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Subjective responses to amphetamine in young adults with previous mood elevation experiences

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Abstract

Rationale—One risk factor for alcohol and substance misuse is hypomanic experiences, or periods of mood elevation. Young people who report hypomanic states are more likely to develop bipolar disorder (BP), and BP and other mood disorders increase the risk of addiction. We recently reported that young adults with a history of mood elevation experience less subjective effects from a low dose of alcohol, which may be predictive of future alcohol use. The finding with alcohol raised the question of whether this dampened response to a drug also applies to other drugs, such as amphetamine.

Objective—This study assessed responses of d-amphetamine in healthy young adults with varying experiences of mood elevation, as measured by the Mood Disorders Questionnaire (MDQ).

Methods—Healthy 18–19-year-olds ($N = 30$) with a range of MDQ scores participated in three 4-h laboratory sessions in which they received placebo, 10 mg, or 20 mg d-amphetamine. They completed mood questionnaires and cardiovascular measures.

Results—Individuals with higher MDQ scores reported less stimulation and euphoria after 10 mg, but not 20 mg, d-amphetamine, than individuals with lower scores. MDQ scores were not related to cardiovascular responses to the drug.

Conclusions—A history of mood elevation experiences or hypomania states is related to dampened response to a low dose of a psychostimulant drug, extending previous findings with dampened response to alcohol. This phenotype for mood disorders of dampened responses to drugs may contribute to risk for subsequent drug use or misuse.

Keywords

Amphetamine; Bipolar disorder; Hypomania; Subjective effects

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Compliance with ethical standards

Study procedures were approved by the Institutional Review Board at the University of Chicago and were carried out in accordance with the Declaration of Helsinki.

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Introduction

It has long been known that individuals vary in their subjective responses to stimulant drugs (Brown et al. 1978; Lasagna et al. 1955). This variability has been linked to a wide range of biological and psychological factors, including genetics, personality, sex hormones, dopamine function, and baseline mood states (Abi-Dargham et al. 2003; Harvanko et al. 2016; Miller et al. 2015; Weafer and de Wit 2013; Weafer et al. 2018; White et al. 2002, 2006). Responses to stimulant drugs also appear to be related to psychiatric conditions including depression and bipolar disorder (BD).

BD is characterized by repeated episodes of abnormally elevated, expansive, or irritable mood (in hypomanic or manic states) with abnormally depressed mood (depression). BD presents on a spectrum of severity from mania linked to psychotic features (bipolar I) through milder hypomania with depression (bipolar II), as well as other forms with briefer symptoms (American Psychiatric Association 2013). Individuals diagnosed with BD are more than 3 times as likely to develop substance use disorders (SUDs) compared with healthy controls (Zimmermann et al. 2009). It is evident that certain risks related to BD exist on a continuum and extend below thresholds established for clinical diagnoses (Merikangas et al. 2011). At risk individuals often report experiences of mood elevation in, for example, hypomanic episodes. These individuals are at four times greater risk to receive a lifetime BD diagnosis (alongside intermittent unipolar depression and anxiety), and, despite their lower symptom severity, they are twice as likely to develop a SUD (Zimmermann et al. 2009). High rates of mood elevation are surprisingly common among young adults (Calabrese et al. 2003; Chandler et al. 2008). In an analysis of 2591 individuals, Rock et al. (2013) reported that nearly 18% of college undergraduates reported 7 or more mood elevation experiences, amounting to threshold or probable BD.

Several studies have examined responses to stimulant drugs in individuals with psychiatric symptomatology. Individuals with major depression appear to be hypersensitive to the rewarding effects of a fairly high dose of d-amphetamine (30 mg) (Cardenas et al. 2002; Tremblay et al. 2002, 2005). In one study comparing the effects of d-amphetamine in adult patients with BD with controls, Anand et al. (2000) reported that these patients were also hyperreactive to d-amphetamine (0.3 mg/kg intravenous), on the Brief Psychiatric Rating Scale (Overall and Gorham 1962) and Young Mania Scale (Young et al. 1978). Some studies have examined the therapeutic effect of the stimulant methylphenidate in children with ADHD who also exhibit bipolar symptoms (Carlson et al. 2000; Galanter et al. 2003; Waxmonsky et al. 2008). These studies indicate that the drug produced similar therapeutic benefits among ADHD children with and without bipolar symptoms. Thus, the findings with patient populations vary. However, interpretations of the studies with patients are complicated by the symptom heterogeneity among participants in patient groups, and the possible confounds of current and past use of psychotropic medications.

An alternative approach that may avoid these complications is to examine acute responses to a drug among individuals who report psychiatric symptoms below a diagnostic threshold. We recently examined vulnerability to mood elevation or hypomania as a predictor of

responses to alcohol (Yip et al. 2012). That study assessed acute subjective responses to a moderate dose of alcohol in young men (18–21 years of age) who scored high on the Mood Disorder Questionnaire (Hirschfeld et al. 2003; Hirschfeld et al. 2000). Individuals who reported high scores on the MDQ, amounting to threshold BP symptomology, were *less* sensitive to feeling the subjective effects of alcohol. In the context of addiction risk, this may be important because one prominent theory postulates that lower sensitivity to the effects of alcohol is associated with increased risk for future alcohol abuse (Schuckit 1994).

Here, we sought to extend these previous findings, by testing their generality to a different drug type, d-amphetamine. d-Amphetamine is a prototypic stimulant drug that produces feelings of stimulation and well-being in most healthy adults. We tested whether young adults who reported stronger mood elevation experiences, indicated by reporting higher scores on the Mood Disorder Questionnaire (MDQ) (Hirschfeld et al. 2000, 2003), would also report blunted responses to d-amphetamine. We hypothesized that young adults with elevated MDQ scores would be less sensitive to feel the typical rewarding effects of single, moderate doses of d-amphetamine (10 and 20 mg oral).

Materials and methods

Study design

This study used a placebo-controlled, mixed-model design to examine the effects of d-amphetamine in individuals across a range of scores on the MDQ (Hirschfeld et al. 2000, 2003). We examined responses to the drug in relation to experiences of mood elevation or hypomania as measured by scores on the MDQ (Rock et al. 2013; Yip et al. 2012). Subjects participated in three 4-h laboratory sessions in which they received placebo, 10, and 20 mg oral d-amphetamine. The primary outcome measures were self-reported mood states and cardiovascular measures.

Participants

Thirty healthy young volunteers (ages 18–19) were recruited from the University of Chicago and the surrounding area. To increase the likelihood of identifying participants who would score high on the MDQ, some ads were headed “Have you experienced periods of feeling really good or having more energy than normal?”; others recruited healthy young adults. Participants first completed the MDQ (Hirschfeld et al. 2003; Hirschfeld et al. 2000), formulated on the basis of on diagnostic criteria for hypomania (American Psychiatric Association 2013) it includes 13 Y/N items that describe manic or hypomanic features including lack of a need for sleep, risky behaviors, talkativeness or pressure to speak distractibility, heightened interest in sex, etc. Four separate items covered family history, clinical contacts, frequency of experiences, and whether they are viewed as problematic (Hirschfeld et al. 2003, 2000). Total MDQ scores (0 to 13) indicate the number of listed symptoms that an individual has experienced. Individuals that endorse 7 or more symptoms *and* indicate that the symptoms are co-occurring *and* problematic have been considered probable for BD (Chandler et al. 2008; Hirschfeld et al. 2003, 2000; Rock et al. 2013). In this study, subjects were excluded if they were considered probable for BD or had received clinical BD diagnoses.

Participants underwent medical and psychiatric screening which included an electrocardiogram, medical history, drug use history, a physical exam, and a modified structural clinical interview (SCID; First et al. 2012) conducted by a clinical psychologist. Participants were excluded if they had less than a high school education, had body mass index outside the range 19–26, an abnormal electrocardiogram, current or past year mood, anxiety, eating or psychotic disorders (American Psychiatric Association 2013), past year history of substance use disorder, if they were taking regular prescription medication other than birth control, or if they were pregnant, lactating, or planning to become pregnant. Female participants not using hormonal contraceptives were only scheduled for sessions during the follicular phase of their menstrual cycle (White et al. 2002). Study procedures were approved by the Institutional Review Board at the University of Chicago and were carried out in accordance with the Declaration of Helsinki.

Procedure

Orientation—During an orientation visit, participants were familiarized with the study procedures and provided informed consent. They were told to have a normal sleep the night before the study sessions, consume their normal amount of caffeine, and to refrain from nicotine, alcohol, recreational drugs, and over-the-counter medications for 24 h before each visit. They were told that they would be tested for drugs and alcohol using urine and breath samples before each experimental session. Compliance with drug use instructions were verified using urine tests (Rapid Drug Test Cup, CLIAwaived, Inc., San Diego, CA) and breath samples (Alcosensor III, Intoximeters, Inc., St. Louis, MO). Pregnancy was tested in women (Pregnancy Urine (Dip-Strip), CLIAwaived, Inc., San Diego, CA). No subjects tested positive during the subsequent sessions. On the orientation visit, participants also completed assessments that measured depressive symptoms (Quick Inventory for Depressive Symptomatology (QIDS); Rush et al. 2003), neuroticism (Eysenck Personality Questionnaire's Neuroticism subscale (EPQ-N); Eysenck et al. 1985), and intelligence (Raven's Matrix Reasoning; Raven 2000).

Experimental sessions—Subjects attended three 4-h experimental sessions from 9 am to 1 pm, spaced at least 48 h apart. Sessions were conducted in a comfortable laboratory room. Upon arrival at the laboratory at 9 am, subjects provided urine and breath samples to test for recent alcohol and drug use, and a pregnancy test (for women). Participants consumed a snack (granola bar) upon arrival to standardize food consumption. They completed pre-capsule (baseline) ratings of mood states and cardiovascular measures were obtained. At 9:30 am, participants ingested capsules containing d-amphetamine (10 or 20 mg) or placebo. For the next 3.5 h, they relaxed and watched a movie or read a book, and subjective and cardiovascular measures were obtained every 30 min. Participants were discharged at 1:00 pm.

Drug

d-Amphetamine (10 mg, 20 mg, oral; Dexedrine; GlaxoSmithKline, Research Triangle Park, NC; 5 mg tablets) was placed in size 00 opaque capsules with dextrose filler. Placebo (PLB) capsules contained only dextrose filler. Drug and placebo were administered under double-blind conditions, with dose order counterbalanced across subjects.

Cardiovascular measures

Heart rate and blood pressure were obtained using portable monitors (Omron Automatic Blood Pressure Monitor, Model No BP791IT; Omron Healthcare, Inc., Lake Forest, IL).

Subjective measures

The Drug Effects Questionnaire (DEQ) (Johanson and Uhlenhuth 1980): The DEQ provided a measure of responses to the drug. Participants responded to five questions using 100 mm visual analog scales (VAS): “How much of a drug effect do you FEEL right now?” (“None at all” to “A lot”); “Are you feeling any drug effects that you LIKE?” (“Not at all” to “Like very much”); “Are you feeling any drug effects that you DISLIKE?” (“Not at all” to “Dislike very much”); “Are you HIGH right now?” (“Not at all” to “Very much”); and “Would you want MORE of the drug you took right now?” (“Not at all” to “Very much”).

The Addiction Center Research Inventory (ARCI) (Haertzen 1966; Martin et al. 1971): The ARCI is a 49-item true-false questionnaire designed to assess subjective responses to different categories of abused drugs. It consists of five subscales: sedation (pentobarbital-chlorpromazine group (PCAG)), stimulant-like effects (amphetamine (A) and Benzedrine group (BG)), somatic and dysphoric effects (lysergic acid (LSD)), and euphoria (morphine-Benzedrine group (MBG)).

The Profile of Mood States (POMS) (McNair 1971): The POMS is a 72-item questionnaire designed to assess momentary mood states. It consists of 8 subscales: anxiety, depression, anger, vigor, fatigue, confusion, friendliness, and elation. Participants indicated how they felt at that moment on a 5-point scale from “Not at all” (0) to “Extremely” (4).

Primary outcome measures were the feel, like, high, and more scales from the DEQ. In addition, we focused on the stimulant (A scale) and euphoria (MBG) subscales of the ARCI and friendliness, elation, and vigor subscales of the POMS. These scales represent the typical rewarding and hedonic effects of d-amphetamine. It was hypothesized that individuals with higher MDQ scores (histories of stronger hypomanic experiences) would exhibit reduced subjective responses to d-amphetamine.

Statistical analysis

Cardiovascular, ARCI, and POMS measures were analyzed as the positive or negative peak changes from baseline (i.e., relative to pre-capsule). Baseline ratings were not related to MDQ score on POMS, ARCI, or cardiovascular measures ($ps > .05$). For DEQ measures, in which the baseline ratings are always zero, simple peak ratings were used.

Statistical tests were conducted using SPSS Version 25 (IBM Corp). Cardiovascular and subjective responses to d-amphetamine (0, 10, or 20 mg) were compared using repeated measures multivariate analysis of variance (MANOVAs) with mean centered MDQ Score entered as a continuous variable. MANOVA does not rely on the univariate assumptions of sphericity (Vasey and Thayer 1987) which can be violated (Mauchly's test $< .05$) in psychopharmacology studies. If, however, the sphericity assumption was met (Mauchly's test $> .05$), univariate statistics (ANOVA) were chosen. All significant interactions between

dose and MDQ score were decomposed in terms of the estimated effect (i.e., slope) of MDQ at each dose. Finally, planned contrasts compared the regression slopes for each dose with placebo.

Results

Demographic information

Participant demographics, psychometrics, and recent and lifetime drug use data are presented in Table 1. Pearson correlation or ANOVA tests indicated that MDQ scores were not related to the QIDS, EPQ-N or Raven's Matrix Reasoning scores, recent drug use, lifetime drug use, or a family history of BD ($ps > .05$). Cardiovascular or subjective measures that were not related to either MDQ score or drug are not described below.

Overall amphetamine effects

Amphetamine produced its expected effects on cardiovascular measures and subjective ratings scales. These results, summarized in Table 2, indicate that the drug increased heart rate, $F(2, 56) = 4.67$, $p = .01$, and systolic blood pressure, $F = 8.29$, $p = .001$ (see Fig. 1). The drug increased DEQ ratings of "feel drug," $F = 15.95$, $p < .001$; "like drug" $F = 13.57$, $p < .001$; "feel high," $F = 5.94$, $p < .01$; and "want more," $F = 13.57$, $p < .001$; as well as ARCI-A (stimulation), $F = 8.08$, $p = .002$; ARCI-MBG (euphoria), $F = 9.65$, $p = .001$; POMS elation, $F = 7.50$, $p = .001$; and POMS positive mood, $F = 5.46$, $p = .01$. Planned simple contrasts comparing responses at each dose with placebo indicated that the 20 mg dose produced greater than placebo peak changes on each scale, smallest $F(1, 28) = 7.17$, $p = .01$. However, the lower 10 mg dose failed to produce significant increases on any measure, largest $F = 3.83$, $p = .06$.

Interactions with mood elevation experience

MDQ scores were related to peak changes in self-reported stimulation and euphoria and were associated with smaller changes from baseline on the ARCI-A and ARCI-MBG scales at the lower dose (10 mg). As detailed in Table 2, and graphically presented in Fig. 2, significant dose $\times$ MDQ score interactions emerged for ARCI-A (stimulation), $F(1, 28) = 3.86$, $p = .034$, and ARCI-MBG (euphoria) ratings, $F = 3.50$, $p = .045$. Estimated regression effects indicated that MDQ score predicted peak changes in ARCI-A, $F = 18.34$, $p < .001$, and ARCI-MBG ratings, $F = 9.83$, $p = .004$, but only at the 10 mg dose. Contrasts that compared the β scores indicated that each slope differed from placebo (smallest $F = 5.37$, $p = .028$). The estimated regression slopes indicated that, at the 10 mg dose, every 1 unit increase in MDQ score predicted decreases in ARCI-A and ARCI-MBG ratings of .462 and .677, respectively. MDQ scores were not related to ARCI-A or MBG ratings after the 20 mg d-amphetamine or placebo doses,

An interaction between dose and MDQ scores was observed in DEQ "like the drug" ratings, $F(2,56) = 3.62$, $p = .033$. However, planned contrasts did not reveal differences between either dose and placebo (largest $F = 3.87$). Similarly, the estimated regressions indicated that MDQ scores were not consistently associated with responses at any dose (largest $F = 2.61$).

Exploratory analyses with sex and stimulant use

Exploratory analyses indicated that subjective responses did not differ in men and women, and sex did not moderate interactions between MDQ scores and the subjective measures (ARCI-A, ARCI-MBG, and DEQ “like the drug”). When added as a factor, sex did not produce main effects, (largest $F(1,27) = 1.22, p = .28$), or interact with dose (largest $F(2,54) = 1.77, p = .19$).

Another exploratory analysis determined that removal of the seven subjects who reported any lifetime stimulant did not affect the interpretation of dose $\times$ MDQ interactions for ARCI-A and ARCI-MBG measures. However, the dose $\times$ MDQ interaction for DEQ “like the drug” was not significant in an analysis without these subjects ($F = 1.21, p = .32$).

Discussion

In the current study, we sought to examine subjective responses to acute d-amphetamine (10 and 20 mg) among young adults reporting hypomanic experiences. d-Amphetamine produces its expected, dose-dependent subjective and cardiovascular effects. However, participants who reported greater hypomanic symptomatology tended to report weaker subjective effects from acute administration of 10 mg, but not 20 mg, d-amphetamine on ARCI ratings of stimulation and euphoria. MDQ scores were not related to cardiovascular responses to the drug: Similar dose-dependent increases in heart rate and blood pressure occurred across the entire range of MDQ scores.

Our hypothesis was partially supported. That is, consistent with our hypothesis and earlier results in the study with alcohol, individuals with previous experiences of mood elevation or hypomania appeared to be less sensitive to the subjective effects of 10 mg d-amphetamine. In the previous study, Yip et al. (2012) reported that young men with MDQ scores of 7 and above (Hirschfeld et al. 2003, 2000) reported blunted subjective responses after a single dose of 0.8 g/kg alcohol, and this dampened response was also observed here, with 10 mg d-amphetamine. However, in the present study, the higher dose of d-amphetamine (20 mg) was not related to MDQ scores. The reasons for the differential results at the 10 and 20 mg doses are not clear. It is possible that the vulnerability to hypomanic experiences is associated with altered sensitivity to drugs only at threshold doses, and that with higher doses, these individual differences are masked. Relatedly, it is possible that individuals with previous hypomanic experiences have more difficulty attributing the subjective effects to a drug because they are hard to distinguish from fluctuations in mood without a drug. The subjective effects of d-amphetamine may resemble certain hypomanic or manic symptoms (Janowsky et al. 1972). It is notable that MDQ scores were not related to the cardiovascular effects of d-amphetamine, suggesting that pharmacokinetic factors did not contribute to the observed differences in subjective responses.

The differences in sensitivity to d-amphetamine may reflect differences in sensitivity to reward. d-Amphetamine is known to produce rewarding subjective effects, which are thought to be mediated by increased synaptic levels of dopamine in the “reward circuit.” It has been reported that a genetic polymorphism linked with BD is associated with dampened neural responses to reward (Trost et al. 2016), raising the possibility that individuals who

experience high rates of elevated mood are less reactive to rewards in general. Several imaging studies have reported that individuals with high MDQ scores or BD exhibit altered neural responses to reward, but the findings are conflicting. While one fMRI study (Yip et al. 2015) reported that euthymic, unmedicated BD subjects (either DSM-IV Bipolar II or Bipolar NOS) exhibited blunted anticipatory and consummatory responses to monetary rewards in limbic reinforcement circuits, other investigators have reported increased reward sensitivity in BD patients (Berghorst et al. 2016; Caseras et al. 2013; Nusslock et al. 2014). The interpretation of the latter studies is complicated by the fact that some of the participants were currently receiving medication to treat their severe bipolar symptoms. In the current study, the subjects were both unmedicated and their mood elevation symptoms were not severe enough to satisfy the criteria for a formal clinical diagnosis.

The quality and magnitude of initial responses to drugs are thought to predict susceptibility to future use, but there is controversy about the nature of these relationships. On one hand, greater hedonic responses to certain drugs have been linked with greater use and abuse (de Wit and Phillips 2012), and there is some evidence that greater stimulant-like responses to alcohol predict progression in use (King et al. 2011). However, a contrasting line of study suggests that low sensitivity to the subjective effects of alcohol predicts risk for developing alcoholism (Schuckit 1994). No longitudinal studies have examined initial responses to stimulants in relation to future use or abuse, and so it is not known whether lower sensitivity to the subjective effects of d-amphetamine, such as that observed here among those with high MDQ scores, is predictive of risk for future use or abuse of stimulant drugs.

There has been speculation, and some evidence, that BD and SUDs have similar etiologies. Certain genetic factors associated with BD are also linked with greater risks for SUDs (Levey et al. 2014; Patel et al. 2010; Trost et al. 2016). Some researchers have suggested that excessive drug use and manic or hypomanic experiences have similar effects on the neural reward system (Koob and Le Moal 2001). The idea is that excessive drug use causes dysregulation of the neural reward system, which ultimately requires an individual to use greater and greater amounts to achieve a desirable drug effect. More recently, Pettorruso et al. (2014) speculated that a similar process occurs in bipolar disorder, and that over time, fluctuations in mood have similar allostatic dysregulating effects on the reward and stress systems to promote addiction. The relationships between a history of elevated mood experiences and sensitivity of the reward circuit and responses to acute or chronic drug administration remain to be clarified.

The strength of the current study is in its rigorous double-blind placebo-controlled within-subject design. The participants were carefully screened to exclude those with psychiatric symptoms or taking psychiatric medications, and participants with varying MDQ scores were matched as closely as possible on demographic variables including drug use. Despite its strengths, the current study also has several limitations. First, our study assesses the strength of previous mood elevation or hypomanic experiences as assessed using a self-report the MDQ (Hirschfeld et al. 2000, 2003), rather than clinician-rated symptoms. There are associations between BP features, as identified using the MDQ, and severity of ADHD symptoms and elevated rates of alcohol and drug use (Bergsholm et al. 2010; Chiu and Chokka 2011). In this study, individuals with current or past ADHD were excluded, but we

did not collect information about specific ADHD symptoms or severity of nicotine dependence. Although use of nicotine or other drugs was not significantly related to MDQ score, higher MDQ scores were nonsignificantly related to frequency of drug use (smallest $p = .12$). Individuals with high MDQ scores likely exhibit characteristics such as impulsiveness and residual lower state mood that have been linked to drinking behaviors and nicotine use (Yip et al. 2012). Another limitation is that the current study did not examine expectancies of amphetamine's effects. Yip et al. (2012) found that those with higher rather than lower MDQ scores reported dampened responses to alcohol despite reporting more positive expectancies of alcohol's effects.

Despite its limitations, the current study expands our understanding of individual variation in acute responses to drugs. Further, it suggests a relationship between bipolar symptomatology and altered stimulant responses that may affect risks for future use. The current study indicated that responses to a low, but not high, dose of amphetamine were related to MDQ scores. Future research using longitudinal study designs and multiple drug doses will be necessary to understand these relationships better. Finally, a future research question is whether bipolar symptomatology is related to altered responses to other drugs in addition to alcohol and amphetamine. Better understanding individual variation in responses to drugs may reveal mechanisms of risk and have implications for treatment.

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Fig. 1.

Estimated regressions for placebo and d-amphetamine (10 and 20 mg) in relation to MDQ score and **a** mean peak change in heart rate (BPM) and **b** systolic blood pressure (mmHg). Labels on the X axes represent 1 SD below (low MDQ; MDQ = 1.03), 1 SD above (high MDQ; MDQ = 9.10); the mean MDQ score in this sample was 5.07

Fig. 2.

Estimated regressions for placebo and d-amphetamine (10 and 20 mg) in relation to MDQ score and **a** mean peak change ARCI-A (stimulation) and **b** ARCI-MBG (euphoria) ratings. Labels on the X axes represent 1 SD below (low MDQ; MDQ = 1.03), 1 SD above (high MDQ; MDQ = 9.10); the mean MDQ score in this sample was 5.07. Significant slopes: * < .05, ** .01, *** .001)

Table 1

Demographic, psychometric, and drug use characteristics of participants. Data indicate mean (SE) unless indicated otherwise. None were related to MDQ score

	<i>N</i> = 30
Sex (M/F)	14/16
Age (years)	18.6 (0.5)
Education (years)	13.5 (0.9)
BMI (kg/m ²)	23.2 (2.8)
MDQ	5.1 (4.0)
QIDS	4.6 (3.1)
EPQ-N	7.9 (4.9)
Raven's Matrix Reasoning	22.0 (2.1)
Current drug use (total in last 30 days)	
Alcohol (drinks)	12.3 (9.9)
Caffeine (servings)	39 (32.7)
Cannabis (times)	2.6 (5.0)
Current nicotine users	12
No. of cigarettes	8.1 (28.9)
Lifetime recreational use (no. of ever used)	
Cannabis	27
Hallucinogens	6
Inhalants	3
MDMA	5
Opiates	4
Sedatives	4
Stimulants	7
Family history of bipolar disorder	4

Table 2

Subjective reports and cardiovascular effects of placebo and d-amphetamine (10 and 20 mg) (group differences: * < .05, ** .01, *** .001)

Subjective effects	Statistical tests		
	Dose <i>F</i> value	MDQ <i>F</i> value	MDQ × Dose <i>F</i> value
DEQ			
Feel	15.95 ***	0.08	2.81
Like	13.57 ***	0.23	3.62 *
High	5.94 **	1.16	0.57
More	10.41 ***	0.45	0.97
ARCI			
MBG	9.65 **	2.46	3.5 *
A	8.08 **	7.8 **	3.86 *
POMS			
Elation	5.57 **	0.02	0.34
Positive mood	8.50 **	0.94	2.22
Cardiovascular effects			
Heart rate	4.67 *	0.02	0.83
Blood pressure (systolic)	8.29 ***	0.00	0.05

ARCI Addiction Research Center Inventory, DEQ Drug Effects Questionnaire, POMS Profile of Mood States

* $p < .05$,

** $p < .01$,

*** $p < .001$