Rethinking Explicit Expectations: Connecting Placebos, Social Cognition, and Contextual Perception

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Expectancy effects are a widespread phenomenon, and they come with a lasting influence on cognitive operations, from basic stimulus processing to higher cognitive functions. Their impact is often profound and behaviorally significant, as evidenced by an enormous body of literature investigating the characteristics and possible processes underlying expectancy effects. The literature on this topic spans diverse fields, from clinical psychology to cognitive neuroscience, and from social psychology to behavioral biology. We present an emerging perspective on these diverse phenomena and show how this perspective stimulates new toeholds for investigation, provides insights into underlying mechanisms, improves awareness of methodological confounds, and can lead to a deeper understanding of the effects of expectations on a broad spectrum of cognitive processes.

Expectancy Effects on Cognition and Behavior
Expectancy effects are ubiquitous. Be it in clinical contexts [1–5], academia [6,7], or sports [8–10], their impact is investigated, discussed, and debated in diverse scientific fields. Part of their appeal is certainly their profound impact on a wide range of cognitive processes such as perception, motor performance, working memory, and subjective evaluations, among others. However, there is more to it than scientific interest: knowledge about these effects and their consequences also informs applied fields such as modern clinical practice and scientific methodology [1,2,4]. By definition, an expectancy (see Glossary) is a ‘belief that something will happen or is likely to happen’ (www.merriam-webster.com/dictionary(expectation)). As such, the word ‘expectation’ entails a variety of concepts, and it is therefore important to clarify which type of expectations will be discussed in this review. Expectations can stem from implicit knowledge about statistical regularities, which is then used incidentally to adapt behavior [11–13], or they can stem from explicit beliefs about, for instance, situations, other agents, oneself, or specific events. Explicitly acquired expectations can be further subdivided into those that are deliberately employed for decision making and those which exert their influence incidentally. It is this latter type of expectations on which we will focus in this review.

A particularly well-studied effect of such expectations on perception and behavior is the placebo effect. That is, the expectation of symptom improvement can evoke strong effects on psychological variables and bodily functions, to the point of significant pain alleviation and improved motor performance. However, the impact of expectations is not restricted to treatment

Trends
A lasting impact of expectancy effects has been documented in clinical and non-clinical settings.
Placebo/nocebo effects are major topics for study in clinical research, whereas non-clinical research has focused on phenomena such as stereotype threat and self-efficacy.
Recent studies have begun bridging these fields by investigating different ways of inducing expectations and new types of outcome variables.
Commonalities between superficially dissimilar expectancy effects are beginning to emerge.

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outcomes – expectations elicited in social situations can have similar effects on perception and behavior. Moreover, basic perception itself has been studied in relation to influences by expectations. In light of the huge body of literature on such expectancy effects, the impact of expectations on perception and behavior seems to be profound, elicited by a wide range of situational and personal factors, and pertaining to an equally wide range of outcome variables.

However, most of the fields describing and investigating these effects have so far worked in parallel, rather than in conjunction. The goal of this review is to provide a first step into broadening the current view to integrate multiple approaches and instances of expectancy effects into a single framework. This framework specifically considers general expectations pertaining to entire situations, time-periods, or treatments rather than expectations pertaining to specific singular events, which have been studied extensively in domains such as perception and motor control [14,15]. Comparing different instances of expectancy effects reveals startling similarities as well as discrepancies between these effects. However, so far, few studies have attempted to bridge these different fields, and the methodological focus within these fields has been decidedly different, as we will argue in the course of this review. Thus, instead of presenting a full-scale model, which seems premature at this time, we hope to provide strong incentive for future scientific investigations in this vein. To this end, we will present an emerging perspective on the behavioral and physiological effects of such general expectations, and show how this perspective has the potential to provide new insights into the mechanisms involved, stimulate new roadblocks for experimental approaches, improve awareness for methodological pitfalls, and ultimately lead to a deeper understanding of the effect of expectations on a broad spectrum of cognitive processes.

**Placebo and Nocebo: Treatment Expectations in Clinical Contexts**

Expectancy effects in clinical contexts have been reported for centuries (Box 1) [16,17], and recent interest in this topic has led to a surge of investigations concerning the behavioral and neurophysiological underpinnings of these phenomena. The most intensively studied phenomena in this context are placebo and nocebo effects on pain [3,18–25], although recent studies have targeted a wide range of additional fields such as psychiatric conditions, respiratory diseases, immune function, and many more [4,5,26–29].

To gain traction in the flood of empirical evidence for placebo and nocebo effects, recent efforts have aimed at providing theoretical frameworks to account for the many aspects associated with treatment expectations. A learning perspective on placebo responses suggests that conditioning cues connected to prior experience with the treatment work in concert with verbal and social

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**Box 1. Historical Roots of the Study of Expectancy Effects**

In 1787 a textbook on empirical psychology written by Ferdinand Ueberwasser dedicated a paragraph to the then current knowledge on the ‘impact of the imagination on the body’. In particular, Ueberwasser describes how ‘bread crumbs, taken in the shape of pills have, by means of vivid imagination and expectations, yielded the same effects as the medication itself’ (117), p. 141; for a perspective see [16] and that ‘vivid imaginations, confident expectations of recovery or relief, and therefore firm trust in the physician, or in the medication alone, even if the medication is without effect by itself, can sometimes lead to real relief, or even recovery, for the invalid’ (117), p. 146. Ueberwasser does not limit his descriptions to placebo effects, he generalizes that ‘these and other observations lead to the general law of the impact of imagination on the body: especially those bodily changes that are caused by external and internal sensations are restaged by the awakened feelings of these sensations, though only more or less, and to a weaker degree’ (117), p. 142). Moreover, Ueberwasser emphasizes in his textbook that expectancy effects rely on physiological changes originating in the brain: ‘if an image is awakened in the mind, then (as physiology teaches us) specific changes in the brain arise, corresponding to this image and its intensity (…). Now, because the nerves originate in the brain and because they are the instruments of sensation and movement in the entire body, it ensues that also other, more remote body parts can be affected by imagination’ (117), p. 143).

It has been over 220 years since Ueberwasser described the impact of expectations on body and mind, and we are only now about to fully appreciate the widespread influence of expectations on cognition and behavior.
cues to generate widespread changes in the central nervous system which, in turn, lead to outcome changes based on treatment expectations [30,31]. Moreover, predictive coding accounts of placebo effects go one step further in postulating that the integration of learning and prior experience during placebo hypoalgesia occurs at multiple levels via recurrent systems in the ascending and descending pathways connected to placebo hypoalgesia [3,32].

These theoretical frameworks are specifically concerned with the role and implementation of both, prior experience and verbal suggestions, in the generation of placebo expectancies. Indeed, this question has occupied researchers for some time [21,23] and, although findings have been somewhat controversial, a lasting consensus in the field assumes roles for both processes in the formation of treatment-affecting expectations. Whereas verbal suggestions alone may or may not lead to changes in pain experience, the combination of conditioning mechanisms with verbal suggestions leads to robust placebo effects (Figure 1) [33,34]. This finding stands in contrast to nocebo hyperalgesia where verbal suggestions alone elicit strong nocebo effects without any further conditioning procedure [35]. Moreover, it seems that lessons from prior experience with the treatment cannot only stem from one’s own experience, but also from the observation of the experience of others, lending a strong social component to treatment expectancy effects [34]. This social aspect in placebo hypoalgesia might be modulated by oxytocin and vasopressin, that is, hormones involved in the regulation of social behavior [36,37].

Diverse physiological systems underlie the placebo effect, resulting in the idea of not one single effect, but many (Figure 2) [38]. Endogenous opioids are released during placebo hypoalgesia [39–42] and have effects on the rostral anterior cingulate cortex (rACC), the orbitofrontal cortex (OFC), lateral prefrontal cortex (LPFC), the anterior and posterior insular cortex (aIns, pIns), the nucleus accumbens (NAcc), the amygdala (Amy), and the periaqueductal grey (PAG) [24,43]. The modulatory descending pain control system further includes the thalamus, the hypothalamus, and the rostral ventromedial medulla (RVM), and descends even further down to the dorsal horn in the spinal cord [41,44–46]. Nocebo hyperalgesia additionally elicited modulated blood oxygen level-dependent (BOLD) activity patterns in the hippocampus [47,48]. Other transmitter systems have also been implicated in placebo effects, such as the endocannabinoid system in placebo hypoalgesia [49] and the release of endogenous dopamine, especially in the NAcc, in Parkinson’s disease [26] and in placebo hypoalgesia [43,50]. The dopamine system and the NAcc are both strongly implicated in the processing of reward, leading to the formulation of the placebo-reward hypothesis [51]. This hypothesis states that the expectation of a treatment effect, that is, of clinical benefit, could be considered a reward and therefore rely on similar structures to reward processing [51].

Treatment expectations have been studied almost exclusively in typical clinical outcome measures such as pain experience, motor performance, or scores on diagnostic scales. However, recent efforts have broadened this approach by targeting cognitive functions including working memory and cognitive control [52,53]. Interestingly, placebo instructions did not enhance actual performance in these studies, but significantly influenced the participants’ subjective perception of their performance [53] and produced changes in subjective drug effects and in the participants’ mood [52,54]. This pattern has also been found for some clinical outcome measures [28]. These findings suggest that the influence of treatment expectations on subjective measures is more widespread and robust than their influence on objective measures. A possible explanation for this difference can be found in response expectancy theory [55,56]. This theory postulates that expectations can directly affect subjective experience; in other words, the effects of expectations on subjective experience are at least partly unmediated [23,55,56]. However, this hypothesis only applies to subjective experience and its direct physiological correlates, whereas other factors are needed to mediate the effects on objective measures.
The study of treatment expectations has stimulated a spirited debate on how to use the emerging knowledge on placebo and nocebo effects in clinical practice [2,4,38–59]. Possible direct applications of the gained knowledge are manifold and form a promising avenue towards improving care and treatment of patients. However, clinical practice is not a faceless operation; it has at its core social processes such as clinician–patient interactions. As it is, these social settings hold a prominent spot in the generation of treatment expectations [31,34], and they even harbor their own types of expectations within and outside of the clinical environment. The next section will focus on such expectations.
Social Expectancies and their Effects

The interactive element of social settings adds another layer to expectancy effects. Not only one’s own expectations, but also those of others, are relevant in human interaction – and these latter expectations are particularly relevant for oneself when they relate to oneself. For instance, the expectations of teachers have been shown to affect their students’ academic performance (Pygmalion effect) [60,61]. Furthermore, even if the expectation is not issued by a specific person, but instead by society as a whole in the form of predominant stereotypes, these expectations can have negative effects on stigmatized individuals (stereotype threat). Stereotype threat describes the phenomenon that the performance of an individual can be severely impaired when that individual is aware of negative cultural stereotypes denying him or her proficiency in the ability in question. For example, when a test was labeled as diagnostic of intellectual ability, African American college students performed worse than their Caucasian counterparts, but this effect did not occur when the test came without such labeling [62]. Even though some seminal observations have been proven difficult to replicate – such as those relating to gender-based stereotypes and math performance (https://replicationindex.wordpress.com/2015/01/06/why-are-stereotype-threat-effects-on-womens-math-performance-difficult-to-replicate/) – many studies have shown effects of stereotype threat in various stigmatized groups [63–65]. Most of these findings concern outcome measures related to higher cognitive functions such as working memory (Figure 1). Recent evidence further points towards stereotype threat effects on basic processes such as motor performance [8–10,66]. In a broader sense, effects of stereotypes could be construed as nocebo effects because they epitomize the effects of negative expectations on higher cognitive functions and motor performance. This poses the question whether mechanisms behind these two phenomena overlap in parts or whether they are fundamentally different.

An influential model on stereotype threat postulates that such threat diminishes executive function by interfering with working memory in cognitive and social tasks. This effect is mediated by several processes, including the biased appraisal of personal experiences, constant
monitoring processes, and the suppression of unwanted thoughts [65]. Even so, further factors might affect threatened individuals. Such an additional factor seems to be the individuals’ self-efficacy because stereotype-vulnerable individuals have been found to show more unstable self-efficacy patterns than non-vulnerable individuals [67].

The exact underlying physiological changes connected to such social expectancy effects remain elusive at present, but initial evidence allows first insights into possible mechanisms mediating this effect. Social identity threats have been found to increase salivary levels of the stress hormone cortisol [68,69]. Cortisol is part of the physiological stress response and its release is stimulated via the activation of the hypothalamic–pituitary–adrenal (HPA) axis. Cardiovascular threat responses and increases in proinflammatory cytokines have also been connected to stereotype threat [70–72]. Moreover, stereotype threat affects neural processing in response to errors and negative feedback [73,74] as well as electroencephalographic (EEG) activity in the default mode network [75]. A possible brain area moderating changes in neural activity is the ACC, which has shown stronger BOLD activity in threatened than in non-threatened individuals [76,77].

However, the focus of studies on social expectancy effects has mainly been directed at characterizing the phenomenon at a behavioral rather than physiological level. This contrasts strongly with research on placebo effects where the focus is on physiological mechanisms and clinical outcome variables. While there seems to be overlap between BOLD activity associated with both expectancy effects (Figure 2), future research will be necessary to systematically compare possible mechanisms at the behavioral and physiological levels in placebo and social expectancy effects. First studies in this direction have targeted social expectations in clinical practice, showing that stereotype threat effects can promote avoidance behavior in patients, impair communication, and lead to poorer adherence to treatment plans [1]. Social expectancies can also influence clinical outcome measures more directly. For instance, common expectations based on traditional gender roles also seem to partly mediate sex differences in pain responsivity [78–82]. Moreover, manipulating gender roles affects the perception, processing, and report of pain [83–86].

Modulations of Perception
Expectancy effects in clinical or social contexts alike, are based on how individuals perceive their environment. However, expectations can also affect how this environment is perceived. Contextual cues and prior notions are analyzed and integrated with the sensory input in question, resulting in a conscious perception of our environment that is colored by expectations. Indeed, prior expectations have been shown to influence stimulus processing already in the visual cortex [87]. This interplay of basic stimulus input and top-down modulation has been extensively investigated in various fields, such as face perception [88–94], language processing [95–97], and the perception of ambiguous figures [98,99], among many others. It would be beyond the scope of this review to account for all findings in this regard (see e.g., [100]). Instead, we have elected to exemplify the impact of expectations on perception by a closer view on contextual effects on face perception and processing, a field that has been well investigated with both, behavioral and physiological measures.

Contextual elements conveying affective or self-referential information have been found to modulate the perception or, at the very least, the judgment of human faces (Figure 1) [93,101,102]. Emotions in facial expressions are categorized depending on an interaction between the facial expression itself and affective contextual information. For example, faces expressing disgust can be perceived as angry or even proud if the context indicates the validity of such a categorization [101]. Participants rated neutral faces as more arousing when they were cued by self-related information as opposed to other-related information, and they perceived
neutral faces cued by negative and positive information as more negative and positive, respectively [93,102]. Facial and contextual information thus seems to be automatically and routinely integrated to form a common perception [88,103]. This modulation of face perception by expectations is accompanied by differential neural processing of these stimuli dependent on context. BOLD activity in the fusiform gyrus (associated with face processing), the Amy (associated with affective processing), the medial prefrontal cortex, and the ACC, among others, proved to be sensitive to additional contextual information (Figure 2) [89,90,93]. Neural processing seems to be affected in its early and its late stages [92,102]. Interestingly, several of the brain areas showing differential BOLD activity in response to different contextual information have also been affected by other types of expectancy effects, as argued above (Figure 2). Moreover, facial expressions are processed differently under social threat, especially in individuals with dispositional social anxiety, that is, in individuals predisposed to expect negative feedback [91,93]. This evidences considerable overlap between social threat effects and modulation of face perception.

The investigation of expectancy effects has primarily focused on humans. We provide short remarks about experience-based expectancy effects in non-human animals in Box 2.

Friend or Foe? Methodological Implications of Expectancy Effects

As outlined in the preceding paragraphs, expectancy effects are found at all levels of cognitive processing from perception to ultimate behavior, with effects on behavioral measures and physiological parameters. It seems reasonable to assume that these effects cannot only be studied experimentally but that these effects also affect our experiments when we actually wish to study something else entirely. Various examples of such inadvertent biases have been reported and, in part controversially, discussed in the past. Awareness of these potential pitfalls during study design is crucial to allow experimenters to improve interpretability of the later results.

While the placebo effect, for instance, is now a popular topic of scientific investigation, it has long been seen (and still is) as a cumbersome confound in clinical research that should be minimized if possible [4]. This is not an easy task because placebo responses to a given treatment vary between individuals [104] and responses to different placebo treatments vary within individuals.

Box 2. Expectancy Effects in Non-Human Animals?

It seems particularly difficult to study the influence of expectations in non-human animals, especially the influence of explicit expectations on which we focus in this review. However, interesting comparisons between human and animal research can be drawn if the concept of ‘expectations’ is viewed more broadly.

An example of introducing the study of traditional expectancy effects to non-human animals is the placebo effect. Placebo effects elicited by conditioning mechanisms have been demonstrated in mice and rats [118–121]. Interestingly, several parallels with findings in humans have emerged: placebo effects seem to be mediated via opioidergic pathways when the conditioning process employs an opioidergic drug; however, if a non-opioid is used for conditioning, placebo effects do not depend on opioidergic pathways [120]. Similar findings have been reported in human studies [39]. These studies suggest that there seem to be, at least partly, comparable processes in humans and rodents regarding placebo effects.

Other taxa have also shown evidence of experience-based expectations, including other mammals, fish, birds, reptiles, crustaceans, arachnids, and insects [122–125]. Winner and loser effects are a prime example of direct effects of experience on subsequent behavior. More precisely, animals that have won a previous fight are more likely to win the next fight, and animals that have lost the previous fight are more likely to lose the next fight, than could be explained by external features such as opponent identity, size, etc. [125]. Interestingly, evidence suggests that there is an adaptive advantage for both, winners and losers, if animals behave according to their social experience [124]. It seems that winner and loser effects are partly based on a re-assessment of one’s own fighting ability [123,125,126], which then in turn affects the fight outcome. This finding offers striking resemblance to the self-efficacy phenomenon in humans [127]. Moreover, winner and loser effects seem to primarily affect the subjective perception of the fighting parties, not objective variables of actual fighting ability [123,125] – a phenomenon that also bears resemblance to expectancy effects in humans, as we have discussed in the main text.
Furthermore, placebo effects might interact with treatment [106,107]. Consequently, this leads to an inability to reliably predict expectancy effects in any given individual. Even when experimenters are careful to minimize placebo effects by choosing active control groups, these active control groups and the treatment group could nevertheless differ in prevalent expectations in the (supposed) treatment, which in turn affects treatment outcome [108]. Indeed, patient and control groups in clinical research might generally differ not only in terms of health but also in terms of performance expectations. For instance, patients after a neurological injury expect cognitive deficits [109] and such differences in expectations potentially affect a variety of outcome measures [85]. That is, the very process of investigating a particular disease might be biased by expectations if the data are only compared to a healthy control group [85].

In addition to expectancy effects in clinical research, potential confounds have been documented in a range of other fields. Pertinent examples include the Hawthorne effect [110–112] and the Pygmalion effect [60,61]. Both of these effects claim that outcome measures could be altered through an intervention not because of the effectiveness of the intervention itself but simply because an intervention was performed (Hawthorne effect) or because the experimenter (or teacher in case of traditional Pygmalion effects) expected a change to occur. Avoiding such biases seems vital for data interpretation. Reasonable countermeasures include the use of active control groups which also receive interventions and, if possible, blinding experimenters to the specific experimental condition investigated, especially when experimenters are asked to assess the performance or progress of participants.

Towards a Holistic View of Expectancy Effects

The previous paragraphs constitute a synthesis of expectancy effects in prominent scientific fields. To characterize specific effects of specific expectancies, researchers in these fields have mostly worked within their own disciplines. This approach is excellent when the goal is to delineate the behavioral and physiological details of the expectancy effects in question, and to later use these findings to improve specific situations and procedures in real life. This has been done, for example, in the case of expectancy effects in clinical practice [2,4,38,57–59] as well as in stereotype threat situations in academia [113,114].

However, we suggest here that this approach can be complemented by interconnecting these separate fields. Two main reasons make such efforts appear promising: (i) as outlined throughout this review, there is substantial overlap between different expectancy effects, in their effects on outcome measures in controlled studies as well as in real life situations (e.g., in clinical practice), and (ii) interconnecting these fields into a holistic approach to expectancy effects provides synergies, offers a deeper understanding of expectancy effects on perception and behavior, and provides new directions for theory-driven investigations.

(i) The previous paragraphs of this review have revealed a substantial overlap between different expectancy effects. For instance, treatment expectations affect clinical outcome measures such as pain, motor performance, or questionnaire scores, and so do social expectations. Moreover, such expectations might also affect a variety of other factors such as the participants’ perception of the experimenter or physician. Little is known whether and how such effects interact, and whether these modulations are separate effects or combine to a single modulatory signal.

(ii) Interconnecting research on different types of expectations appears to be a promising avenue to elaborate the mechanisms underlying their effects. For example, placebo and nocebo studies emphasize the impact of both, situational cues as well as previous experience, on expectancy effects (Figure 1). Such a strong learning component is also likely to play a role in social expectations. Although stereotype threat has been shown to also occur in typically non-threatened individuals when situational cues provoke a threatening environment [115], it is well conceivable that previous experience with performance
decrements under stereotype threat increases the impact of stereotypes. Moreover, different types of expectancy effects come with distinct methodological tools: whereas social expectations have been mostly investigated in behavioral studies with a strong emphasis on forming a conceptual framework, studies on treatment expectations have focused more on the physiological underpinnings mediating the behavioral effects. Because of this discrepancy, it is at this point difficult to ultimately argue for a common physiological mechanism, but it is evident that there is some overlap here as well (Figure 2). Modulatory areas in the brain, such as the ACC, have been found to show differential BOLD activity to treatment and social expectations alike as well as to contextual modulations of perception [24,41,43,76,94]. The dopaminergic system, including the NAcc, also seems to be involved in the mediation of different expectations, as has been found in studies investigating traditional treatment expectations on clinical outcomes as well as treatment expectations regarding cognitive enhancement [26,43,50,51,54]. The NAcc is further involved in the modulation of pain processing by stereotype-related information [85], and specific dopaminergic genes have been associated with susceptibility to external suggestions [116]. The physiological stress response seems a likely candidate to mediate negative expectations because it has been implicated in social identity threat [68,69], in effects of stereotype-related information on pain processing [85], as well as in the nocebo effect [40]. More studies spanning these different fields will be necessary to elaborate on a common framework for different expectations.

A holistic view on expectancy effects thus inspires new toeholds for investigation and can provide new ideas on how to approach a particular subject of study. Questions arising include, for instance, the following: is the mental downward spiral involved in stereotype threat possibly also a factor in nocebo effects? Does the reversibility and longevity of stereotype threat depend on the amount of previous experience with performance decrements under stereotype threat? Several key questions emerging from a holistic view on expectancy effects are outlined in the Outstanding Questions; they clearly await empirical investigation and may lay the foundation for a comprehensive theoretical model covering expectancy effects in many different fields.

Concluding Remarks
Expectancy effects are a widespread phenomenon, and they come with a lasting influence on cognitive operations, from basic stimulus processing to higher cognitive functions. In this review we have aimed at providing a synthesis of expectancy effects in prominent scientific fields, and at presenting first steps towards a common framework for these diverse phenomena. We demonstrated how such a common framework may stimulate new directions for investigation, may give insights into general physiological underpinnings of modulatory effects, and increase awareness of methodological confounds associated with expectations. There are still many open questions regarding the impact of expectations on cognitive processes. However, with the multitude of findings we already have at hand, and more yet to come, a holistic view on expectancy effects might be within our grasp.

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