

Caitlin Chheda

Personal Statement

I have always enjoyed science, ever since I was 7 and read that over 6 billion bacteria live in your mouth. For a 7 year old, this was a scary thought. I refused to eat during meals. I never closed my mouth, as to let the invaders out. I stopped breathing through my mouth and relied only on my nose. However, I am proud to say that I am no longer afraid of being a home to my microscopic friends. Instead, I enjoy their company as they allow me to be immersed daily by science. In high school, when I had just finished studying for an AP Psychology exam, something caught my eye: something that I had glanced over when I was studying - a sentence on the psychostimulant drugs. Curious as to how these drugs could help humans, I Googled it. To my surprise, they are a lot more important and interesting than I actually thought. It was then that I decided that I wanted to research the brain.

Since that fateful internet search, I began to look into research programs where I could learn more about the brain. Unfortunately, I had trouble finding a mentor due to the various COVID restrictions in my area. I reached out to researchers at universities and institutions across the nation so that I could work with them, virtually. I reached out to Dr. Harriet de Wit at the University of Chicago after coming across one of her papers which focused on how the effects of alcohol can predict alcohol choice. Dr. de Wit then directed me to her postdoctoral fellow, Dr. Hanna Molla. After exchanging emails, we decided to meet virtually so that I could gauge what her research entailed. During this meeting, she told me that her research involved the study of MDMA, or ecstasy, on social anxiety. She also revealed to me that the research had already been conducted, and, because this would be a virtual mentorship, I would be analyzing the pre-collected data. After this, I officially asked her to be my mentor; I found her research question to be of interest, especially since examining potential positive effects of recreational drugs, in moderation, in patients with mental health disorders is gaining more recognition within

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the scientific community. It was with this research and through Dr. Molla's leadership and guidance that I was able to submit my paper to Regeneron STS.

Throughout my project, I used several mathematical techniques as a means to understand the scientific work behind the research actually meant. Although I was a junior who had been taught basic statistics and how to compute certain values, the impacts of COVID had made me confused with all of my equations and the meanings behind them. So, in order to proceed with my research, I re-taught myself how to calculate standard deviation, chi square, t-tests, how to read a p-value, and how to use Excel spreadsheets properly. Being able to partake in this research and actually put meaning behind the work that had already been conducted was extremely rewarding to me and gave me an experience that has changed my perspective of research.

Overall, this project has been an incredible experience for me, and I hope that by contributing my story I will be able to touch the lives of others and encourage others to partake in this amazing opportunity. Although the initial step of reaching out to a mentor may seem scary, in reality, you both are working towards one goal and one question to answer, allowing that fear to magically float away. My advice would be to motivate yourself to try something that you think you may like, as it could become a real passion.

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The Impact of Sex and MDMA on Social Anxiety Evaluated by Subjective Responses

Abstract

Psychiatrists continue to seek effective methods to treat social anxiety disorder. The current standard treatment for social anxiety disorder is a combination of psychotherapy and medications, yet, several limitations still exist including high costs and subjects failing to follow prescribed medication. Individuals with this disorder may experience anxiety or fear in some, if not all, social situations. 3,4-Methylenedioxymethamphetamine, or MDMA, is a psychostimulant drug which, apart from its recreational uses, produces prosocial effects in humans. Previous studies have found the drug to increase empathy and interpersonal closeness. Thus, the prosocial effects of MDMA may be examined in social anxiety situations to determine a more effective treatment for the disorder. This study evaluated prosocial effects of MDMA through the administration of modified questionnaires that addressed social anxiety, depressive experiences, and different mood states with sex as a contributing factor. Participants ($n = 18$) were separated into low or high social anxiety groups, as determined by SAQ-A30 scores and were provided questionnaires. From my study, elation was shown to be significant in males ($p = 0.032$) and, in females, sociability ($p = 0.026$), confidence ($p = 0.023$), and friendliness ($p = 0.004$) were significant, when on MDMA. Findings suggest that females, when on MDMA, may experience increased feelings of sociability, confidence, and friendliness, thus mitigating anxiety symptoms. These seminal findings may inform the future use of MDMA as a potential treatment for mitigating social anxiety disorder.

The Impact of Sex and MDMA on Social Anxiety Evaluated by Subjective Responses

1. Introduction

1.1. Rationale

Social anxiety disorder is a mental health disorder, where people feel immense trepidation of people watching and/or judging them [1]. Psychiatrists continue to seek more effective methods for treating social anxiety disorder in humans [2]. Cognitive behavioral therapy (CBT), also called psychological counseling or talk therapy, medications such as selective serotonin reuptake inhibitors (SSRIs), and antidepressants are commonly used for effectively treating social anxiety disorder [1,2]. However, despite advancements in medicine, this type of treatment is still costly for many and some patients fail to follow their medication schedule [3,4]. Medications including Zoloft, benzodiazepines, and Paxil may increase serotonin levels and target adrenaline action to help individuals manage their fear and stress responses[2]. However, randomized controlled trials have shown that adding CBT to antidepressants only relieved social anxiety symptoms in less than 50% of people [2,5,6]. Without proper treatment, social anxiety may progress and lead to low self-esteem, negative thoughts, depression, sensitivity to criticism, poor social skills, and even suicide [1,7]. Past traumatic life experiences, drug use, and medications may be the potential causes of social anxiety, however, the exact cause of social anxiety disorder is unknown [8]. In previous studies, there has been an apparent sex difference in other disorders, such as PTSD (Post Traumatic Stress Disorder) [9]. From these studies, it has been shown that females are more likely to experience PTSD after exposure to a traumatic event [9]. Despite this connection, a sex difference has not yet been identified in social anxiety [9,10]. However, it is known that females tend to experience more positive emotions (such as happiness) compared to males[10]. Additionally, it has been shown through numerous studies that females score higher than males on standardized tests of emotion recognition, social sensitivity, and empathy [10].

Despite its recreational abuse, 3,4-Methylenedioxymethamphetamine (MDMA) is a psychostimulant drug that is widely used in social contexts to produce prosocial effects in both laboratory animals and humans [11]. Previous studies have found MDMA to be effective when used as a treatment for social anxiety in humans on the Autism spectrum and as a treatment for Post Traumatic Stress Disorder (PTSD) [12,13]. However, current studies have yet to examine the effects of MDMA on social anxiety in healthy human volunteers while also considering sex as a factor. Thus, this study evaluated prosocial effects of MDMA through the administration of modified questionnaires that addressed social anxiety, depressive experiences, and mood states with sex as a contributing factor.

1.2. Background

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1.2.1 3,4-Methylenedioxyamphetamine

3,4-Methylenedioxyamphetamine (MDMA), commonly known as ‘ecstasy’ or ‘molly,’ is a psychostimulant and a widely abused synthetic drug that alters mood and perception [14,15]. The first synthesis of MDMA occurred in 1912 by the German pharmaceutical company, Merck KGaA [16], but it was not widely available until later in 1979, when Alexander Shulgin developed a new synthesis method and shared it with psychotherapists for mental health purposes [14]. This ultimately led to the publication of the subjective effects of the drug by David Nichols from Purdue University [16]. This publication - which included MDMA’s effects of increasing empathy and reducing fear - may have contributed to the use of the drug in psychotherapy settings and recreationally [14].

MDMA changes the brain by increasing the activity of three neurological chemicals: dopamine, norepinephrine, and serotonin [17]. It primarily releases serotonin and temporarily inhibits its reuptake [14]. MDMA is an empathogen, meaning that it may increase feelings of empathy and compassion [18]. Chemically similar to stimulants and hallucinogens, MDMA produces feelings of energy increase, pleasure, emotional warmth, and distorted sensory perception and time [14]. However, it should be noted that MDMA affects each individual differently based on different factors: size, weight, health, whether the person is used to taking it, whether other drugs are taken around the same time, the amount taken, and the strength of the drug, which varies for each batch [18,19]. The effects from the drug last from 3 to 6 hours, during which users may experience a range of effects: irritability, impulsiveness, aggression, depression, euphoria, confidence, etc [14, 18]. In high doses, MDMA may affect the ability to regulate temperature which may lead to a fever that may sometimes result in liver, kidney, or heart failure, or death [14,20,21].

However, in moderate doses, MDMA has been shown to increase self-reported ratings of sociability and friendliness, trust, openness, and closeness to others [22]. Due to its prosocial effects, MDMA has been of interest in psychotherapeutic contexts such as its efficacy when treating posttraumatic stress disorder (PTSD) and Autism spectrum disorders [23,12,13]. In 2010, the first controlled clinical study with MDMA-assisted psychotherapy was published [24]. In this study, twenty patients with treatment-resistant PTSD received either an inactive placebo or two or three sessions of MDMA [25]. At two and twelve-month follow-up, 83% of the group no longer met the requirements for PTSD [24]. Yet, it is unknown if the mechanisms underlying MDMA’s prosocial effect and abuse potential may be separated. Thus, it is important for the prosocial effects of MDMA to continue to be examined for the treatment of disorders, such as social anxiety.

1.2.2 Social Anxiety Disorder

Anxiety is the normal response of fear that occurs during threatening or stressful situations, but, if this feeling persists, it could be diagnosed as an anxiety disorder [1]. More specifically, social anxiety disorder is a common anxiety disorder. Social anxiety disorder affects 15 million adults, or about 6.8% of the United States’ population [26]. Symptoms for the disorder appear in both females and males around age

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13 ^[26]. Females have been found repeatedly to be more likely than males to suffer from and be diagnosed with anxiety, including social anxiety ^[27]. People who experience this disorder feel symptoms of anxiety or fear in specific if not all social situation (e.g. meeting people for the first time) and doing daily tasks in front of others ^[1]. These people have a fear that they will be humiliated, judged, and/or rejected ^[1]. This disorder may be hereditary, but it is unknown why some family members may experience social anxiety while others do not ^[28,29].

Neurologists have identified several parts of the brain that may be involved in social anxiety ^[30]. fMRI brain scans have shown that people with the disorder suffer from hyperactivity in their amygdala, which is the center for emotions, emotional behavior, and motivation ^[30,31,32,33]. However, the amygdala also mobilizes the body to respond to perceived threats, whether they are real or not^[31]. This action triggers symptoms identified with intense anxiety: rapid heartbeat, sweaty palms, a freezing of the brain that leaves individuals with anxiety unable to think or reason as they would normally, etc. ^[31,34,35]. In individuals who experience social anxiety, the prefrontal cortex increases the activity in the amygdala^[31]. These individuals interpret social interactions as actual threats, so no amount of rational thinking may calm these fears ^[31]. Interestingly, brains may be reprogrammed to form new circuits at any age with cognitive-behavioral therapy ^[31]. Through this therapy, individuals may retrain their brains to react more rationally in social situations that hold no real threat ^[31]. Yet, no current treatment may cure or effectively help the disorder, leading researchers to look at recreational drugs for possibilities.

1.2.3 Social Anxiety Questionnaires

In order to measure social anxiety levels and changes in mood states, researchers use several tests: SAQ-A30, profile of mood states (POMS), depressive experiences questionnaire (DEQ), and visual analog scale (VAS). The social anxiety questionnaire, or SAQ-A30, measures psychometric properties of an innovative self-report ^[36]. The SAQ-A30 contains thirty items including a social phobia/anxiety structure of five solid dimensions, or factors, each of them including six items ^[36]. The profile of mood states, or POMS, test has been commercially available for over forty years with several different versions developed over time ^[37]. POMS assesses changes in mood states on several scales including friendliness, elation, anxiety, depression, anger, vigor, fatigue, and confusion ^[38]. To make the scale easy for participants with social anxiety to use, the POMS scale is a analog scale that prompts the user to move a cursor along it to rank the question ^[39]. The DEQ, or the Depressive Experiences Questionnaire, assesses self-criticism, dependency and self-efficacy, and a sociodemographic questionnaire^[40]. Similar to POMS, DEQ is also an analog scale so that participants may use it with ease^[40]. And finally, the VAS, or Visual Analog Scale, is a measurement that tries to measure a characteristic (such as anxiety) in clinical research ^[41]. Taken together, these questionnaires may help determine specific feelings of people at a certain time, and compare it to a previous time.

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1.3 Objectives/Hypothesis

1.3.1 Objectives

The primary objective of this study was to evaluate prosocial effects of MDMA through the administration of previously administered modified questionnaires that addressed social anxiety, depressive experiences, and mood states with sex as a contributing factor, in adults (21-40 male and female).

1.3.2 Hypothesis

Based on previous laboratory findings dealing with the prosocial effects of MDMA, I hypothesized that 1) lower levels of self-reported social anxiety would be associated with increased friendliness and positive mood while the subjects were on MDMA and 2) females would have heightened levels of self-reported positive moods while the subjects are on MDMA.

2. Methodology

**All methods were conducted by Author unless otherwise stated*

2.1. Trial Design

Researchers at the University of Chicago employed a double-blind, randomized, and placebo controlled methodology conducted from October 2019 to April 2021.

2.2 Screening, eligibility, and participants *(Performed by Mentor)*

Healthy males and females between the ages of 21-40, who were fluent in English and had at least a high school diploma were recruited through social media (Instagram and Facebook) and flyers distributed across the University of Chicago. Volunteers were screened by researchers at the University, which included a physical, EKG, psychiatric screening interview and detailed drug use history questionnaire. Volunteers had to report using MDMA at least 4 but no more than 40 times, with no adverse responses. Individuals that were excluded from the study for dosage safety reasons had a BMI < 19 or > 30, or weighed under 130 lbs. Individuals who had a history of heart disease, had high blood pressure, (self-reported) or an abnormal EKG (conducted by medical screener) were also excluded from the study, due to potential unwanted side effects with MDMA.

2.3 Pre-experimental Procedures *(Performed by Mentor)*

Before the study, participants arrived at the University in order to complete their orientation, which involved having a physical, signing consent documentation, and completing a series of questionnaires. During the orientation, participants completed the SAQ-A30 in order to determine which category they would fall into - low or high social anxiety. It should be noted that this questionnaire was only given before the experimental sessions and not after or during.

2.4 Experimental Sessions *(Performed by Mentor)*

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For experimental sessions, participants arrived at the University at 09:00 and stayed until 14:00. The study took place in a laboratory setting and during sessions, participants stayed in a subject room that contained a couch, television, and a desk with a computer (this type of room). Upon arrival, subjects completed a urine drug screening and breathalyzer test to verify no drugs were present in their system prior to drug administration. Subjects received a placebo on one session and MDMA (1.5mg/kg) during the other session in a randomized, counter balanced order. Capsules were administered at 9:30 am, and following this, subjects were allowed to eat food. Each hour, participants filled out the DEQ, POMS and VAS questionnaires, and had their blood pressure and heart rate monitored.

2.5 Measures

2.5.1 The social anxiety questionnaire for adults (SAQ-A30) (Performed by Mentor)

The SAQ-A30 consists of 30 items with 5 dimensions: 1) Speaking in public/talking with people in authority, 2) Interaction with the opposite sex, 3) Assertive expression of annoyance, disgust or displeasure, 4) Criticism and embarrassment, and 5) Interactions with strangers. Each dimension has 6 items rated on a 5-point Likert scale ranging from 1 (Not at all or very slight) to 5 (Very high or extremely high). This questionnaire and its items originate from Caballo et al., 2012 ^[42].

After all data was collected from the pre-experimental sessions, I found the total SAQ-A30 score for each participant in the study and then found the median of the 18 participants to be 70.5. This median then determined the high and low social anxiety cohorts - scores lower than 70.5 were placed in the low social anxiety cohort and scores higher than 70.5 were placed in the high social anxiety cohort - of 9 participants each. These cohorts were used for the rest of the study to compare the results from other questionnaires that the participants filled out on both MDMA and a placebo.

2.5.2 Depressive Experiences Questionnaire (DEQ) (Performed by Mentor)

The DEQ consists of 5 items: 1) Like, 2) Dislike, 3) High, 4) More, and 5) Feel. Each item is rated on a 100-point analog scale ranging from 0 (Not at all) to 100 (Very high). This questionnaire and its items originate from Fischman and Foltin, 1991 ^[43].

After all data was collected from both the MDMA and placebo trials, I subtracted the placebo score from the MDMA score for each item (DEQ Feel, DEQ Like, DEQ Dislike, DEQ High, and DEQ More) for each participant.

2.5.3 Profile of Mood States Questionnaire (POMS) (Performed by Mentor)

The POMS consists of 8 items: 1) Friendliness, 2) Anxiety, 3) Elation, 4) Anger, 5) Fatigue, 6) Depression, 7) Confidence, and 8) Vigor. Each item is rated on a 100-point analog scale ranging from 0 (Not at all) to 100 (Very high). It should be noted that although participants were asked all 8, only 3 were used when measuring the statistical analysis: 1) Friendliness, 2) Anxiety, and 3) Elation. This questionnaire and its items originate from McNair et al., 1971 ^[39].

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After all data was collected from both the MDMA and placebo trials, I subtracted the placebo score from the MDMA score for each item analyzed (POMS Friendliness, POMS Anxiety, and POMS Elation) for each participant.

2.5.4 Visual Analog Scale Questionnaire (Performed by Mentor)

The VAS consists of 13 items: 1) Anxious, 2) Stimulated, 3) Sedated, 4) Elated, 5) Insightful, 6) Sociable, 7) Confident, 8) Lonely, 9) Playful, 10) Dizzy, 11) Loving, 12) Friendly, and 13) Restless. Each item is rated on a 100-point analog scale ranging from 0 (Not at all) to 100 (Very high). It should be noted that although participants were asked all 13, only 3 were used when measuring the statistical analysis: 1) Confident, 2) Friendly, and 3) Elated. This questionnaire and its items originate from Bershad et al., 2019 [44].

After all data was collected from both the MDMA and placebo trials, I subtracted the placebo score from the MDMA score for each item analyzed (VAS Confident, VAS Friendly, and VAS Elated) for each participant.

2.6 Statistical Analysis

In order to determine the statistical significance between the MDMA and social anxiety results and the female and male MDMA results, I ran statistical tests. For the DEQ, I totaled added the DEQ Like scores for participants placed in the low social anxiety cohort and then found the mean using Excel Spreadsheet. Then, I used this Excel Spreadsheet to calculate the Standard Error of the Mean and generate bar graphs with the respective data. I then ran t-tests using the function on Excel Spreadsheet to generate the p- value for this item. I used this same process for all other items and questionnaires for both high and low social anxiety. p values < 0.05 were considered significant. This same process was repeated for sex (male or female) in place of social anxiety.

3. Results/Discussion**3.1 SAQ-A30 Data**

Table 1 This table shows the participants with their respective sex and total SAQ-A30 score. From this data table, the median of SAQ-A30 scores was found (70.5), which determined the cohorts for high or low social anxiety rating - scores lower than 70.5 were placed in the low social anxiety cohort and scores higher than 70.5 were placed in the high social anxiety cohort. (Author)

Subject ID	Sex	SAQ-A30 Total	Rating
532	F	71	High
531	M	73	High
530	F	51	Low
529	M	63	Low
528	M	86	High
526	F	76	High
525	M	122	High
524	F	57	Low
523	F	64	Low
520	M	77	High
518	F	54	Low
517	M	90	High
516	M	70	Low
515	M	68	Low
512	M	60	Low
510	F	101	High
507	M	63	Low
504	M	74	High

In order to evaluate social anxiety and sex, the participants and their SAQ-A30 scores were totaled. Based on, the mean was found (70.5) and the participants were split into high (above 70.5) and low (below 70.5) social anxiety cohorts. This set up the rest of the study when trying to determine if there was statistical significance between social anxiety and MDMA.

3.2 DEQ Graphs

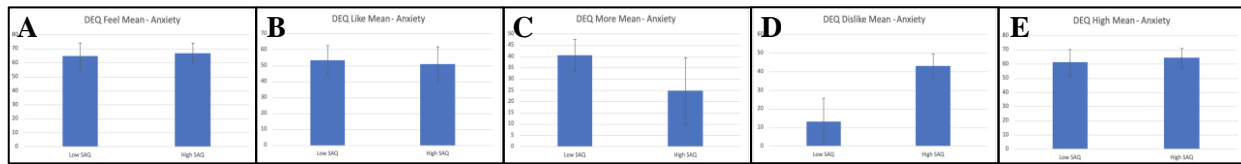


Figure 1 These graphs show the correlations between each item on the DEQ and the high and low social anxiety cohorts. No statistical significance found because all p values were greater than 0.05. **(A)** Graphical representation of DEQ feel question and low/high social anxiety ($n = 18$) $p = 0.864$. **(B)** Graphical representation of DEQ like question and low/high social anxiety ($n = 18$) $p = 0.867$. **(C)** Graphical representation of DEQ more question and low/high social anxiety ($n = 18$) $p = 0.350$. **(D)** Graphical representation of DEQ dislike question and low/high social anxiety ($n = 18$) $p = 0.069$, showing slight correlation between the dislike of MDMA and high social anxiety. **(E)** Graphical representation of DEQ high question and low/high social anxiety ($n = 18$) $p = 0.781$. (Author)

In **Figure 1**, the effect of the drug on five different items was compared to whether or not the participant experienced high or low social anxiety based on the SAQ-A30. In **Figure 1A**, it is seen that the mean for high social anxiety in response to the “Feel” question on the DEQ was 66.778, with a standard error of the mean (SEM) of 7.325, and the mean for low social anxiety being 64.667, with a SEM of 9.749. The p -value was 0.864, showing that there was no statistical significance between high or low social anxiety on the DEQ Feel question. In **Figure 1B**, it is seen that the mean for high social anxiety in response to the “Like” question on the DEQ was 51, with a SEM of 11.056, and the mean for low social anxiety being 53.444 with a SEM of 9.254. The p -value was 0.867, showing that there was no statistical significance between high or low social anxiety on the DEQ Like question. In **Figure 1C**, it is seen that the mean for high social anxiety in response to the “More” question on the DEQ was 24.667, with a SEM of 14.922, and the mean for low social anxiety being 40.556 with a SEM of 7.055. The p -value was 0.350, showing that there was no statistical significance between high or low social anxiety on the DEQ More question. In **Figure 1D**, it is seen that the mean for high social anxiety in response to the “Dislike” question on the DEQ was 42.889, with a SEM of 6.548, and the mean for low social anxiety being 13.111, with a SEM of 12.852. The p -value was 0.069, which although shows no statistical significance, it should be mentioned that it shows a slight correlation between the dislike of MDMA and high social anxiety. In **Figure 1E**, it is seen that the mean for high social anxiety in response to the “High” question on the DEQ was 64.333, with a SEM of 6.859, and the mean for low social anxiety being 61.111, with a SEM of 9.144. The p -value was 0.781, showing that there was no statistical significance between high or low social anxiety in response on the DEQ High question.

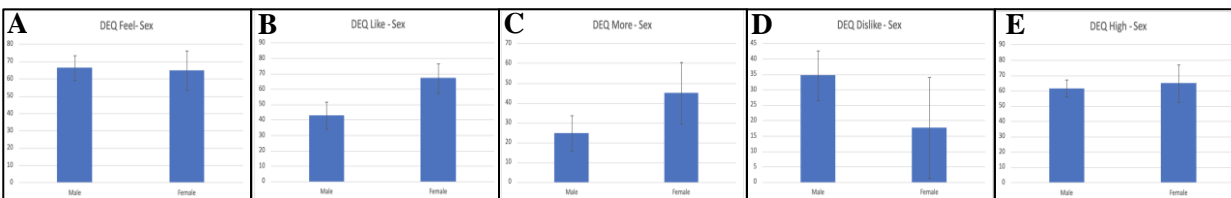


Figure 2 These graphs show the correlations between each item on the DEQ and sex (female or male). No statistical significance found because all p -values were greater than 0.05. **(A)** Graphical representation of DEQ feel question and sex (female or male) ($n = 18$) $p = 0.896$. **(B)** Graphical representation of DEQ like question and sex (female or male) ($n = 18$) $p = 0.091$, showing slight correlation between the like of MDMA and females. **(C)** Graphical representation of DEQ more question and sex (female or male) ($n = 18$) $p = 0.235$. **(D)** Graphical representation of DEQ dislike question and sex (female or male) ($n = 18$) $p = 0.327$. **(E)** Graphical representation of DEQ high question and sex (female or male) ($n = 18$) $p = 0.784$. (Author)

In **Figure 2**, the effect of the drug on five different items was compared to the sex (either female or male) of the participant. In **Figure 2A**, it is seen that the mean for females in response to the “Feel” question on the DEQ was 64.714, with a SEM of 11.407, and the mean for males being 66.363, with a SEM of 7.133. The p -value was 0.896, showing that there was no statistical significance between females or males in response on the DEQ Feel question. In **Figure 2B**, it is seen that the mean for females in response to the “Like” question on the DEQ was 67, with a SEM of 9.504, and the mean for males being 42.818, with a SEM of 8.862. The p -value was 0.091, which although shows no statistical significance, it should be mentioned that it shows a slight correlation between the like of MDMA and females. In **Figure 2C**, it is seen that the mean for females in response to the “More” question on the DEQ was 45.142, with a SEM of 15.491, and the mean for males being 24.636, with a SEM of 8.983. The p -value was 0.235, showing that there was no statistical significance between females or males in response on the DEQ More question. In **Figure 2D**, it is seen that the mean for females in response to the “Dislike” question on the DEQ was 17.571, with a SEM of 16.382, and the mean for males being 34.636, with a SEM of 8.029. The p -value was 0.327, showing that there was no statistical significance between females or males in response on the DEQ Dislike question. In **Figure 2E**, it is seen that the mean for females in response to the “High” question on the DEQ was 64.714, with a SEM of 11.989, and the mean for males being 61.454, with a SEM of 5.537. The p -value was 0.784, showing that there was no statistical significance between females or males in response on the DEQ High question.

3.3 POMS Graphs

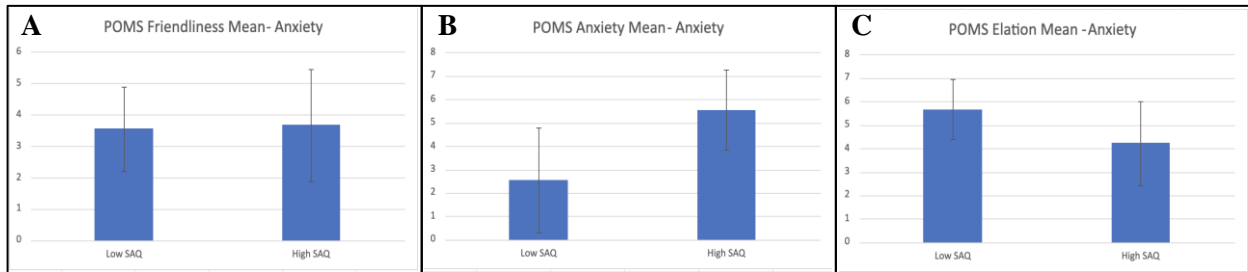


Figure 3 These graphs show the correlations between each item on the POMS and the high and low social anxiety cohorts. No statistical significance found because all p -values were greater than 0.05. **(A)** Graphical representation of POMS friendliness question and low/high social anxiety ($n = 18$) $p = 0.961$. **(B)** Graphical representation of POMS anxiety question and low/high social anxiety ($n = 18$) $p = 0.319$. **(C)** Graphical representation of POMS elation question and low/high social anxiety ($n = 18$) $p = 0.554$. (Author)

In **Figure 3**, the effect of the drug on three different items was compared to whether or not the participant experienced high or low social anxiety based on the SAQ-A30. In **Figure 3A**, it is seen that the mean for high social anxiety in response to the “Friendliness” question on the POMS was 3.667, with a SEM of 1.795, and the mean for low social anxiety being 3.556, with a SEM of 1.344. The p -value was 0.961, showing that there was no statistical significance between high or low social anxiety in response on the POMS Friendliness question. In **Figure 3B**, it is seen that the mean for high social anxiety in response to the “Anxiety” question was 5.556, with a SEM of 1.708, and the mean for low social anxiety being 2.556, with a SEM of 2.236. The p -value was 0.319, showing that there was no statistical significance between high or low social anxiety in response on the POMS Anxiety question. In **Figure 3C**, it is seen that the mean for high social anxiety in response to the “Elation” question was 4.222, with a SEM of 1.785, and the mean for low social anxiety being 5.667, with a SEM of 1.278. The p -value was 0.554, showing that there was no statistical significance between high or low social anxiety in response to the POMS Elation question.

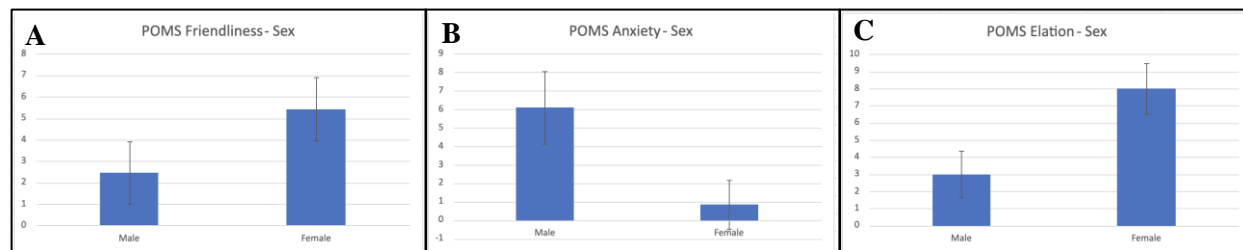


Figure 4 These graphs show the correlations between each item on the POMS and sex (female or male). Statistical significance was found in males experiencing high levels of elation when on MDMA. (A) Graphical representation of POMS friendliness question and sex (female or male) (n = 18) $p = 0.190$. (B) Graphical representation of POMS anxiety question and sex (female or male) (n = 18) $p = 0.080$, showing slight correlation between anxiety and males when on MDMA. (C) Graphical representation of POMS elation question and sex (female or male) (n = 18) $p = 0.032$, showing statistical significance between males and elation when on MDMA. (Author)

In **Figure 4**, the effect of the drug on three different items was compared to the sex (either female or male) of the participant. In **Figure 4A**, it is seen that the mean for females in response to the “Friendliness” question on the POMS was 5.428, with a SEM of 1.477, and the mean for males being 2.454, with a SEM of 1.454. The p -value was 0.190, showing that there was no statistical significance between females or males in response on the POMS Friendliness question. In **Figure 4B**, it is seen that the mean for females in response to the “Anxiety” question on the POMS was 0.857, with a SEM 1.31, and the mean for males being 6.09, with a SEM of 1.972. The p -value was 0.080, which although shows no statistical significance, it should be mentioned that it shows a slight correlation between anxiety and males when on MDMA. In **Figure 4C**, it is seen that the mean for females in response to the “Elation” question on the POMS was 8, with a SEM of 1.48, and the mean for males being 3, with a SEM of 1.361. The p -value was 0.032, which does show statistical significance between males and elation when on MDMA.

3.4 VAS Graphs

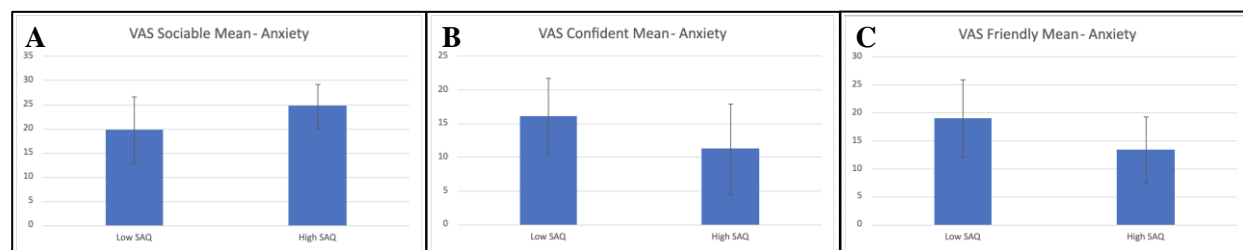


Figure 5 These graphs show the correlations between each item on the VAS and the high and low social anxiety cohorts. No statistical significance found because all p -values were greater than 0.05. (A) Graphical representation of VAS sociable question and low/high social anxiety (n = 18) $p = 0.561$. (B) Graphical representation of VAS confident question and low/high social anxiety (n = 18) $p = 0.584$. (C) Graphical representation of VAS friendly question and low/high social anxiety (n = 18) $p = 0.541$. (Author)

In **Figure 5**, the effect of the drug on three different items was compared to whether or not the participant experienced high or low social anxiety based off of the SAQ-A30. In **Figure 5A**, it is seen that the mean for high social anxiety in response to the “Sociable” question on the VAS was 24.667, with a SEM of 4.582, and the mean for low social anxiety being 19.778, with a SEM of 6.861. The p -value was 0.561, showing that there was no statistical significance between high or low social anxiety in response on the VAS Sociable question. In **Figure 5B**, it is seen that the mean for high social anxiety in response to the “Confident” question on the VAS was 11.222, with a SEM of 6.732, and the mean for low social anxiety being 16.111, with a SEM of 5.608. The p -value was 0.584, showing that there was no statistical significance between high or low social anxiety in response on the VAS Confident question. In **Figure 5C**, it is seen that the mean for high social anxiety in response to the “Friendly” question on the VAS was 13.333, with a SEM of 5.918, and the mean for low social anxiety being 19, with SEM of 6.877. The p -value was 0.541, showing that there was no statistical significance between high or low social anxiety in response on the VAS Friendly question.

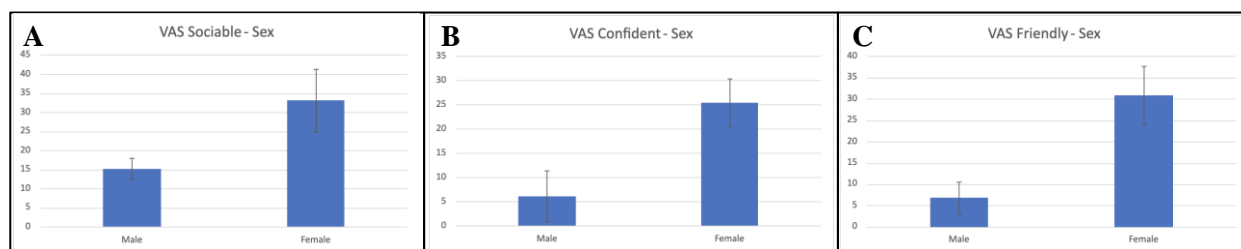


Figure 6 These graphs show the correlations between each item on the VAS and sex (female or male). Statistical significance was found in females experiencing high levels of sociability, confidence, and friendliness when on MDMA. **(A)** Graphical representation of VAS sociable question and sex (female or male) ($n = 18$) $p = 0.026$, showing statistical significance between females and sociability when on MDMA. **(B)** Graphical representation of VAS confident question and sex (female or male) ($n = 18$) $p = 0.023$, showing statistical significance between females and confidence when on MDMA. **(C)** Graphical representation of VAS friendly question and sex (female or male) ($n = 18$) $p = 0.004$, showing statistical significance between females and friendliness when on MDMA. (Author)

In **Figure 6**, the effect of the drug on three different items was compared to the sex (either female or male) of the participant. In **Figure 6A**, it is seen that the mean for females in response to the “Sociable” question on the VAS was 33.142, with a SEM of 8.189, and the mean for males being 15.272, with a SEM of 2.74. The p -value was 0.026, which does show statistical significance between females and sociability when on MDMA. In **Figure 6B**, it is seen that the mean for females in response to the “Confident” question on the VAS was 25.428, with a SEM of 4.913, and the mean for males being 6.181, with a SEM of 5.249. The p -value was 0.023, which does show statistical significance between females and confidence when on MDMA. In **Figure 6C**, it is seen that the mean for females in response to the “Friendly” question on the VAS was 30.857, with a SEM of 6.874, and the mean for males being 6.818, with SEM of

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3.832. The p -value was 0.004, which does show statistical significance between females and friendliness when on MDMA.

4. Conclusion and Future Studies

The primary goal of this project was to further investigate the relationship between social anxiety (high or low), sex, and MDMA. My results suggest a potential prosocial effect of elation that males experience when given MDMA ($p = 0.032$) (**Fig. 4C**) and a potential prosocial effect of sociability, confidence, and friendliness that females experience when given MDMA ($p = 0.026$, 0.023 , and 0.004 , respectively) (**Fig. 6**). This study showed some of the benefits of MDMA when used appropriately in sex. I identified the total SAQ-A30 for each participants and their respective high or low anxiety rating (**Table 1**), found the mean of each item for each item per questionnaire when compared to both social anxiety (high or low) and sex (female or male) (**Fig. 1-6**). This study showed that elation is significant in males when compared to sex (female or male) on MDMA. Additionally, this study showed that sociability, confidence, and friendliness are significant in females ($p = 0.026$, 0.023 , and 0.004 , respectively) (**Fig. 6A-C**) when compared to sex (female or male) on MDMA. Overall, this suggests that females tend to have increased feelings of sociability, confidence, and friendless when on MDMA than males.

4.1 Sex and MDMA

The data collected from the study showed statistical significance between females and increased levels of friendliness, confidence, and sociability when on MDMA (**Fig. 6**). Due to the p values being less than 0.05, females exhibited increased levels of friendliness ($p = 0.026$), confidence ($p = 0.023$), and sociability ($p = 0.004$). Also, statistical significance was shown between males and increased levels of elation (**Fig. 4C**). Due to the p values being less than 0.05, males exhibited increased levels of elation ($p = 0.032$). Although males did show this increase in elation, females showed an increase in multiple factors, suggesting that they were impacted by MDMA more than males.

4.2 Limitations and Future Work

This study was limited primarily due to the study being conducted remotely. Not all software was available for use in performing various analyses remotely. Additionally, the study had been performed previously by the University of Chicago researchers, so the data had been already collected. This leads to several limitations since it would have been ideal to gauge the full range of the experiment. Also, the study conducted by the researchers at the University of Chicago had several limitations itself. The participants were recruited via flyers spread across the University and social media and must have used MDMA prior to experimentation. The sample size of the participants - 18 - was also relatively small. Thus, the participants are not representative of the general population. If this study were continued, the

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participants must be representative of the population in order to be generalizable. So, more participants should be taken from multiple age groups across the country. It should also be noted that future studies involving MDMA should not be random, as MDMA may impact those with severe diseases or disorders. Thus, psychiatrists should be involved in the selection process for participants.

The SAQ-A30 determined the social anxiety cohorts. However, more measures should be used or people diagnosed with social anxiety should be used instead of relying on one test to limit outliers. If given more time, more measures - including the ones associated with elation, friendliness, confidence, and sociability - could be analyzed in participants diagnosed with social anxiety when compared to sex to determine its significance. Also, other measures could be compared in larger groups of people to determine an accurate significance with social anxiety.

4.3 Conclusion

My study successfully determined benefits, increased positive moods, in terms of sex (female or male) in males (elation) ($p = 0.032$) (**Fig. 4C**) [but more so females when given MDMA on their mood (specifically confidence, friendliness, and sociability ($p = 0.026, 0.023, \text{ and } 0.004$, respectively) (**Fig. 6A-C**)]. These results support previous findings of durable and rapid improvement in social anxiety symptoms in autistic adults following MDMA psychotherapy [12,13]. Although sex was not analyzed in the previous study, my results show that it sex should be a factor considered in future experiments. Females are more likely than men to have generalized anxiety disorders and score higher on self-reported fear tests [45,46]. Thus, exploring these sex differences, or specifically MDMA in females, may lead to an effective way for treating social anxiety, especially for females. Additionally, these results could support previous findings of MDMA use for PTSD patients as well as Autism patients [12,13]. 3,4-Methylenedioxymethamphetamine (MDMA) is a psychostimulant drug that is widely used for its recreational use, however its prosocial effects are only now starting to be analyzed, as they were in this study, and should be continued with larger cohorts focused on sex after noticing trends and significance in this study.

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