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Adherence, Expectations, and the Placebo Response: Why is Good Adherence to an Inert Treatment Beneficial?

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Objective

The current study soughtto better understand why good adherence to a placebotreatment has been reliably associated with health benefits. We proposed a model where initial expectations shape adherence, which then influences subsequent expectations that affect placebo response. Design: Seventy-two participants were told they were enrolling in a study of physical activity and memory and were asked to increase their physical activity by 35% for two weeks (placebo treatment). Main outcome measures: Adherence to this physical activity target was measured by pedometer. Expectations and short-term memory (free recall) were assessed before and after physical activity. Results: Initial expectations predicted adherence to physical activity ($r = 0.27$, $p < 0.03$), but adherence did not predict subsequent expectations ($r = 0.06$, $p = 0.60$). Testing a multi-step meditational model revealed that initial expectations predicted better memory even after controlling for adherence, subsequent expectations, baseline memory, and gender (c'= 1.10, 95% CI = 0.46 – 1.74). Stronger expectations for memory improvement predicted better memory performance, but adherence and later expectations did not mediate this association. Conclusions: Good adherence to a placebo may reflect strong treatment expectations which may convey benefits by enhancing the non-specific effects of treatment.

Keywords

adherence; expectations; placebo response; physical activity; memory

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A growing body of evidence suggests that good adherence to treatment is an important predictor of positive treatment outcomes, regardless of whether the treatment is an active therapy or an inert placebo. A meta-analysis of randomized controlled trials (RCTs) involving a variety of medications found that good adherence to a placebo was associated with a roughly 50% reduction in mortality risk, equal to that associated with good adherence to an effective active drug (Simpson et al., 2006). Subsequent studies have also reported similar results (e.g. Avins et al., 2010; Curtis et al., 2011; Granger et al., 2005; Pressman et al., 2012).The fact that good adherence among the placebo group is beneficial across a variety of medication trials, health outcomes, and patient samples suggests that this is a robust and reliable effect, not merely attributable to bias in a single trial. Given the persistence of this remarkable effect, an explanation seems necessary.

How can it be that faithfully taking an inert pill reduces morbidity and mortality risk? Some have suggested that good adherence is merely a marker of other healthy behaviors that are more directly responsible for the health benefits (Shrank, Patrick, & Brookhart, 2010). Although some evidence consistent with this explanation has been reported (Brookhart et

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al., 2007; Dormuth et al., 2009), others have found that the association between adherence and mortality still holds even after controlling for healthy lifestyle factors (e.g Curtis et al., 2011; Pressman et al., 2012). If a generally healthier lifestyle among high placebo adherers cannot completely account for the risk reduction they experience, another explanation is warranted. In order to better understand why good adherence is associated with larger placebo effects, it may be useful to consider existing explanations for placebo effects.

Response expectancies, the self-confirming belief that a particular response will result from a particular treatment, behavior, or situation, can explain many placebo effects (Kirsch, 1985; Kirsch, 1997; Stewart-Williams & Podd, 2004). For example, expectations have been shown to predict responses to placebo analgesics (Benedetti et al., 2003), placebo caffeine (Fillmore & Vogel-Sprott, 1992), and placebo alcohol (Marlatt & Rohsenow, 1980). Patients may adhere well to a placebo because they think they are taking an active medication and thus expect to experience benefits. The belief that one is taking an active medication (regardless of one's actual group assignment) has been associated with larger therapeutic benefit in the context of RCTs (Bausell, Lao, Bergman, Lee, & Berman, 2005; Colagiuri, Morley, Boakes, & Haber, 2009; Dar, Stronguin, & Etter, 2005; McRae et al., 2004). Expectations and adherence are likely to be linked, although the exact nature of their association in the context of a RCT is unclear. The current study seeks to determine whether a relationship between expectations and adherence exists, as well as the direction of that association, by using a prospective design.

Expectations may predict adherence. Patients may adhere well because they have strong expectations for treatment benefit. A theoretical basis for this prediction lies in all the dominant conceptual models of health behavior, including Bandura's social cognitive theory (Bandura, 1998); the Health Belief Model (Rosenstock, 1974), and the Theory of Planned Behavior (Ajzen & Madden, 1986). Each of these theories contains a role for expectations as a predictor of behavior. In the context of a RCT, this would look something like "I think this treatment is likely to benefit me, so I am going to take it as directed". Many correlations between treatment expectations and adherence behavior across a variety of health conditions have been published (e.g. Horne & Weinman, 1999; Menckeberg et al., 2008; Olsen, Smith, & Dei, 2008). Stronger support comes from a recent study that manipulated expectations in order to examine their effect on adherence. In this study, asthma patients who viewed an expectation-enhancing video regarding their asthma medication were more adherent to the medication one month later compared to patients who saw a control video (Clerisme-Beaty et al., 2011). Thus increased outcome expectancies produced greater adherence to a medical treatment.

Adherence may also predict expectations. The act itself of adhering to a medication regimen may produce stronger expectations of therapeutic benefit. A supporting rationale for this possibility can be derived from self-perception theory (Bem, 1972) which proposes that an individual will inferone's attitude based on one's past behavior. In the current context, this would look something like: "I've been taking this medication regularly as directed, so I must expect it to have health benefits". To our knowledge, no study has examined the role of treatment adherence on subsequent expectations. One goal of our study is to determine the direction of the association between expectations and adherence. We believe that the association is likely to be bidirectional. Initial expectations of treatment benefit may lead to greater adherence, which then further reinforces treatment expectations. This sort of reciprocal relationship was proposed by Czajkowski, Chesney, and Smith (2009) in their model of adherence and placebo effects.

A second goal of the study is to determine how expectations and adherence predict placebo responses. We propose a model in which initial expectations about a treatment affect adherence to the treatment, which in turn influences subsequent expectations about the treatment, and thus affects the placebo response (see Figure 1). In our model, adherence and subsequent expectations act as mediators of the effect of initial expectations on the placebo response. We also allow for a direct effect of initial expectations on placebo response in our model, based on previous research. In order to address these two goals and gain a better understanding of why adherence to a placebo is beneficial in RCTs, the current study employed a prospective design in which expectations were assessed before and after a period of treatment, during which time adherence was assessed.

The treatment consisted of a placebo treatment given to healthy adults. Using a placebo eliminates the verum effects of an active treatment, and recruiting healthy adults minimizes the variability associated with a clinical sample. Participants were told they were enrolling in a study of the effect of physical activity on memory. Physical activity served as a placebo here because a modest increase in physical activity for only two weeks is unlikely to directly produce improvements in short-term memory. Thus a brief, moderate increase in physical activity could be considered a sub-therapeutic dose of a treatment that could improve memory when done over a longer period of time (Colcombe & Kramer, 2003). Desharnais and colleagues (1993) have demonstrated that exercise and the expectations created around it can be used effectively as a placebo. Physical activity is also something that can be measured objectively outside the lab, rather than relying on self-report. We chose to use a memory-enhancing placebo for a several reasons. First, memory has been shown to be subject to placebo effects (Kvavilashvili & Ellis, 1999; Nash & Zimring, 1969; Oken, et al., 2008; Parker, Garry, Einstein, & McDaniel, 2011; Van Oorsouw & Merckelbach, 2007). Second, memory performance could plausibly change over a few weeks, and third, memory performance can also be assessed objectively.

Method

Participants

Participants were recruited for a study of physical activity and memory from the community via flyers and direct-mail based advertisements as well as email lists of local alumni. Interested individuals were directed to contact the lab for further information about the study and eligibility screening. Eligibility requirements included being 18 years or older, and in good physical and mental health i.e. no chronic or acute medical conditions that could interfere with physical activity (e.g. emphysema, broken bones, arthritis) or impair memory or cognitive function (e.g. concussions, dementia, epilepsy).

Seventy-four participants enrolled in the study. Two failed to complete the baseline assessment of physical activity and were excluded from further analyses. The final sample consisted of 72 individuals, 58 women and 14 men. The average age was 46.14 years (SD = 14.12; range: 18–72). The majority of the sample (91.7%) identified their race/ethnicity as Caucasian, two participants identified as Hispanic, three as Black, and one as multi-racial.

Design and Procedure

Participants were told that the study was examining whether increases in physical activity could improve memory. We chose to use physical activity (rather than an inert pill) as a placebo for several reasons. Although the long-term benefits of exercise on cognitive function are clear (e.g. Erickson et al., 2011), the level of physical activity used in the current study would not actually cause any changes in memory, as a moderate increase in physical activity sustained over a brief period of time is unlikely to produce reliable improvements in memory among healthy adults (see Results section for analyses supporting this assertion). Thus any improvements in memory could be attributable to something other than increased physical activity. Second, physical activity and memory made a believable cover story for the participants. Third, pilot testing suggested that people would be much more willing to enroll in a study of physical activity than a "memory-enhancing" drug i.e. placebo pill.

Participants made a total of three visits to the lab. At an initial lab visit (Visit 1), participants gave informed consent and then received instructions for using the pedometer. Participants wore the pedometer for three days in order to establish a baseline level of physical activity. Previous research has demonstrated that three days of pedometer data are sufficient to estimate physical activity levels in healthy adults (Tudor-Locke et al., 2005). The readout on the pedometer was covered with opaque tape during this baseline phase in order to reduce reactivity to the novelty of wearing a pedometer. After getting dressed in the morning, participants placed the pedometer on their clothes at waist-level and wore it until going to bed each night. After three days, participants returned to the lab (Visit 2) where the pedometer's data were uploaded to a computer. The number of steps was averaged across the three days in order to compute that participant's baseline. Participants were then asked to increase their level of daily physical activity by 35% above their baseline for the next 14 days. A target increase of 35% was chosen based on the physical activity literature (Bravata et al., 2007) and our own pilot testing that showed acceptable variability in adherence at that level. Participants were informed of both their baseline level and target number of steps. In order to enhance the cover story, participants then read an article from a popular health magazine on the benefits of exercise for memory (Tsai, 2008).Participants also completed measures of expectancy as well as the memory task. Participants then received a new pedometer to wear daily for the next 14 days (adherence phase) and were scheduled for a return lab visit. The readout on this pedometer was not covered by tape during this phase. At the next lab visit (Visit 3), participants returned their pedometers, completed the expectancy and memory measures (in that order), were debriefed, and received $40 compensation.

Measures

Expectations—The degree to which participants expected to experience a change in their memory was assessed using three items created for this study. All items were administered twice, once before the adherence phase (Visit 2), and once after (Visit 3). The exact wording of each item varied slightly depending on when it was administered. The first item asked "How much do you think your memory will be (was) affected by an increase in your physical activity?". The second item asked "If you reach(ed) the target number of steps each day, what type of memory performance do think will result (resulted)?". The third item asked "How do you believe your performance on today's memory tasks will compare to your memory performance at the next (previous) lab visit?".Responses at Visit 2 were reverse coded for this item. Participants responded to these items using a 9-point scale from −4 "much worse" to 4 "much better" with the middle point, 0, representing "no change". Cronbach's alphas for these three items at each visit were $\alpha = 0.89$ (Visit 2) and $\alpha = 0.82$ (Visit 3). Mean level of initial expectations (Visit 2) was 3.34 (SD: 1.56). The mean level of expectations at Visit 3 was 0.81 (SD: 0.95).

Physical activity—Physical activity was assessed using a pedometer (Omron HJ-720; Omron Healthcare, Kyoto, Japan) which recorded and saved the number of steps taken by the participant each day. This type of pedometer has been established as a valid and reliable way to measure physical activity (Zhu & Lee, 2010). After wearing the pedometer, participants returned to the lab where the pedometer data was uploaded to a computer.

Adherence—Adherence to physical activity was assessed two ways using the pedometer data. First, the number of steps recorded each day was compared to the target number of steps (baseline + 35%) for that participant. The number of days (out of 14 possible) that a participant met or exceeded his or her target number of steps was totaled. The average participant met the target on 7.04 days (SD: 4.22; range 0 – 14).Second, we calculated the average percent of the target met by the participant across all 14 days. This method captures the days when a participant may have come close to but not met their target. The average percent of target met across all days and participants was 96% (SD = 28%, range 39% – 175%).

Memory—Short-term memory was assessed at each lab visit with a delayed free-recall task. Participants were seated at a computer screen where they saw 24 words presented one at a time for one second each. There was a one second delay between each word. After viewing the words, participants were asked to count backwards by threes from a 3-digit number out loud for 30 seconds. This served as a distractor task. Then participants were given two minutes to recall as many words from the original list as they could. Participants saw two separate word lists at each lab visit, separated by a 10-minute filler task; the number of words recalled was summed across the two lists. The order of the lists was counter-balanced across participants and visits. The average participant was able to recall 14.92 (SD = 5.96; range 6.50 – 31) words at Visit 2 and 16.72 (6.35; 6.50 – 30) words at Visit 3.

Effort—Because it is possible that memory performance could be influenced by effort on the memory task, we included a single-item measure of effort at Visits 2 and 3. Participants rated the effort they put into the memory task on a 1 (no effort) to 7 (maximal effort) scale. At Visit 2, the average effort rating was 6.3 (SD = 0.84) with a modal rating of 7. At Visit 3, the average effort rating was 6.49 (SD = 0.78) with a model rating of 7. No participant reported an effort score lower than 4 (moderate effort).

Missing Data

Three participants failed to return for Visit 3 and were missing memory and expectancy data. We used their memory and expectancy scores from Visit 2 in place of the missing data. Four participants failed to return their pedometers and were missing adherence data. Because dropping these participants from the analysis entirely would have meant a loss of statistical power, we used hot deck imputation in order to model their missing data. Hot deck imputation is a technique in which missing data is imputed from participants who most closely match the participants with missing data on some pre-specified variable (Myers, 2011).It has been reported as the most effective method for handling missing data of this type (Hawthorn & Elliot, 2005). In our study, adherence was significantly associated with baseline physical activity ($r = -0.34$, $p< 0.01$). Thus we imputed the missing adherence data from participants matched on baseline level of physical activity. Of note, the significance of any statistical analysis was unchanged by using hot deck imputation compared to excluding participants with missing data (i.e. list wise deletion). We chose to report the analyses based on hot deck imputation, as doing so maximizes statistical power and most closely reflects the original sample of participants.

Results

The first goal concerned the direction of the association between expectations and adherence. In order to address this question, we took advantage of the prospective nature of our study to examine (1) the association between initial expectations (at Visit 2) and subsequent adherence and (2) the association between adherence and subsequent expectations (measured at Visit 3). We found a significant correlation between expectations at V2 and number of days the target was met ($r = 0.27$, $p < 0.02$) such that participants with stronger initial expectations tended to achieve their target level of physical activity on more days. There was no such association between number of days at target and expectations at V3 (r = 0.06, p = 0.60). How often participants met their target levels of physical activity did not predict the strength of their subsequent expectations. There was no significant association between the average percent of target achieved and expectations at either V2 or V3 (p's > 0.23). As such, subsequent analyses include only the number of days that the target was met as the measure of adherence. Table 1 summarizes the intercorrelations among expectations, adherence, and memory scores.[1]

The second goal was to test a model in which initial expectations about a treatment's effects determine adherence to the treatment, which in turn influences subsequent expectations about the treatment, and thus affects the placebo response (Figure 1). Also embedded in this model is the direct effect of initial expectations on placebo response. In order to model both the direct and indirect effects of expectations on memory, we used conditional process modelling developed by Hayes (2013). We employed the PROCESS technique (in SPSS v21) that allows for the testing of multi-step mediation using an ordinary least-squares approach. This method has advantages over other commonly used approaches to testing mediation. It provides a quantitative, rather than inferential, estimate of the indirect path coefficient. This method also employs a bootstrapping technique that is more powerful and does not assume normality for the sampling distribution of the indirect effect, as the Sobel test does (see Hayes, 2009 for complete explanation).For these bootstrapping analyses, we set z = 5000 resampling iterations. Because all paths are tested simultaneously using this method, it is also possible to include covariates in the model. Not surprisingly, free recall score at Visit 2 was positively associated with free recall score a Visit 3 (r = 0.82, p< 0.001). In the current sample, women recalled significantly more words at Visit 3 (17.43 (SD = 6.38) words) compared to men (12.36 (SD = 4.68); $t(70)$ = −2.79, p < 0.01). Thus, free recall score at Visit 2 and gender were included as covariates in the full mediational model[2].

Figure 2 depicts the path coefficients for this model. Expectations at V2 predicted adherence (a = 0.71, SE = 0.30, p = 0.02), but adherence did not predict V3 expectations (d = 0.003, SE = 0.03, p = 0.91).V3 expectations did significantly predict free recall (b = 1.14, SE = 0.44, p = 0.01).Bootstrap results for indirect effects did not support adherence and V3 expectations as a mediators(indirect effect estimate = 0.003, bias corrected 95% CI: −0.05 – 0.07). Although the total indirect effect of V2 expectations on V3word recall (via adherence and V3 expectations in serial) was non-significant, the direct effect remained significant (c' = 1.10, SE = 0.32, p = 0.001). High initial expectations about the benefits of physical activity for memory predict better memory scores, even after controlling for adherence, subsequent expectations, baseline memory score, and gender. Overall, this model explained 75% of the variance in V3 free recall scores (R^2 = 0.75; F(5, 66) = 39.56,p < 0.001), much of this likely due to the high correlation between free recall scores at V2 and V3. In order to understand the unique amount of variance explained by V2 expectations, we ran a hierarchical linear regression model using all the same predictors (but not testing mediation). Results of this model suggest that initial expectations accounted for 4.5% of the variability in V3 free recall (ΔR^2 = 0.045; F(1, 66) = 11.8, p = 0.001).

We wondered whether effort on the memory tasks explained the association between initial expectations and memory performance. The correlation between initial expectations and effort at V3 was non-significant (r = −0.10, p> 0.50) as was the correlation between effort

[1]Importantly, neither the average, maximum, or total number of steps taken during the 14 days were associated with free recall scores (r's = −0.17, p > 0.17), supporting our assertion that physical activity is acting as a sub-therapeutic placebo in the current study.
[2]We also included baseline physical activity as a covariate in both correlational and PROCESS mediational analyses, but doing so did not change the current pattern of results.

and word recall at V3 ($r = 0.24$, $p > 0.10$). These findings do not support greater task effort as an explanation for why initial expectations predicted subsequent memory performance.

Discussion

We examined the direction of the association between expectancies and adherence to a memory-enhancing placebo treatment. Stronger expectations at the outset of treatment predicted greater adherence. Given the demands of a treatment, strong initial beliefs in the benefits that treatment will provide may facilitate persistence in the face of obstacles. However, adherence did not predict subsequent expectations. One possibility is that participants who increased their physical activity some, but failed to reach their daily target, may still have adjusted their expectations. This possibility was tested by also computing adherence as the average percent of target achieved. Doing this better captures adherence for participants who may have increased their physical activity above baseline, but come up short of achieving their daily target. When computed this way, adherence was not significantly associated with either initial or subsequent expectations. Expectations of benefit may help you meet a daily goal when one is personally assigned. While few studies have examined adherence-related goals in the context of treatment expectations, exercisers who were given specific, process-related goals were more adherent to an exercise regimen compared to other exercisers given no goal, an effect that lasted six months (Wilson & Brookfield, 2009). In our study, individuals with stronger initial expectations met or exceeded their daily targets for physical activity more often, rather than just generally increasing physical activity.

Another possible explanation for the lack of association between adherence and subsequent expectations is a restriction of range. Expectations at V3 were generally lower (with less variability) compared to those at V2. Thus adherence may not have predicted expectations because of a range restriction in expectations at V3. To evaluate this possibility, we used the formula from Cohen & Cohen (1983) for estimating a correlation under better measurement conditions. If the standard deviation in expectations at V3 were set equal to the standard deviation for expectations at V2, the correlation between adherence and expectations at V3would still be non-significant for this sample. Thus we do not believe that the null finding is due to a restriction of range issue (calculations available upon request).Rather, the association between expectations and adherence appears to be uni-directional. Subsequent expectations may be formed based on other factors that occur during treatment, such as mental/physical changes or side effects, that we did not measure.

Adherence and subsequent expectations did notmediate the relationship between initial expectations and memory performance. In fact, stronger initial expectations for memory improvement predicted better memory performance even after controlling for these variables (as well as baseline memory performance and gender).The effect of expectations on memory performance in response to a placebo is consistent with previous studies e.g. Parker, Garry, Einstein, & McDaniel, 2011; Van Oorsouw & Merckelbach, 2007. The current study adds to this literature in one important way. While the majority of previous studies manipulated expectations for a single-dose placebo, our study examined the role of expectations over a longer treatment period, a timeframe more similar to treatment in a clinical setting. Even after two weeks, initial expectations were still predictive of treatment outcome, in line with the findings of Nash & Zimring (1969) and Oken et al. (2008). However, neither of those studies assessed adherence or examined its role in their expectancy effects.

A study by Leedham and colleagues (1995) does provide some evidence that is also consistent with our model. These researchers prospectively examined expectations, adherence, and physical health outcomes among heart transplant patients. Pre-operative positive expectations predicted subsequent adherence to the post-operative treatment regimen three months later. Positive expectations prior to the transplant also predicted better physical health outcomes at 6-months post-transplant (as rated by a nurse), even after controlling for the effects of adherence on health in this seriously ill sample. Thus initial expectations regarding the health benefits of an upcoming treatment predict future health above and beyond the effects of improved adherence. However, subsequent expectations were not assessed in this study, nor was a meditational model tested.

The current study tested, but did not find support for, a meditational model. Although the effect of initial expectations on memory performance was independent of adherence and subsequent expectations, we do not believe that these factors are unimportant. Regarding adherence, some minimal level is certainly necessary, as one could not expect a placebo effect to occur if the placebo treatment is never experienced. The precise level of adherence that is minimally necessary remains unclear, and may vary between individuals. Participants may have considered themselves to be adherent even if they did not meet their target every day; this perception of "sufficient adherence" may have then justified their expectations for memory improvement. One review found that self-reports tended to overestimate adherence by about 15% compared to electronic monitoring devices (Shi et al., 2010).Although the readout on the pedometer was uncovered during the adherence phase, we cannot be sure of participants' awareness because we did not measure adherence via self-report. It may be that perceived, rather than actual, adherence does mediate the expectations-placebo relationship.

In our study self-reported effort on the memory tasks did not explain the association between initial expectations and memory performance. However, such a self-report measure of effort may be subject to demand characteristics, such that participants are unlikely to validly report low to moderate effort. We cannot definitively rule out this possibility in our data. Future studies should employ objective measures of cognitive effort such as time spent on recall or a vigilance task in order to better assess the role of effort in explaining the expectation and memory association. Another limitation of the current study is its correlational nature. Despite our prospective analyses, we cannot say for sure that initial expectations are causing a larger placebo response, although our results are consistent with such a conclusion. In order to demonstrate causality, future studies should manipulate expectations by strengthening some patients' treatment outcome beliefs.

The current study was designed to be an analogue of the placebo arm of a RCT. However, the generalizability of the current findings to patients in a randomized controlled trial or a clinical setting is unclear, because our study differed from a RCT in a number of ways. We included healthy adults rather than a clinical sample. Our placebo treatment was in the form of physical activity rather than a pill. Our outcome of interest was memory performance, rather than a process directly related to physical health. Although limiting generalizability, this design also had several advantages. By using healthy adults from the community, we were able to reduce the variability associated with a disease process. Physical activity is generally perceived to be beneficial both mentally and physically, facilitating our cover story. Adherence to physical activity can be measured objectively, and is associated with adherence rates comparable to those of medication regimens (DiMatteo, 2004).It is acting as a placebo (i.e. sub-therapeutic dose of treatment) in this study because the absolute level of physical activity (number of steps taken daily) did not predict memory performance. Memory, although not directly related to physical health, could plausibly change over a two-week period and can be assessed objectively. All of these features create an analogue study in which we investigate the reasons why adherence may be associated with larger placebo responses in RCT's.

The results of the current study support a direct, unmediated effect of initial expectations on later placebo response. Initial expectations appear to be important for two reasons. First, they are associated with better adherence, which can increase a patient's exposure to an effective treatment. Second, expectations can increase the non-specific components inherent in all treatments (Caspi & Bootzin, 2002), thus maximizing potential treatment response. Good adherence, although not directly contributing to placebo effects, may serve as a behavioral marker of strong treatment expectations. Among previous studies linking reduced mortality risk with greater adherence to a placebo, patients in those studies may have been highly adherent because they believed they were receiving the active treatment (rather than placebo) and thus had a strong belief in the effectiveness of their treatment. Of course our ability to generalize from an outcome like short-term memory to an outcome like mortality is very limited. The current study is an initial attempt to better understand the role of expectations in explaining the benefits of adherence within the placebo arm of RCT's. Good adherence to an inert treatment may be beneficial because it reflects, but does not necessarily produce, stronger expectations of treatment benefit. Consistent with previous research, it is these stronger expectations that directly predict placebo responses. Based on our findings, researchers designing future RCT's may now have another reason to incorporate a measure of treatment expectations in their study. Clinicians should consider strengthening patient expectations at the beginning of treatment. Doing so may improve adherence, giving patients greater exposure to effective treatments. It may also enhance the non-specific effects of treatment, producing greater health benefits overall.

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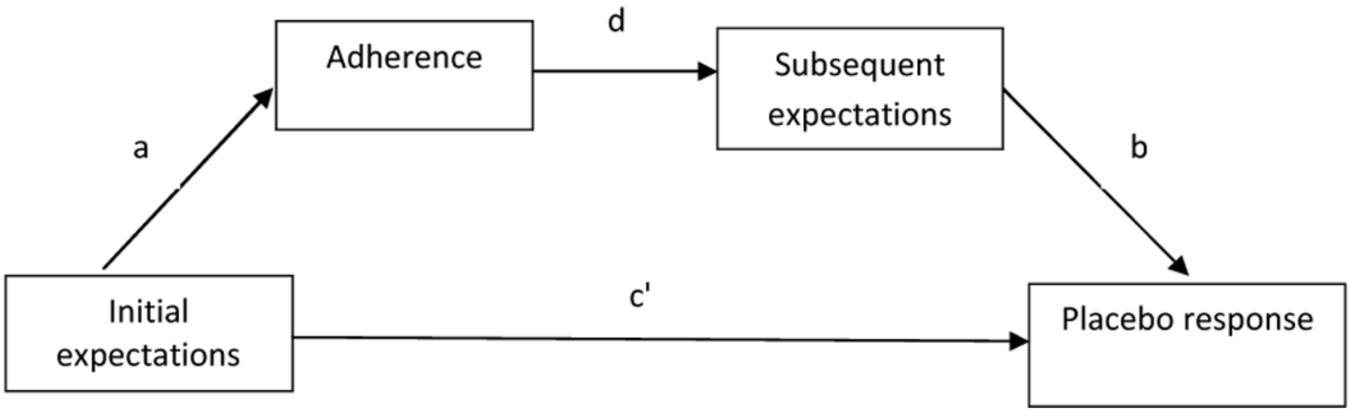

Figure 1.
Model tested in the current study. Initial expectations will influence later placebo responding by affecting treatment adherence, which then informs subsequent expectations about the treatment.

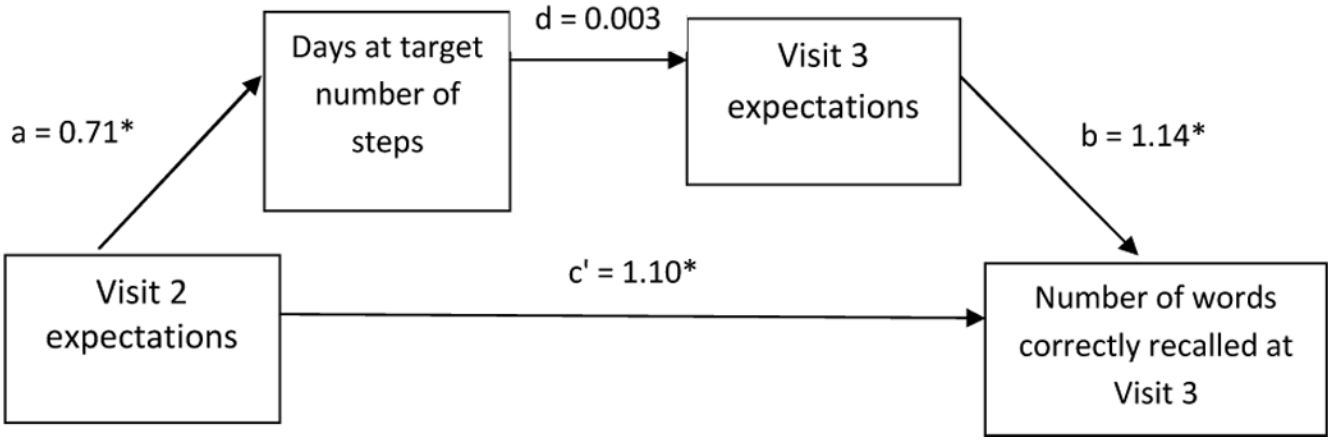

Figure 2.

Path coefficients for mediational model.* $p < 0.02$.Also included in this model are the covariates gender and Visit 2 free recall score. The total indirect effect (a + d + b) = 0.003, SE = 0.03, 95% CI = −0.05 to 0.07.

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Table 1

Summary of Intercorrelations, Means, and Standard Deviations for Expectations, Adherence, and Free Recall scores

Measure	1	2	3	4	5	6	M	SD
1. Initial expectations (V2)	–	0.27*	0.15	0.19	0.45**	0.48**	3.37	1.56
2. Adherence (days at or above target)		–	0.86**	0.06	0.22	0.22	7.04	4.22
3. Adherence (mean percent target)			–	0.06	0.23	0.28*	96%	28%
4. Subsequent expectations (V3)				–	0.07	0.16	0.81	0.95
5. Free recall score V2 (# of words)					–	0.82**	14.92	5.96
6. Free recall score V3 (# of words)						–	16.72	6.36

Note.

* $p < 0.05$

** $p < 0.01$