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Utilization of Placebo Response in Double-Blind Psychopharmacological Studies, Contextual Perspective

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UTILIZATION OF PLACEBO RESPONSE IN DOUBLE-BLIND
PSYCHOPHARMACOLOGICAL STUDIES, CONTEXTUAL PERSPECTIVE

A Dissertation

Presented to the Faculty of
Antioch University Seattle
Seattle, WA

In Partial Fulfillment
of the Requirements of the Degree
Doctor of Psychology

By

Margarita O. Ashirova

October 2015

UTILIZATION OF PLACEBO RESPONSE IN DOUBLE-BLIND
PSYCHOPHARMACOLOGICAL STUDIES, CONTEXTUAL PERSPECTIVE

This dissertation, by Margarita O. Ashirova, has been approved by the committee members signed below who recommend that it be accepted by the faculty of the Antioch University Seattle at Seattle, WA in partial fulfillment of requirements for the degree of

DOCTOR OF PSYCHOLOGY

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ABSTRACT

UTILIZATION OF PLACEBO RESPONSE IN DOUBLE-BLIND
PSYCHOPHARMACOLOGICAL STUDIES, CONTEXTUAL PERSPECTIVE

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Placebo response has been an elusive phenomenon in the fields of medicine, medical research, and psychology. Even though it has been heavily utilized as a comparator treatment in double-blind psychopharmacological studies, the reliable definition and consistent understanding of placebo response are missing. In this contextual exploration, I outlined the state of current placebo response research and variable rates of placebo response reported in double-blind studies. I identified the gap in the literature—lack of consistent understanding of placebo response—that has led to a waste of resources by the psychopharmacological research industry. Further, I compared and contrasted the current inconsistent Western medical understanding of placebo as outlined by a leading expert on placebo research (Fabrizio Benedetti) and the potential new understanding of placebo response based on philosophical concepts of Hans-Georg Gadamer. I concluded that placebo response appeared to be a contextual phenomenon and therefore could be expected to behave similarly to other contextually based healing modalities as described by Gadamer. I determined that the positivistic approach of modern medical research was not an appropriate method for understanding, researching, or defining placebo. Thus, I argued that psychopharmacological research could be improved by changing the way it

used placebo in its control groups and maximizing placebo response in both placebo and active treatment groups instead of minimizing it. I argued that this new approach would bring the drug trial environment closer to the real life treatment environment and improve the quality of the drug trials. The electronic version of this dissertation is at AURA: Antioch University Repository and Archive, <http://aura.antioch.edu/> and OhioLINK ETD Center, <https://etd.ohiolink.edu>

Dedication

I dedicate this work to my mother who taught me to never settle and always try harder.

Acknowledgements

I want to thank my husband who provided so much love and support throughout my academic career and can finally see the result—my completed dissertation research. I want to express love and gratitude to my mom, who always pushed me to do better and not give up. I am grateful to my dissertation chair, Dr. Alex Suarez, who helped me deal with my writer's blocks and arguably saw the most tears come out of one person's eyes in one sitting. My friends Anna and Aly deserve a special mention for being there for me every single week during the 6 months of intense writing making sure that I was nourished, that I continued to write, and that I was not giving up. Thank you also to my supervisors, Drs. Nancy Cook and Sean Kitaoka who provided their support in some of the most critical times, read my drafts, gave feedback, and allowed me to take time during my internship to finish this work. I am also grateful to the two professors in my academic career whose courses made this research possible: Dr. Jaime Diaz and Dr. Phillip Cushman. One taught me the importance of psychopharmacological research for clinical psychology, the significance of placebo response, and the ability to evaluate scientific research, while the latter taught me the philosophical stance to critique the research I encounter and to question the mainstream ideals. Thank you to all my friends and relatives for believing in me.

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Introduction to Placebo Response Understanding

Placebo response is an intriguing phenomenon that has been puzzling medical doctors, psychiatrists, and psychologists alike for many centuries (Benedetti, 2009). It has been both a nuisance and a welcome mystical phenomenon in modern science. Despite numerous recent studies attempting to understand and explain how the phenomenon occurs, lack of clarity persists in the definition of placebo response and in understanding of its mechanisms of action (Benedetti, 2009).

Medical professionals had long been prescribing placebos with often positive results for conditions that did not have a known etiology or cure (Walach & Jonas, 2004). Moreover, Benedetti (2009) claimed that historically most medical interventions as well as many interventions available currently had been relying mainly on the placebo effect, because they did not contain any proven specific efficacious element otherwise:

Most, if not all, of these medicaments and procedures were based neither on scientific rationale nor on the assessment of real efficacy, but rather they emerged from metaphysical beliefs, social influences, and scientific ignorance about anatomy and physiology related to that particular historical period. (Benedetti, 2009, p. 2)

Many such treatments included rather bizarre and odd concoctions of “skulls of victims of violent death, frogs, worms, feathers, hair, horns, hoofs, ants, scorpions, viper flesh, crab eyes, bee glue, fox lung, spider webs, teeth, sexual organs, and so forth” (Benedetti, 2009, p. 2). In modern medicine for example, many different antidepressants with different neurological effects considered effective without a convincing unifying theory that would explain why the neurological effects that they produce alleviate depression. Not surprisingly, placebo response has produced a controversy in current pharmaceutical and medical research. Understanding placebo response could both increase and diminish the effect attributed to an active treatment (de la Fuente-Fernandez et al., 2001; Zubieta et

al., 2005). This has happened due to the difficulties in the conceptualization of the placebo response (Benedetti, 2009).

In this study, I looked more closely at this conceptualization predicament as it applied to the area of research where placebo response is most utilized: psychopharmacological studies. Indeed, pharmacological research is one of the few areas in which placebo response has been actively used. Placebo response has been commonly used as an *inactive* comparator in double- and single-blind studies. By utilizing this kind of comparator group, pharmacological companies aspire to establish whether their newly developed medications perform better than just the treatment routine alone (Benedetti, 2009).

In this case, the psychopharmacological researchers assume that the placebo arm treatment group is equivalent to the active treatment in every way except for the active ingredient exposure. The assumption here is that all of the cumulative improvement that happens in the placebo group is due to the process of treatment (i.e., coming to research clinic on a specific schedule, being assessed by doctors regularly, having one's blood and urine taken for chemical analyses, routine of taking pills as prescribed).

Benedetti (2009) suggested that this assumption described above might not be warranted. In fact, he was quite critical of the pharmacological researchers lumping together the spontaneous improvement, statistical regression to the mean, natural progression of an illness, psychosocial factors, biases, and co-interventions that were not accounted for properly (p. 5). According to the author's conclusions, placebo response is not a cumulative positive effect that a person experiences while in treatment. Instead, he

suggested that placebo response is a phenomenon in its own right, separate from the factors above.

Despite the pharmaceutical researchers' many attempts to control the placebo response via intricate study designs and controlling for the few identified contributing factors such as patient-provider relationship and treatment environment (Benedetti, 2009, p. 33), the response continues to fluctuate and has recently been on the rise (Benedetti, 2009; Bridge, Birmaher, Iyengar, Barbe, & Brent, 2009; Walsh, Seidman, Sysko, & Gould, 2002). Walsh and colleagues conducted an analysis of published studies and found a robust association between the year of publication and the response rate to placebo in adult major depressive disorder trials. In their analysis of published studies, Bridge et al. also found a significant correlation between the date of publication and placebo response rate in children and adolescents. These findings suggest an increase of placebo response over time. Increasing and out of control placebo response can complicate interpretation of study results and, clearly, contributes to an increasing number of so called "failed studies." Failed studies are those whose results were unsuccessful in producing clear separation of measured efficacy between placebo and treatment groups. Currently, no reliable explanations exist for predicting and thus being able to control placebo response (Benedetti, 2009). Researchers continue to explore the phenomenon, but it is still difficult to grasp. Thus, its application in clinical work often remains unpredictable.

The psychopharmaceutical industry has long been using the placebo response phenomenon as a comparator treatment in their randomized trials (Benedetti, 2009). The double-blind placebo-controlled study became a gold standard of the pharmacological

research (Enck & Klosterhalfen, 2013; Relton, 2013). However, due to the lack of knowledge about predictors of and factors influencing placebo response, the researchers in the industry are not able to design studies in a way that protects from a large number of failed and inconclusive studies resulting from unexpectedly high placebo response.

Comprehensive analysis of studies published by pharmacological companies revealed a number of concerns (Song et al., 2010). Specifically, Song and colleagues identified the tendency by the pharmacological companies to not publish studies whose results were negative or inconclusive. Others also reported that this selective publishing occurs (Turner, Matthews, Linardatos, Tell, & Rosenthal, 2008) despite the FDA requirement to publish all of the results whether positive or negative (Prayle, Hurley, & Smyth, 2012). This inevitably leads to a skewed understanding of efficacy of various psychopharmacological products. Moreover, as also highlighted by Song et al., these failed studies lead to a considerable waste of resources. This is particularly concerning to consumers, as it is a common practice for businesses to push their increasing expenses onto the consumer in a form of a higher price of their product.

Most importantly, however, thousands of studies conducted by the psychopharmaceutical industry seem to contribute little to further the understanding of placebo response. It is somewhat understandable, because psychopharmacological companies are not in business to study placebo. They attempt only to study their own products as “the main interest of both physicians and drug companies is to demonstrate the efficacy of the therapy under test” (Benedetti, 2009, p. 9) not the limitations or benefits of placebo. On the other hand, this tendency to ignore lack of understanding of placebo appears somewhat irresponsible given that the industry has to rely on such a

poorly understood phenomenon. The meta-analyses based on the psychopharmacological studies data provide limited understanding of predictors of placebo response, as they can look only at information collected by the studies (i.e., age, gender, length of trial, number of visits, and severity of a diagnosis).

A main difficulty in identifying predictors of placebo response lies in the theoretical weaknesses of placebo response conceptualization (Benedetti, 2009). The researcher stated that clinical researchers conceptualize the placebo response as “any improvement that may occur in the placebo group, regardless of whether it is a spontaneous remission or a psychological phenomenon; whereas most psychologists referred to the placebo response as: the psychological phenomenon that involves expectations and anticipation of clinical improvement” (Benedetti, 2009, p. 5). The author further considered that the placebo response is, in fact, “a context effect” (p. 34), though through his descriptions it is evident that Benedetti still assumed that a specific “baseline placebo” (p. 11) effect can eventually be identified. This is very much a positivistic point of view, which assumes that one identifiable element, placebo response in this case, can be pinpointed through a series of meticulous and targeted searches. However, this theoretical approach has now been used for decades in placebo response studies, and has been producing inconclusive and often contradictory results as the current state of events shows (Benedetti, 2009; Enck & Klosterhalfen, 2013; Enck, Klosterhalfen, Weimer, Horing, & Zipfel, 2011; van Haselen & Jütte, 2013).

In summary, it has been demonstrated that the psychopharmaceutical industry tends to not publish their failed or inconclusive studies (Prayle et al., 2012; Song et al., 2010; Turner et al., 2008). It is also known that placebo response in the double-blind

studies has been on the rise and is contributing to the said failed and inconclusive studies rate (Benedetti, 2009; Bridge et al., 2009; Song et al., 2010). I believe that the lack of a firm and reliable understanding of placebo response is likely due to the inadequate positivistic theory applied in describing this state-based phenomenon. A conceptualization of placebo response from a theoretical point of view that accounts for its contextual nuances is necessary to adequately describe the phenomenon and make it applicable for research.

Purpose Statement

This study is a theoretical dissertation research exploring placebo response using the philosophical arguments of Hans-Georg Gadamer (2004, 2011) as an alternative to the currently accepted model in the medical field the positivistic approach illustrated by the placebo conceptualization of Benedetti (2009). The purpose of this theoretical study was to explore the understanding of placebo response from a contextual point of view in an attempt to develop a better conceptualization of this phenomenon and broaden the placebo phenomenon body of knowledge. Specifically, I explored placebo response as a state-related and meaning-related phenomenon assuming that meaning is created through cultural discourse. The understanding of placebo response through the work of Gadamer was then compared to the current understanding of placebo by the medical community presented via Benedetti's work.

I completed a qualitative comparison of the differences between the two theoretical conceptualizations and outlined the applicable implications for experimental and clinical work with placebo. The main research question of this dissertation was as follows: What are the differences between placebo response as it is understood by the

mainstream Western medicine community and placebo response as it is understood by a contextual theory of Gadamer's hermeneutics? I believe that this alternative understanding of placebo response would contribute to the general body of knowledge on this subject. Additionally, since unpredictability and variability in strength of placebo response lead to a waste of resources in the pharmacological research, resulting in excessively highly priced pharmaceutical products, I hope with this research to augment the current mainstream concept of placebo response to possibly help reduce this wasteful trend in the future.

Contextual Theory Versus Trait Based Understanding of Placebo

In this section, I illustrated that a contextual theory is necessary to address some of the common deficiencies of current placebo research. There is great variation in placebo response from study to study and from condition to condition (Benedetti, 2009). In line with positivistic thinking, placebo response studies and studies utilizing this effect for comparison have assumed that placebo response is a trait-phenomenon and few studies have actually marginally supported this idea (Bagby, Ryder, & Cristi, 2008; Entsuah & Vinall, 2007; Grant, Kim, Hollander, & Potenza, 2008). Due to the assumption that inherent (e.g., gender), historical (e.g., age), or present (e.g., current diagnosis) traits are responsible for placebo response susceptibility, the studies that were evaluating predictors of placebo response continued to search for correlations between specific trait characteristics of subjects and their tendency to respond to placebo positively (Benedetti, 2009).

Currently, psychopharmacological studies experience significant difficulty controlling the rising placebo response (Benedetti, 2009; Bridge et al., 2009).

Researchers appear to be attempting to control for the known trait and context related variables affecting placebo response, but to no avail, as demonstrated by the number of failed trials. Other scientists also confirmed that little could be gained from the current studies involving placebo in understanding placebo response and individual factors influencing it (Enck et al., 2011; van Haselen & Jütte, 2013).

Therefore, I showed in this work that a contextual theory could be used instead to explore the elusive placebo response phenomenon. I conducted a qualitative exploration of theoretical works by Hans-Georg Gadamer with an emphasis on the books *The Enigma of Health* (2004) and *Truth and Method* (2011) to offer a contextual theoretical conceptualization of placebo response. I believe that a qualitative comparison of the differences between conceptualizations of placebo response, can advance theoretical understanding of this powerful and elusive effect.

Why Gadamer's Hermeneutics?

Hans-Georg Gadamer was one of the prominent philosophers of the 20th century. His philosophy is most completely described in his seminal work *Truth and Method*, originally published in German language in 1960. Though Gadamer did not directly address the phenomenon of placebo response in his work, the principles for application of his theory, hermeneutics, are clearly outlined in the most recent English translation of *Truth and Method* (2011). Additionally, Gadamer dedicated a significant part of his research career to understanding health, illness, and healing. The majority of his essays on these topics are collected in the book *The Enigma of Health* (Gadamer, 2004). I believe that Gadamer's understanding of health, illness, and healing are indeed very applicable to understanding placebos and placebo response.

I postulated that Gadamer's hermeneutics provided the necessary theoretical underpinning for understanding such a contextual phenomenon as placebo response. As suggested by Richardson, Fowers, and Guignon (1999), Gadamer provided a way to understanding not by giving a specific method to understanding, but describing where the understanding takes place. According to hermeneutics, understanding is a dynamic occurrence that depends on what is the context of the person who attempts to understand. Hermeneutics originated as a form of religious text interpretation and an auxiliary discipline in theology. Later, "the idea of general hermeneutics" has developed, which applied "to all forms of human communication" (Richardson et al., 1999, p. 200). However, at the turn of the 20th century, another shift has occurred in understanding hermeneutics, which "reflected the growing awareness that devising rules for interpreting humans is impossible and that the whole fascination with method is a by-product of the very scientism being called in question" (Richardson et al., 1999, p. 200). Since then, hermeneutics has been successfully used as a process and a philosophical foundation from which to analyze and interpret "the being of the entities that interpret and understand, namely, ourselves" (Richardson et al., 1999, p. 200).

Moreover, Gadamer's (2004, 2011) hermeneutics provides specific constructive criticisms of positivistic theories as they apply to natural sciences. I therefore have directly applied his theoretical work to understanding placebo response as a phenomenon in a natural science. Additionally, Gadamer's work offers ways of understanding phenomena as part of a socially constructed world where everything exists through being defined linguistically, socially, culturally, and being situated historically. I hold that the placebo response, as a contextual state-based phenomenon, is best conceptualized

utilizing understanding of how linguistic, social, and historical aspects affect individuals experiencing this phenomenon.

Summary

In this chapter, I demonstrated that placebo response is a puzzling phenomenon in the fields of medicine, psychology, and clinical research. Part of what makes it difficult to study is the lack of consistent definition, which would take into account the state-based nature of this phenomenon. Despite the lack of understanding, placebo response is heavily utilized by the psychopharmacological research industry as a comparator in their double-blind studies. In last decades, the psychopharmacological industry has been experiencing increased placebo response rate in studies, which led to failed trials and waste of resources. Lack of proper placebo response definition appears to contribute to the problem, because the drug research industry is unable to control the rising placebo response rate in drug trials. I concluded that it was necessary to study placebo response from a contextual point of view, because the current positivistic approach to understanding placebo has not been successful. I proposed that Gadamer's (2004, 2011) hermeneutics—a contextual philosophical theory—would be one of the perspectives from which to explore placebo response and compare it to current scientific, albeit inconsistent, understanding of placebo response represented by Benedetti (2009, 2013) (one of the lead scientists in placebo research).

Literature Review

Narrowing the Scope of the Study

The purpose of this dissertation was to explore further my ongoing interest in the study of placebo response that began almost a decade ago in an undergraduate psychology class. This fascinating phenomenon intrigued me particularly with how widely it spread over almost all areas of human physiological and mental functioning. This remarkable connection between mind and body was impossible for me to ignore. I later pursued a career in psychopharmacological research, which gave me firsthand experience of how people respond to placebo in a single- and double-blind placebo-controlled study setting.

In over five years of coordinating Phase II, III and IV psychopharmacological trials and seeing placebo response occur in humans, my curiosity about placebo response transformed into a strong belief that humans can heal their mental disorders separately from direct medication effects. I have seen depressed, anxious, and hypertensive people taking a “dummy” pill become remarkably better in a matter of days. What made them improve? Placebo response mechanisms are clearly not sufficiently understood (Benedetti, 2009; Moerman, 2000).

The psychopharmacological research industry warns its research investigators and clinical staff of harmful effects of high placebo response that can ruin years of research and waste millions of dollars due to a “failed” trial. The industry is interested in learning how to minimize placebo response in double-blind trials and to stop wasting so many resources on “failed” trials, but seemingly has reached an impasse on how to achieve that and it just continues to do more of the same (i.e., minimize contact with patients, avoid

excessive niceness and friendliness, only accept people in the study with a severe enough level of a disorder, etc.).

Defining placebo response. A positive change in a patient's condition following administration of a substance or a device that is known to be inactive is what is usually called placebo effect (Walach & Jonas, 2004; Zubieta et al., 2005). Correspondingly, a negative change in response to an inert substance or device is often called nocebo (Enck, Benedetti, & Schedlowski, 2008). Active and inert/inactive placebos are currently identified in research and medicine where active placebos produce some specific measurable effects in the body, but the effects cannot be directly attributed to the expected changes in the body. The scope of this dissertation is limited to the effects of inactive placebos. See Definitions section in Methodology and Delimitations for definitions of *active* and *inactive placebo* and *nocebo* effects.

In previous decades, a number of different kinds of changes like “spontaneous remission, measurement artifacts, and regression to the mean” (Walach & Jonas, 2004, p. S-103) have been lumped under the phenomenon of placebo effect by confused and careless writers (Benedetti, 2009; Walach & Jonas, 2004). This lead many researchers, who used placebo as their control group in studies of pharmacological and other treatments, to assume that placebo effect is the average improvement in their placebo arms. However, I believe that the most helpful way of describing placebo response, as Walach and Jonas suggest, is to specifically define it as “self-healing capacities of a person” because research studies conducted with human subjects are unable to control for all other possible artifacts that contribute to improvement.

Current Knowledge and Understanding of Placebo Response

Currently, the psychopharmacological research industry attempts to reduce placebo response through some logical steps: asking investigators and study staff to reduce chatting with patients beyond common courtesy and medical necessity, create studies that call for fewer procedures (i.e., less time spent with study doctor and staff in the clinic), begin studies with a single-blind placebo, and eliminate responders prior to having them start study drug treatment. However, there are no specific studies that support these steps as being effective placebo response prevention/reduction measures. On the contrary, an overview article by Moerman (2000) showed a tendency for studies with more visits (i.e., more contact with study doctor and study staff) to show a smaller placebo response rate.

Experience of placebo response. In the substudy of a larger double-blind trial that explored acupuncture treatment for irritable bowel syndrome (IBS), Kaptchuk with colleagues (2009) interviewed 12 patients who were assigned to a placebo arm of the study. They were able to reveal the double-blind treatment assignment to their subjects after the main study was completed. Participants ranging in age from 23 to 65 were interviewed a few times during the main study while on their assigned treatment. They were also interviewed during post-study briefing after the treatment code was revealed to them.

They found that most placebo arm participants found their study treatment to be beneficial and reported moderate to dramatic improvement in their IBS symptoms. Additionally, when asked about their thoughts on placebo treatment, participants revealed a clear understanding of placebo was and what treatment with placebo meant. During the

treatment phase of the study, most participants also shared that they thought about the possibility of being assigned to the placebo arm and tried to determine whether they were assigned to the placebo or the treatment arm. Participants reported carefully observing the manipulations of their study acupuncturists, paying attention to how the needles felt when applied to their skin, and noticing any variations in their IBS symptoms while trying to identify the most likely cause for those variations.

These findings showed that participants assigned to the placebo treatment were thinking critically throughout the process and spent considerable time trying to figure out through personal observations whether they were on placebo. Additionally, Kaptchuk et al. (2009) found that many of the participants were questioning their improvement during the study and wondering if it was a treatment effect, a normal variation in their IBS symptoms, or if their minds were “tricking” them into feeling better. Overall, by the end of the study, most of the participants who responded to placebo believed that they were assigned to a real treatment, not a placebo (Kaptchuk et al., 2009). One participant even refused to accept that she was given the placebo treatment during study, because her improvement was so significant and because her personal observations led her to believe that she was on a real acupuncture treatment.

The study by Kaptchuk et al. (2009) showed the complexity of placebo response as it might be experienced by humans. Most of the participants assigned to the placebo arm (except for the woman who refused to believe that she was on placebo) were surprised to learn about this assignment, but during the briefing found a way to understand and explain it. Such explanations included beliefs that IBS has a lot more to do with mental activity than they realized, that placebo acupuncture could also be a good

treatment, etc. The study also showed how real the effects of placebo can be to those experiencing them and that they could constitute a real treatment for some rather than being a nuisance variable.

Mechanism of placebo response. It is not surprising that participants found placebo treatment so tangible. As shown in Benedetti, Mayberg, Wager, Stohler, and Zubieta (2005) overview, placebo response mimicked the same neurological mechanisms as an active treatment. Moreover, in some cases placebo response was more precise at targeting only areas of the brain responsible for the main effect and not causing additional side effects. Benedetti et al. did not make any speculations regarding how various trait characteristics of a subject could influence suggestibility, expectation, or conditioning. Wager et al. (2004) showed that placebo analgesia produced brain activity changes in anticipation of pain rather than changing the experience of pain as it occurred. Again, this study was not making any predictions or speculations regarding trait-based characteristic differences in such anticipation effects.

Additionally, placebo response, though naturally associated with mental activity and therefore expected to be more prominent in more brain-related disorders, actually appeared in treatment of less mind-linked conditions (Kemeny et al., 2007; Shetty, Friedman, Kieburtz, Marshall, & Oakes, 1999). Researchers found a significant placebo response in the double-blind pharmacological treatment of asthma symptoms (Kemeny et al., 2007). The reported placebo response in this study was conservatively measured at 18% of participants responding to placebo with significantly reduced bronchial hyperreactivity compared with baseline.

In studying children, Goodenough et al. (1997) found that placebo cream application prior to venipuncture did not produce a significant placebo response. In their randomized controlled trial of three groups of children varying in age from 3 years and 5 months to 17 years and 7 months, researchers found no significant differences in reported amount of pain following a venipuncture. Additionally, they did not find any significant age or sex correlation and the amount of pain reported. The significant predictors of pain were only prediction of pain by participants (i.e., when participants predicted that the venipuncture would hurt, they were more likely to actually experience pain) and whether a person was a “looker” versus not a “looker” (e.g., not looking at the needle during venipuncture). The results of this study were not conclusive and should be used with caution, since the study failed to produce placebo response altogether. Moreover, it was difficult to draw conclusions regarding age differences in placebo response since no significant placebo response was observed.

Placebo response prevalence in double-blind studies. Placebo response in depression studies has been rather considerable. Bridge et al. (2009) conducted a meta-analysis of 12 randomized controlled trials of pediatric double-blind pharmacological treatment of major depressive disorder (MDD), where 2,862 patients were involved. Ages of the participants ranged from 6 to 18 years old. The meta-analysis provided information regarding the average placebo response in all of these trials and attempted to find the predictors of placebo response in pediatric MDD trials. Researchers found that on average 46% of participants who were assigned to placebo responded to it. This response rate varied across studies from 34 to 58% responders to placebo, whereas from 48 to 70% of the participants were responders to antidepressant. Bridge et al. found that

neither age nor sex were good predictors of placebo response. However, severity of MDD was negatively correlated with placebo response. As follows from this large meta-analysis, children ages 6 to 18 participating in pediatric MDD double-blind studies responded to placebo on average in 46% of cases and the more severe their MDD symptoms the less likely they were to respond to placebo.

Unfortunately, in a similar meta-analysis of late-life depression treatment by Sneed et al. (2008), the placebo response rates were not reported. Only antidepressant response rates were reported, which ranged from 35 to 77%. It appeared that these response rates in individuals over 60 years old were somewhat higher than in pediatric trials. However, studies included in the late-life MDD meta-analysis by Sneed et al. also included active comparator treatment studies, not only placebo-controlled studies. Researchers stated that in the active comparator research designs, response to study medication was higher than in the placebo-controlled designs (60% vs. 46% response rate to study medication). Sneed et al. speculated that the difference in response due to study design might be due to participants' expectations, as they might be less likely to respond positively to a treatment when a chance of being on placebo was present.

In IBS syndrome, double-blind studies showed a more varied tendency. Specifically, Patel et al. (2005) in their meta-analysis of randomized controlled double-blind pharmacological treatments of IBS found that placebo response ranged from 16 to 71% of people improved while on placebo. Though on average it was similar to a placebo response in pediatric MDD trials at 40.2%, it varied much more and was dependent on the number of office visits. Patel with colleagues found that with each additional visit at the research office for treatment, a reduction in placebo response was

observed by 4.4%. Notably, Patel et al. also observed the lack of consistency across studies in definition of response for both placebo response and active treatment response:

The definition of a global response varied widely among studies, ranging from binary to continuous variables. Some trials recorded ‘improvement vs no improvement’ whereas others evaluated the Subject’s Global Assessment of Relief (SGAR) with a predefined scale that characterized response to treatment. In our study, ‘responders’ were patients who showed a global response according to the study’s definition, or, in studies lacking a global response definition, patients who showed global improvement in symptoms. (p. 333)

Diversity in placebo response. Few studies reported differences in placebo response across cultures. A literature review conducted by Moerman (2000) provided some information on such variations. As reported by the researcher, differences existed in placebo response rates between ulcer disease double-blind studies conducted in Germany and Brazil. The German participants in Germany tended to have higher placebo response compared to their Brazilian counterparts in Brazil.

Additionally, such aspects as culture-specific response to size, color, and shape influenced treatment response (Moerman, 2000). For instance, branding of a medication pill and coloring it culturally expected color increased the medication potency (p. 54). Specifically, a Dutch study showed that “cool” colors like blue (a culture-dependent perception) were used more for depressants and “hot” colors like red or orange for stimulants (de Craen, Roos, de Vries, & Kleijnen, 1996). Moerman made a side note that “[c]olor and form are not invariably this clear: Viagra, for example, is marketed in a blue tablet” (p. 66). I speculate that the light blue color of Viagra may be explained if it is meant to represent the maleness (i.e., baby blue stands for male and manhood in Western culture).

Cultural aspects may also play into the notion of *nocebo* which has the opposite effects of placebo (i.e., making someone’s condition regress due to some external factors

or due to taking an inactive substance). Moerman (2000) provided an example of Chinese Americans affected by chronic diseases having lower life expectancy than their White American counterparts with the same disease do if according to their belief system the year of their birth made them susceptible to the disease in question. It provides an excellent example of how powerful one's beliefs may be and how that may affect one's treatment in general.

Furthermore, Moerman (2000) urged researchers to not misinterpret the data from placebo-controlled trials or trials where "no treatment" was the treatment. If a condition appeared to resolve "on its own" during a "no treatment" observational trial, one could not definitively state that the condition did not require treatment. Instead, the conditions under which the patient was observed should be considered the effective treatment. Coming to a doctor's office, receiving a physical exam, and being interviewed by a doctor regarding symptoms might be just as potent as a pill. However, if a study concluded that one did not require active treatment to heal, those suffering from the disorder would be unlikely to experience the "no treatment" conditions as they might not be seen at all, and instead be advised to wait and let the condition resolve on its own. Walach, Sadaghiani, Dehm, and Bierman (2005) also agreed that conditions under which participants were treated account for a great proportion of treatment success in the double-blind trials. This also highlights the importance of examining contextual variables in placebo research.

Open-label placebo. Sandler, Glesne, and Geller (2008) conducted a sub-study in an open-label (vs. blinded) randomized pharmaceutical trial of dose extension of child Attention Deficit/Hyperactivity Disorder medication. Children and their parents in a

placebo group (who were aware that they were in a placebo group) were interviewed (open-ended questions, one 20–30 minute interview) about their 3-month experience on a placebo extender (taken mid-day in addition to a morning dose of an actual stimulant medication). Curiously, researchers found that most (75%) of the participants found the experience positive and beneficial. They found that patients and their parents found taking it beneficial at least to some degree, even when aware of being in a placebo arm and having a clear understanding of what placebo was. One child participant described the placebo pill as an “extension of his medicine” regimen and after a while thought of it as part of a treatment, not a dummy pill.

Suggestibility (“Suggestibility,” n.d.) explanation of placebo response assumes that a patient is, in a sense, fooled by a doctor or a researcher into believing that the treatment they are receiving is going to be beneficial for them. The findings of the Sandler et al.’s phenomenological study (2008) made the positivistic definition of suggestibility rather questionable, since patients were acutely aware of the sham nature of the placebo treatment they received and were not fooled.

More Positivistic Explorations of Placebo Response

The first documented successful attempt to describe how placebo response might manifest itself on a neurological level was done by Levine, Gordon, and Fields (1978). They discovered that analgesic effects of placebo could be reversed by administering the opioid-blocking substance naloxone. This blocking effect was assumed to occur in a similar manner to how morphine analgesic effects were reversed by naloxone and it led the scientists to believe that placebo analgesia must work on the same neural pathways as opioids. This discovery triggered a long line of successive research exploring the

analgesic properties and pathways of placebo (Kong et al., 2006; Petrovic, Kalso, Peterson, & Ingvar, 2002; Wager et al., 2004; Zubieta et al., 2005).

With the help of modern technology, it became a lot easier to study the neurological bases of placebo response in analgesia and a number of other conditions. In fact, Levine and colleagues' original hypothesis (1978) of opioid pathways activation by placebo was verified and expanded by a number of recent studies using positron emission tomography (PET) scans and functional magnetic resonance imaging (fMRI) (Kong et al., 2006; Petrovic et al., 2002; Wager et al., 2004; Zubieta et al., 2005). Moreover, the analgesic placebo effect was one of the most widely studied phenomena, possibly due to the fact that the analgesic effects could be quickly seen and easily measured (Benedetti et al., 2005; Kong et al., 2006). These new technologies provide an important insight into how placebo response takes place in the human brain.

More specifically, Petrovic et al. (2002) discovered using PET scans that analgesic effects of placebo in a heat-induced pain response activated similar areas as opioids did. Surprisingly, the reduction in pain after administration of placebo was reported by all subjects in this study, though it varied considerably interindividually. The specific areas the researchers found activating in both opioid-induced and placebo-induced analgesia were in the rostral anterior cingulate cortex (rACC) and brainstem. The effects of the placebo were much more specific and did not affect as many cortical and subcortical areas as an opioid administered in this study. The main effect of remifentanyl, the opioid analgesic used in this study, was the significantly increased activity bilaterally in both rostral and caudal anterior cingulate cortex (ACC) (extending also to ventromedial prefrontal cortex), insula, orbitofrontal cortex (OFC) (extending into

the temporopolar areas), and lower pons. The effect was defined as PET-captured activity with pain administration minus PET-captured activity without pain administration. This effect was especially prevalent in the rACC and in the anterior insula. This activity was imitated by the brain during placebo administration, though to a much lesser degree. The increased activity was found in the OFC regions bilaterally, but mainly in the right hemisphere and the contralateral rACC (the pain stimulus was applied to the left hand of right-handed participants) (Petrovic et al., 2002). Most importantly, the areas that overlapped in both the opioid and the placebo analgesia network were OFC in the right hemisphere and rACC.

It was shown that in general caudal ACC was activated during pain and unpleasantness, but rACC was activated in conditions involving suggestion and resulted in modulation of pain. One of the post-hoc findings by Petrovic et al. (2002) was that high placebo responders had rACC activation in response to pain while low responders did not. This made a strong case for viewing rACC as an area involved in modulation of pain experience. Petrovic and colleagues further suggested that placebo responders might have a more efficient opioid system. Additionally, it was speculated that brainstem activation (pons area specifically) was produced by the higher cortical systems. This activation happened during both opioid and placebo analgesia effect.

Wager and colleagues (2004) aspired to understand whether placebo-induced analgesia was achieved via altering pain transmission, changing pain affect, or by producing compliance with suggestion of investigators. They conducted two fMRI studies and concluded that placebo did not numb the pain, but instead changed the experience of it. Their major finding was that both dorsolateral prefrontal cortex (PFC)

and OFC activation correlated with midbrain activation during pain anticipation after placebo administration, consistent with the idea that prefrontal mechanisms trigger opioid release in the midbrain. Wager et al. (2004) agreed that “OFC and midbrain regions are not typically associated with directed attention” (p. 1166). However, they speculated, “activation of these regions seems more consistent with the view that anticipation during placebo involves a specific expectancy process that may be related to opioid system activation” (p. 1166). This important finding opened another window into placebo-induced analgesia—it seemed to change the experience of pain by anticipating pain experience and activating specific brain regions getting ready for the experience.

A study by Kong et al. (2006) used fMRI scans and sham acupuncture needles to test their hypotheses regarding the neurobiology of placebo analgesia. The pain stimulus in this study was administered to the right hand of the right-handed participants. The activation was seen in the bilateral lateral/OFC, rACC, cerebellum, right fusiform, parahippocampus, and pons. Most importantly, it was found that placebo analgesia was positively correlated with the activity in rACC even in a study with a different analgesic paradigm (acupuncture worked on different analgesic mechanisms than opioids). The more strongly subjects exhibited placebo-induced analgesia, the more activated were their rACC. Therefore, the hypothesis regarding rACC mediating pain in suggestion scenarios was once again supported with this study.

Additional information regarding placebo analgesia pathways was gained by Zubieta et al. (2005). They used PET to examine the activation of μ -opioid receptors in sustained pain with and without placebo administration. Their findings suggested that placebo activated both higher-order and sub-cortical brain regions like rACC,

dorsolateral PFC, insula, and nucleus accumbens. They found significant differences across their subjects in activation of these areas, but overall their results supported the previous findings where rACC, PFC, and insula were involved in placebo-induced analgesia. It was now shown, however, that μ -opioid receptors specifically were involved in producing the analgesic effect.

Placebo for Parkinson's disease and depression. Interestingly, placebo response in relieving Parkinson's disease symptoms was also found to be very prominent and was often used in research (Benedetti et al., 2004; de la Fuente-Fernandez et al., 2001). The neurobiology of placebo response in patients with Parkinson's is quite different from neurobiology of placebo-induced analgesia. As hypothesized by the researchers in their study (de la Fuente-Fernandez et al., 2001), "the placebo effect is mediated through the activation of the pathway relevant to the disorder under study" (p. 1164).

In their PET experiment, de la Fuente-Fernandez and colleagues (2001) discovered significant changes in the caudate nucleus and the putamen with greater changes seen in the posterolateral part of the putamen. These changes (increases in dopamine availability) were comparable to the effects of therapeutic dose of levodopa. Consequently, "placebo-induced release of endogenous dopamine in the striatum" (p. 1164) was observed and this finding was consistent with current etiology theory of Parkinson's disease. Placebo seemed to be working on the same networks as active medication to relieve symptoms of Parkinson's. Similar results were found by Benedetti et al. (2004). The researchers also tested a hypothesis regarding use of placebo as a control in medication trials and concluded that at least in some patients most of the

benefit obtained from an active drug might derive from placebo response (de la Fuente-Fernandez et al., 2001).

Moreover, placebo response could be seen on neurological levels not only immediately following placebo administration, as in pain and in Parkinson's research, but also in a more long-term placebo administration. A 6-week double-blind trial for depression that used a placebo control group and an active-medication (fluoxetine) group utilized PET to look at changes following the treatment period (Mayberg et al., 2002). The researchers discovered a common pattern in cortical and subcortical regions activation that was close to identical in both placebo-responders and fluoxetine-responders. They found that placebo-responders specifically had increased metabolic activity in neocortical and limbic-paralimbic regions with significant increases in PFC, premotor cortex, inferior parietal cortex, posterior insula, and posterior cingulate. Additionally, researchers saw a statistically significant decrease in metabolism in subgenual cingulate, hypothalamus, thalamus, supplementary sensory area, insula and parahippocampus. Responders to fluoxetine showed additional changes in metabolism in subcortical and limbic regions and more specifically in striatum, hippocampus, and anterior insula.

The studies of placebo use in pain modulation, Parkinson's symptoms relief, and depressive symptoms relief showed that there was no placebo-specific pathway in the brain that produced general placebo response (Enck et al., 2008). Each placebo response pathway was expectation-specific and worked in ways very similar to the ones active medications used. Expectation and Pavlovian conditioning were suspected to be at work mediating these processes (Benedetti et al., 2005; Walach & Jonas, 2004).

One of the hypotheses of placebo response was that an expectation network activated in the brain. The expectation network when activated was responsible for the experience. The expectation was triggered by the investigator/doctor suggestion, previous knowledge, or classical (Pavlovian) conditioning.

Understanding and implementing placebo response. The results of the neuroimaging studies of placebo responses and psychotherapy effects suggested that “beliefs and expectations can markedly modulate neurophysiological and neurochemical activity in brain regions involved in perception, movement, pain, and various aspects of emotional processing” (Beauregard, 2007). Based on the imaging evidence presented above, it is now known that direct physical or biological/chemically-active intervention is not required to produce significant and specific changes in the brain. Therefore, by using information gained from placebo and other non-biological interventions, psychologists and medical doctors might be able to deliver more appropriate care to their patients: the care that harnesses the natural healing capacities of humans (Stefano, Fricchione, Slingsby, & Benson, 2001; Walach & Jonas, 2004).

Further Research

There is a lot to learn about this phenomenon of “self-healing” (Walach & Jonas, 2004). For instance, it is yet to be determined if placebo response mediated by suggestion is different from placebo response that is explained by classical conditioning (Enck et al., 2008). Additionally, Brody and Brody (2000) suggested that multidisciplinary research was needed to integrate qualitative measures of meaning and perception with quantitative measures of biochemical mediators. Such research would allow scientists to better predict how well someone would respond to placebo and

possibly to an active treatment, as “meaning has biological consequences” (Moerman & Jonas, 2002).

Meaning assigned to treatment by a patient in a conscious way does not always explain the placebo response phenomenon. For instance, placebo response seen in immune, hormone, and respiratory systems seemed to be occurring as a subconscious classical conditioning process rather than a conscious expectation (Price, Finniss, & Benedetti, 2008). However, Moerman and Jonas (2002) were discussing the meaning and meaning-making in the hermeneutic sense, where subconscious processes took part by manifesting the values and beliefs of the cultural-historical context in which patients existed.

Summary of Positivistic Research and Implications

Thanks to neurocognitive research, more is now known about the illusive phenomenon of placebo response and it now appears more measurable (Benedetti et al., 2005; Price et al., 2008). Placebo response in double-blind pharmacological studies tends to vary greatly from study to study, but on average remains around 40 to 46%. The condition for which one receives treatment also determines the placebo response. For instance, in treatment of pediatric MDD, placebo response ranged from 34 to 58%—the percentage of individuals in the placebo groups who scored ≤ 2 on the improvement item of the Clinical Global Impression scale (Bridge et al., 2009), whereas in treatment of ulcers the range of placebo response was from 0 to 100%, which was measured by percentage of people in the placebo groups who had “endoscopically observed healed ulcer craters” (Moerman, 2000, p. 58). It appears that studies of placebo response are difficult to conduct and often hard to interpret.

Placebo response is still often considered an unexplained side effect by the general public and primary care physicians (Brody & Brody, 2000). The response is discarded as not attributable to a “real” intervention and thus as not a “real” effect. However, the effects produced by placebo through suggestion, expectation, and Pavlovian conditioning are visible and measurable on neurobiological level using the modern technology. Nonetheless, the above studies continue to be restricted by the same limitations that are inherent in using positivistic theory: inherent reductionism of positivistic studies is often insufficient to describe and explain complex systems. Placebo response phenomenon, I believe, is a complex system and requires a different approach for studying it.

Contextual Explorations of Placebo Response

A contextual exploration is a method of annotation, which takes into account context. So far, very few studies have attempted to look at placebo response using a contextual theory. A contextual theory would attempt to understand placebo response as a phenomenon that exists within a set of circumstances surrounding it rather than a phenomenon that is interrupted or contaminated by contextual variables. Thompson, Ritenbaugh, and Nichter (2009) proposed an anthropological conceptualization of placebo where the “whole systems” approach was taken to the healing (p. 139). In many ways, the authors provided an important reconceptualization of placebo response as a full range human experience as it is located socially, culturally, and linguistically. They also brought out the important aspect of discourse when it came to understanding placebo as an underresearched topic. They identified that placebo response conceptualization in literature overly relied on conscious cognitive approaches rather than direct embodied

experience common in meaning-making of healing. The researchers believed that by taking a more holistic approach to understanding placebo, one might better understand its healing qualities. Unfortunately, Thompson and colleagues did not suggest what implications their conceptualization could have on current double-blind study designs.

Summary

In this chapter, I provided an overview of current state of research on placebo response. Majority of placebo research in the literature is of quantitative positivistic type. I began the chapter with describing my personal interest in placebo response and its direct connection with drug research. I narrowed the scope of this study to placebo response and its use in psychopharmacological industry. I provided examples of placebo response experience by study participants. These examples showed how real that experience of healing from illnesses felt to them.

I highlighted that in recent decades neurocognitive research, had helped to make placebo response more measureable. However, placebo response had remained unpredictable and varied across studies of various conditions and age groups. It appeared to me that studies of placebo response were difficult to conduct and their findings were just as difficult for researchers to interpret. I concluded that the inconsistencies found in studying placebo response contributed to dismissal of the phenomenon as something made up and unproven. Yet, the effects produced by placebo were visible and measurable on neurobiological level using modern technologies. The literature review highlighted the need for an alternative understanding of placebo response to counteract the inherent reductionism of positivistic empirical studies and to help explain a complex system (placebo response).

Methodology and Delimitations

Research Questions

The following are the questions I intended to answer with this study. What are the differences between placebo response as it is understood by the mainstream Western medicine community and placebo response as it is understood by a contextual theory of Gadamer's hermeneutics? How could these differences inform the psychopharmacological double-blind study design?

Research Approach

A hermeneutic exploration using Gadamer texts and observation of modern culture were used as primary ways to identifying aspects of placebo response as a contextual phenomenon. Then contextual definition of placebo response was discussed. The new definition of placebo response was applied to the double-blind psychopharmacological trials, and derived implications were recorded.

Delimitations of the Study

The topic of placebo response is very vast. It is a phenomenon that is manifesting in various aspects of healing such as psychotherapy, treatment of medical conditions, as well as in performance on cognitive and physical tasks (Benedetti, 2009). To delimit the study and identify the scope of this research, only placebo response as used in psychopharmacological trials was explored for application of this theoretical treatise. Possibly, similar contextual perspective might need to be taken when identifying placebo response in other areas of healing listed above. However, the identified purpose of this study was to illuminate the differences between the positivistic approaches in defining placebo response and Gadamer's (2004, 2011) hermeneutical understanding as applied to

the psychopharmacological studies. Psychopharmacological research industry historically had used placebo response phenomenon and had been relying on it most heavily in the scientific study of psychopharmacology.

I used the work of Fabrizio Benedetti (2009, 2013), an Italian researcher specializing in studying placebo response phenomenon, as the primary source that represented Western medicine's point of view. The reason for this choice was Dr. Benedetti's worldwide recognition as an authority on the subject of placebo response. Since mid-1990s, he authored and coauthored numerous research articles exploring the extent of placebo response (Benedetti, n.d.). Benedetti, one of the major researchers of this phenomenon, brought together research from various subfields of science (such as medicine, psychology, and pharmacology) in an attempt to streamline and define placebo response, while he highlighted inconsistencies across the subfields.

For the contextual point of view, I used hermeneutics as a base from which to describe a contextual phenomenon as well as to critique the modern Western medicine's empirical point of view. Hermeneutics, although comparable to other interpretive theories such as discursive, constructionist, and dialogical theory, had been used specifically to provide an alternative to empirical, scientific research methods in psychology and medicine (Kirschner & Martin, 2010). It challenges core positivistic assumptions of modern psychology and medicine research. I used Gadamer's hermeneutics as a lens through which to assess placebo response phenomenon. Gadamer's work is known for its extensive critique of human sciences in modern research. He specifically argued against using natural science model for human sciences. Additionally, Gadamer greatly contributed to the hermeneutic literature with his writings

on modern medicine and the ideas of illness, health, and healing. I considered his work critical to the hermeneutical exploration of placebo response. Thus, I based my theoretical exploration of placebo response primarily on Gadamer's hermeneutics.

Definitions

Active comparator is a medication whose efficacy for a specific condition is already established and it is being used in a double-blind research design as a comparator to a study medication.

Active treatment, in the context of pharmacological treatments research, refers to a pharmacological intervention that has known pharmacological effects of therapeutic value.

Active placebo is a chemical compound used in pharmacological research that produces some felt physiological response that is not by itself found to be therapeutic, but mimics the side effects of the treatment under test (Benedetti, 2009, p. 7).

Inactive placebo is a chemical compound used in pharmacological research that is commonly referred to as "sugar pill" and does not necessarily contain any sugar or possess any ability to produce therapeutic effects in a living organism for the condition under study.

Double-blind treatment, in the context of pharmacological research, refers to an active or placebo treatment that is hidden from both the participant and the researcher. Neither of them knows during study whether the participant is taking an active medication or a placebo.

Nocebo is the term which was introduced in contrast to the term placebo ('I shall harm' vs. the classical Latin meaning of placebo: 'I shall please') by some authors to distinguish the pleasing from the noxious effects of placebos (Benedetti, 2009, p. 35).

Nocebo response or *nocebo effect* is a negative response associated with an inert treatment that does not possess any therapeutic and/or toxic properties. In this negative response, negative context and/or verbal suggestions of clinical worsening prompt the negative expectations about the outcome (Benedetti, 2009, p. 35).

Open label treatment, in the context of pharmacological research, refers to an active or placebo treatment, where the nature of this treatment is known to (i.e., not hidden from) the research participant as well as to the researcher administering the treatment. In an open-label treatment, the participant and the researcher both know what exactly the participant is prescribed during the study.

Placebo response/placebo effect—the definition of placebo response applied throughout this study is that explained by Benedetti (2009, 2013) for clinical research—it constitutes an improvement in someone who has taken placebo, and the improvement is due to either regression to the mean, spontaneous remission, or a body's natural ability to heal itself via some not yet identified mechanism. See a more extensive discussion about placebo response definition in Definition Confusion subsection of this chapter.

Regression to the mean is a phenomenon in pharmacological studies where the condition under study reduces in severity not due to a treatment, but because of the nature of all conditions to go up and down in severity. If participants' severity of the condition was measured during the exacerbation of the condition, it is expected that when the

severity of the condition is measured again it will likely be lower as it would go down to its average, or mean, rate of severity.

Definition confusion. As previously stated in the Delimitations section, only placebo response within a context of psychopharmacological double-blind placebo-controlled studies is discussed in this study. Thus, the psychopharmacological industry's global understanding of placebo response is employed in this research. *Placebo response* and *placebo effect* are interchangeable terms describing the improvement in a placebo group (also known as a group that received placebo treatment during study) due to either regression to the mean, spontaneous remission, or a body's natural ability to heal itself via some not yet identified mechanism.

As summarized by Benedetti (2009), the term *placebo effect* brings confusion into science, which “resides in the fact that the improvements that may take place in patients who receive placebo may be due to many factors, for example spontaneous remission or expectation of therapeutic benefit or other factors” (p. 5). Other researchers have observed that in clinical research, improvement in placebo groups regardless of the reason is attributed to placebo effect. However, psychologists typically refer to placebo effect as a psychological phenomenon associated with expectation of improvement (p. 5). Moreover, Hoffman, Harrington, and Fields (2005) proposed to discriminate between the terms placebo response and placebo effect by using the word *response* to define the psychological phenomenon and the word *effect* to refer to the global outcome in the placebo group. More about the differentiation between response and effect of placebo is discussed in Suggestions for Future Research. Even though Benedetti (2009) stated, “placebo effect, or placebo response, is a psychobiological phenomenon that must not be

confounded by other phenomena, such as spontaneous remission and statistical regression to the mean” (p. 19), the clinical research industry does not clearly define placebo response. In fact, spontaneous remission, regression to the mean, the natural history of a disease, as well as “expectation-modulated anxiety, expectation of reward, learning-reinforced expectations, social learning, Pavlovian conditioning, personality traits, genetics” (Benedetti, 2013, p. 1220) together constitute the placebo response category for clinical trial purposes. Therefore, for the purposes of this study, a placebo response constitutes an improvement in someone who has taken a placebo, and the improvement is due to either regression to the mean, spontaneous remission, or a body’s natural ability to heal itself via some not yet identified mechanism.

Healing in the Modern World

As I illustrated in the Literature Review, until now, placebo response has been studied mostly as a natural science phenomenon. In this chapter, I provide a case for placebo response being a phenomenon to be studied by human sciences. I begin with illustrating that health, illness, and treatment are important parts of Western culture. I then provide a summary of Gadamer's (2004, 2011) understanding of health, illness, and treatment from hermeneutic point of view. Hermeneutically, treatment is understood as a process of restoration to health, which is affected by cultural-historical influences. Using Gadamer's hermeneutics, I provide a critique of natural science being used for describing human phenomena. I outline a summary of Benedetti's (2009, 2013) understanding of placebo response and compare them to Gadamer's understanding of treatment. I conclude that placebo phenomenon appears to be a subject to be studied by human sciences.

Health, Healthy, and Healing as Part of Social Discourse

The conversation about health, healthy, and healing techniques and procedures dominates the social discourse. This preoccupation with health and healing is evident any time one is exposed to the media: internet sites, popular and scientific literature, newspapers, magazines, television programs, and radio broadcasts are full of information about healthy practices, new illnesses, and new treatment methods. The methods discussed may be either carefully researched or carried over from traditional healing practices.

Food, clothing, household and hygiene products, dishware, and furniture are covered with labels that appeal to the current ideas of what is healthy. Labels like

“organic,” “locally-grown,” “natural,” “does not contain [list whatever the unhealthy contaminant of the day here]” are found in abundance any time one opens one’s pantry or walks into a supermarket. The marketing techniques in capitalist society end up telling quite a bit about the values the society currently holds. Thus, observation of the marketing messages in modern Western society clearly illuminates the value it places on health and healing.

What Is Health and What Is Illness?

To have a conversation about placebo and placebo response, it is important to identify what constitutes health and illness. As discussed earlier in this paper, placebo response is defined as an improvement in a placebo group due to either regression to the mean, spontaneous remission, or a body’s natural ability to heal itself via some not yet identified mechanism. One would need to know what constitutes illness and what constitutes health to know how the placebo response might be helping humans to go from one condition to the other.

Gadamer’s View

In *The Enigma of Health* (2004), Gadamer provided a hermeneutic understanding of modern medical practice and healing practices in general. His work is a philosophical account of the meaning of healing. He described the embeddedness of healing practices in modern Western culture. Hermeneutics concedes the idea that there is meaning-making behind all human communications and practices. Thus, illness and methods of healing should carry meaning in each culture. Gadamer in his writings talked about the culture most familiar to him—modern Western culture—from the point of view of an elderly German citizen.

The author (Gadamer, 2004) provided an important historical overview of science and of medical practice as a subset of science. He also offered a critique of the current Western medical practice for its overreliance on natural science research model. Gadamer stated that the modern medical practice is a scientific practice and as such “requires knowledge, which means that it is obliged to treat the knowledge available at the time as complete and certain. The knowledge known from science, however, is not of this sort” (p. 4). The main assumption of scientific knowledge is that it is never final or definite. Furthermore, science, Gadamer argued, historically was not sought out for its practical applicability, “[science] understood itself . . . as pure *theoria*, that is, as knowledge sought for its own sake and not for its practical significance” (p. 4).

For Egyptian geometricians and Babylonian astronomers, knowledge accumulated from practice and was not valued apart from it. In Ancient Greece for the first time, “science and its application, theory and practice, parted ways” (Gadamer, 2004, p. 5). The “modern relation between theory and practice, which was formed by the seventeenth-century idea of science” was based on Cartesian “ideal of certainty [that] became the standard for all understanding” (p. 5). Furthermore, Gadamer stated,

Only that which could be verified could have validity as experience. In seventeenth century, experience thus ceased to be a source of starting point of knowledge but became, in the sense of ‘experiment’, a tribunal of verification before which the validity of mathematically projected laws could be confirmed or refuted. (p. 5)

In other words, Gadamer suggested here that only experience that was verified by experiment could serve as a datum for knowledge. Modern science still lives by these ideals of verifiability and testability. However, Gadamer provided an important observation—modern natural science is not “knowledge,” but a “know-how.” This,

Gadamer stated, made knowledge a practice. Know-how is an expertise on how to do something (“Know-how,” n.d.) rather than an accumulation of information on a subject.

Gadamer (2004) discussed the idea of science as an instrument of technology and its impact on human development. He particularly warned his readers to pay attention to the ethics in scientific practice. Gadamer postulated, regarding the significant pressures that science was facing in modern times,

On the one hand this leads to the emotional blindness with which a mass critique of culture reacts to these phenomena, and it is necessary to avert in time the iconoclasm which threatens from this quarter. On the other hand there is the superstitious faith in science which strengthens the technocratic unscrupulousness with which technical know-how spreads without restraint. In both respects science must carry on a kind of demythologization of itself and indeed by its very own means: critical information and methodical discipline. (p. 7)

Thus, Gadamer disclosed his concern about the rapid progress with which science was taking over our day-to-day lives. He provided two possibilities: blind following of scientific progress might lead to unquestioned spread of technology, which could be destructive to humanity. On the other hand, the society might renounce the scientific progress altogether, which consequently could be detrimental as well. Science has brought many important innovations into the modern world. Specifically when it comes to medicine and healing, modern science inventions provide an unmatched level of care for traumatic injuries and disabilities. It is unimaginable the way modern medicine can reattach torn parts of the body, safely deliver babies in the most complicated births, and bring functional artificial limbs to people, who lost theirs in traumatic accidents or in wars. Throwing away *all* of the inventions that science brings to people would not be humane. However, for Gadamer, it remained important to keep science doing what science did best—natural phenomena—and not allow it to uncontrollably permeate

human phenomena. When science does the latter, it reduces the rich and complex human experience to nuts and bolts of a mechanical machine and takes away its humanity.

Additionally, the philosopher explained his apprehension about modern science's inaccessibility. Gadamer (2004) argued that science as it was developing prior to the twentieth century was still available to the layperson or scientists from other fields via the "paths of well-organized information" (p. 8), which made it possible to partake in scientific knowledge. However, starting in the early twentieth century, the "expansion of research and its increasing specialization have led to a deluge of information which turns against itself" (p. 8). This made scientific knowledge difficult to organize and store and, therefore, difficult to access. This difficulty of access makes the scientific information privileged and scarcely available for examination by the society or other fields for ethical or political reasons. This inaccessibility of scientific knowledge was risky, Gadamer implied, as it prohibited public critique, discourse, and accountability.

It is important to note that Gadamer (2004) wrote his collection of essays, *The Enigma of Health*, in the time before the internet became as widespread as it is today in 2015. Along with the availability of internet access, scientific publications also became very accessible. Nowadays, anyone with a smartphone and internet connection can have almost any published scientific article literally at their fingertips within seconds or minutes. Some of these publications are free, although access to many may become prohibitively expensive, at \$30 or more per article. However, despite these apparent improvements in accessibility of scientific data, the difficulties remain in integration of these data and ability to analyze the data by the public. These difficulties, I agree with Gadamer, are there because of specialization of subfields. Each subfield of science

creates different jargon and different understanding of similar or sometimes the same phenomena. Thus, communication between various fields of study and integration of this information by public or even by the scientists from other subfields becomes increasingly problematic and, I agree with Gadamer, eventually impossible. Additionally, in science, the bias for publishing mostly positive results remains a big problem, leading to misrepresentation of scientific data in each subfield.

Gadamer (2004) further stated, “our progress of knowledge is subject to law of increasing specialization and, hence, to increasing obstacles to comprehensiveness” (p. 10). This directly contradicts the ultimate scientific expectation that all knowledge eventually will come together in a comprehensive theory of the world and of all living beings in it. Given Gadamer’s carefully outlined perspective on science and knowledge, however, his conclusion appears to have merit: we can expect that the more specialized each subfield of science is, the more difficult it will be to bring all of those fields together into a comprehensive whole. I argue that such a comprehensive theory, which would be capable of bringing together all of the knowledge collected by science to date, appears highly improbable given the fragmentation of knowledge that specialization created.

What further complicated things, Gadamer (2004) argued, was what he called “the institutionalization of science into a business” (p. 17). He stated, “[science] belongs to the larger context of economics and social life in the industrial age. Not only is science a business, but all the work performed in modern life is organized like a business” (p. 17).

There is the artificial creation of needs, above all by means of modern advertising. In principle what is at stake is dependence on the means of information. The consequence of this condition is that both the specialist who acquires new information and the journalist—that is, the informed informer—become social

factors in their own right. The journalist is well informed and decides how far others should be informed. The specialist presents us with an unassailable judgment. If no one other than the specialist is able to judge the specialist, and if even misadventures or mistake can be criticized only by specialists—one thinks of the ‘malpractice’ of doctors or architects—an area thereby has become in a precise sense autonomous. (p. 18)

Furthermore when it came to health and illness, Gadamer (2004) postulated, “illness is a social state of affairs. It is also a psychological-moral state of affairs, much more than a fact that is determinable from within the natural sciences” (p. 20). Therefore, in Gadamer’s opinion, the therapeutic factors are in the patients’ cooperation and the doctors’ power of persuasion. These factors are affecting an organism beyond the chemical influences of a so-called medical intervention. It is possible then to draw the conclusion that the personal qualities of a doctor and his or her talent are of great importance to the healing process. On the other hand, application of scientific knowledge should not be affected by such factors as personality and/or special talent. Scientific knowledge is expected to depend only on testable and verifiable facts. Peculiarly, Gadamer chose the following words to describe the modern attitude towards medical doctors and it is surprisingly similar to the one humans had towards their healers many centuries ago,

in spite of all the progress which the natural sciences have brought about for our knowledge of sickness and health, and in spite of the enormous expenditure on rationalized technology for diagnosis and treatment which has taken place in this area, the sphere of the unrationalized element within it is particularly high. This shows itself in the fact that even now, as in the oldest times, the idea of a good doctor or even of the medical genius has much more of the prized esteem we think characteristic of an artist than of a man of science. (p. 21)

Modern Western society highly values scientific developments and greatly relies on the knowledge and the know-how they provide. However, relying so heavily and blindly on scientific knowledge can be risky. Gadamer’s (2004) main critique of

scientific know-how is that it is hermeneutically “limited to what it must answer by its questions. This is a hermeneutic structural element of all research. In itself it is still not ‘practical’ knowledge” (p. 28). In other words, the science will only provide answers to the questions that the scientists ask. Moreover, the questions that are asked are formed within the current *cultural* and *temporal horizons* thus are not universal in their nature, but relevant only to today’s reality. Another important hermeneutical limitation is the fact that “researchers cannot always eliminate value expectations or that they will often interpret their findings under the impress of inappropriate prejudices—I am reminded again of the Darwinism in social research” (p. 29).

According to Gadamer (2004), a physician is simply a “man [sic] with a body of knowledge” (p. 31), thus his or her personal genius and talents will play a role in how he or she delivers healing. The physician would not just make somebody healthy, Gadamer stated, “Thus it must always remain an open question just how much the successful restoration of health owes to the experienced treatment of the physician and how much nature itself has assisted in the process” (p. 33). Moreover, to Gadamer, health was a natural state of equilibrium, and thus healing someone from an illness involved reestablishing the lost equilibrium. He observed that when one attempted to produce an equilibrium, then one was “thrown back, as it were, by something that is somehow self-sufficient and complete” (p. 37). Therefore, the medical field is not concerned with establishing an equilibrium of health, but instead works on “arresting and assisting” the already existing and ever shifting equilibrium (p. 37).

Physicians are facing the task of having to address the whole to achieve convalescence, because Gadamer’s equilibrium affects the wholeness of the human

experience. Moreover, Gadamer (2004) stated that the loss of such equilibrium did “not merely represent a medical-biological state of affairs, but also a life-historical and social process” (p. 42). To Gadamer, the person who has succumbed to an illness is not the same person who was there before. The ill individual loses the balance and figuratively speaking “falls out” of his or her “normal place in life” (p. 42). One of the important aspects for physicians, when keeping in mind Gadamer’s idea of equilibrium, is to “neither make patients wholly dependent on them, nor needlessly prescribe dietary or other conditions of lifestyle which would only hinder patients from returning to their own equilibrium of life” (p. 43).

There are other dangers of accepting science without question as the only means to healing. For example, Gadamer (2004) discussed the idea of objectification of bodily experiences and of the body—the same objectification that science enhanced. Scientific exploration requires the objectification, the breaking down of the whole into its parts, and a careful analysis of each separate fragment of the human body. Such objectification, Gadamer stated, “demands of all of us a violent estrangement from ourselves, irrespective of whether we are doctors, patients, or simply responsible and concerned citizens” (p. 70). He found risky this estrangement of humans from their bodies because, in his opinion, the idea of health was broader and more comparable to an equilibrium that kept both the internal physical states, emotional states, and external environments in balance. However, through the methodological procedures that the modern science brings, it objectifies the experience of living in the world. In his work, Gadamer expressed his fear of losing the greater whole by breaking it into its parts via reductionism coupled with objectification.

Etymologically, Gadamer (2004) noted, the word *health* had its origins in “the Greek experience of the world” (p. 73) and reflected the idea of “whole of being” or *holousia*. Meanwhile, the illness feels like *Es fehlt mir etwas* or “I am lacking in something” when translated from German (p. 73). Gadamer further noted that when illness was upon their bodies, humans noticed a disruption in something (health) that usually, when not disturbed, escaped human attention. In his opinion, the condition of well-being was the condition of not noticing. This is the condition of not noticing the body or equilibrium in which the body resides. Thus, the author asked the question, “what does illness tell the one who is ill? (p. 76). He then logically proceeded to ask an even more provocative question—“Can learning to ask such a question of oneself perhaps even contribute to helping the one who is ill?” (p. 76).

The fundamental fact remains that it is illness and not health which ‘objectifies’ itself, which confronts us as something opposed to us and which forces itself on us. In fact, we always describe something as a ‘case’ of illness. The German word for case is *Fall*. What does *Fall* mean here? The use of the word undoubtedly comes from the game of dice. From there it has entered into the language of grammar and the rules of declension. It refers to the role which ‘falls’ to a noun within a sentence. (The Greek for *Fall* is *ptosis*, which in Latin becomes *casus*). Similarly, illness is something which ‘befalls’ or ‘falls’ to us, something we experience as a chance or accident (*Zufall*). (p. 107)

Gadamer (2004) made another important conclusion from his careful observation of our modern culture—health was not what was observable to us. Instead, it was illness that humans were able to observe, measure, analyze, and treat. Therefore, he concluded, when medical science established standard values for health and imposed those standard values onto a healthy human being that resulted in making him or her ill. “The appeal to standard values which are derived by averaging out different empirical data and then simply applied to particular cases is inappropriate to determining health and cannot be forced upon it,” he postulated (p. 107). Gadamer further explained the reason for using

the word *inappropriate* in this case. Inappropriateness was due to health not being truly measurable for each separate individual, as it was a “condition of inner accord, of harmony with oneself that cannot be overridden by other, external forms of control” (p. 108). Consequently, one of the most important indicators of someone’s illness is their self-report of not feeling well.

The author illustrated how our use of language highlighted the importance of the inner experience that could not be measured:

The role of the doctor is to ‘treat’ or ‘handle’ the patient with care in a certain manner. The German word for treating a patient is *behandeln*, equivalent to the Latin *palpare*. It means, with the hand (*palpus*), carefully and responsively feeling the patient’s body so as to detect strains and tensions which can perhaps help to confirm or correct the patient’s own subjective localization, that is, the patient’s experience of pain. The function of pain in the living body is to register through subjective sensation a disturbance in that harmonious balance of bodily processes which constitute health. (Gadamer, 2004, p. 108)

Similarly, the word *handle* in English implies the use of hands as well. Gadamer further believed that the doctors who were able to identify the location of the pain accurately “are in possession of a true ‘art’” (p. 108). To strengthen his point, Gadamer provided a couple of examples where a doctor’s skill of identifying an anomaly in the human body without the use of supplemental devices had been admired and acknowledged as a superior skill and a true talent.

Additionally, illness does not manifest the same way in everyone. Instead, Gadamer (2004) observed, human ability to think about themselves contributed to the experience. For example, psychosomatic conditions illustrate this point quite clearly—human suffering in one’s environment (e.g., conflicts at a workplace) may translate into various somatic symptoms.

The last important factor that Gadamer (2004) identified as contributing to treatment was human “desire for authority” (p. 120). He wrote, “even in a state of perfect enlightenment we cannot ground everything we hold to be true through strict proof or conclusive deduction. Rather, we must permanently rely on something, and ultimately on someone, in whom we have trust” (p. 121). It was “genuine authority” that humans sought, he believed. This genuine authority “is recognized as involving superior knowledge, ability and insight” (p. 121). Hence, the authority of science is so important and understandable in modern medicine—it fulfils the need so perfectly. In our “scientific age” the authority of science “is grounded in the superiority of that knowledge which has been accumulated and passed on by science as an institution” (p. 122). Of course, the authority of science ultimately relies on humans conducting science.

Gadamer stated,

Now method and methodology are, in fact, the hallmark of science. But they possess a human background. The self-discipline which allows someone to keep to a method—against those inclinations, assumptions, prejudices and subjective interests which tempt all of us into believing to be true only what suits us—here claim its superior value and validity. It is on this that the true authority of science rests. . . . In truth, modern science presents an impressive embodiment of critical freedom that is to be marveled at. But we should also be aware of the human demand that is placed on all those who personally participate in this authority: the demand for self-discipline and self-criticism, and this is an ethical demand. (p. 122)

On Health, Illness, and Treatment

As summarized above, to Gadamer (2004), *health* was an equilibrium between one’s self, parts of one’s body, and his or her environment (including one’s relationships with other people and objects around a person). Thus, *illness* was an *unbalanced* state of events and a lack of equilibrium. Similarly to Gadamer, Eisenberg (1977) almost four decades earlier also noticed that doctors deal with diseases; however, the illnesses

included social aspects of diseases as well. Thus, when doctors focus on treating organs and dysfunction in organs, patients also experience the impact of disease on their states of being and social functioning (i.e., loss of equilibrium described by Gadamer).

When illness comes and the equilibrium is lost, several if not all of the person's aspects of being are affected. For instance, if someone has a common cold, they feel discomfort in various parts of their body. They often choose to stay inside as it becomes difficult or impossible to complete the simplest tasks. They are not able to talk and engage with others at the same level they could prior to the onset of their symptoms. These behaviors in turn trigger changes in the environment and the person's relationships with the world are affected. All become difficult to do: performing their jobs, carrying for their children, sustaining relationships with colleagues/peers and loved ones. The person now feels ill not only because of the physical challenges (e.g., achiness and fever), but also because many of the meaningful things in the environment qualitatively have changed.

Therefore, in accordance with Gadamer's (2004) conclusions, *treatment* is the restoration of the lost equilibrium via various approaches. Thus, treatment should and often does address the bigger picture, not only the common cold symptoms, or a broken foot, for instance. The treatment process is meaningful as we associate this process with the restoration of the lost equilibrium.

Television commercials for cold and flu remedies are a good illustration of this loss of equilibrium and of the following restoration of it by means of the advertised treatments. When people in the commercial video succumb to the common cold symptoms, they behave as if in a fog, unable to interact with their environment. They

appear disconnected from the world around them and look miserable. They are then displayed taking the advertised remedy and it provides them with the ability to talk to the coworkers again, give presentations, care for their children, etc. Visibly, the equilibrium has been restored.

Such advertisements are the products of our culture. They are *historical artifacts* as hermeneutists would say. By the virtue of being a cultural artifact, an advertisement is situated within a culture and it embodies and reflects the culture. In other words, it is meaningful to the representatives of a culture, which produced this artifact.

These commercials illustrate how the advertisers appeal to the meaning of treatment. Treatment is not just a relief from the cold symptoms. Most importantly, treatment is a reconnection with the rest of the world and feeling like oneself again. These commercials appeal to the audiences and help to sell the products because they address that which the individuals with the cold symptoms are actually seeking—restoration of equilibrium in their meaning-laden lives. The meaning of treatment, in the end, is not primarily concerned with physical well-being, but to a great extent with what the physical well-being represents.

There is another important aspect of treatment—treatment should be restoring the equilibrium and not creating a different one. Just as in the cold medicine commercial, people expect the treatment to happen without much disruption to their usual ways of being. Activities such as quickly popping a pill for a few days or drinking a tablespoon of syrup at night only minimally disrupt the person's usual way of life. Then the equilibrium is restored via reducing the flu symptoms and making one's body feel less achy or feverish. Another way of restoring the equilibrium, for instance, could be to ask

people to power through their symptoms and not miss family gatherings or important office presentations. Alternatively, one could be asked to change their environments in a way that would allow the sickness to continue while not interrupting other aspects of life. If one does not have a job to go to, then why not just stay in bed all day?

These latter options of achieving the equilibrium seem less appealing because they propose to *reset* the equilibrium itself, not to restore the previously existing one. It is the restoration of the previously existing equilibrium that people seek when they seek treatment, according to Gadamer (2004). In line with his postulates, people wish for a treatment process that would not cause significant change to their routine. The goal is to restore the equilibrium, but not to create a different one.

Additionally, people seek treatments which they are already used to and tend to associate with positive results. This idea of familiar treatments associated with positive results resembles the elements of the concept of classical conditioning. Thus, both the idea of restoring the equilibrium and the idea of classical conditioning, referenced by Benedetti (2013), appear to refer to similar processes. People seek healing methods that are meaningful to them and classical conditioning phenomenon may be contributing to creating that meaning. Through the process of classical conditioning, one builds an expectation of what is to come. Sometimes that expectation is covert, but often it is overt and, therefore, the connection between the stimulus and the response becomes meaningful for people. Thus, when certain treatments are associated with certain results, people learn to make a more conscious connection of positively associating the healing procedures with the positive results (e.g., with feeling better).

Furthermore, meaningfulness of a treatment is bound to a particular culture. In the United States, treatment options that involve taking tablets, capsules, pills, or syrups are some of the most popular. The healing ritual of taking a pill is very meaningful in mainstream U.S. culture. Most diseases, disorders, maladies, or ailments have at least one drug developed to treat them or symptoms associated with them. Representatives of the mainstream U.S. culture may find nothing unusual or noteworthy about the fact that they take pills so commonly to treat various ailments. However, not in every culture do healing rituals favor pill taking. For example in Russia (also a country with predominantly Western views), many people find a series of painful intramuscular injections to be a superior treatment for a severe cold or other ailment. They find injections to be a meaningful and powerful form of treatment. Injections are often considered more potent than pills in Russia. The treatment preferences of Americans and Russians that I described here are personal observations from the point of view of a bicultural person. To my knowledge, there are no studies that show the prevalence of injectable treatments in Russia. In my experience, injectable treatments are commonplace in Russia as a home treatment, whereas I rarely hear of such treatments outside of clinics and hospitals in the United States. This observation, of course, is debatable in absence of specific data. I provided this observation of the difference in treatment options to illustrate that even in Westernized societies mainstream treatments may vary due to cultural differences.

Bhugra and Ventriglio (2015) also acknowledged that culture influences how one perceives his or her distress or healing. Other research in the past showed that cultures sometimes attached opposite meanings to healing methods. Buckalew and Coffield

(1982) discovered that Caucasians were more likely to see white capsules as analgesics and black capsules as stimulants. However, African Americans in the same study saw black capsules as analgesics and white ones as stimulants. These variations appear to result from the differences in aspects that make up a culture at any particular historical point in time and location.

Natural Sciences Versus Human Sciences

In modern Western society, there is an accepted distinction between natural and human sciences that Gadamer (2011) alluded to in his writings. Human sciences are fields of study that explore the nature of humans, human relationships, aspects of human psyche, and individual and public relationships within human societies. Examples of human sciences are sociology, psychology, and anthropology. Natural sciences, on the other hand, deal with the matters of the material world in which humans exist. Natural sciences include fields like mathematics, physics, chemistry, biology, geology, hydrology, and dozens of other fields and subfields. Additionally, medicine and engineering are treated as scientific subfields and fall into the category of applied sciences (Ossenbrink & Stephan, 2013). They deal with specific practical applications of natural sciences like physics, chemistry, or biology for solving various issues that humans face.

Sciences have originated and triumphed in Western culture. In this culture, humans clearly label and distinguish the differences between the fields and subfields of sciences. Moreover, there are some differences between human and natural sciences that appear categorically significant and important. Specifically, there is a general sense in Western culture that human sciences are inferior to natural sciences. Even though in

Ancient Greece, all arts and sciences were equally important and worthy of pursuit, but this changed in the time of Descartes. Gadamer wrote about this shift in *The Enigma of Health* (2004). Also, Clarke (1982) wrote that Descartes had

a pivotal role in the history of this development, in the transition from a widely accepted scholastic concept of science to its complete rejection by practicing scientists and the endorsement of some kind of hypothetical, empirically based knowledge of nature. (pp. 258–259)

Since Descartes, a more positivistic approach has been cultivated in science in which experience is valid only if observable and measurable (Carnap, 1936). Certainty is now of most importance. Gadamer (2004) wrote that the truth had been reduced to certainty (p. 148). However, certainty is difficult if not impossible to achieve. Some experiences studied by human sciences are not easily observable or measurable. This makes human sciences less objectifiable, less quantifiable, and consequently presumed to be inferior to natural sciences, where subjects by their nature are more likely to be objectively measured and quantified.

In scientific discourse as well as in general public, the bias exists in favor of natural sciences. In addition, there exists a prejudice against things not quantifiable or measurable. Gadamer (2011) stated, that even when human sciences were acknowledged for producing a different kind of knowledge, one might still “describe the human sciences in a merely negative way as the ‘inexact sciences’” (p. 5). It appears as though Western culture produced not only science and scientific inquiry, but also a *cult* of science and of such scientific inquiry based on natural sciences methodology. I use the word *cult* here to describe a system of religious-like worship and ritual (“Cult,” n.d.). Usually, scientific inquiry is viewed as a way to understand and describe the world in which humans live. However, the difference between *a way* something is done and *a cult* is in the amount of

open questioning of the process. In a cult, the authority of the idol is not questioned. Similarly, Western culture rarely questions the goodness of rigid, objective scientific inquiry. There is a strong assumption, that scientific inquiry is always good and the more precision the better.

This idea of blind following of scientific ideals has already been described and critiqued. Psychotherapist and author Phil Cushman (1995) warned modern psychologists and other professionals of the risks they took when they did not question science. One of the most commonly used terms is the word *scientism* or its adjective form, *scientistic*. They describe the invasion of science into every aspect of human functioning with an exaggerated belief in the principles and methods of science (“Scientistic,” n.d.). Scientism is defined as “the belief that the assumptions, methods of research, etc., of the physical and biological sciences are equally appropriate and essential to all other disciplines, including humanities and the social sciences” (“Scientism,” n.d.).

The assumption that science is always good is not always accurate. Let us review the process of scientific inquiry in human sciences for example. When it comes to describing and measuring human phenomena, few things are easily identifiable and measurable. In natural sciences, researchers name, describe, and then measure various aspects of nature (e.g., rocks, chemical elements, electrical and magnetic forces, etc.). In human sciences, on the other hand, there are no analogous clearly identified objects of study. Hence, scientists develop constructs for which they can later develop measuring procedures. For instance, such aspects of human experience as *mind* or *emotion* cannot be easily isolated and measured. First, the construct has to be created—a word to

describe the experience. Not every human culture has words to describe these concepts—mind and emotion. When they do, the concepts would not necessarily represent the same aspects as mind and emotion do for English speakers. Thus, linguistics largely determines what is studied by the human sciences.

Social constructionists argue that human language determines human experience in general and this is not only true of human sciences (Gergen, 2009). An important fact to acknowledge is that any distinctions that humans identify between natural and human sciences are abstract and constructed by humans as a form of cultural artifact. Science accepts these constructs as hypothetical. However, mainstream Western culture as well as individual scientists often forget that these constructs are artificial and hypothetical and instead accept them as objective experiences. These constructs are meaningful in the particular way only in the given time, place, and culture. These ideas of constructed reality are described in more detail in the writings by social constructionists like Gergen (2009) and hermeneutists like Gadamer (2011) and Cushman (1995).

In Gadamer's *Truth and Method* (2011), he addressed a number of points now relevant to this study. He made a strong argument for medicine being a human science rather than a natural science. In Western society, medicine is an applied science and generally follows the natural science model. Thus, it is under the influence of the cult of science and scientific inquiry, in other words, of scientism. This metaphorical cult of science dictates that all information gathering should ascribe to the logic of natural science. Cushman (1995) stated, "the modern Western society . . . slowly developed an intense belief in rationality and the scientific practices of quantification and objectification" (p. 21). Cushman and Gadamer appear to agree that quantitative methods

of inquiry are favored in the modern Western world. Indeed, anyone can experience this favoritism by simply looking at the research section at a local library or by doing a simple internet search. One is likely to notice that the majority of textbooks and scientific publications include an abundance of quantitative data and complex statistical analyses to investigate and draw conclusions from those data.

For instance, in the fields of clinical and counseling psychology, research plays a fundamental role in establishing understanding of psychological phenomena and best clinical practices. An example of a popular research methods textbook that graduate students in psychology use is *Research Design in Counseling* by Heppner, Wampold, and Kivlighan (2008). This textbook consists of 22 chapters. Out of these, 19 have information pertaining to research methods and clarifications around such methods. The headings of these chapters do not specify what type of research methods they are. Instead, they use generic names such as: “Science and counseling,” “Research training,” “Choosing research designs,” and “Major research designs.” In Part 2 of the textbook, which is labeled “Major research designs,” there are five chapters. Four of them discuss quantitative research designs without overtly specifying that they are quantitative. However, one chapter stands out—it is named “Qualitative research.” It is of note that qualitative research methods—the research methods developed specifically for studying phenomena in human sciences—take only one fifth of the section on research designs in the textbook developed for human science graduate programs. Additionally, only this chapter in the textbook contains a subsection called “Myths and facts about qualitative research” (p. 259), which in many words outlines common misunderstandings about qualitative research. The misunderstandings outlined by the authors show the common

thread—qualitative research is less trusted and is not considered scientific enough. It is also the type of research that is usually labeled with a specifier “qualitative” in literature and textbooks. Quantitative research methods are rarely clarified with a label “quantitative,” as simply writing “research” is usually enough.

The example of the *Research Design in Counseling* textbook (Heppner et al., 2008) is only one in many and suggests that the field favors quantitative over qualitative methods and often requires that qualitative methods defend themselves and prove that they too provide valid research by having sections such as the “Myths and facts about qualitative research” in textbooks, dissertations, or scientific articles. The implicit message here is that all knowledge gathered in other ways or that is not measurable by quantitative methods is not valid or is of less value than knowledge gathered using positivistic scientific methods.

Gadamer (2011) stated, “the logical self-reflection that accompanied the development of the human sciences in the nineteenth century is wholly governed by the model of the natural sciences” (p. 3). However, human sciences, he argued, had their own logic. In the culture where natural sciences and natural-science ways prevail, however, it is difficult for human sciences to stay credible unless they succumb to the natural sciences logic.

Human science too is concerned with establishing similarities, regularities, and conformities to law which would make it possible to predict individual phenomena and processes. In the field of natural phenomena this goal cannot always be reached everywhere to the same extent, but the reason for this variation is only that sufficient data which the similarities are to be established cannot always be obtained. Thus method of meteorology is just the same as that of physics, but its data is incomplete and therefore its predictions are more uncertain. (Gadamer, 2011, pp. 3–4)

In human sciences, it appears that it is not the lack of data that creates uncertainty. Instead, the uncertainty seems to be there because it is a different dynamic system altogether. Where humans, human psyches, and behaviors are involved, there exists a great deal of uncertainty and unpredictability. Psychological theories are at best operating on low percentages of probability when predicting individual human behavior. This occurs for the simple reason that scientists cannot ever create a laboratory condition where an individual human behavior can be predicted. Humans live, breathe, and, most importantly, think at all times. It is now evident, even using limited scientific data, that humans' context creates their reality. For instance, body language of a person is a powerful communicator and has been found to not only send signals outward to the community, but also inwardly in terms of changing the person's own neurochemistry within a short time of just two minutes (Carney, Cuddy, & Yap, 2010). When a person's hormonal and neurochemical balance is changed, that person reacts and behaves differently. Modern imaging techniques are now capable of showing that the neural pathways of the brain change constantly under the influence of drugs, medications, meditation, and even conversations (i.e., psychotherapy) (Cozolino, 2010).

Human culture and social behavior consist of many individual behaviors, thoughts, and choices. This makes the system of social interaction and individual human behavior too complex and dynamic to be able to make clear predictions. Many human actions appear to be based on people's belief systems and cultural backgrounds as well as individual circumstances in the moment. Moreover, even when the current scientific understanding of human behavior is applied (i.e., things that appear observable and measurable such as changes in human biochemical makeup and brain activity), scientists

run into problems in being able to understand and predict human phenomena. This is because biochemical makeup and neural pathways in the brain and even human genes change due to not only biochemical or physical interventions but also to various contextual phenomena.

When scientists think of observable and measurable changes in physiology as a way to prove that some change in a human has occurred, they connect the observable changes to a physical or biochemical intervention that they performed. Since they do not have a way of observing, measuring, or testing a constantly changing cultural, historical, temporal, and other contextual environment, they tend not to connect the observable changes in humans to context as readily as they do with other interventions. Therefore, even when observable changes happen and are carefully measured (such as in imaging studies of placebo response), scientists are hesitant to attribute these changes to contextual factors. Benedetti (2013) warned scientists and public that even though placebo response produced measurable changes, this did not put the placebo response on the same level of efficacy as drug interventions. Moreover, efficacy of study drugs in the psychopharmaceutical studies is argued to be representative of their effectiveness in real world, so the drugs may be sold on the market. However, the same logic is not applied to placebos, and their efficacy in the clinical studies is not argued to suggest a possibility that they could be effective as a treatment in real world.

Summary of Benedetti's 2013 Review

This article, "Placebo and the New Physiology of the Doctor-Patient Relationship" (Benedetti, 2013), is one of the most complete summaries of the placebo response as it is understood by modern medicine and psychology. I provided highlights

of this article here as an attempt to give the most recent overview of the current state of research on placebo. I chose to rely on Dr. Benedetti's work as one of the most prominent experts in the field of placebo research. In this recent work, Benedetti provided a thorough synopsis of placebo research and the new understanding of placebo response as a contextual phenomenon. Benedetti (2013) wrote that the context was mediated to the large extent by the relationship with the doctor. He began his 2013 overview by identifying the term placebo and its history. Specifically, he stated that back in the 18th century placebo was first used as a comparator to identify whether mesmerism was indeed an efficacious treatment modality. This was the first time that a sham treatment successfully demonstrated that mesmerism was not what it claimed to be. Eventually, the word *sham* was replaced with the word *placebo*. Since that first official use of a sham procedure, placebo entered the world of clinical investigation as a comparator treatment for efficacy evaluation of various treatment modalities.

Benedetti (2013) next provided a summary of how placebo was used in modern science to help researchers understand the way the human brain works. The researchers used the terms placebo effect and placebo response very much interchangeably. The author identified that various aspects were influencing placebo response "such as the relationship between the doctor and his patient, the patient's expectations and needs, the patient's personality and psychological state, the severity and discomfort of the symptoms, the type of verbal instructions, the preparation characteristics, and the environment milieu" (p. 1208). Additionally, he stated that "the merits of conceptualization of the placebo effect as a mind-body phenomenon reside in the fact that it makes us understand that the placebo effect is due to the psychosocial context around

the patient and the therapy” (p. 1208). Moreover, he underlined that “when a treatment is given to a patient, be it sham or real, it is not administered in a vacuum, but in a complex set of psychological states that vary from patient to patient and from situation to situation” (p. 1208). Thus, Benedetti identified the following contextual pieces that influenced placebo response: “words by doctors and medical personnel,” “sight of health professionals, hospitals, and medical instruments,” “interactions with other patients and people,” “touched by needles and other devices,” “color, shape, smell and taste of medications” (p. 1209). It appeared that the author recognized that symbolisms and rituals mediate placebo response.

Benedetti (2013) further discussed other changes that may be confused with placebo response, such as regression to the mean, natural history of the disease, unidentified co-interventions, and biases of patients and healers. Overall, the author provided the following breakdown of what placebo response was made of when used as a comparator to active treatment: natural history (i.e., spontaneous remission), regression to the mean, co-interventions, experimenter’s and patient’s biases, and psychobiological factors (p. 1210). The combination of all or some of the above leads to clinical improvement when placebo is administered. The author acknowledged that because these variables constituting placebo response were not controlled for in clinical trials, clinical trials were not a good way for understanding placebo response.

Next, Benedetti (2013) discussed the effect of the doctor-patient relationship on placebo response. He made an argument for the evolutionary nature of grooming behaviors, where both the groomer and the groomed (i.e., the healer and the patient) were genetically predisposed to feel the benefits of the process and changed in response to the

grooming. The biological changes identified via MRI studies showed the patient's response in expectations, trust, and hope when the patient met his or her doctor. The doctor's brain also showed changes that involved activation of empathy and compassion. Additionally, the author discussed auditory/language systems that affected one's placebo response. Specifically, using reassuring language, as his earlier research had shown, produced considerably stronger placebo response (Benedetti, 2002). Humans additionally took into consideration the facial expression of their healers (e.g., medical personnel), eye contact, gestures, and touch, with all influencing improvement. Benedetti stressed that trust and hope were activated in response to the above factors and "these, in turn, lead to expectations and beliefs, which represent some of the principal elements involved in placebo response" (p. 1216). Benedetti explained the participation of various brain areas in those processes and particularly underscored the involvement of amygdala in trust assessment.

Benedetti reviewed an additional aspect of placebo response as a meaning response in the 2013 article. Specifically, he provided an example of a postoperative pain experience as compared to a cancer pain experience. People reported that cancer pain was more unpleasant than postoperative pain. The researchers identified the reason for the difference in experience as the difference in attribution of meaning: cancer pain meant death and postoperative pain meant healing (p. 1218). He admitted, however, that the researchers still did not know what mechanisms of placebo response took place and under what conditions.

It appeared from the research, Benedetti (2013) concluded, that placebo response involved classical conditioning and expectation as some of the primary driving factors.

However, the author did not explain how those were involved in nocebo response and in situations where no previous conditioning occurred. There is some evidence that certain personalities are more susceptible to placebo response. However, the author did not discuss why sometimes the same person might respond or not respond to placebo, making the scientific identification of placebo response mediators very difficult.

Benedetti (2013) additionally discussed the idea of nocebo effect or worsening of one's condition based on the expectations derived from the meaning. For example, the author stated that "negative diagnoses may lead to amplification of pain intensity" as well as to "unwanted side effects" or to reduced "efficacy of some treatments" (p. 1226). Interestingly, even the known efficacious treatments or known powerful drug effects lost their potency when the expectation of receiving those treatments or drugs was removed or reduced. Specifically, Benedetti provided examples of pain not subsiding as expected when morphine was administered if the patient was not aware of the drug administration (p. 1235). Similarly, the cocaine addicts had an increase in glucose metabolism in response to methylphenidate smaller by almost 50% when they were told that it was not the drug, but placebo (p. 1233).

Benedetti (2013) acknowledged the placebo response being "activated by social stimuli and therapeutic rituals on one hand and by drugs on the other" (p. 1236). He also underlined the important observation that all of the drugs introduced to patients worked because there were already neural receptors in place that could be activated (p. 1236). This means that the human body already has the neuronal pathways that are activated internally using the self-produced neurotransmitters within the chemically closed system in the absence of externally introduced chemicals.

Moreover, Benedetti (2013) stated, “drugs are not injected into a vacuum but into a complex living organism that has expectations and beliefs” (p. 1236). It is not known to science “whether therapeutic rituals can indeed modify a receptor, so as to change the drug-receptor binding properties,” but the author also noted that this “seems unlikely as far as we know today” (p. 1236). He then continued to explain that, according to current research, even though drugs and rituals might “use the same type of receptors,” the “receptorial pathways are independent from each other, being located in different areas of the brain” (p. 1236). Furthermore, placebo response might be heavily dependent on prefrontal cortex functioning, as Benedetti’s own study showed reduction in placebo response in patients with Alzheimer’s disease (Benedetti et al., 2006).

Further, Benedetti (2013) described how placebo response might be manipulated in the lab and that both placebo responders and placebo nonresponders could be created in a lab setting (p. 1237). For example, placebo analgesia was more robust after first preconditioning with a real analgesic agent (p. 1237). It appeared that “placebo responses were found to be affected by learning” and, more interestingly, they were also comparably affected by social learning (p. 1237).

In conclusion, Benedetti’s (2013) summary article provided the most comprehensive and most up-to-date scientific overview of placebo response phenomenon, touching on its history, implementation, and the current theories of placebo’s mechanism of action. He additionally mentioned the ethical considerations for using placebo and creating placebo responders and nonresponders in both medicine and pharmacological research. Benedetti appeared to view placebo as an interesting phenomenon that was useful for medical research and neuroscience, but which use in

healing was ethically questionable. He specifically warned of the dangers of “bizarre” therapies that some could justify as techniques that induced placebo effect.

Nonetheless, Benedetti (2013) acknowledged the significance of placebo effect as a response to the bedside manner and additionally expressed the hope that this knowledge could be used by health professionals to “boost” their “empathic, humane, and compassionate behavior further” (p. 1238). Furthermore, he also stated, “understanding the physiological underpinnings of the doctor-patient relationship will lead to better medical practice and clinical profession, as well as to better social/communication skills and health policy” (p. 1238). At the end of the article, Benedetti made an important observation that by connecting placebo response to the tangible and observable neurological and physiological changes, science also risked sending the wrong message that placebo was somehow equivalent to other traditional medicines (i.e., pharmacological treatments). He suspected that such a conclusion could be made by the general public and the media, and that therefore the scientific community should insure proper communication between science, ethics, and the media.

Benedetti (2013) identified the following seven factors that might be contributing to clinical improvement in the presence of placebo or sham treatment: “expectation-modulated anxiety, expectation of reward, learning-reinforced expectations, social learning, Pavlovian conditioning, personality traits, genetics” (p. 1220). I conclude that if these factors indeed play a role in a person’s clinical improvement while in the presence of placebo, these same factors must also be contributing to a person’s improvement in the presence of a proven medical treatment. Thus, Benedetti’s strong opposition to the use of placebo as a form of treatment is almost surprising. In his writings, he defended the use

of drugs, because their efficacy was evident through measurable biochemical changes. On the other hand, placebo response was equally measurable, yet placebo efficacy was questioned as a potential form of treatment. Such contradictory opinion is understandable, if one is working within a narrower scientific worldview. Scientific approach does not question the validity of natural science methodology. Moreover, it questions the validity of experience that is not confirmed directly by empirical research. Gadamer (2004) also pointed out this questioning of validity of experience. Since there is no strong generally accepted scientific hypothesis that explains how exactly placebos work in an organism, the experience is dismissed as unscientific and of questionable value.

Gadamer Versus Benedetti on Healing

In this section, I provide a comparison between Gadamer's and Benedetti's assumptions about healing. It is difficult to compare the philosopher's and the scientist's views on placebo response directly. Gadamer never discussed placebo at length in his writings. Correspondingly, Benedetti did not focus his work directly on the process of healing. Therefore, I compared the assumptions that both made about the processes of health, illness, and healing/treatment and drew my conclusions based on this comparison. As stated earlier in my work, Benedetti's views are to represent mainstream Western medicine views.

As seen in Table 1, there were differences in the way Gadamer and Benedetti viewed health and medical treatment, and similarities in the way they viewed illness. To Gadamer, health was the state of equilibrium between body, mind, and environment of a person. To Gadamer the experience of health went unnoticed. It was the experience of

illness that would make humans notice that something was “off.” To Benedetti, health was simply a lack of disease. The disease in Western medicine is typically identified via a set of measurements by medical doctors such as blood tests or X-rays to identify any abnormality as compared to standard (aka normal) set of values.

Illness to Gadamer (2004) was a loss of equilibrium: a sense of being off balance between the body, mind, and/or environment—a subjective experience. Moreover, Gadamer also stated that illness was a social and psychological moral state of affairs (p. 20). On the other hand, illness to Benedetti (2013) was similarly a state of feeling sick (subjective experience), where both the physical sensations of discomfort and psychological interpretation of the sensations were at play. However, Benedetti never put significance on the role of society in illness.

Medical treatment or, in other words, healing was viewed differently by Gadamer and Benedetti. Gadamer (2004) believed that treatment included meaningful rituals and a process of meaning-making. Benedetti (2013) wrote that medical treatment context included rituals such as sight of medical environment and personnel, words spoken by doctors, touch, taste and smell of medications, and interactions with other people. Benedetti stressed in his writings that the context described above was influencing treatment, but never constituted treatment. Moreover, he stated that “the very act of administering a treatment is a psychological and social event that is sometimes capable of inhibiting a symptom such as pain, even though the treatment is fake” (Benedetti, 2013, p. 1213). Therefore, I concluded that a real treatment to Benedetti was only an active treatment. Placebo would never constitute a true treatment to Benedetti. However, based on Gadamer’s assumptions about treatment, placebo could constitute a true treatment.

There were both similarities and some differences in the way the two men saw aspects of healing/treatment. Trust was something that both Gadamer and Benedetti agreed was a necessary part of healing. Gadamer (2004) called this aspect “authority” and described a need humans had to have someone they could trust. They needed someone who would have “superior knowledge, ability and insight” because alone one human was not capable of having the necessary knowledge and ability to heal (p. 121). Unlike Gadamer, Benedetti (2013) viewed trust as an evolutionary adaptation of species to live as a social group and help each other.

Context was an important part of healing to both Gadamer and Benedetti. However, Gadamer (2004) considered culture or cultural-historical context as the primary setting in which healing occurred and from which healing was, essentially, made. To Benedetti (2013), psychosocial context, personal expectations, and Pavlovian conditioning constituted context that influenced therapy.

Both authors believed that beliefs and expectations influenced healing. The beliefs and expectations that Gadamer referred to were part of culture-specific beliefs and expectations. To Benedetti, those were personal beliefs, expectations, and memories of previous treatment experiences. Benedetti did not place a significant role on cultural context and social consciousness, but instead focused on cognitions of a specific individual.

Doctor-patient relationship was another important aspect of healing that both Gadamer and Benedetti identified. Gadamer (2004) viewed doctor-patient relationship as a place where the important meaning-making that constituted healing took place. Authority, words, concepts, and care that doctors shared with their patients provided

healing. Benedetti, on the other hand, believed that experimenter's (a form of doctor) and patient's biases contributed to clinical improvement following placebo administration. He also stated that doctors' words of reassurance and the trust patients placed in doctors contributed to healing outcomes. Nonetheless, Benedetti's (2013) words (i.e., "biases") suggested that he believed improvement associated with doctor-patient relationship to be important and yet not the main aspect of healing. There was negative connotation in the words he chose to describe improvement following placebo administration, which suggested his own bias against placebo as a true treatment.

In conclusion, there were many similarities in Gadamer's and Benedetti's views about healing. Specifically, they both considered context an important part contributing to improvement. However, one of the most important differences between their assumptions was the value they placed on cultural-historical context. To Gadamer, such context constituted the place where and through which healing occurred. To Benedetti, social-cultural or historical aspects were of no significance as he placed value only on individual beliefs, attitudes, and previous experiences.

Table 1
Differences and Similarities Between Gadamer's and Benedetti's Assumptions

Health, Illness, and Treatment	Gadamer	Benedetti
Health	Unobservable state of equilibrium in the absence of illness, a balance between environment, body, and mind (Gadamer, 2004)	Lack of disease
Illness	Loss of the equilibrium, some sort of unbalance in body, mind, and/or environment. It is also a social and psychological moral state of affairs (Gadamer, 2004)	Illness (feeling sick)—bottom-up processing (detection of sensory stimuli), top-down modulation (psychological influences) and seeking relief (motivation to suppress discomfort, reward mechanisms) (Benedetti, 2013, p. 1213)
Medical treatment	Includes meaningful rituals conducted by doctors and/or caregivers who are trusted as authority that can restore the equilibrium. Treatment is culture-specific. It includes cultural-historical beliefs about health, illness, and healing rituals and utilizes words, sight, touch, smell, beliefs, expectations, interactions with other people, being subjected to procedures, etc. (Gadamer, 2004)	Medical treatment is administration of active treatment Medical treatment <i>context</i> includes: Sight, words, touch, smell of medications, medical personnel, and clinical environment (Benedetti, 2009) Personal beliefs & expectations, memories about previous treatments, interactions with other people, in addition to sight, words, touch, smell (Benedetti, 2013)
Aspects of healing/treatment		
Authority/Trust	Authority is an important aspect of healing/treatment. One needs to subject him/herself to authority of “superior knowledge, ability and insight” (Gadamer, 2004, p. 121)	Trust is an important aspect of placebo effect (Benedetti, 2009, p. 52)
Context	Culture is an important context for meaning-making and therefore for healing (Gadamer, 2004)	Psychosocial context of medical treatment plus expectations and/or conditioning are important parts of therapy (Benedetti, 2009)
Beliefs and expectations	Healing rituals and beliefs are culture-specific (Gadamer, 2004)	Personal beliefs and expectations, memories about previous treatment (Benedetti, 2013, p. 1209) along with social learning (p. 1220) are important aspects of placebo effect
Doctor-patient relationship	Meaning-making essential for healing occurs between doctor and patient (Gadamer, 2004)	Experimenter's and patient's biases contribute to clinical improvement following placebo administration (Benedetti, 2013, p. 1210) “The very act of administering a treatment is a psychological and social event that is sometimes capable of inhibiting a symptom such as pain, even though the treatment is fake” (Benedetti, 2013, p. 1213)

Placebo Phenomenon as a Human Science Subject

Both human sciences and natural sciences are interested in studying placebo response and/or utilizing it in some fashion. Benedetti (2009) referred to psychologists and clinical researchers (who are usually medical doctors such as psychiatrists) both playing a role in advancing placebo research. However, they appear to define placebo somewhat differently, albeit still inconsistently, with the former group understanding placebo response as a psychological phenomenon and the latter group thinking of placebo response as a composite of various factors such as regression to the mean, classical conditioning, spontaneous response, etc. More about this difference in definition is discussed in the final chapter of this dissertation.

Placebo response in psychopharmacological research is a comparator to a medication effect. Thus, it falls in the same category of phenomena as the natural sciences-based applied science of medicine. For the clinical research community in the setting of medical research, placebo phenomenon is implied to be of natural science and thus is treated as a natural science occurrence. As I argued earlier in the section On Health, Illness and Treatment, medicine as a scientific field fits better in the human science category than in natural science, because so much of its healing depends on the relationship between the doctor and the patient. Therefore, I conclude that placebo response should also be treated as a human science occurrence.

Summary

In this chapter, I discussed the ideas of health and illness as presented by Gadamer in his book *The Enigma of Health* (2004). I illustrated that health, illness, and healing were an important topic of public discourse in modern Western culture. I further

provided a summary of Gadamer's essays discussing the nuances of health, illness, and healing from hermeneutic point of view. Gadamer offered his view on health as the state of equilibrium of mind, body, and environment of a human. He compared it to a sense of balance, a sense of not being disturbed, and a state of "not noticing." He equated a state of illness to loss of such equilibrium—a state when humans would notice that something was off-balance, or something was bothering them. Further, he concluded, a healing process would be a meaningful set of rituals enlisted to restore the lost equilibrium. From a hermeneutic point of view, restoration of the equilibrium would consist of rituals that were meaningful in a specific cultural-historical space and were delivered by some form of authority. Gadamer pointed out that authority was an important aspect of healing. Thus, healers had been individuals who received great respect from their communities at all times.

Gadamer (2004) stated that natural science model prevailed in conceptualizing health, illness, and healing, and he provided the historical reasons for this. Conventional Western medicine, backed by scientific research methods, provided both the meaningful rituals of healing (i.e., pill taking, exams at doctors' offices) as well as the necessary authority—science. Gadamer outlined his critique of overreliance on science when it came to healing as it brought dehumanization and objectification to the process. He demonstrated the importance of humanness in illness and healing experiences and stressed the fact that science did not make someone a good doctor, but certain talent and personal genius did. He believed that conventional medicine based on natural science model could do great things for treating physical injuries, but by itself was less equipped to deal with healing as the restoration of the equilibrium. He pointed out that medicine

should not be conceptualized as a natural science, but instead should be treated as human science. I further explored the idea of human sciences and contrasted it with the natural science model that had prevailed in medicine.

Further, I provided a summary of placebo response understanding and its use in healing as viewed by Benedetti (2013), one of the leading experts on placebo research in modern Western science. Benedetti, acknowledged the inconsistency of placebo response definition in scientific literature and clinical research. He stated that placebo response and placebo effect had been used interchangeably in research. Additionally, for the purposes of clinical research, scientists identified placebo response as consisting of five contextual elements—words of doctors and staff, sight of medical staff and instruments, interacting with staff and other patients, being touched by medical devices and needles, and medicaments' color, shape, smell, and taste. He made a strong case for importance of doctor-patient relationship in healing. Benedetti also stressed the significance of meaning that patients gave to their experiences that would shape their experience of healing. He acknowledged that many contextual and personal meaning aspects shaped placebo response in patients. I observed that the meaningful contextual pieces that Benedetti identified seemed to resonate with Gadamer's meaningful rituals and authority necessary for healing. Nonetheless, for Benedetti as he indicated in his writings, placebo remained an interesting phenomenon that was useful to study and to implement as a booster in active medical interventions by enhancing the contextual and meaning-laden aspects of patient healing. He strongly opposed the use of placebo as a separate healing method in its own right.

I further presented evidence for considering placebo phenomenon a human science subject rather than a natural science subject. I made that conclusion based on the observation that contextual elements appeared to constitute placebo response. Many of these contextual elements were dependent on human culture, history, and attitudes. I further stated that psychopharmacological industry had been treating this phenomenon as a natural science phenomenon similarly to the rest of medical interventions.

Discussion

Why Science Is So Culturally Relevant

Modern Western society is embedded in a culture of perpetual anxiety. This may seem like a strong statement until we observe how much we worry about our survival and well-being at all times. This preoccupation with avoidance of harm is evident when one notices the kind of laws humans in this society pass, the type of messages they give to each other and to their children, and even the way they advertise products. The emphasis on safety and health is strong.

It would logically follow that a society as anxious as ours needs a lot of reassurances, a lot of certainty, and a lot of authority that Gadamer discussed in *The Enigma of Health* (2004) to help soothe its anxiety. Understandably, science takes on the role of such an authority that can provide an illusion of certainty, logic, predictability, and ability to answer questions that humans are facing. When we observe this cultural process from a hermeneutic point of view a so-called hermeneutic circle predictably appears: the anxious society constructs a method for soothing its anxiety (i.e., science). However, science, being the product of the anxious society, asks and answers questions that perpetuate the anxiety rather than only soothe it. Thus a treatment created to deal with one disorder, inevitably is criticized for risks it poses for creating another disorder or a side effect. Now the society is worried not only about the disorder, but also about the risks its treatment poses. Thus, science often does not eliminate fears, but multiplies them instead.

Despite the circular nature of science in modern Western culture, it provides answers and a feeling of certainty, which are reassuring and calming (at least temporarily) to the people in this culture.

Placebo Defined Contextually

Researchers in the Western scientific community have extensively studied placebo response, which is often called placebo effect in the literature. They widely used the phenomenon to prove efficacy of medications and to better understand various neuropsychological mechanisms (Benedetti, 2009). Additionally, many researchers attempted to understand the placebo response itself. One of the predominant hypotheses used to understand placebo response included an idea that there existed a certain number of placebo responders, people who were more likely to respond to placebo. With time, that hypothesis became weaker as evidence suggested that placebo responders were not a consistent group of individuals. In fact, the same individual might respond to placebo in one study and not respond in another (Hoffman, Harrington, & Fields, 2005, p. 255) and placebo responders and nonresponders could be created in a lab setting (Benedetti, 2013). In recent years, understanding of placebo has taken a new turn where placebo response is viewed as a contextual state-based phenomenon (Kong et al., 2013) rather than a trait-based phenomenon as previously hypothesized.

The new understanding of placebo response emphasizes the importance of context and minimizes the contribution of personal traits. The new hypothesis appears more beneficial in explaining certain inconsistencies. For instance, the state-based hypothesis can explain the difficulties that the researchers encounter when using placebo in double-blind studies or in studies of the placebo response itself. The state-based hypothesis does

this in a way that the trait-based hypothesis could not. Hoffman et al. (2005) stated, “the fact that we see such variation in the percentages of responders across different studies further underscores the need for more research designed to tease out the contextual and other factors that affect the likelihood of a response” (p. 255). Based on the wording Hoffman and colleagues used, it was evident that they continued to view placebo response as a phenomenon which was interwoven with the contextual variables rather than itself created by those variables.

Medical and psychopharmacological research are applied sciences that are governed by natural science ideals and logic. Therefore, these ideals and logic predominate in the hypotheses and the assumptions made by researchers in medicine and psychopharmacology. This logic was apparent throughout the Benedetti’s writings (Benedetti, 2009, 2013) even when he endorsed the idea that context and relationship with the treatment personnel were important contributors to a patient’s recovery. Even though he admitted that context and relationships were important, Benedetti still viewed those factors as contributing to placebo response and not as factors that were responsible for creating the placebo response.

The theme that dominates the scientific literature on placebo response is that layers of context can be peeled away to reveal the kernel that is placebo response. Presumably, what is to be revealed is a psychobiological phenomenon representing the innate ability of human mind to heal the mind and body. However, there is no evidence that such a kernel actually exists. The idea appears to be based on a natural sciences presumption that everything can always be broken into its constituting parts and then further into smaller and smaller parts that constitute the constituting parts. However,

based on a hermeneutic understanding of context, under the layers there are only more layers and no kernel. From hermeneutical point of view, the layers themselves are valuable. The layers of context or the layers of meaning are what make up human understanding of the world and the humans in it. Thus, I consider the contextual nature of placebo response to be like an onion. One can peel away the onion's layers one after another and reveal nothing in the end. There will be no onion left. From a scientific point of view, on the other hand, one could see placebo response as an artichoke where underneath all of the layers there can be found a heart.

The presumption that the smaller constituting parts exist follows the usual natural sciences logic. In natural sciences, this presumption, indeed, is very helpful. It is a presumption that allows scientists to identify key phenomena (i.e., independent variables) and how they are affected by numerous identifiable confounding variables. This presumption helps to understand physical phenomena and to explain how the physical world around us functions. For example, humans have benefited greatly from science: they build better shelters, produce more food, are able to tell what food is safe to eat and what water is safe to drink. Nevertheless, I argue, based on Gadamer's (2004) view of human sciences, medicine, illness, and treatment that placebo response belongs in the category of human sciences along with medicine.

Even though human sciences are forced to follow the logic of natural sciences, it is rarely possible to do so. Human phenomena, particularly those that are to do with psychology and relationships, have poor predictability. In accordance with natural sciences model, psychology and even medicine both operate on probabilities and statistical chances. Treatments of various psychological and medical conditions typically

have percentage rates associated with them, with best treatment practices having most data supporting their efficacy. The idea of empirically-based practice is based on the natural science principles. However, this logic is not always best for treatment of specific individuals. If most people are helped by a specific treatment, there is no guarantee that a specific individual at the doctor's office will be helped by this treatment. In home improvement, however, the natural science logic works perfectly—if a special waterproof coating covers a roof, it will deflect water no matter to what roof or who applies the coating.

Conclusions of This Study

Science and scientific method are attractive as means of gaining knowledge in the modern world. One of the reasons for popularity of science is its supposed neutrality and impartiality. Other forms of knowledge gaining and research methods (e.g., case studies and qualitative research methods) often have to prove that they too are valid options for research as they are scrupulously compared to the natural science model. These other methods are often accused of not being neutral enough. However, the assumption that natural science model is neutral or impartial is false. Even though it aspires to be impartial, scientific research is done by people and is designed to answer questions posed by people. Since people are always embedded in their culture, they carry within them their systems of values and meaning-making. Scientists cannot be completely impartial: the topics they study and questions they pose for their research are all dictated by the values scientists hold as individuals as well as cultural values that they perpetuate by being embedded in the culture.

The drug-taking and scientific research-oriented culture has been created by people in the West and has perpetuated itself over the past decades. Placebos in the pill form are sometimes found to be just as effective as medications (Howick et al., 2013).

One of the major legal changes that had an effect on the U.S. culture is the law allowing for direct-to-consumer advertisement of prescription medications. The therapeutic effect has been rising in both the placebo groups as well as in the active medication groups during clinical trials (Biegler, 2014; Walsh et al., 2002) since the implementation of the law. Study by Kamenica, Naclerio, and Malani (2013) showed that exposure to brand-name advertisement can increase the efficacy of a medication measured on the physiological level. Additionally, researchers acknowledged that the consumers were led to believe that the medications were well-researched and were superior to previously trusted treatments Biegler. Additionally, He (2015) stated that such advertisement methods were misleading to the public and thus were harmful. I argue that the reason why people believe the direct-to-consumer advertisement and have an increased expectation of the power of medications is due to the scientific methods being part of the Western culture. Thus, any association with research, research methods, study, or tests taps into the general cultural understanding that these methods are what bring healing.

In the context of double-blind psychopharmacological studies, most of the time placebos are taken in the form of a pill. Therefore, the same cultural values, meanings, and expectations apply to the placebos as they do to medications described above. Additionally, culture-wide belief in scientific method and expectations of superiority of science must affect research participants during psychopharmacological trials. During a

study, research participants are constantly surrounded by the meaning-laden context of “research,” “researchers,” “science,” “scientists,” “study,” “study doctor,” “medication” and various other meaningful terms associated with science and research.

Context is larger than what clinical researchers assume. Benedetti (2013) and clinical researchers concluded that context consisted of the following typical variables: “words by doctors and personnel,” “color, shape, smell and taste of medications,” “sight of health professionals, hospitals and medical instruments,” “interaction with other patients and people,” “touched by needles and other devices,” “personal beliefs and expectations,” and “memories about previous therapies” (p. 1209). However, I argue that context is greater than what researchers can account for using positivistic approach. Historically, people of the West have been living in a culture (i.e., context) that predisposed them for believing in authority of science, superiority of quantitative research, and trustworthiness of medications developed by scientists. This is in addition to any individual cultural-historical systems of belief that each person carries with them. Positivistic research cannot isolate or account for each one of these pieces that constitute the greater context. Additionally, there is no way to predict how each one of the above variables would affect a specific individual, because it is not known what meaning an individual assigns to each of them.

Gadamer (2004) as well as other modern researchers (Bhugra & Ventriglio, 2015) suggested that culture played a large role in healing and specifically in placebo response. I believe culture therefore constitutes part of the context. Culture is a set of beliefs and practices in any given place and time. Many of such beliefs are not conscious. They are also dynamic and continue to change with time and be influenced by outside and inside

forces. For instance, the mainstream Western culture's belief in scientific approach to exploring the world is both a conscious and an unconscious occurrence. People are driven to scientific methods because they consider them superior to other methods of knowledge gathering. In fact, the belief in scientific approach is so strong that simply an association with the scientific process produces a halo effect. This blind belief in the superiority of scientific method has been often used by marketing specialists. The belief in superiority of scientific approach can be easily illustrated by an advertising example. The marketing specialists appeal to the belief in superiority of scientific method by stating in their advertisement videos and marketing spiels that the products have undergone studies, research, and/or tests. They state this even in instances where there is no evidence that such studies were conducted in accordance with best research practices. They appeal to the society's belief in science, because appealing to it works for selling products. They do not have to produce credible research to be able to appeal to the belief. In most instances where government regulations do not require a specific standard for research, marketing specialists are free to mention any testing of a product to the potential customers. There is no need to explain who exactly the researchers were, what their credentials and expertise are, and how specifically they conducted their tests. Just mentioning the fact that the product was tested by researchers produces the halo effect.

Strictly positivistic approach is not appropriate for practicing medicine. As outlined in the previous section, placebo response belongs in the general category of healing along with medicine. If the goal of medicine is to produce the best clinical outcomes and make people feel better, then the medical field should not be benefiting from the positivistic approach alone. Medicine is an applied science, which gathers

important knowledge from various fields of natural science like biology, chemistry, physics, etc. However, medicine could also benefit more from humanities and from less emphasis on the positivistic approach. Because medicine deals with diseases that are embedded in humans and in human nature, it is under the influence of the ever-changing cultural dynamics. It is important to apply scientific research methods to treatment, but it is inappropriate to consider the humanness of the healing experience inferior or less important than the scientifically supported treatments. Within their positivistic framework, Bhugra and Ventriglio (2015) and Benedetti (2013) agreed that paying attention to the patient's culture and to the doctor-patient relationship were both important for promoting best healing practices. I argue that studying culture and relationships should not be treated as another positivistic venture in isolating patterns and probabilities. Perhaps, a qualitative research approach to these aspects would be more beneficial than another quantitative inquiry that is likely to produce less meaningful numbers. Similarly, a qualitative approach to healing by medicine might also prove beneficial—connecting with the individual story of each patient might allow doctors to find treatment methods that are more likely to help a specific individual.

Context influences humans on a biological level. It is difficult to overestimate the importance of culture and context. Humans are greatly influenced by context. Moreover, as hermeneutic approach suggests, they create the context and are, in fact, embedded in the context that they create, thus creating a hermeneutic circle. The context consists of the humans' own thought processes, ideas, beliefs, and conscious and unconscious influences of ever-changing culture. A human's physiology is constantly undergoing changes throughout lifetime: blood sugars fluctuate, blood pressure and heart

beat change depending on activity and time of day, hormonal levels vary due to food intake, emotional responses, and even due to body postures minute to minute (Carney et al., 2010). Both thoughts and behaviors influence human physiology, increasing and decreasing the neurochemicals in their brains and hormones in their bodies.

Conversations and relationships with other people influence physiology as well (Cozolino, 2010). If Western doctors measure healing and illness by the biochemistry of the body, because that is what can be measured with their instruments, it is irrational to conclude that only biologically-based and scientifically-tested treatments are capable of producing healing. There is abundant evidence to show that other contextual elements are capable of producing biochemical changes (Carney et al., 2010; Cozolino, 2010).

Another strong example of the context influencing patients' healing experience is the recent study by Read, Cartwright, Gibson, Shiels, and Magliano (2015). They conducted a survey of 1827 adults from New Zealand, which revealed interesting findings about people's beliefs surrounding their depression and the self-reported effectiveness of their antidepressant medications. Specifically, Read and his colleagues found a positive association between reported effectiveness of the medications and the responders' belief in the biogenetic etiology of depression. Similarly, there was a positive correlation between the quality of the relationship with the prescribing doctor and the respondents' belief in the chemical imbalance as a cause of the depression. Curiously, the researchers in this study also found a negative correlation between the quality of the relationship with the prescribing doctor and the belief that unemployment was the cause of the respondents' depression. These findings appear to suggest that a positive association with a person of science (i.e., the prescribing doctor) makes one more

susceptible to view one's illness through a lens of scientific explanations rather than circumstantial or contextual ones. Additionally, findings of Read et al. suggested that personal beliefs affected how one perceived his or her improvement and supported the idea that personal understanding of cause and effect of illness might determine how well someone responded to the active treatment. Though this study's findings may not be fully generalizable to the rest of the world's population, the study had a rather large sample of people who were indoctrinated into the Western medicine approach and thus could reveal a trend that might be expected in the patients in other Westernized countries such as the United States of America.

Cultures determine cognitive schema and interpretation of symbols of relevance and importance within that culture. This is the crux of understanding placebo response. However, this aspect of placebo response must be seen in the context of how patients perceive their illness experience—what names and explanatory models they give to it, but also the actual therapeutic communication and encounter. (Bhugra & Ventriglio, 2015, p. 1)

Placebo response is a contextual phenomenon. Based on Gadamer's (2004) understanding of healing and illness, it appears that placebo response is a phenomenon of restoration of the equilibrium that is created by context. Gadamer stated that healing from an illness occurred through engaging in meaningful rituals that people associated with healing. To Gadamer, health was an absence of illness and thus a state of the equilibrium of all systems (i.e., mind, body, and environment being in balance). Illness, on the other hand, was a loss of such an equilibrium. Therefore, healing needed to focus on the restoration of the lost equilibrium and bring all systems back in balance. Taking a pill in Western culture is a meaningful healing ritual. Therefore, placebo response that follows taking a placebo pill is a healing response, because it is a meaningful healing ritual which brings about the restoration of the equilibrium. Moerman and Jonas (2002)

also observed that placebo response was a meaning response. Bhugra and Ventriglio (2015) noted that “placebo response must be seen in the context of how patients perceive their illness experiences—what names and explanatory models they give to it, but also the actual therapeutic communications and encounter” (p. 1). Many if not most illnesses are affected by contextual circumstances, because humans live in a meaning-laden world. Notably, Miller, Colloca, and Kaptchuk (2009) argued that placebos affected the illness rather than the disease:

Disease consists of biological dysfunction of the human organism—the primary focus of diagnosis and treatment within biomedicine. Illness is the experience of detriments to health, including the symptomatic manifestation of disease. Disease adversely affects the organism; illness adversely affects the person. The body is the locus of both disease and illness; however, the impact on the body is understood differently in these two domains. Disease is understood scientifically in terms of pathophysiology; illness is understood phenomenologically, as lived experience. (p. 5)

This is supportive of the idea that placebo response is an equilibrium-restoring experience using Gadamer’s terminology.

Bhugra and Ventriglio (2015) talked about expectations and speculated that what the doctor provided to patients was meaning: “the key is what meaning patients give to their experiences and distress which are culturally influenced” (p. 2).

I argue that placebo response is not simply influenced by various contextual variables, as the medical field might see it. Instead, it appears that placebo response is likely *created* by the individual as well as his or her historical context. Moreover, these contextual variables that participate in creating placebo response are likely too numerous and too dynamic to be able to account for using positivistic approach. Perhaps chaos theory, as it was proposed for social sciences by Kiel and Elliott (1997), is a way to deal with nonlinearity and uncertainty of human phenomena. The chaos theory and its

potential application are too complex to be addressed at length by this theoretical exploration and fall outside the scope of this study. Therefore, exploration of the complex systems theory is not done in this contextual exploration of placebo response definition and application to double-blind psychopharmacological studies. The relationship of placebo phenomenon and chaos theory (also known as complex systems theory) needs to be addressed by future research.

Implications for Double-Blind Psychopharmacological Studies

Some researchers suggested that clinical research studies could produce better data by introducing treatment context similar to the one that existed in clinical practice (Severus et al., 2012). Specifically, Severus and colleagues suggested that by setting an expectation for the study participants that they were guaranteed to eventually receive active treatment (i.e., receive regular-type medical care), researchers could improve the placebo outcomes of the studies. In my working within the psychopharmacological research industry, I learned from experience as a certified clinical research coordinator that many clinical trial sites already provided free follow up treatment to the study participants once the study was completed. Thus, it is reasonable to assume that the participants have had the experience of a regular medical care and an expectation to be eventually treated with an active medication as part of their participation.

The practice as described above is certainly more ethically appropriate than the one that allows only chance to determine whether a participant receives an active treatment. However, in my experience, following this practice did not improve the outcome of the studies (i.e., it did not decrease the placebo response at a specific research site). Moreover, the performance at clinical research sites that followed such practice

was comparable to the performance of clinical research sites that did not provide follow up treatment.

The psychopharmacological research industry continues to struggle with this question: What are the variables that constitute the context of placebo response? I argue that the better question to ask is: What are the context variables that constitute placebo response? The answer, based on this study, is that the context variables appear to constitute placebo response and are too numerous and too dynamic to be accounted for using positivistic approach.

As the findings of this study suggest, medical practice is a healing practice grounded in various cultural and historical influences. For the healing practice to be useful, it has to be meaningful in the culture in which it has originated. Conventional medicine originated in Western culture, which valued scientific methods and followed positivistic ideas. Therefore, healing methods that incorporate science and scientific methods are meaningful to the members of this culture and thus provide the healing that they seek.

Healing effect comes, according to Gadamer (2004), from the restoration of the lost equilibrium. The restoration of the equilibrium, on the other hand, is accomplished by using the rituals and objects that the culture meaningfully associates with healing. In Western culture's conventional medicine, it is the meaning-laden visits to doctors, measurement of vital functions, receipt of a prescription followed by a medicine regimen that are associated with the process of healing in addition to caring relationships one develops with medical personnel, staff, and/or family members. It is reasonable to conclude, as Gadamer already has done in his *The Enigma of Health* (2004), that healing

that follows a medical intervention in Western culture happens to the large degree due to the meaning response.

Given the understanding that healing in Western culture occurs largely due to the meaning that people associate with the healing rituals, it is possible to conclude that the current ways of testing the efficacy of the psychopharmacological medications is less than optimal. Currently, the double-blind method that uses placebo control group as a comparator to active treatment exists within the context of the same meaning-laden beliefs and rituals (e.g., belief in scientific research methods, going to the doctor, taking medicine, etc.). If Gadamer's conclusions are correct, the difference between placebo and active medicine is rather small (particularly when it comes to psychotropic medications) given the strength of the cultural and historical contextual influence. This conclusion is also supported by some traditional scientific research: the meaning people associate with their healing is powerful enough to override the effects of chemicals in their bodies. Specifically, in studies done by Benedetti and colleagues (2003) as well as by Levine, Gordon, Smith, and Fields (1981), even the proven pain relief treatment such as morphine was significantly less effective when patient was unaware that they were being administered a painkiller. It appears that a significant part of pain relief is coming from the meaning patient associates with a ritual of being treated (the researchers of these studies called it "expectations").

Therefore, it is my conclusion that double-blind placebo control studies, as they are conducted today, may not be the proper way to studying the efficacy of active psychotropic medications. Positivistic double-blind placebo-controlled studies have been the gold standard in pharmacological research under the assumption that in both active

medication and placebo groups the conditions are equal aside from the active ingredient in the medication. Thus, by attempting to isolate the healing to only the active ingredient of the medication under study, the comparison of the two groups appeared justified. Unfortunately, the context of pharmacological treatment in modern Western society has been changing in the recent decades. The society has become more drug-focused than ever with the ever-present direct-to-consumer pharmaceutical advertising. The psychopharmaceutical industry has been particularly susceptible to the changes—the placebo response in the placebo groups has been on the rise and detrimental to the studies' outcomes (Benedetti, 2009; Bridge et al., 2009; Song et al., 2010). There needs to be a change in the way psychopharmacological industry tests its products.

Conducting Psychopharmacological Research by Incorporating Context

Benedetti (2013) encouraged incorporating what was known about placebo response into healing by improving the doctors' bedside manner and enhancing the healing environment with encouraging words, etc. He concluded that placebo was a contextual phenomenon. Gadamer (2004) made an even more overreaching conclusion that all healing was about meaning-making in the context of cultural and historical circumstances. Bhugra and Ventriglio (2015) also concluded that culture played a great role in healing and should be incorporated in healing and research.

Indeed, placebo response appears to be a contextual phenomenon. It consists of layers of context, which are both cultural-historical and individual ideas, beliefs, and expectations. Thus, placebo response cannot be isolated by removing the layers of context one after another. It is not possible, because context is larger than is generally thought—it stretches to cultural-historical circumstances that people are embedded in and

often take for granted without analyzing. Some healing practices simply make sense to us—representatives of this date and time. Contextual phenomenon of placebo response cannot be decontextualized. Therefore, attempts at limiting placebo response or minimizing it are doomed to fail. Up until now, psychopharmacological research have attempted to minimize placebo response across both placebo and active medication groups.

Based on the findings of this contextual exploration, I suggest that one of the ways to circumvent the issue with ever-rising placebo response is to maximize it instead. Maximizing placebo response was exactly what Benedetti (2013) proposed for treatment purposes. He acknowledged the significance of placebo response as a response to the bedside manner and additionally hoped that this knowledge could be used by the health professionals to “boost” their “empathic, humane, and compassionate behavior” (p. 1238). He also added that understanding the effects of doctor-patient relationship would improve “medical practice and clinical profession” and lead to a “better social/communication skills and health policy” (p. 1238). Benedetti’s suggestions listed above were limited to the medical treatment. I believe that one could also enhance healing context for clinical research purposes.

In many efficacy studies of various new products, developers attempt to test their inventions in conditions closely resembling real life utilization. For example, during crash tests, new cars are smashed into concrete walls head on, sideways, and hit from behind with another moving vehicle. These simulated high impact crashes at high speeds and at different angles are important. They show the developers how the new car is going to behave in similar difficult situations on the road. Will it prevent injuries to

people inside? If the car does not perform up to the standards the developers set for themselves, they go back to the drawing board and attempt to reinforce the identified weak areas. Testing the car at slower speeds and in softer impact situations will not do much for predicting its behavior in a real road accident.

Unfortunately, current ways of testing new psychiatric medications do not resemble real life utilization. In real life, patients often come to a clinic, where they are met with friendly personnel and calming music. They have pleasant conversations with the staff and have a chance to discuss their illness with them. Then, they meet with a physician or a psychiatrist with whom patients already have built (or have a chance to build) a therapeutic relationship and whom they trust. After that, this clinician prescribes them medications. The therapeutic context there is strong. Benedetti (2013) argued that the doctor-patient relationship in a clinical setting should be further enhanced by improving doctors' bedside manner and should ensure that the healing potential was maximized. Relationship with their doctors and reassurance by them have been shown to affect people's response to treatment. These are the therapeutic rituals, without which drugs are less effective, according to Benedetti (Benedetti, 2013, p. 1234). In research setting, however, medications and placebos are administered in double-blind fashion under strict laboratory conditions. Any reassurance by the doctors and staff as well as other typical medical office pleasantries are discouraged and minimized in an attempt to reduce placebo response. The environment of a research clinic is supposed to feel cold to patients by design. This cold laboratory environment does not match real life clinic surroundings.

Instead, I propose to incorporate the important meaning response and context into research to bring the research conditions to closely resemble real life treatment.

Currently, psychopharmacological research is limited to laboratory and so-called clean research environments. However, the purpose of the psychotropic drugs that are being developed is to treat psychiatric conditions. Laboratory-based and research clinic-based study treatments are too dissimilar from the typical treatment/healing environments of psychiatrists' offices. It would be more appropriate to conduct research of human conditions (i.e., psychiatric illnesses and healing from such) in the environments that are designed to be healing. The design of such studies can remain double-blind with active medications and placebo-control groups. The major change I propose is maximizing the placebo response across these groups instead of minimizing it. It can be done by providing the most healing environment possible. Such environment Benedetti (2013) recommended to create in general medical practice: increasing expectation of positive effect and utilizing socially appropriate therapeutic rituals. Additionally, per recommendation of Bhugra and Ventriglio (2015) cultural expectations for healing also needed to be taken into account. This can be achieved by developing a therapeutic rapport with each individual research participant through building a meaningful relationship with him or her.

Once the contextual placebo response is maximized in both groups (active medication and placebo), we can observe whether study medications are performing better than placebos and have effects that are superior to the general healing environment. Medications rigorously tested by such process, which pass the test of maximized healing responses, are bound to be a great addition to the medical field as additional tools for

healing people. These would be the effective medications that have proven themselves to work in the real-life treatment conditions.

Summary of the Study

I conducted this theoretical exploration to address an important gap in the literature—definition of placebo response. This was an attempt to bring together two different schools of thought and break the artificial separation of humanities and medicine. Introducing hermeneutics as a way to interpret medicine was not a novel idea. Various scholars had explored this thought and agreed that medicine, despite its desire to be seen purely as a natural science, was a study of meaning-making (Cooper, 1994; Gadamer, 2004; Leder, 1990).

I concluded that using the philosophical lens of Hans-Georg Gadamer, placebo response belonged in the area of human sciences (aka social sciences) and thus needed to be understood as a human phenomenon. Additionally, placebo response is a context phenomenon, not a human trait phenomenon, and the context appears to be greater than researchers can generally account for using positivistic research methods. Context does more than just influence someone's experience—it influences humans on a biological level too. Double-blind psychopharmacological studies cannot properly ascertain the influence of medication versus placebo using the current design. Current double-blind clinical studies attempt to equalize the contextual variables between placebo and medication groups. However, the greater cultural context in modern Western world dictates that scientific research, drugs, and allopathic medicine are healing and to be trusted, thus increasing the efficacy of both placebo and medicine. This dynamic may

change (strengthen or weaken) in the future with natural fluctuations and shifts in the culture.

A different way of testing efficacy of psychotropic medications is necessary. By maximizing the placebo response (i.e., meaningful healing context), researchers could put medications to a much more realistic test. Medications that prove to be superior to placebo under such conditions could indeed be considered a helpful addition to healing process.

Culture is a dynamic entity. In the West, it is currently in a state of deep belief in scientific progress and unlimited possibilities of science. However, science too has limits. One of them is its inability to properly critique itself. It needs other theoretical models to be able to address its own blind spots. Other philosophical approaches that counterpoise the philosophical approach of natural science are necessary to effectively look at its limitations. In summary, one should not forget that everything humans do and create is produced within a context that has cultural and historical aspects.

Strengths and Limitations of the Study

This study is a theoretical exploration that used philosophical approach of Hans-Georg Gadamer (hermeneutics) to critique and add to the current positivistic natural science approach of modern clinical research. The strength of this study is offering a new way of seeing the deficiencies of natural science model when it is applied to human (aka social) sciences. There are a number of limitations to this study of placebo response. First, the study aimed at outlining the deficiencies of psychopharmacology's current understanding of placebo response. I outlined one concrete suggestion to help the current double-blind placebo-controlled design to better account for the complex contextual

nature of placebo response. However, further research is needed for developing a more comprehensive theory that specifically accounts for the dynamic context that creates placebo response. Second, from the point of view of natural science, this study may appear lacking in empirical support. However, this theoretical exploration did not aim to provide concrete answers to the outlined issues with current state of placebo response understanding. I hope that further research will be able to address these gaps. Third, as with most philosophical theories, Gadamer's hermeneutics is simply a way of looking at and describing the cultural artifacts within a culture. Philosophical theories usually provide a direction for future research, but rarely are able to serve as solutions themselves. According to the findings of this study, it appears that placebo response is a phenomenon that is created by context. Thus, the human experience within the context needs to be explored further via means of qualitative research, instead of isolation or streamlining of the potential context variables.

Phenomenon or phenomena? In this work, I consistently referred to placebo response as a singular occurrence—placebo response phenomenon. However, some researchers, including Benedetti (2009), talked about placebo effects and/or placebo response phenomena—plural—in their writings. For the purposes of this contextual exploration, it is irrelevant whether placebo response occurs via one or multiple mechanisms in an organism. I concluded that whether placebo response or responses, they occur as a result of a cultural historical and personal contexts. I did not explore in this study specific physiological or other mechanisms via which organisms respond to placebos.

Suggestions for Further Research

In current placebo research, the terms placebo effect and placebo response are commonly used interchangeably. Raz, Zigman, and de Jong (2009), who stated, “many researchers and clinicians conflate placebo effects and placebo responses into one transposable term” (para. 4), questioned this difference in terminology. Such interchangeability initially appears insignificant. In the recent past, some of the researchers acknowledged that the terms placebo response and placebo effect were used interchangeably in the scientific community and literature (Benedetti, 2009; Colloca, Sigauco, & Benedetti, 2008) and some even attempted to change this inaccuracy by suggesting that the two terms be distinguished from each other (Hoffman et al., 2005). Hoffman et al. proposed that placebo effect would stand for the global outcome in the placebo group and that placebo response would stand for the psychological phenomenon. However, clinical trial investigators did not follow this suggestion (Benedetti, 2009, p. 6).

When measuring effect or response, clinical researchers are concerned with describing measurable changes in an organism. Thus, when it comes to interchangeability of the two terms, one might consider a different point of view. Both words effect and response can similarly describe such changes. However, in the world of linguistic nuances and intricate meanings, using the terms placebo response and placebo effect hardly means the same thing. When one talks of the effects of something, it is presumed that the subject is affecting the object in some important way where changes are observable and/or measurable. When one describes the response of something, the agency changes. Now the subject is what undergoes the changes in the presence of the object whether the object actively affects the subject or not.

Therefore, when one talks about placebos it would be improper to talk about placebo effects, since placebos by definition are inert and are incapable of producing an effect. However, placebo response is a more fitting description of the phenomenon. It implies that some changes occur in the subject whereas the object, placebo, may not necessarily be the one causing the changes to occur. Moreover, when one describes the changes in organism due to medications, it is appropriate to talk about the medication effects, because it is the medical community's presumption that medications are active and are capable of producing effects. Medication response is an unusual term, yet it would also be appropriate for describing the reactions to or effects of the medication. In double-blind psychopharmacological studies, however, the comparison is of medication effects to placebo response and such comparison may not be fully justified.

Additionally, it would be important to investigate in the future the differences in the use of the terms placebo effect and placebo response in the scientific literature. Raz et al. (2009) identified important effects of the interchangeable use of the terms in the literature:

Lack of uniformity underscores inherent ambiguity and fosters a climate of uncertainty. Moreover, it may adversely influence the direction and nature of research efforts. In addition, placebo-like effects often occur without the administration of an actual placebo, highlighting the central role of expectation and suggestion in placebo-related phenomena. (para. 4)

Given the assumptions identified in Benedetti's (2009, 2013) overviews of placebo research, it is reasonable to assume that psychotherapy community and clinical psychology field in general might be more likely to use the term placebo response, whereas the medical community is less likely to differentiate between the two terms. Future research is needed to find out whether such differences exist and if they do, what they can tell about the attitude towards placebo and the self-healing properties of humans.

The ever-changing nature of contextual variables that constitute culture is impossible to predict and constructively use by the methods of natural science's positivistic approach. It appears that a different model is needed for understanding context. Some of the potential approaches include qualitative methods of study where individual human experiences of phenomena are studied and themes are identified (Creswell, 2012). This approach has been successfully used in the past to understand the placebo response phenomenon (Kaptchuk et al., 2009; Sandler et al., 2008; Thompson et al., 2009). The results of such studies informed the researchers about the commonalities in experience without reducing the human experience to numbers. Instead, meaningful and relatable themes were identified. Placebo response research would benefit from an increase in research that uses qualitative methodologies.

Alternatively, a mathematical model of chaos theory could potentially help researchers understand placebo response as a dynamic system. This theory was proposed to solve issues with social sciences by Kiel and Elliott (1997). More research in this area is needed to ascertain whether chaos theory could be a helpful model for understanding the dynamics of contextual phenomena such as placebo response.

Moreover, psychiatric medications appear to be sometimes helpful to people. This is probably due to the combination of both the contextual as well as the biological effects on the human body. Thus, the clinical studies of the psychiatric medications are necessary to insure that the medications that are put on the market are safe. However, it is difficult to judge the efficacy of psychiatric medications using the positivistic approach and placebo as a comparator because context determines response in both placebo groups and active medication groups. In this study, I proposed a change to the current double-

blind clinical study design that could better incorporate context. The proposed design would not exclude context as a nuisance variable when testing psychiatric medications. Instead, the new design would embrace the context and placebo response factors. By maximizing healing context, researchers might be able to develop medications that truly contribute to the healing of individuals beyond meaning-response.

Lastly, the concepts placebo and placebo response or placebo effect themselves carry meaning in Western culture. For instance, Huculak (2013) explored the views associated with these concepts using a keywords approach. She noted that placebo had pejorative views associated with it. However, placebo effect was “more nuanced” (p. 164). Undoubtedly, these sudden differences are likely to have an effect on someone’s perception of placebo and the response associated with it. In many ways, this negative interpretation of placebo is already playing a role in the way researchers are treating it and in the way they interpret study results. It would be important to explore these differences further via both quantitative and qualitative approaches in patients and in doctors.

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