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Affect and emotions in placebo and nocebo effects: What do we know so far?

Andrew L. Geers[1] | Kate Faasse[2] | Darwin A. Guevarra[3] | Kelly S. Clemens[1] | Suzanne G. Helfer[4] | Ben Colagiuri[5]

[1]Department of Psychology, University of Toledo, Toledo, Ohio, USA

[2]School of Psychology, University of New South Wales, Sydney, New South Wales, Australia

[3]Department of Psychology, Michigan State University, East Lansing, Michigan, USA

[4]Department of Psychology, Adrian College, Adrian, Michigan, USA

[5]School of Psychology, University of Sydney, Sydney, New South Wales, Australia

Correspondence
Andrew L. Geers, Department of Psychology, University of Toledo, Toledo, OH, USA.
Email: andrew.geers@utoledo.edu

Abstract

Once considered nuisance variance in clinical trials, placebo effects and nocebo effects are now widely recognized as important and mutable psychobiological contributors to mental and physical health. Psychological theory explaining these effects emphasizes associative learning and conscious expectations. It has long been suggested, however, that affective states such as moods, emotions, and distress could play a significant role. In this paper, we draw together and review the empirical data linking affective states to placebo and nocebo effects. To organize this disparate literature, three questions are addressed: (1) Does pre-existing state and trait affect modulate placebo and nocebo effects? (2) Does administering placebo and nocebo treatments change affective states, and if so, does the resulting affect causally influence placebo and nocebo effects? Finally, (3) Can placebo treatments be successfully employed as a regulation strategy to modulate different affective states? In reviewing the evidence in relation to these three questions, it is clear that affect does play a key role in placebo and nocebo effects in many circumstances, and further, there may be a reciprocal dynamic at play between a treatment event, affect, and placebo/nocebo effects. The paper concludes by discussing implications for theory and intervention and recommends future research priorities.

1 | INTRODUCTION

Placebo effects refer to psychobiological phenomena whereby cues associated with a treatment trigger health improvements independent of any active ingredients of the treatment itself (Colagiuri, Schenk, Kessler, Dorsey, & Colloca, 2015). The prototypical example involves a sugar pill administered under the guise of a painkiller that relieves pain despite containing no active ingredients. Nocebo effects are the "dark side" of the placebo effect, whereby harmful outcomes are similarly triggered by aspects of the treatment context (Faasse, Helfer, Barnes, Colagiuri, & Geers, 2019). For example, warnings about side effects can induce side effects from inert treatments (Neukirch & Colagiuri, 2015).

Although once dismissed as patient reporting bias, placebo and nocebo effects are now widely recognized as complex psychobiological phenomena involving a rich interplay between physiological processes, individual characteristics, and sociocultural factors (Carlino & Benedetti, 2014; Frisaldi, Piedimonte, & Benedetti, 2015; Petrie & Rief, 2019). Supporting this, recent evidence indicates that in addition to subjective experiences, placebo and nocebo effects influence a range of neurobiological pathways, including the pain processing network, neurotransmitter systems, immune and neuroendocrine responses, and the autonomic nervous system (Schedlowski, Enck, Rief, & Bingel, 2015; Wager & Atlas, 2015). Most importantly, placebo and nocebo effects are not confined to sugar pills and other inert treatments, but also shape the effectiveness (placebo) and burden (nocebo) of *active* medical treatments (Benedetti et al., 2003). For example, Bingel et al. (2011) found that a positive treatment expectation doubled the pain-relieving effect of the active drug remifentanil, whereas a negative treatment expectation completely eliminated the drug's pain-relieving effect. Simply put, research into placebo and nocebo effects offers opportunities for improving mental and physical health treatments and interventions through nonpharmacological channels.

While various theoretical explanations have been put forward for placebo and nocebo effects, most propose that they are primarily driven by expectancies triggered by verbal, contextual, and social cues and acquired via learning processes (Colagiuri, Quinn, & Colloca, 2015). For example, there is evidence of both placebo and nocebo effects resulting from changes in expectations, and being evoked by social observation, cues in the health care contexts, and classical conditioning (Colloca, Sigaudo, & Benedetti, 2008; Faasse & Petrie, 2016; Testa & Rossettini, 2016). Furthermore, pain studies report changes in opioid release from both placebo (increase release) and nocebo manipulations (decrease release; Blasini, Corsi, Klinger, & Colloca, 2017; Scott et al., 2008; Tracey, 2010). As research has progressed, however, there has been increasing evidence of the involvement of feeling states in both of these effects (Colloca & Benedetti, 2007; Flaten, Aslaksen, & Lyby, 2013). This is noteworthy because affect is not commonly incorporated into models of placebo and nocebo effects. Understanding the involvement of affect could account for some of the substantial unexplained variation in when and how these effects manifest. Moreover, affect could play multiple roles in placebo and nocebo effects. For example, affect may bias how treatment cues are perceived and treatment cues may, in turn, alter affect, such as by reducing anxiety about one's health. Thus, there might be a reciprocal dynamic in medical care between affect, treatment events, and placebo/nocebo effects. If affect is implicated in this process, social and personality psychology theories could help elucidate the different connections.

Toward this end, the current paper draws together and reviews the diverse evidence linking affect to placebo and nocebo effects in order to provide a springboard for research and theoretical development. Before delving into the review, we begin with brief discussions of why affect may relate to placebo and nocebo effects.

2 | HOW COULD AFFECT INFLUENCE PLACEBO AND NOCEBO EFFECTS?

Affect is a central characteristic of the human mind (Barrett & Bliss-Moreau, 2009), and affective experiences both shape and are shaped by thought and action. Definitions of "affect" vary, but for the purpose of this review can broadly be viewed as the experience of a feeling with a positive or negative quality (Slovic, Finucane, Peters, &

MacGregor, 2007). Affect is typically used as an umbrella term that includes mood, distress, anxiety, and discrete emotions (Gross, 2015). Individuals can differ in their dispositional tendency to experience positive or negative feelings ("trait affect"), as well as in experiences of short-term or current affect ("affective state" or "state affect"; Diener & Emmons, 1984). Substantial research indicates that both state and trait affect have important health consequences (Consedine & Moskowitz, 2007; DeSteno, Gross, & Kubzansky, 2013).

There are good reasons to suspect that affect can influence placebo and nocebo effects. Individuals do not experience treatment messages (e.g., this pill will reduce pain) in a vacuum. Rather, treatment messages are one salient input among many. There is likely an integration of both semantic and affective information in the minds of individuals during a treatment event (Leventhal, Brissette, & Leventhal, 2003), which collectively determine when a placebo or nocebo effect manifests. Affect represents a particularly important class of inputs, as it substantially impacts cognition and physiology. Affective states and traits bias information encoding, evaluation, judgment, and recall (Bower, 1981; Forgas, 1995; Lerner, Li, Valdesolo, & Kassam, 2015; Schwarz & Clore, 2007) and likely shape cognitions concerning treatment messages (e.g., treatment expectations and confidence; Takahashi & Earl, 2020). One often observed outcome is that affect leads to valence-congruent judgments and predictions. For example, negative mood states and anxiety can increase expectations of negative or harmful outcomes (Johnson & Tversky, 1983; Lerner, Gonzalez, Small, & Fischhoff, 2003; Lyubomirsky, King, & Diener, 2005; Meissner et al., 2019). Consequently, positive affect may encourage processes leading to placebo effects, whereas negative affect may encourage processes leading to nocebo effects.

Based on prior literature, state and trait affect, including state affect evoked from receiving a treatment, are likely to influence somatic attention, symptom attributions, and coping processes (Costa & McCrae, 1987; Eysenck, Derakshan, Santos, & Calvo, 2007; Lazarus & Folkman, 1984; Pervin, 1993; Pressman, Jenkins, & Moskowitz, 2019; Salovey & Birnbaum, 1989; Watson & Pennebaker, 1989). For example, being in a positive mood when given a (placebo) treatment for an ailment could lead to the appraisal that one has sufficient resources to overcome the illness and shift attention and attributions toward somatic indicators of health and healing.

Another reason placebo and nocebo effects are likely to occur is that anticipating a beneficial treatment outcome reduces distress, whereas anticipating a harmful treatment outcome increases distress. Thus, receiving treatments both influences, and is influenced by, affect (Flaten, 2014). Based on the broader literature on affect and physiology it can be anticipated that, due to their relation to distress, placebo and nocebo manipulations (i.e., a positive or negative treatment message coupled with sham treatment administration and other contextual and social cues) alter physiological reactivity, including activation of the sympathetic nervous system, the hypothalamic-pituitaryadrenal axis, and cortisol output and immune system changes (Blascovich &Mendes, 2000; Dickerson & Kemeny, 2004; Marsland et al., 2007; Pressman & Cohen, 2005; Segerstrom, 2007). Affect, such as anticipatory anxiety, could also influence placebo and nocebo effects by directly changing neurological activity related to pain and threat (Bishop, 2007; Pourtois, Schettino, & Vuilleumier, 2013). This same circuitry has been implicated in nocebo effects (Benedetti, 2014; Wager & Atlas, 2015). As such, from the outset there is good reason to suspect that affect should relate to placebo and nocebo effects. We now turn our attention to our three questions pertaining to this potential relationship.

3 | THE ORGANIZATION OF THIS REVIEW

This literature review is arranged around three key questions. The first question asks if pre-existing state and trait affect modulate placebo and nocebo effects. Thus, in the first section, we summarize the studies that measured or manipulated affective states *prior* to a placebo or nocebo manipulation to assess if pre-existing affect predicts or causally influences these effects. We also evaluate whether trait affect measures reliably predict placebo and nocebo effects. The second section asks if placebo and nocebo treatments change affective states, and if so, does the resulting affect causally influence placebo and nocebo effects. In this section, we review studies that measure

affect after a placebo and nocebo manipulations to assess whether these manipulations change affective states. Here, we also evaluate whether such changes in affect serve to mediate resulting placebo and nocebo effects. The third section asks if placebo treatments can be successfully employed as a regulation strategy to modulate different affective states. In this section, we summarize data on placebos regulating affect, review the psychological and neural mechanisms by which placebos exert their regulatory effect, and consider the possibility of using placebos in interventions for regulating affect. In each of these three sections, we discuss data on psychological processes, when available. Finally, following these sections, we discuss limitations to this literature and highlight new avenues for future research.

4 | DOES PRE-EXISTING STATE AND TRAIT AFFECT CHANGE PLACEBO AND NOCEBO EFFECTS?

In the placebo/nocebo literature, researchers have periodically examined whether pre-existing state and trait affect alter placebo and nocebo effects. In this section we review these studies. We first summarize studies measuring naturally occurring affect prior to placebo and nocebo manipulations. Next, we examine studies in which affect was experimentally altered prior to the delivery of a placebo or nocebo manipulation. Finally, we describe the literature on trait affect.

4.1 | Naturally occurring state affect

Some studies have examined the relationship between naturally occurring state affect and placebo/nocebo effects. State anxiety has been related to both nocebo and placebo effects. For example, in nonclinical samples, Morton, Watson, El-Deredy, and Jones (2009) found higher state anxiety predicted reduced placebo analgesia, and Colloca, Petrovic, Wager, Ingvar, and Benedetti (2010) found higher state anxiety predicted nocebo hyperalgesia. Other studies that looked at both nonclinical and clinical samples demonstrate a similar pattern of heightened state anxiety negatively predicting placebo effects and positively predicting nocebo effects (Andrykowski et al., 1987, 1985; Devriese et al., 2000; Ober et al., 2012; Van den Bergh, Winters, Devriese, & Van Diest, 2002). A number of other studies, however, have yielded null results (Elsenbruch et al., 2012; Hashish, Haia, Harvey, Feinmann, & Harris, 1988; Ho, Hashish, Salmon, Freeman, & Harvey, 1988; Stam & Spanos, 1987; van der Meulen, Kamping, & Anton, 2017; Vögtle, Barke, & Kröner-Herwig, 2013), which further complicates this relationship. Furthermore, little data exists regarding naturally occurring positive state affect predicting placebo or nocebo effects.

4.2 | The causal role of state affect

Another avenue for determining the involvement of state affect on placebo and nocebo effects is through experimental manipulation. In this section, we review experiments in which variables that change state affect were manipulated in an effort to determine if state affect causally impacts placebo and nocebo effects.

Benedetti et al. conducted pioneering pharmacological experiments to test the role of anxiety in placebo and nocebo effects. In two studies, participants were administered doses of either proglumide or diazepam to reduce anxiety prior to placebo or nocebo manipulations and experimental pain induction. Pharmacological anxiety reduction resulted in both enhanced placebo analgesia and reduced nocebo hyperalgesia (Benedetti et al., 1996, 1997). Later, Benedetti, Amanzio, and Thoen (2011) showed that analgesia from a placebo manipulation was reduced in participants who were first administered the drug pentagastrin, which induces panic and fear. Relatedly, studies have found mixed evidence that administering the neuropeptide oxytocin, which has been associated with

positive feelings, increases placebo analgesia (Colloca, Pine, Ernst, Miller, & Grillon, 2016; Kessner, Sprenger, Wrobel, Wiech, & Bingel, 2013; Skvortsova, Veldhuijzen, Middendorp, Van den Bergh, & Evers, 2018).

Investigators have also used non-drug strategies to alter state affect. For example, two experiments by Geers et al. (2019a, 2019b) employed video inductions to provoke either a positive or neutral mood in volunteers prior to a nocebo manipulation. In one study, participants subsequently completed a laboratory pain task, whereas in the other they took part in a sham task said to cause headaches. In both studies, participants given the neutral mood induction experienced increased pain in response to the nocebo manipulation. Importantly, participants given the positive mood induction showed no evidence of nocebo effects, despite being similarly warned that the treatment would increase their experience of pain (also see Jacobs, Schagen, Thijssen, & Das, 2019).

In another study using nonpharmacological affect inductions, a nonclinical sample used a brief progressive muscle relaxation exercise with the intention of reducing stress, and found that the relaxation exercise facilitated placebo analgesia compared to a control group (Elsenbruch, Roderigo, Enck, & Benson, 2019). Lyby, Forsberg, Åsli, and Flaten (2012) tested a complementary hypothesis that experimentally inducing fear with a threat of an electric shock would reduce placebo effects. In this study, fear induction abolished the placebo effect on self-reported pain and the startle reflex. Notably, chronic fear of pain moderated this effect, with individuals high in fear of pain displaying the effect most prominently. Likewise, Roderigo et al. (2017) reported that inducing stress using the Trier social stress test increased nocebo effects in an experimental pain paradigm.

4.3 | Psychological mechanisms

There is little data regarding the processes by which state affect alters placebo and nocebo effects. However, two study did test the mediating role of expectations. Roderigo (2017) found the Trier stress test increased nocebo hyperalgesia, but it did not do so by changing self-reported expectations. Similarly, Elsenbruch et al. (2019) found no evidence that expectations mediate the influence of a relaxation intervention on placebo analgesia. Thus, the psychological mechanisms linking state affect to placebo and nocebo effects are unclear, and merit further study.

4.4 | Trait affect as a predictor

Do trait affect measures predict placebo and nocebo effects? Researchers have frequently tested whether individual differences in affect can predict placebo and nocebo effects. These studies have relied heavily on measures of trait anxiety and positive and negative affectivity. Lee et al. (2012), for example, found lower levels of trait anxiety predicted greater placebo analgesia in visceral pain for patients with irritable bowel syndrome, and these patients showed greater changes in affective brain regions (e.g., insula, ventrolateral prefrontal cortex) than healthy controls. Trait measures of anxiety likewise have predicted placebo and nocebo effects (Colloca et al, 2010, 2016; Corsi & Colloca, 2017; Lee et al., 2012) as have measures of trait negative affect (Put et al., 2004), particularly in studies using conditioning to evoke nocebo effects (De Peuter et al., 2007; Van den Bergh et al., 2002). Other studies have identified individual differences in fear of pain and trait pain anxiety as predictors of placebo and nocebo effects (Aslaksen et al., 2015; Bąbel et al., 2018; Forsberg, Gjerstad, Flaten, & Aslaksen, 2018; Lyby et al., 2010, 2012; Schienle, Höfler, Übel, & Wabnegger, 2018; Staats, Staats, & Hekmat, 2001).

Despite these encouraging findings, there are ample studies in which trait measures of affect have not served as significant predictors (e.g., Bogaerts et al., 2010; Butler & Steptoe, 1986; Goodenough et al., 1997; Ho et al., 1988; Schmid, Langhorst, Gaß, Theysohn, & Benson, 2015; Weimer et al., 2019). As a result of these frequent null effects, it is currently unclear if there are any reliable influences of trait affect on placebo and nocebo effects. One possibility is that these individual differences shift attributions and perceptions of negative symptoms,

regardless of a placebo and nocebo treatment (Petrie, Moss-Morris, Grey, & Shaw, 2004; Salovey & Birnbaum, 1989). Given the uncertainty on this topic, there is a need for theory-driven research to test how and when trait affect may change placebo and nocebo effects.

4.5 | Summary

Naturally occurring state anxiety and state negative affect can alter nocebo and placebo effects, although studies report non-significant effects. It may be that the influence of state affect is context dependent or modest in magnitude and frequently overwhelmed by other inputs in the treatment context. Consistent with this second possibility, Colloca et al. (2010) found the ability of state anxiety to predict nocebo effects was eliminated when greater experiential pre-conditioning of nocebo effects took place. There is also strong experimental evidence that manipulating affective states changes placebo and nocebo effects, but the psychological mechanisms underlying these effects remain unclear. Finally, the evidence linking trait measures of affect to placebo and nocebo effects has not been reliable and warrants further consideration.

5 | DOES AFFECT STIMULATED BY RECEIVING A TREATMENT CHANGE PLACEBO AND NOCEBO EFFECTS?

It is a common assumption that placebo manipulations for illnesses change affective states, particularly anxiety, which thereby improve outcomes (Rosenthal & Frank, 1956; Shapiro, 1964). In contrast, nocebo manipulations are expected to cause negative affect, which in turn, exacerbates psychological and physical conditions (Evans, 1974; Hahn, 1997). These assumptions can be broken down into two questions which this section addresses: (1) do placebo and nocebo manipulations result in changes in affect and (2) can these changes in affect help mediate placebo and nocebo effects.

5.1 | Placebo and nocebo treatments changing affect

There is considerable evidence that placebo administration increases positive feelings and reduces negative affect. In pain and distress paradigms, placebo manipulations tend to reduce anxiety and worry, elevate mood, and produce changes on stress-related physiological markers such as heart rate and heart rate variability (e.g., Aslaksen & Flaten, 2008; Bąbel et al., 2018; Crichton et al., 2014; Gryll & Katahn, 1978; Lyby et al., 2010; Stam & Spanos, 1987). Complementing these findings, nocebo manipulations increase anxiety and worry, depress moods, and increase hormonal and autonomic measures of distress (e.g., Colagiuri & Quinn, 2018; Crichton et al., 2014; Elsenbruch et al., 2012; Staats et al., 2001). In pharmacological and neurobiological studies, placebo and nocebo manipulations have been linked to activity in brain regions associated with anticipatory anxiety and emotional processing as well as changes in endogenous opioid, dopaminergic, and cholecystokinin systems (for reviews, see Benedetti, 2014; Blasini et al., 2017; Wager & Atlas, 2015). In paradigms without a pain stimulus, nocebo treatments also raise negative affect. For example, exposure to sham WiFi and electromagnetic fields increases anxiety as well as reported side effects (Bräscher, Raymaekers, Van den Bergh, & Witthöft, 2017; Verrender, Loughran, Dalecki, Freudenstein, & Croft, 2018). Drug information leaflets describing treatment side effects can also induce negative affect, reduce willingness to take a medication, and increase side effect reports (Prediger, Meyer, Büchter, & Mathes, 2019; Schmitz et al., 2017). In clinical settings, explicit warnings that a medical procedure would be painful increases both patient anxiety and pain (Lang et al., 2005).

Other features of the treatment context modulate affective responses from placebo and nocebo manipulations. For example, in several studies participants displayed stronger placebo effects and weaker nocebo effects when given the opportunity to choose between sham treatments (Bartley, Fasse, Home, & Petrie, 2016; Brown et al, 2015; Rose et al., 2012, 2014). This opportunity for personal control also reduced anxiety and raised positive affect. Social elements in the treatment context may also work by changing affect. For example, nocebo effects from social observation are stronger when the target being observed displays facial expressions associated with negative emotions (Vögtle, Kröner-Herwig, & Barke, 2019). Further, practitioner characteristics, such as warmth and empathy, appear to increase positive feelings in individuals during treatment administration (Losin, Anderson, & Wager, 2017; Van Osch, van Dulmen, van Vliet, & Bensing, 2017).

In sum, there is reliable evidence that placebo and nocebo manipulations, and in many cases, simple messaging about possible drug side effects, modulates affect.

5.2 | Affect as a mediator

The findings discussed above provide evidence that placebo and nocebo manipulations can elicit positive and negative affect. However, in many studies, affect is measured concurrently with the placebo and nocebo dependent measures. The timing makes it unclear if affect serves as a mediation variable or is simply a corresponding change that accompanies the placebo and nocebo effect (Flaten et al., 2013). Evidence against this corresponding change interpretation comes from studies measuring self-reported or physiological markers of affect between the administration of the treatment and the placebo and nocebo outcome. These studies find affective changes occur in this intervening time period which may mediate the relationship between treatment and subsequent placebo and nocebo effects (Aslaksen & Lyby, 2015; Elsenbruch et al., 2012; Petersen et al., 2012, 2014; Vase, Robinson, Verne, & Price, 2005). For example, Aslaksen, Bystad, Vambheim, and Flaten (2011) found that anticipatory stress recorded between placebo manipulation and a pain task predicted placebo effects on pain. In a similar paradigm, Aslaksen and Lyby (2015) reported that changes in subjective stress and systolic blood pressure mediate placebo and nocebo effects on pain. Finally, Colagiuri and Quinn (2018) found that nocebo effects are more enduring than placebo effects and this increase in duration is mediated by changes in autonomic arousal—a marker of distress.

Evidence concerning the possible mediating role of affect on placebo analgesia also comes from studies utilizing neural measures such as functional magnetic resonance imaging or positron emission tomography scans. Although there are many brain regions associated with placebo effects, including a host of prefrontal regions and regions linked with affective appraisal processes, here we focus on brain regions that are associated with affective reactivity from placebo and nocebo manipulations. The periaqueductal grey (PAG) and surrounding regions have high density of opiate neurons; anticipatory activity from this region positively predicts placebo effects (Wager et al., 2004, 2011). A meta-analysis also shows robust anticipatory activity in the PAG after placebo administration (Amanzio, Benedetti, Porro, Palermo, & Cauda, 2013). Another candidate region is the nucleus accumbens (a subcortical region associated with reward processing); Scott et al. (2007) observed that activation of dopamine release in the nucleus accumbens was associated with subsequent placebo effects on pain.

Although affect can mediate placebo and nocebo effects, changes in affect are not necessary for them to occur. For example, Elsenbruch et al. (2019) found that, whereas changes in expectations predicted placebo analgesia, changes in state anxiety and physiological arousal did not. In a clinical setting, changes in affect following placebo administration did not predict reductions in postoperative swelling (Ho et al., 1988). Moreover, there is little direct evidence for the frequently hypothesized serial mediation prediction, that placebo/nocebo treatments alter expectations, which alters affect, that in turn, causes placebo and nocebo effects (Shapiro, 1964). Instead, affective measures and self-reported expectations frequently account for separate variation in placebo and nocebo effects (Bjørkedal & Flaten, 2012; Vase et al., 2005).

5.3 | Summary

Placebo and nocebo manipulations change affective states and in some cases predict placebo and nocebo effects. However, placebo and nocebo effects can occur without the mediating role of affective states and there is little direct evidence for the serial mediation prediction. This may be a function of measurement. Expectations are assessed with conscious self-report measures, which are unlikely to fully capture cognitive change (Nisbett & Wilson, 1977). Future studies should identify situational, individual, methodological, and treatment-related factors that impact when affect mediates placebo and nocebo effects.

6 | CAN PLACEBOS REGULATE AFFECTIVE STATES?

Although the previous sections focused on how affect can moderate or mediate placebo and nocebo effects, this section focuses on affective states as the *target* of placebo interventions. When the target of placebos is affect, they can be conceptualized as a type of affect regulation strategy (Braunstein, Gross, & Ochsner, 2017). Currently, affect regulation and placebo theory suggest that placebo manipulations involve a conscious goal to regulate affect but the appraisal processes involved in this change tend to be more automatic compared to other internally generated appraisal-type strategies (Ashar, Chang, & Wager, 2017; Braunstein et al., 2017). In this section, we first summarize current evidence on placebos regulating affect. Second, we review psychological and neural mechanisms by which placebos exert their regulatory effect. Lastly, we discuss translational applications of placebos regulating affect.

6.1 | Placebos regulating affect

Researchers have demonstrated robust regulatory effects of placebos on self-report measures of affect. For example, placebo treatments have reduced negative affect evoked from a variety of induction procedures, including adverse emotional images (Petrovic et al., 2005; Schienle, Gremsl, Übel, & Körner, 2016; Übel, Leutgeb, & Schienle, 2015), fear of impending shock (Meyer et al., 2015, 2019), and stress from a social speech task (Abrams, Kushner, Lisdahl Medina, & Voight, 2001; Balodis, Wynne-Edwards, & Olmstead, 2011). In study with distressed individuals, participants given a placebo treatment experienced larger reductions in depression, stress, and anxiety over a 3-day period compared with controls (Darragh et al., 2016). Other studies find that expectations about treatment efficacy can be altered and thereby reduce depression and negative emotions (Jurinec & Schienle, 2020; Long et al., 2020). Moreover, as described next, these placebo effects extend to autonomic and neural measures of affect reactivity, providing evidence that they are more than response bias (Schienle et al., 2018).

6.2 | How placebos regulate affect

An intriguing finding is that placebos exert a general dampening effect on affective reactivity, even when the treatment instructions are specific to one emotion. For example, when the target of the placebo manipulation are emotions of disgust, some studies have found that it also reduced ratings of fear (Schienle, Übel, Schöngaßner, Ille, & Scharmüller, 2014; Übel et al., 2015). Moreover, there are instances when placebos reduce self-reported negative affect as well as autonomic and neural measures linked to distress when observing both negative and neutral stimuli (Meyer et al., 2015, 2019). Reduced skin conductance levels (Meyer et al., 2015) and medial thalamus activity (Meyer et al., 2019) during the presentation of both neutral and negative stimuli in blocks followed by placebo administration suggest a general dampening of arousal and reactivity to any incoming salient stimuli. Another intriguing result is that EEG and eye tracking data suggest that placebos increase attention engagement

with salient stimuli (Gremsl, Schwab, Höfler, & Schienle, 2018; Schienle et al., 2016; Übel et al., 2015). This is consistent with the interpretation that placebos reduce overall emotional reactivity which may in turn increase people's confidence in their ability to engage with any salient stimuli.

Our understanding of placebo neural mechanisms also comes from studies directly comparing placebos with other affect regulation strategies such as cognitive reappraisal. Two studies show that placebos and cognitive reappraisal both downregulate self-reported negative affect and activation in the amygdala and insula; however, they do so through different ways. Zhang, Guo, Zhang, and Luo (2013) showed that cognitive reappraisal led to increased activation in regions associated with cognitive processing of emotions such as right cingulate and bilateral inferior prefrontal cortex (among other regions), regions that are less active during placebo regulation. Schienle, Übel, and Wabnegger (2017) found that cognitive reappraisal was associated with increased activity in the dorsolateral prefrontal cortex (DLPFC) while the placebo was not. Even more intriguing, cognitive reappraisal was associated with increased connectivity between the DLPFC and amygdala while the placebo was associated with decreased connectivity between these two regions, suggesting different routes of regulation.

6.3 | Placebo interventions

Despite robust findings that placebos can be used successfully for the downregulation of affect, placebos are still not used actively and regularly in clinical and nonclinical contexts. This is likely due to the prevalent belief that deception, which violates medical guidelines, is necessary to induce placebo effects (Colloca & Howick, 2018; Kaptchuk et al., 2010). However, preliminary research on placebos without deception (i.e., open-label or nondeceptive placebos) suggests translational possibilities in harnessing the effects of placebos to promote emotional well-being (Evers et al., 2018; Haas et al., 2020; Kirsch, 2019). For example, placebos administered without deception can reduce both self-report and neurological measures of emotional distress (Guevarra, Moser, Wager, & Kross, 2020), improve self-reported emotional well-being in healthy participants (El Brihi, Horne, & Faasse, 2019), and reduce text anxiety (Schaefer et al., 2019). These findings help open-up the translational potential of using nondeceptive placebos as interventions for acute and chronic distress.

6.4 | Summary

Placebos can regulate affective states. Despite both being appraisal-type strategies, placebos exert their regulatory effects differently from cognitive reappraisal strategies. Moreover, new research on placebos administered without deception opens up translational possibilities of utilizing placebos not only in clinical contexts, but also in the daily regulation of prevalent, debilitating unwanted affective experiences. A fruitful future direction for research is testing nondeceptive placebos as potential co-interventions or tools with existing therapies for those suffering from mood or anxiety disorders which are associated with emotion dysregulation (Sheppes, Suri, & Gross, 2015).

6.5 | Limitations and future directions

This review highlights limitations to the available data on affect and placebo/nocebo effects and points to directions for future inquiry. Much of the existing research employs single-session experimental pain paradigms, which raises questions regarding generalization. Longitudinal designs with repeated measurements would address this gap and provide information on possible reciprocal relations between affect and placebo/nocebo effects over time (Vase et al., 2005). Expanding the types of symptom domains, particularly ones that inherently evoke less negative affect than pain, would also be enlightening. For example, a placebo relaxation treatment may change positive affect

rather than negative affect. Additionally, as health care occurs in a complex psychosocial context, more can be done to identify social psychological factors (e.g., social comparisons) that change affect during treatment events.

Future research could also take a more nuanced approach to conceptualizing and measuring affect. First, affect has typically been measured via self-report. There is now a wide array of techniques for assessing affect, and incorporating different measures would further clarify the links between affect and placebo/nocebo effects (Mauss & Robinson, 2009). Further, researchers could explore effects from a range of discrete emotions (DeSteno, Petty, Rucker, Wegener, & Braverman, 2004; Saarimäki et al., 2018), like awe, that have been linked to important downstream cognitive and physiological consequences (Stellar et al., 2015). Finally, researchers may profit from considering goals, values, and self-views, thereby taking into account the dynamic motivational-emotional system (Kenrick, Griskevicius, Neuberg, & Schaller, 2010).

There is limited evidence regarding the psychological processes involved in the interplay between affect and placebo and nocebo effects (Geers & Miller, 2014). Conscious expectations have been tested as mediators of changes due to affect, with limited support. Future research should examine other mediators, including non-conscious cognitions and basic affect heuristics (Peters, Lipkus, & Diefenbach, 2006). Theoretical accounts, such as the elaboration likelihood model (Petty & Briñol, 2012), have been useful in accounting for the multiple roles of affect in communication effects more broadly and could serve as an organizing framework for such investigations (Geers, Briñol, & Petty, 2019c). Finally, we noted at the outset that it is generally theorized that placebo and nocebo effects result from similar processes, such as expectations and conditioning. There is, however, evidence for differences between how and when placebo and nocebo effects manifest. For example, nocebo effects appear easier to induce and more difficult to extinguish than placebo effects (Faasse, 2019). Future research should explore the potential causal role of affect in these placebo/nocebo effect differences. Indeed, Colagiuri and Quinn (2018) have provided evidence that the persistence of nocebo effects over placebo effects is due to the heightened autonomic arousal of nocebo effects.

Additional work is needed to clarify the role of trait affect in placebo and nocebo effects. Although trait affect has predicted placebo and nocebo effects in some studies, these effects are thus far unreliable. This inconsistency is reminiscent of prior literatures in which attitudes and traits served as weak and variable predictors of responses (Ajzen & Fishbein, 1977; Funder, 2006). As such, researchers may profit by leveraging the lessons learned in those established literatures. For example, stable psychological constructs are better predictors of responses aggregated across context rather than within a single context (Epstein, 1979; Fleeson, 2004). Consequently, trait affect may predict placebo effects more reliably in longitudinal rather than cross-sectional studies. Also, prediction may improve if the specificity of the individual difference measure matches the specificity of the response (Ajzen & Fishbein, 1970). Thus, a chronic fear of pain from needles could more reliably predict nocebo hyperalgesia involving needle pain than generalized trait anxiety. Indeed, some studies suggest fear of pain and pain-related anxiety can be more reliable in predicting placebo and nocebo effects (Aslaksen et al., 2015; Lyby et al, 2010, 2011, 2012; Forsberg et al., 2018; Staats et al., 2001).

Finally, this review has applied a demarcation between affective and cognitive constructs. The stance is that there is a phenomenological difference between affect and cognition, and further, that in some cases cognition changes affect, and other cases, affect changes cognition. This perspective is consistent, for example, with research on risk perception and health behavior that finds differences among indicators of affect and cognition (for reviews, see Williams, Rhodes, & Connor., 2018). It should be noted, however, that it's plausible that in placebo/nocebo studies, measures of affect are often not revealing affective states, but instead, affect measures are serving as proxies for changes on cognitive constructs such as expectations and perceptions of control. This is certainly an open question. Some relevant data comes from studies in which both expectations and affect were measured after placebo and nocebo manipulations. These studies find low and moderate correlations between the measures (de Jong, van Baast, Arntz, & Merckelbach, 1996; Geers, Fowler, Helfer, & Murray, 2019d; Vase et al., 2005). Several studies have found expectations and affect measures to yield different relationships with placebo/nocebo effects (Bąbel et al., 2018; Corsi & Colloca, 2017; Colagiuri & Quinn, 2018; Świder, Bąbel, Wronka, van Rijn, &

Oosterman, 2019), which is not fully in-line with this alternative account. Also challenging to explain from this perspective is that pharmacological inductions known to change affect (e.g., diazepam to reduce anxiety) alter placebo and nocebo effects, presumably without changing cognitions (Benedetti et al., 1996, 1997). Clearly more data is required on this point. One possibility is that, changes in expectations, control perceptions, and affect are often closely tied and meticulous experimental techniques are needed to disentangle their ongoing relations.

7 | CONCLUSIONS

Placebo and nocebo effects play an important role in mental and physical health. This review indicates that affective states can influence placebo and nocebo effects, and in turn, placebo and nocebo manipulations can influence affective states. Thus, there is a reciprocal dynamic between a treatment event, affect, and placebo/nocebo effects. Affect is not always a reliable predictor of placebo and nocebo effects; however, it should be considered one of many critical inputs. Finally, placebo treatments, particularly open-label placebos, may provide a novel emotion regulation strategy for reducing negative feeling states. Importantly, current limitations in the available data provide openings for social and personality psychologists to employ precision and systematic techniques to provide a fuller understanding of the relationship between affect and placebo and nocebo effects.

ORCID

Andrew L. Geers https://orcid.org/0000-0002-4413-7098
Darwin A. Guevarra https://orcid.org/0000-0002-5093-355X

REFERENCES

Abrams, K., Kushner, M., Lisdahl Medina, K., & Voight, A. (2001). The pharmacologic and expectancy effects of alcohol on social anxiety in individuals with social phobia. *Drug and Alcohol Dependence*, *64*(2), 219–231. https://doi.org/10.1016/S0376-8716(01)00125-9

Ajzen, I., & Fishbein, M. (1977). Attitude-behavior relations: A theoretical analysis and review of empirical research. *Psychological Bulletin*, *84*(5), 888–918. https://doi.org/10.1037/0033-2909.84.5.888

Ajzen, I., & Fishbein, M. (1970). The prediction of behavior from attitudinal and normative variables. *Journal of Experimental Social Psychology*, *6*(4), 466–487. https://doi.org/10.1016/0022-1031(70)90057-0

Amanzio, M., Benedetti, F., Porro, C. A., Palermo, S., & Cauda, F. (2013). Activation likelihood estimation meta-analysis of brain correlates of placebo analgesia in human experimental pain. *Human Brain Mapping*, *34*(3), 738–752. https://doi.org/10.1002/hbm.21471

Andrykowski, M. A., & Redd, W. H. (1987). Longitudinal analysis of the development of anticipatory nausea. *Journal of Consulting and Clinical Psychology*, *55*(1), 36–41. https://doi.org/10.1037/0022-006X.55.1.36

Andrykowski, M. A., Redd, W. H., & Hatfield, A. K. (1985). Development of anticipatory nausea: A prospective analysis. *Journal of Consulting and Clinical Psychology*, *53*(4), 447–454. https://doi.org/10.1037/0022-006X.53.4.447

Ashar, Y. K., Chang, L. J., & Wager, T. D. (2017). Brain mechanisms of the placebo effect: An affective appraisal account. *Annual Review of Clinical Psychology*, *13*(1), 73–98. https://doi.org/10.1146/annurev-clinpsy-021815-093015

Aslaksen, P. M., Bystad, M., Vambheim, S. M., & Flaten, M. A. (2011). Gender differences in placebo analgesia: Event-related potentials and emotional modulation. *Psychosomatic Medicine*, *73*(2), 193–199. https://doi.org/10.1097/PSY.0b013e3182080d73

Aslaksen, P. M., & Flaten, M. A. (2008). The roles of physiological and subjective stress in the effectiveness of a placebo on experimentally induced pain. *Psychosomatic Medicine*, *70*(7), 811–818. http://doi.org/10.1097/PSY.0b013e31818105ed

Aslaksen, P.M., & Lyby, P. (2015). Fear of pain potentiates nocebo hyperalgesia. *Journal of Pain Research*, *8*, 703–710. https://doi.org/10.2147/JPR.S91923

Aslaksen, P. M., Zwarg, M. L., Eilertsen, H. I., Gorecka, M. M., & Bjokedal, E. (2015). Opposite effects of the same drug: Reversal of topical analgesia by nocebo information. *Pain*, *156*(1), 39–46. https://doi.org/10.1016/j.pain.0000000000000004

Bąbel, P., Adamczyk, W., Świder, K., Bajcar, E., Kicman, P., & Lisińska, N. (2018). How classical conditioning shapes placebo analgesia: Hidden versus open conditioning. *Pain Medicine*, *19*(6), 1156–1169. https://doi.org/10.1093/pm/pnx177

Balodis, I. M., Wynne-Edwards, K. E., & Olmstead, M. C. (2011). The stress–response-dampening effects of placebo. *Hormones and Behavior*, *59*(4), 465–472. https://doi.org/10.1016/j.yhbeh.2011.01.004

Bartley, H., Fasse, K., Home, R., & Petrie, K. J. (2016). You can't always get what you want: The influence of choice on nocebo and placebo responding. *Annals of Behavioral Medicine*, *50*(3), 445–451. https://doi.org/10.1007/s12160-016-9772-1

Benedetti, F. (2014). Placebo effects: From the neurobiological paradigm to translational implications. *Neuron*, *84*(3), 623–637. https://doi.org/10.1016/j.neuron.2014.10.023

Benedetti, F. (1996). The opposite effects of the opiate antagonist naloxone and the cholecystokinin antagonist proglumide on placebo analgesia. *Pain*, *64*(3), 535–543. https://doi.org/10.1016/0304-3959(95)00179-4

Benedetti, F., Amanzio, M., Casadio, C., Oliaro, A., & Maggi, G. (1997). Blockade of nocebo hyperalgesia by the cholecystokinin antagonist proglumide. *Pain*, *71*(2), 135–140. https://doi.org/10.1016/S0304-3959(97)03346-0

Benedetti, F., Amanzio, M., & Thoen, W. (2011). Disruption of opioid-induced placebo responses by activation of cholecystokinin type-2 receptors. *Psychopharmacology*, *213*(4), 791–797. https://doi.org/10.1007/s00213-010-2037-y

Benedetti, F., Maggi, G., Lopiano, L., Lanotte, M., Rainero, I., Vighetti, S., & Pollo, A. (2003). Open versus hidden medical treatments: The patient's knowledge about a therapy affects the therapy outcome. *Prevention & Treatment*, *6*(1), 1a.

Bingel, U., Wanigasekera, V., Wiech, K., Mhuircheartaigh, R. N., Lee, M. C., Ploner, M., & Tracey, I. (2011). The effect of treatment expectation on drug efficacy: Imaging the analgesic benefit of the opioid remifentanil. *Science Translational Medicine*, *3*(70), 70ra14.

Bishop, S. J. (2007). Neurocognitive mechanisms of anxiety: An integrative account. *Trends in Cognitive Sciences*, *11*(7), 307–316. https://doi.org/10.1016/j.tics.2007.05.008

Bjørkedal, E., & Flaten (2012). Expectations of increased and decreased pain explain the effect of conditioned pain modulation in females. *Journal of Pain Research*, *5*, 289–300. https://doi.org/10.2147/JPR.S33559

Blascovich, J., & Mendes, W. B. (2000). Challenge and threat appraisals: The role of affective cues. In J. P. Forgas (Ed.), *Studies in emotion and social einteraction, second series. Feeling and thinking: The role of affect in social cognition* (pp. 59–82). Cambridge, UK: Cambridge University Press.

Blasini, M., Corsi, N., Klinger, R., & Colloca, L. (2017). Nocebo and pain: An overview of the psychoneurobiological mechanisms. *Pain Reports*, *2*(2), e585. http://doi.org/10.1097/PR9.0000000000000585

Bogaerts, K., Van Eylen, L., Li, W., Bresseleers, J., Van Diest, I., De Peuter, S., … Van den Bergh, O. (2010). Distorted symptom perception in patients with medically unexplained symptoms. *Journal of Abnormal Psychology*, *119*(1), 226–234. https://doi.org/10.1037/a0017780

Bower, G. H. (1981). Mood and memory. *American Psychologist*, *36*(2), 129–148. https://doi.org/10.1037/0003-066X.36.2.129

Bräscher, A. K., Raymaekers, K., Van den Bergh, O., & Witthöft, M. (2017). Are media reports able to cause somatic symptoms attributed to WiFi radiation? An experimental test of the negative expectation hypothesis. *Environmental Research*, *156*, 265–271.

Braunstein, L. M., Gross, J. J., & Ochsner, K. N. (2017). Explicit and implicit emotion regulation: A multi-level framework. *Social Cognitive and Affective Neuroscience*, *12*(10), 1545–1557. http://doi.org/10.1093/scan/nsx096

Brown, J. A., Oikawa, M., Rose, J. P., Haught, H. M., Oikawa, H., & Geers, A. L. (2015). Choosing across cultures: The effect of choice complexity on treatment outcomes. *Journal of Behavioral Decision Making*, *28*, 515–528.

Butler, C., & Steptoe, A. (1986). Placebo responses: An experimental study of psychophysiological processes in asthmatic volunteers. *British Journal of Clinical Psychology*, *25*(3), 173–183. https://doi.org/10.1111/j.2044-8260.1986.tb00693.x

Carlino, E., & Benedetti, F. (2014). Placebo and nocebo effects. In D. Mostofsky (Ed.), *The handbook of behavioral medicine* (pp. 26–57). New Jersey, NJ: John Wiley & Sons Ltd. https://doi.org/10.1002/9781118453940.ch3

Colagiuri, B., Schenk, L. A., Kessler, M. D., Dorsey, S. G. S., & Colloca, L. (2015). The placebo effect: From concepts to genes. *Neuroscience*, *307*, 171–190. https://doi.org/10.1016/j.neuroscience.2015.08.017

Colagiuri, B., & Quinn, V. F. (2018). Autonomic arousal as a mechanism of the persistence of nocebo hyperalgesia. *The Journal of Pain*, *19*(5), 476–486. https://doi.org/10.1016/j.jpain.2017.12.006

Colagiuri, B., Quinn, V. F., & Colloca, L. (2015). Nocebo hyperalgesia, partial reinforcement and extinction. *The Journal of Pain*, *16*(10), 995–1004. https://doi.org/10.1016/j.jpain.2015.06.012

Colloca, L., & Benedetti, F. (2007). Nocebo hyperalgesia: How anxiety is turned into pain. *Current Opinion in Anesthesiology*, *20*, 435–439.

Colloca, L., Sigaudo, M., & Benedetti, F. (2008). The role of learning in nocebo and placebo effects. *Pain*, *136*, 211–218.

Colloca, L., & Howick, J. (2018). Placebos without deception: A review of their outcomes, mechanisms, and ethics. *International Review of Neurobiology*, *138*, 219–240. https://doi.org/10.1016/bs.irn.2018.01.005

Colloca, L., Petrovic, P., Wager, T. D., Ingvar, M., & Benedetti, F. (2010). How the number of learning trials affects placebo and nocebo responses. *Pain*, *151*(2), 430–439. https://doi.org/10.1016/j.pain.2010.08.007

Colloca, L., Pine, D. S., Ernst, M., Miller, F. G., & Grillon, C. (2016). Vasopressin boosts placebo analgesic effects in women: A randomized trial. *Biological Psychiatry*, *79*(10), 794–802. https://doi.org/10.1016/j.biopsych.2015.07.019

Consedine, N. S., & Moskowitz, J. T. (2007). The role of discrete emotions in health outcomes: A critical review. *Applied and Preventive Psychology*, *12*(2), 59–75. https://doi.org/10.1016/j.appsy.2007.09.001

Corsi, N., & Colloca, L. (2017). Placebo and nocebo effects: The advantage of measuring expectations and psychological factors. *Frontiers in Psychology*, *8*, 1–11. http://doi.org/10.3389/fpsyg.2017.00308

Corsi, N., Andani, M. E., Tinazzi, M., & Fiorio, M. (2016). Changes in perception of treatment efficacy are associated to the magnitude of the nocebo effect and to personality traits. *Scientific Reports*, *6*(1), 30671. https://doi.org/10.1038/srep30671

Costa, P. T., & McCrae, R. R. (1987). Neuroticism, somatic complaints, and disease: Is the bark worse than the bite? *Journal of Personality*, *55*(2), 299–316. https://doi.org/10.1111/j.1467-6494.1987.tb00438.x

Crichton, F., Dodd, G., Schmid, G., Gamble, G., Cundy, T., & Petrie, K. J. (2014). The power of positive and negative expectations to influence reported symptoms and mood during exposure to wind farm sound. *Health Psychology*, *33*(12), 1588–1592. http://doi.org/10.1037/hea0000037

Darragh, M., Yow, B., Kieser, A., Booth, R. J., Kydd, R. R., & Consedine, N. S. (2016). A take-home placebo treatment can reduce stress, anxiety and symptoms of depression in a non-patient population. *Australian and New Zealand Journal of Psychiatry*, *50*(9), 858–865. https://doi.org/10.1177/0004867415621390

de Jong, P. J., van Baast, R., Arntz, A., & Merckelbach, H. (1996). The placebo effect in pain reduction: the influence of conditioning experiences and response expectancies. *International Journal of Behavioral Medicine*, *3*(1), 14–29.

De Peuter, S., Put, C., Lemaigre, V., Demedts, M., Verleden, G., & Bergh, O. V. D. (2007). Context-evoked overperception in asthma. *Psychology and Health*, *22*(6), 737–748. https://doi.org/10.1080/14768320601151702

DeSteno, D., Gross, J. J., & Kubzansky, L. (2013). Affective science and health: The importance of emotion and emotion regulation. *Health Psychology*, *32*(5), 474–486. https://doi.org/10.1037/a0030259

DeSteno, D., Petty, R. E., Rucker, D. D., Wegener, D. T., & Braverman, J. (2004). Discrete emotions and persuasion: The role of emotion-induced expectancies. *Journal of Personality and Social Psychology*, *86*(1), 43–56. https://doi.org/10.1037/0022-3514.86.1.43

Devriese, S., Winters, W., Stegen, K., Van Diest, I., Veulemans, H., Nemery, B., … Van den Bergh, O. (2000). Generalization of acquired somatic symptoms in response to odors: A Pavlovian perspective on multiple chemical sensitivity. *Psychosomatic Medicine*, *62*(6), 751–759. https://doi.org/10.1097/00006842-200011000-00003

Dickerson, S. S., & Kemeny, M. E. (2004). Acute stressors and cortisol responses: A theoretical integration and synthesis of laboratory research. *Psychological Bulletin*, *130*(3), 355–391. https://doi.org/10.1037/0033-2909.130.3.355

Diener, E., & Emmons, R. A. (1984). The independence of positive and negative affect. *Journal of Personality and Social Psychology*, *47*(5), 1105–1117. https://doi.org/10.1037/0022-3514.47.5.1105

El Brihi, J., Horne, R., & Faasse, K. (2019). Prescribing placebos: An experimental examination of the role of dose, expectancies, and adherence in open-label placebo effects. *Annals of Behavioral Medicine*, *53*(1), 16–28. https://doi.org/10.1093/abm/kay011

Elsenbruch, S., Schmid, J., Bäsler, M., Cesko, E., Schedlowski, M., & Benson, S. (2012). How positive and negative expectations shape the experience of visceral pain: An experimental pilot study in healthy women. *Neuro-Gastroenterology and Motility*, *24*(10), 914-e460. https://doi.org/10.1111/j.1365-2982.2012.01950.x

Elsenbruch, S., Roderigo, T., Enck, P., & Benson, S. (2019). Can a brief relaxation exercise modulate placebo or nocebo effects in a visceral pain model?. *Frontiers in Psychiatry*, *10*, 144. https://doi.org/10.3389/fpsyt.2019.00144

Epstein, S. (1979). The stability of behavior: I. On predicting most of the people much of the time. *Journal of Personality and Social Psychology*, *37*(7), 1097–1126. https://doi.org/10.1037/0022-3514.37.7.1097

Evans, F. J. (1974). The placebo response in pain reduction. In J. J. Bonica (Ed.), *Advances in neurology* (Vol. 4, pp. 289–296). New York, NY: Raven.

Evers, A. W. M., Colloca, L., Blease, C., Annoni, M., Atlas, L. Y., Benedetti, F., … Kelley, J. M. (2018). Implications of placebo and nocebo effects for clinical practice: Expert consensus. *Psychotherapy and Psychosomatics*, *87*(4), 204–210. http://doi.org/10.1159/000490354

Eysenck, M. W., Derakshan, N., Santos, R., & Calvo, M. G. (2007). Anxiety and cognitive performance: Attentional control theory. *Emotion*, *7*(2), 336–353. https://doi.org/10.1037/1528-3542.7.2.336

Faasse, K. (2019). Nocebo effects in health psychology. *Australian Psychologist*, *54*(6), 453–465. https://doi.org/10.1111/ap.12392

Faasse, K., Helfer, S. G., Barnes, K., Colagiuri, B., & Geers, A. L. (2019). Experimental assessment of nocebo effects and nocebo side effects: Definitions, study design, and implications for psychiatry and beyond. *Frontiers in Psychiatry*, *10*, 396. https://doi.org/10.3389/FPSYT.2019.00396

Faasse, K., & Petrie, K. J. (2016). From me to you: The effect of social modeling on treatment outcomes. *Current Directions in Psychological Science*, *25*, 438–443.

Feldman Barrett, L. F., & Bliss-Moreau, E. (2009). Affect as a psychological primative. *Advances in Experimental Social Psychology*, *41*(8), 167–218. https://doi.org/10.1016/S0065-2601(08)00404-8

Flaten, M. A. (2014). Pain-related negative emotions and placebo analgesia. In F. Benedetti, P. Enck, E. Frisaldi, & M. Schedlowski (Eds.), *Placebo, handbook of experimental pharmacology* (pp. 81–96). Berlin, Heidelberg: Springer.

Flaten, M. A., Aslaksen, P. M., & Lyby, P. S. (2013). Affect positive and negative emotions and placebo analgesia. In L. Colloca, M. A. Flaten, & K. Meissner (Eds.), *Placebo and pain: From bench to bedside* (pp. 73–81). London, UK: Academic Press.

Fleeson, W. (2004). Moving personality beyond the person-situation debate: The challenge and the opportunity of within-person variability. *Current Directions in Psychological Science*, *13*(2), 83–87. https://doi.org/10.1111/j.0963-7214.2004.00280.x

Forgas, J. P. (1995). Mood and judgment: The affect infusion model (AIM). *Psychological Bulletin*, *117*(1), 39–66. https://doi.org/10.1037/0033-2909.117.1.39

Forsberg, J. T., Gjerstad, J., Flaten, M. A., & Aslaksen, P. M. (2018). Influence of catechol-O-methyltransferase Val158Met on fear of pain and placebo analgesia. *Pain*, *159*(1), 168–174. https://doi.org/10.1097/j.pain.0000000000001081

Frisaldi, E., Piedimonte, A., & Benedetti, F. (2015). Placebo and nocebo effects: A complex interplay between psychological factors and neurochemical networks. *American Journal of Clinical Hypnosis*, *57*(3), 267–284. http://doi.org/10.1080/00029157.2014.976785

Funder, D. C. (2006). Towards a resolution of the personality triad: Persons, situations, and behaviors. *Journal of Research in Personality*, *40*(1), 21–34. https://doi.org/10.1016/j.jrp.2005.08.003

Geers, A. L., Close, S. R., Caplandies, F., Pertiwi, Y., Murray, A., Vogel, C., … Vase, L. A. (2019). Testing a positive affect induction to reduce verbally-induced nocebo hyperalgesia in an experimental pain paradigm. *Pain*, *160*(10), 2290–2297. https://doi.org/10.1097/j.pain.0000000000001618

Geers, A. L., Close, S. R., Caplandies, F., & Vase, L. (2019). A positive mood induction for reducing the formation of nocebo effects from side effect information. *Annals of Behavioral Medicine*, *53*(11), 999–1008. https://doi.org/10.1093/abm/kaz005

Geers, A. L., Briñol, P., & Petty, R. E. (2019). An analysis of the basic processes of formation and change of placebo expectations. *Review of General Psychology*, *23*(2), 211–229. https://doi.org/10.1037/gpr0000171

Geers, A. L., Fowler, S. L., Helfer, S. G., & Murray, A. B. (2019). Test of psychological and electrodermal changes immediately following the delivery of three analgesic treatment messages. *Pain Reports*, *4*(3), e693. https://doi.org/10.1097/PR9.0000000000000693

Geers, A. L., & Miller, F. G. (2014). Understanding and translating knowledge about placebo effects: The contribution of psychology. *Current Opinion in Psychiatry*, *27*, 326–331.

Goodenough, B., Kampel, L., Champion, D. G., Laubreaux, L., Nicholas, K. M., Ziegler, B. J., & McInerney, M. (1997). An investigation of the placebo effect and age-related factors in the report of needle pain from venipuncture in children. *Pain*, *72*(3), 383–391. https://doi.org/10.1016/S0304-3959(97)00062-6

Gremsl, A., Schwab, D., Höfler, C., & Schienle, A. (2018). Placebo effects in spider phobia: An eye-tracking experiment. *Cognition & Emotion*, *32*(8), 1571–1577. https://doi.org/10.1080/02699931.2017.1422698

Gross, J. J. (2015). Emotion regulation: Current status and future prospects. *Psychological Inquiry*, *26*, 1–26.

Gryll, S. L., & Katahn, M. (1978). Situational factors contributing to the placebo effect. *Psychopharmacology*, *57*(3), 253–261. https://doi.org/10.1007/BF00426747

Guevarra, D. A., Moser, J. S., Wager, T. D., & Kross, E. (2020). Placebos without deception reduce self-report and neural measures of emotional distress. *Nature Communications*, *11*, 1–8. https://doi.org/10.1038/s41467-020-17654-y

Hahn, R. A. (1997). The nocebo phenomenon: Scope and foundations. In A. Harrington (Ed.), *The placebo effect: An interdisciplinary exploration* (pp. 56–76). Cambridge, UK: Harvard University Press.

Hashish, I., Haia, H. K., Harvey, W., Feinmann, C., & Harris, M. (1988). Reduction of postoperative pain and swelling by ultrasound treatment: A placebo effect. *Pain*, *33*(3), 303–311. https://doi.org/10.1016/0304-3959(88)90289-8

Haas, J. W., Wittkowski, J., Rief, W., Glombiewski, J. A., Winkler, A., & Doering, B. K. (2020). Expectation-induced placebo effect on acute sadness in women with major depression: An experimental investigation. *Journal of Affective Disorders*, *274*, 920–928. http://doi.org/10.1016/j.jad.2020.05.056

Ho, K. H., Hashish, I., Salmon, P., Freeman, R., & Harvey, W. (1988). Reduction of post-operative swelling by a placebo effect. *Journal of Psychosomatic Research*, *32*(2), 197–205. http://doi.org/10.1016/0022-3999(88)90055-4

Jacobs, W., Schagen, S. B., Thijssen, M., & Das, E. (2019). Preventing adverse information effects on health outcomes: A self-affirmation intervention reduced information-induced cognitive decline in gastrointestinal cancer patients. *Social Science & Medicine*, *226*, 47–55. https://doi.org/10.1016/j.socscimed.2019.02.013

Johnson, E. J., & Tversky, A. (1983). Affect, generalization, and the perception of risk. *Journal of Personality and Social Psychology*, *45*(1), 20–31. https://doi.org/10.1037/0022-3514.45.1.20

Jurinec, N., & Schienle, A. (2020). Utilizing placebos to leverage effects of cognitive-behavioral therapy in patients with depression. *Journal of Affective Disorders*, *277*, 779–784. https://doi.org/10.1016/j.jad.2020.08.087

Kaptchuk, T. J., Friedlander, E., Kelley, J. M., Sanchez, M. N., Kokkotou, E., Singer, J. P., … Lembo, A. J. (2010). Placebos without deception: A randomized controlled trial in irritable bowel syndrome. *PLoS One*, *5*(12), e15591. https://doi.org/10.1371/journal.pone.0015591

Kenrick, D. T., Griskevicius, V., Neuberg, S. L., & Schaller, M. (2010). Renovating the pyramid of needs: Contemporary extensions built upon ancient foundations. *Perspectives on Psychological Science*, *5*(3), 292–314. https://doi.org/10.1177/1745691610369469

Kessner, S., Sprenger, C., Wrobel, N., Wiech, K., & Bingel, U. (2013). Effect of oxytocin on placebo analgesia: A randomized study. *Journal of the American Medical Association*, *310*(16), 1733–1735. https://doi.org/10.1001/jama.2013.277446

Kirsch, I. (2019). Placebo effect in the treatment of depression and anxiety. *Frontiers in Psychiatry*, *10*, 407. https://doi.org/10.3389/fpsyt.2019.00407

Lang, E. V., Hatsiopoulou, O., Koch, T., Berbaum, K., Lutgendorf, S., Kettenmann, E., … Kaptchuk, T. J. (2005). Can words hurt? Patient–provider interactions during invasive procedures. *Pain*, *114*(1–2), 303–309. https://doi.org/10.1016/j.pain.2004.12.028

Lazarus, R. S., & Folkman, S. (1984). *Stress, appraisal, and coping*, New York, NY: Springer.

Lee, H. F., Hsieh, J. C., Lu, C. L., Yeh, T. C., Tu, C. H., Cheng, C. M., … Chang, F. Y. (2012). Enhanced affect/cognition-related brain responses during visceral placebo analgesia in irritable bowel syndrome patients. *Pain*, *153*(6), 1301–1310. https://doi.org/10.1016/j.pain.2012.03.018

Lerner, J. S., Gonzalez, R. M., Small, D. A., & Fischhoff, B. (2003). Effects of fear and anger on perceived risks of terrorism: A national field experiment. *Psychological Science*, *14*(2), 144–150. https://doi.org/10.1111/1467-9280.01433

Lerner, J. S., Li, Y., Valdesolo, P., & Kassam, K. S. (2015). Emotion and decision making. *Annual Review of Psychology*, *66*(1), 799–823. https://doi.org/10.1146/annurev-psych-010213-115043

Leventhal, H., Brissette, I., & Leventhal, E. A. (2003). The common-sense model of self-regulation of health and illness. In L. D. Cameron & H. Leventhal (Eds.), *The self-regulation of health and illness behaviour* (pp. 42–65). New York, NY: Routledge.

Long, Q., Hu, N., Li, H., Zhang, Y., Yuan, J., & Chen, A. (2020). Suggestion of cognitive enhancement improves emotion regulation. *Emotion*, *20*, 866–873. https://doi.org/10.1037/emo0000629

Losin, E. A. R., Anderson, S. R., & Wager, T. D. (2017). Feelings of clinician-patient similarity and trust influence pain: Evidence from simulated clinical interactions. *The Journal of Pain*, *18*(7), 787–799. https://doi.org/10.1016/j.jpain.2017.02.428

Lyby, P. S., Aslaksen, P. M., & Flaten, M. A. (2010). Is fear of pain related to placebo analgesia? *Journal of Psychosomatic Research*, *68*(4), 369–377. https://doi.org/10.1016/j.jpsychores.2009.10.009

Lyby, P. S., Aslaksen, P. M., & Flaten, M. A. (2011). Variability in placebo analgesia and the role of fear of pain—An ERP study. *Pain*, *152*(10), 2405–2412. https://doi.org/10.1016/j.pain.2011.07.010

Lyby, P. S., Forsberg, J. T., Åsli, O., & Flaten, M. A. (2012). Induced fear reduces the effectiveness of a placebo intervention on pain. *Pain*, *153*(5), 1114–1121. https://doi.org/10.1016/j.pain.2012.02.042

Lyubomirsky, S., King, L., & Diener, E. (2005). The benefits of frequent positive affect: Does happiness lead to success? *Psychological Bulletin*, *131*(6), 803–855. https://doi.org/10.1037/0033-2909.131.6.803

Marsland, A. L., Gianaros, P. J., Prather, A. A., Jennings, J. R., Neumann, S. A., & Manuck, S. B. (2007). Stimulated production of proinflammatory cytokines covaries inversely with heart rate variability. *Psychosomatic Medicine*, *69*(8), 709–716. https://doi.org/10.1097/PSY.0b013e3181576118

Mauss, I. B., & Robinson, M. D. (2009). Measures of emotion: A review. *Cognition & Emotion*, *23*(2), 209–237. http://doi.org/10.1080/02699930802204677

Meissner, K., Talsky, N., Olliges, E., Jacob, C., Salat, C., Braun, M., … Stoetzer, O. J. (2019). Individual factors contributing to nausea in first-time chemotherapy patients: A prospective cohort study. *Frontiers in Pharmacology*, *10*, 410.

Meyer, B., Yuen, K. S. L., Ertl, M., Polomac, N., Mulert, C., Buchel, C., & Kalisch, R. (2015). Neural mechanisms of placebo anxiolysis. *Journal of Neuroscience*, *35*(19), 7365–7373. https://doi.org/10.1523/JNEUROSCI.4793-14.2015

Meyer, B., Yuen, K. S. L., Saase, V., & Kalisch, R. (2019). The functional role of large-scale brain network coordination in placebo-induced anxiolysis. *Cerebral Cortex*, *29*(8), 3201–3210. https://doi.org/10.1093/cercor/bhy188

Morton, D. L., Watson, A., El-Deredy, W., & Jones, A. K. P. (2009). Reproducibility of placebo analgesia: Effect of dispositional optimism. *Pain*, *146*(1), 194–198. https://doi.org/10.1016/j.pain.2009.07.026

Neukirch, N., & Colagiuri, B. (2015). The placebo effect, sleep difficulty, and side effects: A balanced placebo model. *Journal of Behavioral Medicine*, *38*, 273–283. http://dx.doi.org/10.1007/s10865-014-9590-5

Nisbett, R. E., & Wilson, T. D. (1977). Telling more than we can know: Verbal reports on mental processes. *Psychological Review*, *84*(3), 231–259. https://doi.org/10.1037/0033-295X.84.3.231

Ober, K., Benson, S., Vogelsang, M., Bylica, A., Günther, D., Witzke, O., … Schedlowski, M. (2012). Plasma noradrenaline and state anxiety levels predict placebo response in learned immunosuppression. *Clinical Pharmacology & Therapeutics*, *91*(2), 220–226.

Pervin, L. A. (1993). Personality: Theory and research (6th ed.). New York, NY: John Wiley & Sons.

Peters, E., Lipkus, I., & Diefenbach, M. A. (2006). The functions of affect in health communications and in the construction of health preferences. *Journal of Communication*, *56*(suppl_1), S140–S162. https://doi.org/10.1111/j.1460-2466.2006.00287.x

Petersen, G. L., Finnerup, N. B., Grosen, K., Pilegaard, H. K., Tracey, I., Benedetti, F., … Vase, L. (2014). Expectations and positive emotional feelings accompany reductions in ongoing and evoked neuropathic pain following placebo interventions. *Pain*, *155*(12), 2687–2698. https://doi.org/10.1016/j.pain.2014.09.036

Petersen, G. L., Finnerup, N. B., Nørskov, K. N., Grosen, K., Pilegaard, H. K., Benedetti, F., … Vase, L. (2012). Placebo manipulations reduce hyperalgesia in neuropathic pain. *Pain*, *153*(6), 1292–1300. https://doi.org/10.1016/j.pain.2012.03.011

Petrie, K. J., Moss-Morris, R., Grey, C., & Shaw, M. (2004). The relationship of negative affect and perceived sensitivity to symptom reporting following vaccination. *British Journal of Health Psychology*, *9*(1), 101–111. https://doi.org/10.1348/135910704322778759

Petrie, K. J., & Rief, W. (2019). Psychobiological mechanisms of placebo and nocebo effects: Pathways to improve treatments and reduce side effects. *Annual Review of Psychology*, *70*(1), 599–625. https://doi.org/10.1146/annurev-psych-010418-102907

Petrovic, P., Dietrich, T., Fransson, P., Andersson, J., Carlsson, K., & Ingvar, M. (2005). Placebo in emotional processing—induced expectations of anxiety relief activate a generalized modulatory network. *Neuron*, *46*(6), 957–969. https://doi.org/10.1016/j.neuron.2005.05.023

Petty, R. E., & Briñol, P. (2012). The elaboration likelihood model. In P. A. M. Van Lange, A. W. Kruglanski, & E. T. Higgins (Eds.), *Handbook of theories of social psychology* (pp. 224–245). Los Angeles, CA: Sage Publications Ltd. https://doi.org/10.4135/9781446249215.n12

Pourtois, G., Schettino, A., & Vuilleumier, P. (2013). Brain mechanisms for emotional influences on perception and attention: What is magic and what is not. *Biological Psychology*, *92*(3), 492–512. https://doi.org/10.1016/j.biopsycho.2012.02.007

Prediger, B., Meyer, E., Büchter, R., & Mathes, T. (2019). Nocebo effects of a simplified package leaflet compared to unstandardised oral information and a standard package leaflet: A pilot randomised controlled trial. *Trials*, *20*(1), 458. https://doi.org/10.1186/s13063-019-3565-3

Pressman, S. D., & Cohen, S. (2005). Does positive affect influence health? *Psychological Bulletin*, *131*(6), 925–971. https://doi.org/10.1037/0033-2909.131.6.925

Pressman, S. D., Jenkins, B. N., & Moskowitz, J. T. (2019). Positive affect and health: What do we know and where next should we go?. *Annual Review of Psychology*, *70*(1), 627–650. https://doi.org/10.1146/annurev-psych-010418-102955

Put, C., Van den Bergh, O., Van Ongeval, E., De Peuter, S., Demedts, M., & Verleden, G. (2004). Negative affectivity and the influence of suggestion on asthma symptoms. *Journal of Psychosomatic Research*, *57*(3), 249–255. https://doi.org/10.1016/S0022-3999(03)00541-5

Roderigo, T., Benson, S., Schöls, M., Hetkamp, M., Schedlowski, M., Enck, P., & Elsenbruch, S. (2017). Effects of acute psychological stress on placebo and nocebo responses in a clinically relevant model of visceroception. *Pain*, *158*(8), 1489–1498. https://doi.org/10.1097/j.pain.0000000000000940

Rose, J. P., Geers, A. L., Rasinski, H. M., & Fowler, S. L. (2012). Choice and placebo expectation effects in the context of pain analgesia. *Journal of Behavioral Medicine*, *35*, 462–470. https://doi.org/10.1007/s10865-011-9374-0

Rose, J. P., Geers, A. L., Fowler, S. L., & Rasinski, H. M. (2014). Choice-making, expectations, and treatment positivity: How and when choosing shapes aversive experiences. *Journal of Behavioral Decision Making*, *27*(1), 1–10. https://doi.org/10.1002/bdm.1775

Rosenthal, D., & Frank, J. D. (1956). Psychotherapy and the placebo effect. *Psychological Bulletin*, *53*(4), 294–302. https://doi.org/10.1037/h0044068

Saarimäki, H., Ejtehadian, L. F., Glerean, E., Jaaskelainen, I. P., Vuilleumier, P., Sams, M., & Nummenmaa, L. (2018). Distributed affective space represents multiple emotion categories across the human brain. *Social Cognitive and Affective Neuroscience*, *13*, 471–482. https://doi.org/10.1093/scan/nsy018

Salovey, P., & Birnbaum, D. (1989). Influence of mood on health-relevant cognitions. *Journal of Personality and Social Psychology*, *57*(3), 539–551. https://doi.org/10.1037/0022-3514.57.3.539

Schaefer, M., Denke, C., Harke, R., Olk, N., Erkovan, M., & Enge, S. (2019). Open-label placebos reduce test anxiety and improve self-management skills: A randomized-controlled trial. *Scientific Reports*, *9*, 1–6. https://doi.org/10.1038/s41598-019-49466-6

Schedlowski, M., Enck, P., Rief, W., & Bingel, U. (2015). Neuro-bio-behavioral mechanisms of placebo and nocebo responses: Implications for clinical trials and clinical practice. *Pharmacological Reviews*, *67*(3), 697–730. https://doi.org/10.1124/pr.114.009423

Schienle, A., Gremsl, A., Übel, S., & Körner, C. (2016). Testing the effects of a disgust placebo with eye tracking. *International Journal of Psychophysiology*, *101*, 69–75. https://doi.org/10.1016/j.ijpsycho.2016.01.001

Schienle, A., Höfler, C., Übel, S., & Wabnegger, A. (2018). Emotion-specific nocebo effects: An fMRI study. *Brain Imaging and Behavior*, *12*(1), 180–187. https://doi.org/10.1007/s11682-017-9675-1

Schienle, A., Übel, S., Schöngaßner, F., Ille, R., & Scharmüller, W. (2014). Disgust regulation via placebo: An fMRI study. *Social Cognitive and Affective Neuroscience*, *9*(7), 985–990. https://doi.org/10.1093/scan/nst072

Schienle, A., Übel, S., & Wabnegger, A. (2017). When opposites lead to the same: A direct comparison of explicit and implicit disgust regulation via fMRI. *Social Cognitive and Affective Neuroscience*, *12*(3), 445–451. https://doi.org/10.1093/scan/nsw144

Schmid, J., Langhorst, J., Gaß, F., Theysohn, N., & Benson, S. (2015). Placebo analgesia in patients with functional and organic abdominal pain: A fMRI study in IBS, UC, and healthy volunteers. *Gut*, *64*(3), 418–427. https://www.doi.org/10.1136/gutjnl-2013-306648

Schmitz, J., Kamping, S., Wiegratz, J., Müller, M., Stork, J., Colloca, L., … Klinger, R. (2017). Impact of patient information leaflets on pain medication intake behavior: A pilot study. *Pain Reports*, *2*(6), e620. https://doi.org/10.1097/PR9.0000000000000620

Schwarz, N., & Clore, G. L. (2007). Feelings and phenomenal experiences. In A. W. Kruglanski & E. T. Higgins (Eds.), *Social psychology: Handbook of basic principles* (pp. 385–407). New York, NY: The Guilford Press.

Scott, D. J., Stohler, C. S., Egnatuk, C. M., Wang, H., Koeppe, R. A., & Zubieta, J. K. (2007). Individual differences in reward responding explain placebo-induced expectations and effects. *Neuron*, *55*(2), 325–336. https://doi.org/10.1016/j.neuron.2007.06.028

Scott, D. J., Stohler, C. S., Egnatuk, C. M., Wang, H., Koeppe, R. A., & Zubieta, J. K. (2008). Placebo and nocebo effects are defined by opposite opioid and dopaminergic responses. *Archives of General Psychiatry*, *65*, 220–231.

Segerstrom, S. C. (2007). Stress, energy, and immunity: An ecological view. *Current Directions in Psychological Science*, *16*(6), 326–330. https://doi.org/10.1111/j.1467-8721.2007.00522.x

Shapiro, A. K. (1964). Etiological factors in placebo effect. *Journal of the American Medical Association*, *187*(10), 712–714. https://doi.org/10.1001/jama.1964.03060230040010

Sheppes, G., Suri, G., & Gross, J. J. (2015). Emotion regulation and psychopathology. *Annual Review of Clinical Psychology*, *11*, 379–405. https://doi.org/10.1146/annurev-clinpsy-032814-112739

Slovic, P., Finucane, M. L., Peters, E., & MacGregor, D. G. (2007). The affect heuristic. *European Journal of Operational Research*, *177*(3), 1333–1352. https://doi.org/10.1016/j.ejor.2005.04.006

Staats, P. S., Staats, A., & Hekmat, H. (2001). The additive impact of anxiety and a placebo on pain. *Pain Medicine*, *2*(4), 267–279. https://doi.org/10.1046/j.1526-4637.2001.01046.x

Stam, H. J., & Spanos, N. P. (1987). Hypnotic analgesia, placebo analgesia, and ischemic pain: The effects of contextual variables. *Journal of Abnormal Psychology*, *96*(4), 313–320. https://doi.org/10.1037/0021-843X.96.4.313

Stellar, J. E., John-Henderson, N., Anderson, C. L., Gordon, A. M., McNeil, G. D., & Keltner, D. (2015). Positive affect and markers of inflammation: Discrete positive emotions predict lower levels of inflammatory cytokines. *Emotion*, *15*(2), 129–133. http://doi.org/10.1037/emo0000033

Skvortsova, A., Veldhuijzen, D. S., Middendorp, H. V., Van den Bergh, O., & Evers, A. W. M. (2018). Enhancing placebo effects in somatic symptoms through oxytocin. *Psychosomatic Medicine*, *80*(4), 353–360. https://doi.org/10.1097/PSY.0000000000000571

Świder, K., Bąbel, P., Wronka, E., van Rijn, C. M., & Oosterman, J. M. (2019). Placebo analgesia induced by verbal suggestion in the context of experimentally induced fear and anxiety. *PLoS One*, *14*(9) e0222805. https://doi.org/10.1371/journal.pone.0222805

Takahashi, K. J., & Earl, A. (2020). Effect of extraneous affect on health message reception. *Personality and Social Psychology Bulletin*, *46*(2), 270–284. https://doi.org/10.1177/0146167219855042

Testa, M., & Rossettini, G. (2016). Enhance placebo, avoid nocebo: How contextual factors affect physiotherapy outcomes. *Manual Therapy*, *24*, 65–74.

Tracey, I. (2010). Getting the pain you expect: Mechanisms of placebo, nocebo and reappraisal effects in humans. *Nature Medicine*, *16*(11), 1277–1283. https://doi.org/10.1038/nm.2229

Übel, S., Leutgeb, V., & Schienle, A. (2015). Electrocortical effects of a disgust placebo in children. *Biological Psychology*, *108*, 78–84. https://doi.org/10.1016/j.biopsycho.2015.03.015

Van den Bergh, O., Winters, W., Devriese, S., & Van Diest, I. (2002). Learning subjective health complaints. *Scandinavian Journal of Psychology*, *43*(2), 147–152. https://doi.org/10.1111/1467-9450.00280

van der Meulen, M., Kamping, S., & Anton, F. (2017). The role of cognitive reappraisal in placebo analgesia: An fMRI study. *Social Cognitive and Affective Neuroscience*, *12*(7), 1128–1137. https://doi.org/10.1093/scan/nsx033

Van Osch, M., van Dulmen, S., van Vliet, L., & Bensing, J. (2017). Specifying the effects of physician's communication on patients' outcomes: A randomised controlled trial. *Patient Education and Counseling*, *100*(8), 1482–1489. https://doi.org/10.1016/j.pec.2017.03.009

Vase, L., Robinson, M. E., Verne, G. N., & Price, D. D. (2005). Increased placebo analgesia over time in irritable bowel syndrome (IBS) patients is associated with desire and expectation but not endogenous opioid mechanisms. *Pain*, *115*(3), 338–347. http://doi.org/10.1016/j.pain.2005.03.014

Verrender, A., Loughran, S. P., Dalecki, A., Freudenstein, F., & Croft, R. J. (2018). Can explicit suggestions about the harmfulness of EMF exposure exacerbate a nocebo response in healthy controls?. *Environmental Research*, *166*, 409–417. https://doi.org/10.1016/j.envres.2018.06.032

Vögtle, E., Barke, A., & Kröner-Herwig, B. (2013). Nocebo hyperalgesia induced by social observational learning. *Pain*, *154*(8), 1427–1433. https://doi.org/10.1016/j.pain.2013.04.041

Vögtle, E., Kröner-Herwig, B., & Barke, A. (2019). Nocebo hyperalgesia can be induced by the observation of a model showing natural pain expressions. *The Clinical Journal of Pain*, *35*(9), 737–743. https://doi.org/10.1097/AJP.0000000000000734

Wager, T. D., Atlas, L. Y., Leotti, L. A., & Rilling, J. K. (2011). Predicting individual differences in placebo analgesia: Contributions of brain activity during anticipation and pain experience. *Journal of Neuroscience*, *31*(2), 439–452. https://doi.org/10.1523/JNEUROSCI.3420-10.2011

Wager, T. D., & Atlas, L. Y. (2015). The neuroscience of placebo effects: Connecting context, learning and health. *Nature Reviews Neuroscience*, *16*(7), 403–418. https://doi.org/10.1038/nrn3976

Wager, T. D., Rilling, J. K., Smith, E. E., Sokolik, A., Casey, K. L., Davidson, R. J., … Cohen, J. D. (2004). Placebo-induced changes in FMRI in the anticipation and experience of pain. *Science*, *303*(5661), 1162–1167. https://doi.org/10.1126/science.1093065

Watson, D., & Pennebaker, J. W. (1989). Health complaints, stress, and distress: Exploring the central role of negative affectivity. *Psychological Review*, *96*(2), 234–254. https://doi.org/10.1037/0033-295X.96.2.234

Weimer, K., Hahn, E., Mönnikes, N., Herr, A.-K., Stengel, A., & Enck, P. (2019). Are individual learning experiences more important than heritable tendencies? A pilot twin study on placebo analgesia. *Frontiers in Psychiatry*, *10*, 679. https://doi.org/10.3389/fpsyt.2019.00679

Williams, D. M., Rhodes, R. E., & Connor, M. T. (2018). *Affective determinants of health behaviour*. New York, NY: Oxford University Press.

Zhang, W., Guo, J., Zhang, J., & Luo, J. (2013). Neural mechanism of placebo effects and cognitive reappraisal in emotion regulation. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *40*, 364–373. https://doi.org/10.1016/j.pnpbp.2012.10.020

AUTHOR BIOGRAPHIES

Andrew Geers is a Professor of Psychology at the University of Toledo. He is interested in the advancement and application of personality and social psychology theory within health and medical contexts. His primary research interests are in the areas of placebo effects, nocebo effects, health behavior, affect, and emotion. He received his BA from the University of Cincinnati and his PhD in Experimental Psychology from Ohio University.

Kate Faasse is a senior lecturer and Australian Research Council DECRA Fellow in health psychology at the University of New South Wales in Sydney, Australia. Kate's research in health psychology focuses on the impact of beliefs and expectations on both health behaviour and mind-body interactions. Her work examines a range of beliefs and outcomes related to aspects of illness and medical care, including nocebo and placebo effects, treatment adherence, perceptions of generic medicines, and beliefs about and responses to health threats including COVID-19. Kate teaches health psychology and research and writing skills.

Darwin A. Guevarra is a Postdoctoral Fellow at Michigan State University working with Jason S. Moser. He is broadly interested in affect and affect regulation processes and their implications for health and well-being. His primary research interests are in emotion regulation, placebo effects, affective neuroscience, and well-being.

His dissertation was examining the effectiveness of non-deceptive placebos (i.e., placebos administered without deception) in regulating emotional distress as indexed by self-report and neural measures. He received his BA from San Francisco State University and his PhD in Psychology (Social Area) at the University of Michigan.

Kelly Clemens is a doctoral student in Social Psychology at the University of Toledo in Toledo, OH. She completed her BS in Education from Central Michigan University and MA in Counseling from Oakland University. Her research examines how thoughts and feelings influence treatment perceptions and decision-making, particularly in the area of alternative medicine. She is also interested in factors which modulate placebo and nocebo effects.

Suzanne G. Helfer is a professor of psychology at Adrian College, specializing in health psychology. In her research she has examined pain, exercise, affect and emotion, placebo and nocebo effects, and cardiovascular reactivity to stress. She received her BA from Pennsylvania State University and her PhD in Experimental Psychology from Ohio University.

Ben Colagiuri is an Associate Professor in the School of Psychology, University of Sydney, Australia. His research focuses on how expectancies influence human behaviour with a specific interest in placebo and nocebo effects.

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