. Compared in this latter way, one study reported little difference between a placebo and no treatment [2]; however, this information is tempered by the inclusion of numerous physical diseases and did not evaluate the nature of the interaction between caregiver and patient. Pain, however, did show a significant placebo response when compared with no treatment.

Generally, symptoms unrelated to serious underlying organic diseases, such as pain or fatigue, are most likely relieved by a placebo. That is not to say, however, that these symptoms are not real or are imagined. I believe the relief of symptoms in this context is real, but the underlying physiological mechanisms are not well understood. A beneficial response occurs most often when the treatment is provided by a caregiver who explains that he/she expects improvement. It is also most likely to occur in individuals who are, in general, highly receptive to suggestion [3]. Additionally, the responses are more profound when a given medication is thought to be more expensive than a cheaper one [4].

Perhaps the most potent placebo effects result from physical interventions, such as acupuncture. Various studies have shown marked improvement with either traditional acupuncture, or a sham which employs superficial needling at non-acupuncture points. For example, in a trial of over 1,100 patients with chronic low back pain who received ten 30-minute sessions over 5 weeks [5], the improvement rate after 6 months was 48% for traditional acupuncture and essentially the same for the sham procedure, compared to 27% for patients receiving customary care (physiotherapy plus as-needed pain medication), clearly confirming the placebo effect. The same observations have been found with migraine and tension-type (formerly called tension) headaches, irritable bowel syndrome, chronic low back pain, and even arthritis of the knee.

These findings establish two important points; the sham procedure is as effective as the real procedure, qualifying both as effective placebos, and the efficacy of both acupuncture procedures far exceeded those of ordinary medical management, indicating that the placebo effect is powerful indeed. Moreover, it demonstrates that acupuncture is likely only effective as a placebo. These and many other similar trials strongly suggest that this type of invasive but safe intervention, characterized by an elaborate treatment ritual and frequent clinician-patient interaction, may be a potent method of interpersonal healing by means of the placebo effect [6]. In general, physical manipulations demonstrate a more profound beneficial effect than do placebo tablets.

A study [7] involving patients suffering from irritable bowel disorder reinforces the importance of personal interaction in any treatment encounter. In this study, patients received sham acupuncture twice a week for 3 weeks. In one (first) group, initial communication between practitioner and patient was businesslike and limited to 5 minutes; in the second, there was a 45-minute conversation with the practitioner at the initial visit regarding the patient's condition. This talk was purposefully supportive, with the idea of promoting positive expectations of acupuncture therapy. A third group received no treatment. Patients in the second group had superior outcomes of symptom relief and quality of life compared to those in the first group, which in turn had better outcomes than those in a third group who received no treatment. At 3 weeks after the "treatment", 62% of patients in the second group reported adequate symptom relief, compared with 44% in the first group and 28% in the third group. This experiment suggests that simulation of treatment can account for therapeutic benefit. When enhanced by supportive communication, however, the placebo response is more profound. Thus, the placebo effect is closely bound to interpersonal contact.

Recognizing that the placebo effect is so closely bound to interpersonal contact, Kleinman, *et al.* [8] advocate an informal process of medical psychotherapy as a basic component of care, focusing on the experience of chronically ill patients: "It is of the utmost importance that physicians achieve the highest possible placebo effect rates. To do this, doctors must establish relationships that resonate empathy and genuine concern for the well-being of their patients". They add that "The chief sources of therapeutic efficacy are the development of a successful therapeutic relationship and the rhetorical use of the practitioner's personality and communicative skills to empower the patient and persuade him toward more successful coping".

Sham surgeries have also demonstrated dramatic placebo effects, as demonstrated by an early study [9] that showed that angina pectoris could be relieved by superficial thoracic incisions without any cardiac effects.

The interaction between mind and body is so potent that it can affect the course and outcome of certain organic, or physical, diseases. Mental depression is a well-known cause of poor outcomes in patients who have suffered myocardial infarctions. The cause of this relationship is not well understood. In those who suffered an attack, treatment with antidepressant drugs has been found to improve not only quality of life but also probably reduces recurrent heart attacks and even mortality, although the data are currently too limited to enable a firm conclusion [10]. Since depression responds profoundly to placebos, one questions whether the placebo effect could be lifesaving [11].

The placebo effect may be beneficial in such physical conditions as Parkinson's disease [12], asthma [13], duodenal ulcer and inflammatory gastrointestinal conditions [14]. Although placebos have no effect on progression of cancer, they have been found to reduce associated symptoms of pain, loss of appetite, anxiety, and depression [15].

Of the manifold responses to the placebo, what is perhaps most amazing is its effect on physical sports performance! Enhancement of performance has been demonstrated in several trials. Clark, *et al.* [16] provided one notable example, when they studied the endurance of 43 cyclists in a 40 kilometer timed trial. After suitable allocation into subgroups, those given placebos that were told they had received performance-enhancing carbohydrate performed 3.8% better than those given the same drink but told it was a placebo. Similar observations have been made in studies of muscle endurance and power in other athletes [17]. This raises the intriguing-albeit facetious-question: Should the administration of performance-enhancing placebos be considered "doping", and worthy of disqualification from competition?

The placebo effect clearly reflects the strong interplay between brain and body, and recipient and caregiver. More dramatic treatments, such as mechanical or surgical procedures, seem to evoke the greatest response. I believe that the personality of the caregiver strongly influences the results. Some physicians likely obtain optimum results by having a placebo personality—a positive and upbeat attitude toward an expected successful outcome. Additionally, of all patients seen in most general clinics, I would estimate that approximately 50% - 70% have self-limiting conditions that will improve or resolve without treatment. This means any action taken by a physician will usually be followed by a favorable outcome and, according to the post hoc fallacy, both the patient and physician are seduced into believing the treatment brought about subsequent improvement. Thus, all practitioners, legitimate or otherwise, will achieve success through a combination of natural outcome, placebo effect and post-hoc reasoning. This can easily account for the apparent success of alternative medicine and faith healing.

The mechanism for the placebo's influence on brain/body connection had always been obscure until clues began to surface in the 1970s. The discovery of substances produced by the brain, called endorphins, has provided one possible answer to this enigma, at least in regard to the role of the placebo in combating pain. Endorphins are chemically similar to opiates like morphine and, therefore, likely provide pain relief. But does the placebo stimulate the brain's production of endorphins? The answer is they probably do, for one study demonstrated that Naloxone, a drug that blocks the physical effects of morphine, also was capable of nullifying relief of pain that was attributable to the placebo effect [18]. This may account for some of the real and physical pain relief afforded by placebos.

Since standard medical caregivers are keenly aware of the placebo effect, it is not surprising that this principle would be applied in clinical practice. Placebos may be administered in a “subtle” form, wherein a barely effective medication (such as a mild tranquilizer) is given together with strong reassurance that said nostrum will be effective. Highly attenuated preparations are said to be “homeopathic” in nature, which is simply a form of alternative medicine. Vitamin B12, when given by injection in the absence of this vitamin’s deficiency, provides a more dramatic example of this effect. Probably less often, a medication without any physical effect whatever may be delivered with the same fanfare. Actual surveys of practitioners in mainstream medicine confirm the widespread use of placebos: in a study by Nitzan and Lichtenberg [19], 60% of physicians and nurses used placebos, usually as often as once a month or more, and in most cases the patients were told they were receiving “real” medication. Of this latter group, 94% reported they found placebos generally effective. Another survey among academic physicians in the United States [20] disclosed that 45% had used placebos in clinical practice, most commonly to reduce anxiety and as supplemental treatment for physical problems. As many as 96% of these physicians believed placebos can have therapeutic effects, and 40% reported placebos could even benefit patients’ physical problems. These studies serve to add additional support garnered worldwide from earlier surveys showing the same overall findings. Very few practitioners in any of these surveys considered placebo-giving as immoral or worthy of prohibition. Regardless of one’s opinion about this issue, however, the placebo’s safety profile is absolutely unbeatable!

The “reverse” placebo effect”: the brain as a cause of illness

As presented above, the brain can be a powerful cause of relief-or even cure-of many illnesses. This effect is based, at least in part, on the positive anticipations from placebo treatments. But the flip side of this coin, illness resulting from expectation or fear of a bad effect, can be even more powerful. This has been labeled the “nocebo” effect, or the “placebo’s evil twin” [21]. A nocebo response refers to harmful, unpleasant, or undesirable effects a subject manifests after receiving a placebo. These reactions are due basically to a subject’s pessimistic belief and expectation that the inert drug will produce negative consequences. The actual responses range widely in nature, often taking the form of headaches, gastrointestinal upset, and many others. If the administration is accompanied by warnings of specific potential reactions, those effects are more apt to actually materialize. This fact alone accounts for why almost all drug trials demonstrate rates of undesirable “side effects” in the control (placebo) group. This provides ample reason for why proper research must include these latter comparisons.

Several common maladies seem to emanate solely from the brain, often called “psychosomatic” or “somatoform” disorders. These usually feature various aches and pains not explainable by objective medical testing. I believe these symptoms are really felt, i.e. they are not “all in the head”, as is sometimes alleged. By contrast, pure fakery of symptoms, i.e. malingering, falls outside of this discussion. Sometimes these disorders are hidden behind other names such as psychogenic arthritis, fibromyalgia, chronic widespread pain disorder and chronic fatigue syndrome [22]. More focused areas of pain also can result from emotional factors, and these include, among others, tension-type headaches, back and chest pain. All are usually associated with emotional tension and/or depression, which often is associated with an unexplained sense of fear. These conditions are quite prevalent and can be severely disabling, persistent, and often resistant to treatment. Aggravating the anxiety embedded in these conditions are occasional “panic attacks”, which are marked by as extreme fear, sweating, breathlessness, light-headed sensations, numbness and tingling of the extremities, bodily pains (often in the chest), general weakness and even fainting. Extreme fear also usually triggers inappropriately rapid breathing-termed “hyperventilation”-which reduces carbon dioxide in the blood and contributes to many of the symptoms, including numbness and tingling of the extremities, weakness, and disturbed consciousness with fainting. Excessive breathing probably owes its existence to our evolutionarily adapted ancestors, whose anxious response in preparing for “flight or fight” triggering rapid breathing necessary to meet the upcoming heavy metabolic demands required by these activities. In modern times, however, anxiety and hyperventilation are not followed by increased physical activity and are thus inappropriate. This part of the disorder is easily combated by simply preventing the loss of carbon dioxide by either breath holding or rebreathing air in a simple paper bag. These maneuvers not only relieve these symptoms but help to allay the underlying fear and anxiety that initially triggered the attack. This combination of emotionally induced symptoms combined with the real physical consequences of hyperventilation is quite common, and may account for as much as ten percent of individuals seen in general medical clinics [23,24].

Some disorders defy classification as purely physical, mixed psychosomatic, or completely somatoform. For instance, irritable colon (bowel) disorder was once considered as having purely mental causes, but subsequent research has shown significant differences in the behavior of the intestines in these sufferers. On the other hand, there are no actual structural changes in these individuals and research shows that stress and emotions are still aggravating factors in producing the unpleasant symptoms of this disorder.

Inasmuch as almost all physical illnesses have associated mental factors that determine their onset, presentation, clinical course, and susceptibility to treatment, there is little benefit in classifying disorders as purely physical or mixed psychosomatic. All management strategies must include identification of stress and include its remediation whenever possible.

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