THE ACTIVATING PLACEBO EFFECT AND ITS USE IN TREATMENT

by

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Abstract

Prior studies have shown that placebos have had similar effects when treating symptoms of an illness or ailment. Placebo studies have shown that the placebo can reduce symptoms of the common cold, depression, phobias and many more ailments both biological and psychological. This proposed study will be on the fear of public speaking. The purpose is to build upon prior research of the placebo affect by introducing an *activating placebo effect*. Most placebo studies are conducted in such a way that the participants self-report a reduction in symptoms where they don't have to do anything but take the placebo and report back their symptom changes. An activating placebo effect is when the participants will have to actually do a task that involves facing their fear while undergoing their intervention. This way, the participants have taken as active role in reducing their symptoms. The hypothesis of this proposed study is that the participants will speak for longer on a public speaking task and will report less fear while performing the task. There will be 75 participants recruited through an online forum from a Northeastern public college. The participants will be randomly assigned into three groups of 25 each. The three groups are the Propranolol group, the open placebo group, and the no-treatment control group. Every participant must complete a brief 3 minute public speaking task twice, once at baseline and again a week later after their intervention. The first group will be given a placebo but is told it is propranolol, a drug performers take before going on stage, the second group will receive a placebo and told it is a placebo, while the third group will receive nothing. The researchers will ask the participants to fill out the Public

Speaking Anxiety Scale (PSAS) both time they perform the public speaking task and to rate their fear on a Likert scale of 1-7 on their level of fear once they stop performing the public speaking task. They are allowed to stop speaking at any point during the speaking task. The expected results are that the participants taking the placebo but believe it is propranolol will speak fro longer than the participants taking the placebo and know it is a placebo. The no-treatment control group is to prevent a nocebo effect which is the negative expectation of taking a placebo that can skew the results of the open placebo group. If these results are proven, it means that an activating placebo effect can be used to treat severe ailments without using an active substance.

A placebo is a substance or drug with no active medical ingredient, usually a sugar pill, that is given to a person for treatment of a certain ailment, such as anxiety, depression, headaches, or the common cold (Howick et al., 2013). The placebo effect is a psychological phenomenon where a belief or a mindset can alter how a person responds to a treatment and reduce physical symptoms. The placebo effect has been widely researched in the psychological field (Benedetti, 2014). The patient is usually told the placebo may be an active treatment for their symptoms which do become less severe or go away. The belief is the key component of a placebo. If the patient believes in the treatment, then their symptoms will be reduced with the placebo regardless of the inactive ingredient in the placebo. The placebo has been used on itch, phobias, depression, anxiety and many more ailments. These studies have proved that the placebo is effective in reducing symptoms (Kirsch et al., 2014).

Randomized controlled trials (RCT) are used to test the effectiveness of drugs and placebos. In an RCT of a drug, participants are randomly assigned to one of two groups. One group of participants are given the active drug, and another group is given the placebo. Most RCTs are double-blind, meaning that the participants don't know which substance they are being given; the placebo or the active drug. The placebo effect, however, is usually tested with a third group who is given no treatment. The placebo group gets compared to the treatment group to determine the effect of the treatment, while the placebo group gets compared to the no treatment group to determine the effect of the placebo.

Most placebo studies involve testing for passive symptom relief where the

participants self-report if their symptoms have been reduced. The participants do not have to do anything to reduce their symptoms, they just have to report if their symptoms were reduced by the treatment. In the current study, by contrast, the participants will have to take action in reducing their symptoms after taking a placebo. They will do so by participating in a public speaking task before treatment and after treatment to test if their public speaking anxiety levels have decreased. This will be measured by the duration of their public speaking task as well as self-reporting their anxiety levels.

The current proposed study focuses on social anxiety disorder. Social anxiety disorder is most common in college students (Barlow, D. & Durand, V.M. 2003) and is manifested especially in public speaking tasks. Social anxiety disorder can be very severe and often impairs students to perform due to the fear it can cause, especially when they are asked to speak publicly or present something. In the proposed study we would specifically manipulate the belief about the placebo to test if the belief that the placebo is a real drug will reduce public speaking fear. One group will believe it is a fear-reducing drug, a beta blocker, while the comparison group will be told it is a placebo. There will be a third no treatment group to test if their could be a nocebo effect; if the drug believing group speaks longer because the placebo group knows they have taken an inert substance. I hypothesize that the belief of the placebo is a beta blocker will reduce public speaking fear relative to the belief that the placebo is just a placebo. Before presenting how the hypotheses will be tested, I will first present a review of prior placebo studies in order or put the proposed study into

proper perspective.

Meta-analyses are an analysis of results of multiple studies. Howick et al. (2013) tested for differences between treatment and placebo effects across a wide range of medical conditions within similar randomized controlled trials. For each study, there were three groups: a treatment group, a placebo group, and a no treatment control group. The no treatment group is a control for the placebo group; it is necessary to measure the effect of the placebo. The results demonstrated that the treatment groups and the placebo groups had similar effect sizes in terms of how effective they were at reducing symptoms. This shows that across a variety of medical conditions, the effect size of placebos is quite similar to the effect sizes of active treatments. Placebos have as much of an effect on reducing symptoms as treatments. Indeed, about 50% of the effect of treatments can be attributed to the placebo effect. Thus, the psychological factors of medical treatments are as powerful as the treatments themselves.

Kirsch (1998) reviewed studies comparing the efficacy of antidepressants and the placebo effect. Across the clinical trials 83% of the anti-depressant drug effect were accounted for by the placebo effect. Meaning only 13% of the reduction in depression symptoms was due to the biologival effects of an anti-depressant. Most of the effect of anti-depressants is due to the placebo. Moreover, there was only a difference of two points on the Hamilton Depression Scale between the antidepressant and placebo groups. In another meta-analysis of 19 clinical trials, Kirsch (1998) found a .90 correlation between drug effects and placebo effects, showing that the

efficacy of placebos on patients was quite similar in reducing symptoms.

Other studies demonstrate the effect of placebos on specific medical conditions. This next article specifically tests the effect of placebos in the common cold. The purpose of this study (Barrett et al. 2011) was to test whether symptoms of the common cold would have different severity or duration based on its treatment, either echinacea or a placebo. Echinacea is an herbal remedy. There were 955 participants that had to present at least 2 common cold symptoms. There were 4 parallel groups in this experiment; one given no pill, one that was blinded to placebo, one that was blinded to echinacea, and one open label echinacea. The participants improved when they believed in the efficacy of the treatment, regardless of whether it was a placebo or echinacea. The conclusion of this study was that what the participants believe about a treatment is more important than the treatment itself. A limitation of this study was that echinacea recently received negative media attention, which could have impacted the results if the participants had seen the media attention.

The belief of the efficacy of a placebo versus a drug is researched as well to eliminate the possibility of a belief skewing the results. The purpose of this study was to test whether a person's belief of a drug versus a placebo had an effect on the treatment efficacy. There were 66 participants in this study that all suffered from migraines. They were told to rate their pain of one migraine with no treatment to serve as baseline data to compare the efficacy of the treatments. They then had 6 migraines randomized to six different treatment options. The treatment options were: given Maxalt (a migraine drug) labeled as Maxalt, given Maxalt labeled as placebo, and

given Maxalt labeled as Maxalt or placebo; given the placebo labeled as Maxalt, given the placebo labeled as placebo, and given the placebo labeled as Maxalt or placebo. The information given to the patients about which treatment they are receiving is meant to instill beliefs about the treatment, which in turn is supposed to affect the response to that treatment. Both treatments were most effective when labeled as Maxalt, and least effective when labeled as placebo. However, the efficacy of the drug was not different when the placebo was labeled as Maxalt or Maxalt labeled as placebo. When they took Maxalt but they believed it was a placebo, it reduced headache pain as much as when they took a placebo but believed it was Maxalt. This proves that positive information or beliefs of a treatment has a positive effect on headache pain and has as much of an effect as the actual treatment.

Expectations have been showed to influence the effect of placebos as well. The purpose of this study (Geers et al 2010) was to test if people that are optimistic will respond better to the expectation of a substance that reduces pain than pessimists. There were 116 participants that aged between 18 and 45 and all had no history of chronic pain. The participants were given a series of questionnaires that recorded their disposition of optimism or pessimism a month before they were to be given a cold pressor task. A month later they were randomly assigned to an expectation and no expectation condition prior to the task. The expectation group was told they were being given a topical cream that would reduce their pain, and the no expectation group were given a cream that they were told was just a cleansing balm and would not alter their pain. The cold pressor test is when participants are asked to put their hands

in freezing cold water then having them self-report their pain. The participants heart rate and blood pressure was measured before and during the task. The expectation/placebo intervention only worked for the optimists, and there was no effect on the pessimists. A limitation of this study is that there was not a no treatment group and that could have resulted in the possibility of a nocebo effect. There was no way to have known if the cleansing balm did not work due to a negative expectation in the group who knew they were getting a placebo.

Positive information in and of itself greatly influences the placebo effect even when people know they are receiving a placebo. If participants are given positive information about the placebo before they are given it, it tends to increase its efficacy. This study (Bartels 2017) tested the effects of an open label placebo on (OLPs) improving test anxiety and self-management skills more than a no-treatment control group. 58 students were allocated to a two week randomized controlled trial comparing an open-label placebo to no-treatment controls. For both groups, participant-provider interaction and the amount of contact time was held similar. After two weeks and before taking an exam, the researchers tested whether test anxiety and self-management abilities had changed. The results showed that open-label placebos reduced test anxiety and improved self-management skills before an academic exam compared to the control group with the same quality of interaction with advisers. Moreover, the improvement of the self-management resources in the OLP group was positively correlated with the exam results. Thus, the results suggest that an OLP treatment may improve self-management abilities and test anxiety.

Placebos have also been shown to test if nocebo effects occur. A nocebo effect is a negative reaction to a placebo so that participants do worse than the no treatment group due to a negative expectation about a placebo.The purpose of this study (Bartels 2017) was to test if a nocebo effect could be reduced by positive verbal suggestion. This randomized control trial had 129 participants . There were two phases to this study. The first phase was to induce a nocebo effect in all of the participants by giving them negative suggestions about the placebo, for example, “A placebo is not going to have a therapeutic effect”. In the second phase, the participants were divided into three groups; one was given positive information about the placebo, one was given negative suggestions about the placebo, and the third was given no suggestion about the placebo. Next, every participant got either a histamine injection to induce itching. Their severity of their itching was measured by self-report and observation. The experimental group that received positive suggestions about the placebo showed significantly smaller nocebo effects, so much so that the nocebo effect was actually reversed into a placebo effect; their amount of itching was reduced.

Placebos have been used in phobia studies as well. The participants believe they are receiving a real treatment when they are really receiving a placebo to show just how effective the placebo can be. For example, prior studies have shown that spider phobics avoid looking at pictures of spiders. The purpose of this study (Gremel 2018) was to see if a placebo could alter the eye tracking patterns of people with a spider phobia. There were 37 participants who were all women with arachnophobia. This used a within-subjects design in which each participant would look at a spider picture

and a control picture for 7 seconds. The measurements were the visual fixation count and dwell time. Half the participants were given a drug and told it was propranolol first and then given the placebo second, while the other half were told they were receiving the placebo first and propranolol second. The participants were split like that) to counterbalance the study, which controls for order effects and practice effects. The results showed that there was less visual avoidance and more visual approach behavior when the participants took the placebo but believed it was the drug. A major limitation of this study is the lack of a third, no treatment control group to rule out a possible nocebo effect.

Public speaking tasks cause severe anxiety for socially anxious people, especially college students. In the proposed study, we will be testing the effects of participants' anxiety levels during a public speaking task. We will be giving one group a placebo and telling them it is a beta blocker that professional performers take before going on stage to reduce fear. Another group will be given the placebo and told it is a placebo. A third control group will be given no treatment. Our hypothesis is that the group receiving the placebo but are being told it is a beta blocker will be able to speak for longer on the public speaking task, and rate a lower level of anxiety after their treatment, than the group who knows they took the placebo.

Methods

Participants:

In this proposed study there will be 75 undergraduate students from a public northeastern college that all have a fear of public speaking. They will take a fear of

public speaking questionnaire (described below) and score within the top 15%. Scoring within the top 15% means that their fear of public speaking is similar to that of people that are diagnosed with social anxiety disorder according to the DSM-V. There will be an average of 4:1 females versus males in the study. Every participant will receive either money or research credit towards their psychology course.

Experimental Design:

I will be conducting a randomized control trial on the effects of placebos on the fear of public speaking. There will be three groups in this experiment. The first group will be the drug-believing group. This group will be given a placebo, but told it is propranolol, a drug that performers take before going on stage too reduce anxiety. The second group will be given a placebo, and honestly told it is a placebo. This group is used to test the effect the placebo has when participants know they are receiving a placebo versus when they are not told they are taking a drug. The third group will be a no treatment group who receives no intervention. This group is compared to the placebo believing group to see if a nocebo effect occurs. A nocebo effect is a negative expectation about one knowing they are taking a placebo that is an inert substance. The belief that a participant is taking a placebo has a negative effect on behavior. All participants will be placed in a group randomly assigned to the groups with 25 in each group. Before taking the placebo, the drug-believing group will be given an article about how propranolol has helped performers and how they like how it reduces their fear. The open placebo group will read an article about placebos and their results. And the no treatment group will read a regular newspaper. The first and third groups are

blind in this study. Every participant will do a public speaking task at baseline to measure their level of fear as how long they speak for and again one week later right after the participants receive their intervention.

Measures

Each participant will take the the Public Speaking Anxiety Scale (PSAS; Bartholomay & Houlihan, 2016). The PSAS is a questionnaire to asses the anxiety level of each participant. The PSAS has been shown to be reliable and valid in measuring an individuals fear and anxiety of public speaking. The top 15% of scored in the distribution is an indicator that an individuals anxiety is similar to people who have Social Anxiety Disorder (SAD) as diagnosed by the DSM-5. This shows that the participants that score highly on the PSAS are likely to SAD. The PSAS measures the three components of public speaking anxiety; behavioral, cognitive, and physiological.

Each participant will complete a public speaking task once at the beginning of the experiment and again a week later after receiving their intervention. The purpose of this task is to measure the level of public speaking anxiety of the participants.
The public speaking task consists of asking the participants to stand in front of a stranger and speak about a topic, of their choosing, as long as they can within a three minute session. They are given a pen and paper and allowed to prepare and write notes their topic for three minutes. They are asked to stand up in front of the researcher and present their topic like when giving a real speech. They can use and look at their notes but must keep eye contact with the researcher. The participants are

told they can stop at any time but should try to speak for as long as they can and to stop when their anxiety becomes unpleasant to the point where they would stop in a real life situation. We will measure two things, the duration of each participants speech and a behavioral measure of their speaking fear. As soon as the participant stops speaking, we will measure their anxiety level because that will be when their speaking fear is at its peak. Participants will be asked to rate how much anxiety they are receiving right right after they stop speaking on a scale from 0-10: zero being "no fear at all", 5 being a "moderate but tolerable amount of fear", and 10 being "an intolerable amount of fear".

Procedure

This study will consist of two sessions that will be administered one week apart. In the first session, the researcher will have each participant take part in a public speaking task. In the second session, each participant will take the public speaking task again with their intervention to assess the changes in their fear level. The participants are randomly assigned into three groups: active placebo, placebo control, and no treatment.

In week one, the public speaking task is given (as described above) to collect a baseline measurement of the participants fear. The researcher will say to the participant: "*In the next part of the study, we want to find out when you start to feel anxious. In a few minutes, I would like you to give a 3-minute speech about a topic of your own choosing – anything that you feel comfortable talking about, and that you are familiar with. You will give the speech to me and to another person who will come*

into the room. No one is watching behind that mirror (point to mirror). *While it should be a 3-minute speech, you should stop giving the speech when you become fairly uncomfortable - the point at which you would usually want to leave the situation if it happened in your daily life. Otherwise, you should keep speaking – until you feel pretty uncomfortable. To stop the speech at any time, pick up this STOP sign next to you on this desk."* The participant will then be given 2 minutes to prepare a list of points they wish to make during their speech. While the participant gives their speech, the researcher will sit and watch while keeping a neutral facial expression throughout. The experimenter will record the participants speaking time and when the participant stops speaking, the researcher will ask them to give them a fear rating on a scale from from 0-10.

In week two, the participants will come back and will be assigned randomly into three groups. The researcher will speak to each group in the following The experimenter told participants who were randomly assigned to the active placebo group: "*Remember the task last week when you gave a speech? We are going to do that task again today. But before we do it, I want to give you something that will help you feel less afraid – a pill that is able to reduce fear. It is a beta-blocker called "propranolol". Performers commonly use it before they go on stage to reduce stage fright and other kinds of performance anxiety. The propranolol should help you feel less afraid and speak for a longer period of time. It does not have any negative effects. The only effect it has is to reduce fear. The effect lasts about 15 minutes. Would it be OK if I gave you the drug to take with a glass of water?"* - Experimenter also shows

the participant a white bottle labeled "Propranolol" as the experimenter introduces it. The experimenter then told the participant: "*It will take about 5-10 minutes for the pill to take effect. While we are waiting, please read this article. It's about propranolol."* – the participant is given a professional study report about the effects of propranolol. The researcher will remain in the room for seven minutes while the participants read the article. If the participant has any questions about the article the researcher tells them they will be answered at the end of the experiment.

The open placebo group is told, "*Remember the task last week when you gave a speech? We are going to do that task again today. By chance, you have been assigned to the placebo group. That means I'm going to ask if you are willing to take a placebo - an inactive, sugar pill - before we do the speaking task. The placebo does not have any negative effects at all. It is simply a sugar pill. Would it be OK if I gave the placebo to you to take with a glass of water?"* The researcher then explains that the participants will have to wait for a few minutes before doing the task and gives the participant a newspaper to read while they wait together for 7 minutes. Then the participants will be administered the public speaking task again.

The no treatment control group are only administered the public speaking task each week. In the debriefing, there will be a full account of the deception, and why some participants were deceived.

Discussion

The purpose of this proposed study is to test if a placebo effect will work to reduce symptoms associated with a fear of public speaking. We will test participants

in three groups: the placebo believing group, the open placebo group, and the no treatment control group. The placebo believing group will be deceived by the researchers telling them they are receiving propranolol, a fear-reducing drug that performers take before going on stage. The open placebo group is told they are receiving a placebo, and the no treatment control group is receiving no intervention. All participants will perform a public speaking task once at baseline and again one week later after receiving their intervention.

The predicted results are that at the second week the group that was given the placebo but told it was propranolol will speak longer than the open placebo group, and the open placebo group will speak longer than the no-treatment group. These results would support the hypotheses. However, if the open label placebo group spoke for a significantly shorter amount of time than the no treatment control group, then there is a likelihood that a nocebo effect occurred. A nocebo effect is the negative expectation of the participants being told they are being given a placebo, which interferes with the potential efficacy of the placebo.

If the hypotheses are confirmed, it would be the first indication of an activating placebo effect. This would potentially mean that treatments that use a placebo could be similarly effective for patients being prescribed active drugs. These results would be consistent with prior research done on the placebo effect, such as Kirsch's meta-analysis in 1998 and also the reduction of common cold symptoms as tested by Howick et al. (2013). These results would confirm that there is a therapeutic use for deception that is possible to be used as a treatment. Showing that placebos, presented

as real drugs, can have therapeutic effects on phobic behavior can be a major breakthrough for the psychology community.

As with all studies, there are some limitations to consider. One limitation of this study could be that the public speaking task causes too much fear. A solution to that would be to make the task less difficult by involving a more gradual increase in speaking time for the participants. Another limitation could be some participants not believing the deception, which would cause the researchers to rework the deception technique and make it more believable or the training of the researchers to be more believable when presenting the deception.

Another possible limitation is some participants may not believe that the palcebo was given to them, and think that the researchers were trying to deceive them, when in fact the participants are being given a placebo. Most placebo studies use deception by not telling participants they are receiving a placebo which in this study can lead some participants to believe that they are still being misled.

There are ethical questions to consider about this study and if it is ethical to deceive participants. Future studies could add an ethical element, like giving the participants a questionnaire on how they felt about the deception after the debriefing.

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