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Journal

Journal of Psychopharmacology, 38(3)

Authors

Bershad, Anya
Hsu, David
de Wit, Harriet

Publication Date

2024-03-01

DOI

10.1177/02698811231224153

Peer reviewed

HHS Public Access

Author manuscript

J Psychopharmacol. Author manuscript; available in PMC 2024 September 17.

Published in final edited form as:

J Psychopharmacol. 2024 March ; 38(3): 297–304. doi:10.1177/02698811231224153.

MDMA enhances positive affective responses to social feedback

Anya K Bershad[1], **David T Hsu**[2], **Harriet de Wit**[3]

[1]Department of Psychiatry and Biobehavioral Sciences, UCLA, Los Angeles, CA, USA

[2]Department of Psychiatry, Renaissance School of Medicine at Stony Brook University, Stony Brook, NY, USA

[3]Department of Psychiatry and Behavioral Neuroscience, University of Chicago, Chicago, IL, USA

Abstract

Background: The prosocial compound ± 3,4-methylenedioxymethamphetamine (MDMA) is an amphetamine derivative that has shown promise as an adjunct to psychotherapy in the treatment of post-traumatic stress disorder. MDMA increases positive responses to social images, and it has been suggested that the ability of MDMA to positively bias social perception may underlie its therapeutic efficacy as a psychotherapy adjunct. However, the effect of the compound on affective responses to positive or negative social feedback has not been tested.

Aims: In this study, we aimed to test the effects of MDMA compared to placebo and the prototypical stimulant, methamphetamine (MA), on responses to positive and negative social feedback.

Methods: This was a double-blind, placebo-controlled, crossover trial (NCT03790618), comparing the effects of two doses of MDMA (0.75 mg/kg, 1.5 mg/kg) to both placebo and MA (20 mg) on responses to a personalized social feedback task, similar to a dating app, in healthy adult volunteers ages 18–40 (N = 36, 18 women, 18 men).

Results/Outcomes: The high dose of MDMA increased positive affective responses to social feedback.

Conclusions/Interpretations: These findings suggest one process by which MDMA may facilitate social connection. Further work is needed to understand how MDMA affects responses to more generalized types of social feedback and to understand these effects in clinical populations.

Keywords

MDMA; social feedback; social rejection; social acceptance

Corresponding author: Harriet de Wit, Department of Psychiatry and Behavioral Neuroscience, University of Chicago, 5841 S. Maryland Ave., MC3077, Chicago, IL 60637, USA. hdew@uchicago.edu.
David T Hsu is now affiliated to Tonix Pharmaceuticals, Chatham, NJ, USA.

Declaration of conflicting interests

HdW is on the board of PharmAla Biotech, Inc. and is a consultant to Awakn Life Sciences and Gilgamesh Pharmaceuticals. DTH is currently employed by Tonix Pharmaceuticals.

Supplemental material

Supplemental material for this article is available online.

Introduction

Responding appropriately to social feedback is critical to functioning in society and to maintaining healthy family, social, and professional relationships. Deficits in affective responses to social input are symptomatic of many disorders across the spectrum of psychiatric illness, many of which lead to significant functional impairment (Fulford et al., 2018; Kupferberg et al., 2016; Ventura et al., 2013). From autism to mood, personality, and psychotic disorders, many patients experience either heightened responses to negative social input or blunted responses to positive social input (Kennedy and Adolphs, 2012). Such alterations in social function and their resulting social disconnection have serious health consequences. One recent metanalysis suggested the effect of social disconnection on mortality is comparable to that of smoking (Holt-Lunstad et al., 2015). Yet, to date, there are no effective pharmacologic treatments for impaired social processing.

The amphetamine derivative ± 3,4-methylenedioxymethamphetamine (MDMA), which is known as an “empathogen” for its ability to induce feelings of social connection, may be a promising way to positively bias social perception. MDMA is a psychostimulant that shares many pharmacological properties with amphetamines, but in addition, reportedly produces feelings of empathy and closeness with others and increases motivation to socialize (Bershad et al., 2016; Kamilar-Britt and Bedi, 2015). The drug is used recreationally in social contexts, but has garnered recent interest as an adjunct to psychotherapy in the treatment of post-traumatic stress disorder (PTSD) and other psychiatric disorders (Mitchell et al., 2021). Some clinical trials investigating MDMA in the treatment of PTSD have suggested that the drug acts by enhancing therapeutic alliance (Sottile and Vida, 2022). In pre-clinical studies, MDMA consistently increases prosocial behavior (Thompson et al., 2007). In laboratory studies in healthy human volunteers, MDMA enhances subjective feelings of sociability, friendliness, and confidence, in addition to positive affective responses to social cues (Baggott et al., 2016; Bedi et al., 2009; Bershad et al., 2019; Kirkpatrick et al., 2014; Wardle and de Wit, 2014). Furthermore, it reduces responses to negative social input, such as blunting neural responses to threatening social stimuli and alleviating social anxiety (Bedi et al., 2009; Danforth et al., 2018). It is perhaps partly as a result of these prosocial effects that MDMA has shown promise as an adjunct to psychotherapy in the treatment of PTSD (Mitchell et al., 2021).

MDMA has a somewhat unique mechanism of action that may contribute to its prosocial effects. Like other amphetamines, MDMA induces the releases of dopamine, norepinephrine, and serotonin. However, unlike other amphetamines, MDMA induces the release of dopamine indirectly, through its induction of the release of serotonin (Rothman et al., 2001; Rudnick and Wall, 1992). These preferential effects on the serotonergic system lead to the release of oxytocin (Thompson et al., 2007) and are thought to underlie some of the prosocial effects of the drug (Liechti, 2015).

The effects of MDMA on social function not only resemble effects of other prototypic stimulant drugs, but also differ in certain key measures. Other amphetamines, such as *d*-amphetamine and methamphetamine (MA), produce several prosocial effects. They increase subjective ratings of sociable emotions, including how talkative, friendly, and social

individuals report feeling (Tancer and Johanson, 2003; van Wel et al., 2012) and increase emotional empathy in some contexts (Dolder et al., 2018). Both MA and *d*-amphetamine increase speech quantity (Griffiths et al., 1977; Ward et al., 1997; Wardle et al., 2012), and MA increases fluency of speech (Marrone et al., 2010). MDMA produces many of these effects, but in addition, it has distinctive effects on trust, generosity, and feelings of connection (Bershad et al., 2016).

Thus far, the effects of MDMA on social processing have been tested using simple, standardized social processing tasks. These tasks have included visual attention and reactivity to static images of emotional faces (Bedi et al., 2009; Bershad et al., 2019; Wardle and de Wit, 2014), emotion identification using static images or short morphed video clips of actors (Hysek et al., 2012; Wardle and de Wit, 2014), and reactivity to images with social content (Kuypers et al., 2014, 2017; Schmid et al., 2014; Wardle and de Wit, 2014). Other studies have demonstrated effects of MDMA on social decision-making in prisoner's dilemma and resource-allocation tasks (Gabay et al., 2019; Kirkpatrick et al., 2015) and speech (Agurto et al., 2020; Baggott et al., 2015; Bedi et al., 2014; Wardle and de Wit, 2014). One study showed that MDMA buffered the decrease in positive mood following simulated social exclusion using the Cyberball paradigm (Frye et al., 2014). However, the Cyberball task uses only implied social exclusion, when the participant stops receiving the ball from the other players. Thus, it is not known whether MDMA alters responses in the context of overt social acceptance and rejection.

The present study used The Social Feedback Task (Hsu et al., 2013) to assess effects of MDMA and a comparison drug, MA, on positive and negative social feedback in a laboratory setting. This task was administered in this trial as part of a battery of other behavioral tasks, previously published in Bershad et al. (2019). In this task, participants first view profiles of individuals and select the profiles that they consider to be most likely to have a mutual connection with them. Then, they receive feedback about whether these others like (acceptance) or do not like them (rejection). This task has previously been used with positron emission tomography (PET) imaging to assess opioid responses to social feedback in healthy volunteers (Hill et al., 2022; Hsu et al., 2013) and patients with major depressive disorder (Hsu et al., 2015). The task has also been used to investigate neural responses to social feedback using functional magnetic resonance imaging (fMRI) in healthy volunteers (Hsu et al., 2020) and patients with depression (Sankar et al., 2019; Yttredahl et al., 2018). The present study tested the effects of MDMA, compared to both placebo, and the prototypical stimulant, MA, on affective responses to overt social acceptance and rejection in healthy volunteers. We hypothesized that MDMA would both reduce negative affective responses to rejection and enhance positive affective responses to acceptance.

Methods

Study design

The behavioral task described here was part of a previously published study (Bershad et al., 2019), and we thus report the subjective and cardiovascular effects of MDMA and MA as previously reported. In this double-blind, placebo-controlled crossover study, participants attended four study sessions at which they received placebo, 0.75 mg/kg MDMA, 1.5 mg/kg

MDMA, or 20 mg MA in randomized order. They completed the Social Feedback Task (and other behavioral tasks published in Bershad et al., 2019) during expected peak drug effect. In the Social Feedback Task, participants received acceptance or rejection feedback from images of preferred-sex individuals whom they had identified as likely to form a mutual connection. Measures of subjective and cardiovascular drug effects were collected at regular intervals throughout the sessions. All procedures were carried out in accordance with the Declaration of Helsinki and approved by the University of Chicago Institutional Review Board.

Participants

Healthy volunteers (N = 36), 18–40 years old, with some reported previous MDMA experience (4–40 uses), were recruited from the University of Chicago and surrounding area. Participants underwent a physical and psychiatric screening, which included an in-person psychiatric interview, drug use history questionnaire, and electrocardiogram. Exclusion criteria were current diagnoses of psychiatric disorders including major depressive disorder (Diagnostic and Statistical Manual (DSM-V); American Psychiatric Association, 2013), serious medical condition, history of cardiac or liver disease, current or past substance abuse, individuals regularly using any contraindicated medications, and individuals with a previous negative reaction to MDMA. Women who were pregnant, planning to become pregnant, or lactating were excluded. Inclusion criteria were: fluency in English, a minimum of a high school education, and BMI between 19 and 30 kg/m^2.

Study drugs

MDMA in powdered form (0.75 mg/kg or 1.5 mg/kg; Organix Inc., Woburn, MA) or MA (20 mg; Desoxyn) was placed in opaque size 00 capsules with lactose (United States Pharmacopeia) filler. Placebo capsules contained only lactose.

Session procedures

Orientation.—Participants attended a 1-h orientation during which they received details of the study, provided informed consent, and completed profile ratings for the Social Feedback Task. To minimize expectancy effects, participants were told they could receive a stimulant drug such as MDMA or MA, a sedative drug such as Valium, a cannabinoid such as marijuana, or placebo.

Study sessions.—The four drug sessions took place from 9:00 am to 1:30 pm separated by at least 72 h. They were conducted in a comfortably furnished room in a research laboratory containing chairs, a desk, computer, a television, video player, and reading materials. During the sessions, the participants were allowed to watch movies, read, or relax when not completing study questionnaires or tasks. They were asked to abstain from drug and alcohol use for 48 h before each session, and compliance was verified at the start of each session with a urine drug (ToxCup, Branan Medical Corporation, Irvine, CA) and breathalyzer tests (AlcosensorIII, Intoximeters, St. Louis, MO). Women were tested for pregnancy before each session (AimStickPBD, hCG professional, Craig Medical Distribution). Participants then completed baseline measures of mood, heart, rate, and blood pressure. At 9:30 am, participants ingested a capsule containing MA (20 mg),

MDMA (0.75 or 1.5 mg/kg), or placebo. Participants then relaxed for 1 h, and subjective and cardiovascular measures were collected again at 10:00 am and 10:30 am. At 11 am, participants completed the Social Feedback Task and other tasks reported elsewhere (Bershad et al., 2019). Cardiovascular measures were re-assessed at 12:30 pm and 1:00 pm. Finally, participants completed an end of session questionnaire and left the laboratory. Participants were debriefed after the final drug session.

Subjective questionnaires

Drug Effects Questionnaire.—The Drug Effects Questionnaire consists of five questions on a visual analog scale assessing subjective drug effects. Subjects were asked to rate the extent they felt a drug effect, whether they liked or disliked the drug effect, if they felt high, and if given a choice, whether they would want more of the drug.

End of Session Questionnaire.—The End of Session Questionnaire consists of questions about what drug participants believed they received and how much they would like to take the drug again.

Behavioral tasks

The Social Feedback Task (Hsu et al., 2013; Figure 1) is designed to test affective responses to simulated social acceptance and rejection. During the orientation session, participants completed an online personal profile that included age, major/occupation, a list of their interests, a short paragraph of their positive qualities, and a picture of themselves. Participants also selected at least 120 online profiles of preferred-sex individuals with whom they would be most interested in forming an intimate relationship, from a collection of 500 profiles of men and women. For each profile, subjects answered two questions (“Would I like this person?” and “Do I think this person would like me?”) on a seven-point Likert scale from “definitely no” to “definitely yes.” To increase feedback salience, only profiles with the highest ratings for both questions were used (Hsu et al., 2013). Separate sets of profiles were used for each drug session.

During the drug sessions, at expected peak drug effect, subjects were presented with their highest-rated profiles along with feedback that they were not liked (rejection condition), liked (acceptance condition), or that the ratings had not been completed (neutral condition). Blocks each contained 12 unique trials of equal length with varying levels of rejection/acceptance (seven trials “definitely no/yes,” four trials “very likely no/yes,” and one trial “likely no/yes”). Subjects were asked to imagine that the profiles and feedback were real. During each trial, subjects reported on a five-point Likert scale how much they felt sad, rejected, happy and accepted (order randomized in each trial).

Cardiovascular measures

Portable monitors were used to measure heart rate and blood pressure (Omron 10 Plus, Omron Healthcare) at five time points throughout session (−15, 30, 60, 180, and 240 min post-drug administration). Mean arterial pressure was calculated with the following equation: MAP = (systolic BP+2 × diastolic BP)/3.

Power calculation and statistical analysis

With a sample size of 36 and significance level of $\alpha = 0.05$ and a moderate within-subject correlation of $r = 0.5$, there was 80% power to detect MDMA effects of size $f = 0.2$, a standard medium effect. This effect size is consistent with previously published studies investigating the prosocial effects of MDMA. Analyses were conducted using IBM Statistial Package for the Social Sciences (SPSS). Missing cases (due to equipment malfunction or other data collection problems) were deleted list-wise, which led to smaller sample sizes for some analyses. For subjective measures collected at multiple time points, peak change from baseline was calculated for the purpose of analysis. Subjective effects of the drug were assessed using repeated measures analysis of variance (ANOVA), with dose as a within-subjects factor. The Social Feedback Task was analyzed using repeated measures ANOVA, with dose and condition as within-subject factors. Significant main effects and interactions were followed with post hoc *t*-tests.

Results

Demographics

The subjects were equal numbers of men and women (mean age 24.8 ± 4.2 years), mostly Caucasian (61%), with some post-graduate education. Demographic characteristics are summarized in Table 1.

Subjective drug effects

MDMA (both doses) and MA significantly increased ratings of “feel drug” [Table 2, Supplemental Figure 1: Dose $F(3,105) = 38.04$, $p < 0.001$]. All doses also increased ratings of “like drug,” [Dose $F(3,105) = 20.21$, $p < 0.001$]. All doses also increased ratings of “feel high,” [Dose $F(3,105) = 24.11$, $p < 0.001$]. The 1.5 mg/kg dose of MDMA increased ratings of “dislike drug” [Dose $F(3,105) = 4.59$, $p = 0.01$]. All doses increased ratings of “want more” [Dose $F(3,105) = 12.69$, $p < 0.001$].

Cardiovascular drug effects

Both doses of MDMA and MA significantly increased heart rate [$F(3,105) = 11.33$, $p < 0.001$] and MAP [$F(3,105) = 13.87$, $p < 0.001$], compared to placebo.

Social Feedback Task

The Social Feedback Task induced its expected effects on emotion following social acceptance and rejection. Participants reported feeling more “sad and rejected” in the reject condition, compared to neutral and accept [Condition $F(2,62) = 43.49$, $p < 0.001$; reject > neutral and accept $p < 0.001$] and more “happy and accepted” after being accepted [Condition $F(2,62) = 70.51$, $p < 0.001$; accept > neutral and reject $p < 0.001$]. The higher dose of MDMA increased ratings of “happy and accepted” following social feedback [Dose $F(3,93) = 2.92$, $p = 0.04$; 1.5 mg/kg MDMA vs. placebo $p = 0.01$, no significant differences between MDMA and MA or the two doses of MDMA; Figure 2(a)]. There were no significant effects of dose on ratings of “sad and rejected” (Figure 2(b)). There were no

significant dose by condition interactions. There were no significant effects of dose order on either positive or negative ratings following social feedback.

Blinding

During the placebo session, 23 participants (63.9%) correctly guessed what they had received. On the MA session, nine participants (25%) correctly guessed that they had received a stimulant. During the low-dose MDMA session, 17 participants (47.2%) correctly guessed that they had received MDMA, and during the high-dose MDMA session, 25 participants (69.4%) guessed correctly. The other guesses of the participants are reported in Table 3.

Discussion

In this study, we investigated the effects of MDMA, compared to placebo and MA, on affective responses to social feedback. We predicted that MDMA would both enhance positive affective responses to social acceptance and diminish negative affective responses to social rejection, as compared to both placebo and MA. In partial support of our hypothesis, we found that high doses of MDMA increased positive affective responses to social feedback, and that MA did not significantly influence responses to either condition.

The finding that MDMA increased positive affective responses is in line with a body of work suggesting that the drug enhances reactivity to social rewards. MDMA increased ratings of positivity of images with social content (Wardle and de Wit, 2014) and enhanced the pleasantness of social touch (Bershad et al., 2019). Beyond subjective ratings, MDMA selectively facilitated visual attention and psychophysiological responses to faces expressing positive emotions, suggesting increased salience of these positive social cues (Bershad et al., 2019; Wardle and de Wit, 2014). The results reported here build upon these previous findings by showing that the drug also boosts positive mood responses to a more complex, overt form of social feedback.

We did not find a significant effect of MDMA on feelings of rejection following social feedback, contrary to our hypothesis. Our prediction was based on a number of studies that have shown that MDMA dampened several dimensions of responses to negative social input. In particular, Frye et al. (2014)reported that MDMA reduced affective responses to perceived social rejection using the Cyberball paradigm. Others have shown that MDMA reduced the ability to identify negative facial expressions (Hysek et al., 2012, 2014; Kirkpatrick et al., 2014; Wardle and de Wit, 2014; Schmid et al., 2014;), blunted amygdala reactivity to threatening faces (Bedi et al., 2009), enhanced fear extinction and fear extinction retention (Vizeli et al., 2022), and reduced social anxiety (Baggott et al., 2016; Danforth et al., 2018). It is not clear why MDMA did not dampen feelings of rejection during the Social Feedback Task in the present study. It appears that the simulated social rejection was realistic enough, or salient enough, to significantly increase negative mood and induce feelings of rejection. However, this increase was not large; indeed the negative mood following rejection was not greater than positive mood following rejection, and it is possible that MDMA would have an effect on stronger feelings of rejection that we were not able to observe.

Although the present study was conducted with healthy volunteers, the findings are nevertheless relevant to individuals with psychiatric disorders involving aberrant responses to social input. MDMA has shown promise as an adjunct to psychotherapy in the treatment of PTSD (Mitchell et al., 2021), but the behavioral mechanisms underlying its effectiveness in facilitating therapy are not known. Our results suggest that MDMA may enhance affective receptiveness to positive social environments, which may relate to the accepting, empathic environment cultivated during therapeutic sessions (Mithoefer, 2017). Furthermore, our results may be relevant to other psychiatric disorders involving social anhedonia, such as schizophrenia (Barkus and Badcock, 2019; Xie et al., 2014), major depressive disorder (Sherdell et al., 2012), PTSD (Nawijn et al., 2015), and autism spectrum disorder (Delmonte et al., 2012). In schizophrenia, for example, despite their profound functional consequences for patients, no medications are available to treat deficits in social motivation that commonly occur in the illness (Fulford et al., 2018; Ventura et al., 2013). Given its social effects, a compound like MDMA may be helpful in these populations when used a limited number of times in combination with a psychosocial intervention, such as social skills training. The drug may be particularly helpful during these types of training interventions, the effectiveness of which can be limited by poor patient motivation. More work investigating the effects of MDMA on affective responses to social feedback in clinical populations is warranted.

It should be noted that while our findings may have implications for the use of MDMA in therapeutic settings (as an adjunct to psychosocial interventions, for instance), they also may suggest risks and have implications for the misuse of the drug. If MDMA increases positive affective responses to social feedback, this could make individuals vulnerable in nonmedical settings, such as recreational settings. The drug could make individuals more susceptible to dangerous social situations in which they may be taken advantage of, and this underscores the importance of rigorous safety measures and monitoring in clinical contexts.

Our study had a number of strengths. First, we used a double-blind, placebo-controlled, crossover study design and included an active comparator drug. This allowed for careful consideration to expectancies, and the effectiveness of our blinding is reported. The inclusion of MA as a prototypical stimulant drug allowed for the assessment of prosocial effects unique to MDMA. Furthermore, we included two doses of MDMA to assess dose-related effects. Finally, the Social Feedback Task is a novel way to assess the effects of MDMA on affective responses to different social feedback, and the task is specially tailored to each participant to increase the salience of the social cues.

There are a few limitations to our design that warrant discussion. While the task was designed to closely resemble a virtual social interaction that someone might encounter (i.e., on a dating app), the task was a simplified paradigm rather than a real-world exchange. In line with how this task has previously been implemented (Hsu et al., 2013), subjects were not led to believe that their interactions in the task involved real people who liked or disliked them, but were asked to imagine how they might feel receiving the social feedback they received. This decision not only allowed us to avoid the issue of inconsistency in the effectiveness of deception, but it also limited the validity of the task. Furthermore, a simulated dating app scenario may have limited applicability to social interaction outside

the realm of romantic relationships. Another limitation is that plasma levels of MDMA were not collected, limiting our ability to assess drug absorption. Additionally, sessions were spaced 72 h apart, but there is some evidence that CYP2D6 activity might not be fully recovered for several more days after MDMA administration (O'Mathúna et al., 2008). Therefore, although we did not show significant order effects in this study, there may have been lingering effects of MDMA that we did not detect. Finally, our primary measure is a self-report measure, and it is possible there exist discrepancies between self-reported mood and more objective measures (behavioral, physiological, neural) of affective reactivity.

In summary, we investigated the effects of MDMA and MA on responses to social feedback. We report that MDMA, but not MA, enhanced positive affective responses to social feedback compared to placebo. This finding has implications for understanding one mechanism by which MDMA acts as a prosocial compound.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by NIH grant R01DA02812 to HdW. AKB is supported by NIH grant DP5OD036172 to AKB.

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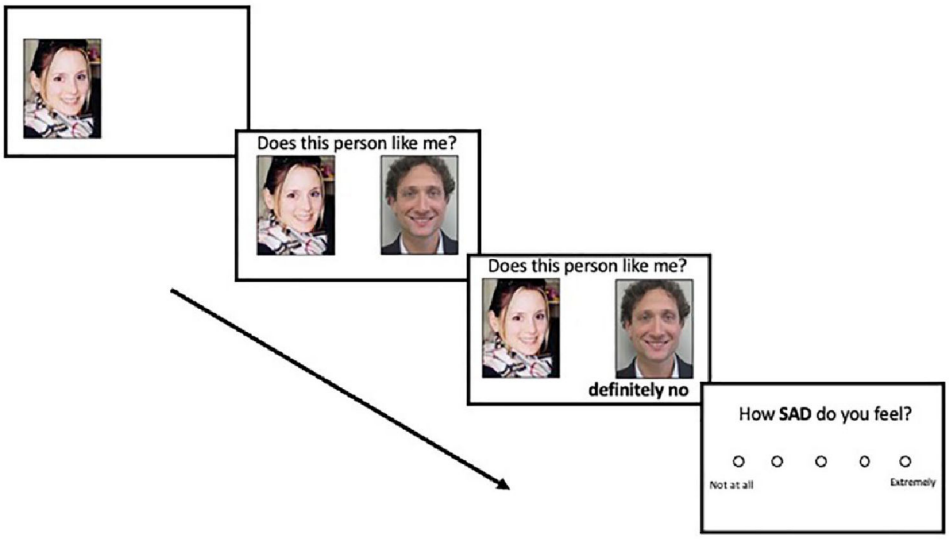

Figure 1.

The Social Feedback Task. During each trial, the participant was first presented with a picture of themselves, followed by a picture of a highly rated profile along with the other person's rating of the participant. Stimuli were arranged into blocks of social acceptance, social rejection, and neutral feedback. Subjects were subsequently asked to rate their mood and feelings of rejection and acceptance. A fixation cross was presented between blocks.

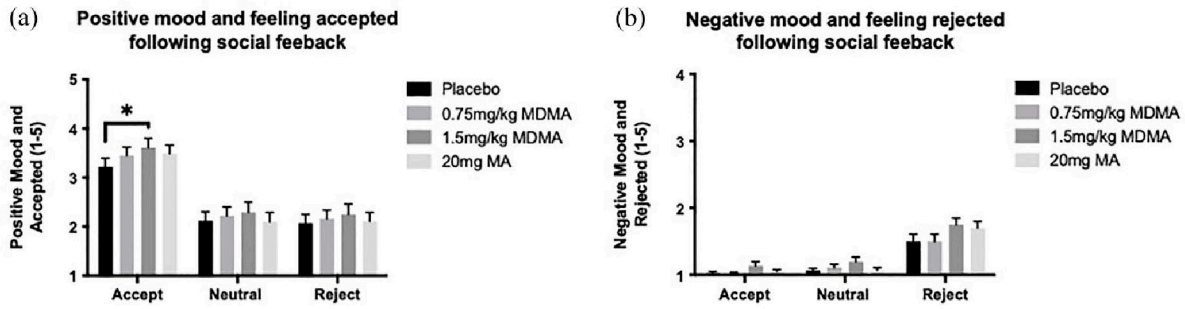

Figure 2.

Effects of MDMA and MA on positive (a) and negative (b) mood during the Social Feedback Task by condition. Bars depict mean ± SEM. Asterisk indicates significant difference from placebo, $p < 0.01$.

MDMA: 3,4-methylenedioxymethamphetamine; MA: methamphetamine; SEM: standard error of the mean.

Table 1.

Participant demographics.

Sex	
Male	18 (50)
Female	18 (50)
Race	
Caucasian	22 (61)
African American	5 (14)
Asian	5 (14)
Other	4 (11)
Age	24.8 (4.2); range 19–39
BMI	23.3 (1.1); range 19–26
Education in years	15.2 (1.5); range 12–16
Substance use	
Alcoholic drinks/week	3.7 (2.3); range; 2–10
MDMA (lifetime number of times used)	11.1 (9.8); range; 4–40

Demographic and drug use characteristics reported as *N* (%) or *M* (SD).

SD: standard deviation; BMI: body mass index; MDMA: 3,4-methylenedioxymethamphetamine.

Table 2.

Subjective and cardiovascular drug effect means, standard deviations, and time to peak effect.

Measure	Placebo	0.75 mg/kg MDMA	1.5 mg/kg MDMA	20 mg MA
DEQ (peak change; 1–100)				
Feel	22.75 (26.12)	47.83 (26.94)***	77.97 (21.72)***	46.28 (27.49)***
	60 min	120 min	60 min	120 min
Like	29.67 (34.76)	59.47 (30.88)***	78.75 (22.40)***	70.81 (30.66)***
	60 min	120 min	120 min	120 min
High	19.92 (26.95)	43.94 (30.59)*	71.75 (26.89)***	24.5 (25.18)***
	60 min	60 min	60 min	60 min
Dislike	15.67 (21.78)	25.08 (21.72)	34.97 (28.51)***	24.50 (25.18)
	120 min	120 min	60 min	120 min
Want more	25.56 (33.24)	55.22 (32.47)***	64.25 (35.32)***	63.83 (35.01)***
	60 min	120 min	120 min	180 min
Cardiovascular Measures (peak change)				
Heart rate (bpm)	79.97 (12.41)	87.64 (15.79)**	92.53 (16.29)***	91.19 (15.01)***
	30 min	60 min	180 min	180 min
Mean arterial pressure (mm Hg)	92.45 (11.23)	96.65 (10.94)*	102.91 (11.47)***	101.41 (12.92)***
	60 min	60 min	120 min	180 min

MDMA: 3,4-methylenedioxymethamphetamine; MA: methamphetamine; DEQ: Drug Effects Questionnaire.

*Signifies significant effect of dose versus placebo $p < 0.05$.

**Signifies significant effect of dose versus placebo $p < 0.01$.

***Signifies significant effect of dose versus placebo $p < 0.001$.

Table 3.

Participants' reports of which drug they believed they received on each session.

Drug guesses	Placebo session (%)	Low MDMA session (%)	High MDMA session (%)	MA session (%)
Placebo	63.9	13.9	2.8	19.4
Valium	22.2	25.0	11.1	5.6
Marijuana	2.8	8.3	0.0	11.1
MDMA	5.6	47.2	69.4	38.9
MA	5.6	5.6	16.7	25.0

Correct guesses are shaded gray.

MDMA: 3,4-methylenedioxymethamphetamine; MA: methamphetamine.