JOURNAL OF MANUAL & MANIPULATIVE THERAPY, 2017
VOL. 25, NO. 3, 151–159
https://doi.org/10.1080/10669817.2017.1298699

Taylor & Francis
Taylor & Francis Group

Placebo disclosure does not result in negative changes in mood or attitudes towards health care or the provider

Joel E. Bialosky[a] and Michael E. Robinson[b]

[a]Department of Physical Therapy, Center for Pain Research and Behavioral Health, University of Florida, Brooks-PHHP Research Collaboration, Gainesville, FL, USA; [b]Department of Clinical and Health Psychology, Center for Pain Research and Behavioral Health, University of Florida, Gainesville, FL, USA

ABSTRACT

Objectives: The purposes of this study were to (1) determine whether disclosure of having received a placebo treatment following participation in a randomized manual therapy trial resulted in changes in negative mood or attitudes towards health care and the provider and (2) examine the association between changes in mood or attitude and changes in clinical outcomes over the two-week study period.

Methods: Participants with low back pain ($N = 110$) were randomly assigned to receive a spinal manipulative therapy (SMT), a standard placebo SMT in which participants were aware of a chance of receiving a placebo, an enhanced placebo SMT in which participants were instructed 'the manual therapy technique you will receive has been shown to significantly reduce low back pain in some people,' or no treatment. Outcomes included pain (Numeric Rating Scale), disability (Oswestry Disability Index), and negative mood and attitudes towards health care and the provider (visual analog scales). Pain and disability were obtained at baseline and two weeks. Mood and attitude measures were assessed at baseline, at the start of the final session, and upon completion of the final session following disclosure of group assignment.

Results: Disclosure of having received a placebo treatment was not associated with worsening of mood or attitudes towards health care or the provider ($p > 0.05$). A small, but significant ($p < 0.05$) association was observed between two-week changes in disability and immediate changes in mood ($r = 0.31$–0.36) upon disclosure of having received a placebo. This analysis indicates an association between larger improvements in disability and more positive changes in mood.

Discussion: Placebo treatment use in clinical practice is common yet controversial due to the deceptive nature. Our findings suggest disclosure of having received a placebo treatment is not associated with adverse changes in negative mood or attitudes towards health care or the provider.

KEYWORDS
Placebo; pain; low back pain; spinal manipulation; ethics

Introduction

Placebo is traditionally considered inert suggesting a lack of a treatment effect [1,2]. Furthermore, researchers often view placebo as an annoyance capable of confounding study results [3,4]. In fact, one of the highest levels of evidence, the randomized controlled trial, frequently defines the success of a studied intervention on the observed efficacy in comparison to placebo – implying 'no better than placebo' is the equivalent of an ineffective intervention. In contrast to this perspective, recent literature supports a large placebo analgesic effect [5]. Furthermore, placebo is a psychological and physiological process [6]. For example, recent studies using functional magnetic resonance imaging suggest placebo related analgesia is associated with supraspinal responses in brain regions related to pain modulation [7–9], emotion [9–11], and cognitive appraisal [10]. Beyond a specific supraspinal mechanism, more recent imaging studies demonstrate spinal cord related responses to placebo [12,13] suggesting placebo related pain modulation occurs throughout the continuum of the nervous system. Collectively, these findings support placebo as an active analgesic agent functioning throughout the central nervous system.

Despite the potential analgesic benefit, placebo treatment use in clinical practice is controversial. Deception is inherent to placebo treatment related analgesia as the magnitude of a placebo response is dependent upon expectation for the provided intervention. Specifically, greater placebo related analgesia is observed when individuals are given a placebo; however, informed they are receiving an effective intervention in order to enhance their expectations of pain relief [5]. This need for deception has raised significant ethical issues regarding the use

CONTACT Joel E. Bialosky bialosky@phhp.ufl.edu

of placebo treatments in clinical practice [14]. Particularly concerning is the withholding of informed consent and breach of trust inherent to the patient provider relationship through deceptive medical practice [15–18]. Medical research requires participants are educated on the goals, aims, and methods of a research study and provide consent prior to participation [19]. Participants in placebo controlled research studies provide informed consent with the knowledge of potentially receiving a placebo treatment. Subsequently, placebos are considered ethical with informed consent in studies to establish efficacy or safety of an intervention; however, their use in clinical care is questionable [20].

Despite these ethical concerns, the use of placebo treatment in clinical practice is common both internationally and across disciplines [21–25]. For example, 75% of nurses in Iran [21], 88% of general practitioners in Germany [24], and 50% of internists and rheumatologists in the United States [25] admit to the deceptive use of placebo treatment in clinical practice. Reasons for the use of placebo treatment by health care providers appear well intentioned and include calming the patient, as supplemental treatment, to control pain, and as a bridge to the next regular dosage of medication [26]. The concern inherent to deception results from older studies of 'deception to cause harm [27]'. Placebo treatment related deception differs markedly in that deception is provided with the intention of a beneficial effect such as pain relief. Consequently, deception in and of itself is not necessarily negative [28] and particularly if provided with therapeutic intentions. Furthermore, deception by a health care provider with the goal of lessening pain may be acceptable to patients [29–31].

The purpose of this study was to determine whether disclosure of having received a placebo treatment following participation in a placebo controlled study of manual therapy was associated with changes in negative mood or attitudes towards health care and the provider. Additionally, we wished to determine the association between changes in mood or attitude following disclosure of having received a placebo treatment and changes in clinical outcomes observed over the two-week period of the study. Based on prior studies [31,32], we hypothesized changes in negative mood and attitude would not differ between participants receiving the placebo treatment and those receiving the studied manual therapy intervention or no treatment. Furthermore, we hypothesized changes in mood and attitude would be associated with clinical outcomes with better clinical outcomes related to more positive changes in mood and attitudes upon disclosure of having received a placebo treatment.

Methods

The current study is a secondary analysis of a previously completed randomized controlled trial [33]. The study was approved by the Institutional Review Board of the University of Florida. Details of the study design and primary analyses are reported in more detail elsewhere [33]. Briefly, we recruited a sample of convenience from the general community of the University of Florida campus and Health Science Center. Participants between the ages of 18 and 60, currently experiencing low back pain (LBP) rated ≥ 4/10 at worst over the past 24 h on a numeric rating scale (NRS) (0 = no pain at all, 10 = worst pain imaginable) were included in the study. Participants were excluded for; (1) pain or paresthesia below the knees; (2) potential non- musculoskeletal causes of LBP such as (a) unexplained weight loss of greater than 10 pounds, (b) fever corresponding to LBP, (c) non- mechanical pain, (d) bowel or bladder dysfunction; (3) surgery to the low back within the past 6 months; (4) systemic illness known to affect sensation i.e. diabetes; (5) chronic pain condition unrelated to LBP; (6) fracture as the cause of LBP; (7) pregnancy. All individuals meeting the criteria for participation and providing informed consent were enrolled in the study.

Measures

Demographic and clinical characteristics

Demographic information was obtained at baseline through a questionnaire specific to age, sex, education, and duration of LBP.

Mood

Separate 100-mm visual analog scales anchored with 'none' to 'most severe imaginable' were provided for 'depression,' 'anxiety,' 'frustration,' 'anger,' and 'fear.' Participants were instructed to draw a vertical line perpendicular across the horizontal line at the location best describing their current level of each construct and their ratings were quantified in terms of millimeters. Visual analog scales are reliable measures of both pain intensity as well as the affective dimension of pain [34] and similar methodology has been used in a prior study of placebo disclosure [32]. Mood was assessed at baseline and at the two-week conclusion of the study both prior to and immediately following disclosure of the assigned treatment group.

Attitudes towards health care and the provider

Separate 100-mm visual analog scales anchored with 'not at all' to 'most likely' were provided for the questions of 'how likely are you to:' (a) use medical treatments (e.g. surgery and medication prescribed or non-prescribed, but not including herbal medication) for your pain?; (b) use non-medical treatments for your pain?; (c) to participate in future studies in general?; (d) participate in future studies conducted in our lab? On separate visual analog scales anchored with 'not at all' to 'very much,' participants were asked to indicate 'how much you:' (a) like experimenters in general?; (b) like the experimenters in this study?; (c) trust experimenters in general?; (d)

trust the experimenters in this study? Participants were instructed to draw a vertical line perpendicular across the horizontal line at the location best describing their current level of each construct and their ratings were quantified in terms of millimeters. Similar methodology has been used in a prior trial of placebo disclosure [34]. Attitude was assessed at baseline and at the two week conclusion of the study both prior to and immediately following disclosure of the assigned treatment group.

Clinical outcomes

Clinical pain intensity

Clinical pain intensity was assessed for changes over the two weeks of the study using a 101 point numeric pain rating scale (NRS) for 'usual pain over the past week' anchored with 0 = 'no pain at all' to 100 = 'worst pain imaginable.' NRSs are reliable and valid [35,36] and a common measure of clinical pain intensity.

Low back pain related disability

Low back pain related disability was assessed through the Oswestry Disability Index (ODI). The ODI is a 10 item questionnaire specific to LBP. Each item contains a 6 point adjectival scale scored from 0 to 5. We doubled the total score as is commonly done [37] to provide a percentage, with higher scores indicating greater perceived disability. The ODI is a commonly used measure of disability in the study of LBP and has demonstrated strong reliability and validity [38–40].

Interventions

Participants were randomly assigned to one of four groups.

The spinal manipulative therapy group (SMT) group received a SMT previously shown to be effective in the treatment of some individuals experiencing low back pain [41,42] and applied twice to each side. Participants receiving the SMT were instructed through the informed consent process they would receive either a studied SMT or a placebo intervention and were provided no additional information regarding which intervention they received. SMT was performed twice on each side.

The standard SMT placebo group received a placebo SMT intended to mimic the studied SMT; however, differ biomechanically. Specifically, the placebo SMT did not include rotation and sidebending components inherent to the studied SMT and the mechanical force was applied with the pelvis and spine in full contact with the treatment table. Similar to the studied SMT, the placebo SMT was performed twice on each side. Participants receiving the placebo SMT were instructed through the informed consent process they would receive either a studied SMT or a placebo intervention and were provided no additional information regarding which intervention they received.

The enhanced SMT placebo group received the same placebo as the standard placebo group. Participants receiving the enhanced SMT placebo were told, 'The manual therapy technique you will receive has been shown to significantly reduce low back pain in some people' immediately prior to the first intervention and subsequent intervention sessions. Similar instructional sets have been incorporated in mechanistic studies of placebo and are associated with enhanced placebo analgesia in subjects with irritable bowel syndrome [5,43]. Similar to the SMT and the standard placebo group, the enhanced placebo SMT group received the placebo SMT twice on each side.

The no treatment control group sat quietly for 5 min during the initial session and final session.

Procedures

Individuals agreeing to participate signed an informed consent form approved by the University of Florida Institutional Review Board and then completed the intake demographic form, the NRS, the ODI, the mood scales, and the attitude scales. The entire study procedure is described in detail elsewhere [33]. Briefly, participants receiving the SMT and both placebo treatment groups were scheduled for 5 additional sessions during the next 2 weeks to receive their assigned intervention. Following the two-week period of the study, all participants were seen for a final session in which they completed the NRS, ODI, and mood and attitude scales. Upon completion of the study, participants were debriefed regarding their group assignment and the purpose of the study. Immediately following the debriefing session, participants again completed the mood and attitude scales.

Data analysis

Univariate ANOVAs were used to assess for post-randomization group differences in demographic variables. Mixed model repeated measure ANOVAs were used to assess group (SMT, placebo, enhanced placebo, no treatment control) related changes in measures of mood and attitude over time (final session prior to disclosure of group assignment, and final session immediately following disclosure of group assignment). Baseline measures of mood and attitude were included as covariates in the analyses. We did not combine the placebo groups in this initial analysis as we were interested in whether changes in mood and/or attitude differed by how the placebo was presented, i.e. awareness of an equal chance of receiving a placebo or SMT (standard placebo group) versus having been informed, 'The manual therapy technique you will receive has been shown to significantly reduce low back pain in some people' (enhanced placebo group). Interaction effects were decomposed with simple contrasts. Pearson correlation coefficients were calculated for two-week changes in clinical outcomes (pain and disability) and within session changes in mood and attitude

(prior to and immediately following disclosure of group assignment only in the 2 placebo groups). Correlation coefficients were considered very weak (*r*-values less than 0.19), weak (*r*-values between 0.20 and 0.39), moderate (*r*-values between 0.40 and 0.59), strong (*r*-values between 0.60 and 0.79), and very strong (*r*-values between 0.80 and 1.00) [44]. The two placebo treatment groups did not differ in changes in any clinical outcome, mood, or attitude variables, so they were combined for the correlation analysis. Significance was set at 0.05 and all analyses were performed using the SPSS statistical package, version 21.0 (SPSS Inc, Chicago, IL)

Results

One hundred and ten individuals signed the informed consent form and agreed to participate. Seventy percent of participants were female and mean age was 31.68 (SD = 11.85) years. Baseline measures of the sample as a whole and by group assignment are presented in Table 1. Individual groups did not differ by baseline demographic measures, clinical measures, or measures of mood or attitude ($p > 0.05$).

Changes in mood

A group by time interaction was not observed for any measures of mood ($p > 0.05$); however, a main effect for time was observed for improvements in anxiety after disclosure of group assignment ($F_{(1,99)} = 5.79$, $p = 0.02$, partial $\eta^2 = 0.06$) (Table 2).

Changes in attitudes towards health care and the provider

Neither a group by time interaction ($p > 0.05$) nor a main effect for time ($p > 0.05$) was observed for any measure of attitude towards the use of health care or the provider (Table 3).

Association between changes in mood and clinical outcomes

Significant, but weak, positive correlations were observed between two-week changes in disability and immediate changes in depression ($r = 0.31$, $p = 0.02$) and anger ($r = 0.36$, $p = 0.01$) upon disclosure of having received a placebo treatment, suggesting an association between larger improvements in disability and more positive changes in these factors (Table 4).

Association between changes in attitudes towards health care and the provider and clinical outcomes

Very weak to weak and non- significant ($p > 0.05$) correlations were observed between two-week changes in disability and immediate changes in attitudes towards health care and the provider upon disclosure of having received a placebo treatment (Table 5).

Table 1. Baseline comparison of intervention groups.

	SMT *n* = 28	Placebo *n* = 27	Enhanced placebo *n* = 27	No treatment control *n* = 28	Total sample *n* = 110	*p*- value for difference
Sex (% female)	21/28 (75.0)	17/27 (63.0)	20/27 (74.1)	19/28 (68.0)	77/110 (70.0)	0.74
Age (years)	32.07 (10.98)	33.22 (13.29)	31.56 (11.85)	29.85 (12.09)	31.68 (11.85)	0.78
Education (years)	16.04 (2.33)	15.59 (2.50)	15.89 (2.38)	16.57 (2.60)	16.03 (2.45)	0.51
Duration of LBP (weeks) (median, interquartile range)	12 (164.50)	24 (100)	36 (543)	4 (108)	16.03 (153)	0.43
ODI	17.04 (9.17)	14.22 (8.56)	17.92 (13.31)	20.04 (15.27)	17.32 (11.95)	0.35
Pain (NRS)	45.26 (26.21)	43.78 (22.45)	37.89 (22.13)	33.93 (26.21)	40.16 (23.33)	0.24
Mood (VAS)						
Depression	18.81 (21.00)	15.04 (16.39)	12.52 (16.64)	14.65 (23.09)	15.23 (19.34)	0.43
Anxiety	22.04 (16.00)	17.88 (15.54)	19.22 (18.81)	24.81 (27.66)	21.00 (20.01)	0.18
Frustration	25.50 (20.54)	23.64 (17.96)	22.30 (22.47)	29.15 (29.17)	25.13 (22.77)	0.57
Anger	6.19 (8.34)	8.60 (9.99)	7.96 (10.96)	15.85 (25.52)	9.64 (15.56)	0.41
Fear	10.35 (10.96)	11.32 (15.17)	10.15 (16.82)	16.38 (23.68)	12.04 (17.23)	0.37
Attitudes (VAS)						
Use medical treatment	36.19 (30.31)	50.12 (37.08)	38.56 (32.27)	52.36 (37.54)	44.12 (34.57)	0.83
Use non- medical treatment	67.42 (26.45)	70.32 (26.32)	68.15 (30.23)	52.40 (34.18)	64.67 (29.87)	0.28
Participate in future studies in general	78.44 (21.87)	79.32 (16.96)	79.81 (23.41)	77.16 (20.81)	78.71 (20.66)	0.70
Participate in future studies in our lab	80.80 (20.00)	82.68 (14.63)	77.33 (24.83)	76.04 (21.43)	79.18 (20.52)	0.64
Like experimenters in general	73.19 (24.40)	74.60 (21.02)	69.74 (25.67)	73.56 (22.84)	72.72 (23.32)	0.72
Like experimenters in this study	64.68 (22.19)	72.80 (20.80)	72.73 (22.57)	73.54 (22.85)	70.93 (22.08)	0.29
Trust experimenters in general	63.50 (21.53)	67.76 (18.07)	68.30 (26.12)	74.24 (23.51)	68.40 (22.56)	0.80
Trust experimenters in this study	71.52 (22.59)	75.20 (19.35)	71.70 (24.47)	75.58 (24.81)	73.45 (22.65)	0.43

Notes: All data are reported as mean (standard deviation) ratings unless otherwise noted.
Abbreviations: LBP = low back pain, NRS = Numeric Rating Scale, ODI = Oswestry Disability Index, VAS = visual analog scale.

Table 2. Changes in mood following disclosure of having received a placebo treatment.

		Depression	Anxiety	Frustration	Anger	Fear
Control $n=28$	2- week pre- disclosure	13.15 (24.26)	24.46 (22.17)	23.38 (25.86)	15.08 (25.48)	16.27 (27.32)
	2- week post disclosure	8.88 (16.80)	13.46 (21.94)	13.58 (22.74)	8.81 (21.35)	9.00 (21.36)
SMT $n=27$	2- week pre disclosure	14.73 (19.11)	20.73 (20.07)	26.00 (25.89)	5.88 (10.73)	12.69 (19.35)
	2- week post disclosure	11.38 (17.31)	12.77 (15.46)	15.92 (20.82)	4.46 (11.50)	6.19 (15.62)
Placebo $n=27$	2- week pre disclosure	13.72 (16.66)	18.32 (21.35)	20.68 (22.83)	8.96 (14.22)	9.80 (13.99)
	2- week post disclosure	10.04 (18.42)	12.84 (20.84)	12.36 (21.67)	5.92 (10.89)	5.00 (7.56)
Enhanced placebo $n=28$	2- week pre disclosure	8.30 (13.17)	12.85 (18.14)	12.78 (15.63)	4.52 (7.61)	5.89 (8.41)
	2- week post disclosure	5.81 (10.71)	7.52 (11.64)	5.63 (9.02)	2.33 (4.10)	3.59 (5.44)
Total sample $n=110$	2- week pre disclosure	12.42 (18.61)	19.04 (20.61)	20.63 (23.10)	8.57 (16.25)	11.13 (18.72)
	2- week post disclosure	8.99 (15.92)	11.60 (17.78)	11.81 (19.39)	5.35 (13.43)	5.93 (13.96)

Notes: All data are reported as mean (standard deviation) of ratings on a visual analog scale (in millimeters).
Group related changes were not observed for any measures of mood ($p > 0.05$); however, a main effect for time was observed for improvements in all measures of mood ($p < 0.01$).

Table 3. Changes in attitude following disclosure of having received a placebo treatment.

		Use medical treatment	Use non-medical treatment	Participate in future studies in general	Participate in future studies in our lab	Like experimenters in general	Like experimenter in this study	Trust experimenters in general	Trust experimenters in this study
Control $n=28$	2- week pre-disclosure	41.32 (33.09)	60.64 (32.20)	76.56 (24.57)	78.12 (23.54)	71.32 (20.95)	71.38 (24.25)	73.44 (22.77)	80.46 (21.75)
	2- week post disclosure	39.64 (30.08)	60.72 (28.58)	76.52 (23.66)	77.68 (22.64)	74.08 (23.84)	73.50 (27.03)	72.04 (24.71)	79.75 (23.53)
SMT $n=27$	2- week pre disclosure	50.50 (28.61)	64.65 (25.68)	80.32 (20.69)	82.88 (24.38)	73.54 (26.82)	87.20 (18.94)	73.92 (23.36)	88.64 (14.63)
	2- week post disclosure	50.15 (31.99)	64.11 (31.42)	77.32 (27.58)	85.72 (18.19)	75.46 (27.47)	87.64 (19.72)	73.11 (27.26)	90.52 (14.75)
Placebo $n=27$	2- week pre disclosure	37.44 (30.52)	64.28 (24.52)	80.44 (17.67)	83.56 (17.51)	75.92 (20.79)	81.28 (21.28)	70.36 (21.90)	84.52 (18.44)
	2- week post disclosure	40.48 (29.97)	63.12 (22.03)	79.92 (14.80)	83.28 (14.29)	72.76 (18.00)	83.84 (16.40)	73.96 (19.57)	86.84 (15.17)
Enhanced placebo $n=28$	2- week pre disclosure	28.25 (33.26)	59.93 (34.09)	79.19 (23.33)	78.85 (23.98)	75.11 (21.76)	83.08 (17.15)	72.07 (23.47)	84.81 (17.15)
	2- week post disclosure	30.41 (32.62)	58.00 (30.55)	77.48 (23.90)	78.15 (24.22)	74.41 (24.39)	81.50 (22.48)	71.33 (24.35)	82.59 (22.07)
Total sample $n=110$	2- week pre disclosure	39.27 (32.02)	62.35 (29.12)	79.13 (21.49)	80.81 (22.35)	73.99 (22.47)	80.85 (21.00)	72.46 (23.47)	84.65 (18.07)
	2- week post disclosure	40.07 (31.58)	61.45 (28.14)	77.80 (22.68)	81.15 (20.29)	74.19 (23.40)	81.70 (21.98)	75.59 (23.84)	84.93 (19.44)

Notes: All data are reported as mean (standard deviation) of ratings on a visual analog scale (in millimeters).
Neither group differences nor a main effect for time were observed immediately pre to immediately post- disclosure of having received a placebo ($p > 0.05$).

Table 4. Correlation between two-week change in outcomes and within session change in mood amongst placebo treatment groups.

	Depression	Anxiety	Frustration	Anger	Fear
2- week change in pain	0.26 $p=0.06$	0.21 $p=0.14$	−0.06 $p=0.66$	0.08 $p=0.58$	0.05 $p=0.70$
2 week change in disability	0.31 $p=0.02$	0.25 $p=0.08$	0.16 $p=0.27$	0.36 $p=0.01$	0.28 $p=0.05$

Note: Values are Pearson correlation coefficients.

Discussion

Many health care providers admit to the use of placebo treatment with the desire to help and/or satisfy their patients [26]. Such practice is ethically questionable due to the deceptive nature; however, the patient's view of well-intentioned deception has not been extensively considered. Two qualitative studies nested within a larger study have considered the perspective of participants in a clinical trial towards placebo treatment [45,46].

Table 5. Correlation between two-week change in outcomes and within session change in attitude amongst placebo treatment groups.

	Use medical treatment	Use non-medical treatment	Participate in future studies in general	Participate in future studies in our lab	Like experimenters in general	Like experimenter in this study	Trust experimenters in general	Trust experimenters in this study
2- week change in pain	0.17 $p=0.23$	−0.14 $p=0.32$	0.02 $p=0.86$	0.08 $p=0.58$	−0.08 $p=0.55$	−0.07 $p=0.63$	−0.09 $p=0.52$	−0.22 $p=0.11$
2 week change in disability	0.21 $p=0.14$	0.04 $p=0.80$	0.18 $p=0.19$	0.14 $p=0.32$	−0.19 $p=0.18$	−0.12 $p=0.39$	−0.18 $p=0.21$	−0.27 $p=0.05$

Note: Values are Pearson correlation coefficients.

Each study included 12 participants with irritable bowel syndrome in the placebo arm of a trial of acupuncture. Participants in these studies perceived placebo treatment responses along a continuum from valuable and resulting from psychological aspects of treatment to not valid and deceptive with the concern of appearing gullible. In the current study, we found disclosure of having received a placebo treatment was not related to negative changes in mood or attitude towards health care or the provider of participants in our randomized controlled trial. Furthermore, placebo treatment disclosure was not related to mood or attitudes of participants regardless of whether they were instructed during the consent process of having a 50% chance of receiving a placebo OR whether they were informed they were receiving a manual therapy intervention 'shown to significantly reduce low back pain in some people.' Our findings are similar to those observed in a previous study of both participants with irritable bowel syndrome and healthy participants [32] in which placebo treatment disclosure did not result in worsening of mood or negative attitudes towards health care or the provider and extends these findings to individuals with low back pain participating in a study of a manual therapy intervention.

A previous study surveyed 57 participants with chronic musculoskeletal pain regarding the acceptability of placebo treatment in clinical practice [29] and found concern was mitigated by improved clinical outcomes suggesting deception was acceptable as long as improvements in clinical outcomes resulted. Our findings add to this body of knowledge as we found small, but significant associations between two-week improvements in disability and more positive changes in mood following disclosure of having received a placebo intervention. Together, these findings suggest detrimental effects of deception are influenced by a positive clinical response.

Our findings suggest the disclosure of having received a placebo treatment does not result in negative mood or negative attitudes towards health care or the provider and particularly if the resulting clinical outcomes are favorable. These findings have clinical implications for practicing manual therapists. Placebo treatment use in clinical practice has been differentiated between 'pure' placebo treatments or those devoid of an active ingredient such as a sugar or starch pill and 'impure' placebo treatments or those containing active physical ingredients thought ineffective for the treated condition such as prescribing antibiotics for a viral infection [22]. While practitioners admit to the clinical use of both pure and impure placebo treatments, impure placebo treatment use is much more common in clinical practice [24,47,48]. The mechanisms are undetermined through which many of the interventions applied by a manual therapist result in improved clinical outcomes. Factors such as expectation [5], conditioning [43], and therapeutic alliance [49] are known to enhance the magnitude of placebo analgesia as well as influence clinical outcomes [50,51]. Subsequently, placebo mechanisms are likely to play a role in outcomes related to all interventions for pain including those commonly used by manual physical therapists. In fact, treatment effects sizes are similar across multiple, differing interventions for some pain conditions suggesting the importance of common mechanisms related to the treatment context rather than the specific parameters of an individual intervention [52].

Consider a patient presenting to a clinic with an episode of acute low back pain with signs and symptoms suggesting the likelihood of benefitting from SMT [41]. The treating clinician may evaluate this patient and recommend SMT as the initial treatment. Ultrasound is not recommended for acute low back pain [53]; however, suppose this patient expressed a strong preference for ultrasound and preferred not to receive SMT. One approach would be for the manual therapist to present the current evidence to the patient and recommend the patient accept SMT as the provided treatment. The patient may agree to this approach when presented with the best evidence, but suppose the patient still preferred to receive ultrasound and preferred not to receive SMT. Having presented the patient with the best evidence and, the patient still preferring to receive ultrasound, the treating manual therapist may decide to provide the patient with ultrasound and educate the patient (truthfully) that although the best evidence does not support the use of ultrasound for acute low back pain, he has seen or heard of individuals with acute low back pain for whom it was very effective. Ultrasound in this instance could perhaps be considered an 'impure'

placebo treatment. Clinical care occurs at the individual level and is not always reflective of the average response indicated by a clinical trial. Subsequently, while counter to the literature, the manual therapist may feel justified in providing this intervention based on the potential for the individual patient preferences [54] and expectations [55] to influence clinical outcomes.

Our findings along with those of others [30–32] suggest patients are agreeable to good intentioned deception in clinical practice. Furthermore, well intentioned deception does not result in an adverse effect on mood or the relationship with the health care provider particularly if a positive outcome is experienced. Importantly, we do not interpret these findings as supporting the clinical use of sugar pills or a manual therapy equivalent on unsuspecting patients. Furthermore, we do not advocate for the intentional deception of patients by manual therapists. These findings support the practice of considering and honestly manipulating patient expectations and preferences for interventions lacking strong evidence based support when interventions supported by the literature are either not acceptable to the individual patient or not effective for the individual patient.

An interesting alternative to the deceptive use of placebo is the use of "pure" placebo treatments without deception [56,57]. For example, a recent study compared treatment as usual to treatment as usual plus open label placebo pill for individuals with low back pain of greater than three months duration [57]. The treatment as usual plus placebo pill group received chemically inert pills (containing microcrystalline cellulose) in a container labeled 'placebo.' Participants in this group were instructed they were receiving a placebo pill and received a 15-min educational intervention describing the placebo effect and placebo analgesia. The study observed moderate to large significant improvements in pain and disability favoring the treatment as usual plus placebo pill group. Furthermore, a recent study found educating patients about placebo could enhance its acceptability [58]. Subsequently, 'pure' placebo treatments may be a viable and ethically acceptable [59] option for patients with pain conditions.

Limitations of the current study include the clinical trial design. Clinical trial participants are instructed during the consent process they will receive either a studied intervention or a placebo and are aware of a chance of receiving a placebo treatment. In clinical practice, patients expect to receive a standard intervention. Subsequently, attitudes towards the use of placebo treatment in participants of a clinical trial may differ from those of patients seeking care. We believe this limitation is partially ameliorated by our inclusion of the enhanced placebo treatment group in which participants were instructed, 'The manual therapy technique you will receive has been shown to significantly reduce low back pain in some people.' This more closely resembles clinical practice in which interventions are provided by enthusiastic health care providers.

Conclusion

We observed disclosure of having received a placebo treatment was not associated with worsening of mood or attitudes towards health care or the provider. A small but significant association was observed between two-week changes in disability and immediate changes in specific measures of mood and attitude towards the provider upon disclosure of having received a placebo treatment. This suggests any small adverse responses to disclosure are partially mitigated by improvements in clinical outcomes.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

This study was supported by the University of Florida Research Opportunity Fund.

Notes on contributors

Joel E. Bialosky is a clinical assistant professor in the Department of Physical Therapy.

Michael E. Robinson is a Professor in the Department of Clinical and Health Psychology.

References

[1] Hawk C, Long CR, Rowell RM, et al. A randomized trial investigating a chiropractic manual placebo: a novel design using standardized forces in the delivery of active and control treatments. J Altern Complement Med. 2005;11(1):109–117.

[2] Vernon H, MacAdam K, Marshall V, et al. Validation of a sham manipulative procedure for the cervical spine for use in clinical trials. J Manipulative Physiol Ther. 2005;28(9):662–666.

[3] Fava M, Evins AE, Dorer DJ, et al. The problem of the placebo response in clinical trials for psychiatric disorders: culprits, possible remedies, and a novel study design approach. Psychotherapy and psychosomatics. Psychother Psychosom. 2003;72(3):115–127. Epub 2003/04/23.

[4] Yang H, Cusin C, Fava M. Is there a placebo problem in antidepressant trials? Curr Top Med Chem. 2005;5(11):1077–1086. Epub 2005/09/27.

[5] Vase L, Petersen GL, Riley JL III, et al. Factors contributing to large analgesic effects in placebo mechanism studies conducted between 2002 and 2007. Pain. 2009;145(1–2):36–44.

[6] Price DD, Finniss DG, Benedetti F. A comprehensive review of the placebo effect: recent advances and current thought. Annu Rev Psychol. 2008;59:565–590.

[7] Bingel U, Lorenz J, Schoell E, et al. Mechanisms of placebo analgesia: rACC recruitment of a subcortical antinociceptive network. Pain. 2006;120(1–2):8–15.

[8] Lu HC, Hsieh JC, Lu CL, et al. Neuronal correlates in the modulation of placebo analgesia in experimentally-induced esophageal pain: a 3T-fMRI study. Pain. 2010;148(1):75–83. Epub 2009/12/08.
[9] Zubieta JK, Bueller JA, Jackson LR, et al. Placebo effects mediated by endogenous opioid activity on mu-opioid receptors. J Neurosci. 2005;25(34):7754–7762. Epub 2005/08/27.
[10] Craggs JG, Price DD, Verne GN, et al. Functional brain interactions that serve cognitive-affective processing during pain and placebo analgesia. NeuroImage. 2007;38(4):720–729. Epub 2007/10/02.
[11] Petrovic P, Dietrich T, Fransson P, et al. Placebo in emotional processing–induced expectations of anxiety relief activate a generalized modulatory network. Neuron. 2005;46(6):957–969. Epub 2005/06/15.
[12] Eippert F, Finsterbusch J, Bingel U, et al. Direct evidence for spinal cord involvement in placebo analgesia. Science (New York, NY). 2009;326(5951):404. Epub 2009/10/17.
[13] Matre D, Casey KL, Knardahl S. Placebo-induced changes in spinal cord pain processing. J Neurosci. 2006;26(2):559–563. Epub 2006/01/13.
[14] Miller FG, Wendler D, Swartzman LC. Deception in research on the placebo effect. PLoS Med. 2005;2(9):e262. Epub 2005/09/22.
[15] Braillon A. Placebo is far from benign: it is disease-mongering. Am J Bioeth: AJOB. 2009;9(12):36–38. Epub 2009/12/17.
[16] Finniss DG, Kaptchuk TJ, Miller F, et al. Biological, clinical, and ethical advances of placebo effects. Lancet (London, England). 2010;375(9715):686–695. Epub 2010/02/23.
[17] Grace PJ. The clinical use of placebos. Is it ethical? Not when it involves deceiving patients. Am J Nurs. 2006;106(2):58–61. Epub 2006/02/03.
[18] Cahana A, Romagnioli S. Not all placebos are the same: a debate on the ethics of placebo use in clinical trials versus clinical practice. J Anesth. 2007;21(1):102–105. Epub 2007/02/08.
[19] World Medical A. World medical association declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013;310(20):2191–2194. Epub 2013/10/22.
[20] Sullivan M, Terman GW, Peck B, et al. APS position statement on the use of placebos in pain management. J Pain. 2005;6(4):215–217. Epub 2005/04/12.
[21] Baghcheghi N, Koohestani HR. Placebo use in clinical practice by nurses in an Iranian teaching hospital. Nurs Ethics. 2011;18(3):364–373. Epub 2011/05/12.
[22] Fassler M, Meissner K, Schneider A, et al. Frequency and circumstances of placebo use in clinical practice–a systematic review of empirical studies. BMC Med. 2010;8:15. Epub 2010/02/25.
[23] Fent R, Rosemann T, Fassler M, et al. The use of pure and impure placebo interventions in primary care – a qualitative approach. BMC Fam Pract. 2011;12:11. Epub 2011/03/26.
[24] Meissner K, Hofner L, Fassler M, et al. Widespread use of pure and impure placebo interventions by GPs in Germany. Fam Pract. 2012;29(1):79–85. Epub 2011/08/03.
[25] Tilburt JC, Emanuel EJ, Kaptchuk TJ, et al. Prescribing "placebo treatments": results of national survey of US internists and rheumatologists. BMJ (Clinical research ed). 2008;337:a1938. Epub 2008/10/25.
[26] Kermen R, Hickner J, Brody H, et al. Family physicians believe the placebo effect is therapeutic but often use real drugs as placebos. Fam Med. 2010;42(9):636–642. Epub 2010/10/12.
[27] Milgram S. Behavioral study of obedience. J Abnorm Psychol. 1963;67:371–378. Epub 1963/10/01.
[28] Herrera CD. Ethics, deception, and 'those milgram experiments'. J Appl Philos. 2001;18(3):245–256. Epub 2002/05/02.
[29] Kisaalita N, Staud R, Hurley R, et al. Placebo use in pain management: the role of medical context, treatment efficacy, and deception in determining placebo acceptability. Pain. 2014;155(12):2638–2645. Epub 2014/10/01.
[30] Kisaalita NR, Robinson ME. Analgesic placebo treatment perceptions: acceptability, efficacy, and knowledge. Journal Pain. 2012;13(9):891–900. Epub 2012/08/03.
[31] Kisaalita NR, Roditi D, Robinson ME. Factors affecting placebo acceptability: deception, outcome, and disease severity. J Pain. 2011;12(8):920–928. Epub 2011/08/06.
[32] Chung SK, Price DD, Verne GN, et al. Revelation of a personal placebo response: its effects on mood, attitudes and future placebo responding. Pain. 2007;132(3):281–288. Epub 2007/03/21.
[33] Bialosky JE, George SZ, Horn ME, et al. Spinal manipulative therapy specific changes in pain sensitivity in individuals with low back pain. J Pain. 2014;15(2):136–148. Epub 2013/10/27.
[34] Wade JB, Dougherty LM, Archer CR, et al. Assessing the stages of pain processing: a multivariate analytical approach. Pain. 1996;68(1):157–167. Epub 1996/11/01.
[35] Gagliese L, Weizblit N, Ellis W, et al. The measurement of postoperative pain: a comparison of intensity scales in younger and older surgical patients. Pain. 2005;117(3):412–420.
[36] Jensen MP, Karoly P, Braver S. The measurement of clinical pain intensity: a comparison of six methods. Pain. 1986;27(1):117–126.
[37] Fairbank JC, Pynsent PB. The Oswestry disability index. Spine (Phila Pa 1976). 2000;25(22):2940–2952; discussion 52. Epub 2000/11/14.
[38] Changulani M, Shaju A. Evaluation of responsiveness of Oswestry low back pain disability index. Arch Orthop Trauma Surg. 2009;129(5):691–694. Epub 2008/06/04.
[39] Fritz JM, Irrgang JJ. A comparison of a modified Oswestry Low Back Pain Disability Questionnaire and the Quebec Back Pain Disability Scale. Phys Ther. 2001;81(2):776–788. Epub 2001/02/15.
[40] Frost H, Lamb SE, Stewart-Brown S. Responsiveness of a patient specific outcome measure compared with the Oswestry Disability Index v2.1 and Roland and Morris Disability Questionnaire for patients with subacute and chronic low back pain. Spine (Phila Pa 1976). 2008;33(22):2450–2457; discussion 8. Epub 2008/10/01.
[41] Childs JD, Fritz JM, Flynn TW, et al. A clinical prediction rule to identify patients with low back pain most likely to benefit from spinal manipulation: a validation study. Ann Intern Med. 2004;141(12):920–928.
[42] Flynn T, Fritz J, Whitman J, et al. A clinical prediction rule for classifying patients with low back pain who demonstrate short-term improvement with spinal manipulation. Spine. 2002;27(24):2835–2843.
[43] Price DD, Milling LS, Kirsch I, et al. An analysis of factors that contribute to the magnitude of placebo analgesia in an experimental paradigm. Pain. 1999;83(2):147–156.
[44] Evans JD. Straightforward statistics for the behavioral sciences. Pacific Grove (CA): Brooks/Cole Publishing; 1996.
[45] Bishop FL, Jacobson EE, Shaw JR, et al. Scientific tools, fake treatments, or triggers for psychological healing: how clinical trial participants conceptualise placebos. Social Sci Med (1982). 2012;74(5):767–774. Epub 2012/01/31.

[46] Kaptchuk TJ, Shaw J, Kerr CE, et al. "Maybe I made up the whole thing": placebos and patients' experiences in a randomized controlled trial. Cult Med Psychiatry. 2009;33(3):382–411. Epub 2009/07/15.
[47] Fassler M, Gnadinger M, Rosemann T, et al. Use of placebo interventions among Swiss primary care providers. BMC Health Serv Res. 2009;9:144. Epub 2009/08/12.
[48] Howick J, Bishop FL, Heneghan C, et al. Placebo use in the United Kingdom: results from a national survey of primary care practitioners. Plos One. 2013;8(3):e58247. Epub 2013/03/26.
[49] Kaptchuk TJ, Kelley JM, Conboy LA, et al. Components of placebo effect: randomised controlled trial in patients with irritable bowel syndrome. BMJ. 2008;336(7651):999–1003.
[50] Kalauokalani D, Cherkin DC, Sherman KJ, et al. Lessons from a trial of acupuncture and massage for low back pain: patient expectations and treatment effects. Spine. 2001;26(13):1418–1424.
[51] Ferreira PH, Ferreira ML, Maher CG, et al. The therapeutic alliance between clinicians and patients predicts outcome in chronic low back pain. Phys Ther. 2013;93(4):470–478.
[52] Artus M, van der Windt DA, Jordan KP, et al. Low back pain symptoms show a similar pattern of improvement following a wide range of primary care treatments: a systematic review of randomized clinical trials. Rheumatology (Oxford, England). 2010;49(12):2346–2356. Epub 2010/08/18.
[53] Chou R, Huffman LH. Nonpharmacologic therapies for acute and chronic low back pain: a review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline. Ann Intern Med. 2007;147(7):492–504.
[54] Preference Collaborative Review G. Patients' preferences within randomised trials: systematic review and patient level meta-analysis. BMJ. 2008;337:a1864. Epub 2008/11/04.
[55] Myers SS, Phillips RS, Davis RB, et al. Patient expectations as predictors of outcome in patients with acute low back pain. J Gen Intern Med. 2008;23(2):148–153.
[56] Kaptchuk TJ, Friedlander E, Kelley JM, et al. Placebos without deception: a randomized controlled trial in irritable bowel syndrome. Plos One. 2010;5(12):e15591. Epub 2011/01/05.
[57] Carvalho C, Caetano JM, Cunha L, et al. Open-label placebo treatment in chronic low back pain: a randomized controlled trial. Pain. 2016;157(12):2766–2772. Epub 2016/10/19.
[58] Kisaalita NR, Hurley RW, Staud R, et al. Placebo use in pain management: a mechanism-based educational intervention enhances placebo treatment acceptability. Journal Pain. 2016;17(2):257–269. Epub 2015/11/26.
[59] Blease C, Colloca L, Kaptchuk TJ. Are open-label placebos ethical? Informed consent and ethical equivocations. Bioethics. 2016;30(6):407–414. Epub 2016/02/04.