

Designer's Corner

Alternative Therapies and Placebos: Conceptual Clarification and Methodologic Implications

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The past decade has witnessed increased public awareness and use of alternative therapies for the management of diseases and symptoms (Schwartz, Chesney, Irvine, & Keefe, 1997). Spiro (1997) relates the increased use of alternative therapies to the need for personal connection, belonging, and comfort. A variety of biochemical, psychophysiological, and psychological therapies are available, including homeopathic preparations such as sulphur for dermatoses (Linde et al., 1997), acupuncture, reflexology, massage therapy, therapeutic touch, and self-help approaches. Margo (1999) reports that alternative therapies are used by 20% to 50% of persons in industrialized countries, with some \$14 billion being spent on such therapies in the United States. A large number of publications have been devoted to alternative therapies (e.g., *Journal of the American Medical Association*, 280, 1998); medical and nursing schools are offering courses in alternative therapies; and funding has been made available to systematically investigate the effects of alternative therapies (e.g., National Institutes of Health) (Kwekkeboom, 1997).

Despite the interest in alternative therapies and the accumulating empirical evidence supporting their effectiveness, some scholars view these therapies with scepticism. Many consider them as placebos (Linde et al., 1997; Shapiro & Shapiro, 1997). The arguments for or against considering alternative therapies as placebos are based on differences in professional paradigms and perspectives on what constitutes a placebo

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(Brody, 1985) and in the theory underlying the therapeutic effects of the treatment being evaluated (Grunbaum, 1985). Thus, what one professional considers as a placebo another views as a therapeutic intervention (Spiro, 1997). In this paper we will clarify two perspectives of placebo: the traditional and the alternative. We will review the conceptualizations of placebo within each perspective and the mechanisms underlying placebo effects. We will also discuss the methodological implications of addressing placebo effects in intervention evaluation research from the two perspectives. Addressing these effects is essential to enhancing the validity of the study conclusions.

Definitions

The term *placebo* was introduced in medicine, and later in psychotherapy, to refer to *sham* treatments. Sham treatments consist of inert substances, preparations, or pills given by physicians, or innocuous interventions delivered by therapists, to please or satisfy patients rather than to benefit patients in relation to the specific ailment or symptom being treated (Harrington, 1997; Peck & Coleman, 1991; Straus & Cavanaugh, 1996). Although placebos are assumed to be inert and harmless, they have the power to produce actual clinical improvement in the patient's condition (Sullivan, 1993). The effectiveness of placebos ranges from 15% to 58%, depending on the patient population and the conditions or symptoms presenting (Elander & Hermeren, 1995; Ilnyckyj, Shanahan, Anton, Cheange, & Bernstein, 1997; Jospe, 1978; Quitkin, 1999; Shetty, Friedman, Keiburtz, Marshall, & Oakes, 1999).

The term *placebo effects* refers to changes in the patient's condition or symptom that are produced by the placebo (Grunbaum, 1985; Peck & Coleman, 1991). It can be reflected in favourable outcomes such as improvement in the patient's condition, or in unfavourable outcomes such as worsening of the condition or development of side effects (for details, see Hahn, 1997).

The classic example of a placebo in the field of medicine is a sugar pill or saline injection given for pain relief. Studies have found that placebos are effective in reducing pain intensity by about half in approximately a third of patients who experience severe pain (Evans, 1985; Jospe, 1978). The examples of placebo in the field of psychotherapy are limited. Wilkins (1985) provides two: (1) pre-therapy — conducting an initial interview and psychological assessment but not providing any form of psychotherapy, and (2) pseudotherapy — involving the patient in general conversation during the scheduled session(s) but not addressing the patient's actual problems.

Placebo is, therefore, any treatment that is used in the same way as an active treatment; it may produce therapeutic effects similar to those expected of an active treatment (Ross & Buckalew, 1985). The similarity in the therapeutic effects achieved by a placebo and an active treatment is perplexing. Both types of treatment have been shown to produce clinical improvement in the patient's physiological and psychological functioning (Harrington, 1997; Jospe, 1978). These observations raise some fundamental theoretical questions: What distinguishes a placebo from an active treatment? How can the therapeutic effects of a placebo treatment be explained? Can an active treatment include a placebo treatment? If yes, how validly can we attribute the observed therapeutic effects to the causal effects of the active treatment?

Conceptualization of Placebo Treatments and Effects

Clinical observations and results of studies have led scholars to acknowledge the healing power of placebos. Scholars, however, differ in their conceptualization of placebo treatments and effects. Some view placebos as innocuous treatments and contend that placebo effects are non-specific noise, or nuisance; they dismiss these effects from further consideration since, in their opinion, they defy scientific explanation. Other scholars view placebos as aspects of any treatment and contend that placebo effects are clinically important processes that warrant further investigation (Harrington, 1997; Peck & Coleman, 1991; White, Tursky, & Schwartz, 1985). We label the first view the traditional perspective and the second the alternative perspective of placebo.

Traditional Perspective

The traditional conceptualization of placebo as innocuous treatment and its effects as nuisance is consistent with the traditional, reductionistic, mechanistic paradigm of science. This paradigm is dominant in contemporary medicine and guides investigation of the effectiveness of medications. Medicine is focused mainly on the bio-physio-chemical processes underlying a disease, and on treating these ailments with medications. Medications contain active ingredients or substances, which, when administered, initiate a series of bio-physio-chemical mechanisms that ultimately lead to resolution of the disease and to clinical improvement in the patient's condition. Within this paradigm, the therapeutic effects observed following the administration of an active medication are the direct results of the mechanisms initiated by the active ingredients of the medication. In contrast, the therapeutic effects observed following the administration of a placebo cannot be attributed

to the bio-physio-chemical mechanisms, since, by definition, a placebo is an inert substance that does not contain the active ingredients capable of initiating these mechanisms. Rather, placebo effects refers to phenomena outside the boundaries of specific, active, bio-physio-chemical causes; they are the result of psychosocial factors associated with the "pill-taking ritual" (Kirsch, 1997; Wilkins, 1985). The psychosocial factors relate to the patient's beliefs and expectations; the physician's attitudes, expectations, and beliefs; and the physician-patient relationship that develops during the treatment period. These psychosocial factors could also be present, and have been recognized as taking place, during the administration of active medications. They may, however, confound the therapeutic effects expected of the active medications, because they have been shown to produce the same therapeutic effects. Thus, it becomes difficult to claim, validly, that the observed therapeutic effects are the direct and sole result of the bio-physio-chemical mechanisms initiated by the active ingredients of the medication. Medical research is geared towards demonstrating that the therapeutic effects are a direct result of the bio-physio-chemical mechanisms initiated by the active ingredients of the medication, and not a consequence of the psychosocial factors; the latter factors present major threats to the construct validity of the study.

While attributing placebo effects to psychosocial factors is admissible in medicine, where the primary focus is the bio-physio-chemical processes, it is not acceptable in the field of psychotherapy (Wilkins, 1985). By definition, these psychosocial factors and their associated effects are the primary focus in psychotherapy. Many psychotherapists argue that placebo effects, as conceptualized above, are psychological processes representing aspects of psychotherapy and cannot be viewed as placebo (Shapiro & Shapiro, 1997). In psychotherapy, placebo treatment has been redefined as: (1) any therapy prescribed knowingly or unknowingly by a healer, or used by a layman, for its therapeutic effects on a symptom or disease, but which actually is ineffective or not specifically effective for the symptom or disorder being treated (Shapiro & Shapiro); and (2) an intervention for which there is no clearly defined mechanism of action (Ilnyckyj et al., 1997).

The elements that characterize a placebo are lack of specificity of the placebo therapy to the condition or symptom for which it is given, and lack of understanding of the mechanisms that explain the changes in the patient's condition observed following the administration of placebo. The two elements relate to the notion that placebo therapy, compared to active therapy, lacks specific components that are presumed to initiate the mechanisms responsible for producing the thera-

peutic effects; therefore, the placebo exerts its effects through alternative, non-specific processes that are not known.

Alternative Perspective

The alternative conceptualization of placebos as aspects of any treatment and their effects as clinically important, favourable outcomes is consistent with the emphasis on the bio-psycho-social, holistic view of health, and with the recognition of the complexity of clinical reality. In this perspective, patients are viewed as complex beings, actively interacting with their environment. The complex nature of human beings demands multidimensional treatments that address the multiple domains of health. Treatments are delivered to and received by individuals who interact with each other within a socio-cultural context. The therapeutic effects of treatments result from a complex system of multiple factors (Hegyvary, 1991; Paul, 1985). Consequently, all factors that influence the expected outcomes of an intervention need to be identified based on the theory underlying the intervention effects, and empirically investigated (Sidani & Braden, 1998).

Placebo effects are considered an integral part of a patient's treatment. They represent the non-specific aspects of any treatment, whether the treatment is an active medication or psychotherapy, but produce specific effects (Kirsch, 1997; Ross & Buckalew, 1985; Straus & Cavanaugh, 1996; Sullivan, 1993). Grunbaum (1985) clarifies this conceptualization of placebo effects. He proposes that any treatment consists of two categories of factors: characteristic and incidental. Characteristic factors refers to the specific or unique ingredients or components of the treatment that are presumed to initiate the mechanisms known to produce the intended changes in the disorder or symptom being treated. Incidental factors refers to the non-specific or generic ingredients or components of the treatment that also produce the intended therapeutic effects. Incidental factors involve aspects or procedures performed as part of the treatment that influence outcome either directly or indirectly. The indirect influence can take two forms: through specific mechanisms (i.e., a series of changes leading to the intended outcomes), or by moderating (i.e., strengthening) the effects of the characteristic factors on the outcomes. The theory underlying the treatment delineates the characteristic and incidental factors, and specifies how the factors produce the therapeutic effects (Borkovec, 1985; Grunbaum; Straus & Cavanaugh). Thus, what is considered a placebo depends on the intervention theory, and placebo effects are not necessarily artifacts (Peck & Coleman, 1991; Sullivan). For instance, the patient's beliefs and

expectancies, considered as nuisance in the traditional perspective, could be viewed as important factors mediating the effects of a medication, and should be taken into consideration, rather than controlled for, when the effectiveness of the medication is being determined. Evans (1985) summarizes this perspective: "The placebo effect should be considered as a potent therapeutic intervention in its own right, rather than merely a nuisance variable. The placebo can be understood as if it were another active agent whose effects can be independently evaluated and whose mode of action is worthy of independent investigation" (p. 215).

Mechanisms Underlying Placebo Effects

The exact mechanisms explaining placebo effects are not yet well known. Several psychological and psycho-physiological processes have been suggested as mediating placebo effects, which could be psychological and/or physiological in nature.

Endorphins

The placebo effects specific to pain may be mediated by the release of endorphins (Hrobjartsson, 1996; Peck & Coleman, 1991). Kirsch (1997) explains the release of endorphins after the administration of placebo by the following processes: The effects of placebo medications generally mimic those of active drugs. Taking the placebo engenders expectancies of improved outcomes; these expectancies may produce some feature of the expected physiological response and may be accompanied by the release of endogenous opioids in the brain. The findings of studies testing the role of endorphins in mediating the placebo effects have been inconsistent (Jospe, 1978; Kwekkeboom, 1997).

Expectancies

The concept of expectancy is central to cognitive theories. Cognitive theories propose that the therapeutic effects of a treatment are mediated by the expectancies of the individual. Two expectancies are of interest: (1) outcome expectancy, which is the belief that a given treatment will lead to improvement; and (2) efficacy expectancy, which is the belief that one can successfully execute the treatment. Expectancies are developed in different ways, including previous experience with the treatment, previous learning, provision of information, and persuasion. Outcome expectancy is frequently assumed to be responsible for placebo effects (Bootzin, 1985; Peck & Coleman, 1991); the expectation

that a condition or symptom will improve results in actual improvement in the condition or symptom, regardless of how the expectation was developed (Kirsch, 1997). Results of several studies provide evidence supporting the contribution of expectancy to placebo effects (e.g., Price et al., 1999), particularly in pain management (Jospe, 1978; Price & Fields, 1997).

Suggestion

Suggestion consists of the practitioner or researcher providing the patient with information about the treatment, such as its nature, mode of action, and anticipated effects, and emphasizing its benefits. Suggestion is believed to influence the individual's perception of the treatment and expectancy for improvement (Jospe, 1978; Kwekkeboom, 1997). The effects of suggestion have been investigated in few studies, with no consistent relationship between suggestion and placebo effects being found (Evans, 1985).

Conditioning

Conditioning refers to learning through previous experience or association, as proposed by classical and operant conditioning theories. If a patient experiences repeated instances of a treatment having positive effects, those same positive effects tend to occur when the treatment is given again (Hrobjantsson, 1996; Peck & Coleman, 1991; Straus & Cavanaugh, 1996). Although results of studies provide evidence that previous exposure to an effective treatment enhances placebo effects, Price and Fields (1997) and Kirsch (1997) contend that such experience is not a necessary or contingent condition for the occurrence of placebo effects. Rather, they propose that conditioning leads to the formation of expectancy improvement, which, in turn, contributes to the placebo effects.

Motivation

Motivation is defined as the degree to which individuals desire to experience an improvement in their condition (Price et al., 1999). The influence of motivation on placebo effects has been demonstrated in laboratory studies of pain, which have found that with increased pain there is a greater need and desire for relief, and therefore greater placebo effects (Price & Fields, 1997). Thus, patients experiencing distressing symptoms may exhibit a strong desire for relief and consequently increased

placebo effects. Motivation (i.e., desire for treatment to relieve pain) was not found to contribute significantly to placebo effects when tested against expectancy (i.e., expectation that pain will be relieved) in an experimental study of pain (Price et al.).

Reduced Anxiety

Reduced anxiety has been suggested as a mechanism underlying placebo effects. The experience of alteration in health condition or development of a symptom is associated with increased anxiety, which adversely affects health and symptom perception and experience. Seeking treatment, speaking with a health-care provider, receiving attention from the health-care provider, and receiving treatment (even if it is a placebo treatment) are believed to alleviate anxiety and subsequently to improve the individual's condition or symptom (Evans, 1985; Quitkin, 1999). The influence of reduced anxiety and the exact mechanism underlying its influence on placebo effects have not been investigated and remain unclear (Kwekkeboom, 1997).

Meaning Model

Brody (1985, 1997) developed the meaning model to explain the placebo effects in a clinical context. The model proposes that positive placebo effects are likely to occur when the meaning attached to an illness or treatment experience by a patient is altered in a positive manner. Alteration of meaning occurs when the patient is provided an understandable and satisfying explanation of the illness or treatment experience and is supported by caring health-care providers, and when the patient's sense of mastery and control over the illness is enhanced. These alterations take place within the physician-patient relationship. The contribution of this relationship to the development of placebo effects has been recognized by several scholars and clinicians (Finkel, 1985; Margo, 1999; Peck & Coleman, 1991; Straus and Cavanaugh, 1996).

While several mechanisms have been proposed to explain placebo effects, there is insufficient empirical evidence to support them or to favour one over the other. This "state of affairs" endorses the complexity of placebo effects in that they can be attributed to multiple, interrelated factors and mechanisms. The contributing factors are associated with the patient, the therapist, the therapist-patient relationship, and the treatment itself.

Methodological Implications

Theoretical and empirical knowledge related to placebo treatments and effects has developed over the years. Placebo effects are acknowledged; they are likely to occur with the delivery of any treatment, to any patient population, by any therapist, in either a clinical or a research context. Nonetheless, our understanding of placebo effects remains limited. This knowledge gap could be partly associated with the traditional conceptualization of placebo treatments and effects that has dominated scientific endeavours and that has influenced the design of intervention evaluation studies.

The traditional conceptualization acknowledges placebo effects but considers them as artifacts or threats to the construct validity of the study, as they are confounded with treatment effects (Cook & Campbell, 1979). Studies aimed at evaluating treatment effectiveness should be carefully designed to minimize these potential threats and/or to allow for dismantling the placebo from the intervention effects. The double-blind, placebo-controlled, randomized-clinical-trial design is viewed as the gold standard design for evaluating the effectiveness of an intervention (Margo, 1999; Quitkin, 1999). It is extensively used in drug-effectiveness studies (Straus & Cavanaugh, 1996). Eligible patients are randomly assigned to receive the medication that contains the active ingredients (treatment group) or an inert substance (placebo group). The active and placebo medications should have identical properties to maintain the double-blind condition, whereby the patients and the therapists are unaware of the nature (i.e., active vs. placebo) of the medications being given. The double-blind condition minimizes hypothesis-guessing and/or expectancies in the patient, and minimizes bias, enthusiasm, and expectancies in the therapist. The statistical analysis involves comparison of the post-test outcomes between the two groups. A statistically significant difference, in which the intervention group shows more improvement in the outcomes than the placebo group, indicates the effectiveness of the active medication (Peck & Coleman, 1991; Quitkin; Wilkins, 1985).

Designing and conducting double-blind, placebo-controlled trials can be challenging. "Blind" conditions cannot be maintained if the active and placebo medications are not identical in all their properties (such as label, form, mode of administration, dosage, effects, and side effects). Differences between the two medications in dosage, onset of effects, and development of side effects have been reported because of the difficulty in finding a placebo that mimics the active medication

(Ross & Buckalew, 1985; Straus & Cavanaugh, 1996). Such differences can be noticed by either the patient or the therapist, or both.

In the field of psychotherapy it is very difficult to find identical or equivalent treatments. Pre-treatment activities and pseudotherapy have been proposed as placebo treatments. The delivery of placebo psychotherapy is entrusted to a therapist who can easily differentiate a placebo from an active therapy. Therefore, it is impossible to keep the therapist unaware of which therapy is being delivered to which patient. The blind condition is breached. The therapist's awareness of the type of therapy being delivered may influence the patient's response, intentionally or unintentionally (Wilkins, 1985).

In addition, the double-blind, placebo-controlled design has been criticized for its limited utility in minimizing other threats to the validity of the study conclusions. These threats include regression to the mean in studies of severe pain (Straus & Cavanaugh, 1996) and Hawthorne effects (Weihrauch & Gawler, 1999). Finally, this design has been criticized on ethical and theoretical grounds. It is considered unacceptable to provide placebo treatment for conditions for which there are therapies that are deemed safe and effective (Margo, 1999; Straus & Cavanaugh). These trials do not entirely eliminate mechanisms that are believed to contribute to placebo effects, such as: expectancy that treatment will be delivered and improvement gained through participation in research; knowledge of the treatment, its effects, and its side effects acquired through the process of obtaining informed consent (Elander & Hermeren, 1995; Peck & Coleman, 1991; Weihrauch & Gawler); spontaneous or natural recovery from the illness (Hrobjartsson, 1996; Margo); and influence of the context or environment (Paul, 1985).

Modifications of the double-blind, placebo-controlled clinical trial have been suggested to address some of the above-mentioned limitations of this design. For example, a third, no-treatment, control group could be incorporated into the double-blind, placebo-controlled design. Any changes in the outcomes observed in the no-treatment control group will be spontaneous and related to natural recovery, or will be a result of the patient's guess of the investigator's hypothesis about the anticipated changes in outcomes (Peck & Coleman, 1991). The difference between the placebo control group and the no-treatment control group provides an estimate of the placebo's impact. A waiting-list control group design could be used to overcome the ethical issue and/or to generate a placebo treatment in psychotherapy research. In this design, patients are randomly assigned to (a) receive the treatment immediately, or (b) a waiting list. Patients assigned to the waiting list

serve as a placebo control group, since they have been involved in a study and received initial assessment. They are given the treatment after taking the post-test measures from the immediate-treatment group (Hrobjantsson, 1996).

The alternative conceptualization considers placebos as part of the treatment and their effects as clinically important. The incidental factors of the treatment that contribute to the placebo effects are identified by the theory underlying the treatment. Once identified, these treatment factors can be incorporated into a study designed to evaluate the treatment of interest, and their influence on outcomes determined. The mechanisms underlying the placebo effects presented earlier are examples of incidental factors of treatments. They can be incorporated into the design of a treatment evaluation study as suggested by Peck and Coleman (1991). These authors propose a balanced placebo design. In this factorial design, half the patients are told they will receive the treatment while the other half are told they will not. In each of the two groups, half the patients actually receive the treatment while the other half do not. This factorial design enables the researcher to disentangle the effects of expectancy from those of treatment. The authors also recommend the use of a within-subject design, in which patients are given first the active treatment, then the placebo treatment. This design allows for testing of the mechanism of conditioning that explains the placebo effects. A more complex design involving three groups — active treatment, waiting-list control, and active treatment followed by control condition — is proposed by Schwartz et al. (1997). The theory-driven approach to intervention evaluation research is another strategy for investigating placebo effects. This approach is consistent with the alternative conceptualization of placebo treatments and effects, which advocates: (1) identifying factors related to the patient, therapist, setting, and intervention that affect the achievement of outcomes expected of the intervention, based on the theory underlying the intervention; (2) measuring these factors; and (3) determining the influence of these factors through multivariate statistical analyses (for details, see Sidani & Braden, 1998).

Conclusions

Placebo treatments have been traditionally defined as non-specific causes that result in therapeutic effects. As long as the characteristic ingredients or components, as well as their mechanisms of action, remain unclear, they will be looked at unfavourably and considered as artifacts or nuisance, since they confound the treatment and its effects.

Such confounding presents threats to the validity of the claim that the treatment is effective in producing the expected outcomes.

Alternative therapies may be viewed as placebos because their characteristic components and their mechanisms of action are not well articulated or understood. Delineating the components and mechanisms underlying the effects of alternative therapies is an essential step in the process of clarifying this misconception and establishing their value. Future research should be guided by the theory underlying alternative therapies and identifying their characteristic and incidental factors, and should be directed towards testing the theory. This approach to research is advantageous and useful for any intervention evaluation study, as it allows for dissociation of the therapeutic effects of the intervention from those effects resulting from the incidental factors (placebo) and understanding which aspects of the intervention are characteristic and which are incidental.

References

- Bootzin, R.R. (1985). The role of expectancy in behavior change. In L. White, B. Tursky, & G.E. Schwartz (Eds.), *Placebo: Theory, research, and mechanisms* (pp. 196–210). New York: Guilford.
- Borkovec, T.D. (1985). Placebo: Defining the unknown. In L. White, B. Tursky, & G.E. Schwartz (Eds.), *Placebo: Theory, research, and mechanisms* (pp. 59–64). New York: Guilford.
- Brody, H. (1985). Placebo effect: An examination of Grunbaum's definition. In L. White, B. Tursky, & G.E. Schwartz (Eds.), *Placebo: Theory, research, and mechanisms* (pp. 37–58). New York: Guilford.
- Brody, H. (1997). The physician as therapeutic agent: A placebo effect research agenda. In A. Harrington (Ed.), *The placebo effect: An interdisciplinary exploration* (pp. 77–92). Cambridge, MA: Harvard University Press.
- Cook, T.D., & Campbell, D.T. (1979). *Quasi-experimentation: Design and analysis issues for field settings*. Boston: Houghton Mifflin.
- Elander, G., & Hermeren, G. (1995). Placebo effect and randomized clinical trials. *Theoretical Medicine*, 16, 171–182.
- Evans, F.J. (1985). Expectancy, therapeutic instructions, and the placebo response. In L. White, B. Tursky, & G.E. Schwartz (Eds.), *Placebo: Theory, research, and mechanisms* (pp. 215–228). New York: Guilford.
- Finkel, M.J. (1985). Placebo controls are not always necessary. In L. White, B. Tursky, & G.E. Schwartz (Eds.), *Placebo: Theory, research, and mechanisms* (pp. 419–422). New York: Guilford.
- Grunbaum, A. (1985). Explication and implications of the placebo concept. In L. White, B. Tursky, & G.E. Schwartz (Eds.), *Placebo: Theory, research, and mechanisms* (pp. 9–36). New York: Guilford.

- Hahn, R.A. (1997). The nocebo phenomenon: Scope and foundations. In A. Harrington (Ed.), *The placebo effect: An interdisciplinary exploration* (pp. 56–76). Cambridge, MA: Harvard University Press.
- Harrington, A. (1997). Introduction. In A. Harrington (Ed.), *The placebo effect: An interdisciplinary exploration* (pp. 1–11). Cambridge, MA: Harvard University Press.
- Hegyvary, S.T. (1991). Issues in outcomes research. *Journal of Quality Assurance*, 5(2): 1–6.
- Hrobjartsson, A. (1996). The uncontrollable placebo effect. *European Journal of Clinical Pharmacology*, 50, 345–348.
- Ilnyckyj, A., Shanahan, F., Anton, P.A., Cheang, M., & Bernstein, C.N. (1997). Quantification of the placebo response in ulcerative colitis. *Gastroenterology*, 112, 1854–1848.
- Jospe, M. (1978). *The placebo effect in healing*. Lexington, MA: D.C. Heath.
- Kirsch, I. (1997). Specifying nonspecifics: Psychological mechanisms of placebo effects. In A. Harrington (Ed.), *The placebo effect: An interdisciplinary exploration* (pp. 166–186). Cambridge, MA: Harvard University Press.
- Kwekkeboom, K.L. (1997). The placebo effect in symptom management. *Oncology Nursing Forum*, 24(8), 1393–1399.
- Linde, K., Clausius, N., Ramirez, G., Melchart, D., Eitel, F., Hedges, L., & Jonas, W.B. (1997). Are the clinical effects of homeopathy placebo effects? A meta-analysis of placebo-controlled trials. *Lancet*, 350(20), 834–843.
- Margo, C.E. (1999). The placebo effect. *Survey of Ophthalmology*, 44, 31–44.
- Paul, G.L. (1985). Can pregnancy be a placebo effect? Terminology, designs, and conclusions in the study of psychosocial and pharmacological treatments of behavioral disorders. In L. White, B. Tursky, & G.E. Schwartz (Eds.), *Placebo: Theory, research, and mechanisms* (pp. 137–166). New York: Guilford.
- Peck, C., & Coleman, G. (1991). Implications of placebo theory for clinical research and practice in pain management. *Theoretical Medicine*, 12, 247–270.
- Price, D.D., & Fields, H.L. (1997). The contribution of desire and expectation to placebo analgesia: Implications for new research strategies. In A. Harrington (Ed.), *The placebo effect: An interdisciplinary exploration* (pp. 117–137). Cambridge, MA: Harvard University Press.
- Price, D.D., Milling, L.S., Kirsch, I., Duff, A., Montgomery, G.H., & Nicholls, S.S. (1999). An analysis of factors that contribute to the magnitude of placebo analgesia in an experimental paradigm. *Pain*, 83, 147–156.
- Quitkin, F.M. (1999). Placebos, drug effects, and study design: A clinician's guide. *American Journal of Psychiatry*, 156, 829–836.
- Ross, S., & Buckalew, L.W. (1985). Placebo agency: Assessment of drug and placebo effects. In L. White, B. Tursky, & G.E. Schwartz (Eds.), *Placebo: Theory, research, and mechanisms* (pp. 67–82). New York: Guilford.

- Schwartz, C.E., Chesney, M.A., Irvine, J., & Keefe, F.J. (1997). The control group dilemma in clinical research: Applications for psychosocial and behavioral medicine trials. *Psychosomatic Medicine*, 59, 362-371.
- Shapiro, A.K., & Shapiro, E. (1997). The placebo: Is it much ado about nothing? In A. Harrington (Ed.), *The placebo effect: An interdisciplinary exploration* (pp. 12-36). Cambridge, MA: Harvard University Press.
- Shetty, N., Friedman, J.H., Kieburtz, K., Marshall, F.J., & Oakes, D. (1999). The placebo response in Parkinson's disease. *Clinical Neuropharmacology*, 22(4), 207-212.
- Sidani, S., & Braden, C.J. (1998). *Evaluating nursing interventions: A theory-driven approach*. Thousand Oaks, CA: Sage.
- Spiro, H. (1997). Clinical reflections on the placebo phenomenon. In A. Harrington (Ed.), *The placebo effect: An interdisciplinary exploration* (pp. 37-55). Cambridge, MA: Harvard University Press.
- Straus, J.L., & Cavanaugh, S.V.A. (1996). Placebo effects: Issues for clinical practice in psychiatry and medicine. *Psychosomatics*, 37, 315-326.
- Sullivan, M.D. (1993). Placebo controls and epistemic control in orthodox medicine. *Journal of Medicine and Philosophy*, 18, 213-231.
- Weihrauch, T.R., & Gawler, T.C. (1999). Placebo-efficacy and adverse effects in controlled clinical trials. *Arzneimittel-Forschung/Drug Research*, 49, 385-393.
- White, L., Tursky, B., & Schwartz, G.E. (1985). Placebo in perspective. In L. White, B. Tursky, & G.E. Schwartz (Eds.), *Placebo: Theory, research, and mechanisms* (pp. 3-8). New York: Guilford.
- Wilkins, W. (1985). Placebo controls and concepts in chemotherapy and psychotherapy research. In L. White, B. Tursky, & G.E. Schwartz (Eds.), *Placebo: Theory, research, and mechanisms* (pp. 83-109). New York: Guilford.