A Critical (and Cautiously Optimistic) Appraisal of Moerman's "Meaning Response"

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ABSTRACT In this article we propose a critical reassessment of Daniel Moerman's "meaning response." First, we reconstruct and criticize Moerman's original proposal of introducing the "meaning response" as a way of clarifying some terminological and conceptual issues in the placebo debate. Next we evaluate the criticisms that Moerman's proposal is epistemically moot since other existing and more empirically grounded models already account for all the phenomena that fall under the concept of the "meaning response." We conclude that Moerman's original proposal is inherently problematic and that, in order to be instrumentally useful in the future, the meaning response must be reconceived so that it may finally support, rather than oppose, other theoretical and empirical lines of research currently ongoing in the field of placebo studies.

Shamans, healers, and doctors have always known that patients may improve even if no real therapy is administered. In the *Charmides,* Plato noted

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that to soothe a headache, one needed "a kind of leaf, which required to be accompanied by a charm, and if a person would repeat the charm at the same time he used the cure, he would be made whole; but that without the charm would be of no avail" (Jowett 1892, 12). Similarly, more than two millennia later, Thomas Jefferson (1898) observed, "One of the most successful physicians I have even known has assured me that he used more bread pills, drops of colored water, and powder of hickory ashes, than of all other medication put together"; Jefferson famously labeled this practice a "pious fraud" (199).

Today, this phenomenon is routinely observed in clinical trials where patients assigned to control groups often report measurable improvements even if they have received a placebo or no medicine at all. Patients' improvement in control groups is usually explained in terms of three major components (Benedetti 2011). The first is the natural history of the disease: sometimes patients improve because conditions like colds spontaneously improve over time. The second component is the statistical phenomenon of "regression to the mean": sometimes patients "improve" because symptoms tend to regress toward a mean value after reaching their peak intensity. Finally, patients may improve because of the different phenomena lumped under the term "placebo effects."

The definition of *placebo* is, however, notoriously controversial. Usually, the term refers to something that mimics a therapy but lacks those features of it that are believed to affect patients' outcomes (Howick 2017). According to this approach, in order to call something a "placebo," one must first know that *something else* is a "therapy." Yet, often determining what a therapy might be is unclear: the concept of "therapy" may depend on culturally situated and historically fluid epistemic norms—just like the concept of "disease." Also, it may not yet be known which "characteristic features" of a particular therapy are the ones affecting patients' outcomes. The case of acupuncture is an example: although evidence seems to indicate that acupuncture is slightly more effective that placebo acupuncture, its characteristic features are still (at least) partially unclear. In general, then, one cannot satisfactorily define the concept of "placebo" unless one also provides a sound epistemic criterion for distinguishing between "placebos" and "therapies"—a task that raises complex issues in, and for, the branch of the philosophy of medicine known as medical epistemology.

A second difficulty is that placebo effects may occur even when no placebo is administered. Using an open-hidden paradigm, researchers have demonstrated that the same medicine—for example, a painkiller—may induce different effects depending on how it is presented to patients (Colloca et al. 2004). In these studies, patients who receive painkillers in full view of the physician report a significantly lower pain compared to patients who receive the exactly the same dose of medication administered by an automatic infusion machine. The difference between the improvements measured in the open and hidden groups provides a measure of the magnitude of the placebo effect. Indeed, the same results have

been replicated in conditions other than pain, including depression and Parkinson's motor syndrome (Benedetti 2011; Finniss et al. 2010; Miller et al. 2013). These studies demonstrate that placebo effects may occur even without placebos.

In the wake of these difficulties, scholars have advocated two strategies. Some have argued that we should largely conserve the present theoretical placebo constructs but revise their definitions (Grünbaum 1981, 1986; Howick 2017; Miller and Kaptchuk 2008). Others, instead, have argued that we should abandon these concepts altogether, replacing them with new theoretical constructs (Gotzsche 1995; Moerman 2013a; Nunn 2009; Turner 2012). In this paper, we analyze one of the latter alternatives: the concept of "meaning response" originally proposed in 2002 by Daniel Moerman.

Moerman's Concept of the "Meaning Response"

In a series of influential contributions, Moerman argues that we must substitute the concept of the "placebo effect" with the concept of the "meaning response" (Moerman 2002, 2013a, 2013b; Moerman and Jonas 2002).[1]

Moerman (2013b) defines a placebo as "an inert substance (a sugar or starch pill, a saline injection) used in place of, or next to, an ordinary drug. By 'inert,' we mean a substance that 'doesn't do anything,' that has no effect on human physiology" (183). Thus, distinguishing himself from the majority of commentators, Moerman holds that the concept *placebo* is "perfectly legitimate" and should retain its currency in medicine.

By contrast, he argues that the concept of the placebo effect is an oxymoron, for nothing that is "inert"—in other words, the placebo—can cause an "effect" or a "response" (183). Hence, he proposes replacing the concept of placebo effect with the concept of the meaning response, defined as "the psychological and physiological effects of meaning in the treatment of illness" (Moerman 2002, 14).

In this view, placebo effects—that is to say, the responses to placebos—are just a special case of meaning responses. All placebo effects for Moerman are meaning responses, but not all meaning responses are placebo effects, for a meaning response may occur even without a placebo. Thus—Moerman argues—the concept of the placebo effect concept mistakenly confuses a part for the whole and should be replaced with the concept of the meaning response.

Moerman's proposal has the prima facie advantage of avoiding the inherent confusion of calling something a placebo effect even when no placebo is given. However, his view has also attracted some objections. In particular, in this article we discuss two criticisms of Moerman's strategy, namely (1) that Moerman's

[1]In this paper we restrict our attention to Moerman's conceptualization of placebo effects as meaning responses. We also note that Howard Brody's conceptualization of placebo responses as "meaning responses" predates Moerman's account (Brody 1988, 2000). However, our criticisms of Moerman's account, we believe, also apply to Brody's articulations of the meaning response.

concept of placebos as "inert substances" is flawed, and (2) that the concept of the meaning response is epistemically moot, since other more empirically sound theories can already account for the phenomena that fall under this concept.

Are Placebos Inert?

Several scholars have criticized Moerman's view that placebos are definable as "inert substances" (Brody 2000; Howick 2017). According to these critics, no substance is "inert," if by *inert* one wishes to refer, as Moerman does, to a "substance that 'doesn't do anything,' that has no effect on human physiology" (Moerman 2013b, 183). The objection is simply that no physical object falls under this definition of *inert*—not even traditional placebos.

Sugar pills are not inert for people with diabetes, and lactose pills are not inert for people who are lactose-intolerant. Indeed, nothing is inert if by *inert* one means something that has absolutely no physiological effect. To be meaningful, the adjective *inert* must therefore be understood in relative terms. That is to say, something can be inert with respect to something else *only* against some background assumptions—such as, for example, a particular biomedical theory of health and disease. Thus, in order to define placebos as inert substances, one must first clarify what these assumptions are—otherwise the concept of inertness becomes ipso facto useless.

For this reason, and in absence of further qualifications, we agree with other critics that defining placebos as inert substances begs the question, as it only shifts the problem from the definition of *placebo* to the definition of *inertness*, which is, again, a difficult concept to define with precision. This conclusion has important implications for what follows. A primary objective of Moerman's proposal was to clarify the terminological and conceptual quandaries hindering the placebo debate. To do so, he proposed to retain the concept of placebo and substitute the concept of placebo effect. This strategy, however, falls short, inasmuch as to define placebos as "inert substances" raises just as many issues as the ones it was meant to solve. Therefore, from the standpoint of conceptual and terminological clarity, there is no reason to abandon the current placebo constructs.

This objection, however, is not sufficient to reject Moerman's proposal, as in his view the concept of placebo is decoupled from the concept of meaning response. In fact, to define the meaning response one does not, strictly speaking, need to define the term *placebo*. Thus, it is possible to reject (or refine) Moerman's definition of placebo while at the same time hold to his definition and concept of the meaning response. In the next section we shall move to explore the relative epistemic advantages of adopting the concept of the meaning response.

Is the Concept of the "Meaning Response" Epistemically Moot?

A second and more direct criticism of Moerman's view has been articulated, among others, by Howick (2017), who asserts that

> Perhaps the most serious problem with Moerman's account is that conditioning and expectancy theories can account for all the phenomena Moerman describes in his [2002] book. . . . Unlike the meaning hypothesis, which Moerman himself acknowledges has not been tested directly in any experiments, conditioning and expectancy have been tested and confirmed in hundreds of studies starting with Pavlov's famous experiments. . . . By contrast the term "meaning" . . . is by Moerman's own admission unsupported by direct empirical tests. (1367)

Howick's criticism is that Moerman's proposal is epistemically moot, since other theories can account for the same phenomena and are better supported by empirical evidence. As we argue, this critique hits the mark and it can also be generalized to nocebo effects.

In order to unpack this claim, consider the famous experiment in which Braithwaite and Cooper (1981) showed that branded aspirins were more effective than unbranded aspirins to reduce headache, and that (deceptively) branded placebos were also more effective than (deceptively) unbranded placebos. Recent empirical studies have similarly shown that pills presented as more expensive have greater analgesic effects than pills presented as less costly, even if both are placebos (Waber et al. 2008). Branding has also been found to influence the effectiveness both of "verum" therapies and placebos in reducing the pain of episodic migraine (Kam-Hansen et al. 2014). Collectively, these studies demonstrate that the effectiveness of therapies and placebos may vary depending on the modalities of their administration and their presentation. In particular, the same substance—a placebo or a real analgesic—may induce different effects depending on the verbal clues that are associated with its administration.

Yet we do not need the concept of the meaning response to explain these effects: the different effects of branded and unbranded pills may be explained by current accounts based on expectancy and conditioning. These accounts draw from a converging series of empirical studies that, in the last decades, have uncovered some of the underlying mechanisms of placebo effects (Benedetti 2011; Finniss et al. 2010). These studies reveal that there are several intertwined mechanisms that mediate placebo effects, some of which can now be described at the biological level. Given that such accounts may explain the effects observed by both Braithwaite and Cooper (1981) and Kam-Hansen and colleagues (2014), it is unclear why we need to introduce another construct such as the meaning response.

One retort to this criticism of the meaning response is that exactly the same challenge can be leveled at the concept of the placebo effect. If expectancy and conditioning-based models already explain all the phenomena at stake, why indulge in conceptual proliferation? As Turner (2012) argues, why not simply refer to such effects as "expectancy" or "conditioning responses" rather than as "placebo effects"?

In our view, answering these questions involves two considerations. First, in the last decades, the concept of placebo response or effect has played a major role as a driver of scientific and public attention, unifying diverse strands of research across disciplines such as neurocognitive sciences, neurophysiology, clinical research, biomedical ethics, and medical anthropology, eventually leading to the emergence of the new interdisciplinary field of "placebo studies." To use Imre Lakatos's (1974) terminology, placebo studies is a progressive research program. At this stage, we propose that fragmenting the concept of placebo effect into diverse and seemingly unrelated concepts would be detrimental for such a nascent yet cutting-edge area of research (Finniss et al. 2010).

Second, there is still considerable scientific debate about the best model for conceiving placebo effects and thus about whether—and to what extent—known placebo mechanisms might be interpreted as instances of a unique phenomenon, such as, for example, "response expectancies" (Benedetti 2011; Finniss et al. 2010). Researchers still disagree on theoretical issues, including how expectancy and conditioning ought to be defined, or whether one is entirely reducible to the other. Furthermore, in the last decades, the terms *placebo* and "placebo and nocebo effects" have provided a highly focused target for a growing and lively debate in biomedical ethics, as well as a suitable target for institutional policies and regulations (Annoni and Miller 2014, 2016; Blease, Bishop, and Kaptchuk 2017).

Amidst such open-ended debates, we argue that it would be premature and counterproductive to abandon the only unifying abstraction—as problematic as it is—around which the discussions are presently anchored. Therefore, even if expectancy and conditioning models may account for a significant class (or even all) of placebo effects, there are strong practical reasons for conserving the placebo construct—at least in the short and medium term.

By contrast (and as noted) there seems to be no equally compelling reason to endorse Moerman's justification for replacing the term "placebo effect" with "meaning response." As discussed in the previous section, the latter does not add clarity to the debate, as it only shifts the problem from the definition of *placebo* to the definition of *inertness/efficacy*. Moreover, today the concept of the meaning response has little currency within the scientific community of contemporary placebo scholarship; hence, its adoption would demand a massively onerous cooperative effort (Turner 2012).

Therefore, to the extent that the concepts of meaning response and placebo effect overlap, Moerman's proposal ought to be rejected. While both concepts

still have residual definitional problems, at the very least the placebo construct is an important anchor for ongoing empirical and theoretical debate and provides an important practical focus for regulatory and normative action.

Conclusions and Recommendations

Moerman's view of the meaning response is inherently problematic. Contrary to its intent, it does not aid clarification of the conceptual and terminological paradoxes intrinsic to the placebo debate, as it rests on an equally problematic definition of placebos as inert substances. Furthermore, there are no good reasons to replace the concept of placebo effect with the concept of the meaning response: while both constructs rely on problematic definitions, the former is already at the forefront of a new and fruitful program of theoretical and empirical research as well as a target of regulatory and normative action.

By contrast, it is unclear how the meaning response concept *could* support existing or new lines of theoretical and empirical inquiry. Moerman has never defined the term *meaning* in a technical and precise way to help differentiate it from other possible conceptions and theories of meaning. *Meaning*, however, may refer not only to a plurality of diverse concepts in everyday language, but also to many—sometimes directly contrasting—technical notions belonging to specialized fields such as the philosophy of language, lexicography, linguistics, logic, and semiotics. Currently, there are several competing definitions, models, and accounts of *meaning* that are available across these different disciplines, each of which may lead to diverse research programs and (possibly) to different empirical hypotheses.

Since Moerman has never provided a technical definition of *meaning*, his definition of the meaning response as "the psychological and physiological effects of meaning in the treatment of illness" (Moerman 2002, 14) has so far remained inescapably vague. In the absence of further qualifications, it is hard—if not impossible—to indicate which conceivable series of experiments could support or disprove the meaning response model proposed by Moerman. This conclusion casts further doubts about the value to scholarship and research of adopting the meaning response framework.

Against this backdrop, however, we also believe that meaning response could potentially play a significant role within the contemporary and future health-care landscape. This admittedly narrow path, we argue, would need to reconceptualize the meaning response so that it might finally integrate and support, rather than oppose, other lines of theoretical and empirical research currently ongoing in placebo studies. Essentially, this reconceptualization involves two steps. First, it is necessary to redefine the role of the meaning response against the current landscape of placebo studies. As we have seen in the previous section, there are well-documented and empirically measurable effects that cannot be explained by

resorting to the same models currently used to explain placebo and nocebo effects. This is also true of many other salubrious effects routinely observed in other therapeutic contexts including psychotherapy (Blease and Kirsch 2016). How we should think about these other effects in relation to placebo and nocebo effects is, at present, a highly contested and open issue.

Amidst this debate, the meaning response could potentially provide a higher-order and useful unifying abstraction. Just like the placebo construct has acted as a catalyst and driver for diverse strands of research over different psychobiological mechanisms, the meaning response could act as a catalyst and driver for a broader and multidisciplinary program of research—one in which the field of placebo studies would represent just one among many related strands of scientific inquiry. In this view, the meaning response would retain and include, rather than substitute, the placebo effect construct as it is currently utilized by the majority of scholars and scientists in placebo studies.

In order for this to occur, however, the meaning response must also be endowed with a theory of meaning up to the task; we argue it would need to fulfill two conditions. First, this theory must rely on a sufficiently general concept of *meaning,* so that all the different effects that fall under the concept of the meaning response might be interpreted as diverse instances of a single concept. Second, this concept of *meaning* must also be sufficiently precise as to be then translatable into a series of empirically testable hypotheses.

In conclusion, in the past 15 years, Moerman's meaning response has provided an intriguing perspective for scholars and scientists interested in placebo effects and medical anthropology. Because of its inherent limitations, however, so far Moerman's proposal has failed to reshape the placebo debate in a substantial way, nor has it heralded a new scientific research program in placebo studies. Thus, in order to be relevant, and to inspire future generations of researchers, the time has come either to eliminate the meaning response in favor of existing conceptualizations of placebo effect in placebo studies, or to critically rethink the concept to render it amenable to a program of scientific research.

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