The Placebo Effect and Declarative Memory

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Abstract

The placebo effect has been shown to have significant impacts across many psychological domains. This study investigated the impact of an expectancy-inducing placebo on declarative memory. 21 participants were asked to memorize a series of nonsense syllables after viewing either a memory-positive or memory-neutral placebo stimulus. Participants were also assessed on their knowledge of the placebo effect. No significant differences were observed in terms of memory performance between treatment and control, or across different levels of placebo knowledge; however, a significant interaction effect emerged, with larger treatment-control differences in those with higher levels of placebo knowledge. These results highlight the importance of expectancies in conscious processing.

Keywords: placebo effect, declarative memory

Introduction

The human mind may be one of the most powerful medicines that the world has to offer: through placebo effects, the brain itself can become an important tool in the healing process. With placebo treatments achieving compelling results in reducing pain, treating depression anxiety, and even improving academic performance, it only follows to think that placebo may also have a powerful effect on another fundamental aspect of human cognition--memory. In our modern world, with a rapidly-aging world demographic, the importance of studying memory cannot be understated. A study of British adults by Barker, Jones, Jennison (2018) found that nearly 20% of adults over age 50 reported experiencing noticeable memory loss; compounding this issue is the current lack of effective and easily-accessible treatment for those suffering from memory issues. Moreover, memory plays an important role in learning and knowledge acquisition in all age populations, not just older adults. Schater (2013) found that children and young adults with better memory, particularly in the conscious (declarative) domain, performed better in both occupational and educational settings. Memory, in other words, is a crucial yet often-ignored aspect of daily life.

The study and measurement of different types of memory have been operationalized through a variety of scales; however, one of the first and still most-commonly-used methods for assessing declarative memory is lists of nonsense syllables. Ebbinghaus (1885) pioneered this technique by documenting his retention of nonsense syllables over time to measure the processes of declarative memory. Nonsense syllables are particularly useful in research involving memory, due to the fact that such syllables have few to no associative ties in memory, which can eliminate extraneous variables related to past experience in memory-measuring experiments. In particular,

Hull (1993) identified several groups of nonsense syllables low on “meaningfulness”, which shared very few memory associations with words in ordinary language. This study utilizes such low-meaningfulness nonsense syllables to investigate the placebo effect and memory.

It is only recently that placebos themselves have become a subject of major scrutiny, rather than just a tool for researching other treatments and medications. Bendetti et al. (2005) defined the placebo effect as a psychobiological response to an inert treatment due to expectancies and conditioning effects. A few past studies have attempted to investigate placebos and memory; for example, Ashor (2011) studied the effect of placebo and beliefs on working memory. In this study, participants’ reaction times and task performance were measured by a computer program after taking a placebo cast as either a stimulant, an inert substance, or an unknown drug. Results showed that participants in the stimulant placebo condition had a significant effect improvement in working memory; those that believed they were taking a stimulant drug had faster reaction times and better recall for memory-sequencing tasks.

Most previous studies have used a similar paradigm as the study by Ashor. With this, an issue arises with the lack of inquiry into placebo and conscious memory processing. Declarative memory is arguably just as important, if not more, than unconscious working memory, in terms of impact on day-to-day life such as work and academics. As such, it is vitally important to understand the role expectancies can play in conscious memory. Moreover, the majority of past studies have relied on the so-called “sugar pill” to induce placebo effects, using fake drugs or injections in order to stimulate participants’ expectancies of cognitive change. However, this is a limited view of the placebo effect, as human expectancies can be influenced by many environmental and social factors outside of taking physical medication.

Since the placebo effect depends on expectancies, awareness of the placebo effect may cause changes in its effectiveness. For a long time, it was commonly believed that a person knowing about a placebo would render it ineffective. Recent research on so-called "open-label" placebos, though, has begun to counter this belief. In such "open-label" placebo treatments, participants are told that the treatment they are receiving is inert. In a landmark study by Carvalho (2016), researchers found that informing patients about a placebo still resulted in effective pain reduction. Applying this to the domain of memory, then, it follows that even participants who suspect a placebo may still experience enhanced memory when exposed to a memory-positive placebo.

The present study attempts to investigate both these questions--the impact of placebos in declarative memory, and the impact of placebo knowledge (PK) on the effectiveness of a placebo. Participants were exposed to an expectancy-inducing stimulus, either memory-positive or memory-neutral, and assessed through an objective self-report test of 20 nonsense syllables. Using nonsense syllables allows for the measurement of placebo effects on declarative memory, a conscious aspect of cognition, as compared to previous studies on working memory, emotion, or pain, which are relatively more difficult to consciously access and control. Additionally, rather than employing the "sugar-pill" paradigm, this study uses the technological integration of video and text to induce memory-enhancing expectancies. If effective, this could potentially allow for a more efficient and accessible method of enhancing memory, as compared to creating and administering mock drugs. This study also attempts to extend the concept of open-label placebos to a more general idea--the awareness and knowledge of any particular participant of the placebo effect itself.

The hypotheses investigated by this study are:

	Null Hypothesis	**Alternative Hypothesis**
Hypothesis 1 [memory ~ placebo + error]	Watching a placebo-inducing video will have no effect on participants' performance on a declarative memory task.	Watching a placebo-inducing video will increase participants' performance on a declarative memory task.
Hypothesis 2 [memory ~ placebo knowledge (PK) + error]	More knowledge about the placebo effect has no effect on memory.	More knowledge about the placebo effect will cause a change in memory performance, as compared to those with no knowledge about the placebo effect.
Hypothesis 3 [memory ~ placebo * placebo knowledge (PK)+ error]	Psychological knowledge has no effect on the placebo effect or memory.	For those with more knowledge about the placebo effect, the impact of the placebo effect on memory improvement will be reduced.

Table 1. Predictions.

Methods

For this study, 26 participants were recruited anonymously through an online survey platform, Qualtrics. However, 4 responses were discarded immediately due to incomplete answers, and one response was later removed due to an abnormally high number of missing fields. Thus, a total of 21 participants' data was included in the final analyses. A majority of participants were recruited from a large public college on the West Coast through an online thread, with additional data collection through personal referrals. The median age was 20, with a range from 15 to 58 years. The participant pool was heavily female-skewed, with 18 females (85%) and 3 males (15%). An option for participants to self-identify as another gender was not

used by any survey taker. No incentives were offered for participation. 12 participants were randomized into the treatment condition, and 9 into the control condition. Demographics for each group are shown below:

	Median Age	Gender Distribution
Treatment (n = 12)	20 (range: 15 - 51)	10 F, 2 M
Control (n = 9)	22 (range: 15 - 58)	8 F, 1 M

Table 2. Treatment and control demographics

The majority of data collection took place through Qualtrics, an online survey creator and distributor. Participants were linked to the survey through a generalized link, which randomized about 50% of redirects to the control survey, and the rest to the treatment survey. The survey began with a paragraph paired with a video. For those in the treatment (memory-positive placebo) condition, the introductory paragraph stated: “This study is investigating the effect of color on memory. Previous studies have shown that the color red boosts arousal and thus recall (Dzulkifli and Mustafar 2013, Loftus 1977, Tavalossi 2001). This study will explore this effect. Please watch this video below to begin the memory-enhancement process.” The control (memory-neutral placebo) group received the exact same survey and video, but with only a neutral message stating, “Please watch this video to test your device’s video capabilities”. A 10-second Youtube video of red text and images was then played.

After watching the video, participants were shown another video of 10 nonsense syllables, each at a 1.5-second interval. Immediately afterwards, participants were asked to recall as many of these syllables as possible, in any order, by filling out ten blanks as short-response questions. The “back” button on the survey was disabled after each video as to prevent cheating

by participants attempting to re-watch the video. The same process was then repeated with another group of 10 nonsense syllables.

After the assessment, participants answered additional demographic questions regarding age, sex, and education level, as well as a 3-item questionnaire about their knowledge about the placebo effect. The three items were:

1. Have you ever taken a psychology class? (Yes: only an intro class, Yes: upper-division/multiple, No)
2. Have you ever heard of the placebo effect? (Yes, no)
3. If yes, how familiar are you with the placebo effect? (not familiar at all, somewhat familiar, very familiar)

Finally, participants were debriefed with another short paragraph: "This study was actually investigating the placebo effect and memory. The placebo effect occurs when a person's beliefs affect some aspect of their physical or cognitive abilities. You were in the [control or treatment] group." The survey then terminated, with a final form for additional questions and concerns.

The primary measurement was participants' recall of nonsense syllables, the dependent variable. This was regarded as a highly valid method of measuring declarative memory, due to the use of a similar paradigm in numerous previous studies regarding declarative memory. The two sets of nonsense syllables were scored separately for accuracy, then combined into a twenty-point scale and z-scored. Only perfectly matching syllables were counted as correct; responses off by a single letter were scored as incorrect. The alpha reliability between scores on the two sets of nonsense syllables was 0.65. Participants' level of "placebo knowledge" (PK) was also assessed. The two multi-level questions, regarding placebo familiarity and previous

psychology classes, were scored on a normalized 0-4 point scale, with 4 indicating maximum PK. The second question (Have you ever heard of the placebo effect?) was excluded due to its high level of redundancy with the third question, as well as its categorical nature. The alpha-reliability of this scale was low, at only 0.43; this may partially be due to the low number of items included in this scale. However, despite low reliability, this measure was still included as part of the study, due to the face validity of its items.

Results

All continuous variables, including demographic, are summarized in the table below:

	Mean (± SD)	Range	**α**
Age	27.52 (± 14.78)	15 - 58	n/a
Placebo knowledge	2.24 (± 1.02)	1 - 4	0.43
Memory score	5.00 (± 2.57)	1 - 11 (20-pt scale)	0.65

Table 3. Descriptive statistics for continuous variables

Categorical measures included sex (18 F, 3 M), education level (college = 11, graduate school = 5, high school = 4, less than high school = 1), and if the participant had heard of the placebo effect (no = 1, yes = 20). Education level was initially collected as a variable of interest but not used in final analyses, due to a change in the direction of inquiry. The yes/no placebo measure was also excluded due to redundancy and the lack of variation in responses. There were no significant differences between treatment and control in any demographic variables.

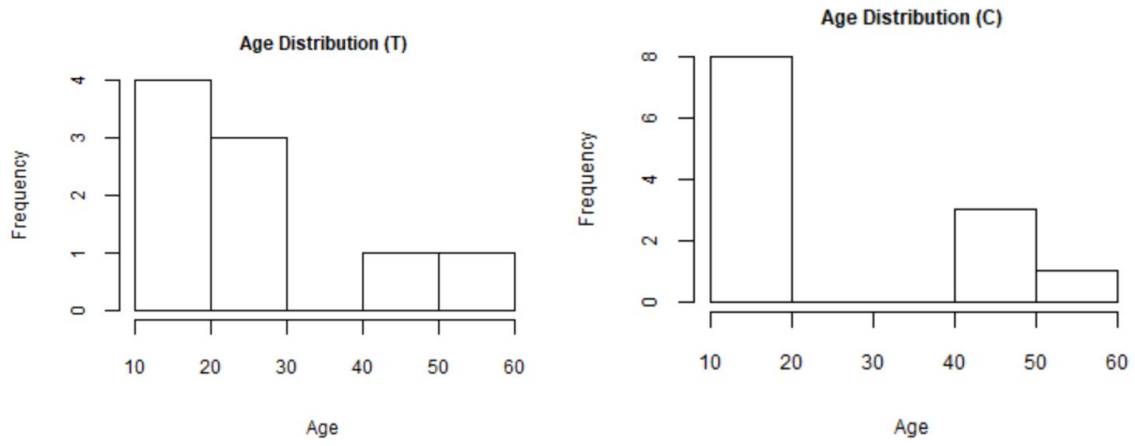

Figure 1. Age distribution across treatment and control conditions

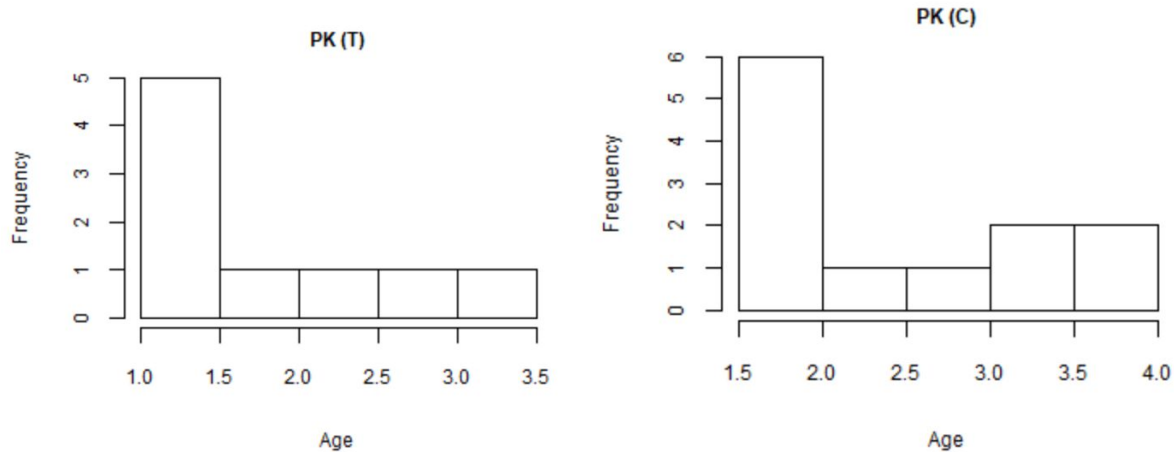

Figure 2. Placebo knowledge (PK) distribution across treatment and control

A standardized bivariate linear regression model was fitted to memory scores between the treatment and control groups. Contrary to Hypothesis 1, the treatment group actually performed worse on nonsense syllable recall (β = -.15); however, these results were not significant (t = -0.677, p = 0.506, R^2 = 0.024). This suggests that the experimental manipulation had little to no effect on memory scores, with condition explaining only about 2% of the variation in scores.

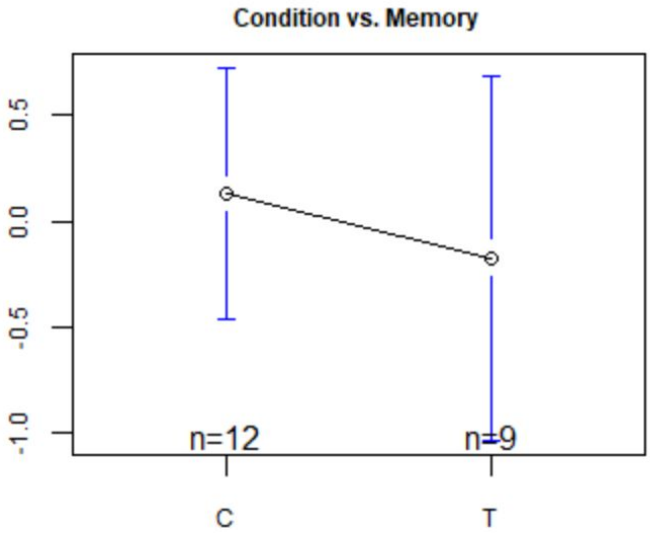

Figure 2. Scores in memory-positive vs. memory-neutral conditions

A second bivariate linear regression model was fitted to the continuous variable of placebo knowledge (PK). Contrary to Hypothesis 2, there was no significant relationship between PK and memory performance in either direction (β = 0.028, t = 0.125, p = 0.902, R^2 = 0.001). Thus, participants' level of knowledge about placebos had no impact on their declarative memory capabilities.

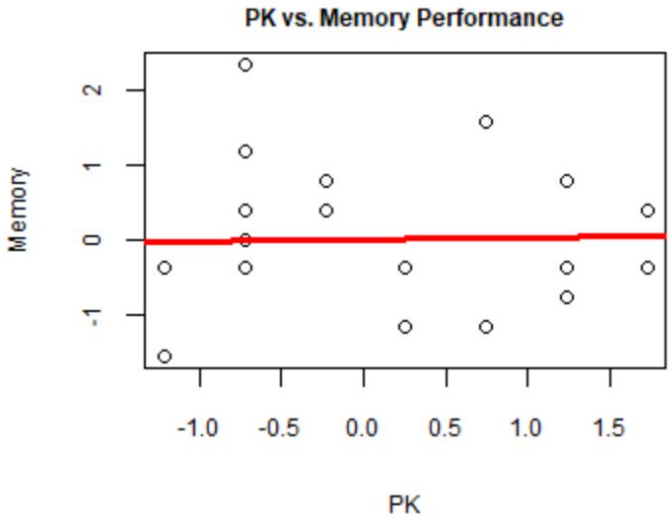

Figure 2. Standardized PK and Memory Scale Score

A multivariate linear regression model was run to observe any interaction effects between placebo knowledge (PK) and condition (treatment or control) on memory scale performance. A significant interaction effect was observed between condition and PK; namely, in the treatment group, those with higher levels of PK performed better on the memory test ($\beta_{interaction}$ = 1.306, t = 3.144, p = 0.006, R^2 = 0.383). This directly contradicts Hypothesis 3, which expected results in the opposite direction, in that at higher levels of PK, the difference between the treatment and control condition would decrease. The opposite was observed: in the control group, memory scale performance decreased with higher levels of PK (β = -0.547, t = -2.066, p = 0.066, R^2 = 0.299), while in the treatment group, memory scale performance increased with higher levels of PK (β = 0.658, t = 2.312, p = 0.054, R^2 = 0.433). This suggests that PK may have opposing effects depending on whether a memory-positive placebo is present; and that when present, PK has a significant interaction with the effectiveness of a placebo, explaining about 38% of the variation in memory scores.

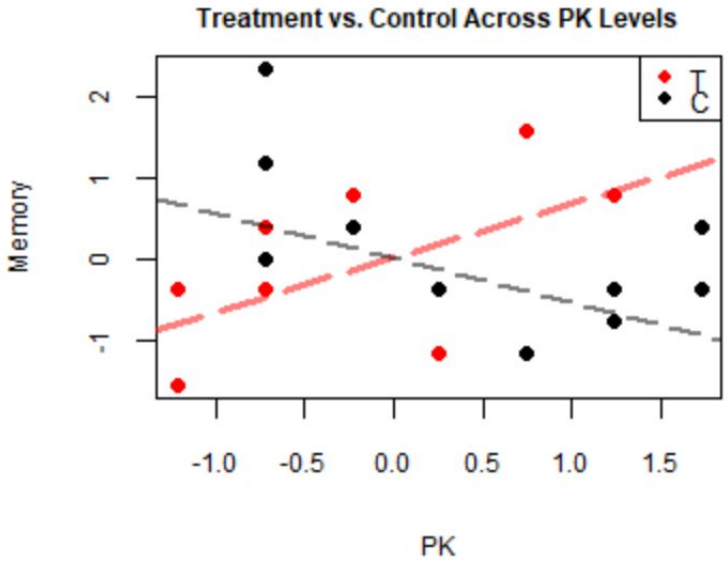

Figure 3. Interaction effect of PK and condition

The findings from each of the three models above are summarized in the following table:

DV = memory scale performance	**Model 1: Condition**	**Model 2: PK**	**Model 3: Condition * PK**
Condition	-0.151	--	-0.076
PK	--	0.029	0.064
Condition * PK	--	--	1.306 **
R^2	0.024	0.001	0.383
df	19	19	3, 17

Table 4. Z-scored bivariate and multivariate models

**** indicates p-value below 0.01**

Discussion

Results demonstrated that, contrary to the original hypotheses, a memory-positive placebo had no impact on declarative memory. There was a decrease in memory scores for the treatment group; however, this result was nonsignificant. Several factors could have contributed to the lack of significant results in regard to placebo manipulation, first of which is the small sample size (22 participants) and limited participant pool. A replication of the current study with a more diverse and larger group of participants could potentially yield different or more significant results. Additionally, unlike previous placebo studies that used physical pills or injections, the placebo in this study was administered virtually in the form of text and video; this may be a less effective form of inducing expectancies in participants. Future research will need to explore the effectiveness of different forms of placebos, and whether those other forms may cause more significant cognitive changes. Placebo knowledge (PK) alone also had no impact on memory scores as part of a bivariate model; this was relatively expected as there is no previous

research suggesting that simply having more knowledge about placebos or psychology will improve memory by itself.

However, in conjunction with the experimental placebo manipulation, PK had a significant effect on memory scores. This effect was in the opposite direction originally hypothesized, in that for the treatment group, performance increased with higher levels of PK. This contradicts some previous research, in which knowing about a placebo or suspecting a treatment was actually inert would render the placebo treatment ineffective. In light of more recent research, though this finding is not too surprising; many studies have found so-called "open-label" placebos to be effective. In other words, suspecting that a placebo treatment may still cause the treatment to induce placebo effects. In this study, participants with higher levels of PK performed better in the treatment group, but not in the control group. This suggests that this improvement is not due to external factors (for example, those with more knowledge about placebos also being more educated), but rather due to the experimental manipulation. One reason for this may be that the placebo effect may itself induce a kind of placebo effect--a "placebo placebo effect". In recent years, the placebo effect has become a relatively mainstream topic; thus, participants who suspected they were receiving a memory-positive placebo and had high levels of PK may have experienced increased expectations due to their expectations surrounding placebos, not necessarily due to the sham video treatment. Such a finding suggests, then, that the effectiveness of open-label placebos may be caused by a higher-order placebo effect--in other words, believing in the placebo effect may itself cause a placebo effect. Now that the placebo effect is relatively well-known by the general public, future studies will have to explore the expectancies surrounding placebos and their impact on cognitive change.

In several respects, however, this study was limited in its methods and generalizability. First of all, the sample size was small, and participants were limited to mostly college-age students and females, rather than a more representative sample of the general population. A larger, and more diverse, replication of this study will be necessary to confirm any results. Moreover, this study used an untested method of inducing placebo effects using video and text, rather than a traditional medication-based approach; this may have caused different or weaker expectancies in participants. The scale used to assess placebo knowledge (PK) also had very low alpha reliability and contained too few items to achieve full construct validity; thus, a future study with a more comprehensive and reliable assessment of PK may find different results. Additional research on how placebos can influence memory is critical in advancing the development of new, non-drug-based treatment for memory loss, as well as improving the daily functioning of all individuals. Memory and the placebo effect is now, more than ever, a relevant and critical topic that cannot be forgotten.

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