

Studies on the Mechanism and Impacts of Placebo Effect: Illness and Interpersonal Healing

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Abstract:- A placebo effect, also known as a nonspecific effect, is a psychological or psychophysiological improvement achieved through the administration of an inert substance or through a simulated procedure. Positive thinking about the effectiveness of a treatment is not the only component of the placebo effect. The goal is to create a strong connection between the mind and the body in order for them to function effectively. There is empirical proof that the mind and body are reciprocally influenced by each other through the placebo effect.

In this research paper, authors understand how the placebo is a factor of self-healing and the impact it has on the mind of the receiver. The studies revealed that how placebo is the pivot on which the whole treatment bases. In the second half of the research, a relationship between drug effect and placebo has also been discovered which helps to prove the increase in demand of placebos. It has been found that drug effect and placebos go hand in hand. While placebos mentally cure a person, drugs help physically. The results suggest that contextual factors such as expectations and altered perception can treat inflammatory diseases and Parkinson's disease. This research aimed at analyzing the mechanism and impacts of placebo effect on human mind.

Keywords:- Placebo Effect, Psychophysiological, Psychological, Self-Healing, Expectations, Drug Effect.

I. INTRODUCTION

An inert substance can produce the placebo effect if it is administered in a situation that encourages positive expectations of its effects, thereby improving the symptoms of the patient [15]. A modern concept of the placebo effect dates back to 1955, when US physician Henry Beecher analyzed 15 studies and concluded that one-third of patients responded to a placebo regardless of their complaints [4]. For placebos to work, there must be some form of deception or concealment. This effect, validating the existence of innate self-healing mechanisms in the body, is the result of the interaction between mind and body with their psychosocial environment [6]. Dr. Levine's study was the first to suggest that patients aren't just pretending they're experiencing pain relief when receiving placebos. A person's ability to feel pain is mediated by endogenous opioids, such as endorphins, released by the brain [20]. Biological changes can, of course, not be caused by inert substances. Levine *et al.* claim that the active component of a placebo is the person's psychological response to treatment [20]. Tor Wager, a neuroscientist at the University

of Colorado Boulder, is of the same opinion. He was one of the first to demonstrate that placebos reduced brain activity in relevant areas when individuals were exposed to pain through functional magnetic resonance imaging (fMRI). It appears, however, that fMRI scans taken before pain reveal something different: the prefrontal cortex and ventral striatum, two brain areas involving emotion and valuation, are more active after receiving a placebo. Wager *et al.* concluded that the placebo has the power to cause a re-evaluation of pain [32]. It is possible for learned responses to override conscious expectations in certain circumstances. Pavlov noticed that dogs salivated in response to a buzzer that was associated with food; the same mechanism is probably driving placebo responses previously assumed solely to be based on conscious expectations. Using a placebo cream, Wager *et al.* found that pain was reduced even in volunteers who knew it was a placebo after four pre-conditioning sessions. According to Schafer *et al.*, because your brain has already learned, what you think doesn't matter [29]. It is important to recognize that the recollection of previous treatments, character traits, and expectations of the patient will change in response to the doctor's interaction, and that a patient's characteristics and expectations will influence the context of the encounter. A placebo effect is therefore caused by the therapeutic ritual itself [7]. Dr. Benedetti, observed that placebos can modulate the same biochemical pathways that are modulated by drugs. An experiment revealed that patients with Parkinson's disease who had been preconditioned with apomorphine would respond just as well to a placebo as to the active drug [8]. By alternating drug treatments and placebos, it has been suggested that tolerance development might be delayed [8]. To be able to harness the effectiveness and power of the placebo effect, it is critical to understand that "placebo effect" is the framework upon which the result of the treatment can be placed [13]. Based on analysis of previous studies the aim of this research is to analyze the mechanism behind the placebo effect, i.e., placebo as a factor of self-healing and co-relating it with the impact it has on the mind of the receiver. This research will also be focusing on how placebo is the pivot on which the whole treatment bases and certain plausible reasons for its recent growth in the medical field.

II. RESULTS AND DISCUSSIONS

A. Mechanism behind the placebo effect and the impact it has on the mind

According to Rossettini *et al.* [25], the placebo effect is a consequence of changes in behavior, neurophysiology and cognition prompted by a remedial encounter. In the neurophysiological network there are several distinct systems including endogenous opioid, endocannabinoid, and dopaminergic channels, as well as brain regions such as the dorsolateral prefrontal cortex, the rostral anterior cingulate cortex, the periaqueductal gray, and the dorsal horn of the spine. In a report by the psychologist Bruno Klopfer, a patient's beliefs and expectations can greatly affect and impact the course of an illness is illustrated. In addition to treating illnesses that display a psychological component, such as anxiety, anxiety-related pain, and depression, placebos can also treat inflammatory diseases and Parkinson's disease [19].

Here are a few ways how placebo impacts our mind thus initiates the self-healing mechanism:

- **Expectations:** These refer to a person's anticipation of the future events. Expectation is the most important factor behind the working of a placebo. They are a powerful modulator of the patients cognitive, physical and emotional experiences [23]. Expectations are constantly shaped and modified on the basis of inputs coming from the surrounding environment [10].
- **A change in behavior:** Placebos have the power to motivate a person to take better care of themselves. An improvement in the diet, regular exercise or even rest may be the actual cause behind the ease of a symptom.
- **Altered perception:** In many cases, the patient is not told that they are being given a placebo. The patient takes the placebo to be any normal medicine prescribed by their doctor with the expectation and hope of feeling better. Thus, leading to a change in the person's interpretation of their symptoms. For instance, after having taken a placebo, a sharp pain may be perceived as uncomfortable tingling.
- **Reduced anxiety:** Stress chemicals such as adrenaline produced by the body maybe reduced after having taken the placebo and the expectation to feel better may also calm a person down thereby reducing the anxiety.
- **Altered brain state:** Researchers have found that the brain responds to imagined scenes much the same way it does to actual visuals. In theory, a placebo may cause the brain to recall a time before symptoms were present, causing the body to respond. A theory such as this is called the 'remembered wellness' theory.
- **The characteristics of the placebo pill:** Due to the appearance of the pill, the person taking it is more likely to think it contains an active ingredient. It is more likely that a person will heal faster if the pill looks real. Additionally, research indicates that larger pills suggest stronger doses than smaller pills. It has also been shown that taking two pills has a greater impact on a person's recovery rate compared to swallowing just one pill. When injections are used instead of pills, the placebo effect is stronger.
- **Doctor-patient relationship:** A patient is more likely to have faith in the power of the placebo based on his or her

relationship with their health care practitioner. If the patient trusts their doctor, then they are more likely to believe that the placebo will work.

- **The person's attitude:** It is more likely for the placebo effect to occur if the patient expects that the treatment will work. However, even if a person has a slight skepticism regarding the effectiveness of the placebo, it will still work. Clearly, the power of suggestion is the key here.

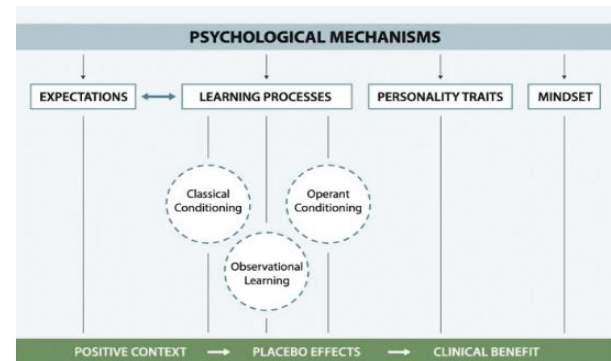


Fig. 1 Mechanism behind Placebo effect

In figure 1, It has been clearly seen how a number of psychological mechanisms underlie placebo, nocebo, and context-related effects. The cognitive functions involved in this are anticipation, memory processes like classical conditioning and observational learning, reinforced expectations, mindsets, and personality traits. In the past, multiple scientists have studied the placebo effect in patients with Parkinson's disease and its physiological mechanisms. The patients were told that they were being given an anti-parkinsonian drug that will enhance their motor skills but, it was nothing more than a sugar pill (a placebo). This study demonstrated that placebos not only minimize the symptoms of Parkinson's disease, but also help the patient produce more dopamine, which the disease destroys, thus helping the patient recover. These effects were visible within minutes showing that expectations generate neural changes almost instantaneously [34]. One of the underlying components of this effect is classical conditioning, a type of implicit learning. For example, being escorted to an examination room, getting one's heart rate, body temperature, blood pressure and so on while waiting for the doctor are contextual clues linked with healing. There appears to be a progressive association between these and effective medical therapies, and this, ultimately, may cause conditioned responses in patients [1]. Behavioral, cognitive and emotional modifications can be elicited while expecting a certain result. These in turn elevate the probability of a certain outcome [24]. In another study, a doctor obscured a drug treatment from a patient and the external factors that contribute to the expectation were removed. The result was that this hidden medical treatment was not as effective as compared to those administered overtly by clearly emphasizing the role of expectations in the treatment. The concept behind this is that when a patient is unaware of the treatment he or she is receiving and do not expect any benefits from the same, there is almost no effect in the treatment [11, 12]. A patients' experiences because of their illness and treatment change pre-existing mindsets. A patient who considers his or her body to have the capability to recover will

be able to better notice the signs of their body coping well with an illness. They perhaps have anticipated that their body can handle this illness and the side effects it brings along due to the treatment [35].

Positive thinking about the effectiveness of a treatment is not the only component of the placebo effect. The goal is to create a strong connection between the mind and the body in order for them to function effectively [17]. Surely, placebo will not cure the disease, they will not shrink a tumor or fix a valve in the heart. Instead, they will work on those symptoms that are controlled and generated by the brain such as pain. They are very effective when it comes to pain-management, insomnia and such conditions that associated with the brain and its psychology. A recent study published by PLOS Biology investigates what is going on in the brain when people receive a placebo. As a part of this study researchers used functional magnetic resonance imaging to scan brains of individuals with chronic knee osteoarthritis pain. Following the scans, people were given a placebo and another scan was performed. A third of the frontal lobe in the brain comprises the middle frontal gyrus, where those who felt pain relief experienced more activity.

Researchers have revealed the impact of expectations on the effectiveness of a placebo. In addition to this, the context of health care plays an important role, since it is an enhanced relational space that consists of a number of elements that are defined as contextual factors [2, 18, 21, 3, 14, 30, 26]. Together, these increase the effectiveness of a placebo and the impact it has on the mind of the receiver. These factors include the practitioners' professionalism, mindset and appearance; the patient's beliefs, experience about the ailment and expectation from the therapy as discussed above; the kind of language used during the sessions and lastly, the overall impression of the clinic [16]. Although these factors are not directly associated with the placebo, the impact they create on the person and his or her mind, have a huge contribution to the working of the placebo. As discussed above, if the patient trusts their doctor, thinks positively about the situation, and feel comfortable in the place they are in, i.e., the hospital, they are more likely to heal faster as they are more likely to have confidence on the usefulness of the placebo provided by their doctor [16, 22, 28, 9, 27]. For example, a patient is provided with a medicine and the medical practitioner says that "This medication will ameliorate your symptoms", this verbal statement along with the medicine provided will lessen the pain and enhance the physical and mental strength of the patient. Parallely, if the doctor says, "This medication sometimes might reduce your symptoms", i.e., the doctor is uncertain himself, then this could even worsen the symptoms and the confidence of the patient. Thus, we established a link between the power of social entities on the mindset of a patient.

B. Placebo is the scaffolding upon which the entire treatment is based and thus it is growing stronger by the day

A placebo is a pill, injection or something that makes the patient believe that it is a medical treatment but in reality, isn't. For instance, a sugar pill. The placebo effect on the other hand is when an improvement in symptoms is observed despite

using this fake, nonactive treatment. As we discovered and discussed above, it is most likely to occur due psychological factors such as classical or implicit conditioning and expectations. Placebos, make the affected individual feel better. Drugs on the other hand, are certain molecules given to the body with the intention to produce a biological effect. It works by altering one or more biochemical pathways such as by binding to a receptor molecule or enzyme activity. Thus, drugs are responsible for curing a person while placebos are involved with the improvements that derive from the active processes in the brain [5]. Clearly, placebos are essential in any treatment as they can, without developing any kind of antibiotic resistance, help alleviate the symptoms of a person. As shown in figure 2, Drug effect and placebos thus go together. While placebos mentally cure a person, drugs help physically.

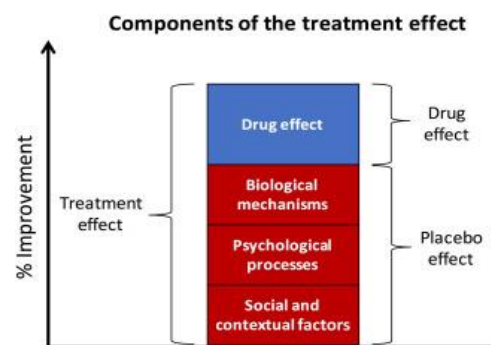


Fig. 2 – Components of the treatment effect

Levine et al., [33] reported that biochemical blocks can prevent the placebo reaction placing a strong link between placebos and the body's natural opiates (endorphins), which, as long as their release was not cut off organically, would provide us with relief. Through the study it was found from the responses that drugs remained steady over the years, whereas placebo responses have amplified considerably over the decades. This resulted in lower treatment advantage. This got multiple researchers to think as to why is it that placebos are posing a tough competition to active drugs? According to Silberman, patients seeking trials in the USA have been inundated with prescription drug advertisements since 1997. According to him, if one associates a medication's brand name with aspects of life that advance happiness and peace, this can cause a powerful placebo effect.

However, research suggested that it is not the drugs that are getting weaker, rather, we are finally realizing that most pain drugs don't really work [31]. Well, if pain drugs don't work then how is pain relieved? In simple words, it's the placebo effect. Since the patient is being given a medicine by their trusted doctor, they expect the pill will cure their symptoms and heal them. Thus, their pain is relieved. Modern medicine, for example, looks at diabetes as a "root cause" involving the body not producing enough insulin, so the patient is advised to take insulin supplements and epinephrine injections. In reality, it is the pancreas' failure to produce enough insulin that causes diabetes, which is the catalyst for its inefficiency. This may explain why most drugs essentially act as placebos. The patient is often the only person who truly understands or perceives the cause of their illness or prescribes

the correct treatment. As a result, it can be clinched that the placebo effect, namely the expectations and subconscious cues, make the overall treatment effect more personal and effective for each patient. Research showed that when pharmaceutical industries tried to outperform placebo by using psychiatric drugs, they faced a lot of difficulty [35]. Drugs proved to be inefficient when it came to curing mental illness due to their inability to accurately define what the illness is about. In parallel, the placebo response can be boosted due to this inconsistency in diagnosis as clearly, the drugs' role is ambiguous making it harder for drug companies to manufacture effective treatments. Mental disorders, on the other hand, engage higher cortical centers of the brain that generate the contextual factors required for effective working of the placebo. In a similar manner, chronic pain, Parkinson's disease and other illnesses also respond to placebo. Any medicine that brings out the desired result in the symptoms of the patient only when the patient is subconsciously aware that they have been given a drug are placebos themselves. As a result, the placebo effect is proving to be effective and is likely to grow stronger in the future.

ACKNOWLEDGMENT

I would like to thank our Principal, Mrs. Nargish Khambatta, Principal, Gems Modern Academy, Mr. John Gomes, Vice Principal, GMA, and the entire senior leadership team for their support throughout this review. I would like to specially thank Dr. Vimaldeep Kaur for her continued guidance. Without their support, it would have been impossible for me to have curated this research paper.

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