E-only Article

Expectancy Effect in Three Mind-Body Clinical Trials

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Abstract

Expectancy, arguably the prime component of the placebo effect, has been shown to significantly modify the effects of many treatments. Furthermore, various forms of mind-body interventions have demonstrated effective improvements in outcomes. The aim of this study was to examine the relationship between pretreatment expectations and symptom reduction in a secondary analysis of 3 mind-body intervention programs. An adjusted correlation and regression analysis compared data from a 6-question expectancy questionnaire to a self-reported clinical impression of change score. Only 1 of the 6 expectancy questions in 1 of the 3 studies reached significance ($B = 0.087$; $P = .025$). The combined data from all 3 studies did not reveal significant expectancy effects. The positive effects of mindfulness meditation appear to be independent of an expectancy effect.

Keywords

mind-body, expectancy, mindfulness-based stress reduction, meditation

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The placebo effect has been thought of as either a nuisance to research or a fascinating and interdisciplinary problem in understanding the healing process.[1,2] Evidence indicates that among certain conditions, placebo can have therapeutically significant effects.[3] Among these conditions are pain,[4,5] migraine,[6] cognitive performance,[7] insomnia,[8] epilepsy,[9] depression,[10] and irritable bowel syndrome.[11] However, a series of meta-analyses have cast doubt on the impact of the placebo effect.[12] These contradictory findings cannot be easily dismissed when one considers the difficulties of collecting data on placebo effect from clinical trials. In particular, publication bias against negative results in controlled trials would tend to suppress results showing large effects of placebo control treatments.[13] Despite its variable history, current placebo research is attempting to better understand both the mechanisms that mediate the placebo effect as well as the conditions and populations that are susceptible to it or not, with the ultimate goal of improving standards of care.

A useful consideration in understanding the placebo effect is the biocultural model. In that theory, there was once an evolutionary selective pressure to believe in the healing powers of shaman and/or supernatural phenomena.[14] This model suggests that making a bigger show (ie, more elaborate procedure) will have a more profound effect resulting in greater optimism and survival. Supporting this theory is the fact that more invasive procedures seem to have greater effect than less invasive,[15] placebo surgery is more effective than placebo pills, capsules are better than tablets, and bigger and brighter colored pills are better than smaller and dull colored pills.[16] Furthermore, this model accounts for studies that demonstrate that longer and more empathetic personal interactions with health professionals giving a placebo treatment produce a larger placebo response when compared to the same placebo treatment with minimal interaction.[11] This is known as the Hawthorne effect and may account for smaller studies with fewer participants reporting greater placebo response than larger studies and why study participants may exhibit response bias, which is a tendency to self-report better results because of psychosocial expectations.[17] While a detailed review of the physiological role of the placebo effect is beyond the scope of this article, they include dopaminergic and opioid pathways in the brain that regulate the perception of pain,[18,19] and immunological responses that can be manipulated by conscious or unconscious thoughts and attitudes, some of which are subject to behavioral conditioning.[20-22]

The growing body of knowledge about placebo treatment benefits has begged the question of how to use placebos in an ethical way, assuming that they require deception to be

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effective. However, using placebo as an intentional treatment has been proposed as a mind-body therapy in that it is using intentions or the power of the mind to heal the body.[23] One approach pioneered by Dr Ted Kaptchuk was to tell patients with irritable bowel syndrome that the pill being prescribed was a placebo. Despite the patient's knowledge that they were not receiving any real treatment, their condition greatly improved.[24] This demonstrates that deception is not a necessary element in all cases in order to achieve a placebo effect. This leaves open the notion that mind-body interventions, such as meditation, hypnosis, yoga, tai chi, and so on, may be an effective form of intentional "placebo" without deception.

In this study, we examine the role of beliefs or attitudes about treatments before they are given and how these beliefs influence outcomes. This phenomenon is known, more specifically, as the expectancy effect and is an important part of, and often synonymous with, the placebo effect. Previous studies looking specifically at expectancy have shown that a positive belief about a treatment can improve outcomes.[25] Measuring expectancy-based outcomes in mind-body interventions may offer new insight into their effectiveness and underlying mechanisms. As a mind-body medicine, meditation is an attractive therapy because of the relatively low cost, low physical and emotional risk, ease of implementation, and its ability to allow patients to take a more active role in their treatment. It has been successfully used in, among other populations, veterans with posttraumatic stress disorder.[26] In this secondary analysis of three clinical trials using meditation, we attempted to determine if participant expectations influenced self-perceived impressions of clinical improvement. Our hypothesis was that higher expectations would correlate with higher global impression of change.

Methods

The study analyzed secondary data collected from 3 separate studies. Results and complete methods for these trials are reported elsewhere.[27-30] Methods relevant to this analysis are included here. The first trial (referred to as MB III by the original lab for Mind-Body trial 3) was a 3-arm randomized controlled trial of mindfulness meditation in healthy adults, aged 50 to 85, who are caregivers for people with dementia. There were 17 participants from this study included in this analysis, 4 in the meditation group, 5 in a caregiver education class, and 8 in a respite only group. They were randomized after the assessment of baseline measures, including expectancy (Figure 1). The second study (referred to as MB IV) was a randomized controlled trial examining mindfulness meditation in healthy older adults ages 50 to 85. After baseline measures were taken, the participants were randomized to receive a 6-week meditation program either between the first and second visits or between the second and third visits (these participants served as a waitlist control; Figure 2). Data from the intervention portion of both groups were used in this analysis. The third study (referred to as VetMind) was a randomized controlled trial examining the mechanistic pathways of mindfulness meditation for combat veterans with posttraumatic stress disorder. One hundred participants were enrolled. At the completion of a 6-week program of either mindful meditation (n = 27), slow breathing (n = 25), meditation and slow breathing (n = 23), or sitting quietly (n = 25), the relevant outcome measures were taken a second time (Figure 3). In all 3 studies, before randomization participants were informed about all potential groups and filled out an expectancy questionnaire for each. Only the data for the intervention received was analyzed. Analyses were run using all groups as well as only those groups using meditation.

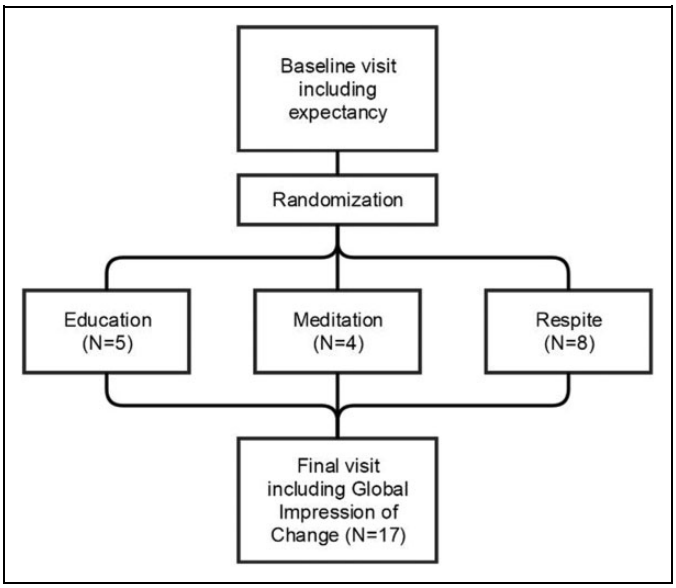

Figure 1. Study design of MB III.

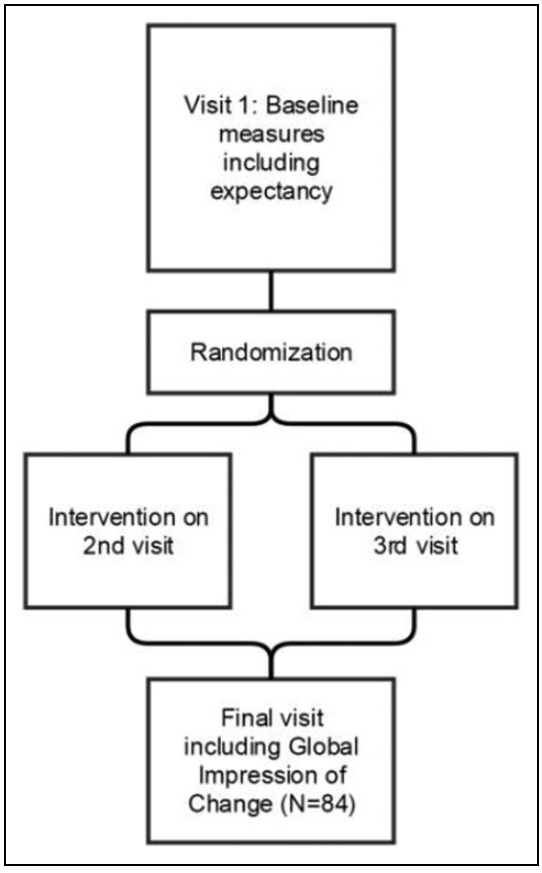

Figure 2. Study design of MB IV.

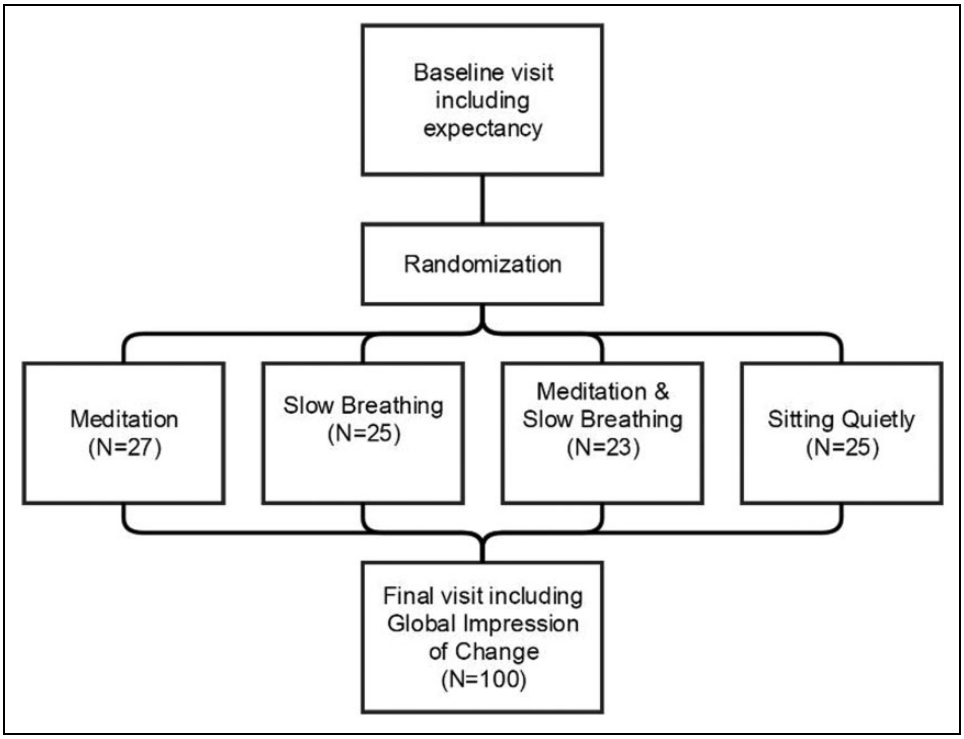

Figure 3. Study design of VetMind.

Questionnaires

Expectancy Questionnaire. Expectancy has been shown to be a strong predictor in both degree and direction not only in meditation research but also in all clinical research.[31] The Expectancy Questionnaire is a self-report questionnaire with 6 questions and Likert-type scale responses. It was used in all 3 studies before randomization to assess the participant's expectation of the training program in reducing their feelings of stress. For the VetMind study, participants filled out one expectancy questionnaire for each of the 4 treatments they would be potentially randomized to receive. The questionnaire asks participants to evaluate the expected effectiveness of the program both by how much they *think* it will improve their symptoms and also how they *feel* it will improve their symptoms.[32] The 6 questions were the following:

1. How logical does the intervention program seem? (1-9) (abbreviated: "Logical")
2. How successful do you think the intervention will be in reducing your symptoms? (1-9) (Success)
3. How confident would you be in recommending the intervention to a friend who shares a similar situation? (1-9) (Recommend)
4. By the end of the study, how much improvement in reducing your symptoms do you think will occur due to the intervention? (0% to 100%) (Improve [think])
5. How much do you really feel that the intervention will help to reduce your symptoms? (1-9) (Improve[feel])
6. How much improvement in reducing your symptoms do you really feel will occur due to the intervention? (0% to 100%) (Improve due to intervention)

Global Impression of Change (GIC). At the end of all 3 studies participants were asked, "How much improvement in your clinical symptoms did you experience from the training?" and self-rated on a 7-point Likert-type scale from "very much worse" (−3) to "very much better" (3). Clinicians often rely on patient observation to help them improve their treatment. However, in clinical trials the participant's perception of clinical change is not always taken into account. The participant's perception may be different than what is objectively recorded and this is important to capture in mind-body medicine trials.[33]

Statistical Analysis

Means and standard deviations for each measure within each primary study are presented. A simple correlation analysis was then conducted in order to determine Pearson correlations between each expectancy outcome and GIC for participants in each study. Then, a regression analysis was conducted for each expectancy measure to evaluate potential predictors of relationship with GIC. Potential predictors included Race, Gender, Marital Status, Education, and Age.

Results

Participant Characteristics

Table 1 shows the study population demographics. All the participants were from the Portland, Oregon, metropolitan area.

Table 1. Study Population Demographics.

	MB III (n = 17)	MB IV (n = 84)	VetMind (n = 100)	Combined (N = 201)*
Race				
Caucasian	100%	92.86%	86%	90.05%
African American	0%	1.19%	3%	1.99%
Native American	0%	0%	4%	1.99%
Asian	0%	5.95%	2%	3.48%
Other	0%	0%	1%	0.50%
Hispanic	0%	0%	4%	1.99%
Gender				
Male	11.76%	16.67%	94%	54.73%
Female	88.24%	83.33%	6%	45.27%
Marital status				N = 184
Single	Not available	45.24%	33%	38.59%
Married		52.38%	67%	59.78%
Other		2.38%		1.63%
Education				N = 184
<12th grade	Not available	0%	2%	1.09%
12-14		15.48%	46%	32.07%
15-16		39.29%	26%	32.07%
>16		45.24%	26%	34.78%
Age				
Range	55-81	49-79	25-65	25-81
Mean ± SD	67.29 ± 7.65	60.07 ± 7.13	52.52 ± 12.06	56.93 ± 10.99

*Except for marital status and education, which were not collected in the MB III study.

Table 2. Mean Values and Standard Deviations[a].

	MB III	MB IV	VetMind	Statistics	Combined
Global Impression of Change	0.706 ± 1.358	0.593 ± 1.282	0.820 ± 0.770	$F(197) = 1.03$; $P = .36$	0.717 ± 1.062
Logical	7.412 ± 2.123	7.153 ± 1.680	5.940 ± 2.164	$F(201) = 10.83$; $P = .0001$	6.574 ± 2.060
Success	6.706 ± 2.257	6.541 ± 1.516	5.220 ± 2.106	$F(201) = 11.99$; $P < .00005$	5.901 ± 2.002
Recommend	7.706 ± 1.490	6.835 ± 1.969	5.570 ± 2.413	$F(201) = 11.80$; $P < .00005$	6.282 ± 2.284
Improve (think)	60.588 ± 24.101	50.941 ± 21.023	37.576 ± 25.358	$F(201) = 12.86$; $P < .00005$	45.373 ± 24.576
Improve (feel)	6.706 ± 1.929	6.412 ± 1.879	4.640 ± 2.250	$F(201) = 19.37$; $P < .00005$	5.559 ± 2.259
Improve due to intervention (feel)	61.765 ± 22.977	55.176 ± 25.383	38.556 ± 25.987	$F(201) = 12.60$; $P < .00005$	47.547 ± 26.939

[a]Global Impression of Change and 6 expectancy questions for each study and combined.

Consistency of Expectancy and Global Impression of Change Across Groups

The 6 expectancy questions showed good internal consistency (standardized Cronbach's $\alpha = .923$ on all 6 items for the combined sample, N = 201), exceeding the standardized alpha of .84 to .85 reported in a previous validation study.[32] Table 2 shows the mean and standard deviation values for each question of the expectancy and GIC questionnaires for each of the three studies and one for the three studies combined. GIC was not significantly different across the three studies. Mean responses to all of the expectancy questions were significantly different across studies, with post hoc comparisons revealing the VetMind scores as being significantly lower than the MB III and MB IV scores.

Relationship Between Expectancy and Global Impression of Change

Table 3 shows the correlation coefficients and P values for the relationship between the expectancy questions and the GIC score. Although there was a positive correlation for nearly all expectancy questions with GIC, which were highest in the VetMind study, none of the expectancy questions were significantly correlated. This analysis was repeated with only those participants randomized to the meditation groups, but the results were fundamentally unchanged.

Potential Predictors

Table 4 shows the adjusted regression coefficients and standard error for each expectancy outcome against the Global Impression of Change for each study and for data from all three studies. Only Improve (Feel) in the VetMind study had a significant relationship with GIC ($B = 0.087$; $P = .025$). In terms of the potential demographic predictors, only Race was significant for some analyses. Those results were as follows: in MB IV, African American race was significant for Success ($B = 2.947$; $P = .031$), for Improve (Feel) ($B = 2.704$; $P = .047$), and for Improve (Think) ($B = 2.741$; $P = .045$). In the VetMind

Table 3. Correlation of Questions With Global Impression of Change.

Expectancy Question	MB III	MB IV	VetMind	Combined
Logical	$r = .088$, $P = .737$	$r = .131$, $P = .242$	$r = .157$, $P = .119$	$r = .090$, $P = .206$
Success	$r = .113$, $P = .667$	$r = -.016$, $P = .887$	$r = .130$, $P = .196$	$r = .024$, $P = .741$
Recommend	$r = .078$, $P = .766$	$r = .205$, $P = .066$	$r = .110$, $P = .276$	$r = .104$, $P = .145$
Improve (think)	$r = .025$, $P = .925$	$r = .084$, $P = .455$	$r = .149$, $P = .141$	$r = .075$, $P = .296$
Improve (feel)	$r = -.011$, $P = .966$	$r = .066$, $P = .560$	$r = .172$, $P = .087$	$r = .046$, $P = .517$
Improve due to intervention (feel)	$r = -.002$, $P = .993$	$r = .127$, $P = .258$	$r = .060$, $P = .556$	$r = .049$, $P = .498$

Table 4. Adjusted Regression Coefficients and Standard Error Against Global Impression of Change[a].

	MB III	MB IV	VetMind	Combined
Logical	.017 ± .181	.090 ± .091	.076 ± .039	.067 ± .041
Success	.019 ± .180	−.068 ± .102	.055 ± .040	.013 ± .044
Recommend	.126 ± .273	.098 ± .078	.053 ± .036	.054 ± .037
Improve (think)	−.010 ± .021	.064 ± .760	.006 ± .003	.003 ± .003
Improve (feel)	−.0123 ± .232	.020 ± .086	.087 ± .038*	.034 ± .039
Improve due to intervention (feel)	−.012 ± .022	.378 ± .625	.003 ± .003	.002 ± .003

[a]Adjusted for race, gender, marital status, education, and age.
*$P = .025$.

study, Asian race had a significant effect for Improve (Feel) ($B = -1.239$; $P = .037$).

Discussion

Population

Participants in the VetMind study had lower expectations on all six questions than the participants of the other two studies, yet reported higher impressions of change (see Table 2). While there is no clear explanation for why their expectations were lower, it is worth noting that they were evaluating different, albeit similar, meditation interventions. They were also predominantly male and younger in comparison to the other studies. However, in a study validating the expectancy questionnaire, Vietnam veterans and their spouses were compared and the two populations were found to have no significant differences.[32] With only a few exceptions[34] in the literature, placebo effects seem not to be modified by age, race, or gender.[35] As with any condition and intervention being studied there is often a regression to the mean. In other words, those in a worse condition have a greater capacity for improvement and are therefore more likely to do so. It is not possible to say within the context of these studies that veterans are in a worse condition than the older adults in the other two studies, some of whom were caregivers to persons with dementia. However, if we took average pessimism (lower expectancy) in a population as indication of a worse condition we could predict a larger average improvement. This may account for the differences in outcomes in the VetMind population in relation to the other two populations.

Some research has shown that expectations are in part due to conditioning[36] and are therefore malleable.[37] Accordingly, two studies using mind-body interventions demonstrated expectancy effects by eliciting and controlling for both positive and negative expectations.[37,38] Other studies using Tai Chi[39] and mindfulness-based stress reduction[40] have found correlations, but are likely confounded by the recruitment process which promoted the benefits of the intervention, in effect only using participants with high expectations in the study. An advantage to this study was that our populations represented a variety of expectancy levels and may account for our results varying from comparable studies.

Future Research

Although it appears that more recent research is beginning to account for expectancy there is no consistent method of accounting for this data. One study testing the effectiveness of Tai Chi and meditation in reducing stress after a stressful stimulus found that the otherwise significant benefits of Tai Chi were negated after adjusting for expectations, which were generally positive.[39] Other studies simply note the levels of expectation without any statistical analysis. There is need for research into reliable methods of accounting for this kind of data. There is also further need to more definitively establish the role of expectancy in mind-body interventions. This could be accomplished with clinical trials that control for levels of expectation.

Limitations

One major limitation of this study was the inclusion of combined data results from the three different studies. This is an issue because the studies were heterogeneous with regard to population, design, and meditation format. The study populations varied on gender and race. MB III was 88% and MB IV

was 83% female, while VetMind was 94% male accounting for nearly all the males in the combined results. The combined race breakdown was 90% Caucasian, which is hardly representative. Although the questionnaires used were the same in all three studies, participants were evaluating different interventions and symptoms. While we presented the data for each study separately, we also wanted to examine the combined data knowing the studies were heterogeneous. The combined data should be viewed with this understanding.

Conclusion

The literature suggests that expectations play a role in the effectiveness of mind-body interventions. However, the available data are insufficient to reach such a conclusion. Our results demonstrate that the role of expectancy in the meditation techniques we examined was marginal. This suggests that the effects of some mind-body interventions may be independent of preconceived expectations. Although this was not our hypothesis, it is consistent with the notion that the objective of mind-body interventions is to alter one's state of mind or perception of bodily experiences, and as such, the starting point is less relevant than the end goal.

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Author Contributions

Matthew Hicks was the primary author. Helané Wahbeh was the primary mentor who oversaw the study design and made editing comments. Douglas Hanes was the statistician.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Approval

The secondary data used in this study resides in an institutional review board–approved data repository. HIPAA and all institutional guidelines for the protection of participant data were followed in the original collection of the data.

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