RUNNING HEAD: CONDITIONING AND PLACEBO

A Functional-Cognitive Perspective on the Relation between Conditioning and Placebo Research

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Abstract

From a functional-cognitive perspective, conditioning is relevant for placebo research because it (a) highlights stimulus pairings (e.g., taking a pill that contains an active pharmacological substance causing a drop in blood pressure) as a potential environmental cause of creating or boosting placebo effects (e.g., reduction in blood pressure after taking a similar pill that no longer contains the active substance) and (b) orients researchers to potential mental mechanisms that might underlie those effects (e.g., the formation of associations or propositions). After describing the functional-cognitive perspective on conditioning, I provide a brief overview of three generations of conditioning theories (Stimulus-Response, Stimulus-Stimulus, and propositional theories) and evaluate different ways in which conditioning and placebo research can be related. Finally, I discuss the implications of the functional-cognitive perspective on conditioning for the status of the placebo phenomenon.

Keywords: placebo, conditioning, association formation, cognition, functional psychology

Extensive empirical evidence supports the conclusion that conditioning plays a crucial role in establishing and boosting placebo effects (e.g., Colloca & Miller, 2011). In this article, I put forward a functional-cognitive perspective on the relation between conditioning and placebo effects. This perspective is built on a definition of conditioning that does not refer to any explanatory mental mechanisms such as expectations or associations. By separating conditioning as a to-be-explained effect from the mental processes that might explain this effect, new light can be shed on different claims about conditioning and its role in placebo effects. In a first section, I describe what it means to define conditioning as an effect rather than a mental process. Next I present a brief overview of various ideas about the mental processes that might explain conditioning effects. Afterwards, I discuss the implications for placebo research.

Conditioning as an Effect

In a recent paper, my colleagues and I defined learning as ontogenetic adaptation, that is, as the impact of regularities in the environment on behavior during the lifetime of the organism (see De Houwer, Barnes-Holmes, & Moors, 2013, and De Houwer & Hughes, in press, for more details). From this perspective, different types of learning can be distinguished on the basis of the type of regularity that changes behavior. Non-associative types of learning encompass the effects of regularities in the presence of one stimulus. For instance, habituation refers to the decline in intensity of an original response that occurs as the result of the repeated presentation of the response evoking stimulus. The term conditioning, on the other hand, refers to associative types of learning in which a change in behavior is due to regularities in the presence of two events. In this article, I focus on classical conditioning (also known as Pavlovian conditioning), in which behavior changes are a function of the pairing of two stimuli, namely a conditioned stimulus (CS) and an unconditioned stimulus (US). For instance, dogs that initially do not salivate upon

hearing a buzzer, start salivating in response to the buzzer (CS) after it was paired with food (US) (Pavlov, 1927).

This definition of conditioning is functional in nature, that is, it defines conditioning as a function that maps regularities in the environment onto changes in behavior. Put differently, it defines conditioning as an effect, that is, as the impact of CS-US pairings on behavior (also see Eelen, 1980; Stewart-Williams & Podd, 2004). As such, the claim that a particular change in behavior is an instance of classical conditioning implies a functional explanation of that change in behavior. More specifically, it implies that the change in behavior (e.g., increased salivation in response to the buzzer) is due to the pairings of stimuli (e.g., buzzer and food) rather than other environmental events (e.g., the mere repeated presentation of food). Crucially, a functional definition of conditioning does not entail any assumption about the mental processes via which CS-US pairings influence behavior. Instead, it allows for all kinds of mental explanations of the conditioning phenomenon and therefore does not limit conditioning to a subclass of effects that is supposedly mediated by one particular mechanism. In fact, the theoretical freedom offered by functional definitions of psychological phenomena such as conditioning is one of the important strength of those types of definitions. It allows one to adopt a functional-cognitive framework that combines the strength of functional (e.g., Skinnerian) approaches directed at explaining behavior in term of environmental events and cognitive approaches aimed at explaining psychological phenomena in terms of mental mechanisms (see De Houwer, 2011, and Hughes, De Houwer, & Perugini, 2016, for more details).

Rather than accepting a particular mental explanation of conditioning in an a priori manner by incorporating it in the definition of conditioning, theories about the mechanisms that mediate conditioning effects can be substantiated only by examining the moderators of

conditioning, that is, the variables that influence its presence and magnitude (De Houwer, 2011; Hughes et al., 2016). A good theoretical model of conditioning is one that can explain the effect of known moderators (high heuristic value) and correctly predicts the effects of yet untested moderators (high predictive value). Unfortunately, like most other humans, scientists are not immune to the logical fallacy known as "affirming the consequent". Hence, when they observe that the prediction of a theoretical model is confirmed, they often conclude too quickly that the model is correct. This fallacy sometimes even results in scientists conflating a phenomenon with one possible explanation of that phenomenon. In fact, as will become clear in the next section of this chapter, much of the confusion surrounding the conditioning literature resulted from this kind of conflation. In order to clear up some of this confusion, I will list and evaluate a number of theoretical models of classical conditioning while keeping those explanations clearly separated from the to-be-explained phenomenon.

A Brief History of Conditioning Models

First Generation: S-R Association Formation Models

Conditioning effects were initially explained in terms of the automatic formation of stimulus-response (S-R) associations (e.g., Byrne & Bates, 2006). Before the CS and US are paired, the US (e.g., food) already evokes a certain unconditioned response (UR; e.g., salivation). A prototypical S-R model postulates that, as the result of pairing the CS and US, the CS co-occurs with the UR, which is a necessary and sufficient condition for the formation of an association between the CS and UR. As the S-R associations gradually grow in strength with each CS-US pairing, the presentation of the CS also starts to evoke the UR, which is now called the conditioned response (CR; e.g., salivation upon hearing the buzzer). From this perspective, conditioning is simply about allowing neutral stimuli (CSs) to evoke novel responses that are

initially evoked only by the stimuli it is paired with (USs). This process is assumed to be (a) low-level in that it does not depend on (conscious) cognitive processes and (b) automatic because it can occur even under conditions that typically hamper cognitive processing (e.g., lack of awareness, time, attention, or intention).

Although this type of model was popular in the 1940s and 1950s, it was abandoned by most learning researchers from the 1960s onwards. In a high profile review article published thirty years ago, Rescorla (1988) reproduced a number of descriptions of this prototypical S-R model as they were provided in psychology textbooks at that time. He noted that "these quotations will certainly sound so familiar that many readers may wonder what is wrong with them. I want to suggest that the answer is "almost everything". … [they] come from … the reflex tradition … which sees conditioning as a kind of low-level mechanical process in which control over a response is passed from one stimulus to another." (pp. 151-152, parentheses added). Rescorla then pointed out that "the prevalent modern view [is] that conditioning involves the learning of relations among events … [this] is not a stupid process by which the organism willy-nilly forms associations between any two stimuli that happen to co-occur. Rather, the organism is better seen as an information seeker using logical and perceptual relations among events, along with its own preconceptions, to form a sophisticated representation of its world. Indeed, in teaching undergraduates, I favor an analogy between animals showing Pavlovian conditioning and scientists identifying the cause of a phenomenon." (pp. 153-154, parentheses added).

Rescorla's conclusions (1988) are based on a wide range of findings that contradict the predictions of S-R models of conditioning. For instance, it is abundantly clear that the CR (i.e., the new response to the CS that occurs as the result of CS-US pairings) can be fundamentally different from the UR (i.e., the response evoked by the US). Just think of a tone that is repeatedly

followed by a painful electric shock. Whereas the shock evokes the experience of pain as an UR, the tone will not evoke pain but rather fear as a CR. Fear is not part of the UR but is induced by the anticipation of the US. Although it is difficult to exclude the possibility that not a single instance of conditioning is due to the formation of S-R associations, at least in humans, there is surprisingly little strong evidence for the operation of these processes (see Hogarth & Troisi, 2015; Moors, Boddez, & De Houwer, 2017).

Second Generation: S-S Association Formation Models

The next generation of conditioning models remained true to the mechanism of association formation but integrated it within a cognitive approach in at least three ways. First, the second-generation models postulated that associations were formed between cognitive representations of stimuli, that is, nodes in memory that encode information about the sensory properties of those stimuli (e.g. Wagner, 1981). Because of this assumption, these types of models are often referred to as stimulus-stimulus (S-S) models. Second, these models typically assume that CS-US pairings have an impact on S-S associations only when the cognitive conditions are right. For instance, the pairing of a CS and US will lead to an association between the CS and US representation only to the extent that the US (Rescorla & Wagner, 1972) and CS (e.g., Mackintosh, 1975) are processed attentively. Third, it is often assumed that S-S associations can influence cognitive states. More specifically, the presentation of a CS can result in an expectancy that the US will be presented, which in turn leads to CRs that prepare the organism for the arrival of the US. Because preparatory responses are often different from URs (e.g., fear of an impending shock versus pain following an actually shock), S-S models can account for the observation that CRs and URs are often fundamentally different.

Many different S-S models have been proposed over the years (see Bouton, 2016, for a

recent review). Although they share the assumption that conditioning is mediated by S-S associations in memory, they differ with regard to the (cognitive) conditions under which associations are formed, the nature of the representations that are associated, and the conditions under which associations influence behavior and thinking. It is safe to say that S-S models are so dominant in the current conditioning literature, that it seems almost self-evident to say that conditioning is mediated by S-S association formation, much like it was self-evident in the 1950s to say that conditioning is due to S-R association formation. In part, this evolution is due to the many successes of S-S models in explaining and predicting the effects of moderators of conditioning (Bouton, 2016, for a review).

Nevertheless, there are reasons to believe that also S-S models do not provide an adequate account of conditioning. Hence, conditioning phenomena cannot simply be equated with an S-S association formation mechanism. In the milestone review paper that I referred to earlier, Rescorla (1988, p. 154) likened conditioning to "scientists identifying the cause of a phenomenon". The S-S association formation models that have been proposed until now, however, are a far cry from models that could underlie scientific discovery. Although S-S models undoubtedly assign a bigger role to cognitive processes than S-R models, they cling on to the idea of an essentially stupid association formation mechanism (i.e., what fires together wires together) that is made "smart" only by calling to arms cognitive processes that modulate the activity of the association formation mechanism and by allowing it to produce expectations. However, current S-S models lack the ability to encode important aspects of relational information, which render them incapable of accounting for higher-order cognitive processes such as analogical reasoning and scientific discovery. As Gentner (2016, p. 651) recently pointed out, "simple associative processes … can tell us that cow is strongly associated with calf and also

with milk, but they cannot record the nature of the relation. Using a purely associative process, we would not be able to discern that the relation between mare and colt is more like that between cow and calf than that between cow and milk".

The fact that current S-S models have little to say about scientific discovery only discredits them as models of conditioning to the extent that conditioning is actually akin to scientific discovery, as Rescorla (1988) claimed. Although surprising from the perspective of S-R and S-S models, evidence is indeed accumulating in support of Rescorla's (1988) proposal. Let us consider the impact of additivity on blocking. Blocking refers to the observation that conditioned responding to CS1 after CS1+CS2-US trials (i.e., CS1 and CS2 are presented together and followed by the US) is weakened or eliminated when CS2 is first paired with the US (i.e., CS2-US followed by CS1+CS2-US) compared to when CS2 is never paired with the US (e.g., only CS1+CS2-US). Typically, blocking is attributed to the fact that CS2 interferes with the formation of the CS1-US association (e.g., because CS2 reduces attention to the US on CS1+CS2-US trials; Rescorla & Wagner, 1972). In fact, the phenomenon of blocking is widely considered as one of the cornerstones on which S-S models of conditioning are built (Rescorla, 1988). My colleagues and I have, however, showed that blocking is often weak and highly parameter dependent (e.g., Beckers, Miller, De Houwer, & Urushihara, 2006; De Houwer, Beckers, & Glautier, 2002; Maes et al., 2016). Based on these findings, we proposed that blocking depends on an inferential reasoning process that allows participants to discount CS1 as a potential cause of the US (De Houwer, Beckers, & Vandorpe, 2005). More specifically, blocking occurs when participants can verify that CS1 does not add anything to the causal effect that CS2 has on the US. For instance, whereas blocking is strong when CSs are described as potential causes of the US, it is weak or absent when there are reasons to doubt that the CSs have

causal (and thus additive) effects on the US (e.g., by telling them the CS are mere effects or predictors of the US; see De Houwer et al., 2002; Waldmann & Holyoak, 1992). Likewise, when the context implies non-additive effects of causal CSs on US intensity (e.g., when USs have their maximal intensity on CS2-US trials and ceiling effects therefore prevent participants from determining whether CS1 adds anything to the effect of CS2), blocking effects are weak or absent, both in humans (De Houwer et al., 2002) and rats (Beckers et al., 2006). In sum, there are reasons to assume that Rescorla (1988) was right in assuming that conditioning has much in common with scientific discovery. Hence, S-S models are fundamentally flawed as models of conditioning.

Third Generation: Propositional Models

In response to growing evidence for the role of higher-order reasoning processes in conditioning, a new type of model was proposed that drops the idea of association formation altogether. Instead, these models postulate that conditioning is mediated by the formation of propositions (De Houwer, 2009; Mitchell, De Houwer, & Lovibond, 2009). Unlike simple associations, propositions can specify the precise way in which events are related. For instance, the propositions “CS causes US” and “CS predicts US” both relate the CS to the US but differ in the way that the CS and US are said to be related. Because they contain relational information and therefore have a truth value (Lagnado, Waldmann, Hagmayer, & Sloman, 2007), they allow for inferences (i.e., the construction of new propositions on the basis of existing ones) and can thus account for the evidence supporting the role of inferences in blocking and other conditioning phenomena (see previous section). They are also compatible with the well-known finding that even instructions about CS-US relations (e.g., “the tone will be followed by a shock”) result in CRs (e.g., tone evokes fear; e.g., Cook & Harris, 1937). From the perspective of

propositional models, actual CS-US pairings are just one source of propositions about CS-US relations, next to other sources such as instructions, observations, and inferences (e.g., Mitchell et al., 2009). Moreover, propositional models fit well with the observation that conditioning effects in humans typically require awareness of the CS-US relation (see Lovibond & Shanks, 2002, for a review). In sum, there are good reasons to believe that at least part of the conditioning effects that have been described in the literature are mediated by propositional processes. As such, propositional models are compatible with the idea that conditioning has much in common with higher-order cognitive phenomena such as problem solving and scientific discovery. In fact, my colleagues and I have recently argued that conditioning in humans is a symbolic phenomenon that is fundamentally similar to learning via instructions (De Houwer & Hughes, 2016). Symbols (defined broadly as stimuli that refer to other events) are not necessarily verbal but also encompass certain gestures (as in sign language) or other movements (e.g., the wink of an eye). We proposed that also spatio-temporal events such as the pairing of a CS and US can function as symbols (also see Hayes, Barnes-Holmes, & Roche, 2001). From this perspective, CS-US pairings are a symbolic cue that signals the type of relation between the CS and US, much like a sentence such as “the CS predicts the US” provides information about the CS-US relation.

Multiple Process Models

Regardless of the merits of the symbolic perspective on conditioning, it is now widely accepted that higher-order cognitive processes mediate at least some instances of conditioning. Many learning researchers, however, cling on to the idea that there are also instances of conditioning that are mediated by S-R association formation (based on the famous aliens in the original Star Trek universe, I sometimes refer to these researchers as first generation Kling-ons)

or S-S association formation (i.e., next generation Kling-ons; e.g., McLaren et al., 2014). As such, these researchers defend a multiple process perspective according to which conditioning effects can result from different types of mechanisms (e.g., McLaren et al., 2014). Although such a perspective seems attractive at first sight, it also has important downsides (see Mitchell et al., 2009, and Boddez, De Houwer, & Beckers, 2017, for a discussion). Most importantly, its merits depend on the extent that specific and plausible assumptions are made about how different types of processes interact (e.g., when which process will underlie conditioning effects). Without these assumptions, multiple process models (i.e., models which assume that different instances of conditioning might be mediated by different mental processes; e.g., McLaren et al., 201) offer little more than posthoc explanations and a false sense of understanding.

Different Ways in Which Conditioning Might Be Involved in the Placebo Effect

S-R Association Formation as a Source of Placebo Effects

So what does all of this tell us about the way in which conditioning might contribute to placebo effects? When placebo researchers claim that conditioning processes contribute to placebo effects, they sometimes seem to use the term “conditioning” to refer to the process of S-R association formation. For instance, in a review paper on placebo-induced relief from nausea, Quinn and Colagiuri (2015, p. 450) wrote that “Conditioning-based models of placebo responding propose that contextual features, such as the treatment setting or ritual of administration, associated with the nauseogenic drug or procedure function as conditioned stimuli (CS). These stimuli become associated with the source of nausea, or unconditioned stimulus (US), and hence the nausea itself, the unconditioned response (UR). In turn, these contextual features could themselves elicit nausea and vomiting, the conditioned response (CR).” Sometimes, conditioning is contrasted with expectancies as being different potential sources of

placebo effects, with the added assumption that both mechanisms operate under different conditions. For instance, Benedetti et al. (2003, p. 4315) argued that “placebo responses are mediated by conditioning when unconscious physiological functions such as hormonal secretion are involved, whereas they are mediated by expectation when conscious physiological processes such as pain and motor performance come into play”.

It should be clear that this perspective on the relation between conditioning and placebo effects is not only limiting but also implausible. It is limiting in the sense that conditioning can be much more than simply the operation of that one mechanism. It is implausible in that many findings question the validity of S-R models of conditioning (Rescorla, 1988) and very little evidence has been found for the operation of the S-R mechanism in humans (e.g., see Hogarth & Troisi, 2015, for a recent review questioning the role of S-R learning in addiction). If there is so little evidence for S-R association formation processes in humans, then maybe those S-R processes also do not play such a big role in placebo effects. In any case, it is important not to simply equate claims about the importance of conditioning for placebo effects with claims about the importance of S-R association formation processes for placebo effects.

S-S Association Formation as a Source of Placebo Effects

Regardless of whether some instances of conditioning are mediated by an S-R mechanism, it is now widely accepted that conditioning cannot simply be contrasted with cognitive accounts of placebo effects. Most notably, the current emphasis on the role of expectancies in placebo effects (e.g., Colloca & Miller, 2011) is perfectly compatible not only with the notion of conditioning as an effect but also with both S-S and propositional models of conditioning effects (Crombez, Baeyens, Vansteenwegen, & Hermans, 1997; Kirsch, 1985; Stewart-Williams & Podd, 2004). As Colloca and Miller (2011, p. 1864) argued, “it is necessary

to overcome any strict dichotomy between conditioning and expectation mechanisms, as the former involves information processing by which a subject anticipates (i.e. expects) a future event". Note, however, that placebo researchers should also be wary of equating conditioning with S-S association formation. Neither S-R association formation, nor S-S association formation is necessarily the only mechanism via which stimulus pairings can produce placebo effects. Hence, claims the relevance of conditioning (defined as the impact of stimulus pairings on behavior) for placebo research can go beyond claims of the relevance of S-S association formation for placebo research.

Propositions about Stimulus Relations as a Source of Placebo Effects

Although S-S models of conditioning provide an interesting perspective on the potential role of conditioning in placebo effects, I believe that this perspective on conditioning is still too limiting.[1] If conditioning is defined functionally as the impact of stimulus pairings on behavior, then one can also consider the possibility that stimulus pairings are not just causes of S-S associations that produce expectancies. From a propositional perspective, stimulus pairings produce full blown propositional beliefs about the way in which events in the world are related. It might well be that these propositional beliefs underlie the expectancies that produce placebo effects. There are a number of reasons for why such a propositional perspective on the role of conditioning is preferable to an S-S perspective. First, one could argue that expectancies are themselves propositional beliefs (e.g., the belief that an event is imminent). Rather than assuming a mysterious transformation from non-propositional associations to propositional expectancies, it seems more plausible to assume that expectancies result from other propositional

[1] Proponents of S-S models of course do not deny that elements other than stimulus pairings (e.g., instructions, context) are important for placebo effects (e.g., Colloca & Miller, 2011). However, defining conditioning in terms of S-S association formation does imply that *stimulus pairings* have an impact only because they result in the formation of S-S associations.

beliefs, including beliefs about the pairing of stimuli (e.g., the proposition that the CS repeatedly precedes the US which might be formed after experiencing the pairing of CS and US). In fact, there is strong evidence to support the conclusion that CS-US pairings result in US expectancies only if people have conscious beliefs about the CS-US pairings (see Lovibond & Shanks, 2002, for a review; but see Jensen, Kirsch, Odmalm, Kaptchuk, & Ingvar, 2015, for evidence of unconscious conditioning in the context of placebo research). Second, a propositional perspective fits well with the finding that conditioning, instructions, and prior beliefs closely interact in determining placebo effects (Colloca & Miller, 2011; Quinn & Colagiuri, 2015). For instance, placebo instructions seem to be much more effective when they are combined with initial conditioning trials in which the treatment is paired with an active pharmacological agent (e.g., Quinn & Colagiuri, 2015). The idea that conditioning experiences (i.e., stimulus pairings) produce propositional beliefs about stimulus relations implies that those beliefs can easily be related to and thus interact with other propositional beliefs that are based on instructions or prior experiences. In sum, compared to S-S models, propositional models of conditioning provide a much richer framework for understanding how conditioning experiences relate to expectancies.

Propositional models also highlight the fact that stimulus pairings can lead to much more than expectancies about the presence of stimuli. Most importantly, they also result in beliefs about the nature of the CS-US *relation* (e.g., CS predicts the US, CS causes the US, CS is an effect of the US, CS sometimes co-occurs with the US, …). Although expectancies might indeed be particularly important in guiding behaviors, some data suggest that propositions about CS-US relations can have an effect even in the absence of (US) expectancies. For instance, research on evaluative conditioning (i.e., changes in liking due to stimulus pairings) suggest that conditioned preferences linger on even after CSs have been extinguished as predictors of the US, thus

showing conditioned responding in the absence of US expectancies (e.g., Hermans, Vansteenwegen, Crombez, Baeyens, & Eelen; 2002; see Hofmann, De Houwer, Perugini, Baeyens, & Crombez, 2010, for a review). Likewise, consider the idea of drinking water from toilet bucket that has been perfectly disinfected. People are uncomfortable with doing so even though they have no reason to expect that there will be any discomfort or risk involved (Rozin, Millman, & Nemeroff, 1986). Examples like these might shed new light on the so-called open placebo effects. Beneficial effects of placebo treatments are sometimes observed even when participants are informed that the placebo treatment does not contain any active pharmacological substance (e.g., Kaptchuk et al., 2010). In these cases, the mere fact of entertaining a proposition that relates a treatment with an outcome might produce that outcome even when there is no expectancy that the treatment will work. Although this idea is highly speculative at this point in time and the merit of propositional models for placebo research does not hinge upon the veracity of this idea, it is worth keeping in mind that there is more to psychology than expectations.

Stimulus Pairings as a Source of Placebo Effects

Despite the merits of a propositional perspective on the role of conditioning in placebo effects, it should be clear that even this perspective is too limiting. At least in principle, it is possible that different conditioning effects are mediated by different mediating mechanisms, even mechanisms that have not yet been considered. Rather than continuing to make the mistake of equating the phenomenon of conditioning with whatever mechanism is in vogue at a certain period in time, it is better to think of conditioning as an effect when considering its relevance for placebo research (also see Stewart-Williams & Podd, 2004).

More specifically, there is merit in examining whether placebo effects qualify as instances of conditioning. Such a claim implies that the placebo effect involves a change in

behavior (in a broad sense that includes motoric, physiological, and neurological responses) that is due to the pairing of stimuli. Take the prototypical example of a pill that initially contains an active pharmacological component that produces a drop in blood pressure. After someone has taken the active pill on multiple occasions, a similar pill without the pharmacological component might also produce a drop in blood pressure. The latter effect could be defined as a placebo effect that is an instance of classical conditioning. If one allows for the possibility that stimulus pairings exert an impact on behavior that occurs a long time after those stimulus pairings, one could even argue that most placebo effects are instances of conditioning. Indeed, effects of many placebo treatments might hinge on having previous experiences in which similar treatments were paired with active components that led to beneficial effects (Colloca & Miller, 2011).

The claim that a particular placebo effect is an instance of conditioning has explanatory value in that it elucidates the environmental causes of the observed change in behavior (De Houwer, 2011; Hughes et al., 2016). For instance, explaining the effect of a placebo pill in terms of conditioning implies that the pill has its effects because similar pills previously went together with a certain active pharmacological substance. Such functional explanations are not trivial because they eliminate other possible functional explanations (e.g., the mere repeated presentation of the pharmacological substance) and imply that the placebo effects might be similar to other conditioning effects in terms of its moderators (e.g., the fact that exposure to the placebo pill prior to receiving an active pill might reduce the placebo effect). Moreover, although the claim that placebo effects are instances of conditioning does not commit itself to a particular explanatory mechanism, it also has implications for mechanistic accounts. Most importantly, it orients researchers to a set of possible mechanisms that *might* produce the placebo effect (e.g., the formation of S-R associations, S-S associations, or propositions). Once it has been

demonstrated that the placebo effect qualifies as an instance of conditioning (i.e., that the observed change is due to stimulus pairings), further studies can be conducted to examine which conditioning mechanism is most likely to mediate the effect.

In sum, a functional-cognitive perspective on the role of conditioning in placebo research can help to reveal the environmental causes and potential moderators of placebo effects while it also facilitates the discovery of mechanistic explanations of those effects. This is why I believe that research about the relation between conditioning and placebo effects is best conceptualized in terms of the contribution of stimulus pairings to those effects (see De Houwer & Hughes, 2016, for a similar conclusion and a more in depth discussion about the nature of evaluative conditioning, that is, the conditioning of preferences).

What are Placebo Effects?

Having said this, the idea that placebo effects might qualify as instances of conditioning raises a number of important questions about the nature and usefulness of the concept of placebo effects. Matters are still relatively straightforward when placebo treatments are defined as "substances, given in the guise of active medication, but which in fact have no pharmacological effect on the condition being treated" (Kirsch, 1985, p. 238). Based on such a definition, stimulus pairings could be seen as one reason for why substances (e.g., placebo sugar pills) can have effects even when they do not contain a pharmacological substance that can have that effect. It becomes more complicated, however, when the concept of placebo is extended to include procedures (e.g., sham operations) in addition to substances (e.g., sugar pills). Procedures could be referred to as placebo procedures when there is no known physical mechanism via which those procedures can exert their effect. Such a definition would, however, relegate all psychological interventions (e.g., psychotherapy) to the domain of placebo effects (Stewart-

Williams & Podd, 2004). One could extend the definition of placebo procedures in such a way that it requires also the absence of any known mechanism via which the procedure could exert its effect, including psychological mechanisms. Apart from the fact that this definition would render it difficult to establish placebo effects (because it requires one to exclude the impact of every possible physical and psychological mechanism) and implies that the boundaries of placebo effects change over time (when new physical and psychological mechanisms are discovered), it ignores scientific explanations that are not situated at the mechanistic level. Most crucially within the context of the present article, knowing that a placebo effect is an instance of conditioning reveals the functional cause of the observed change in behavior (it is due to stimulus pairings) regardless of whether the mediating mechanism (e.g., association formation) is known. Because also functional explanations reveal the causes of behavior, it seems improper to refer to functionally explained behavior as a placebo effect. To put it differently, why would some conditioning effects be referred to as placebo effects (e.g., the reduction in blood pressure due to a pill that no longer contains the active substance it used to contain) when others are not (e.g., the increase in salivation in response to a tone that results from prior tone-food pairings)?

Referring to certain conditioning effects as placebo effects also adds little because it does not provide additional insights in either the environmental causes or mental mechanisms involved in those effects. The concept of placebo effects not only lacks explanatory value, it also does not refer to a clearly delineated set of phenomena given that it is defined primarily in negative terms, that is, in terms of what does not count as a placebo effect (e.g., effects of pharmacological substances). One radical solution would therefore be to drop the placebo concept altogether. Regardless of the eventual fate of the placebo concept, progress in understanding placebo related phenomena is bound to depend on a continuing close integration

of placebo research with other (health) psychological research on environmental factors and mental mechanisms that determine (health related) behavior, including conditioning research.

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