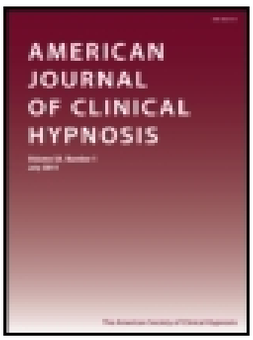

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On Suggestibility and Placebo: A Follow-Up Study

Michael Lifshitz
McGill University, Montreal, QC, Canada; and Chapman University, Irvine, California, USA

Eli O. Sheiner, Jay A. Olson, and Rémi Thériault
McGill University, Montreal, QC, Canada

Amir Raz
McGill University, Montreal, QC, Canada and Jewish General Hospital, Montreal, QC, Canada; and Chapman University, Irvine, California, USA

Identifying what makes some people respond well to placebos remains a major challenge. Here, we attempt to replicate an earlier study in which we found a relationship between hypnotic suggestibility and subjective ratings of relaxation following the ingestion of a placebo sedative (Sheiner, Lifshitz, & Raz, 2016). To assess the reliability of this effect, we tested 34 participants using a similar design. Participants ingested a placebo capsule in one of two conditions: (1) relaxation, wherein we described the capsule as a herbal sedative, or (2) control, wherein we described the capsule as inert. To index placebo response, we collected measures of blood pressure and heart rate, as well as self-report ratings of relaxation and drowsiness. Despite using a similar experimental design as in our earlier study, we were unable to replicate the correlation between hypnotic suggestibility and placebo response. Furthermore, whereas in our former experiment we observed a change in subjective ratings of relaxation but no change in physiological measures, here we found that heart rate dropped in the relaxation condition while subjective ratings remained unchanged. Even within a consistent context of relaxation, therefore, our present results indicate that placebos may induce effects that are fickle, tenuous, and unreliable. Although we had low statistical power, our findings tentatively accord with the notion that placebo response likely involves a complex, multifaceted interaction between traits, expectancies, and contexts.

Keywords: hypnosis, personality, placebo, self-regulation, suggestion

Elucidating predictors of good placebo response is a pressing concern for clinical science (Enck, Bingel, Schedlowski, & Rief, 2013). A growing body of evidence shows that responsiveness to placebo fluctuates as a function of individual differences and context (Horing, Weimer, Muth, & Enck, 2014). And yet, whereas personality, genetics, and brain physiology may shape placebo response in specific contexts

Address correspondence to Amir Raz, Clinical Neuroscience and Applied Cognition Laboratory, Institute for Community and Family Psychiatry, SMBD Jewish General Hospital, 4333 Cote Ste. Catherine Road, Montreal, Québec H3T 1E4, Canada. E-mail: amir.raz@mcgill.ca

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(Darragh, Booth, & Consedine, 2016; Hall, Loscalzo, & Kaptchuk, 2015; Wager, Atlas, Leotti, & Rilling, 2011), the reliability of such determinants tends to waver when comparing across situations (Darragh, Booth, & Consedine, 2015; Kelley et al., 2009). For example, Whalley, Hyland, and Kirsch (2008) reported that individual reliability of placebo response depended on the label of a placebo cream: analgesic responses were similar when comparing different administrations of the same cream but inconsistent when the cream had a different label. In line with such findings, recent models of placebo response typically adopt a multifaceted approach emphasizing interactions between traits, expectancies, and contexts (Darragh et al., 2015; Horing et al., 2014; Weimer, Colloca, & Enck, 2015).

Beyond the complex relationship linking individual differences and placebos, the broader field of psychology faces a replication crisis wherein many reported findings may reflect false positives rather than stable effects (Open Science Collaboration, 2015). Thus, here we briefly report a follow-up on an earlier study from our group probing personality correlates of placebo response (Sheiner, Lifshitz, & Raz, 2016). Our previous experiment demonstrated a relationship between the personality trait of hypnotic suggestibility and subjective ratings of relaxation after ingesting a placebo sedative. Because the relationship between placebo response and personality remains contentious and seems highly sensitive to contextual nuances, the present study probed whether our results would hold up in a replication using similar materials and comparable sample size albeit with minor procedural variations.

Methods

Procedure

Participants were recruited from an undergraduate psychology course taught by the principal investigator (AR). As part of regular course lectures, 117 students completed the Harvard Group Scale of Hypnotic Susceptibility, Form A (scored from 1–11, HGSHS:A; Shor & Orne, 1962). Thirty-four of these students (22 females; age: 20.8 ± 0.97 years [mean ± SD], range: 19–24 years) also completed the placebo component of our study for course credit. In this final sample, the average hypnotic suggestibility score was 6.1 ± 2.3, with a range of 3–10. The placebo component had occurred at an earlier date, in a separate location, and without any mention of linkage to the subsequent measure of hypnotic suggestibility. All participants provided written informed consent and reported abstaining from both caffeine and sedatives for at least 4 hours before the placebo component of the study.

In the placebo component, we randomized participants into two conditions involving different consent forms, audio-visual and verbal instructions, and pill bottles to induce distinct expectations. Participants in the control condition (n = 19) ingested an inert placebo capsule under the impression that they were part of a no-treatment control.

Participants in the relaxation condition (n = 15) consumed an identical capsule under the impression that they were receiving a strong dose of valerian, a common herbal sedative.

As a manipulation check, immediately after ingesting the pill, participants rated how much they expected the pill to affect their mood, energy level, heart rate, and blood pressure. Each of these questions used a 5-point Likert scale ranging from 1 (*not at all*) to 5 (*extremely*). After analysis of the results, the control condition scored 1.3 (bootstrapped 95% CI [1.1, 1.6]) and the relaxation condition scored 2.6 [2.2, 3.0]; these values resembled those of our previous study. The groups, thus, differed in their expectation (Wilcoxon-Mann-Whitney z = 4.06, p < .001), proposing that the experimental manipulation was successful.

Measures

We collected subjective and objective measures of relaxation at two times: immediately before ingesting the pill and 30 min after ingestion. For the subjective measures, we assessed relaxation and drowsiness. Both of these measures consisted of Likert scale items (e.g., "calm," "drowsy") based on an earlier principal component analysis (Sheiner et al., 2016). The internal consistency reliability for each of these measures was acceptable: Cronbach's α was .75 [.54, .96] for relaxation and .85 [.69, 1.00] for drowsiness. We then calculated differences for each individual from pre- to post-ingestion (post minus pre). These difference variables did not correlate (r(32) = .084 [–.262, .410], p = .638). We also measured objective placebo response by calculating pre-to-post differences in systolic blood pressure, diastolic blood pressure, and heart rate (for details, see Sheiner et al., 2016). We aimed to test the relationships between hypnotic suggestibility and these subjective and objective measures. Given our small sample size, statistical power was low: we only had a 19% chance of detecting an effect of the same magnitude as in our previous study (r = .292).

Results

Unlike in our earlier study (Sheiner et al., 2016), here hypnotic suggestibility showed no relation to drowsiness or relaxation (see Appendix A). However, we did find an effect on heart rate in the predicted direction. Participants in the relaxation group showed an average heart rate decrease of 12 [9, 14] beats per minute (from 78 to 66); participants in the control group decreased by only 5 [2, 7] beats (from 71 to 66; Figure 1). This effect was large, with the groups differing by 1.3 [0.5, 2.0] standard deviations (Hedges' g). See Table 1 for descriptive statistics (for main and interaction effects, see Appendix B).

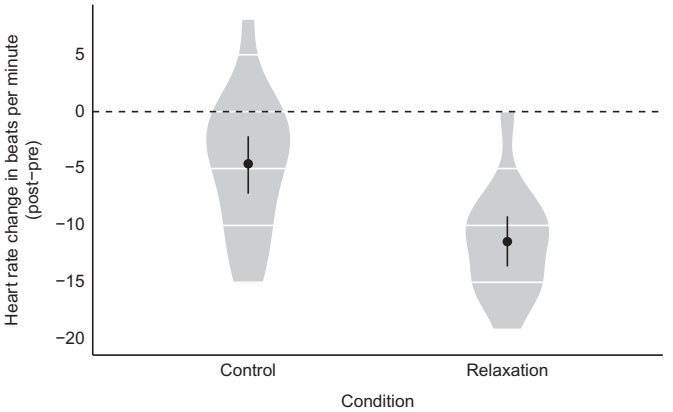

FIGURE 1 Change in heart rate between conditions. Dots show means, width shows frequency, and error bars show 95% bootstrapped Confidence Intervals. The dashed line represents no change.

TABLE 1
Mean Changes (Post Minus Pre) by Condition in Physiological and Subjective Measures in Raw Units

	Control	*Relaxation*
Heart rate	−4.684	−11.533
(beats per minute)	[−7.212, −2.211]	[−13.667, −9.332]
Systolic blood pressure	1.895	−0.867
(mm HG)	[−0.949, 5.212]	[−3, 1.335]
Diastolic blood pressure	−2.316	1.067
	[−5.316, 0.053]	[−4.402, 8.735]
Subjective relaxation	2.526	1.867
	[0.895, 4.316]	[0.133, 4.202]
Subjective drowsiness	1.737	1.933
	[−0.105, 3.789]	[0.067, 3.802]

Note. Square brackets show bootstrapped 95% Confidence Intervals.

Discussion

In this follow-up study, we attempted to replicate our earlier finding showing that hypnotic suggestibility correlated with subjective relaxation in response to a placebo branded as a herbal sedative (Sheiner et al., 2016). Despite employing a similar procedure and identical experimental materials, in the present effort we did not observe the same effects (for a list of methodological differences between the two studies, see Table 2). Though our sample size was small, our findings coalesce with other accounts reporting a lack of robust correlation between placebo response and hypnotic suggestibility (Baker & Kirsch, 1993; Frischholz, 2007; Hilgard & Hilgard, 1975; Lund et al., 2015; McGlashan, Evans, & Orne, 1969).

TABLE 2
Methodological Differences Between Our Earlier Study (Sheiner et al., 2016) and the Present Replication Effort

	Earlier study (Sheiner et al., 2016)	*Present replication effort*
Sample size	50 (22 relaxation, 28 control)	34 (15 relaxation, 19 control)
Order of procedures	Hypnotic suggestibility measure first, then placebo component at a later date	Placebo component first, then hypnotic suggestibility measure at a later date
Course from which we recruited participants	Lower-level undergraduate course on critical thinking in psychology	Upper-level undergraduate course focusing on the cognitive neuroscience of self-regulation
Time of experiment	Spring	Fall
Experimenters	Authors collected data	Authors trained assistants to collect data
Medium of self-report for the placebo component	Paper and pencil	Web-based form

Note. Other procedural factors (e.g., location, audiovisual instructions, consent forms) and sample characteristics (e.g., age, hypnotic suggestibility scores, baseline heart-rate) remained consistent between the two studies.

The discrepancy between the present results and those of our earlier effort (Sheiner et al., 2016) underlines the complex interplay of individual differences (e.g., the personality trait of hypnotic suggestibility) and contextual parameters (e.g., expectations, situational variables) in determining placebo response (Darragh et al., 2015; Horing et al., 2014; Weimer et al., 2015). Supporting this interactionist perspective, one study found that suggestibility predicted placebo response only when expectations for response were strong (De Pascalis, Chiaradia, & Carotenuto, 2002). Moreover, whereas previous reports have emphasized how environmental nuances (e.g., the specific label of a placebo cream in Whalley et al., 2008) may govern individual response, here we observed that—even in a largely uniform context—the relationship between personality and placebo was tenuous.

In addition to the lack of replication concerning the correlation between hypnotic suggestibility and placebo response, here we observed a decrease in heart rate among participants in the relaxation condition—an effect absent from our previous study. Thus, whereas our earlier account showed that placebo ingestion impacted subjective but not physiological indices of relaxation (Sheiner et al., 2016), here we report the opposite pattern: placebos modulated physiological but not subjective measures. This inconsistency highlights how subjective experience may decouple from biological outcomes as a consequence of placebo intervention (Wechsler et al., 2011).

Speculating beyond our data, it may well be the case that subtle differences in sample characteristics drove the inconsistent results between our two studies (see Table 2). For example, participants in our earlier study were recruited from a lower-level undergraduate course and might have been less knowledgeable about placebo effects (Sheiner et al., 2016). They may have been more complacent about the laboratory environment and, thus, more susceptible to demand characteristics. Such differences might potentially account for why we observed subjective changes among the lower-level students in our earlier study but not among the upper-level students in the present replication effort. However, post-hoc *t*-tests revealed no significant differences in expectation ratings between the two samples.

Moreover, it seems hard to explain why only the higher-level students in the present study would have displayed physiological changes—especially given that baseline heart rate was statistically comparable between the two study samples. Thus, future investigations should clarify the potential influence of knowledge and education on placebo response.

The relationship between hypnotic suggestibility and placebo response remains elusive (Parris, 2016; Raz, 2007). Here, we were unable to replicate our earlier finding that hypnotic suggestibility correlated with subjective response to a placebo sedative (Sheiner et al., 2016). In a way, whereas previous studies proposed that placebo effects appear stable in context-specific situations (Whalley et al., 2008), our present results intimate that even within a consistent context of relaxation, personality predictors of placebo response may be unreliable. Nevertheless, the underpowered nature of our statistics forms a salient shortcoming of our current effort. Although we were unable to reproduce our previous findings, our small sample size herein limits the strength of our conclusions. To paraphrase a common research aphorism, lack of replication here does not imply replication of lack. The combination of our two studies —Sheiner et al. (2016) and the present account—should pique the investigative curiosity and whet the empirical appetite of many a researcher to further elucidate the stability and sustainability of good placebo response.

References

Baker, S. L., & Kirsch, I. (1993). Hypnotic and placebo analgesia: Order effects and the placebo label. *Contemporary Hypnosis*, *10*(3), 117–126.

Darragh, M., Booth, R. J., & Consedine, N. S. (2015). Who responds to placebos? Considering the "placebo personality" via a transactional model. *Psychology, Health & Medicine*, *20*(3), 287–295. doi:10.1080/13548506.2014.936885

Darragh, M., Booth, R. J., & Consedine, N. S. (2016). Trait predictors of placebo responses in itch. *Psychology, Health & Medicine*, *21*(6), 769–775.

De Pascalis, V., Chiaradia, C., & Carotenuto, E. (2002). The contribution of suggestibility and expectation to placebo analgesia phenomenon in an experimental setting. *Pain*, *96*(3), 393–402. doi:10.1016/S0304-3959(01)00485-7

Enck, P., Bingel, U., Schedlowski, M., & Rief, W. (2013). The placebo response in medicine: Minimize, maximize or personalize? *Nature Reviews. Drug Discovery*, *12*(3), 191–204. doi:10.1038/nrd3923

Frischholz, E. J. (2007). Hypnosis, hynotizability, and placebo. *American Journal of Clinical Hypnosis*, *50* (1), 49–58. doi:10.1080/00029157.2007.10401597

Hall, K. T., Loscalzo, J., & Kaptchuk, T. J. (2015). Genetics and the placebo effect: The placebome. *Trends in Molecular Medicine*, *21*(5), 285–294. doi:10.1016/j.molmed.2015.02.009

Hilgard, E. R., & Hilgard, J. R. (1975). *Hypnosis in the relief of pain*. Los Altos, CA: William Kaufmann.

Horing, B., Weimer, K., Muth, E. R., & Enck, P. (2014). Prediction of placebo responses: A systematic review of the literature. *Frontiers in Psychology*, *5*, 1079. doi:10.3389/fpsyg.2014.01079

Kelley, J. M., Lembo, A. J., Ablon, J. S., Villanueva, J. J., Conboy, L. A., Levy, R., … Kaptchuk, T. J. (2009). Patient and practitioner influences on the placebo effect in irritable bowel syndrome. *Psychosomatic Medicine*, *71*(7), 789. doi:10.1097/PSY.0b013e3181acee12

Lund, K., Petersen, G. L., Erlandsen, M., De Pascalis, V., Vase, L., Jensen, T. S., & Finnerup, N. B. (2015). The magnitude of placebo analgesia effects depends on how they are conceptualized. *Journal of Psychosomatic Research*, *79*(6), 663–668. doi:10.1016/j.jpsychores.2015.05.002

McGlashan, T. H., Evans, F. J., & Orne, M. T. (1969). The nature of hypnotic analgesia and placebo response to experimental pain. *Psychosomatic Medicine*, *31*(3), 227–246. doi:10.1097/00006842-196905000-00003

Open Science Collaboration. (2015). Estimating the reproducibility of psychological science. *Science*, *349* (6251), aac4716. doi:10.1126/science.aac4716

Parris, B. A. (2016). The prefrontal cortex and suggestion: Hypnosis vs. placebo effects. *Frontiers in Psychology*, *7*, 415. doi:10.3389/fpsyg.2016.00415

Raz, A. (2007). Hypnobo: Perspectives on hypnosis and placebo. *American Journal of Clinical Hypnosis*, *50*(1), 29–36. doi:10.1080/00029157.2007.10401595

Sheiner, E. O., Lifshitz, M., & Raz, A. (2016). Placebo response correlates with hypnotic suggestibility. *Psychology of Consciousness: Theory, Research, and Practice*, *3*(2), 146–153.

Shor, R. E., & Orne, E. C. (1962). *Harvard group scale of hypnotic susceptibility: Form A*. Palo Alto, CA: Consulting Psychologists Press.

Wager, T. D., Atlas, L. Y., Leotti, L. A., & Rilling, J. K. (2011). Predicting individual differences in placebo analgesia: Contributions of brain activity during anticipation and pain experience. *The Journal of Neuroscience*, *31*(2), 439–452. doi:10.1523/jneurosci.3420-10.2011

Wechsler, M. E., Kelley, J. M., Boyd, I. O., Dutile, S., Marigowda, G., Kirsch, I., … Kaptchuk, T. J. (2011). Active albuterol or placebo, sham acupuncture, or no intervention in asthma. *New England Journal of Medicine*, *365*(2), 119–126. doi:10.1056/NEJMoa1103319

Weimer, K., Colloca, L., & Enck, P. (2015). Placebo effects in psychiatry: Mediators and moderators. *The Lancet Psychiatry*, *2*(3), 246–257. doi:10.1016/S2215-0366(14)00092-3

Whalley, B., Hyland, M. E., & Kirsch, I. (2008). Consistency of the placebo effect. *Journal of Psychosomatic Research*, *64*(5), 537–541. doi:10.1016/j.jpsychores.2007.11.007

Appendix A

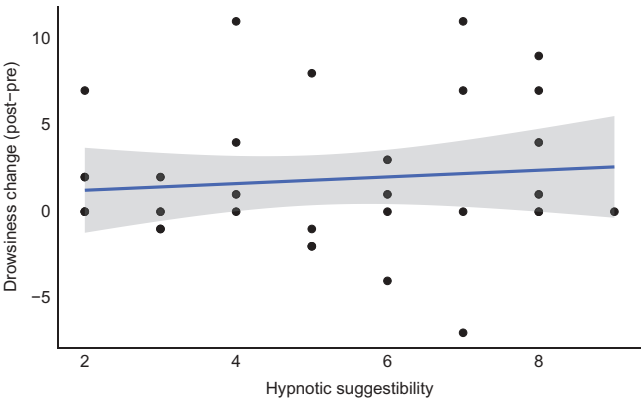

FIGURE A1 Correlation between subjective drowsiness change and hypnotic suggestibility scores. Each dot represents data from one participant. Shaded band shows 95% Confidence Interval.

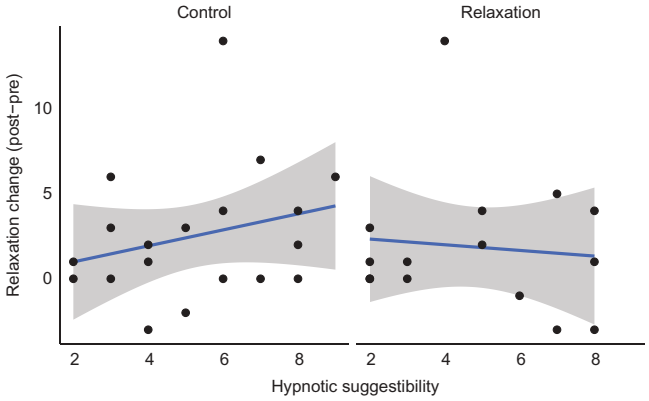

FIGURE A2 Correlations between subjective relaxation change and hypnotic suggestibility scores. Each dot represents data from one participant. Shaded bands show 95% Confidence Intervals.

Appendix B

Regression Tables for Relationships Between Hypnotic Suggestibility and Placebo Response, as Moderated by Condition

Measure/effect	*b**	*t*	*p*
Heart rate			
Condition	−1.073	−3.596	0.001
Hypnotic suggestibility	0.073	0.485	0.630
Interaction	−0.008	−0.027	0.978
Systolic blood pressure			
Condition	−0.494	−1.436	0.161
Hypnotic suggestibility	−0.165	−0.954	0.348
Interaction	0.197	0.562	0.578
Diastolic blood pressure			
Condition	0.310	0.876	0.388
Hypnotic suggestibility	−0.045	−0.253	0.802
Interaction	−0.137	−0.379	0.707
Relaxation			
Condition	−0.149	−0.419	0.678
Hypnotic suggestibility	0.093	0.521	0.606
Interaction	−0.367	−1.023	0.314
Drowsiness			
Condition	0.071	0.198	0.844
Hypnotic suggestibility	0.110	0.612	0.545
Interaction	0.103	0.283	0.779

Note. *b** refers to the standardized regression coefficient. Only heart rate showed an effect. The residual degrees of freedom for each full model was 30. We tested the main effects in the first step followed by the interaction in the second step.