Placebo Effect

How and Why the Placebo Effect is so Effective

How it can be applied in Practice

Literature Review
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Abstract

Objective: The purpose of this literature review is to educate the reader on the Placebo Effect and what research has shown us thus far by studying subjects that it has been applied to. The Placebo effect will be unveiled as a highly effective mechanism that every type of doctor should seek to use; this paper will also discuss ways that any doctor may apply the use of Placebo Effect.

Data Source: The referenced articles were found at Logan College of Chiropractic and Washington University School of Medicine libraries. Pubmed was the search engine used to find articles. The names typed into the Title Search were: "Placebo Effect", "Psychosomatic Pain" and "Treatment with Placebo".

Results: One thousand eight hundred ninety six articles were revealed and twenty-four of the articles deemed relevant to this subject matter and were available for use.

Conclusion: Placebo effect has unveiled as a highly effective mechanism. It can be broken into two different categories: 1) Using it as an adjunct to treatment protocols that are currently being used, 2) Using the placebo effect as its own entity in the treatment of disease. More research must be implemented due to fact that placebo effect can make physiologic changes that cannot be explained at this time.

Introduction

The Latin meaning of the word "Placebo" is I shall please. This is what Doctors do when they deliver there form of treatment to their patients they are pleasing them. The doctors' suggestibility alone can play a major role in the treatment of a patient. A common belief is that when someone finds out that they were treated with placebo it is believed that their sickness was just in their head. Research shows that it is the belief and hope that are the treating factor. Doctors in one study successfully eliminated warts by painting them with a brightly colored, inert dye and promising patients the warts would be gone when the color wore off. In a study of asthmatics, researchers found that they could produce dilation of the airways by simply telling people they were inhaling a bronchiodilator, even when they weren't. Patients suffering pain after wisdom-tooth extraction got just as much relief from a fake application of ultrasound as from a real one, so long as both patient and therapist thought the machine was on. Fifty-two percent of the colitis patients treated with placebo in 11 different trials reported feeling better -- and 50 percent of the inflamed intestines actually looked better when assessed with a sigmoidoscope.(1) When someone is treated with placebo it is assumed that they are dealing with the patient in a psychological way, but this is not the case, it is a physical matter in which they are being treated. The Placebo Effect may be determined by what a

person is told to believe which will ultimately effect their attitude, the change in attitude can be what is actually treating the patient by altering ones body chemistry. The Placebo Effect is a very controversial topic; its existence attacks the philosophy of our health care system today. Through research, its capabilities can be discovered and applied to help patients in our health care system.

Placebo correlates with what good happens to patients when a placebo goes bad it is considered a Nocebo. Headaches were reported by 70% of students told that a (nonexistent) electric current was passing through their heads.(2) Very little research has focused on negative nonspecific influences of health care; this too is a subject that should be more sought after.

The Food and Drug Administration recognize the Placebo Effect, any new drug that is cleared for use must have more physiologic effects than that of the placebo. All physicians should not only be educated on the placebo but should be taught to embrace it and utilize its effectiveness when treating their patients.

Discussion

The Placebo Effect has been around for a very long time. Ancient Chinese cultures to the forefathers of our nation were not only aware of the placebo but actually used it in treatment methods. For example, in 1807, Thomas Jefferson (1743-1826) penned a description of what he called the "pious fraud" and noted that, "one of the most successful physicians I have ever known has assured me that he used more bread pills, drops of coloured water, and powders of hickory ashes, than of all other medicines put together."(3) The placebo went through a dramatic metamorphosis in the years after World War II as the double-blinded randomized controlled trial (RCT) developed. Until 1945 the placebo was a "morally" useful but innocuous management tool without curative or symptomatic consequences. By the time the double-blind randomized controlled trial took form and began to establish itself, around 1955, the placebo was imbued with powerful therapeutic effects and its ethical clinical use was more generally being questioned. In 10 years, the placebo changed from what was called the "humble humbug" to an entity with occult-like powers that could mimic potent drugs. It may be that efforts to bring the precision of science into the evaluation of efficacy with the RCT has its own form of confusion and darkness. (3)

A 1954 *Lancet* article, entitled "The Humble Humbug", depicted the swan song on this old fashioned understanding of the placebo; "a means of reinforcing a patient's confidence in his recovery, when the diagnosis is undoubted and no more effective treatment is possible; that for some unintelligent or inadequate patients life is made easier by a bottle of medicine to comfort their ego; that to refuse a placebo to a dying incurable patient may be simply cruel; and that to decline to humor an elderly 'chronic' brought up on the bottle is hardly within the bounds of possibility". (3) There was an understood ethics throughout society 50 years ago, but today there is no right and there is no wrong. Science has played a wonderful role in treatment protocols that has saved many lives, but it has also set a standard where a placebo would not be valid.

Patrick D. Wall describes his experience with placebo: I will describe here only two examples of the effect. They are unusually provocative. Surgery is not usually subject to placebo test even though "Surgery has the most potent placebo effect that can be exercised in medicine" (Finneson 1969). However, in 1959 Cobb et al. carried out a double-blind trial with sham operations on 19 patients with angina treated with ligation of the internal mammary artery. There was no difference between the two age groups, most of whom showed a marked improvement of their angina and exercise tolerance and some of whom improved the shape of their electrocardiograms. The interest here is not only the evident power of the belief that surgery had been carried out but the fact that improvement was sustained over at least a 6-month period in spite of the general belief that placebos have only a brief and fading action. The second example I wish to quote is the work of Hashish et al. (1988) who examined the effect of ultrasound on the pain and trismus and swelling which follow wisdom tooth extraction. Wishing to determine the

effective dose they found that the ultrasound machine was equally effective whether the machine was turned on or not, provided that the patient and therapist believed it was emitting sound. The interest and surprise of this paper is not that this elaborate placebo was highly effective in reducing pain but that it was also extremely active in reducing swelling. One of the most commonest techniques for ignoring placebo is ignoring pain itself as a mere mental delusion and yet we see here a strong placebo effect on swelling which is usually considered a local expression of tissue damage. (4) This study shows that placebo is not just a psychological processes but it is physical processes by which ones body chemistry is altered to effectively treat a problem. From a medical standpoint the Placebo Effect is what complimentary and alternative medicine practitioners use to treat their patients, such as chiropractors. "Although complementary and alternative medicine (CAM) might not agree, a common view among scientists is that CAM outcomes are mediated through a placebo effect; that is, patients improve because they expect to do so. Our aims in the study described here were to assess the validity of the Attitudes toward Alternative Medicine Scale (AAMS) and to determine whether asthmatic patients who had positive attitudes toward and beliefs about CAM showed greater positive changes in outcomes."(5) This study showed "AAMS scores did not correlate with significant changes in outcomes. The analyses of variance comparing outcomes among patients who believed that they were receiving active treatment and among those who believed that they were receiving a placebo were not significant in regard to any of the outcomes. There was no significant interaction with treatment."(5) This is an article that contradicts the essence of Placebo Effect. It is a stab at

complimentary and alternative medicine by assuming that we simply use people's attitudes as a treatment protocol.

Arthroscopic knee surgery has been a controversial topic in recent studies. The surgery was administered to relieve pain from Osteoarthritis in veterans knee's ages 75 and under. "As suggested by Jackson and Ewing and Ewing, these patients do have improvement after the procedure, but we showed that the benefit of arthroscopy is not greater than the benefit of the placebo effect." (6) This study also touched on the thoughts that the patients receiving the treatment had. Many of the outcomes in patients who guessed that they had undergone the placebo procedure were worse than those who guessed they had undergone one of the arthroscopic procedures. (6) This statement can be looked at from two different perspectives, 1) one might say that placebo is ineffective if the subject believes that they are receiving it, 2) one might see that the mind can control the healing and restoration of post-operative patients.

Irving Kirsch a leader in the fight to utilize the placebo effect states, " If there are placebo effects in conventional medicine, there must also be placebo effects in complementary medicine. Whatever else the herbs, needles and manipulations are doing, they are producing expectations of improvement and expectancy is the foundation of the placebo effect." (7) [7] The effectiveness of a placebo pain reliever varies as a function of its believed effectiveness. (7) [7] The following is an example of effective the placebo effect can be. The most impressive of these reports involves the suggestion-related production and inhibition of contact dermatitis. Contact dermatitis is a skin condition produced by chemical substances to which people have become sensitized. In the study by Ikemi & Nakagawa, 13 students were touched on one arm with leaves from a harmless

tree but were leaves from a lacquer or wax tree (Japanese trees that produce effects similar to poison ivy and to which the boys had reported being hypersensitive). On the other arm, the subjects were touched with poisonous leaves which they were led to believe were from a harmless tree. All 13 subjects displayed a skin reaction to the harmless leaves (the placebo) but only two reacted to the poisonous leaves. Five of the boys were hypnotized before being touched with the leaves but the results wee virtually identical for hypnotized and non-hypnotized subjects. (7) [7] This study alone warrants the demand for intense studies to be conducted concerning the placebo effect. An attempt to deliver the placebo effect has already been performed by the use of ionized bracelets. In testing the bracelets there was a study done where 610 people with similar pain were all told that the bracelets that they were receiving were all ionized and would help with their pain. The results were: "An ionized bracelet is no better than placebo, but many patients experience less pain with it." (8)

Infliximab has recently emerged as the newest form of treatment in patients with Crohn's disease or ulcerative colitis. This drug has been brought forward with inadequate placebo-controlled data and has resulted in reliance on anecdotal reports and very small open-label experiences. (10) This article is not about how good the placebo effect is it is about how researchers keep retesting this drug because the placebo effect is beating it every time. The results of patients in this study were based on standard clinical, endoscopic, and histological findings. At week six of the study 6 out of 20 of the patients receiving the placebo UC's went into remission. That means that there were complete physiologic changes seen on endoscopy and the histology report. Instead of looking at how powerful the placebo is, researchers use it as a dirty word that will keep

them from their paycheck. As a soon to be practioner in the health care field I see this as an outrage in the health care. Researchers keep trying to find their way around the placebo instead of going right through it.

The second part of this literature review is going to show how the placebo works and how the health care provider can deliver the Placebo Effect to his or her patients. In order to investigate external factors that may influence the magnitude of placebo analgesia as well as psychological factors that mediate placebo analgesia. (11) Thirteen irritable bowl syndrome (IBS) patients evoked rectal distension and cutaneous heat pain under the following conditions: natural history, rectal placebo, rectal nocebo, rectal lidocaine, and oral lidocaine. (11) Patients were given verbal suggestions for pain relief and rated expected pain levels and desire for pain relief for both evoked visceral and cutaneous pain, respectively. (11) Large reductions in pain intensity and pain unpleasantness ratings were found in the rectal placebo, rectal lidocaine and oral lidocaine as compared to the natural history condition, whereas no significant difference in pain reduction between the three treatment conditions was found. The Combination of expected pain levels and desire for pain relief may offer and alternative means of assessing the contribution of placebo factors during analgesia. (11)

Attitudes effects how one looks at a situation, this can play a major role in complementary and alternative medicine. When some believes that they are going to get better no matter what the treatment is, they have a higher probability in doing so. Peter J White suggests that, "This might suggest that some factor other than improvement in symptoms could be responsible for increasing a positive attitude toward complementary and alternative medicine or the fact that complementary and alternative medicine was the

subject of a scientific trial, (12) (he completed a clinical trial examining the use of acupuncture vs. placebo in patients with chronic neck pain). After his clinical trial he concluded with "The relationship between belief and treatment outcome, particularly in complementary and alternative medicine, is important and does require further thought and investigation." (12)

"Headache" the journal of head and face pain do a great job at explaining on a neurologic and cellular level the reason why placebo works. In reference (13) Seymour Solomon states, "The doctor patient interaction and the context of administration of therapy are important. Expectations of the administrator of the therapy and that of the recipient influence the placebo response. The time spent with the patient, the enthusiasm of the doctor, nurse, or research coordinator, and many other environmental factors play important roles. Conditioning by past experiences with analgesics or health professionals is another factor. Such factors as white coats, stethoscopes, and emergency room settings are potent stimuli that bear on responsiveness to therapy." (13) The type of placebo can also have a bearing on treatment outcomes; injection placebos are more potent than tablet ones. The bigger the pill the bigger the placebo effect, even intravenous placebo injections are considered more effective than intramuscular. Again, surgery is said to have "the most potent placebo effect that can be exercised in medicine." (13) Two examples are the fake arthroscopic knee surgery and treatment for angina ligation of the internal mammary artery versus sham surgery. These studies counter the common belief that placebo effect is not only of short duration but only deals with psychological components of the patient.

Researchers are now seeing that the placebo effect is a biochemical phenomenon. The reasoning is very complex and demands a good understanding of physiology from the reader. The first explanation for how the placebo effect works is psychological factors. Analgesia may be induced by emotional and cognitive factors. An injury to soldiers in battle unrecognized until the fight is over is the most common example. Cognitive coping strategies such as biofeedback utilize distraction and suggestion to alter pain perception. (13) This coincides with the saying "Fear of pain may be worse than pain itself", these interrelated cerebral factors, expectation evoking the placebo response, and psychological and cognitive factors appear to act by stimulating similar antinociceptive pathways. They generate descending signals that modulate nociceptive impulses. The supraspinal impulses begin in the limbic forebrain and are relayed in the periaqueductal gray matter to the primary afferent nociceptive site in the spinal cord dorsal horn and the medullary nucleus caudalis. (13) The other way that placebo works is by increasing afferent stimuli. To simplify this phenomenon it is the paradoxical relief of pain in one area by evoking pain in another area. This effect has been used for centuries. (13) The pain inhibitory effects of counter irritants and other stimuli appear to be due to depression of the transmission of nociceptive messages at the spinal level. (13) Biochemical changes effect nociceptive synapses and may dampen pain transmission. The most well know are endogenous opioids. In rats and humans, noxious stimuli to the feet evoke an increase in opioid like activity in the brain (of rats) and an increase in analgesia. These responses are reversed by naloxone. The release of endogenous opioids found in blood and cerebrospinal fluid may explain at least part of the pain suppression mechanism of ancient acupuncture and modern transcutaneous electrical nerve stimuli.

(13) This article has described how pain is dealt with in the human body. Unfortunately there is no research that can explain why patients have complete physical improvements under the care of placebo. One theory is that since the body is eliminating the pain that it allows the body to heal itself. This theory also believes that the natural remission of pain is falsely attributed to therapy. When the placebo effect is what is actually taken the patients pain away.

For the placebo effect to play a role in a patient's treatment there must be some favorable factors that must be present according to Phil Latey. He states, "Personal reputation contributes a lot to the favorable preconditions: Reputation, Expectations, Precise problems, Self-motivation, Hurdles, Self-payment and Timelines." (7) [9] If all of these characteristics are in place, the placebo effect will have its greatest effect on the patient. The opposite of these favorable preconditions is what can make the placebo non-effective. An unmotivated patient that expects everything to be done for them will rarely get better and will affect other patients by drawing energy and enthusiasm out of the practitioner. This is an underlying problem with government funded healthcare programs like Medicaid and Medicare. They enable people to be unable. Which in retrospect can affect the health of a nation.

Some practitioners might think that being aggressive and highly persuasive with patients and being in charge is what will bring maximum efficiency to a patient's office visit and treatment protocol. Latey disagrees, "I think that in fact we do best if we try to minimize our persuasiveness and take a great care not to exceed the limits that patients would normally feel comfortable with, both ethically and aesthetically. Even though we are inevitably in charge we must decrease patients' sense of vulnerability and diminish

any tendency to dominate. As body workers we should not overwhelm any aspect of them-no matter how much they may seem to want this." (7) [9] Suggestion is also an important aspect of delivering the placebo, it involves a specific attempt to override and alter perceptions that patients bring to their inner and outer milieu. (7) [9] This is where a practitioner will attempt to alter a patients' lifestyle to maximize the patients' health. One must also be carefully with suggestions that can have dire effects. Strong suggestion applied to suggestible people can have dramatic effects. (7) [9] A practitioner wanting to apply these principles must be aware of these people and be able to perform a quick personality profile for a patient to rule out future excessive behaviors that could be damaging to the patient. It is also stated that good humor can also be very helpful.

Graeme J. Taylor wrote about a leader in psychosomatic medicine named George Engel. Engel enlightened the world on an effective psychoanalytical approach to an internal dialogue that should be present when talking with a patient. He suggests open-ended style of interviewing is what allows a practitioner to read what level of treatment a patient will except. By using the triad of observation, introspection, and dialogue, Engel acquired information that led to a more comprehensive understanding of ways by which mental processes and environmental events can influence bodily processes. (14) Engel had a method of reading patients that was highly effective. Whether he realized it or not using his triad allows a practitioner to implicate the proper level of placebo to each individual patient.

Doctor/Patient relationships are very important but can be very dangerous. There is a fine line between being friends and being an authority. A practitioner cannot conduct intervention without at the same time doing something that has a psychological impact.

In the following Jenny Strong and Anita Unruh give a great depiction of what this relationship should be. "It is a principle of therapeutic communication to provide meaningful information, because information reduces anxiety. Information that is relevant to the clients' needs and concerns is reassuring. In order to fill 'spaces' during therapy, or to respond to the client's distress about their pain, it may be tempting to offer bland reassurance. Such reassurance can increase anxiety." (15) [9] They also go onto say that, "The therapeutic relationship is a powerful influence on the clients' motivation and active involvement in the therapeutic process and persistence with interventions...An approach that focuses on increasing exercise and function, rather than working to a pain limit, depends partially on therapeutic relationship... Compliance will be helped by a relationship which encourages open communication and clear goals." (15) [9] This is the type of relationship that all practitioners must strive to achieve. If the practitioner truly cares about the patients needs the placebo effect will work wonders.

The most controversial aspect of placebo effect is spirituality, not referring to religion. Spirituality is defined as a more individualistic and experiential search for what is sacred in life. (15) [4] Although there is no scientific link in testing the realm of spirituality it is well documented that there have been cases that the unthinkable has happened and the patient credits God and the practitioner credits the placebo effect. It is up to each individual to make their own decision on who is right in those circumstances.

One of the down sides of this power that is withheld in the human body it has capabilities to do harm. In the Book of *Proverbs 18:21*: Death and Life are in the power of the tongue: and they that love it shall eat the fruit thereof. Walter Cannon studied the reasons behind voodoo death the subject alone validates the fact that there is much to be

discovered in the areas of placebo and nocebo. Canon explains nocebo as an emotional state that can override the parasympathetic nervous system and allow the body to kill itself. (18) This parallels with a diagnosis of leukemia or pancreatic cancer. The patient is told to believe they will die and they will do just that. But thanks to technology and positive reinforcing attitudes, which fall under characteristics of the placebo, patients now have a hope and can survive through such outcomes.

The biggest set back of administering the placebo effect is that it sometimes can involve some deception. Categorizing placebos as inert substances contributes to the mistaken notion that their use is harmless. (17) Experimenting with patients requires a deception that can completely ruin the trust factor of the doctor/patient relationship, but it can also make a person feel that they have been betrayed. "Placebos legitimize resentment providers may develop toward difficult patients as demanding, non-compliant and malingerers." (17) If a placebo was used on a patient and documented in his history does this mean that their future complaints would be taken less seriously, and could impede diagnosis of serious health problems. Resorting to placebos stigmatizes the patient and stifles creative thinking by the care team. (17)

Conclusion

The Placebo Effect has many different effects on the body as a whole, some can be good and some can be bad. It has helped in cases such as arthroscopic knee surgery; heart surgery, depression, irritable bowel disease and the list can go on and on. These findings show us that something is present we have learned how opioids play a role in the relief of pain. There is still uncertainty on how it can make complete physiologic changes in the body. Researchers must seek after the subject of placebo aggressively. The effects of it being implicated by practitioners could have a worldwide effect on nations economies and health status. Placebo should be tested as its own entity, like in Ref. (19) " Thus, the natural history condition or group is used to assess the time course of pain intensity that occurs in the absence of any treatment. Additionally, the studies have started to systematically investigate factors that contribute to the magnitude of placebo analgesia, thereby suggesting how the placebo analgesic effect could be optimized in clinical practice." This study is a step in the right direction, more of these trials need to implement and placebo treatment protocols should be made for diseases it is found effective on. Until then is unethical to practice placebo treatment methods due to the lack of research in that area.

In closing, aspects for placebo to take place along with current treatments should be a requirement for being a practitioner of any sort. Caring about patients and under the guide of 'do unto others' is a recipe for the placebo to take place. "Here we are faced with the difference between trying to make change happen and tuning in to engage in such a way as to allow changes to happen." (7) [9]

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