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The Placebo Effect

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Abstract:

The aim of this report is to demonstrate the effects and mechanism of placebo, which is something that's supposed to act through a psychological mechanism. The placebo first came out in 1811 and was first defined in the early 1960s as "any therapeutic procedure which has an effect on a patient, symptom, syndrome or disease, but which is objectively without specific activity for the condition being treated"⁽¹⁾. The placebo is an aid to therapeutic suggestion. The effect that's produced may be psychological or physiological and it may produce a beneficial result or toxic effects like headaches, diarrhea, nausea, vomiting, or even fatigue. The most frequently used placebo is the sugar pill in drug trials, placebos can be and have been used for all kinds of interventions, ranging from placebo pills for headaches and placebo doses for postoperative wound pain to placebo vaccines for preventing cold and placebo surgeries for alleviation of heart disease. The mechanism of action of the placebo is still unknown but it's believed to be either stimulus-expected by inert substances, or might be because of the anticipation of one's own automatic reactions to various situations. There are some factors that may contribute in the effect of the placebo, like the patient's attitudes, habits, educational background, and personality types and characteristics. Other factors include the doses of the placebo taken and the consistency, but the consensus was that no consistent placebo reactor was out there.

Introduction:

The placebo effect is a remarkable phenomenon in which a placebo (a fake treatment), an inactive substance (sugar, distilled water, or saline solution) can sometimes improve a patient's condition simply because the person has the expectation that it will be helpful. If the person expects the pill to do something, it's possible the body's chemistry can cause effects similar to what a drug might have caused. The fact that the placebo effect is tied to expectations doesn't make it imaginary. Some studies show that there are actual physical changes that occur with the placebo effect.

Researchers use placebos during studies to help them understand what effect a new drug or some other treatment might have on a particular condition. For instance, some people in a study might be given a new drug to lower cholesterol. Others would get a placebo. None of the people in the study will know if they got the real treatment or the placebo. Researchers then compare the effects of the drug and the placebo on the people in the study. That way, they can determine the effectiveness of the new drug and check for side effects.

The placebo effect is part of the human potential to react positively to a healer. A patient's distress may be relieved by something for which there is no medical basis. A familiar example is Band-Aid put on a child. It can make the child feel better by its soothing effect, though there is no medical reason it should make the child feel better. People who receive a placebo may also experience negative effects. They are like side effects with a medication and may include, for example, nausea, diarrhea and constipation. A negative placebo effect has been called the nocebo effect.⁽²⁾

Discussion:

In 1801, John Haygarth reported the results of what may have been the first placebo-controlled trial. A common remedy for many diseases at that time was to apply metallic rods, known as Perkins tractors, to the body. These rods were supposed to relieve symptoms through the electromagnetic influence of the metal. Haygarth treated five patients with imitation tractors

made of wood and found that four gained relief. He used the metal tractors on the same five patients the following day and got the same result: four out of five gained relief. It's clear that Haygarth had the concept of the placebo effect when he said "an important lesson in physic is here to be learnt, the wonderful and powerful influence of the passions of the mind upon the state and disorder of the body. This is too often overlooked in the cure of the disease". He also said that the experiment "clearly prove what wonderful effects the passions of hope and faith, excited by mere imagination, can produce on disease"⁽³⁾

The placebo effect though, was first actually scientifically documented by Beecher in 1955, who found that soldiers in World War II experienced an analgesic effect with saline, a placebo which was given because of depleted morphine stocks. His clinical review of generally uncontrolled studies on placebo analgesia found that 30% of clinical effect could be attributable to the placebo effect.

The placebo effect is used as a psychological instrument in the therapy of certain ailments arising out of mental illness, as a resource of the harassed doctor in dealing with the neurotic patient, to determine the true effect of drugs apart from suggestion in experimental work, and finally, as a tool of importance in the study of the mechanisms of drug actions.⁽⁴⁾

In the beginning of the 20th century, a German physician performed a large-scale comparative clinical trial to assess the specific effect of diphtheria antitoxin serum in the treatment of diphtheria. He was concerned whether the antitoxin in the serum was responsible for the effect or whether treatment with serum not containing the antitoxin would give comparable results. He alternately allocated 937 patients to either diphtheria antitoxin serum or normal horse serum, the placebo, and assessed the effect. He concluded that treatment with normal horse serum achieved a similar clinical outcome to that with the antitoxic serum.⁽⁵⁾

In 1938, the word placebo was first applied in reference to the treatment given to concurrent controls in trials. In previous years, uncontrolled observations had given promising results with vaccines in preventing cold, the students in the control groups were treated in exactly the same manner as those in the experimental groups but received placebos instead of vaccines. The subjects in this group were given lactose-filled capsules which were indistinguishable from the capsules containing vaccine. They were prescribed with exactly the same instructions as the capsules containing the vaccine. The conclusion was a great reduction in the number of colds which the members of the control groups reported during the experimental period.⁽⁶⁾

Another important use is the placebo in surgeries. At the end of 1950s, several reports suggested that a surgical procedure, ligation of the internal mammary artery, alleviated heart disease. At that time collateral vessels were believed to originate from the internal mammary artery; thus, ligation of the artery would increase coronary blood flow through collateral vessels proximal to the point of ligation. Two very small randomized clinical trials were made. All patients in both trials were actually operated on, but the artery was ligated in only half of them in one trial⁽⁷⁾, and one-third in the other trial⁽⁸⁾, and the rest of the patients got skin incisions only. In both trials the rates of improvement were the same in ligated patients and those who received skin incisions.

In psychology, two psychologists analyzed data from no-treatment groups in psychotherapy studies and compared them with placebo groups in antidepressant studies. Drug groups showed 33% more improvement over placebo, but placebo groups showed 200% improvement over no-treatment groups. They calculated up to half of the drug effect may be attributable to placebo effect.⁽⁹⁾

Another systematic review in psychiatry was made in 2002 of 75 randomized controlled trials of antidepressants, it demonstrated that up to half of patients on placebo improved significantly.

In 1946, a study was made by Jellinek to test the effect of the placebo on 199 patients with headache and found that 79 of them never found relief from the placebo while 120 did. ⁽¹⁰⁾

The question should be asked here is why the placebo doesn't work for everyone; many factors were suggested in many reports that interfere in the effect of the placebo. In 1954 in a group of 162 patients having steady, severe postoperative wound pain, researchers found that there were no differences in sex ratios or intelligence between reactors and non-reactors. There are however significant differences between reactors and non-reactors in attitudes, habits, educational background, and personality types and characteristics; anxious, emotionally labile, suggestible, dependent on and dominated by others.

On the same study they found that the number of placebo doses was correlated highly with the total number of doses of all kinds. 15 patients with one placebo dose showed 53% relief from the placebo; 21 patients with two placebo doses got 40% relief from the placebo; in 15 patients with three placebo doses 40% showed relief; and of 15 patients with 4 or more placebo doses, 15% gave relief.

And again on this same study it gave an opportunity to examine the consistency of the placebo response. 69% received 2 or more doses of a placebo. 55% (38 patients) of these were inconsistent reactors, sometimes they gained relief and sometimes not. 14% (10 patients) were consistent reactors, all placebo doses were effective. 31% (21 patients) were consistent non-reactors; the placebo doses were never effective. By the end of 1970s, the consensus was that no consistent placebo reactor was out there. ⁽¹¹⁾

Not only do placebos produce beneficial results though, like other therapeutic agents, they have associated toxic effects. In a consideration of 35 different toxic effects of placebos that were observed in one or more studies, here is a sizable incidence of effect attributable to the placebo as follows: dry mouth, 7 subjects out of 77; nausea, 9 subjects out of 92; sensation of heaviness, 14 subjects out of 77; headache, 23 subjects out of 92; difficulty concentrating, 14 subjects out of 92; drowsiness, 36 subjects out of 72; warm glow, 6 subjects out of 77; relaxation, 5 subjects out of 57; fatigue, 10 subjects out of 57; sleep, 7 out of 72. The effects mentioned were recorded as definite but without the subject's or observer's knowledge that only a placebo had been administered. ⁽⁴⁾

On an interesting study made in 1954 of placebos and their associated toxic reactions, they found, in studying a supposedly effective drug and a placebo (lactose) in patients with anxiety and tension as prominent complaints, that these symptoms were made better in about 30% of 31 patients, but 3 of the 31 patients had major reactions to the placebo: one promptly had overwhelming weakness, palpitation, and nausea both after taking the placebo and also after the tested drug. A diffuse rash developed in a second patient after the placebo. It was diagnosed by a skin consultant as dermatitis medicamentosa. The rash quickly cleared after the placebo administration was stopped. In the third patient, within 10 minutes after taking the pills, epigastric pain followed by watery diarrhea, urticaria, and angioneurotic edema of the lips developed. These signs and symptoms occurred twice, after taking the placebo and after taking the drug. The powerful placebo effects are objective evidence that the placebo might produce gross physical changes. ⁽¹²⁾

The mechanism of the placebo effect is still not very much known, but there is some experimental evidence that the placebo response in experimental pain is associated with conditioning, other work points to the response expectancy model as more plausible. There is some evidence that endogenous opioids are implicated in placebo analgesia. In other disease models, a psychoneuroimmunological response has been suggested.

Two theories were also suggested of this matter; the first theory is that inert substances, procedures, people or treatment setting can all act as a conditioned stimulus for the alleviation of symptoms, if they have been repeatedly associated with powerful unconditioned stimuli. This theory focuses on the input; the placebo effect arises because it's stimulus-expected. The second theory, response expectancy, is the anticipation of one's own automatic reactions to various situations. Response expectancy is different from stimulus expectancy in that it focuses on the output rather than the input. However, neither theory offers physiological mechanism. ⁽¹³⁾

Conclusion:

The placebo is something that is given to patients mostly during clinical trials of drugs to know the real effects of the drug, and whether those effects were produced by the actual drug or was it psychological. The use of placebos produced very high beneficial effects in many diseases and clinical trials; it showed that most patients actually felt better after taking the placebo. Though placebos don't only have therapeutic effects, but also many negative and toxic effects like nausea, diarrhea, headache and other effects. The mechanism of its action is still not very much known but there are two theories; one that suggests that the mechanism is related to the inert substances and was stimulus-expected. The second theory depended on the response expectancy.

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