Questioning the Power of the Placebo

Given the Substantial Psychological and Physiological effects Generated by Placebos, should Pharmacologically Inactive Medicines be considered Ineffective or Indispensable?

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Abstract

In recent years, there has been a discernible shift in the way that placebo effects have been perceived by psychologists and medical practitioners alike, largely occurring as a result of research which has shown that placebos can provoke specific physiological reactions and therefore, may have clinical significance beyond their use in double-blind experimental trials. The following literature review explores this ever-changing paradigm through the critical analysis of a number of recent studies in the field of 'placebology.' An overview of the physiological and psychological significance of placebo effects, as well as their underlying mechanisms, is provided, followed by an analysis of studies which focus on placebo effects in relation to non-conscious goals, expectancy in clinical trials, responses to marketing actions and health benefits generated through exercise, as well as the overall robustness of placebo responses for a variety of medical conditions. Conclusions are subsequently drawn regarding the importance of the psychosocial context of the placebo for health and healing.

Introduction

The placebo-controlled, double-blind trial has undoubtedly become the gold standard in psychological research. This design was originally constructed to assess the effectiveness of prescribed medical treatments in comparison with remedies which have no demonstrable therapeutic activity. In such studies, one group is allocated an inert substance or neutral treatment, while the other receives the medication or treatment under investigation. Neither doctors nor patients are aware of which subjects receive the active treatment, though they are generally informed that participants have a 50-50 chance of being assigned the placebo. While it has widely been used in psychological and medical studies, this two-armed research methodology may be far from ideal as the expectation of positive treatment outcomes has been found to enhance placebo effects, thus adding a placebo effect to any benefits generated by the active medication and making it difficult to ascertain how much of the overall effect is attributable to the medication being scrutinised.

The placebo effect is particularly applicable to certain conditions, including pain, hypertension, psychiatric illness, perimenopause symptoms, affective disorders and any condition for which symptoms are subjective or chronic (Kaptchuk, 2002), yet there is evidence that the placebo effect also applies to less subjective measures, including blood pressure readings (e.g. Kirsch & Weixel, 1988). Negative placebo effects (so-called 'nocebo' effects) can also occur, as when those taking a placebo drug experience side effects comparable to those of patients prescribed the real drug (Enck et al., 2008) or when subjects who believe they have been exposed to poison ivy develop rashes, even when the poison ivy is artificial (Crum & Langer 2007, p.165). However, Geers et al. (2005, p.155) note that "positive placebo expectations generally have stronger effects than negative placebo expectations", presumably the desires or goals of the participants are in line with the optimistic beliefs associated with taking the actual medication as opposed to the side effects.

While it has been estimated by Kirsch & Sapirstein (1998) that more placebos have been distributed to research participants than any other experimental drug or medical treatment, research to date has failed to identify a consistent set of placebo responder characteristics. Rather, there are indications that patient preferences for certain types of interventions increase adherence to the intervention, which in turn increases placebo effects (Kaptchuk, 2002). As such, factors including verbal suggestion, health care provider behaviours and conditioning each contribute to the variability of placebo effects (Price et al, 2008). The following paper critically reviews five recent peer-reviewed journal articles by researchers in the field of 'placebology,' the scientific study of placebo effects. These articles are evaluated not only to determine the effectiveness of the experimental measures used and the validity of the conclusions drawn, but also from the perspective of a more modern conception of the placebo effect that questions whether something which produces genuine physiological and psychological responses can justifiably be considered 'inert'.

Background and Theory

Placebos are typically inactive substances which are physically indistinguishable from active medications, though active placebos (those with side effects similar to the drug under investigation but without the purported healing effects) are occasionally used. Placebos were originally considered to be futile substances, as is evident in early definitions of the placebo as "medicines prescribed more to please the patient than for therapeutic effectiveness" (Fox, 1803) and "any therapy...which is actually ineffective or not specifically effective for the symptom or disorder [being treated]" (Shapiro & Shapiro 1997, quoted in Sandler 2005, p.166). However, many modern doctors have updated the definition in recognition of the very real and specific effects placebos appear to generate, including healing peptic ulcers and causing bronchodilation (decreasing airway resistance, thus enabling airflow) in asthmatics (Caspi & Bootzin, 2002). Malani (2006, p.236) describes placebos as medications for which patient responses depend on their expectations regarding the value of the treatment, while Giordano (2008, p.1316) defines a placebo as "any intervention, event, or experience that evokes positive subjective or objective outcomes in a patient."

By the 1980s, to control for placebo effects, the Food and Drug Administration authorised the effectiveness of a drug to be tested via "randomised double-blind placebo trials" (Wampold et al., 2007, p.380). Placebo effects were thought at this time to be an unimportant relic of pre-scientific medicine rather than a legitimate area of inquiry and as a result, very few clinical trials had no-treatment arms (ibid., p.381). As such, it is quite possible that a significant proportion of responses to active medications were attributable to placebo effects (Sandler, 2005), a hypothesis supported by the fact that hidden administration can reduce the effects of pain killing medications (Colloca & Benedetti, 2005).

Physiological Effects

The existence of placebo-induced physiological effects is certainly well established. Colloca and Benedetti (2005) note that placebos can reduce pain through both opioid and non-opioid mechanisms; that opioids produced via placebo effects also have typical side effects such as respiratory depression and, in addition, the opioid blocker nalaxone can block certain placebo responses. Placebo effects have been found in the brain, respiratory system, cardiovascular system and immune system (Colloca & Benedetti, 2005). Furthermore, a number of meta-analyses indicate that the effects of antidepressants are primarily attributable to placebo responses (Geers et al., 2005, p.143) yet clinical trials that show little difference between medications and placebos tend not to be published, thus distorting the overall findings (Kirsch, 2005).

Psychological Effects

Several studies of various psychotherapeutic interventions have found that their effectiveness can be largely attributed to placebo responses (Moerman, 2002). Simply getting one's name on a waiting list can have a positive placebo effect in psychotherapy (Kirsch, 2005, p.796). However, when the benefits accrue from the treatment itself, placebo features are complex and likely to include "the establishment of a therapeutic relationship, discussion of the presenting problem, cognitive restructuring, and the provision of warmth, empathy, positive regard, and response-contingent reinforcement", with hope, expectancy, the release of endorphins and neurotransmitters also contributing (ibid, p.798). As Kirsch (2005, p.798) emphasises, any of these factors could be labelled 'placebo factors'. However, given that endorphins and neurotransmitters are not inert, some question whether it is accurate to label such therapies 'illegitimate'. Kirsch (2005, p.797) identifies a placebo as "something that is sham, fake, false, inert, and empty", and argues that psychotherapy does not deserve such a pejorative descriptor. As Price et al. (2008) emphasise, to define something as 'inert' is to say that it has no effect, and this definition is not applicable to the majority of placebos.

Wampold et al. (2005, p.840) note that it is impossible for psychotherapists who administer what are considered placebo therapies to be 'blind' to which patients are receiving therapy, and so they are less likely to be enthusiastic or convey confidence when providing such therapies, potentially confounding experimental outcomes and giving recognised treatments an advantage over placebo treatments. In addition, removing what are considered the 'active' properties of psychotherapy is problematic; thus, any treatment used as a placebo, such as "sitting quietly with a silent therapist" will be qualitatively different from the actual therapy (Kirsch, 2005, p.796). Even if it is possible to remove specific elements from a psychological treatment, if the elements work synergistically, the effects will be nullified for elements used in isolation even if they are extremely effective when used together. Thus, determining active elements or isolating placebo effects in psychological treatments is problematic, if not impossible.

Theories on Mechanism of Action

Placebos can produce highly specific effects and there are several theories regarding how they exert their influence. Such theories encompass patient expectation, hope, motivation, therapeutic relationships, conditioned responses and other psychological processes (Wampold et al., 2005). However, the two most influential components are undoubtedly expectancy and classical conditioning. The role of expectancy, whereby the placebo effect is generated from the anticipation that a treatment will result in a specific outcome, has been verified by a systematic review of 85 studies (Kaptchuk, 2002, p.819). Yet while this view posits that placebo effects are unmediated consequences of expectation (Geers et al., 2005, p.144), some theorists have argued that expectancies can be moderated by attentional focus, causal attributions, non-conscious goals and

desires (Price et al., 2008). Also, expectancy is not always positively correlated with placebo effects (Thompson, 2005), and conditioned placebo responses can occur in the absence of expectancies, therefore it is evident that a lack of understanding surrounds the mechanisms by which expectations generate the placebo effect (Stewart-Williams & Podd, 2004).

The classical conditioning approach views active medications as unconditioned stimuli, the means by which treatments are administered as the conditioned stimulus and the placebo effect as the conditioned response (Geers et al, 2005, p.144). That conditioning plays a role in some placebo responses is evident in the fact that when a pain stimulus is surreptitiously lowered on a part of the body being "treated with a placebo anaesthetic", the placebo will later reduce pain even when the stimulus is not secretly lowered (Kirsch, 2005, p.795). There is evidence that conditioning is a factor in some contexts but not others, for example, prior experience with an active drug does not always enhance placebo effects, thus calling upon a more cognitive interpretation of classical conditioning effects (Geers et al., 2005, p.144). The fact that placebo effects are stronger when the placebo is administered "after a more potent drug [than] after a less potent drug" provides support for conditioning as an aspect of placebo response (Kirsch, 2005, p.794).

De-conditioned placebo responses may also occur, as when a patient experiences benefits after switching from mainstream medicine to alternative medicine; patients who have lost hope due to a lack of success with standard treatment options may experience renewed optimism by shifting to complementary or alternative options (Kaptchuk, 2002, p.818). In such cases, conventional medicine has come to have a 'nocebo' effect, rendering future treatments provided by mainstream medical practitioners less effective. The medical practitioner plays an important role in both expectation and conditioning; by conveying confidence in a treatment's efficacy, a doctor is more likely to facilitate a strong placebo effect (ibid). Aiding this is prior conditioning; many people have had the experience of feeling better after receiving medical treatment and so come to associate a confident practitioner donning a white coat with feeling better (Sandler, 2005). As such, the white-coated practitioner has become the conditioned stimulus and feeling better the conditioned response.

Another principal theory regarding placebo effects concerns motivation. Placebo effects may occur in response to goals, such as the aim to improve health and feel better or to cooperate with a health care practitioner or experimenter (e.g. demand characteristics). In some cases the expectation or hope of getting better causes individuals to attribute spontaneous recovery, remission or a lessening of symptoms to placebo treatments, or even feel better despite a lack of objective evidence that a condition has been cured or lessened, a misattribution that is most likely to occur with conditions that tend to wax and wane (Sandler, 2005). Improvements in medical or psychological conditions may result from factors other than the administration of active medication or a placebo, such as regression to the mean. People are more inclined to seek treatment when their ailment is at its worst, yet pain tends to be variable and eventually resolves on its own. If an

individual has recently sought medical or alternative treatment, he or she is likely to attribute the remission to the treatment provided as opposed to the body's natural healing mechanisms (Colloca & Benedetti 2005, p.546).

Paradigm Shift

With the eventual recognition of placebo effects came a tendency to label those who dispensed inactive substances or treatments as charlatans, even if they produced the desired effects. As a result, those developing medications and treatments were required to submit their products to placebo-controlled trials (Wampold et al., 2005), with the effectiveness of any given therapy measured as its effects over and above that generated by a placebo. Because fewer than 4% of placebo-controlled studies incorporate a placebo-free or no-treatment control group to evaluate the effect of the placebo itself, it is difficult to determine the magnitude of placebo effects (Geers et al., 2005, p.144).

The placebo effect was originally considered to be a nothing more than a nuisance factor affecting research, but discoveries regarding the real physiological effects placebos can generate have more recently made it "a target of scientific inquiry" (Colloca & Benedetti, 2005, p.545). Increasingly, researchers and medical practitioners have come to understand "that a patient's state of mind can affect, if not determine, clinical outcomes" and as such, placebos may have some clinical value in and of themselves (Giordano, 2008, p.1316). Indeed, a recent study of doctors in Israel found that 60% regularly prescribed placebos and of these, 68% told patients that they were prescribing active medications (Sandler, 2005, p.169), demonstrating the ostensible power of the placebo.

With the dawn of the 21st century came a perceptible paradigm shift. Given that placebos are capable of producing beneficial physiological effects, and that for some conditions these effects are equivalent to those of the active treatment (Wampold et al., 2005), many consider whether it is ethical to label inactive substances that produce significant effects as sham treatments and deny them to patients who could plausibly gain real benefits from them. Kirsch (2005) argues that the difference a given treatment makes to the quality of a patient's life is of more importance in assessing the legitimacy of the treatment than determining whether its effects can be attributable solely to expectancy. Kaptchuk, a primary figure in the placebo effect debate, furthers this idea, noting that "some types of unconventional medicine may produce placebo outcomes that are dramatic and, from the patient's perspective, especially compelling" (2008, p.817). This suggests that rather than merely something to be controlled for in clinical trials, placebo effects may have merit as treatment options, providing that rigorous ethical standards are applied. The following studies investigate this notion and examine the power of placebo effects in numerous contexts.

Goal Activation, Expectations and the Placebo Effect

There is evidence that placebo effects may be influenced by non-conscious desires and goals, yet the majority of recent research into placebo effects has disregarded the potential impact that patient motives can have on responding to placebos (Price et al., 2008). To explore the possibility that "the placebo effect is most likely to occur when individuals have a goal that can be fulfilled by confirmation of the placebo expectation", Geers et al. (2005) conducted five separate but related experiments, concluding that motivational factors such as non-conscious goals do indeed influence a patient's response to the placebo. The overall hypothesis was that participants' expectations of a placebo would produce placebo effects when a compatible goal was held, with the motive of co-operation providing the main focus.

Study 1

The first study used as its sample 45 psychology undergraduates who were given partial course credit as an incentive for participation. All participants completed a Likert-scale instrument to gather information about their emotional states prior to the study, rating items such as 'cheerful', 'headachy' and 'peaceful'. Subjects were then divided into four groups:

1. Placebo-Co-operation-Prime (PCP)
2. Placebo-Independence-Prime (PIP)
3. Placebo-Neutral-Prime (PNP)
4. Control Group

Subsequently, each participant completed a psycholinguistic task in which they created sentences from scrambled words. Geers et al (2005) noted that since "no motivationally oriented placebo effect framework exists", it was necessary to take a self-regulatory approach, steering the thoughts of participants towards a particular motive through priming. Thus, of the 20 scrambled word items assigned to each participant, 16 contained words that differed depending on participants' experimental condition; the purpose of the words being to manipulate the non-conscious goals held by participants in the PCP and PIP groups. In the PCP condition, the task contained words such as 'cooperate', 'assist' and 'helpful' as non-conscious primes for the motive of co-operation. The PIP group, by contrast, completed a task with words such as 'stubborn', 'independence' and 'assert' to prime for independence. This condition was added to determine whether any goal would strengthen placebo-expectation effects or if only goals that could be satiated through confirmation of a placebo expectation would strengthen these effects (ibid). The authors hypothesised that the goal of independence would have no effect on placebo responding as it is not associated with an expectation of the placebo. The PNP group's task contained neutral words, including 'look', 'begin' and 'understood' while

subjects in the control group were not primed with a goal. It was predicted that those participants primed with the specific goal of co-operation would report stronger reactions towards the placebo than each of the other groups.

Next, participants in the experimental groups were told that they would listen to a short piece of music that had been "scientifically developed by neuropsychologists to increase positive feelings and energy levels and reduce headaches" which participants were informed was a result of the inclusion of specific notes and patterns that "unconsciously activate the precise regions of the brain that regulate pain and pleasure sensations" (Geers et al., 2005, p.146). In fact, the piece was selected for the opposite reasons; pilot tests determined that it did not evoke any affective reactions. The control group was not given any expectation regarding the music but was simply asked to evaluate the way it made them feel. Having listened to the music, subjects again completed the affect questionnaire. The results indicated that there was no significant difference between the control group and the PNP, suggesting that no placebo effect was evident when participants were not primed with a goal as in the other two groups. However, there were significant differences between the control group and the PCP, as well as between the PNP and PCP, showing that placebo effects were more likely to result when participants were primed with the goal of co-operation, yet the fact that there were no significant differences between the PNP and the PIP groups suggests that not all goals lead to placebo responses. Evidently, the results support the notion that individuals who have been primed for a goal they are able to fulfil by behaving in a manner consistent with a placebo expectation are more likely to demonstrate placebo effects.

Study 2

Geers et al (2005) recognised that there were several limitations associated with their initial study, namely the inability to generalise the impact of non-conscious goals in a laboratory environment to real-life settings. The study also failed to investigate the prolonged impact of primes on the placebo effect if the goals primed for remain unfulfilled, thus leaving open questions as to the impact of non-conscious goals over a prolonged period of time and in various contexts, both of which were addressed in study 2. In this study, participants' reactions to a placebo therapy deemed to improve sleep quality is investigated, the prediction being that "goals moderate expectancy effects in many different domains of symptomatology and types of medical treatments" (p147).

Geers et al. (2005) randomly assigned subjects to one of six experimental conditions:

1. No-Treatment Control (NTC)
2. Treatment without Expectation (TWE)
3. Treatment with Placebo Expectation (TWPE)

4-6. Treatment, Placebo Expectation and Co-operation Goal Prime (TPEC1, 2, and 3)

Having completed a Likert-scale behaviour questionnaire, which included questions about sleep schedules and perception of sleep quality, the NTC group were asked to proofread a piece of writing about flour and were given no further instructions. The TWE group read the same piece of writing and were then dismissed with the instructions to record their thoughts on paper just before going to bed. The TWPE group were also asked to read the flour passage and to record their thoughts before bedtime, but were told that this writing task was a potent mental relaxation therapy which helped organise thoughts and thus was likely to improve sleep quality.

The TPEC1 group received the same instructions as the TWPE group, but were given a different passage to read, about a man helping the victim of a car accident, confirmed by a pilot study to evoke the concept of co-operation.

The TPEC2 group experienced the same experimental conditions as TPEC1, with one noteworthy exception. They were given an instructional booklet which contained generic instructions about checking that all materials were present and returning the packet after use. However, the booklet contained several co-operation prime words such as ‘volunteer’, ‘co-operate’ and ‘aid’, the purpose of which was to determine whether a co-operation prime could increase placebo responses some time after the expectation was set up.

In the TPEC3 condition, the goal of co-operation was activated in a more overt manner when subjects overheard the experimenter take a phone call while they were reading the passage. The experimenter feigned surprise at the call, pretended to be on the phone with her mother, and took the phone to the next room, staying close enough that participants were sure to overhear. Her scripted conversation contained, embedded amongst numerous filler comments, statements to the effect that she was conducting a study and she hoped that participants would be helpful. It was predicted that this more explicit goal priming would produce more noticeable results to those employed in other TPEC conditions.

The following day, all participants rated their sleep using a self-report questionnaire. The results were as follows:

- NTC and TWE – no significant difference; suggesting participation in the writing task without any expectation had no effect on sleep patterns.
- TWE and TWPE – no significant difference; suggesting that placebo expectation did not alter the way in which participants rated their sleep quality.
- TWE and TPEC 1, 2, and 3 – significant differences for each comparison
- TWPE and TPEC 1, 2, and 3 – significant differences for each comparison.

The last two results indicate that participants were influenced by the placebo expectation when the goal was manipulated by any of the three methods employed. Therefore, further to supporting the findings of study 1, the present study showed the results were applicable outside the laboratory and over a longer timeframe, providing evidence that motivation (at least for the specified goal) has an impact on a range of placebo symptoms. This, suggest the researchers, may be of interest to medical practitioners endeavouring to generate placebo responses.

Study 3

In this experiment, the researchers sought to determine whether the results of the previous two occurred solely due to the non-conscious co-operation goal or whether expectation also played a role, as well as whether non-conscious goals might influence nocebo responses, as well as positive placebo expectations. 93 Psychology undergraduates were randomly assigned to receive a placebo expectation or no placebo expectation and a goal prime or no goal prime.

The procedure was nearly identical to that of Study 2, with one exception: the TWPE and TPEC groups were told that the writing task would have a negative effect on sleep, as excessive thinking stimulates the brain and delays sleep. Participants in the placebo-expectation group were found to report more disturbed sleep than those participants who did not expect the writing task to hinder their sleep pattern. Yet researchers found no statistically significant differences between the expectation and control groups unless there was also a co-operation prime, where half of the participants read the co-operation story from the previous study. As in study 2, the findings of this study support the hypothesis that non-conscious goals moderate the effects of placebo expectations, and can be applied to non-laboratory settings over an extended timeframe. Study 3 adds that such results are relevant to both positive and negative placebo effects and that priming for co-operation alone does not result in the placebo effect.

Study 4

The purpose of study 4 was to determine whether priming for the co-operation motive would moderate placebo responses when participants had prior experience of the placebo symptoms. While in the previous studies participants were presumably unaware of the impact of sleep or music therapy, the majority of people will have had prior experience of the effects of caffeine, which is used as the placebo in study 4 (specifically, 87% of the participants tested reported having at least one caffeinated beverage per day). Therefore, the aim of this experiment was to ascertain whether "goal manipulations will only increase the influence of placebo expectations when the exact treatment effects are ambiguous to participants" (p.151) and whether possessing prior knowledge of a substance may override the priming of co-operation.

In a classic placebo experiment with a twist, participants were given placebo 'caffeine' capsules. The expectation group were told the study's purpose was to examine "the relations among caffeine, physiological reactions and a visual perception task", while the control group, who did not receive the caffeine placebos, were told that they were participating in a study of the relationship "between physiological reactions and performance on a visual perception task" (Geers et al. 2005, p.151).

All participants completed both a lifestyle questionnaire to gather information about their caffeine intake and other behaviours and a Likert-scale affect questionnaire in which participants rated their current feelings with descriptors such as 'mad', 'blue' and 'grieving', as well as caffeine-related items including 'excited', 'drowsy' and 'sluggish'. Having had their baseline blood pressure measured, those in the placebo-expectation groups received a placebo sucrose pill, which they were told contained the equivalent of over two cups of coffee. The expectation and control groups were each split into two groups, with one subgroup in each receiving a co-operation prime via the Scrambled Sentence Test used in Study 1. Next, participants were given a visual perception computer task (a modified version of the Stroop Test) to complete.

In addition to measuring for elevated blood pressure following the computer task, the researchers recorded behaviours that they assumed indicated that participants thought they had ingested caffeine, such as touching their hands and face, and object manipulation. The researchers found that, as anticipated, expectation of the effects of caffeine only altered behaviour if participants had been primed for co-operation. Such participants also had a greater increase in systolic blood pressure than no-expectation participants. Therefore, the current findings support the notion that having no prior experience with symptoms is not responsible for placebo responses.

Study 5

The purpose of the final study was to establish whether priming for the goal of co-operation affects placebo responding beyond an existing placebo effect, as the previously conducted studies failed to provide evidence that placebo effects occur in the absence of such primes. This was accomplished by producing desirable effects and enhancing the placebo expectation by lengthening the music stimulus and enlisting the support of both the experimenter and a confederate, who confirmed the effects of the placebo therapy. Fifty-nine psychology undergraduates completed two questionnaires to gather information on affect and lifestyle, and were randomly assigned to the following experimental conditions:

- No Expectation, No Prime (NENP)
- Placebo Expectation, No Prime (PENP)
- Placebo Expectation, Co-operation Prime (PECP)

While the NENP group were told only that the study would assess the effects that music could have on mood, those in the PENP and PECP groups were informed that they would be participating in a music therapy session, and that the music they would be listening to was designed to produce positive feelings and alleviate anxiety. It was assumed that students would wish this therapy to succeed. During the session, a confederate entered the room pretending to be a student who had participated in the study earlier. The confederate asked the experimenter where he could obtain the music, as it helped him relax. A confederate also interrupted the NENP group session, but asked only if the experimenter had found his notebook.

All participants completed the Scrambled Sentence Test (with the PECP group receiving the co-operation prime words) and subsequently listened to seven minutes of ocean sounds, after which they again completed the affect questionnaire. Participants from all three conditions reported more positive feelings after the experiment, but the PENP and PECP groups experienced more affect enhancement overall, regardless of priming.

Analysis

The above studies clearly contribute a great deal towards current knowledge of how the moderation of goals impacts upon placebo responses, yet they also suffer from a number of limitations. Given the small sample sizes and the fact that all subjects were psychology undergraduates of presumably similar ages, the results of the studies may not apply to other populations. Additionally, because participants received a reward (partial course credit), some may have been biased towards co-operation to begin with, if they subconsciously felt such a 'favour' should be reciprocated. Also, the studies, with the exception of study 4, rely solely on highly subjective self-report instruments. Such instruments are problematic because participants may lack self-awareness regarding their own mind-set or they may misrepresent themselves in order to adhere to what they believe is the experimental aim, thus creating a reporting bias that can distort results (Hróbjartsson & Gøtzsche, 2004). In addition, using Likert scales to rate subjective emotional states may not generate reliable data, as participants may have different ideas about what constitutes a 4 on the 'happy' scale, for example.

The use of the psycholinguistic word test as a co-operation prime is also problematic, as it assumes certain words will evoke the same meanings and responses in all subjects, despite the fact that the personal experience of each subject may create different associations. Thus, it is a leap to assume that encountering such words as 'assist' and 'helpful' will automatically generate the goal of co-operation, and that reading words such as 'assert' or 'stubborn' will have the opposite effect.

In Study 2, the 'co-operation story' presents an additional problem as it may provoke different affective or motivational reactions in subjects. For example, a subject might identify with the accident victim rather than the helper, thus feeling helpless. Geers et al. (2005, p.149) note that "given the large numbers of factors that likely influence the sleeping habits of undergraduate students, [the study results] are quite striking". However, the researchers fail to acknowledge that such factors could act as confounding variables, potentially resulting in a type 1 error, or a false positive result.

Another aspect that was not taken into account in Study 2 was that disclosure itself can provide psychological benefits (Moerman, 2002), and writing thoughts before bedtime may have a relaxing effect that could make it easier to sleep. As such, some participants may have been relaxed by the disclosure activity and thus may have experienced more restful sleep not because of a non-conscious co-operation goal or expectation but due to the placebo effect of disclosure, and it is possible that more of these individuals were in the co-operation-prime groups. Thus, the researchers seem to have attributed the results solely to the co-operation-prime without considering the potential impact of extraneous variables.

Study 3 also fails to take into account a number of confounding variables. Although the authors mention removing three participants who took medication to help them sleep, there is no mention of controlling for other factors that may have affected sleep (such as loud noises in the night, caffeine at bedtime, etc.). Also, participants who had anxious thoughts and wrote them down before bed may have experienced disrupted sleep not because they were warned that the task would keep them awake but because dwelling on their thoughts did.

In Study 4, the authors do not indicate why self-touching is thought to be a reliable indicator for the belief that caffeine has been ingested. Perhaps there is a study attesting to this, yet it is not mentioned. Study 5 used a Likert-scale affect questionnaire with words such as 'carefree', 'tense', 'relaxed' and 'restless' (Geers et al. 2005, p.154). The rating of emotional states is highly subjective; therefore, the researchers might have measured physiological indicators such as blood pressure or heart rate as indicators of tension and stress as they did in study 4.

The researchers admit that the data generated by their series of experiments is at odds with much of the placebo literature, but suggest that they indicate directions for future research and an impetus to test novel hypotheses, such as the "role motivation plays in hypochondria, medical student syndrome, and decisions to take medication or seek healthcare" (Geers et al. 2005, p.155). It is also proposed that rather than "directly altering the evaluation of internal sensations, co-operation primes may actually alter participants' levels of suggestibility, which in turn may increase confidence in the placebo expectation", and thus, it is possible "that there are multiple pathways by which goals cause placebo responding" (Geers et al. 2005, p.155).

Overall, given the small, homogenous sample sizes, the use of subjective measurement instruments and the high potential for confounding, the results of these studies are not able to be generalised and the conclusions cannot be justified without further research. However, if such research did find that co-operation primes do indeed enhance placebo effects, this could have significant implications regarding the psychosocial context in which placebos are administered.

Identifying Placebo Effects with Data from Clinical Trials

The following study suggests placebo effects may be a behavioural rather than a physiological phenomenon, whereby those who are more optimistic about the treatment alter aspects of their behaviour in a manner which enhances their medical treatment. Malani's (2006) study sought to test the hypothesis that subjects in a clinical trial who believe that they have a higher probability of receiving the active treatment rather than a placebo will be more inclined to expect positive results, and thus more likely to experience placebo effects. The conditions chosen for study were ulcers and high cholesterol, as they could be objectively measured and are not generally amenable to placebo responses. Analysing data sets from 200 trials of ulcer medications and more than 30 trials involving the use of statins against LDL (bad) cholesterol, Malani (p.249) found that, as predicted, "a higher probability of treatment" was indeed associated with both a higher rate of ulcer healing and significant LDL cholesterol reduction, as well as more side effects. However, such expectation effects differed from one drug to the next.

Analysis

Milani reviewed a large number of trials, thus increasing statistical power. Also, the medications used in the trials were the first "meaningful" treatments that had been introduced for each condition, diminishing the possibility of self-selection bias among subjects (Malani, 2006, p.244). However, it is probable that people who had less faith in the efficacy of medications in general might have avoided such trials, while those who were more hopeful and optimistic, thus more inclined to have placebo responses, would sign up for any available trials. Having more placebo responders in the trials might magnify any differences between high-probability and low-probability trials. As such, it is unfortunate that subjects participating in clinical trials are not asked beforehand which group they believe they have been assigned to, or about their expectations regarding the treatment's efficacy (Price et al., 2008). As Thompson (2005, p.196) points out, simply participating "in a clinical trial can alter the course of an illness".

Another problematic assumption made by Malani is that subjects who are less optimistic about a treatment's efficacy will prefer the high-probability trial, but if this was the case, given the importance of psychosocial factors, pessimism might suppress placebo effects. Also, subjects may enter a trial not because they are particularly optimistic or pessimistic about the treatment under study, but because they fear the side effects of other available treatments; they may be motivated as much by the perceived safety of the treatment as its potential efficacy.

Another faulty assumption is that subjects are rationally optimistic or pessimistic. In other words, subjects in the low-probability trial will be more pessimistic about the possibility of receiving the active

treatment, whereas those in the high-probability trial will have a greater expectation of receiving it. However, as sales of lottery tickets show, many people anticipate positive outcomes against all odds, while others expect the worst even when there is no reason to. As such, being in a lower-probability trial would not necessarily suppress placebo effects by dampening expectations regarding the likelihood of receiving the active treatment.

A final problem is the lack of information regarding the type of placebo pills used in the trial and the frequency of administration. According to Kirsch (2005), subjects taking placebos who are not told whether they are depressants or stimulants will usually experience stimulant effects after taking red placebos and depressant effects after blue, but if they believe they are taking the placebos for pain relief, red pills work better than blue, white or green, and dose also matters, with higher doses being more effective than lower doses.

To support Malani's hypothesis, a systematic review of a broader array of conditions would be required (particularly those more amenable to placebo effects) and participants in such trials would be questioned beforehand regarding their beliefs about the treatment's efficacy and whether or not they think they will receive the active treatment. Confirmation of Malani's hypothesis in subsequent research would indicate that higher-probably trials have more value for all participants, even those in the placebo group.

Placebo Effects of Marketing Actions

In addition to clinically significant effects of the placebo, placebo effects are pertinent to several areas of everyday life, and can occur as a result of marketing practices. For example, brand-name foods are perceived as being better quality and thus, better tasting than unlabelled products, although objective investigations have found no correlation between price and quality (Shiv et al., 2005). Indeed, "branding accounts for a third of branded aspirin's therapeutic effect" (Thompson, 2005, p.198), suggesting that "discount drug policies may actually impair the efficacy of certain medications" (Berns, 2005, p.400).

Such consumer placebo effects are thought to operate non-consciously, evident in the finding that meat labelled 75% fat-free tastes better than the same meat labelled as containing
25% fat (Shiv et al., 2005). Marketing effects can be generalised to medication; both active medications and placebos are more effective when associated with a well-known brand name, and more elaborate placebos (such as injections or other therapeutic treatments) are more effective than pill placebos (Kirsch, 2005, p.794).

Shiv et al. (2005) conducted a series of experiments designed to test whether beliefs and expectations induced by marketing practices can influence the reported efficacy of a product. Initially, the researchers conducted a study in which 38 regular exercisers consumed an energy drink prior to working out. Participants were split into two groups, one of which was told that the drink had been purchased at regular price and the

other that it had been bought at a significant discount. Subjects who believed they had consumed the regular-priced drink perceived their workout intensity as higher and their post-workout state as less fatigued than those who thought they had consumed the discounted drinks. However, the researchers recognised that the pilot study contained a number of limitations, such as relying on self-report, the failure to include a control group and the fact that participants were merely informed of the price, but incurred no cost for the drink themselves. These were among several problems addressed in the three experiments which followed.

Experiment 1

In Experiment 1, the researchers sought to gather evidence of the effects of price discounts on placebo effects and ascertain whether or not expectancy influenced placebo effects non-consciously. 125 University students were randomly divided into four groups and were each given a popular energy drink, 'SoBe' which claims to boost mental acuity, and then solved word puzzles. Half of the subjects were assigned to the High-Expectancy group and received an expectancy prime in which they were asked to rate the anticipated efficacy of the drink on a scale of 1 (very bad) to 7 (very good), while those in the Low-Expectancy group did not. Half of the subjects in each of the two groups were led to believe that SoBe had been purchased at regular price and the other half that it was purchased at a discounted price. In contrast to the pilot study, the subjects in this experiment gave authorisation for their bank accounts to be charged the price of the drink. The four groups were therefore:

- Regular Price, High Expectancy– RP-HE
- Discount Price, High Expectancy– DP-HE
- Regular Price, Low Expectancy– RP-LE
- Discount Price, Low Expectancy– DP-LE

Another preliminary study was conducted to assess participants' performance on the task without the energy drink. This control group solved 9.1 puzzles on average, while the experimental groups solved the following:

- RP-HE – 9.9 puzzles
- DP-HE – 5.8 puzzles
- RP –LE -9.5
- DP-LE – 7.7 puzzles

Evidently, discounted price was associated with reduced performance in both the High-Expectancy and Low-Expectancy groups, but this effect was more pronounced in the High-Expectancy condition. The Regular-Price

condition results were not significantly different to those from the pilot study control group; thus, no positive placebo effects were found, only negative.

Experiment 2

Shiv et al. (2005) conducted Experiment 2 to discover why they had not seen positive placebo effects in Experiment 1, and to rule out alternative explanations, such as the possibility that those paying the regular price worked harder on the puzzle task to lessen the dissonance they potentially experienced as a result of the price paid. The methodology for this experiment was similar to that of Experiment 1. However, half the participants were assigned to a High-Price-Efficacy-Salience group in which the words "Given the price I was charged for SoBe..." were added to questions regarding the drink's efficacy in boosting performance (Shiv et al., 2005, p.388). Consequently, the difference in puzzle solving performance between the Regular-Price and Discount-Price conditions disappeared, indicating that "awareness of price-efficacy beliefs weakens these beliefs, thus eliminating the placebo effect" (Shiv et al., 2005, p.388). The authors draw the conclusion that such beliefs are ordinarily non-conscious. Once again, there were no positive placebo effects, only a negative placebo effect in the Discount-Price condition where subjects did not receive the prompt regarding price salience.

Experiment 3

The final study sought to further support the findings of the previous two by manipulating the price and purported effects of SoBe. Experiment 3, which had a subject pool of 204 undergraduate students, followed a similar methodology to Experiment 1, but the High-Expectancy group was created by providing information on the cover page of the instruction booklet given to subjects. This cover page attested to SoBe's performance-enhancement effects and the numerous studies that support them. This sort of overt suggestion also generates placebo effects for certain medical treatments, such as enhanced pain relief (Price et al., 2008).

Another goal of this experiment was to determine to what extent participants' levels of motivation and alertness mediated the observed effects. Having completed the puzzles, subjects filled in a Likert-scale questionnaire regarding their levels of motivation and alertness during the task. There was found to be a significant difference between the High-Efficacy and Low-Efficacy groups, both in the Regular-Price and Discount-Price conditions. Results were as follows:

- RP-HE – 10.1 puzzles
- DP-HE –7.4 puzzles
- RP –LE -5.8
- DP-LE – 4.2 puzzles

This dramatic difference between the two expectancy groups is in line with other work in the field which has shown that both advertising claims and price have profound effects on the perceived efficacy of products and services.

Analysis

Several elements of the above series of experiments are subject to criticism, including the fact that participants were drawn from the university population, which is likely to be skewed toward those of high socioeconomic status and a specific age range, limiting the ability to generalise the results. It is possible that price discount effects are more or less pronounced among those of other age groups or backgrounds.

Another problem is the assumption that elaborating upon expectations makes them stronger. As a method for activating expectancies, this strategy has not been adequately justified by the authors. The fact that only the third experiment saw a positive placebo effect indicates that activating expectancies by rating the drink's perceived efficacy was a weak approach at best. Also, while the authors mention that expectations regarding the energy drink's efficacy for improving performance were generally lower in the discounted-price condition, individual expectation ratings are not matched up with individual puzzle scores. It is theoretically possible that subjects who achieved higher scores on the puzzle task had lower efficacy expectancies, yet with only pooled data, there is no way of knowing. Additionally, the researchers used a subjective self-report questionnaire rather than objective physiological measures to determine alertness.

Shiv et al. (2005) conclude definitively that price effects are non-conscious, but given the paucity of research in the field, one study with a limited population will not necessarily generalise to the wider population, and more research is required for confirmation. However, the implications of this study are intriguing, bringing forth a number of potential ethical dilemmas. For example, marketers may significantly increase prices and imply that the quality of a product has been improved, or make false claims regarding a product's benefits in order to generate placebo effects (Shiv et al., 2005). There are also disturbing implications for the marketing of medications and medical procedures.

Mind-Set Matters: Exercise and the Placebo Effect

Increasingly, doctors have begun to recommend behavioural changes such as exercise to treat or alleviate the symptoms of chronic conditions including diabetes, depression and even cancer (Crum & Langer, 2007, p.4). However, it has often been questioned by researchers to what extent the seemingly remarkable benefits of exercise are due to the placebo effect, thereby providing evidence for the "potentially powerful

psychological control people have over their health" (ibid). In order to test the hypothesis that an individual's mind-set mediates the connection between exercise and health, Crum and Langer (2007) conducted a study of 84 women who worked at various hotels as room attendants. The experimental group (44 subjects) were told about the significant health benefits of the sort of exercise they obtained on the job (such as total calories burned for each activity), while the control group was provided with no information. The goal of the study was to examine whether the mind-set of subjects (perceived exercise levels and their expected benefits) could increase the actual health benefits obtained through exercise.

Health information was gathered at the beginning of the study and again four weeks later using both self-report questionnaires (specifically designed to provoke an increase in perceived exercise regardless of actual exercise) and objective physiological measurements, including weight, body fat, body mass index (BMI), waist-to-hip ratio (WHR) and blood pressure (BP). There was no increase in reported exercise levels or dietary changes in either group over the course of the study, nor were subjects aware that their work provided good exercise before being informed of this.

By the end of the four-week study, experimental subjects had lost an average of 2lbs, decreased their BP and body fat, and improved their BMI and WHR. In addition, the average amount of exercise that those in the informed group perceived they were getting increased by 20%, despite the fact subjects did not report higher levels of activity at the end of the study. Thus, the researchers concluded that mind-set did indeed enhance the beneficial effects of exercise, a result which is in line with other placebology findings. For example, favourable prognoses can enhance placebo effects (Thompson 2005, p.196), as can expectancies that are based on prior experience or information perceived as reliable (Caspi & Bootzin 2002).

Analysis

Like those previously detailed, Crum and Langer's study is not flawless. It had a small subject pool, consisting of predominantly Hispanic females, all in the same career. Also, the assumption that subjects' behaviour did not change over the course of the study is based solely upon self-report, which is notoriously unreliable. As Thompson (2005, p.115) emphasises, "placebos control for more than the outcome itself. Changes in the attitudes, incentives, and behaviours...can themselves alter the outcome", and reporting bias may have also been a problem.

Price et al. (2008) note that some placebo effects may actually be misperceptions due to selective attention. For example, if those with fitness goals attend selectively to aspects of physical appearance or

feelings of health that support these goals or desires, they may come to the conclusion that whatever they have been doing to improve their physical fitness is highly effective. This can create a self-affirming feedback loop in which beliefs about a treatment or behaviour's efficacy cause the person to engage in more of that treatment or behaviour, which in turn generates more apparent signs of effectiveness. Subjects may have unknowingly underreported unhealthy behaviours in the pre-study questionnaire because they were less attentive to health-related behaviours until the experimenters encouraged them to focus on such behaviours.

There is also the possibility that experimental subjects obtained more exercise over the course of the study without being consciously aware of it. Subjects may have worked more energetically in the experimental group than the control group because they felt more enthusiastic due to the health benefits they believed their work was generating, or because they now had a more positive impression of their work in general. Studies have found that patients who believe that an outcome will be positive are more inclined to engage in better self-care behaviours, which increase the likelihood of a positive outcome (Thompson, 2005). Also, the positive attitude of a doctor can generate placebo effects (ibid), so it is logical to assume that an experimenter who is enthusiastic about the health benefits of work-related activities could also inspire placebo effects over and above those obtained by belief in the benefits of exercise on its own.

According to Thompson (2005, p.161), "patients with organic disorders have emotional reactions to their disease", and this complex mind-body interaction, particularly with chronic conditions, indicates that there are benefits to improving a patient's mind-set. As such, even placebos that do nothing other than improve mood may generate empowerment and thus more effective coping behaviours, such as adhering to treatment regimes.

It would be extremely difficult to control for all variables in order to ensure that the effects seen in the Crum and Langer study did not result from subtle behavioural changes or reporting biases. However, if providing information on the health benefits of on-the-job exercise inspires modification in health-related behaviours that are notoriously difficult to change, it may be a practice worth encouraging.

Is the Placebo Powerless?

In this final paper, Hróbjartsson and Gøtzsche (2004) revisited their earlier meta-analysis, adding data from an additional 52 new trials to their original 114, pooling all trials together and looking at the average results for a broad array of conditions including jet lag, obesity, alcohol abuse, bacterial infections, enuresis, infertility, epilsepsy, labour, menopause, marital discord and Parkinson's disease, with 46 conditions in total. Their only stated exclusion criteria were studies that were not double-blinded or for which dropout rates were more than 50%. The researchers concluded that there is "no evidence of a generally large effect of placebo

interventions" and that "a possible small effect on patient-reported continuous outcomes, especially pain, could not be clearly distinguished from bias" (p.91). Hróbjartsson and Gøtzsche's remarkable claim that placebo effects are not statistically significant or clinically important stands in direct contrast to the majority of studies published in the field. Others have found placebo responses in clinical trials to be as high as 80% (Thompson, 2005, p.193), and the power of the placebo was indicated by study of 6,928 people, which found that "perceived health was a better predictor of mortality than actual health" (Crum & Langer, 2007, p.166).

Analysis

Unsurprisingly, Hróbjartsson and Gøtzsche have been heavily criticised for failing to account for the fact that various conditions respond differently to placebo treatment. Wampold et al. (2005, p.842) found that conditions such as depression, insomnia and chronic pain are highly responsive to placebos; acute pain, nausea caused by chemotherapy and asthma may be somewhat responsive; and bacterial infection and anemia are not responsive, yet Hróbjartsson and Gøtzsche pooled data from all of these conditions.

Attempting to measure the effects of placebos used in place of treatments such as psychotherapy is notoriously difficult. Because these placebos "are clearly distinguishable from the purportedly active treatment" and administered by "advocates of the active treatment", their effects may be diminished by behavioural signals sent by doctors or therapists (Wampold et al., 2005, p.849). Psychologically 'active' and 'placebo' treatments must be structurally equivalent for true placebo effects to be determined (Wampold et al., 2005, p.850). In addition, researchers have found that doctor expectations regarding whether or not patients are receiving placebos can influence placebo responses (Wampold et al., 2007), which suggests that even in double-blind studies, the beliefs of medical practitioners may still enhance or detract from placebo effects.

According to Wampold et al. (2005), placebo effects are robust for all conditions amenable to placebo responses and placebos are often as effective as active treatments. The authors assert that Hróbjartsson and Gøtzsche's meta-analysis did not detect significant placebo effects because the researchers aggregated their data without regard to the types of disorders included and how amenable each was to placebo effects (p.841). Wampold et al. (2005, p.842) reanalysed the studies used in the meta-analysis, controlling for amenability to placebo effects of individual conditions and determined whether research designs "disadvantaged the placebo treatment". They also looked at the size of placebo effects in relation to no-treatment groups and compared objective and subjective measures of placebo effects. In contrast to Hróbjartsson and Gøtzsche, they found the placebo effect to be extremely powerful.

Nevertheless, there exists some evidence that placebo effects may not be as strong as Wampold et al. (2005) assert. Correlation does not necessarily imply causation; for example, some people become anxious and experience high blood pressure in the presence of a new doctor, but once they have seen that doctor a few times, blood pressure drops. This may suggest a remedy for hypertension has been effective, when in actuality the patient has just become more relaxed in the doctor's presence (Thompson, 2005, p.195). Thompson (2005, p.149) notes that "improvement in the treated individual is the sum of the tested treatment's effect, the placebo effect, and the effect of the treated condition's natural history". However, many studies fail to incorporate a control group that does not receive treatment (Price et al., 2008), which makes the magnitude of placebo effects difficult to assess. Indeed, regression to the mean and the natural course of an illness may generate improvements that could be mistaken for placebo responses, particularly for conditions such as pain that tend to fluctuate or resolve on their own, thus it is near impossible to estimate the magnitude of placebo effects for any given condition (Price et al., 2008).

Overall, the conclusion drawn by Hróbjartsson and Gøtzsche (2004) stands in contrast to the widely held view within the medical community that many alternative medications and possibly even certain analgesics and antidepressants operate predominantly through placebo effects (Malani, 2006). Using trials that included a no-treatment arm and conducing a meta-analysis for each of the conditions individually rather than pooling the data would have been a more effective way to determine the robustness of placebo effects, as evidently, these can vary dramatically from one condition to the next.

Conclusion

Placebos can cause very real physical effects, producing changes in respiration, immune function and neurotransmitter and endorphin levels (Kirsch, 2005). As such, "discarding all placebo effects in a single trash basket of 'untruthfulness'...diminishes our knowledge of important dimensions of health care" (Kaptchuk, 2002, p.817). Also, given that antidepressants often have little more effect than placebos and that drugs such as morphine lose a significant amount of their efficacy when administration is hidden, it appears that many of the effects of many commonly prescribed active medications are actually attributable to placebo responses (Kirsch, 2005).

The studies examined in this paper all, to varying degrees, indicate the importance of the psychosocial context in placebo response and healing. Thompson (2005, p.185) asserts that "patients are more likely to experience placebo effects if they like and have confidence in the doctor and if treatment is prescribed enthusiastically", consistent with the fact that "placebo mechanisms...are driven by the psychosocial context surrounding drug administration" (Price et al., 2008, p.584). The importance of psychosocial factors can be seen in the fact that depressed people are more likely to be diagnosed with and die from heart disease (Thompson, 2005, p.75). This suggests that treating conditions such as depression that are highly amenable to placebo effects may bring concomitant health benefits, and that taking a more holistic approach to medicine may be warranted.

Although it is increasingly recognised that placebos may, in certain cases, be viable treatment options, it is important to balance the need to maintain trust within physician-patient relationships with the benefits that placebo treatments can potentially provide, given that disclosures regarding the fact that a given treatment is a placebo can negate its effects (Giordano, 2008, p.1317). In other words, the value of trust must be weighed against the value of hope. In the case of psychotherapies, viewing placebo effects as inert or a sham particularly

problematic, because practically any aspect of a given psychotherapy could be considered a placebo, but at the same time, psychotherapy can produce specific results that treat the presenting condition. For example, a depressed person who experiences increased hope, happiness and serotonin has been effectively treated (Kirsch, 2005).

Given the difficulty in measuring what might be considered the active aspects of placebo responses, including "expectancy, desire, somatic focus and type of goal" using physiological measures such as brain imaging, placebo responses remain difficult to quantify (Price et al., 2008, p.577). However, Kirsch (2005, p.800) argues that "if the control procedure is effective in treating the disorder, then it is a bona fide treatment", even if the ingredients are "hope or faith or response expectancy".

Ultimately, the question becomes "not just 'what works' but also 'under what conditions' and 'for what reasons'" (Caspi & Bootzin, 2002, p.444). Thompson (2005, p.150) captures the changing perception of placebo effects with his assertion that "a positive approach enhances treatment...placebo therapy is a form of psychotherapy, and one we should recruit and encourage".
This paradigm shift is evident in the changing attitudes of clinical practitioners toward placebo use and their willingness to contemplate conditions under which placebo use would be an acceptable clinical practice. Giordano (2008, p.1371) suggests that for placebo use to be ethical, certain criteria must be met, including a solid physician-patient relationship and a concrete diagnosis that would not be amenable to an 'active' intervention. He suggests that to avoid deception, doctors could tell patients that although the placebo treatment will not directly cure a condition, it can trigger mechanisms which may reduce symptoms.

A review of the literature indicates that placebo effects are robust for certain conditions and strongly influenced by psychosocial context, conditioning, expectancy and non-conscious goals. Contrary to the findings of Hróbjartsson and Gøtzsche, varying conditions produce vastly different placebo responses, so attempting to determine the magnitude of placebo effects in general would be fruitless. Recent advances in the field of placebology suggest that given the specific physiological and psychological benefits that placebo effects are capable of generating, the emphasis is shifting from attempting to rule them out to studying their potential as treatment elements, and applying this fresh perspective to the ethical dilemmas that surround their administration. From the above studies, it may be inferred that the original definition of the placebo as being 'inert' applies only to the pharmacological properties and chemical structure of the placebo. Often, placebos are psychologically and therefore, physiologically potent and so to label them as 'inert' or 'futile' is to overlook the real and measurable physical effects of the psychological expectancies induced by their administration that are of medical benefit to patients.

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