Will Drinking an Artificially Flavored Beverage Lessen my Mental Health Symptoms? (Probably Not):

The Effect of a Placebo on Mental Health Disorders and Blood Pressure

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Abstract

Previous research suggests that placebos, or sham treatments, have a significant effect on mental health disorders but not a significant one on blood pressure. The purpose of this study was to observe the placebo effect on mental health symptoms and blood pressure in high school students. A group of 19 high school students made up of 11th and 12th graders from the Neighborhood Academy, were given a placebo treatment for mental health symptoms presented as a beverage, and their baseline and post stress, anxiety, depression, and blood pressure scores were measured. No significant effects were found on the student's stress, anxiety, and blood pressure after they had received the placebo treatment. However, it was found that the participants' depression symptoms had a significant decline between their baseline and post-measurements. The modality of treatment and the generally healthy baseline scores of the participants may suggest the reason for the study's results to be generally insignificant. Therefore, further research and investigation of these aspects should be considered.

Introduction

Research suggests that placebos, also known as sham treatments, have a generally good effect on mental health disorders (1). As much as 75% of the effect of antidepressant treatments can be credited to placebos (2). Depression is a type of mental health disorder that is common among teens, with 1 in 7 experiencing a mental illness from the ages 10-19 (3). The fact that 75% of the effectiveness of drugs like anti-depressants is possibly credited to the placebo effect is very significant. The effectiveness of placebos in mental health disorders can be found in studies on anxiety, stress, depression, and even physiological responses such as blood pressure (2,4-7). This is important because many teens who experience symptoms of these mental health disorders, take medication for them. If the placebo effect can be shown to be useful in this population, doctors may be able to minimize the number of drugs they need to take. In our study, we exposed high school students to a fake treatment and measured their mental health symptoms before and after to see if there was an improvement.

Many parts of the brain may explain a placebo's effectiveness. A review article by Geuter et al. discussed the different parts of the human brain that allow the placebo effect to work, the most prominent being the ventromedial prefrontal cortex (vmPFC). The vmPFC is part of the brain that controls the autonomic nervous system (ANS), which manages blood pressure, heart rate, and other automatic body responses. The vmPFC expects treatment to work and prepares parts of the body such as the ANS to receive treatment. This may be why a placebo can change how a person feels, as the body is anticipating the effect of a drug (1). Another part of the brain known as the ventrolateral side (the front and right side of the brain) and the periaqueductal gray area (PAG), when stimulated, can reduce a human's blood pressure as well (1).

Studies have shown that placebos have a lot of benefits. Other studies have found effects for pain, Parkinson's disease, nausea, depression, immune response, and cognitive performance, and the effects can even persist for a long time (1). Although for the placebo effect to work, key requirements need to be met: matching cognitive representation of treatment, appropriate social context, the instructions by caregivers, and prior experience with the modality of treatment (1). To match the cognitive representation of treatment, the patient should be able to recognize or understand the relationship between the treatment and a particular situation. For example, if a clinician were to give a patient a donut as a treatment for a sore arm, the patient may doubt the treatment's effectiveness because in their mind they do not associate a donut with pain release. Therefore it is vital to match the patient's cognitive representation of treatment for a particular situation to get the best effect out of the placebo.

As for social context or pressure, there must be testimonies or reliable assessments of the treatment from the patient's peers (1). For example, a patient is more likely to take a treatment if their friends, families, or peers can vouch for its effectiveness. Instructions given by caregivers are additionally very important for the effectiveness of a placebo. Lastly, the patient's prior experience with the treatment modality is essential for the treatment to match the patient's cognitive representation of it (1). A patient should be able to expect that the modality type of treatment is consistent with their cognitive representation of it. Overall, the placebo needs to be something that the patient is used to and they are comfortable with it, so the patient can anticipate the treatment and respond appropriately.

Research suggests the placebo effect can also be effective on mental health disorders such as depression (2). A review by Kirsch argues that placebos work almost as well as antidepressant drugs currently on the market. Anti-depressants are drugs that are designed to fix a chemical imbalance or lack

of serotonin in your brain (2). Some antidepressants can either increase or decrease serotonin levels and some have no effect at all; yet all appear to reduce depression. Utilizing meta-analysis, a statistical tool that gathers the results of a large number of studies and analyzes them together, Kirsch was able to look at the true effectiveness of antidepressants versus placebos. The results showed that the placebo, in some cases, had just as much of an effect on the patients (if not more) as the actual drug did (2).

Kirsch suggested a possible reason for the placebo effect on depression is that depressed people feel hopeless, so promising treatment is in itself a treatment. The anti-depressant drugs were possibly only "active placebos' and didn't do anything for depression. But because they provide side effects, people may have been convinced it was working (2). Kirsch additionally proposed the serotonin myth, which is the fact that we've convinced ourselves that serotonin levels must be increased to treat depression. However, no matter the type of drug (including ones that decrease serotonin, and those that don't work in the brain), all do about the same on a person's symptoms. In the meta-analysis, the placebo was on average, about 75% of the result of the active drug (2). This is important because it shows that placebos can work well on less severe cases of mental health disorders such as depression.

Anxiety, a common mental health disorder, can also be used when testing the true effect of placebos (4). A review article written by Schweizer and Rickels observed there are few new anxiolytics on the market because, in comparison with placebos, they show little difference. For General Anxiety Disorder (GAD), placebo effects can be easy to find because it's an emotion, affected by life experiences, and it's up to the person's interpretation, so suggesting a treatment for it may be easier (4). But it is harder to measure it because anxiety is an emotion and it's hard to quantify emotion. Personality is also a factor because people with high openness and a need for social approval may be open to a therapeutic alliance with a doctor in a clinical setting and might respond to it even though it's not the drug's action that causes the effect. Side effect cueing is also important (4). The author suggests that it may be possible that anxiolytics are essentially just active placebos and this is because of side effect cueing. Experiencing side effects signals to the patient that the treatment may be working, even if it's not. The authors also noted that the severity of mental health disorders such as GAD is also important. This is because the more severe cases may be unaffected by things such as a therapeutic alliance and other placebo treatments and therefore a placebo effect might be more common in patients with mild anxiety disorders (4).

Placebo treatments can have a physical effect on the body, such as by lowering blood pressure. Mutti et al. conducted a study where 41 people got either an antihypertensive drug or a placebo drug, and all of the participants had high blood pressure monitoring. Blood pressure was monitored by a device that was attached to the patient's arms and took readings at regular intervals. Three blood pressure measurements were also taken at the doctor's office and averaged to get the initial measurements. They found that the placebo group's 24-hour average was not affected by the placebo. But, there was a psychological effect due to the measurement procedure during the first eight hours, as the placebo group's average dropped, but it was not long-lasting, as the 24-hour average was not lower. Therefore this shows the placebo effect on blood pressure might only be momentary and not long-lasting, compared to normal blood pressure drugs.

Although placebo treatments have been shown to work well in mental health disorders, it is essential to consider the type of effect to use on a certain condition. Darragh et al. conducted a study in which 77 people received two different sham treatments, one that claimed to have oxytocin (22 people), and one that claimed to have serotonin (22 people) but was actually just spray bottles with water in them. Then lastly they had a waitlist control group of 33 people. The oxytocin and serotonin groups both

received an anti-stress treatment spray to spray on themselves 3 times a day. They then took an online survey in which they rated their stress level from 1-10 before and after the 3 days. They then also took a questionnaire for anxiety and depression before and after the 3 days. The results were that the treatment sprays for oxytocin and serotonin reduced their depression symptoms. The oxytocin group was the only treatment group that had their stress and anxiety levels reduced (5). This is important because the research suggests that placebos can reduce moderate symptoms of things like stress, anxiety, and depression symptoms. It also shows that cognitive representation is an important part of the placebo effect of serotonin, which is associated with depression, but did not work for helping with stress symptoms. But because oxytocin treatment is a "feel-good" drug, people may have believed it would help everything (8).

All previous research on adults and placebos is also relevant for teens. A review article written by Bridge et al. looked at 12 published and unpublished randomized controlled trials of antidepressants on Major Depressive Disorder in teens ages 16-18. The authors observed that placebo effects seem to work more effectively if there is less close control over what is done and how it is done (i.e more clinical sites and doctors). Based on the results of many of the studies they often observed that younger children are easier to influence than older children (6). The severity of the depression also plays a major factor in the effectiveness of the placebo. This article helps support the idea that the placebo effect would most likely work best in people with mild depression. It also shows that therapeutical alliance and catering to patients' individualized needs play an important part in the effect of the placebo (6).

Overall, research says that placebos can have positive effects on mental health disorders, such as anxiety, depression, stress, as well as blood pressure (2, 4-7). It also suggests that therapeutic alliance and matching the patient's cognitive representation of treatment is very important in getting the best effect out of a placebo (4). Other factors such as the severity of mental health and blood pressure cases as well as the age of the patients play an important part in how effective the placebo may be (2, 4-7). This study investigated the placebo effect but used a peer instead of a clinician as the person responsible for administering the sham treatment. Due to this change, the therapeutic alliance may or may not be present within the experiment. Therefore, this study also looked at whether or not a placebo treatment will still work without a proper therapeutic alliance. In this experiment, we gave a mental health symptoms survey before giving the actual placebo "treatment". We then offered treatment for mental health and blood pressure which was a flavored beverage and then had those same patients retake the survey to look for differences in their symptoms. We hypothesize that there is a significant decline between mental health symptoms and blood pressure when exposed to sham treatment (placebo), compared to the baseline scores.

Method and Materials

A total of 19 high school students from The Neighborhood Academy participated in the study. All participants from the study were African American, comprised of males (63%) and females (37%) from grades 11 and 12 and between the ages of 16-18. All students in a particular grade had the same schedules and therefore experienced similar academic environments.

The participants were given a survey known as the DASS21, to get their baseline scores on their stress, anxiety, and depression symptoms (9). The survey consisted of 21 statements in total with 7 statements about either stress, anxiety, or depression symptoms. For example, anxiety had statements such as ¨ I was worried about situations where I might panic and make a fool of myself.¨ For depression, there

were statements such as ¨I couldn´t seem to experience any positive feeling at all¨. Lastly, for stress, there were states such as ¨I found it hard to wind down.¨ Based on the participant's responses to those statements, they would answer 0 meaning that the statement did not apply to them at all, and 3 meaning that it applied to them very much or most of the time. The participants were scored by their ratings being added up on the scale for each statement on anxiety, stress, or depression. Those totals for each disorder would then determine the severity of their symptoms for each disorder. For example, a score of 0-4 in the depression category would mean the person's symptoms are ¨normal¨ and a score of 14+ would mean that their symptoms are ¨extremely severe¨ (9).

For the drinks, we selected a powdered drink mix that tasted like a vitamin drink or herbal tea. Though the drinks were only made up of flavors, colorants, and fake sugars and had no actual vitamins or stimulants. A total of 6 different flavors were available to the participants but we initially only gave them a peach-mango-green tea flavor. If the participant requested another flavor instead, they would then be offered another one of the 6 flavors available.

First, we recruited participants and requested them to sign a permission slip with their parent's signatures in order for them to be able to participate in the study. Within the permission slip, it had stated that they would drink a fruit-flavored drink designed to treat stress/mental health, although the drink did not contain any clinically active ingredients. Once permission slips were collected from the participants, we then collected their baseline blood pressure measurements using an Omron Automatic Blood Pressure Monitor, Model BP710, and the DASS21 survey for their stress, anxiety, and depression symptoms. When measuring their blood pressure baseline scores, they were required to take off bulky sweaters, lay their arms flat while sitting, and were also asked not to speak. After their measurements were recorded, they were then asked to fill out a survey.

Afterward, they were given their first drink and were verbally instructed to drink it throughout the day. They were also told they did not need to finish, as long as they consumed at least a third of it. In addition to that, they were told that the drink was ¨specially designed¨ to reduce their stress and anxiety. Depending on the participant's schedules, the drinks were given out in the morning or early afternoon or before school ended. They were given the drinks for 6 days, not including weekends or absences. For their post-measurements, they were told that they would be receiving their last drink, then asked to fill out DASS21 and blood pressure which was aimed to be measured at the same time it was for their pre-measurements. Pre-score measurements are described in Figure 1.

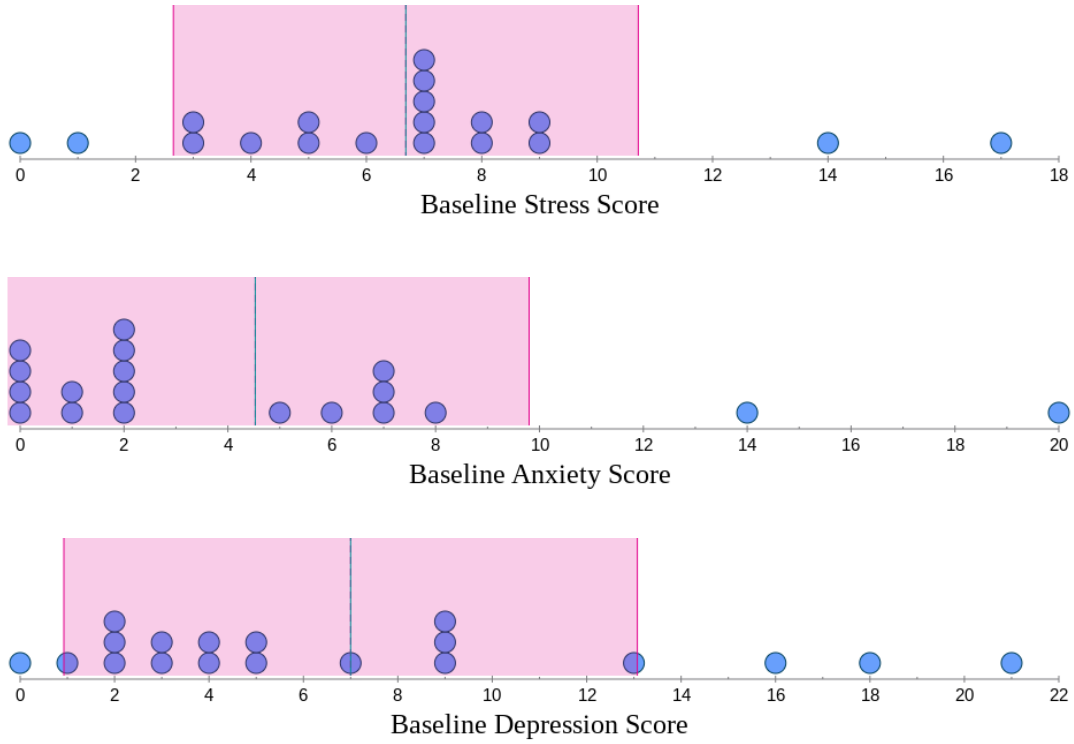

Figure 1. Baseline mental health symptoms score*s. Pictured above are the baseline mental health scores of 19 high school students who participated in my study. The baseline stress scores have a mean of 6.7 and a standard deviation of 6.7 ± 4 and the data was generally symmetrical with a few higher and lower scores. Baseline anxiety scores had a mean of 2 with a standard deviation of 4.5 ± 5.3 with a more skewed set of data with a couple of higher scores. Lastly, for the baseline depression scores, there was a mean of 6 and a standard deviation of 7 ± 6.1, and were somewhat uniformly distributed with a few higher scores. Additionally, there were 4 students with extremely severe or severe mental health symptoms, 2 with extremely severe and 2 with severe.*

Results

In this paper we investigated the effects that a placebo can have on mental health and blood pressure. 19 Students were asked to take a mental health questionnaire and have their blood pressure measured. They then were given a sham treatment (placebo) for a week and had their mental health symptom and blood pressure measured again. We hypothesized that there would be a significant difference between the student's baseline and post-measurements.

Our first hypothesis was that the placebo drink would lower participants' blood pressure. The participant's systolic pressure, diastolic pressure, and pulse were measured before and after they consumed all 6 of the placebo drinks. Two-sample t-tests for correlated samples found no significant differences in systolic ($t(18)= -0.84$, $p=0.21$) and diastolic ($t(18)= +0.16$, $p=0.44$) blood pressures. Additionally, there was no difference in the baseline and final pulse ($t(18)= +1.55$, $p= 0.07$). The average scores are shown in Table 1.

	Baseline	Post
Systolic	121.6 (10.5)	124.4 (16.7)
Diastolic	71.6 (8)	71.3 (12.8)
Pulse	80.8 (10.9)	75.6 (11.6)

Table 1. ***Baseline and final blood pressure measurements.*** *Average systolic pressure, diastolic pressure, and pulse before and after the placebo are depicted above, standard deviations are in parentheses*.

Our second hypothesis was that the placebo would effectively lower depression symptoms. The participant's depression symptoms were measured via the DASS21 survey before and after they consumed six of the placebo drinks. A two-sample t-test found a significant difference in the baseline depression scores and the post-depression scores (t(18)= +2.12, p=0.048). The baseline scores (M=7, SD=6.1) were higher than the final scores (M=5.5, SD=1.3) for depression.

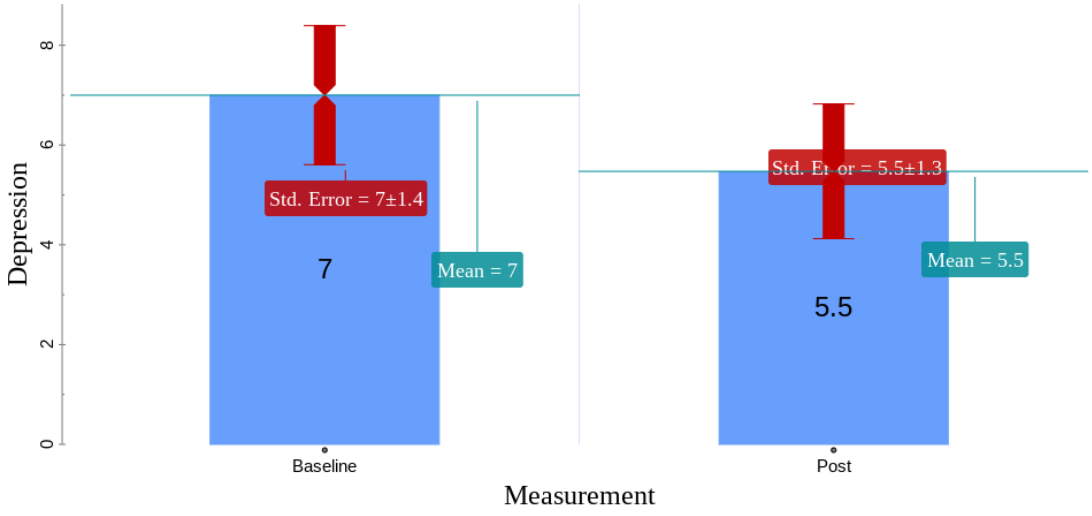

Figure 2. Average depression score before and after placebo. *In the figure above, the horizontal axis is the baseline and post measurements; each participant was measured before and after they were given the placebo drink. The vertical axis is the average depression score.* The post scores were significantly lower. ($p<0.05$).

Our third hypothesis was that the anxiety symptoms would also be lowered due to the placebo effect. The participant's symptoms of anxiety were also measured by the survey before and after the placebo drinks. The two sample t-tests found no significant difference between the baseline and post-anxiety symptom scores (t(18)= +1.54, p= 0.14).

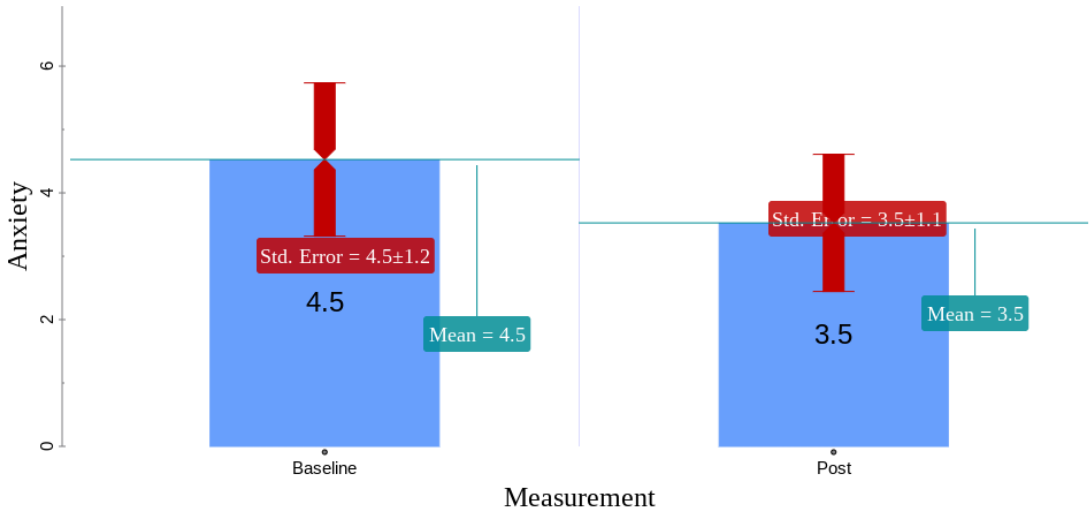

Figure 3. Average anxiety score before and after placebo. *In the figure above, the horizontal axis is the baseline and post measurements; each participant had been measured before and after they drank the placebo drinks. The vertical axis is the average anxiety score.* There was no significant difference in the post and baseline scores ($p>0.05$).

Lastly, our fourth and final hypothesis was that the placebo would be effective in lowering stress symptoms. The participants' stress symptoms were also measured before and after they consumed all six of the placebo drinks. A two-sample t-test found that there was no significant difference between the baseline and post stress symptoms ($t(18)= -0.51$, $p = 0.616$).

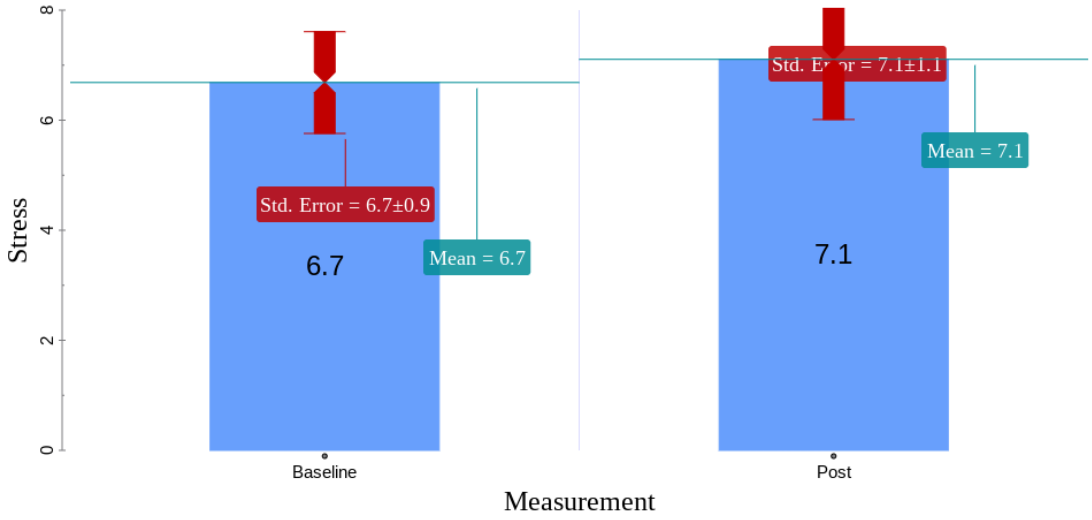

Figure 4. Average stress score before and after placebo. *In the figure above, the horizontal axis is the baseline and post measurements; each participant had been measured before and after they drank the placebo drinks. The vertical axis is the average stress score.* There was also no significant difference in the post and baseline scores ($p>0.05$).

Discussion

In this study, we sought to investigate what effects the placebo had on mental health symptoms and blood pressure. Our first hypothesis was that the placebo drink would lower participants' blood pressure. This was not supported by our data (**Table 1**). Our second hypothesis was that the placebo would effectively lower depression symptoms. This hypothesis was supported by our data (**Figure 2**). For our third hypothesis, it was that the anxiety symptoms would also be lowered due to the placebo effect. This was also not supported by our data (**Figure 3).** Lastly, no effect was also found for stress (**Figure 4**).

Our results for the placebo effect on blood pressure were consistent with other studies done previously (7). Mutti et. al found that the placebo effect only had an immediate reaction on the patient's blood pressure but went back up not soon after. This suggested that the placebo effect has no long-term effect on blood pressure. Our study found that the placebo had no significant effect on the students' blood pressure from the baseline measurements to the post-measurements six days later. The idea that the placebo effect will not have a significant effect on blood pressure after a certain period of time is consistent with Geuter et al.'s review article on the neuroscience behind the placebo effect. According to them, the ventromedial prefrontal cortex (vmPFC) is credited with why the placebo effect works. The vmPFC is part of the brain that controls the autonomic nervous system (ANS), which manages blood pressure, heart rate, and other automatic body responses. These responses usually occur immediately after the treatment is given (1). If the patient is not continually persuaded that the treatment is really effective, then the placebo will begin to lose its effectiveness and the patient would become desensitized to the treatment. In our study after enough exposure to the drinks, people may have begun to think of the treatment as just a drink and not a treatment. The neural connection between their vmPFC and their ANS's control of their blood pressure could have become desensitized. They might have begun only wanting the drink to quench thirst rather than wanting it as a stress or anxiety reliever.

The results for the placebo effect on depression were also consistent with ideas discussed by Kirsch (2). They observed that the placebo, in some cases, had just as much of an effect on the patients as the actual anti-depressant drugs did, owing to side-effect cueing and patient hopefulness (2). Our study found that the patients with the most severe baseline depression scores found a greater decrease in the post scores than those with moderate to no depression symptoms. For students who scored 7 or above (moderate or severe), the average decrease was -2.5 points and for people with no to little depression symptoms, the average was -0.8. Being that most of the effect detected was from people with moderate or severe depression symptoms, our results mostly aligned with what Kirsch argues. It is suggested that this result was to be expected because people with little or no depression may not have felt the need to cure something that they don't necessarily feel that they have (2). Additionally, our study found that while administering the drinks, many of the students felt that the drinks "tasted like medicine". The taste was most likely due to the aspartame within the artificial sugar that can be found in many medicines and our placebo, but because of their association of that taste with medicine, they could have thought the treatment was real and working.

For the placebo effect on anxiety, our results were not consistent with the studies looked at by researchers such as Schweizer and Rickels (4). Schweizer and Rickels observed that for General Anxiety Disorder (GAD), while it is hard to quantify being that it is an emotion, this also makes it easier to influence. (4). Our results found that anxiety symptoms in our sample of students were little to none with the exception of two students whose symptoms suggested that if tested they'd be likely to be diagnosed with anxiety. The day-to-day fluctuations of people without severe anxiety emotions may have hidden the

effect of the placebo. Therefore this may be why most students had no significant change in their anxiety symptoms during the duration of our experiment.

The results for the placebo effect on stress were not consistent with the studies done by researchers such as Darragh et al. They found that their participants had stress and anxiety levels reduced by the sham treatment, which in their case was a spray bottle with water. In contrast, our results found that the placebo effect had no significant effect on stress levels. The reason that the placebo effect may not have had an effect on the participants in our study's stress level may have been because of the context of care. In Darragh et al's study, they conducted the experiment within a hospital on mentally ill patients whereas our study was conducted in a high school on generally healthy high school students. Additionally, Darragh et al's study, specifically named the drug that would be in the spray bottle whereas in our study we were very vague about what "drugs" were included in the drinks the participants were given, calling them vitamins. Therefore this may have been the reason why the participant's stress levels didn't change.

Our study had several limitations, the first being that it was done on mentally healthy people, except for two students out of 19 who had told us, unprompted, that they were receiving mental health treatment. For that reason, it may have been harder to see significant changes in their mental health symptoms if most of them didn't have many in the first place. Another limitation we had was not being able to tell the participants that there was a specific drug within the drink. In order to not alarm the parents and get Institutional Review Board (IRB) approval from the school we had to be very vague and nonmedical in what we told them about the treatment they would be receiving. That may have caused the placebo effect to not work as effectively because of the lack of information we told them about the treatment. Additionally, while we're very careful in making sure each participant received their drinks in a systematic manner or made up their drinks when they were not here, some students had been absent and or nowhere to be found at the scheduled time of treatment, which may have made the treatment less consistent. We recommend future researchers should consider focusing on mentally unwell participants as well as using a different type of sham treatment besides a beverage for perhaps a stronger effect to be detected.

Our research suggests that a drink-based placebo has a limited effect on typical high school teens. For this reason, despite all the research that states that the placebo effect is effective in many situations, it may not be effective as a treatment in the context of generally healthy high school teens. Therefore, further research on placebo effects in this context should be done in order to better understand the role placebos could play in improving the mental health of high school students.

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