



The Neuroscience behind the Mechanism of Placebos: Placebo Effect

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Author's contribution

The sole author designed, analyzed, interpreted and prepared the manuscript.

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ABSTRACT

The science behind any kind of medical treatment is oriented around the effects of the psychology of humans with the corresponding therapeutic mechanism of the treatment. The human mind and its psychology is always an interesting and complex matter of discussion for researchers. The human mind is so powerful that it is even capable of healing the mental and physical health of the human body. To study this psychological concept of a healing mechanism, the Placebos effect is studied. This paper discusses the placebo effect and the physiology neuroscience involved in the whole concept of the Placebos and its mechanism. Because the placebos and its mechanism are so powerful that it is capable of even manipulating the human mind and the body as well the study discussed all the facts in an evidential manner.

Keywords: Depression; physiology; placebos; placebo effect; neuroscience; neurobiological mechanism.

1. INTRODUCTION

In Medical science, the human mind and its association with the mechanisms of the human body lead to the study of psychology between both the human parts. To study the psychosocial

context of the human mind to a treatment they first have to conduct a study in which the observer will monitor how the human body would react to the need for a specific therapy simultaneous to the real treatment but some changes and eliminations of some specific action

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would make what difference in the results of the therapy. To carry out this mechanism Placebos are used in the treatment of illness. The process includes the placebos, which can be drugs, tablets, therapy, or any other treatment mechanism. The person on which this method is practiced believes in its effectiveness and so expects a similar clinical improvement in the symptoms. But the fact is no medication is given in real, the medicines or therapy are fake in real. Then how is this possible that the placebos are believed to give positive effects on the human body [1].

1.1 What Are Placebos?

A placebo is a simulation of any type of therapeutic treatment, which can be medication pills, therapy, or vaccine though these do not consist of any kind of active substance or drug that can change the biochemistry of the human body. Placebo is evidently effective in the treatment of some problems like sleep disorder, depression, menopause anxiety and pain. The placebos are received by a person and based on the expectations in the mind of humans a response is expected [2]. Like if a person takes medicine he will expect pain relief sometimes. Now the effect of placebos completely depends on the attitude of the person as a positive attitude and positive expectations will lead to positive response and symptoms will start improving but if a person is not confident about the medication he is taking expected positive response, this is the psychology of the mind a pictorial representation of this effect is illustrated in Fig. 1.

1.2 The Placebo Effect

The response of the placebo, basically it is the outcome of the false medication or therapy, placebos applied on the patient. Hence it becomes important to highlight the fact that the placebo effect is a concept of physiology and neurological science. Therefore the placebo effect is known as a psychobiological phenomenon. Which can be ascribable in the form of different mechanisms. Depending on the condition and illness of the person different mechanisms are opted based on the different conditions from which the person is suffering with, because there are many types of placebo effect existing in the studies so it needs the proper knowledge before opting it [4].

The presence and outcomes of the placebo effect demonstrate the fact of how powerful the human mind is. To benefit from this phenomenon

a broadened conception is required in medical science. Which helps demolish the limits of internal human capabilities? Scientists are interested in placebo responses because the effects of belief on human experience and behavior provide an entry point for studying internal control of affective, sensory, and peripheral processes. In the last few decades, the placebo effect was underestimated in the sense of utilization of it in clinical treatments of the diseases. Though it is used for the medical inventions trials to check their competence and based on the experimental outcomes of the trials the invention is improved to achieve the highest stage i.e. better than achieved in the placebo effect response. In recent times the people start taking interest in the placebo effects maybe because it gives promising outcomes and also increases self-control in the respective person [5,6].

2. RESEARCH QUESTION

1. Placebos are fake medications and therapy then why it is believed that it gives a positive response in the effect of the false medication and treatment. What makes it even possible?
2. What is the neuroscience involved with the placebos and its famous therapeutic placebo effect on the human body? What neurobiological mechanisms are involved in this treatment?

3. LITERATURE REVIEW

Most of the research papers written about the placebo effect underlining the neurobiological mechanism are only limited to the fields of analgesia and pain. There is very few research paper available which discusses the neurology and physiology of the placebos one of them is "Neurobiological Mechanisms of the Placebo Effect". Written by Mr. Fabrizio Benedetti, Helen S. Mayberg, Jon-Kar, Christian S. Stohler, and Tor D. Wager. The paper demonstrates the neurological mechanism involved with the placebo effect. Including the discussion of the pharmacological approach and the mechanisms. A thorough study of the placebo effect has been discussed and also the immediate clinical effects and the ethical aspect in the implication of the placebo effect [1].

Another paper entitled "The Placebo Effect: How the Subconscious Fits in" was written by Mommaerts, J.L., & Devroey. This paper gives the perspective of placebo effect in the context of

the Biology of Mind and Medical science. Paper argues about the communication of the human body with the subconscious. The paper highlighted the fact that the implication of the placebo effect can be seen effectively without even utilizing the placebo itself just by involving the autosuggestion. Discusses the benefits and side effects related to the placebo effect and its implementation [2]. Referring to these papers this proposed paper has analyzed the placebo effect and has discussed the physiological and neurological aspects of placebo effect.

4. METHODOLOGY

4.1 Design

4.1.1 The placebo effect: A pharmacological approach

The neurobiology of the placebo effect was first implicated in 1978, when it was shown that the placebo effect can be blocked by the opioid antagonist naloxone, which indicates an involvement of endogenous opioids, a type of medicine used for the actions like analgesia relieving the pain by blocking the receptors present in the membrane of the on neuronal cells membranes. By using this approach of pharmacology with the naloxone drugs. For instance, a placebo is capable of reducing the pain by using both the mechanism of indulging the opioid and non-opioid medication. This action can be understood more clearly by referring to the image present in Fig. 1. Considering the first case in which the placebo painkiller points are corporate to be blocked by the use of the opioid antagonist naloxone drug, while it is not very typical in the second case, the placebo analgesic response is induced depending upon the procedure that is being applied [1].

According to the same study, if the placebo effect output response is received only after it is exposed with the opioid medicines, it means it is naloxone drug reversible, But if the response is received only after the exposing the person to the non-opioid medicines then it means it insensitive towards the naloxone drugs. This Information demonstrates that the mechanisms of the opioid and the non-opioid drugs bring out different kinds of action in different kinds of circumstances demonstrated in Fig. 2. A person with placebo activated by using some drug his endogenous opioid systems has a somatotropin organization shown in the experiment because the local naloxone is reversible at the respective place [1].

The pharmacological aspect about the placebo treatment is that it saves the expense of medications, and hence huge cost savings can be incorporated, no serious deception of the patients, a great aspect is the burden of the physicians also got distributed, and a great healing effect in illness domains like depression and distress where usual medication treatment or different therapies may create problematic situations. *How placebo affects the other self-regulatory mechanisms in the:* It is a huge aspect, specifically for the body parts covered by the treatment of placebo, the targeted body part under the placebo effect could be the general circuitry system influenced by the placebos and its affective responses [1]. Some recent studies show that placebo affects the regulation mechanism of the emotions, and the activation occurred by the real opiate drugs. These body regions include the VLPFC, DLPFC and possibly a third cluster part of the rostral PFC [7].

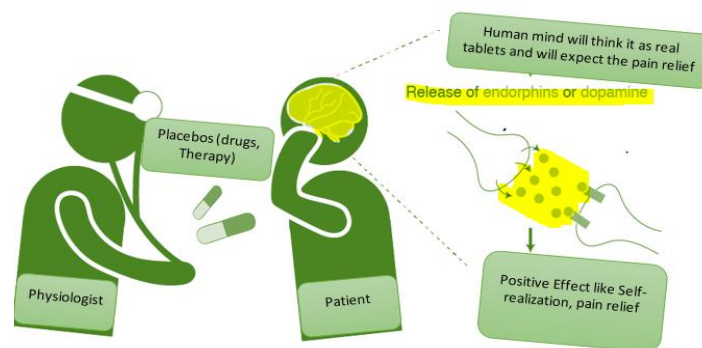


Fig. 1. Illustrating the basic concept of the placebos and placebo effect on the human body. Showing how the human mind convinces the body that even though the medication is fake it will work on the body and will surely give positive effects like pain relief [3]

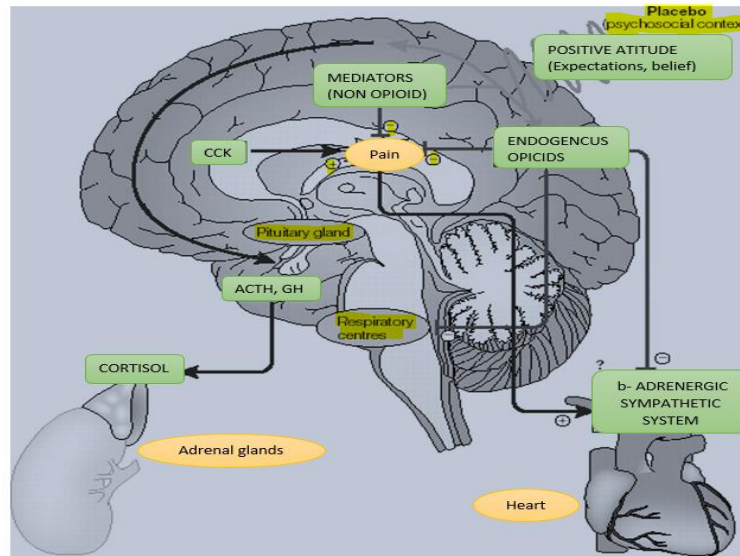


Fig. 2. Demonstrating the effects of the placebos and representing its capability of reducing the pain by using both the mechanism of indulging the opioid and non-opioid medication [1]

4.1.2 Sample

The placebo effect is majorly used to improve the quality expectations of the novel clinical or medical improvement and its utilization conditioning. Clinical practice basically carried out to enhance and reinforce the proportional effects of related expectation in the mind of the person and the conditioning involved in the whole process but this whole mechanism is supposed to be carried out in the arrangements of an already known and tested effective therapeutic method. These conducted research trials are purposely focused with the aim of detecting the important implications received in the medical placebo effects. These can be explicitly attributed to the treatments which are active and are under investigation which eventually leads to the reduction of these corresponding phenomena. Placebo inspired and monitored clinical trial study likely provides a unique chance to analyze the synergist based mechanisms for the depression problem [8]. It includes the study which is specific to the active type treatment and also those which are involved under the conditions and the expectations that are placebo effect.

4.1.3 Data analysis

4.1.3.1 Mechanisms of the placebo effect

Many mechanisms are available to describe and to carry out the placebo effect mechanism Fig. 3.

There are many hypothetical mechanisms available including the conviction, relationship with the prescriber, oneness of body, diversion of attention, symbolic power, optimism and demoralization, magic and many other such as mind, relief of guilt, sense of control, transference, anxiety control, method of fitting in the story, self-hypnosis, emotional appeal theories etc. The neurobiological mechanisms for the positive placebo effect to treat the depression problem have been studied during the randomly conducted controlled clinical trial and examined using quantitative electroencephalography to evaluate the changes that occurred in brain nerve cells and other processes in the effect of the placebo especially in case of severe depressions. For this purpose, two different kinds of antidepressant medicines are being considered. The placebo receptor responders particularly reflect an increased measure in the prefrontal accordance, it is a quantitative electroencephalography measuring tool used for measuring the activities of the regional brain, the sudden effect that starts early during the start of the treatments and was not noticeable in the other medicated or even placebo non-responder category [1,9].

The neural action responses by the placebo effect in the clinical trials of the antidepressants for the case of major depression is another useful model to examine the neurobiological mechanisms affected in the placebo effect because the positive placebo responses are

usual in the antidepressant trials of the many novel interventions, including the medications, the psychotherapy treatment, and other types of somatic treatments. Considering the result of the analyzed functional mechanisms of the brain which are correlated with the placebos and other types of antidepressant therapeutic treatment. This trial of hospitalized people suffering from the unipolar depression condition was treated by utilizing the fluoxetine and by measured alterations in the regions of the brain by glucose metabolism which was determined with the help of PET [10]. On the completion of almost six weeks of the whole therapy, the response of both placebos and fluoxetine drug responders evaluated, the result showed an increase in metabolic activity in the premotor, posterior cingulate, anterior cingulate, and the insular regions of the body and along with a metabolic decrease is also noticed in the regions like thalamus, subgenera cingulate, and the Para hippocampus.

A person suffering from depression is usually inclined towards the initiative to develop a positive group of associations; it could be more or less through some conditions towards a result or to realize the benefit through his or her clinical experience or the procedure faced during the treatment of the psychiatric disease. Though the relevant roles of the individual expectations and the disciplinary are not determined during the depression period, pointing to the depressed patients with the different strategies that evoke the placebos responses in the other neurological conditioning scenarios may lead to an improvement in the outcomes. These planned strategies must include the aspect of maximizing both positive integrated associations through the disciplinarians as well as by the increased

expectations of the huge rewards from the therapy procedure. It is a matter to understand the effects of the cognitive and behavioral procedure of the therapy involved in the depression treatment are not as same as the behaviors reported with the use of placebos antidepressant medications [9,11].

5. RESULTS AND DISCUSSION

The study and analysis of the placebo effect is the study that analyzes the context of the expectations, beliefs and values that shape the human brain. Processes that are related to the perceptions and the emotions of the individual. Ultimately, the study incorporates the brain mechanisms corresponding to mental and physical health. Placebo effect represents a reflection of the current thinking neuroscientific thoughts that has a subjective context of emotions like expectations and hope. The study includes the core discussion of the immediate clinical treatment aspects and the ethical significance of the placebo effect. Also discusses the use of inactive medication, i.e. placebo and its conditions in the medical trials of the new inventions and medical mechanism development. Thus, placebo treatment method effects reflect the human mind aspects of the strength which incorporate the positivity an individual holds or the vulnerability of the human mind which reflects the negativity present in the mind. It's important for the expression and the maintenance of the various states of pathology and their relevant treatment interventions. Overall, the placebo effect appears to be a very good model to understand how a complex mental activity, such as expectancy, interacts with different neuronal systems.

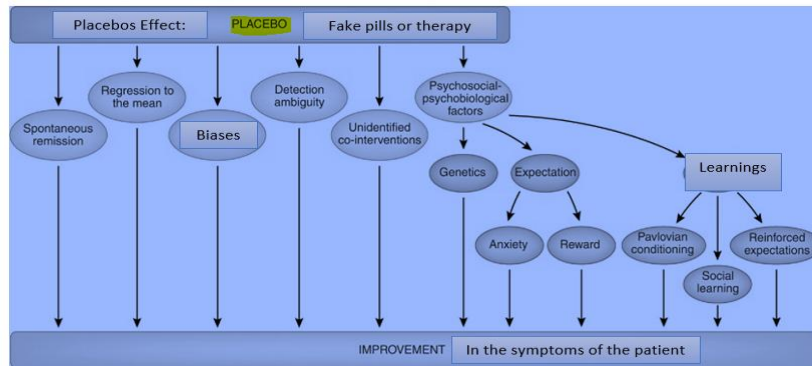


Fig. 3. Picture shows a flowchart representing the processor of mechanism involved in the placebos effect. How the process proceeds from taking the placebos medication till the final placebo effect outcome as a response of placebos [11]

The placebo effect is also proved to be an important strategy to treat patients with depression and distress issues. The neurological mechanisms have shown how it affects the brain and nervous system together control the body functionalities and the other mechanisms. An important fact is that the emotional processes which are involved while the otherwise mechanism of an inactive agent i.e. a placebo, are capable enough of initiation on the internal biological and chemical mechanisms that can modify the physiology of the human system. The regions involved in the whole network of effects include the dorsolateral prefrontal and orbitofrontal cortices, nucleus acumens, and insula, rostral anterior cingulate, and amygdala, periaqueductal gray and medial thalamus. The neurotransmissions of the opioid and dopamine in these regions regulate various aspects of the placebo effect, which looks into the changes occurring in the affective state and pain rating. The neurotransmission gets minimized in the syndromes associated with chronic pain. The relevance between these altered changes in regions and the capacity of placebos to generate the placebo effects in these conditions and other types of clinical trials still remains to be studied and explored.

6. CONCLUSION

The study aims to analyze the psychology and neurological aspects. At the psychological level, there is so much to examine and for decentralization of the psychological mechanisms which are responsible for executing these activities that drive these common activations and influence the placebo effects. Most observations demonstrated show the effects of placebos in controlling the pain symptoms, sleep disorder and depression, but there is evident proof that it has the capability and exists in the treatment of other kinds of psychiatric and neurological conditions. This paper discussed the famous neurobiological mechanisms which result in the success of the placebo effect. AN effort is also made towards the great discussion and use of the clinical trials that were carried out to compare the actions of pharmacological drug agents, it was observed and evaluated that these effects depend substantially purely on the individual emotional and attitude conditions characteristics of the respective patient taking the placebos treatment. More importantly, it shows that the associated expectations with the clinical medication benefit can be stimulated from a placebo response.

In the paper some important mechanisms that are usually carried out in the influence of placebos and do contribute to an effective placebo effect. Which have been generated because of the utilization of functional and molecular neuro imaging. An experiment of the placebo effect in the treatment of pain gives the result according to which the pain is dependent on the activation of the endogenous opioid region and the dopamine systems. According to a hypothesis mentioned in the paper, the placebo effects are driven by the executive attention: appraisals of safety may lead to increased use of self-distraction strategies. However, evidence from the neural and psycho Regions of the frontal lobes showing increased activity in recent studies of self-regulation. The neurobiological mechanisms related to the Placebos and Placebo Effect at logical levels are collected and integrated together to know the depth of these effects and for a better understanding of the emotional, physical health and self-regulatory aspect of the human body.

COMPETING INTERESTS

Author has declared that no competing interests exist.

REFERENCES

1. Benedetti F, Mayberg HS, Wager TD, Stohler CS, Zubieta JK. Neurobiological mechanisms of the placebo effect. In *Journal of Neuroscience*; 2005.
2. Mommaerts JL, Devroey D. "The placebo effect: How the subconscious fits in". *Perspect. Biol. Med*; 2012.
3. Sitn. Hms. Harvard. Edu. "More than just-sugar-pill-placebo-effect-real/."
4. knappily.com. "lifestyle/placebo-effect-when-the-mind-heals-the-body."
5. Papakostas YG, Daras MD. "Placebos, placebo effect, and the response to the healing situation: The evolution of a concept". *Epilepsia*; 2001.
6. Zubieta JK, Stohler CS. "Neurobiological mechanisms of placebo responses". *Ann. N. Y. Acad. Sci*; 2009.
7. Colloca L, Klinger R, Flor H, Bingel U. "Placebo analgesia: Psychological and neurobiological mechanisms". *Pain*; 2013.
8. Price DD, Finniss DG Benedetti, F. "A comprehensive review of the placebo effect: Recent advances and current

- thought". Annual Review of Psychology; 2008.
9. Murray D, Stoessl AJ. Mechanisms and therapeutic implications of the placebo effect in neurological and psychiatric conditions. Pharmacology and Therapeutics; 2013.
 10. HS Mayberg et al. The functional neuroanatomy of the placebo effect. Am. J. Psychiatry; 2002.
 11. Benedetti F, Carlino E, Pollo A. How placebos change the patient's brain. Neuropsychopharmacology; 2011.

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