Published in final edited form as:

J Behav Med. 2011 June ; 34(3): 208–217. doi:10.1007/s10865-010-9301-9.

Placebo expectations and the detection of somatic information

Andrew L. Geers,

Department of Psychology, University of Toledo, Toledo, OH 43606-3390, USA

Justin A. Wellman,

Hartwick College, Oneonta, NY, USA

Stephanie L. Fowler,

University of Toledo, Toledo, OH, USA

Heather M. Rasinski, and

University of Toledo, Toledo, OH, USA

Suzanne G. Helfer

Adrian College, Adrian, MI, USA

Andrew L. Geers: ageers@utnet.utoledo.edu

Abstract

In a laboratory study we examined the hypothesis that placebo expectations enhance the initial identification of placebo-relevant sensations over placebo-irrelevant sensations. Participants ($N = 102$) were randomly assigned to one of three expectation groups. In the first group, participants ingested a placebo capsule and were told it was caffeine (deceptive expectation). In a second group, participants ingested a placebo capsule and were told it may be caffeine or it may be a placebo (double-blind expectation). Participants in the third group were given no expectation. All participants then tallied the placebo-relevant and placebo-irrelevant sensations they experienced during a 7-min period. Participants in the deceptive expectation group identified more placebo-relevant sensations than placebo-irrelevant sensations. No-expectation participants identified more placebo-irrelevant sensations than placebo-relevant sensations. Participants given the double-blind expectation identified an equal amount of placebo-relevant and irrelevant sensations. The amount of both placebo-relevant and placebo-irrelevant sensations detected mediated the relationship between the expectation manipulation and subsequent symptom reports. These data support the position that expectations cause placebo responding, in part, by altering how one identifies bodily sensations.

Keywords

Placebo effect; Expectation; Symptom perception; Attention

The placebo effect is a physiological and/or psychological reaction to an inert or irrelevant substance or procedure (Stewart-Williams and Podd 2004). Over the past 50 years, symptom reduction effects in thousands of research trials and in many clinical settings have been attributed to the placebo effect (Brody and Brody 2000; Jospe 1978; Peters 2001). It has been argued that the placebo effect is partly responsible for beneficial outcomes in virtually every area of medical care and that no medical treatment can be entirely separated from the

placebo effect (for reviews, see Harrington 1997; Jospe 1978; Kirsch 1999; Peters 2001; Shapiro and Shapiro 1997). Many medical scholars have begun to argue that the placebo effect should be harnessed and integrated into clinical practice (e.g., Chaput de Saintonge and Herxheimer 1994). However, the majority of studies administering placebos have failed to include a no-placebo control condition by which to separate the influence of the placebo effect from other non-specific factors such as spontaneous remission and regression to the mean (Ernst and Resch 1995; Keinle and Keine 1997; McDonald et al. 1983). Consequently, the power of the placebo effect remains a source of uncertainty and debate. In controlled studies, the magnitude of the placebo effect varies markedly (Hammersley et al. 1998; Price et al. 2008; Walach et al. 2002) and meta-analyses have come to divergent conclusions regarding the power of a placebo (Hróbjartsson and Gotzsche 2001, 2004; Kirsch and Sapirstein 1998; Madsen et al. 2009; Rief et al. 2009; Sauro and Greenberg 2005; Vase et al. 2002).

Prior research and theory implicate expectations as one of the key determinants of the placebo effect (Fillmore and Vogel-Sprott 1992; Kirsch 1999; Pollo et al. 2001; Rief et al. 2008; Stewart-Williams and Podd 2004). Recently, researchers have begun to disentangle the mechanisms linking expectations to placebo responding, with some studies focusing on neurological and biological factors (Benedetti et al. 2005; De la Fuente-Fernandez et al. 2001; Wager et al. 2004; Zubieta et al. 2006), and others on social, motivational, and personality factors (Geers et al. 2005; Hyland et al. 2007; Hyland and Whalley 2008; Price et al. 1999). In the present experiment we explored the link between placebo expectations and the identification of expectation-consistent and expectation-inconsistent bodily sensations. When one holds an expectation, information that is ambiguous in nature is typically interpreted as congruent with that expectation (Anderson and Pennebaker 1980). As somatic experience can similarly be vague, diffuse, and in a state of fluctuation, expectations may lead to the classification and interpretation of bodily sensations in an expectation-congruent manner (Brown 2004; Pennebaker and Skelton 1981).

The possibility that expectations alter one's initial somatic perception has been discussed previously in theories of the placebo effect (e.g., Caspi and Bootzin 2002; Dinnerstein and Halm 1970; Jospe 1978; Kirsch 1999; Lundh 1987; Ross and Olson 1981). For example, in Lundh's (1987) Cognitive/Emotional Model of the placebo effect, it is proposed that positive placebo expectations lead individuals to selectively attend to signs of improvement even when their physical health has not been altered. Due to this bias in attention, individuals are said to believe that the placebo treatment has been effective. If this attention hypothesis is supported, it has important implications for the role of the placebo effect in medical research and practice, particularly regarding the most likely situations for placebo effects to emerge.

Consistent with Lundh's (1987) theorizing, expectations may produce placebo responding by greater identification of expectation-consistent sensations relative to expectation-inconsistent sensations. However, it is important to recognize that expectations could modify placebo reactions at other stages of information processing. For example, it could be that the initial perception of bodily sensations is actually comparable for individuals in placebo and no-placebo groups but the participants differ in how they cognitively store or recall their experiences (Hirt et al. 1999). As such, there are various information processing stages at which expectancies may alter placebo responding. If we are to understand the placebo effect, it is necessary to explore each of these stages.

Evidence consistent with the notion that placebo expectations alter the perception of symptoms comes from neurological studies in which expectations for reduced pain have been associated with specific brain structures involved in the modulation of attention (e.g., Koyama et al. 2005; Lorenz et al. 2005; Petrovic et al. 2002). Little research exists,

however, regarding the possibility that placebo expectations lead to changes in how individuals subjectively identify somatic symptoms (Price et al. 2008; Smith 2007). In one relevant study (Geers et al. 2006), participants were given one of three expectations before ingesting a placebo capsule. Participants in the first group were told they were ingesting a drug (deceptive-expectation), participants in a second group were told that they were in a double blind study and they may be ingesting an active drug or a placebo (double-blind expectation), and a third group of participants were told the capsule was a placebo (control group). Orthogonal to this expectation manipulation, half of the participants were instructed to closely attend to their somatic experience, whereas the other half were not. The results revealed that the participants given the deceptive expectation reported more placebo symptoms than participants in the control group only when they were also asked to attend closely to their somatic experience. Individuals given the double-blind expectation did not exhibit placebo responding regardless of their level of somatic attention. These data provide evidence that placebo expectations and somatic attention can combine to influence placebo responding.

The present research

Although the research of Geers et al. (2006) suggests that greater somatic attention can amplify placebo responding, it did not assess the hypothesis that placebo expectations alter the *type* of somatic information that individuals initially identify. Consistent with the Cognitive/Emotional Model of the placebo effect (Lundh 1987), the primary hypothesis of the present research is that placebo expectations alter the immediate detection of somatic information such that greater expectation-consistent information is perceived. To this end, after a caffeine placebo manipulation, we gave participants two hand-held tally registers and instructed them to press one of the tally registers when they felt a change in their bodily sensations associated with stimulation and arousal (placebo-relevant sensations), and to press the other tally register when they felt a change in any other type of bodily sensation (placebo-irrelevant sensations).

Ancillary issue 1: self-reported attention

In addition to testing our main hypothesis, we examined three ancillary issues. First, along with recording participants' initial detection of their placebo symptoms, we also recorded their later self-reported symptom attention. Including this self-report measure allowed us to compare the results of our concurrent symptom attention measures with those provided on a self-report scale. These measures represent two divergent ways to test the hypothesis that placebo expectations alter symptom identification and we elected to investigate both.

Ancillary issue 2: summary placebo reports

After participants monitored their placebo-relevant and irrelevant sensations, they also reported on their overall reaction to the placebo. These summary symptom reports provided us an opportunity to examine the relationship between the immediate detection of placebo symptoms with later symptom reporting. It seems plausible that the immediate detection of sensations may mediate the influence of expectations on later placebo symptom measures.

Ancillary issue 3: deceptive versus double-blind placebo expectations

Finally, several studies have found that the strength of the placebo effect differs depending on whether or not participants are given a deceptive expectation or a double-blind expectation (e.g., Geers et al. 2006; Pollo et al. 2001). Clarifying the similarities and differences of these two types of expectancies is important because deceptive expectations are similar to drug expectations in a clinical setting, whereas double-blind expectations are used in placebo-controlled clinical trials (Nash et al. 2002). If these two types of

expectations produce divergent effects, responses in research trials may not generalize to clinical practice (Kirsch and Rosadino 1993; Kirsch and Weixel 1988; Nash et al. 2002). In a meta-analysis, Vase et al. (2002) found weaker placebo effects when participants were given double-blind expectations as compared to studies in which participants were given deceptive expectations. Vase et al. (2002) suggested that this finding emerged because double-blind expectations give individuals the belief that there is only a 50% chance they will feel the anticipated symptoms, whereas deceptive expectations give participant greater confidence that they will feel the anticipated symptoms. In this experiment we included both a deceptive expectation group and a double-blind expectation group to determine if these two types of expectations lead to different styles of somatic perception.

Hypotheses

The following predictions were made: First, we predicted that participants given the deceptive expectation would register more placebo-relevant sensations than placebo-irrelevant sensations on the tally registers. This prediction was based on the expectancy literature which suggests that expectations lead individuals to identify more expectation-congruent information than expectation-incongruent information (Anderson and Pennebaker 1980; Lundh 1987; Pennebaker and Skelton 1981). Second, we hypothesized that individuals given the double-blind expectation would register similar amounts of placebo-relevant and placebo-irrelevant sensations. This prediction is based on the notion that double-blind expectations make participants less certain of the placebo expectation and more open than deceptive-expectation participants to both placebo-relevant sensations and non-placebo relevant sensations (Geers et al. 2006). Third, we predicted that in the no-expectation group, participants would register more placebo-irrelevant sensations than placebo-relevant sensations on the tally registers. We made this prediction because participants in this study could generate countless sensations during this monitoring period and we expected that without an explicit caffeine expectation to guide this process, they would detect a large variety of placebo-irrelevant sensations. Finally, based on prior research (Fillmore and Vogel-Sprott 1992; Vase et al. 2002), it was predicted that the participants given the deceptive expectation would report more caffeine-related symptoms on the placebo response index than participants in the other two groups.

Finally, we investigated two additional issues. First, we examined the possibility that the influence of the placebo expectation on a subsequent placebo response index would be mediated by scores on the hand-held tally registers or on the self-reported attention measure. Second, we also explored the relationships between participant age, sex, and prior caffeine experience and our dependent measures.

Method

Participants and design

One-hundred and two undergraduate students (80 female, 22 male) participated in return for partial course credit (M age = 21, SD = 6.48). The experimenter used a random number generator to randomly assign participants to one of the following three experimental groups: deceptive expectation, double-blind expectation, or no-expectation. Thirty-four participants were in each group. No participant dropped out of the study or was removed from the sample.

Procedure

All procedures were approved in advance by the Institutional Review Board of the University of Toledo where the data were collected. The study was conducted in a university

research laboratory room that was designed to look like a medical office. Participants were run individually and were told that the study concerned the perception of bodily sensations.

Upon arrival at the laboratory room, participants read and signed an informed consent document. Next, participants completed a lifestyle questionnaire that contained 32 free-response items. This questionnaire was administered to provide us with an opportunity to assess caffeine consumption. The instructions on the first part of the questionnaire read “Please indicate the amount you have done each of the following behaviors *today* (since 12:00 am).” Below this sentence, participants were provided with a list of different behaviors (e.g., hours of aerobic exercise, hours of sleep, number of classes attended, number of meals eaten) and a blank line next to each behavior on which they were to provide their response. The important item embedded in this section was “number of caffeinated beverages consumed”. In the second section of the lifestyle questionnaire, participants read the instructions, “Please indicate the amount you do the following behaviors *on an average day*”. Below this sentence, participants were provided with the same list of behaviors found in the first section of the lifestyle questionnaire (e.g., hours of aerobic exercise). The important item in this section was “number of caffeinated beverages consumed”. Participants also made their responses in this section on a blank line next to each behavior listed.

Expectation manipulation

Following the procedures used in prior caffeine placebo studies (e.g., Geers et al. 2005), participants in the *deceptive-expectation group* were given a small cup of water and an orange and white placebo capsule (containing sucrose). Participants were told the capsule contained 250 mg of caffeine. They were then told that the amount of caffeine in the capsule was equivalent to that of two to two and a half average sized cups of coffee. Participants in the *double-blind expectation group* were given the same capsules and caffeine dosage information. Participant in this group were also read additional instructions taken from Geers et al. (2006) to provide the double-blind expectation. Specifically, these participants were told, “participants in studies on the effects of caffeine, such as this one, are randomly assigned to receive either the active drug, the caffeine, or a placebo, which is composed of non-active ingredients that have no effects. So, for the purpose of the study, you may or may not be ingesting caffeine. This is a double-blind study, which means I also do not know which type of capsule you have been randomly assigned to receive”. After ingesting the capsule, participants in both expectation groups were told that it would take approximately 5 min before they would feel the full effect of the caffeine. Participants in the *no-expectation group* were not given the placebo capsule or the caffeine expectation. Instead, after completing the lifestyle questionnaire, the no-expectation participants went directly on to the next part of the study.

Sensation monitoring period

After the expectation manipulation, all participants completed a word puzzle task with a pen and paper for 5 min. This task supported the cover story that it would take 5 min for the caffeine to influence participants. Next, the experimenter told participants that “for the next 7 min, we would like you to focus on your feelings and bodily sensations”. Participants were then given two hand-held tally registers (with the registers labeled A and B) and were told that the tally registers would help them stay engaged in this monitoring task. The experimenter then told participants “we would like you to press a button every time you have a feeling or any discernable bodily sensation. Examples include feeling alert, tired, tingling in your hand, an ache in your leg, nasal congestion, etc. Thus, any feeling you have during the 7-min period should cause you to press one of the two buttons.” The experimenter then indicated when participants should press the button on Tally Register A

and when they should press the button on Tally Register B. Specifically, the experimenter said, “we would like you to press Button A and Button B for different feelings and sensations. We would like you to press Button A whenever you experience a bodily sensation associated with stimulation; such as arousal, anxiety, tension, excitement, and jitteriness. You will press Button B whenever you experience any other type of bodily sensation. That is, press Button B whenever you have a feeling or sensation that is *not* related to stimulation. Example feelings and sensations for Button B could include being happy, hungry, cold, itchy, or experiencing nasal congestion.” We counterbalanced the hand (left and right) that participants used to hold the two tally registers. The experimenter then showed participants how the tally registers worked and made sure participants understood the procedure. Participants then completed the 7-min monitoring period alone in the experiment room.

After the monitoring period, the experimenter collected the tally registers, went to a different room, opened up the covers on the registers that concealed the tally counts, and recorded the number of presses on both devices. During this time participants rated how anxious, sluggish, energized, calm, irritated, lazy, relaxed, and excited they felt on 5-point scales (1 = *very slightly or not at all* to 5 = *extremely*). These items were summed to create a placebo-response index ($M = 23.28$, $SD = 5.04$), with higher numbers on this index equating to more caffeine-related symptoms. As higher scores on half of the items equated to less arousal (i.e., calm, relaxed, sluggish, lazy), the scoring for these items was reversed prior to computing the placebo-response index. These placebo-response items have been used successfully in prior caffeine—placebo studies (e.g., Geers et al. 2005; Walach et al. 2002) and the items demonstrated an acceptable level of internal consistency in the present study, $\alpha = .71$. Finally, using a 1–7 scale (1 = *not at all*, 7 = *very much*), participants also answered the self-reported attention question, “How closely did you pay attention to feelings and sensations that were caffeine-related?” ($M = 4.83$, $SD = 1.57$). Participants were then thanked and debriefed.

Results

Sample characteristics

Table 1 displays participant age, sex, and scores on the caffeine consumption questions broken down by experimental group. To determine if participant age or responses to the caffeine consumption questions differed significantly by experimental group, we submitted each to a one-way (Expectation Group) analysis of variance (ANOVA). None of these ANOVAs produced a significant effect: Participant age, $F(2, 99) = .22$, $P = .80$, $d < .01$; caffeinated beverages consumed today; $F(2, 99) = .74$, $P = .49$, $d = .01$; and average caffeinated beverages consumed, $F(2, 99) = 2.04$, $P = .15$, $d = .03$. Potential group differences in participant sex were examined using a Chi Square analysis. This analysis yielded no significant effect, $\chi^2(2) = 4.13$, $P = .13$.

Sensation detection analyses

We then analyzed the number of placebo-relevant and placebo-irrelevant sensations registered during the monitoring period. To do so, the number of presses on the two tally registers were submitted to a 3 (Expectation Group) $\times$ 2 (Tally Register) mixed factorial analysis of variance (ANOVA), in which the first factor was between-participant and the second factor was within-participant. This ANOVA yielded only an Expectation Group $\times$ Tally Register interaction, $F(2, 99) = 8.42$, $P < .001$, $\eta_p^2 = .15$. Table 2 presents the means and standard deviations for all dependent measures broken down by experimental group. Tests of simple effects revealed that in the deceptive-expectation group, participants registered significantly more placebo-relevant sensations than placebo-irrelevant sensations, $t(99) =$

2.03, $P < .05$, $d = .34$. In the double-blind expectation group, there were no differences between the two types of sensations registered, $t(99) = .12$, $P = .92$, $d = .02$. Finally, in the no-expectation group, participants registered significantly more placebo-irrelevant sensations than placebo-relevant sensations, $t(99) = 3.68$, $P < .001$, $d = .55$.

Self-reported attention analyses

In addition to the tally register task, participants self-reported on how closely they attended to caffeine-related sensations. Responses to this attention question were submitted to a one-way (Expectation Group) ANOVA. This analysis yielded a significant expectation group effect, $F(2, 99) = 4.24$, $P < .05$, $\eta_p^2 = .08$ (see Table 2). An examination of the group means revealed that the deceptive-expectation participants reported attending to caffeine-related sensations more than the no-expectation participants, $t(99) = 2.43$, $P < .05$, $d = .57$, but not more than the double-blind expectation participants, $t(99) = .17$, $P = .86$, $d = .04$. Participants in the double-blind expectation group also reported attending to their caffeine-related sensations more than the no-expectation participants, $t(99) = 2.59$, $P < .05$, $d = .61$.

Placebo-response index analyses

Scores on the placebo-response index were also submitted to a one-way (Expectation Group) ANOVA. This analysis yielded a significant effect of the expectation manipulation, $F(2, 99) = 5.27$, $P < .01$, $\eta_p^2 = .10$ (see Table 2). An examination of the group means revealed that the deceptive-expectation participants reported more caffeine-related symptoms than no-expectation participants, $t(99) = 3.15$, $P < .01$, $d = .93$, and the double-blind expectation participants, $t(99) = 2.27$, $P < .05$, $d = .51$. The double-blind expectation participants did not report more caffeine-related symptoms than the no-expectation participants, $t(99) = .84$, $P = .41$, $d = .21$.

Analyses controlling for sample characteristics

We then performed a set of analyses to explore the role of sample characteristics in our study. To assess for such effects, we re-ran our sensation detection, self-reported attention, and placebo response index analyses. This time, however, we controlled for participants' age, sex, average caffeinated beverage consumption, and caffeinated beverages consumed so far that day. Participant age and responses on the two caffeine consumption measures were not significant predictors of our three dependent variables ($F_s < 1.7$, $P_s > .2$, $\eta_p^2 < .02$). There was, however, one significant effect associated with participant sex. Specifically, men detected a greater number of overall bodily sensations ($M = 7.14$) than women ($M = 4.53$), $t(95) = 2.77$, $P < .01$, $\eta_p^2 = .07$. Importantly, participant sex did not significantly interact with type of sensation detected nor with expectation group. As such, it did not taint the present results. Finally, even though we controlled for these four variables, our analyses of the three dependent variables yielded the same significant effects reported previously. In summary, analyses of the sample characteristics yielded no significant results other than that men detected more sensations overall than women.

Mediational analysis

The previous analyses indicate that the expectation manipulation influenced the initial sensations participants detected, their self-reported attention, and scores on the placebo-response index. To determine if scores on the hand-held sensation detection measures or scores on the self-reported attention measure mediated the effect of the expectation manipulation on the placebo-response index, we conducted a mediation analysis. To do so, we followed the procedures outlined by Kenny et al. (1998) for testing multiple mediators.

Regression analyses were performed to estimate the magnitude and significance of the path coefficients (standardized beta weights) between the factors. (For the regression analyses, the expectation factor was coded as -1 = no expectation, 0 = double-blind expectation, and 1 = deceptive expectation).

The resulting path model is displayed in Fig. 1. As the self-reported attention measure was not a significant predictor of scores on the placebo-response index ($P = .72$), it was dropped from the model. As seen in Fig. 1, the expectation manipulation had a significant impact on both hand held sensation detection measures (i.e., presses on Tally Register A and B) as well as on the placebo-response index (P s $< .05$). Importantly, when scores on the placebo-response index were regressed simultaneously on the expectation manipulation variable and the sensation detection measures, both hand-held sensation detection measures were significantly related to placebo responding (P s $< .05$). The direct relationship from the expectation manipulation to the placebo-response index was reduced in significance from $\beta = .30$, $P = .001$ to $\beta = .19$, $P = .07$.

To determine the value of the two sensation detection measures in the model, we followed the recommendations of Kenny et al. (1998) and conducted modified Sobel tests for each possible mediator. A Sobel test is used to determine if the addition of a mediating path significantly adds to the direct relationship between a manipulated factor and a dependent measure. The first Sobel test was significant ($z = 2.67$, $P < .01$), indicating that the mediational path associated with the placebo-relevant sensations explained unique variance in the model. The second Sobel test was weaker but marginally significant ($z = 1.79$, $P = .07$), indicating that the mediational path associated with the placebo-irrelevant sensations also explained variance in the model. In summary, the mediation analyses provide evidence that the detection of placebo-relevant sensations, and to a lesser degree placebo-irrelevant sensations, partially mediated the relationship between the expectation manipulation and scores on the placebo-response index.

Discussion

In the present study, participants monitored their bodily sensations for a 7 min period following a caffeine-placebo manipulation. As predicted, participants given a deceptive expectation identified more placebo-relevant sensations than placebo-irrelevant sensations. This finding was in direct contrast to the no-expectation participants who identified more placebo-irrelevant sensations than placebo-relevant sensations. Participants given a double-blind expectation did not differ in the two types of sensations they identified. To our knowledge, these are the first data to show variation in the spontaneous identification of bodily sensations as a result of a placebo expectation. The results further reveal that this shift in sensation identification depends upon the type of placebo expectation administered.

In addition to the concurrent sensation detection measures, participants also reported on how closely they attended to their caffeine-related sensations. Responses on this self-reported attention measure were influenced by the placebo expectation manipulation, albeit somewhat differently than the hand-held sensation detection measures. Specifically, participants in the two expectation groups reported attending more closely to their caffeine-related sensations than no-expectation participants, with the two expectation groups giving the same amount of attention. It appears that self-reported attention differs at least to some extent from more immediate sensation detection measures. However, as the self-report measure differed from the concurrent sensation detection measures in both how and when participants used them; more data are needed before the full relationship between these two types of instruments is known. Importantly, the hand-held sensation detection scores did mediate the effect of the expectation manipulation on the placebo-response index, whereas

the self-report attention scores did not. Consequently, the sensation detection measures appear to warrant further investigation.

A key aspect of the present study is that we compared two types of placebo expectations: deceptive expectations and double-blind expectations. Consistent with prior research, participants holding the deceptive expectation responded more to the placebo than those holding the double-blind expectation (Geers et al. 2006). Participants given the double-blind expectation did not differ from controls. Consequently, one important applied implication of the present research is that data derived from clinical trials in which individuals are given double-blind expectations may not fully equate to expectations given in clinical settings. Importantly, scores on the sensation detection measures suggest one reason why these two types of expectations can lead to different outcomes. Specifically, whereas double-blind expectations resulted in equivalent detection of relevant and irrelevant sensations in the monitoring period, deceptive expectations resulted in a biased pool of sensations. As such, these expectations instigate divergent perceptual strategies and these strategies, in turn, generate different levels of placebo responding.

We also examined the possibility that the initial sensations that participants detected statistically mediated the effect of a placebo manipulation on a placebo-response index. We found that the amount of placebo-relevant sensations (and to a lesser extent the amount of placebo-irrelevant sensations) identified by participants accounted for variance in the relationship between the expectation manipulation and scores provided later on the placebo response index. As such, these data provide support for the position that the perception of bodily sensations partially mediates the relationship between a placebo expectation and self-report placebo response measures. It is important to note, however, that the direct effect from the expectation manipulation to the placebo-response index was not completely eliminated with the two sensation detection variables in the model. This indicates that other factors are likely to alter placebo responding without being mediated by initial symptom detection.

An interesting aspect of the mediation data was that both an increase in the detection of placebo-relevant sensations and (to a lesser degree) a decrease in the detection of placebo-irrelevant sensations mediated the influence of the placebo-expectation manipulation on the placebo-response index. These results suggest that it is important to take into account both shifts toward congruent information and shifts away from incongruent information when considering the influence of placebo expectations on perceptual processes. This finding is interesting and may have important implications for harnessing the placebo effect in clinical practice. Specifically, if placebo effects can be produced by both increasing the detection of positive sensations as well as by reducing the detection of negative sensations, this could provide practitioners two distinct methods to enhance the placebo component of a treatment. For example, it may be difficult for depressed individuals to anticipate and focus on positive feelings. As such, to help depressed individuals take full advantage of the placebo component of a treatment, practitioners may need to focus their attention on feeling reduced negativity rather than on feeling increased positivity.

Our findings could have additional implications for researchers and practitioners looking to enhance the placebo component of medical treatments. For example, the data support the position that placebos alter subjective experience in “real time” and that placebo effects are not simply due to memory processes. Thus, to take full advantage of the placebo effect, efforts to strengthen the effect need to occur prior to a placebo treatment or soon after a placebo treatment has been administered. Also, as the present data indicate that placebo effects are at least partially mediated by moment-to-moment identification of symptoms, it may be that placebo responding is greatest when attention is not distracted by external

factors. If this is the case, practitioners should find the strongest benefit from the placebo component of a treatment when patients are instructed to avoid external stressors during the initial phases of a treatment. Further, if placebos work in part by directing attention to symptoms, it may be possible to construct interventions that produce comparable benefits without the actual administration of a placebo. Thus, individuals may be able to gain the advantage conferred by placebos by more directly changing the manner in which they attend to somatic information.

The current results could also have implications for understanding how individuals develop unpleasant medical side effects. For example, recent research shows that men informed about the side effects of prostate medication developed more sexual dysfunction (Mondaini et al. 2007). It may be that informing men of such side effects alters their treatment expectations, which in turn, changes the way in which they attend to unpleasant symptoms. Providing a greater understanding of the process by which expectations guide the identification of symptoms may lead to new methods for reducing the experience of such negative side effects in both clinical practice and research trials.

The finding that placebo expectations influence the subjective detection of placebo-relevant and irrelevant sensations connects well with other studies in the placebo literature; particularly those concerning the neurological underpinnings of the placebo effect. Specifically, consistent with the present findings, prior studies indicate that placebo expectations, induced by conditioning or verbal instructions, prepare the brain for particular perceptions (e.g., Keltner et al. 2006; Petrovic et al. 2002). Researchers have also found that expectations modulate the primary somatosensory cortex and the secondary somatosensory cortex; structures implicated in attentional processing and perceptual sensitivity (e.g., Koyama et al. 2005; Lorenz et al. 2005). These prior findings, taken together with the present data, indicate that placebo expectations produce a broad and perhaps cascading pattern of changes that increase the assimilation of one's current state to a placebo expectation.

The present data offer many avenues for future research. For example, the hand-held sensation measures we used here only gave us the total amount of placebo-relevant and placebo-irrelevant sensations participants detected. As studies have found that placebo effects vary across time (e.g., Kirsch and Rosadino 1993), it would be useful to record the point in time that each sensation is detected during the monitoring period. Such research could give us insight into the time course of placebo responding by clinical patients and participants in research trials. Our results also suggest that the placebo effect is the result of interplay between top-down cognitive processes (e.g., expectations) and bottom-up processes (e.g., perceived sensations and actual physical symptoms). If this is the case, the environment in which individuals evaluate their experience with a placebo, such as whether the individual is in a relaxing or stressful situation, is a contributor to the placebo effect worthy of greater examination.

In this study, the double-blind expectation participants responded very similarly to the no-expectation participants. For example, participants in these two groups provided similar scores on the placebo-response index and registered similar amounts of placebo-relevant sensations. The data for these two groups diverge, however, in one important place: The no-expectation participants registered more placebo-irrelevant sensations than placebo-relevant sensations, whereas the double-blind expectation participants registered an equivalent number of these two types of sensations. The finding that the double-blind expectation participants registered similar levels of placebo-relevant and irrelevant sensations is consistent with our original view that double-blind expectations lead to an even-handed assessment of somatic sensations. However, the small number of placebo-irrelevant

sensations they registered as compared to the no-expectation participants brings forward an intriguing alternative possibility. Specifically, rather than holding two separate expectations that initiated an even-handed assessment of sensations, double-blind expectations may, alternatively, lead to a decrease in attention to placebo-irrelevant sensations; without a corresponding increase in attention to placebo-relevant sensations. Such a decrease in attention to placebo-irrelevant sensations could manifest because double-blind expectations are weaker than deceptive expectations. This fine-grain theoretical difference could have important real-world consequences. For example, if this later explanation is correct, it could mean that individuals given placebos in clinical trials tend to under-report side effects that are irrelevant to a placebo expectation. Future research is certainly required to separate out these two viable explanations for the sensation detection data in the double-blind expectation group.

It is important to acknowledge limitations of the current work. First, in this study we used a caffeine placebo; a drug with which most participants likely had prior experience. Our findings may have been different had we given expectations for a drug that was unknown to participants. Fortunately, this concern is lessened somewhat as participants' self-reported caffeine usage did not influence the findings. Nevertheless, it would be beneficial to test our hypotheses with other placebo treatments. On a related point, it should be emphasized that the present findings may be limited to outcome measures that can be modified by somatic perception. These findings may not extend to measures based on long-term changes in underlying physiology or to biochemical processes (see Meissner et al. 2007). Another issue is that in the present study, we did not include physiological measures (e.g., heart rate). Future research is needed to determine how physiological reactions interface with measures of symptom detection. It would also be advantageous for future research studying the identification of placebo symptoms to obtain baseline symptom detection scores from participants. Such scores could be used to account for variance associated with individual differences in experiencing somatic symptoms. Finally, in the present study we examined a healthy non-clinical sample over a brief span of time. Considering the ethical and financial difficulties of adding a no-treatment control group to clinical trials, laboratory studies of this kind can provide valuable information and can help determine which factors are important for clinical research and practice. However, additional work is required before we can determine fully the implications of the present data for clinical practice.

References

- Anderson DB, Pennebaker JW. Pain and pleasure: Alternative interpretations for identical stimulation. *European Journal of Social Psychology*. 1980; 10:207–212.
- Benedetti F, Mayberg HS, Wager TD, Stohler CS, Zubieta J. Neurobiological mechanisms of the placebo effect. *Journal of Neuroscience*. 2005; 25:10390–10402. [PubMed: 16280578]
- Brody, H.; Brody, D. The placebo response. New York, NY: HarperCollins Publishers; 2000.
- Brown RJ. Psychological mechanisms of medically unexplained symptoms: An integrative and conceptual model. *Psychological Bulletin*. 2004; 130:793–812. [PubMed: 15367081]
- Caspi O, Bootzin RR. Evaluating how placebos produce change: Logical and causal traps and understanding cognitive explanatory mechanisms. *Evaluative and Health Professions*. 2002; 25:436–464.
- Chaput de Saintonge DM, Herxheimer A. Harnessing placebo effects in health care. *Lancet*. 1994; 334:995–998. [PubMed: 7934436]
- De la Fuente-Fernandez R, Ruth TJ, Sossi V, Schulzer M, Calne DB, Stoessl AJ. Expectation and dopamine release: Mechanism of the placebo effect in Parkinson's disease. *Science*. 2001; 293:1164–1166. [PubMed: 11498597]

- Dinnerstein AJ, Halm J. Modification of placebo effects by means of drugs: Effects of aspirin and placebos on self-rated moods. *Journal of Abnormal Psychology*. 1970; 75:308–314. [PubMed: 5423023]
- Ernst E, Resch KL. Concept of true and perceived placebo effects. *Journal of Behavioral Medicine*. 1995; 311:551–563.
- Fillmore M, Vogel-Sprott M. Expected effect of caffeine on motor performance predicts the type of response to placebo. *Psychopharmacology*. 1992; 106:209–214. [PubMed: 1549648]
- Geers AL, Helfer SG, Kosbab K, Weiland PE. Expectations and placebo response: A laboratory investigation into the role of somatic focus. *Journal of Behavioral Medicine*. 2006; 29:171–178. [PubMed: 16374671]
- Geers AL, Weiland PE, Kosbab K, Landry SJ, Helfer SG. Goal activation, expectations, and the placebo effect. *Journal of Personality and Social Psychology*. 2005; 89:143–159. [PubMed: 16162050]
- Hammersley R, Finnigan F, Millar K. Verbal expectancies and performance after alcohol. *Addictive Behavior*. 1998; 23:489–496.
- Harrington, A. The placebo effect: An interdisciplinary exploration. Cambridge, MA: Harvard University Press; 1997.
- Hirt, ER.; Lynn, SJ.; Payne, DG.; Kracknow, E.; McCrea, SM. Expectancies and memory: Inferring the past from what must have been. In: Kirsch, I., editor. *How expectancies shape experience*. Washington DC: American Psychological Association; 1999. p. 93-124.
- Hróbjartsson A, Gotzsche PC. Is the placebo powerless? An analysis of clinical trials comparing placebo with no treatment. *New England Journal of Medicine*. 2001; 344:1594–1601. [PubMed: 11372012]
- Hróbjartsson A, Gotzsche PC. Is the placebo powerless? Update of a systematic review with 52 new randomized trials comparing placebo with no-treatment. *Journal of International Medicine*. 2004; 256:91–100.
- Hyland ME, Whalley B. Motivational concordance: An important mechanism in self-help therapeutic rituals involving inert (placebo) substances. *Journal of Psychosomatic Research*. 2008; 65:405–413. [PubMed: 18940369]
- Hyland ME, Whalley B, Geraghy AWA. Dispositional predictors of placebo responding: A motivational interpretation of flower essence and gratitude therapy. *Journal of Psychosomatic Research*. 2007; 62:331–340. [PubMed: 17324684]
- Jospe, M. The placebo effect in healing. Lexington, MA: Lexington books; 1978.
- Keinle GS, Keine H. The powerful placebo: Fact or fiction? *Journal of Clinical Epidemiology*. 1997; 50:1311–1318. [PubMed: 9449934]
- Keltner JR, Furst A, Fan C, et al. Isolating the modulatory effect of expectation on pain transmission: A functional magnetic resonance imaging study. *Journal of Neuroscience*. 2006; 26:4437–4443. [PubMed: 16624963]
- Kenny, DA.; Kashy, DA.; Bolger, N. Data analysis in social psychology. In: Gilbert, D.; Fiske, S.; Lindzey, G., editors. *The handbook of social psychology*. Vol. 1. Boston, MA: McGraw-Hill; 1998. p. 233-265.
- Kirsch, I. *How expectancies shape experience*. Washington DC: American Psychological Association; 1999.
- Kirsch I, Rosadino MJ. Do double-blind studies with informed consent yield externally valid results? An empirical test. *Psychopharmacology*. 1993; 110:437–442. [PubMed: 7870914]
- Kirsch, I.; Sapirstein, G. Listening to Prozac but hearing placebo: A meta-analysis of antidepressant medication. *Preventative Treatment*. 1998. Retrieved from <http://journals.apa.org/prevention/volume1/pre0010002a.html>
- Kirsch I, Weixel LJ. Double-blind versus deceptive administration of a placebo. *Behavioral Neuroscience*. 1988; 102:319–323. [PubMed: 3365327]
- Koyama T, McHaffie JG, Laurienti PJ, Coghill RC. The subjective experience of pain: Where expectations become reality. *Proceedings of the National Academy of Science*. 2005; 102:12950–12955.

- Lorenz J, Hauck M, Paur RC, et al. Cortical correlates of false expectations during pain intensity judgments—a possible manifestation of placebo/nocebo cognitions. *Brain, Behavior, and Immunity*. 2005; 19:283–295.
- Lundh L. Placebo, belief, and health: A cognitive-emotional model. *Scandinavian Journal of Psychology*. 1987; 28:28–143.
- Madsen MV, Gotzsche PC, Hróbjartsson A. Acupuncture treatment for pain: Systematic review of randomised clinical trials with acupuncture, placebo acupuncture, and no acupuncture groups. *British Medicinal Journal*. 2009; 338:a3115.
- McDonald D, Mazzuca S, McCabe GP. How much of the placebo “effect” is really statistical regression? *Statistics in Medicine*. 1983; 2:417–427. [PubMed: 6369471]
- Meissner K, Distel H, Mitzdorf U. Evidence for placebo effects on physical but not biochemical outcome parameters: A review of clinical trials. *BMC Medicine*. 2007; 5:3. [PubMed: 17371590]
- Mondaini N, Gontero P, Giubilei G, et al. Finasteride 5 mg and sexual side effects: How many of these are related to a nocebo phenomenon? *Journal of Sexual Medicine*. 2007; 4:1708–1712. [PubMed: 17655657]
- Nash JM, Holroyd KA, Rokicki LA, Kvaal S, Penzien DB. The influence of placebo awareness on stimulant drug response in a double-blind trial. *Psychopharmacology*. 2002; 161:213–221. [PubMed: 12021824]
- Pennebaker JW, Skelton JA. Selective monitoring of physical sensations. *Journal of Personality and Social Psychology*. 1981; 41:213–223. [PubMed: 7277203]
- Peters, D. *Understanding the placebo effect in complementary medicine*. London, UK: Harcourt Publishing; 2001.
- Petrovic P, Kalso E, Petersson KH, Ingvar M. Placebo and opioid analgesia: Imaging a shared neuronal network. *Science*. 2002; 295:1737–1740. [PubMed: 11834781]
- Pollo A, Amanzio M, Arslanian A, Casadio C, Maggi G, Benedetti F. Response expectancies in placebo analgesia and their clinical relevance. *Pain*. 2001; 93:77–84. [PubMed: 11406341]
- Price DD, Finniss DG, Benedetti F. A comprehensive review of the placebo effect: Recent advances and current thought. *Annual Review of Psychology*. 2008; 59:565–590.
- Price DD, Milling LS, Kirsch I, Duff A, Montgomery GH, Nicholls SS. An analysis of factors that contribute to the magnitude of placebo analgesia in an experimental paradigm. *Pain*. 1999; 83:147–156. [PubMed: 10534585]
- Rief W, Hofmann SG, Nestoriuc Y. The power of expectation—understanding the placebo and nocebo phenomenon. *Social and Personality Psychology Compass*. 2008; 2:1–14.
- Rief W, Nestoriuc Y, Weiss S, Welzel E, Barsky AJ, Hofmann SG. Meta-analysis of the placebo response in antidepressant trials. *Journal of Affective Disorders*. 2009; 118:1–8. [PubMed: 19246102]
- Ross M, Olson JM. An expectancy-attribution model of the effects of placebos. *Psychological Review*. 1981; 88:408–437. [PubMed: 7025076]
- Sauro MD, Greenberg RP. Endogenous opiates and the placebo effect: A meta-analytic review. *Journal of Psychosomatic Research*. 2005; 58:115–120. [PubMed: 15820838]
- Shapiro, AK.; Shapiro, E. *The powerful placebo effect*. Baltimore, MA: John Hopkins University Press; 1997.
- Smith, EE. Expectancy and the perception of aversive events. In: Shoda, Y.; Cervone, D.; Downey, G., editors. *Person in context*. New York, NY: Guilford Publications; 2007. p. 148–168.
- Stewart-Williams S, Podd J. The placebo effect: Dissolving the expectancy versus conditioning debate. *Psychological Bulletin*. 2004; 130:324–340. [PubMed: 14979775]
- Vase L, Riley JL, Price DD. A comparison of placebo effects in clinical analgesic trials versus studies of placebo analgesia. *Pain*. 2002; 99:443–452. [PubMed: 12406519]
- Wager TD, Rilling JK, Smith EE, et al. Placebo-induced changes in FMRI in the anticipation and experience of pain. *Science*. 2004; 303:1162–1167. [PubMed: 14976306]
- Walach H, Schmidt S, Dirhold T, Nosch S. The effects of a caffeine placebo and suggestion on blood pressure, heart rate, well-being, and cognitive performance. *International Journal of Psychophysiology*. 2002; 43:247–260. [PubMed: 11850090]

Zubieta JK, Yau WY, Scott DJ, Stohler CS. Belief or need? Accounting for individual variations in the neurochemistry of the placebo effect. *Brain, Behavior, and Immunology*. 2006; 20:15–26.

Fig. 1. Path diagram and coefficients (standardized beta weights). Solid paths are significant, $P < .05$

Table 1
Sample characteristics as a function of expectation group

	No expectation (<i>n</i> = 34)	Double-blind expectation (<i>n</i> = 34)	Deceptive expectation (<i>n</i> = 34)
Average caffeinated beverages today	.67 (.97)	.58 (.66)	.83 (.87)
Average daily caffeinated beverages	1.95 (1.82)	1.36 (1.32)	2.03 (1.69)
Participant mean age	21.03 (7.34)	20.52 (6.12)	20.03 (4.73)
Participant sex (females/males)	27/7	29/5	24/10

Note Higher scores on the self-reported caffeine questions equate to a larger number of caffeinated beverages consumed. The numbers in parentheses are standard deviations

Table 2
Means and standard deviations (in parentheses) on the dependent measures as a function of expectation group

	No expectation (<i>n</i> = 34)	Double-blind expectation (<i>n</i> = 34)	Deceptive expectation (<i>n</i> = 34)
Placebo-relevant sensations	4.11 (5.36)	4.69 (3.82)	6.21 (6.16)
Placebo-irrelevant sensations	6.74 (5.40)	4.61 (3.28)	4.73 (4.02)
Self-reported attention	4.22 (1.73)	5.18 (1.37)	5.12 (1.41)
Placebo-response index	21.74 (3.10)	22.72 (5.68)	25.41 (4.65)

Note Higher numbers equate to greater placebo-relevant sensations, placebo-irrelevant sensations, self-reported attention to caffeine symptoms, and placebo responding, respectively