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Article 54

The Placebo Effect

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What is the Placebo Effect?

The term placebo effect refers to the changes in an individual caused by placebo manipulation (Koshi & Short, 2007). In clinical trials, substances or procedures designed to serve as control conditions may actually produce an effect on subjective or biomarker outcomes. Stewart-Williams and Podd (2004) provide a definition for placebo that states "A placebo is a substance or procedure that has no inherent power to produce an effect that is sought or expected" (pp. 326). They also define the placebo effect as "a genuine psychological or physiological effect, in a human or another animal, which is attributable to receiving a substance or undergoing a procedure, but is not due to the inherent powers of that substance or procedure" (pp. 326). These indirect effects of inactive procedures are considered under the umbrella term placebo effects (Kaptchuk, 1998; Oken, 2008).

The placebo effect has been a topic of interest in scientific, as well as clinical communities, for many years (Price, Finniss, & Benedetti, 2008). Until the 1930's physicians used placebos to substitute an inert treatment for a real but dangerous drug or to reassure patients when no actual treatment intervention yet existed. The use of placebos was not malicious, but rather a part of the medical practice at the time. With the invention of clinical pharmacology and double-blind randomized placebo-controlled trial methodology, the inert control groups were referred to as placebos in the literature.

Other terms that have been used to describe the placebo effect include expectancy effects, context effects, and meaning response (Brody & Brody, 2000; Crow, Gage, Hampson, Hart, Kimber, & Thomas, 1999). The actual intervention that elicits the placebo effect is referred to as the placebo. Many non-specific aspects of treatment can help to determine the direction and size of the placebo effect. This can be any clinical intervention including words, gestures, pills, devices, and surgery. Each of these can play a part in conveying the practitioner's confidence in a treatment, empathy with the patient, and professional status. Wampold, Imel, and Minami (2007) argue that a placebo is not simply an inert pill. This is supported by a study conducted by Thomas (1987) that showed results of no difference between placebo treatment and no treatment, but a significant difference between positive and negative statements about prognosis. This study provided some evidence that the words a health professional uses to create

expectations are critical to the remediation of symptoms. Yalom (2005) suggests that the installation and maintenance of hope is crucial to the practice of counseling and that faith in a treatment mode can in itself be therapeutically effective. Several studies have demonstrated the impact a high expectation of helping before the start of counseling can have on a positive therapeutic outcome. Other studies have found that placebo effects can be traced back to verbal cues (Kirsch, 2004; Stewart-Williams, 2004). These authors belief that by a practitioner using verbal cues the suggested reaction leads to the generation of the expected reaction. Non-specific aspects of the placebo remedy itself can also have a powerful influence. For example, the more invasive it is, or the more actively it involves the patient/client, the larger the placebo effect (Chaput de Saintonge & Herxheimer, 1994). This article will focus on the various models of the placebo effect and how both researchers and practitioners may make use of this valuable asset.

Models

Pavlovian

One initial theory concerning the placebo effect is Pavlov's original stimulus substitution model. According to the classical conditioning approach, active medications are the unconditioned stimuli, the methods or techniques used to administer treatments are the conditioned stimuli, and the placebo effect is the conditioned response (Geers, Weiland, Kosbab, Landry, & Helfer, 2005). Studies have shown that conditioning can occur in humans. For example, patients with headache taking regular aspirin can associate the shape, color, and taste of the aspirin to decreases in the amount of pain they feel (Koshi & Short, 2007). After several associations, pain decreased when patients were given a placebo that looked and tasted like aspirin that was previously administered. However, it is assumed that human conditioning does not involve cognition and occurs without the individual knowing it. The response will depend on the individuals' history of learning, or the response generalization. According to such a model, the unexplained variability in placebo response within subjects is due to past medical history and differences in learning history with a particular treatment. Other determinants of placebo effects include verbal suggestions and behaviors manifested by healthcare providers.

In order for this model to fit, the repeated pairing of a treatment, such as a pill, could then set up a stimulus substitution that took place when the person took pills without pharmacological activity. However, numerous problems arise when one accounts for the placebo effect solely through traditional classical conditioning. For example, placebo effects may occur in a way that is different than how classical conditioning is supposed to occur. Classical conditioning cannot explain why prior experience with the active drug often does not increase placebo effects. Montgomery and Kirsch (1997) argues that classical conditioning results in the acquisition of placebo expectancy. This means that the classical conditioning viewpoint may be seen as a special case of the expectancy theory.

Expectancy Theory

Expectancy theory has become the most popular explanation for placebo effects (Frenkel, 2008). An expectation is a belief about the chances associated with a future state of affairs (Geers, et al., 2005). Expectancy theory was developed by Goldstein

(1962; as cited in Koshi & Short, 2007). This theory states that expectancy is a consciously accessible belief about a situation. According to expectancy theory, conditioning trials leave behind an expectancy of what should happen given certain stimuli. This expectancy is then what is responsible for the observed effects. Simply put, expecting the suggested reaction is thought to lead to the generation of the reaction.

The gain of expectancy theory over an explanation solely built upon stimulus substitution is the addition of cognitive content. Expectancies are anticipatory and appear to possess the property of intentionality. Therefore, accessing expectancy puts it in the realm of an intentional state, and the placebo response can then be labeled as an intentional act (Frenkel, 2008). The issue with this account for the placebo effect is that this intentionality fails to include the body as the center of the placebo effects.

Psychosocial Model

Benedetti, Mayberg, Wager, Sohler, and Zubieta (2005) incorporate the previous theories of the placebo effect and discuss that, in the study of the placebo effect, it is important to examine the psychosocial context around the patient or client. They state that the placebo effect is a psychobiological phenomenon that can be attributed to different mechanisms, including expectation of clinical improvement and conditioning. Benedetti et al. also suggest that there is not a single placebo effect, but many. The idea that there are many different placebo effects is something to be considered when examining the placebo effect. In fact, the placebo effect may be conceptualized as an umbrella term or construct since there are multiple biological and psychological shifts that contribute to the phenomenon.

Biomedical Paradigm

Much of the controversy that surrounds the placebo effect can be traced to the evolution in clinical medicine from the biomedical paradigm to the biopsychosocial perspective. The biomedical paradigm relies heavily on the assumption that disease and the treatment of disease are solely reliant on molecular biology and physiology. This paradigm requires health practitioners to understand all treatment outcomes to be understood in terms of changes in underlying and related pathophysiology. However, a multifactorial biopsychosocial perspective considers the potentially rich contribution of nonphysiologic factors and the role they play in treatment. A biopsychosocial perspective considers the potency of social and psychological factors that promote both reliable and desirable clinical outcomes (Roth, 2003). Since the 1950's, interest in the placebo effect has continued to increase and our knowledge of the mechanisms of the placebo effect has advanced a great deal. It has been through this advanced knowledge that many health care professionals believe the use of the placebo effect is of critical importance to their success in working with disease (Frenkel, 2008). We are only beginning to appreciate how the mind or how we think moves molecules in the immune, hormonal, and central nervous systems.

The study of the placebo effect is the study of how beliefs and values may shape brain processes related to perception, emotion, and mental and physical health. Study of the placebo effect in this way reflects a neuroscientific thought that has at its central core the idea that subjective constructs like expectation and value have identifiable and

parallel physiological bases and that these bases are modulators of perceptual, motor, and internal processes (Benedetti et al., 2005).

Neurobiology of the Placebo Effect

The neurobiology of the placebo effect began in 1978, when it was shown that placebo analgesia could be blocked by the opioid antagonist naloxone, which indicates an involvement of endogenous opioids (Levine et al., 1978, as cited in Benedetti et al., 2005). Following this study by Levine et al., further research has confirmed and extended this initial observation (Colloca & Benedetti, 2005). Oken (2008) provides one explanation regarding how the placebo effect occurs. He states that "the central nervous system is the primary location and mediator of the physiological basis of the placebo effects through its role in learning and memory and its outputs on sensory, motor, and autonomic pathways, as well as the immune and endocrine systems" (pp. 2813). Oken proposes that people have individual traits that predispose them to be more or less responsive to certain stimuli. This may explain why there are placebo responders and nonresponders. Due to their predisposition to respond to stimuli, individuals who have a higher predisposition would likely react better to placebo. The response could be a physiological process such as the modulation of sensory processing, the release of neurotransmitters, or alterations in hypothalamic-pituitary-adrenal axis or immune system activity. The placebo effect could also be a more complex physiological process that includes changes in mood, changes in motivation or effort, or cognitive set-shifting.

Neurobiologists have found that placebo effects are accompanied by reductions in neural activity within brain areas known to process symptoms including anxiety and pain. They also have found that these reductions occur along with increases in neural activity within brain areas known to be involved in emotional regulation (Fields, 2004). They propose that placebo responses are generated as a function of reward or aversion and associated neural circuitry.

In the realm of psychopharmacology, major depression provides us the most useful model to examine the neurobiological mechanisms of the placebo effect. This is because placebo responses are common in antidepressant trials of many interventions. These include: medication, psychotherapy, and somatic treatments. The same as in trials for other medical conditions, the effectiveness of a new antidepressant is determined by comparing an active treatment with a controlled comparison condition. PET measures of regional glucose metabolism and regional cerebral blood flow have proven to be sensitive indices of brain function in both the untreated depressed state and after various treatments. Changes in cortical (prefrontal and parietal), limbic-paralimbic (cingulated, amygdale, and insula), and subcortical (caudate/pallidum, thalamus, and brainstem) regions have been described after treatments such as medication, psychotherapy, sleep deprivation, electroconconvulsive therapy (ECT), and repetitive transcranial magnetic stimulation ablative surgery. The functional neural architecture of these observed change patterns provides a foundation to examine putative brain mechanisms mediating placebo effects under comparable treatment conditions. Studies examining placebo effect have found that there were unique ventral striatal and orbital frontal changes in both placebo and active drug responders. An ongoing correlation between ventral striatal activity and lateral prefrontal and subgenual cingulated changes was predictive of clinical outcome with both active drug and placebo (Benedetti et al., 2005). Price et al. (2008) also report

that the neural mechanisms of placebo treatments have been studied in depression. Those patients who received a placebo treatment showed both electrical and metabolic changes in the brain. In one study, placebos induced electroencephalographic changes in the prefrontal cortex of patients with major depression (Price et al., 2008). Mayberg et al. (2002) found changes in brain glucose metabolism in subjects with unipolar depression.

Uses of the Placebo Effect

Although the placebo effect has yielded positive results in many cases, there are important ethical issues to consider when determining whether the use of a placebo is appropriate. The placebo effect has an effect on clinical and ethical implications, because the use of the placebo conditions in clinical trials has created an ethical controversy. However, it has been well-documented that placebo effects may represent points of either strength or vulnerability for the expression and maintenance of various pathological states and their therapeutic interventions (Benedetti et al., 2005). The following discussion will include issues related to both clinical and research settings for mental health professionals to consider.

Use Within Research

This discussion will first focus on the use of placebo for research purposes. The use of placebo remains an issue that is highly debated in psychiatric research (Berk, 2007). The Declaration of Helsinki appears to contradict the use of placebos if an effective treatment for a condition is known. Quitkin (1999) indicates that placebo use is acceptable in disorders characterized by a fluctuating course with only a slight chance that a delay in effective treatment would result in permanent damage and where patients are closely monitored. Most psychiatric disorders have a fluctuating course. The public health implications of approving an ineffective treatment are of great importance. Therefore, when the use of placebo may reduce this risk, it is of greater good than risk (Quitkin, 1999).

Although Quitkin (1999) discussed the benefit of placebo, it is important to be aware of the potential risks. The principal risks when using placebo are classified as increased mortality, permanent serious harm, and reversible but serious harm or discomfort. However, in comparing placebo and active treatment for anti-depressants, research has found no increased suicide in placebo-treated subjects. The same is true for schizophrenia trials (Quitkin, 1999). Those who argue against the use of placebo in these clinical trials state that the burden invoked by placebo treatment against new treatments is not worth the risk. Other situations in which placebo controls are controversial include studies in which known effective therapy will be withheld, the side effects are not intolerable for subjects, and the disease/disorder has serious implications for an individual's health.

The substitute for placebo versus active trials would be for a new treatment to be compared against an already established treatment to determine which is more effective (Berk, 2007). With these concerns being stated, it is important to consider the fact that placebo treatment is often not the equivalent to non-treatment. Berk's (2007) meta-analysis showed that 25% of studies failed to distinguish active antipsychotics from

placebo. This suggests, although a placebo is meant to be an inert procedure of some sort, that the placebo has some effect on those individuals who receive the placebo.

Use of Placebo in Practice Settings

The use of placebo in clinical practice differs from that of research studies. This is not to say that the risks inherent in research studies are not potential factors in clinical practice. Clinicians should always consider the potential for increased mortality, permanent serious harm, and reversible but serious harm or discomfort. Differences are shown in reasoning for placebo between clinical and research settings. In clinical practice, the physician prescribes a placebo in hopes that it will produce a therapeutic effect. However, in research, the physician prescribes a placebo in the hope that it will produce no therapeutic effect. The ethical implications for these two scenarios are different and need to be examined separately (Lichtenberg, Heresco-Levy, Nitzan, 2009).

It is not uncommon for physicians to offer a placebo to a patient. However, there has been question whether the placebo in general has significant therapeutic value. The work of Benedetti et al. (2005) has shown that the placebo effect does, in fact, have therapeutic value. Therefore, the issue with using placebo treatment is not the fact that the patient is receiving an ineffective medicine, since it has been shown to have therapeutic value. The ethical problem is that most frequently it is thought, in the administration of the placebo, that the doctor is deceiving the patient. The patient's right to be honestly and fully informed about treatment may be violated in the administration of the placebo. However, Lichtenberg et al. (2009) suggest that this concern may be greatly overstated by researchers. This is due to the assumption upon which the issue resides is that only through pharmacology or other rational procedures can the doctor aid the patient. This has not been shown to be true, even in an age of evidence based medicine. Since the individual intervenes at many points along the biopsychosocial continuum. This includes intervening through use of his or her personality, air of assurance, words of encouragement, offers of help, and resolution of uncertainty. Placebo is a deception only for those individuals who reduce treatment to a purely biomedical pursuit. The way that the helper reports the nature of the placebo he or she is offering is important in this dilemma. If the placebo being used is that in pill form and the physician prescribing the pill is open and honest with a statement such as: "I would like to offer you a pill which I believe can help lessen your suffering. I do not know exactly how it works. I have other pills to offer whose mechanism is clearer, but I am not sure they will work better for you, and they may also have more serious side effects." This is not an example of deception on the side of the practitioner, yet it does not completely write off the placebo pill being given as ineffective.

Lichtenberg et al. (2009) also offer guidelines for the justified use of placebo in clinical practice. The first of these is that the intentions of the physician must be benevolent and only concerned with the well-being of the patient. The placebo must also be offered in the spirit of assuaging the patient's suffering, not merely appeasing the patient, silencing the patient, or otherwise failing to address his or her distress. Another guideline is that whenever the placebo is proven ineffective, the placebo should be immediately withdrawn and discontinued. The placebo should not be given in place of another medication that the physician reasonably expects to be more effective. Administration of the placebo should be considered when a patient is obstinate to

standard treatment, suffers from its side effects, or in a situation where standard treatment does not exist. Also, if the patient is helped by the placebo, discontinuing the placebo, in absence of a more effective treatment, would be unethical. Finally, the placebo can be of service to physicians in many clinical situations. Therefore, it should not be denied its rightful place in treatment. Offering the placebo as treatment requires that the physician accept that within the therapeutic situation, the physician is an integral part of the cure. This is not always easily accepted by the physician. When placebo treatment is approached with consideration for the issues involved, the placebo can provide legitimate use in medicine.

Placebo Use in Counseling

Given the importance of placebo effects in medical interventions, it was a natural progression that researchers began to question the degree to which the effects of psychological interventions might be placebo effects. To answer this question, studies were designed to include placebo psychotherapies. This strategy is rather problematic practically and conceptually since it cannot be done and makes no sense to try (Kirsch, 2005). However, an important question to be addressed is "How can helping professionals utilize the placebo response?"

Since the placebo effect is hypothesized to be influenced by expectancy there are many things that can increase the potency of the placebo effect. An important mechanism of the placebo response is the nature of the practitioner-client dyad. The placebo response is mediated by client expectancies that result from interaction and communication from the helping professional. This idea was the main way that the placebo effects were initially understood. It has been suggested that any health care delivery system that undermines the helping professional-client relationship will have a detrimental impact on the occurrence and therapeutic benefits of placebos. A demeanor of confidence that a certain treatment will work promotes a positive placebo response. This demeanor of confidence may be known otherwise as instillation of hope. A positive outcome in psychotherapy is more likely when the client and the therapist have similar expectations of treatment outcomes. Counselors can use this factor by acting in a manner that will increase clients' belief and confidence in the efficacy of the treatment being provided. Instillation of hope provides an inspiration to assist clients in more actively coping with the demands placed upon the individual.

Another factor to consider is the emotional bond between the patient and practitioner. A strong emotional bond, otherwise known as the therapeutic relationship, enhances the strength of the placebo response (Roth, 2003). Practitioners can facilitate the therapeutic relationship by utilizing basic counseling skills such as active listening, empathy, congruence, unconditional positive regard, and trustworthiness. Carl Rogers placed a great deal of power in the relationship between the practitioner and client. Through a strong therapeutic relationship, the counselor may put in place a very basic portion of the helping process that may also influence the placebo effect.

Another area in which expectancy may be affected is through the personal history of the client-clinician interactions and shared experiences of the client and clinician (Di Blasi, Harkness, Ernst, Georgiou, & Kleijnen, 2001). This interaction may provide non-specific benefits such as stress reduction, decreased anxiety, or improvement of mood. Oken (2008) also suggested that the clinician's personality or interaction style may

impact outcomes independent of any specific treatment. Therefore, it is important to be aware of how one presents oneself when interacting with the client or patient. When clinicians are more positive and enthusiastic in regard to the effects of an intervention, the outcome has been shown to be better than when the clinician was uncertain and experimental when describing the intervention (Oken, 2008). This suggests that by simply believing in the process of counseling and how it can lead to expected outcomes the counselor is increasing the likelihood of success of counseling. When administering any intervention, an enthusiastic, positive attitude may increase the effectiveness of the intervention and the client may benefit from counseling to a greater extent.

Taking these factors into consideration, practitioners may be effective in influencing the placebo effect by conducting their work with clients using a healthy therapeutic alliance, positive and enthusiastic language, and a personality and interaction style that facilitates client growth. This type of treatment works well with the positive approach to work with clients. By beginning the therapeutic work with an individual from a positive standpoint, this leads to greater enthusiasm by the client.

Conclusion

Inquiry into the placebo effect has provided a wealth of information. The placebo effect has undergone many changes in its role over the years and has gone from being an inert treatment to being recognized as a viable alternative in certain situations. This article focused on explanations of the placebo effect as well as the use of the placebo effect in counseling. The body of literature on the placebo effect suggests that placebo can be utilized to the benefit of counselors. Due to the factor of expectancy and its role in the placebo effect, counselors may use the placebo effect to influence the outcome of counseling and psychotherapy. As Yalom (2005) suggested, instillation and maintenance of hope is crucial to the practice of counseling and the counselor's belief in the process can be infectious, increasing the likelihood of a positive outcome to counseling. This is an area that could be quite beneficial for practitioners to be aware of in order to encourage the process of change that is at the heart of counseling.

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