A comparison of open-label and deceptive placebo analgesia in a healthy sample

Authors: Nathan Disley, MSc[1], Susanna Kola-Palmer, PhD[1] & Chris Retzler, PhD[1]

Affiliations: [1]Department of Psychology, University of Huddersfield, Huddersfield, UK.

Corresponding author: Chris Retzler

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Abstract

Objectives

A small number of studies have supported the efficacy of open-label placebos (OLPs) in reducing pain. However, research comparing the effectiveness of OLPs with deceptive placebos (DPs) is limited, and the relative impact on pain tolerance versus intensity are not yet understood. This study therefore, examined the effectiveness of a nasal placebo administered openly and deceptively on pain intensity and tolerance during a cold pressor test (CPT).

Method

75 healthy participants were allocated to one of three groups; OLP (n = 25), DP (n = 26) and no-treatment (NT; n = 24). A pre-test post-test design was used, with all participants completing a baseline and post-treatment CPT, following placebo administration in the treatment groups.

Results

A one-way ANCOVA revealed significant differences between groups for pain intensity, with planned contrasts revealing that this effect was driven by an increase in pain intensity scores for the NT group within the post treatment CPT, which was not evident in the OLP and DP groups. There were no significant differences between groups for changes in pain tolerance.

Conclusion

The increase in pain intensity reported within the post-treatment CPT in the NT group was not apparent in either the OLP or DP groups, with no significant differences between OLP and DP effectiveness. These findings suggest that deception may not be necessary for effective placebo treatment and have implications for the management of pain.

Keywords: open-label, placebo, deception, analgesia, pain

1. Introduction

Patient reports of pain can be effectively reduced by the use of placebos (1). However, there are ethical debates surrounding the use of deceptive placebos (DPs) for treatment purposes (2). A growing body of evidence now suggests that deception may not be necessary, with open-label placebos (OLP) being shown to be effective in treating a wide variety of disorders such as Attention-Deficit/Hyperactivity Disorder (3), irritable bowel syndrome (4), cancer-related fatigue (5,6), depression (7), allergic rhinitis (8,9), and inducing placebo analgesia within clinical samples (10,11). Despite this body of evidence supporting the effectiveness of OLPs, few studies have compared OLPs with DPs to assess their relative efficacy (12–14).

Two recent studies comparing OLP and DP analgesia using heat pain found mixed evidence for the support of OLPs being as effective as a DPs in reducing pain intensity ratings and increasing pain tolerance in samples of healthy participants (13,14). We aimed to extend knowledge from previous studies by exploring the effectiveness of OLPs and DPs within a cold pressor test (CPT). The pain induced by the CPT is thought to mimic chronic pain, and affects both the skin and deeper structures of the hand and forearm (15), in contrast to the contact heat method used by previous research, which consists of brief presentations of noxious stimuli to a small area of the skin.

The current study utilised a saline nasal spray, administered openly, and deceptively, prior to completing a CPT. The aim of this novel approach was to compare the analgesic effect of the placebos administered openly and deceptively, against a no-treatment (NT) group in reducing subjective pain intensity and increasing pain tolerance.

2. Materials and methods

2.1. Participants

Participants were screened for medical conditions which might be exacerbated by the CPT; including cardiovascular problems, arthritis, diabetes, fibromyalgia, Reynaud's Disease, or circulatory problems (16). 104 healthy participants were initially recruited for this study. As the CPT had a maximum immersion time of three minutes, only those participants who removed their hand from the CPT in less than 160 seconds in the baseline CPT, were included for further analysis. This criterion allowed for a substantial increase in pain tolerance in the second CPT, without which increases would not have been detectable (17). Of the remaining 75 participants, 65 were female, and were aged between 18 and 54 years old (mean = 21.05, SD = 5.04). Participants were assigned to one of three experimental groups using a quasi-random assignment: OLP (n = 25), DP (n = 26) and NT

(n = 24). Ethical approval for the study was granted by the host institution's ethics committee. The study was not intended as a clinical trial as it used healthy participants and induced pain as opposed to a clinical test of a pain reduction method.

2.2 Procedure and Measures

Pain was induced using a CPT whereby participants placed their left hand in cold water at 3 degrees Celsius (18). They were informed that they should withdraw their hand when they could no longer withstand the pain. A constant temperature was maintained using a circulatory water bath (Medline RW-2025). Two measures were recorded for each CPT; pain tolerance and pain intensity. The pain tolerance measurement consisted of the amount of time, in seconds, participants immersed their hand within the CPT, with the maximum time permitted being 180 seconds (16). Once participants removed their hand, they were asked to rate the peak pain experienced during the CPT, using a visual analogue scale ranging from 0-100, with 0 representing no pain sensation and 100 representing the most intense pain imaginable (13).

A pre-test post-test design was used with all participants completing a baseline and post-treatment CPT with a 15-minute interval between CPTs. After the baseline CPT, participants completed a survey lasting 5-10 minutes (not reported here) and an unrelated reading task. Participants in the NT group completed a second CPT, with no rationale provided.

Participants in the treatment groups were asked to stop the reading task after 12 minutes, allowing 3 minutes for them to read additional materials. Those in the OLP group were given a placebo information sheet including several statements to increase participants' expectation of pain relief, similar to the rationale given in previous research (13). Participants were informed the placebo contained no pain-killing properties, however, they may still experience pain relief, given previous research has demonstrated that placebos can reduce pain, even when administered openly. Finally, participants were informed that having a positive attitude may improve the placebo's effectiveness, however, it is not necessary (13).

Participants in the DP group were given a painkiller information sheet informing them that they were going to be given an analgesic nasal spray, containing Lidocaine, the main ingredient used in a painkiller from Switzerland (in line with previous research, 13). Participants were informed the painkiller's effectiveness had been tested worldwide and takes approximately 30 seconds to induce analgesic effects.

Participants in the OLP and DP groups then administered a saline nasal spray and completed a post-treatment CPT, 30 seconds after placebo administration. Finally, participants were fully debriefed. The experimenter was male and consistent for all participants.

3. Results

Two one-way ANCOVAs were conducted with treatment group (OLP, DP and NT) entered as the independent variable, the post-treatment measurement of pain tolerance or intensity entered as the dependent variable, and the corresponding baseline measure inputted as a covariate to account for any differences between groups at baseline[1].

A one-way ANCOVA revealed no significant differences between groups within post-treatment pain tolerance, $F(2, 71) = 1.90$, $p = .16$, $\eta^2 = .05$, with baseline pain tolerance being a significant covariate, $F(1, 71) = 196.26$, $p < .001$, $\eta^2 = .73$. See *Table 1* for descriptive statistics.

A further ANCOVA revealed a significant difference between groups for post-treatment pain intensity, $F(2, 71) = 4.84$, $p = .01$, $\eta^2 = .12$, with baseline pain intensity being a significant covariate, $F(1, 71) = 173.41$, $p < .001$, $\eta^2 = .71$. Planned contrasts revealed significant differences between the OLP and NT groups ($p = .02$, 95% CI [-13.69, -1.19]) and the DP and the NT groups ($p = .005$, 95% CI [-15.70, -2.95]), demonstrating OLPs and DPs were both effective. Furthermore, contrasts revealed no differences between the effectiveness of the OLP and DP ($p = .56$, 95% CI [-4.49, 8.26]). See *Table 1* for descriptive statistics.

Table 1. Table showing the means and standard deviations for pain tolerance times and pain intensity ratings for each group.

		Baseline CPT			Post-treatment CPT		
		OLP	DP	NT	OLP	DP	NT
Pain Tolerance (Seconds)	Mean (SD)	48.36 (26.20)	39.50 (22.05)	46.50 (27.15)	58.76 (46.65)	46.85 (33.94)	46.04 (36.71)
Pain Intensity[a]	Mean (SD)	61.60 (20.67)	48.23 (19.88)	59.79 (17.66)	61.72 (20.01)	48.15 (22.98)	67.58 (16.93)

Notes: [a] despite participants removing their hands from the cold pressor prior to 180 seconds, none reported an intensity score of 100 suggesting that the results were not due to a ceiling effect.

[1] To assess differences at baseline between our groups we ran two one-way ANOVA's on the baseline CPT scores for pain intensity and pain tolerance. There was no effect of group for pain tolerance ($F(2, 74) = .88$, $p = .42$) but there was an effect of group for pain intensity ($F(2, 74) = 3.54$, $p = .03$, $\eta^2 = .09$). Post hoc comparisons revealed a marginally significant difference between only the OLP and DP groups ($p = .05$).

4. Discussion

Using the CPT to induce pain in healthy participants and a novel nasal spray placebo, we found that the increase in pain intensity within the post-treatment CPT that was reported in the NT group was not apparent in either of the placebo administration groups; thus, the placebos effectively prevented the increase in pain intensity within the post-treatment CPT. This finding adds to the existing literature demonstrating that OLP's can effectively reduce symptoms and pain (3–11).

Interestingly, OLPs and DPs did not significantly increase pain tolerance. This finding, along with those of Locher et al. (13) suggests that OLPs mainly impact subjective pain outcomes within healthy samples. However, these findings contrast with those of Kube et al. (14) who found a reduction in pain intensity for only the DP group, with both OLPs and DPs increasing pain tolerance. The second important finding from this study was that there were no significant differences between OLP and DP effectiveness in reducing pain intensity. These findings are consistent with a recent study showing that DPs and OLPs, with a rationale, are similarly effective in reducing pain intensity (13).

To address some limitations, with this study utilising healthy participants, it is important to consider that placebo effects may be underestimated as placebo effects may be stronger within clinical samples (19). Furthermore, this study's sample size was relatively small and future studies should therefore, collect larger samples to provide greater confidence in the results. In order to better understand the effects of our placebos, it would be useful for future studies to record a measure of the expectation of pain relief. Finally, it is important to consider that tolerance and intensity were not independent of each other, however, analysis revealed no correlations between these measures.

These results add to a small body of literature suggesting that, not only are placebos effective at reducing reported pain intensity, but deception may not be necessary for a reduced pain experience. These findings, along with a growing body of evidence, have implications for clinical care and suggest that clinicians could consider non-deceptive placebo medication to enhance treatment outcomes.

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