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Role of Sensation Seeking in Sensitivity to d-amphetamine Reinforcement

Mollie E. Patrick
University of Vermont, mollie.patrick@uvm.edu

ROLE OF SENSATION SEEKING IN SENSITIVITY TO *d*-AMPHETAMINE REINFORCEMENT

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Mollie E. Patrick, M.A.

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Dissertation Examination Committee:

_____Advisor
Stacey Sigmon, Ph.D.

_____
Sarah Heil, Ph.D.

_____
Stephen Higgins, Ph.D.

_____
Timothy Stickle, Ph.D.

_____Chairperson
Jennifer Laurent, Ph.D., FNP-BC

_____Dean, Graduate College
Cynthia Forehand, Ph.D.

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Abstract

Psychomotor stimulant abuse is a significant public health problem. While many individuals experiment with stimulants, there is marked variability in individuals' behavioral and subjective response to these drugs and these differences may be associated with their risk for abuse. One characteristic shown to be associated with drug abuse is sensation seeking, defined as the seeking of novel sensations and experiences and the willingness to take risks for the sake of such experiences. While observational studies have shown that individuals with elevated sensation seeking are more likely to report stimulant use and abuse, less clear is whether subjective and behavioral response to acute stimulant administration may vary as a function of sensation seeking status. We recently completed an outpatient laboratory study in which 37 healthy adults received repeated opportunities to sample and choose between *d*-amphetamine (*d*-AMPH; 5, 10, 20 mg/70kg) or placebo. That study provided an opportunity to examine associations between sensation seeking and *d*-AMPH choice and subjective response under rigorous double-blind experimental conditions. The Zuckerman Sensation Seeking Scale V was administered at intake, providing a Total sensation seeking score as well as four subscales (i.e., Experience Seeking, Disinhibition, Thrill and Adventure Seeking, Boredom Susceptibility). We hypothesized that elevated sensation seeking at intake would be associated with increased preference for *d*-AMPH over placebo in subsequent choice sessions, as well as greater positive *d*-AMPH subjective effects. Among males, increased baseline sensation seeking was associated with increased *d*-AMPH choice and positive subjective effects at the 5 and 10 mg/70 kg doses. Among females we found no significant associations between sensation seeking and *d*-AMPH choice or subjective effects. Finally, when the association between sensation seeking and other baseline characteristics was examined, there was a significant positive association with lifetime drug use as well as impulsivity. Taken together, our data suggest that elevated sensation seeking in males may be associated with increased sensitivity to *d*-AMPH reinforcement and positive subjective effects, suggesting increased vulnerability for stimulant use and abuse.

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Introduction

Abuse of psychomotor stimulants is a serious public health problem in the United States. In addition to the 1.6 million current cocaine users, rates of methamphetamine abuse have increased in recent years, with 133,000 new methamphetamine initiates in 2012 alone (SAMHSA, 2013a). Abuse is also increasing for the stimulant medications widely used to treat attention deficit hyperactivity disorder (ADHD), including methylphenidate (Ritalin®), dextro-amphetamine (Dexedrine®) and mixed-salts amphetamine (Adderall®) (Kaye & Darke, 2012). Between 2005-2010, for example, the number of annual emergency department visits involving these medications more than doubled from 13,379 to 31,244 (SAMHSA, 2013b). The increase in stimulant abuse has been especially marked among adolescents and young adults, with a near four-fold increase in stimulant-related emergency department visits among those ages 18-25 (SAMHSA, 2013b). Abuse of psychomotor stimulants in general is associated with a variety of deleterious health consequences, including autonomic nervous system dysfunction, cardiovascular pathology, cognitive impairment, neurologic and psychiatric problems, poor psychosocial functioning and increased involvement in high-risk sexual, criminal and violent behavior (Cavazos-Rehg et al., 2009; Henry, Minassian, & Perry, 2012; SAMHSA, 2005, 2008; Winslow et al., 2007).

While the abuse potential of stimulants is well established (e.g., Chait, Uhlenhuth, & Johanson, 1987; Johanson & Fischman, 1989; Johanson & Uhlenhuth, 1980; Kollins, MacDonald & Rush, 2001), many individuals experiment with these drugs without transitioning to abuse or dependence. Of those who report lifetime cocaine use, for example, only about 15% will go on to develop dependence (Wagner & Anthony, 2002).

Individuals also vary greatly in both subjective and behavioral response to stimulants and these differences may translate to differences in susceptibility to abuse (de Wit, 1998; de Wit & Phillips, 2012; de Wit, Uhlenhuth, & Johanson, 1986; Silberman, Reus, Jimerson, Lynott, & Post, 1981). In studies examining preference for amphetamine over placebo, for example, those who consistently choose amphetamine typically report increased ratings of positive mood, while those who consistently choose placebo report either no effects or greater negative effects of amphetamine (de Wit, Uhlenhuth, & Johanson, 1986; Gabbay, 2003; Johanson, Kilgore, & Uhlenhuth, 1983). An improved understanding of these individual differences would inform efforts to identify and intervene with those at risk for developing abuse or dependence.

Sensation Seeking

One characteristic shown to be associated with drug use and other risk behaviors is sensation seeking. Sensation seeking (SS) is regarded as a stable personality trait and defined as the "seeking of varied, novel, complex, and intense sensations and experiences, and the willingness to take physical, social, legal and financial risks for the sake of such experiences" (Zuckerman, 1994). The construct of SS is based on the premise that individuals vary widely in their optimal level of arousal, and these differences influence behavior (Zuckerman, 2007). High sensation seekers, for example, are those who are more likely to engage in behaviors that increase the amount of stimulation they experience and therefore are hypothesized to have a greater likelihood of engaging in high-risk behaviors (Zuckerman, 1994).

Sensation Seeking and Risk Behaviors

Research over the past two decades has demonstrated an association between SS

and a wide range of risk behaviors (see Arnett, 1992 for review). These have included gambling (Cyders & Smith, 2008; Powell, Hardoon, Derevensky, & Gupta, 1999; Shead, Derevensky, & Gupta, 2010), risky driving (i.e., racing, unsafe passing, high speeds, DWI; see Jonah, 1997 for review), sports-related risks (i.e., failure to use protective gear; Horvath & Zuckerman, 1993; Ruedl, Abart, Ledochowski, Burtscher, & Kopp, 2012) and risky sexual behavior (i.e., increased number of sexual partners, insufficient condom use; Gonzalez et al., 2005; Wagner, 2001). In a survey of sexual risk behaviors among adolescents, for example, those with elevated SS reported increased frequency of sexual intercourse, a greater number of sexual partners and less consistent condom use (Spitalnick et al., 2007).

Elevated SS scores have also been linked to increased substance use. This has included licit drugs such as tobacco (Gunning, Sussman, Rohrbach, Kniazev, & Masagutov, 2009; Hampson, Tildesley, Andrews, Barckley, & Peterson, 2013) and alcohol (Bekman, Cummins, & Brown, 2010; Puente, Gonzalez Gutierrez, Abellan, & Lopez, 2008; Sargent, Tanski, Stoolmiller, & Hanewinkel, 2010), as well as illicit drugs including marijuana (Kopstein, Crum, Celentano, & Martin, 2001; Martin et al., 2002), opioids (Franques et al., 2003; Kosten, Ball, & Rounsaville, 1994) and stimulants (described below).

SS may also be associated with dependence severity, treatment retention and therapeutic response among individuals with established drug dependence (Ball, Carroll, & Rounsaville, 1994; Kahler, Spillane, Metrik, Leventhal, & Monti, 2009; Patkar et al., 2004). A study evaluating the influence of SS on smoking cessation among heavy social drinkers, for example, found that those with elevated SS at intake had reduced odds of

smoking abstinence, poorer treatment compliance (i.e., nicotine replacement therapy adherence, use of cessation strategies) as well as greater alcohol use during treatment (Kahler et al., 2009).

Sensation Seeking and Psychomotor Stimulant Use

The association between SS and psychomotor stimulant abuse has been of particular focus. In national surveys of the general population, elevated SS scores have been associated with higher prevalence rates of cocaine (Saiz et al., 2003), ecstasy (Wu, Liu, & Fan, 2010) and methamphetamine use (Herman-Stahl, Krebs, Kroutil, & Heller, 2007). Elevated SS scores have also been associated with prescription stimulant misuse, particularly among adolescents (Herman-Stahl, Krebs, Kroutil, & Heller, 2006) and young adults (Arria, Caldeira, Vincent, O'Grady, & Wish, 2008; Herman-Stahl, Krebs, Kroutil, & Heller, 2007; Jardin, Looby, & Earleywine, 2011; Low and Gendaszek, 2002; Van Eck, Markle, & Flory, 2012; Weyandt et al., 2009). In one study, for example, adolescents with elevated SS had almost a 2.5-fold increased odds of past year nonmedical stimulant use compared to lower-SS adolescents (Herman-Stahl, Krebs, Kroutil, & Heller, 2006). Additionally, stimulant-dependent individuals have higher SS scores compared to non-drug dependent siblings and matched controls (Ersche, Jones, Williams, Smith, Bullmore, & Robbins, 2013; Ersche, Turton, Pradhan, Bullmore, & Robbins, 2010). Finally, SS may also be associated with severity of stimulant use in clinical populations. In an analysis of treatment-seeking cocaine users, for example, SS was positively correlated with frequency of cocaine use and having a cocaine-positive urine at treatment intake (Murray et al., 2003). Taken together, these studies have suggested a general association between SS and stimulant use, though more controlled

investigations are needed to improve our understanding of this association.

Laboratory Studies Examining Sensation Seeking and Stimulant Use

Seven laboratory studies have examined the association between SS and participants' sensitivity to the subjective and reinforcing effects of psychomotor stimulants (Carrol, Zuckerman, & Vogel, 1982; Chait, 1993; de Wit, Uhlenhuth, & Johanson, 1986; Hutchison, Wood, & Swift, 1999; Kelly et al., 2006, 2009; Stoops et al., 2007). All used *d*-amphetamine (*d*-AMPH) as the exemplar stimulant, as it is a classic psychomotor stimulant that produces effects similar to those of cocaine, methamphetamine and other commonly-abused stimulants (O'Brien, 2001). Sensation Seeking in those studies was measured using either the Sensation Seeking Scale V (SSS; Zuckerman et al., 1978) or the Zuckerman-Kuhlman Personality Questionnaire (ZKPQ; Zuckerman, Kuhlman, Joireman, Teta, & Kraft, 1993).

All seven studies examined the association between participants' SS scores and their subjective response to *d*-AMPH (Carrol et al., 1982; Chait, 1993; de Wit et al., 1986; Hutchison et al., 1999; Kelly et al., 2006, 2009; Stoops et al., 2007). Subjective effects were measured using the Addiction Research Center Inventory (ARCI; Haertzen, Hill, & Belleville, 1963), Drug Effects Questionnaire (DEQ; Fischman & Foltin, 1991), Profile of Mood States (POMS; McNair, Lorr, & Droppleman, 1971) or Visual Analog Scales (VAS; Folstein & Luria, 1973). In four studies, participants with higher SS scores showed increased sensitivity to *d*-AMPH effects compared to those with lower scores (Hutchison et al., 1999; Kelly et al., 2006, 2009; Stoops et al., 2007), while three found no influence of SS on *d*-AMPH subjective effects (Carrol et al., 1982; Chait, 1993; de Wit et al., 1986). Among those demonstrating increased *d*-AMPH sensitivity among

participants with higher SS scores, the nature of the effect observed varied. In three studies, for example, participants with higher SS showed increased sensitivity to *d*-AMPH's positive effects (e.g., stimulation, elation, drug liking) (Hutchison et al., 1999; Kelly et al., 2006, 2009), while in the fourth study those with higher SS scores showed increased sensitivity to *d*-AMPH's negative effects (e.g., anger, confusion) (Stoops et al., 2007).

Three of the seven studies also examined the role of SS in *d*-AMPH reinforcement (Chait, 1993; de Wit et al., 1986; Stoops et al., 2007). Two employed a discrete-trial choice procedure to investigate the role of SS in *d*-AMPH reinforcement (7.5-20 mg, Chait, 1993; 5 mg, de Wit et al., 1986). In choice procedures, participants are given an opportunity to sample and choose between two concurrently-available alternatives. This arrangement provides an index of the relative preference for one of two alternatives, with the frequency with which one option is chosen over the other providing an index of the relative reinforcing effects of the drug (de Villiers, 1977; Mazur, 1994). Participants in both studies were dichotomized into Choosers and Nonchoosers based on the percentage of sessions wherein they chose active *d*-AMPH over placebo, and there were no significant differences in Total SS scores between Choosers and Nonchoosers in either study. However, while not statistically significant, mean SS scores were in the expected direction with Choosers having higher SS scores than Nonchoosers (de Wit et al., 1986; means not reported in Chait, 1993).

The third study evaluating SS and *d*-AMPH reinforcement used a progressive ratio (PR) procedure (Stoops et al., 2007). In PR procedures, participants are provided the opportunity to work (e.g., pull a lever, press a computer key) to receive a reinforcer.

The response requirement for obtaining each drug reinforcer increases following delivery of the previous reinforcer (Hodos, 1961). Response requirements continue to escalate until responding terminates, and the final ratio completed (i.e., break point) provides an index of the magnitude of the reinforcing effects of the drug. In the Stoops et al. (2007) study, participants with higher SS scores demonstrated greater break points for both 8 and 16 mg *d*-AMPH doses compared to those with lower SS scores, suggesting that elevated SS was associated with increased sensitivity to *d*-AMPH reinforcement.

While these studies have generally suggested that baseline SS may influence individuals' sensitivity to *d*-AMPH's subjective and reinforcing effects, there was variability across studies. Several methodological details may have contributed to this. First, failure to examine a sufficient range of doses could have limited the ability to detect an effect in some studies. Of the three studies that failed to find a significant association between SS and *d*-AMPH, for example, each examined only a single *d*-AMPH dose (Carrol et al., 1982; Chait, 1993; de Wit et al., 1986). Of the four that demonstrated a significant association between SS and *d*-AMPH, three examined multiple doses (Kelly et al., 2006, 2009; Stoops et al., 2007). Considering that individual differences in subjective and behavioral responses to drugs may be dose dependent, assessing multiple doses may be important for obtaining a thorough characterization of the association between SS and stimulant response (White, Lott, & de Wit, 2006).

Second, the prior studies may have been constrained by the failure to consider potential gender differences. Gender differences in SS have been consistently reported, and the developer of the Sensation Seeking Scale V, the most widely-used instrument for measuring SS, has published gender-specific norms for use in data interpretation

(Zuckerman et al., 1978; Zuckerman, 1994). Indeed, in a recent meta-analysis of SS across multiple cultures, men generally had significantly higher scores on the Total, Thrill and Adventure Seeking, Disinhibition and Boredom Susceptibility scales of the SSS compared to women (Cross, Cyrenne, & Brown, 2013). Of the three laboratory studies above that failed to find a significant association between SS and *d*-AMPH, two did not consider gender differences in SS (Chait, 1993; de Wit et al., 1986). Of the four that demonstrated a significant association between SS and *d*-AMPH, three either used gender as a covariate or selected participant groups based on gender-specific SS cutpoints (Kelly et al., 2006, 2009; Stoops et al., 2007).

Finally, limited use of the Sensation-Seeking Scale's subscales may have precluded a full characterization of the SS-stimulant association in prior studies. The questionnaire includes a Total composite SS score as well as four subscales, with each subscale contributing unique variance (Zuckerman, 1994). Of the five studies above that used the Sensation Seeking Scale V (Carrol et al., 1982; Chait, 1993; de Wit et al., 1986; Hutchison et al., 1999; Kelly et al., 2009), only one examined the four subscales. It found a significant association between participants' *d*-AMPH response and their scores on the Experience Seeking, Disinhibition and Boredom Susceptibility scales (Hutchison et al., 1999). Of the four that solely relied on the Total scale as a measure of SS, only one showed a significant association between SS and *d*-AMPH response (Kelly et al., 2009).

Current Study

In the present study, we conducted a secondary analysis of data obtained in an outpatient laboratory study conducted at the University of Vermont from November 2009 to March 2012. As a growing scientific literature suggests that vulnerability for drug

abuse is influenced by genetic factors (Comings & Blum, 2000; Uhl, 2006), the parent study sought to examine the influence of a specific dopaminergic polymorphism, the dopamine D2 receptor (DRD2) A1 allele, on individual differences in sensitivity to *d*-AMPH reinforcement (Sigmon et al., in preparation). Healthy adult volunteers were prospectively identified as DRD2 A1 carriers or noncarriers and then completed double-blind laboratory sessions wherein they received repeated opportunities to sample and choose between *d*-AMPH (5, 10 and 20 mg/70 kg) and placebo. Participants completed a Drug Effects Questionnaire prior to capsule ingestion and again at 1, 2, 4 and 8 hours post-drug administration. Percent of *d*-AMPH choices and self-report DEQ ratings served as measures of *d*-AMPH reinforcing and subjective effects, respectively. Analyses of the primary outcomes are ongoing and the resulting manuscript will be submitted to a peer-reviewed scientific journal in upcoming months (Sigmon et al., in preparation).

While the primary aim of the parent study was to investigate the influence of the DRD2 A1 allele on sensitivity to *d*-AMPH reinforcement, the study provided a unique opportunity to examine the association between participants' SS and their subsequent sensitivity to *d*-AMPH's subjective and reinforcing effects. All participants completed the Sensation Seeking Scale V (Zuckerman et al., 1978) at study intake. We hypothesized that elevated SS would be associated with increased *d*-AMPH choice as well as positive subjective effects. As a secondary exploratory aim, we also examined the association between SS and baseline demographic and drug use characteristics in our sample. Overall, this study is the first to our knowledge to investigate the influence of sensation seeking on *d*-AMPH reinforcement and subjective response within gender

using the SSS-V total scale and each of its subscales. As such, it is positioned to provide a thorough investigation of whether SS influences *d*-AMPH response under controlled conditions, providing data relevant to the issue of whether sensation seeking may influence individuals' vulnerability for stimulant abuse.

Method

Participants

Participants were 37 healthy adult volunteers between the ages of 18-50, recruited through electronic and community postings. To be eligible for that study, participants were required to report a history of limited recreational stimulant (e.g., methylphenidate, cocaine) use but not meet DSM-IV criteria for current or lifetime abuse or dependence and not be seeking treatment for alcohol or drug abuse or dependence. All were required to submit a drug-negative sample to eliminate physically dependent or regular drug users, which is consistent with prior studies investigating vulnerabilities that may predispose individuals to the development of drug abuse (cf. de Wit, 1998). Participants were required to be in good health, be fluent in English and capable of understanding and complying with the protocol. Females had to be non-pregnant and non-lactating, and those of childbearing age were required use appropriate birth control for the study duration. Exclusion criteria included known hypersensitivity or medical contraindication to psychomotor stimulants, history of or current significant medical or psychiatric condition (including a diagnosis of ADHD), diastolic blood pressure >90 mmHg or systolic pressure of >140 mmHg, body weight 20% above or below ideal body weight and use of prescription or over-the-counter medications that could interfere with the study. The study was approved by the local institutional review board and each

participant provided written informed consent prior to participating.

Intake Assessment

Participants completed an intake assessment that included measures previously associated with drug abuse vulnerability and/or stimulant choice: Sensation-Seeking Scale Form V (SSS-V; Zuckerman et al., 1978; described below), Barratt Impulsiveness Scale – 11 (BIS-11; Patton, Stanford, & Barratt, 1995), Beck Anxiety Inventory (BAI; Beck et al, 1988), and Behavioral Inhibition Scale and Behavioral Activation Scale (BIS/BAS; Carver & White, 1994). A drug history questionnaire, modified Time-Line Followback interview (Sobell, Sobell, Leo, & Cancill, 1988) and the DSM-IV psychoactive substance and alcoholism sections (Feingold & Rounsaville, 1995) were used to assess lifetime and recent drug use. Participants also completed a medical history, which the principal investigator and physician reviewed to confirm eligibility. Finally, urine and breath alcohol samples were collected and tested for recent drug and alcohol use.

Measures of Sensation Seeking and *d*-AMPH Response

The SSS-V contained 40 forced-choice questions yielding four subscales of 10 items each (Zuckerman et al., 1978), as well as a Total score. The Experience Seeking subscale assessed the desire to experience novel sensations and experiences through social nonconformity. The Disinhibition subscale assessed the desire to seek sensations through social activities such as parties, drinking and sex. The Thrill and Adventure Seeking subscale measured the desire to engage in sports or risky physical activities. The Boredom Susceptibility subscale assessed intolerance to monotony. Total scores could

range from 0-40 and subscales ranged from 0-10; on both, increased scores represented increased levels of sensation seeking.

The Drug Effects Questionnaire (DEQ) included five items that assess direct drug effects (i.e., Drug Effect, Stimulant Effect, Good Effects, Bad Effects, Liking) shown in previous research to be related to abuse potential (e.g., King, de Wit, McNamara, & Cao, 2011; Morean et al., 2013). All items, with the exception of Liking, were scored using a Likert scale that ranged from 0 (not at all) to 4 (extremely). Subjects rated their Liking of the drug from -4 (dislike very much) to +4 (like very much), in order to permit a neutral or no drug liking rating.

Procedures

The double-blind, discrete-trial choice procedure consisted of 36 sessions (3-5 sessions per week) conducted over approximately 7 weeks, depending on participants' schedules. Three *d*-AMPH doses were evaluated, with each dose involving 12 sessions. Each of these 12-session series involved 4 sequences of 3 sessions per sequence (Sample-Sample-Choice; described below). At each session, participants provided a urine and breath sample, completed a baseline DEQ and ingested 2 color-coded capsules. After leaving the laboratory, participants completed the DEQ at 1, 2, 4, and 8 hours post-drug.

Each 3-session sequence began with two "sample" days during which participants received different color-coded capsules each day (e.g., 2 red capsules on Monday and 2 green capsules on Tuesday). One pair always contained placebo and the other *d*-AMPH. On the subsequent "choice" day, participants reviewed their self-report data from the prior sample days to help recall specific drug effects associated with each pair of color-coded capsules and then chose to ingest one of the two capsule pairs. Participants were

informed that the content of each pair of color-coded capsules in the choice session was identical to that of the preceding two sample sessions. This 3-day sequence (2 sample days followed by 1 choice day) was repeated for a total of 4 experimentally-independent assessments (12 total sessions) at each *d*-AMPH dose (i.e., 5, 10 and 20 mg/70kg). In summary, 36 total sessions were conducted, with 12 (4 Sample-Sample-Choice sequences) sessions at each *d*-AMPH dose. The order of exposure to *d*-AMPH and placebo was counterbalanced within and across trials and subjects, and order of exposure to the different *d*-AMPH doses was counterbalanced across subjects.

Study Medication

d-AMPH capsules (5, 10 or 20 mg/70kg; size 0, opaque hard gelatin) were prepared by the University of Vermont investigational pharmacy using powdered lactose and *d*-amphetamine sulfate. Placebo capsules were weight matched (+/- 5%) and prepared using powdered lactose. Color of *d*-AMPH and placebo capsules varied across sessions, with 7 capsule colors and 28 possible color combinations (including solid-colored capsules and capsules with each half a different color).

Statistical Analyses

T-tests were used to compare male and female participants on mean SS scores, as well as for comparison within gender to published norms. Due to established gender-specific differences in SS scores (Cross, Cyrenne, & Brown, 2013; Zuckerman, 1994), the association between SS and *d*-AMPH reinforcing and subjective effects were analyzed within gender. With regard to *d*-AMPH choice, logistic regression analyses based on generalized estimating equations (GEE) were used to examine the association between each SS scale and *d*-AMPH choice (SAS, PROC GENMOD). This

methodology accounts for the repeated measures structure in the choice data, as each participant had multiple opportunities to choose between *d*-AMPH and placebo at each of the three dose levels. First, the association between SS and choice was evaluated across all three *d*-AMPH dose levels, with dose (5, 10, 20 mg) as additional predictors represented by indicator variables in the model. This reflects a main effect model, as the effect of each SS subscale is assumed to be independent of dose. Subsequently, simple effect models were examined in which SS was used to predict choice at the individual dose levels. Predicted probabilities were computed based on the derived logistic regression equations. In order to have derived odds ratios represent a meaningful change in SS score, a 5-point change was used for the Total SS scale (range: 0-40), and 2-point change was used for each of the subscales (range: 0-10).

With regard to *d*-AMPH's subjective effects, mixed model repeated measures ANCOVAs were used to examine the effects of each SS scale on the five DEQ drug effects items. The dependent variable for each item was the area under the curve representing the cumulative drug effect over time (8 hours). Consistent with prior studies, subjective effects analyses were limited to the data collected from the sample sessions in order to avoid the potential bias associated with choice sessions (Sigmon & Griffiths, 2011). In order to isolate the effect of active *d*-AMPH dose on subjective response, all regression models included participants' subjective effects during placebo administration as a covariate. Similar to the logistic regression methodology reported above, separate models were performed for each SS scale as a predictor. Main effect models were run across the three dose levels with dose as an additional explanatory variable, followed by simple effect models evaluating the dose-specific association.

Finally, the association between SS Total and *a priori* identified baseline demographic, drug use and psychosocial characteristics was examined using Pearson's correlation coefficient. Participants' DRD2 A1 polymorphism status was not considered as a covariate in analyses as there was no evidence that choice or subjective effects varied as a function of allele status (Sigmon et al., in preparation). Analyses were performed using SAS statistical software Version 9.3 (SAS Institute, Cary, NC). Statistical significance was determined based on $\alpha = .05$.

Results

Participant Characteristics

The 37 participants were 22.9 $\pm$ 2.9 years old, 43% male and had completed 15.1 $\pm$ 1.3 years of education (Table 1). In terms of drug use, 14% of participants were current cigarette smokers and 100% reported current alcohol use. All reported lifetime marijuana use, and 22%, 32.4% and 67.6% reported lifetime benzodiazepine, opioid and hallucinogen use, respectively. Consistent with study eligibility criteria, all participants reported prior recreational stimulant use, including cocaine (57%), amphetamines (e.g., Adderall®) (86%), methylphenidate (Ritalin®) (24%) and ecstasy (46%). See Table 1 for participant characteristics within gender. There were no significant differences between males and females in demographic or psychosocial characteristics. However, in terms of drug use, a significantly greater percentage of males had used stimulants > 10 times.

Participants' mean SS scores at study intake are presented in Table 2. Contrary to normative data, there were no significant differences in SS between males and females. However, compared to norms, the mean Total score of our male participants was estimated to be at the 60th percentile, with significantly higher mean scores on the

Experience Seeking subscale compared to published male norms ($p < .001$) (Zuckerman, Kuhlman, Thornquist, & Kiers, 1991). Similarly, our females' mean Total score was estimated to be at the 80th percentile of normative data, with significantly higher mean scores on the Total, Experience Seeking and Thrill and Adventure Seeking scales compared to female norms ($p's < .01$).

Sensation Seeking and *d*-AMPH Choice

Males chose 5, 10 and 20 mg/70kg *d*-AMPH over placebo on 56%, 52% and 61% of occasions, respectively (Wald $X^2(2, N = 16) = 1.55$, $p = .46$). Among males, there was a significant positive association between Total, Experience Seeking, Disinhibition and Thrill and Adventure Seeking scale scores and *d*-AMPH choice *(p's* < .05; Table 3). More specifically, each 5-point increase in Total SS score was associated with a 1.57 odds of choosing *d*-AMPH, while each 2-point increase in Experience Seeking, Disinhibition and Thrill and Adventure Seeking scores was associated with a 1.87, 1.52, and 1.91 odds of choosing *d*-AMPH, respectively. There was no significant association between Boredom Susceptibility and *d*-AMPH choice. When these effects were examined within dose, the association between SS scores and *d*-AMPH choice was strongest at the 10 mg dose. More specifically, each 5-point increase in Total SS score was associated with an odds ratio of 2.20 for choosing *d*-AMPH (Figure 1, top left panel), while each 2-point increase in Experience Seeking (Figure 1, bottom left panel), Disinhibition (Figure 1, top right panel) and Thrill and Adventure Seeking (Figure 1, bottom right panel) subscales was associated with odds ratios of 2.39, 1.81 and 2.85 for *d*-AMPH choice, respectively.

Females chose 5, 10 and 20 mg/70kg *d*-AMPH over placebo on 62%, 67% and 70% of occasions, respectively (Wald $X^2(2, N = 21) = 1.70$, $p = .43$). In contrast to males, analyses performed across and within dose showed no significant associations between any SS scale and *d*-AMPH choice among females (Table 3).

Sensation Seeking and *d*-AMPH Subjective Effects

Males showed a significant dose effect on all five DEQ items ($F = 11.43$-60.27, p's $<.05$). There was a significant positive association between male participants' scores on the Total and Disinhibition scales and their ratings of *d*-AMPH Liking (p's $<.05$), as well as a positive trend between Thrill and Adventure Seeking and *d*-AMPH Liking ($p = .08$) (Table 3). More specifically, each 5-point increase in Total SS score was associated with a β of 1.17, while each 2-point increase in Disinhibition and Thrill and Adventure Seeking scores was associated with β's of 1.00 and 1.39, respectively. Within-dose analyses showed that the strongest associations between *d*-AMPH Liking and the Total (($\beta = 1.35$, $p = .07$; Figure 2, top panel), Disinhibition ($\beta = 1.19$, $p = .04$; Figure 2, bottom left panel) and Thrill and Adventure Seeking ($\beta = 2.10$, $p = .06$; Figure 2, bottom right panel) scales occurred at the 5 mg dose. In addition, there was a significant negative association between the Experience Seeking subscale and ratings of Bad Effects ($\beta = -1.87$, $p = .01$). Within-dose analyses revealed that the negative association between Experience Seeking and Bad Effects was significant at the 10 mg ($\beta = -2.25$, $p = .01$) and 20 mg ($\beta = -2.91$, $p = .04$) doses (Figure 3).

Females showed a significant dose effect on all DEQ items except Bad Effects ($F = 52.17$-60.45, p's $< .05$). There were no significant associations between any of the SS

scales and *d*-AMPH subjective effects in females (Table 3). However, within-dose analyses showed a significant negative association between the Disinhibition subscale and Bad Effects at the 10 mg dose (β = -0.61, p = .04; Figure 4).

Sensation Seeking and Baseline Characteristics

Correlations between participants' SS Total scores and baseline demographic, drug use and psychosocial characteristics were also examined (see Table 1 for variables). There were no significant associations between the Total scale and any demographic characteristics. With respect to drug use, Total scores were significantly correlated with use of stimulants on greater than 10 occasions (r = .58, p = .01), as well as lifetime opioid (r = .55, p < .01) and hallucinogen use (r = .38, p = .02). The Total scale was also significantly correlated with other measures of impulsivity, including BAS Fun Seeking (r = .50, p < .01), BIS-11 Motor Impulsiveness (r = .34, p = .04), BIS-11 Nonplanning Impulsiveness (r = .47, p < .01) and BIS-11 Total (r = .41, p = .01).

Discussion

Stimulant abuse represents a serious public health problem, with over 3.4 million Americans reporting past-month illicit stimulant use (SAMHSA, 2013a). Efforts to identify the characteristics associated with susceptibility for stimulant abuse may help inform the development of more effective prevention and treatment efforts. In the present study, we sought to examine whether sensation seeking, a characteristic commonly associated with drug use and other risk behaviors, was associated with increased sensitivity to *d*-AMPH reinforcement under double-blind experimental conditions.

Among males, there was a significant association between SS and *d*-AMPH choice. Healthy volunteers with increased scores on the Total, Disinhibition, Thrill and Adventure Seeking, and Experience Seeking subscales had significantly greater odds of choosing *d*-AMPH over placebo, particularly at the 10 mg/70kg dose. These results are consistent with those of Stoops and colleagues (2007) in which high-SS participants demonstrated increased break points for both 8 and 16 mg *d*-AMPH compared to low-SS participants. Our findings differ from the two prior discrete-trial choice studies that found no such association between SS and *d*-AMPH choice (Chait, 1993; de Wit et al., 1986), perhaps due to a lack of controlling for gender differences in those studies.

Sensation Seeking was also significantly associated with *d*-AMPH subjective effects in males. With regard to positive *d*-AMPH subjective effects, males with higher scores on the Total, Disinhibition and Thrill and Adventure Seeking scales reported greater *d*-AMPH Liking, particularly at the 5 mg/70kg dose. These results are consistent with previous studies showing increased sensitivity to *d*-AMPH-associated positive effects among participants with higher SS scores (Hutchison et al., 1999; Kelly et al., 2006, 2009), as well as the larger literature showing concordance between *d*-AMPH-related positive effects and increased choice (Rush, Essman, Simpson, & Baker, 2001; Tancer, & Johanson, 2003). In terms of negative *d*-AMPH effects, males with higher Experience Seeking scores reported lower ratings of Bad Effects, particularly at 10 and 20 mg/70kg doses. This is also consistent with a prior study in which higher sensation seekers showed reduced sensitivity to *d*-AMPH-associated unpleasant effects (e.g., anger, light-headed; Kelly et al., 2009). Overall, these findings provide additional support for

increased vulnerability for stimulant abuse among males with elevated SS (Chait, 1994; de Wit, Uhlenhuth, & Johanson, 1986; Jaffe & Jaffe, 1989).

In contrast to males, we found no significant association between SS and *d*-AMPH choice or subjective response in female participants. One possible reason may be related to the inclusion criteria used in the parent study, in which participants were required to have used stimulants in order to be eligible. Thus, our sample of female participants may differ from the general female population in that they represent a more severe subset of the general population. There is some evidence to suggest this, as our female participants had significantly higher scores on the Total, Experience Seeking, and Thrill and Adventure Seeking scales compared to the published norms for females (Zuckerman et al., 1991).

Finally, we also examined correlations between SS and other baseline characteristics. Sensation Seeking scores were significantly associated with lifetime use of stimulants, opioids and hallucinogens, supporting the larger literature showing an association between SS and drug use (Zuckerman, 2012). In addition, SS scores were significantly correlated with other measures of impulsivity, including the BIS-11 and the BIS/BAS. This supports prior assertions that impulsivity and sensation seeking characteristics are likely comprised of related factors (Meda et al., 2009; Magid, & MacLean, 2005; Stanford et al., 2009). Indeed a factor analysis of several impulsivity and sensation seeking scales found that the Zuckerman SSS Total scale and each of the BIS-11 subscales loaded onto the same Self-Reported Impulsivity factor (Meda et al., 2009).

Several strengths of the present study should be noted. First, this study included a range of *d*-AMPH doses with multiple exposures at each dose level. We found that the associations between SS and *d*-AMPH sensitivity were strongest at the 5 and 10 mg *d*-AMPH doses, which supports previous findings suggesting that individual differences may be most pronounced at lower doses (White, Lott, & deWit, 2006). Second, instead of ignoring gender or simply using it as a covariate, we directly examined the effects of SS on *d*-AMPH response within each gender and found a strong association between SS and *d*-AMPH in males that was not evident in females. Third, while prior studies dichotomized participants into Low and High SS subgroups based on arbitrary cut-offs, which can result in suboptimal analyses, we examined SS as a continuous variable (Cohen, 1983). Finally, this is the first study to our knowledge to use the SS Total score as well as each of the four subscales, thus providing the most thorough analysis to date of the association between SS and *d*-AMPH response. Indeed, in males we saw significant associations between *d*-AMPH subjective effects and choice not only with the Total scale, but also the Disinhibition, Thrill and Adventure Seeking and Experience Seeking subscales.

Several potential limitations should also be considered. First, our sample size was restricted by the number of participants who completed the parent study. That said, we observed several statistically significant and potentially important associations between SS and *d*-AMPH response despite the limited sample. Also worth noting is that our sample size (n=37) was generally similar to those in prior studies on this topic (range = 17-36). Second, as we used a convenience sample of participants from a previously-completed study, our participant selection was constrained by its eligibility criteria.

Those criteria may have skewed SS scores in our study sample and, as a result, may have limited our ability to observe an association between SS and *d*-AMPH in females.

In summary, the present study sought to examine whether sensation seeking among healthy volunteers is associated with their sensitivity to *d*-AMPH's subjective and reinforcing effects. We found evidence that increased SS was associated with greater sensitivity to *d*-AMPH's positive effects and greater *d*-AMPH preference in males. Taken together, SS may reflect an important characteristic underlying an individual's sensitivity to stimulant reinforcement and risk for abuse.

Table 1
Baseline demographic, psychosocial and drug use characteristics

	Total Sample (n=37)	Males (n=16)	Females (n=21)	*p*
Demographics				
Age	22.9 (2.9)	22.2 (2.2)	23.4 (3.3)	0.20
Education (yrs)	15.1 (1.3)	15.1 (1.0)	15.2 (1.6)	0.78
Drug Use Characteristics				
Current smoker (%)	13.5	18.8	9.5	0.42
Current alcohol use (%)	100	100	100	1.00
Lifetime THC use (%)	100	100	100	1.00
Lifetime benzodiazepines use (%)	21.6	12.5	28.6	0.24
Lifetime opioid use (%)	32.4	43.8	23.8	0.21
Lifetime hallucinogen use (%)	67.6	68.8	66.7	0.9
Lifetime stimulant use (%)	100	100	100	1.00
Cocaine (%)	56.8	50.0	61.9	0.47
Adderall (%)	86.5	93.8	81.0	0.26
Methylphenidate (%)	24.3	25.0	23.8	0.93
Ecstasy (%)	45.9	62.5	33.3	0.08
Stimulants > 10 times	24.3	43.8	9.5	0.03
Psychosocial Characteristics				
Beck Anxiety Inventory (0-63)	2.6 (2.9)	2.3 (3.0)	2.9 (2.9)	0.58
Barratt Impulsivity Scale-11 (Total) (30-120)	57.6 (9.5)	58.6 (11.1)	56.8 (8.2)	0.57
Attentional Impulsiveness (8-32)	14.5 (3.8)	14.3 (4.3)	14.6 (3.4)	0.85
Motor Impulsiveness (11-44)	21.8 (3.3)	22.3 (3.9)	21.5 (2.8)	0.45
Nonplanning Impulsiveness (11-44)	21.3 (4.6)	22.0 (5.1)	20.8 (4.2)	0.44
Behavioral Inhibition/Behavioral Activation				
BAS Drive (4-16)	11.6 (2.3)	11.1 (1.6)	12.0(2.6)	0.26
BAS Fun Seeking (4-16)	12.7 (2.1)	13.3 (1.6)	12.4 (2.4)	0.22
BAS Reward Responsiveness (5-20)	17.8 (2)	17.8 (1.5)	17.9 (2.3)	0.92
BIS (7-28)	19 (3.3)	18.4 (3.1)	19.4 (3.5)	0.38

Note: Means (±s.d.) unless otherwise specified
p-values based on independent sample t-tests.

Table 2
Sensation seeking characteristics

	Total Sample (n=37)	Males (n=16)	Females (n=21)	*p*
Total Sensation Seeking (0-40)	24.1 ± 5.1	24.5 ± 5.2	23.8 * ± 4.9	0.68
Experience Seeking (0-10)	7.5 ± 1.4	7.2 * ± 1.6	7.7 * ± 1.3	0.28
Disinhibition (0-10)	5.6 ± 2.0	5.9 ± 2.5	5.5 ± 2.3	0.54
Thrill and Adventure Seeking (0-10)	7.9 ± 1.8	8.4 ± 1.5	7.6 * ± 2.0	0.19
Boredom Susceptibility (0-10)	3.0 ± 1.9	3.0 ± 2.0	3.1 ± 2.0	0.92

Note: Means (±SD), significance levels based on t-tests
* indicates that value is statistically greater than published norms ($p<.01$) (Zuckerman, Kuhlman, Thornquist, & Kiers, 1991)

Table 3
Effects of sensation seeking and d-AMPH choice

	Males (n=16)			Females (n=21)		
SS Scale	Odds ratio	95% CI	*p*	Odds ratio	95% CI	*p*
Total	1.57	(1.03, 2.38)	0.03	0.78	(0.49, 1.23)	0.28
Experience Seeking	1.87	(1.05, 3.32)	0.03	0.64	(0.36, 1.13)	0.12
Disinhibition	1.52	(1.10, 2.10)	0.01	0.94	(0.69, 1.28)	0.71
Thrill and Adventure	1.91	(1.04, 3.53)	0.04	0.90	(0.65, 1.25)	0.53
Boredom Susceptibility	0.87	(0.51, 1.48)	0.61	0.80	(0.53, 1.22)	0.31

Note. CI = confidence interval.
Odds ratio represents change in odds of *d*-AMPH choice per 5-point increase in Total SS and 2-point increase in each of the subscores.

Table 4
Dose-specific effects of sensation seeking and d-AMPH choice

	Males (n=16)								
	5mg			10mg			20mg		
SS Scale	Odds ratio	95% CI	*p*	Odds ratio	95% CI	*p*	Odds ratio	95% CI	*p*
Total	1.62	(0.84, 3.10)	0.15	2.20	(1.23, 3.94)	0.01	1.08	(0.60, 1.96)	0.80
Experience Seeking	1.20	(0.51, 2.81)	0.68	2.39	(1.21, 4.72)	0.01	2.50	(0.83, 7.51)	0.10
Disinhibition	1.70	(0.99, 2.92)	0.06	1.81	(0.98, 3.32)	0.06	1.14	(0.76, 1.73)	0.52
Thrill and Adventure	1.86	(0.98, 4.02)	0.11	2.85	(1.19, 6.86)	0.02	1.32	(0.48, 3.65)	0.59
Boredom Susceptibility	1.07	(0.54, 2.13)	0.85	1.11	(0.60, 2.02)	0.74	0.52	(0.25, 1.11)	0.09
	Females (n=21)								
	5mg			10mg			20mg		
SS Scale	Odds ratio	95% CI	*p*	Odds ratio	95% CI	*p*	Odds ratio	95% CI	*p*
Total	0.90	(0.50, 1.62)	0.74	0.69	(0.43, 1.11)	0.12	0.73	(0.42, 1.28)	0.28
Experience Seeking	0.63	(0.33, 1.20)	0.16	0.60	(0.33, 1.09)	0.09	0.68	(0.26, 1.81)	0.44
Disinhibition	1.09	(0.76, 1.57)	0.62	0.80	(0.53, 1.20)	0.28	0.94	(0.61, 1.45)	0.78
Thrill and Adventure	0.92	(0.53, 1.59)	0.77	0.81	(0.56, 1.16)	0.25	0.97	(0.64, 1.46)	0.87
Boredom Susceptibility	0.91	(0.50, 1.63)	0.74	0.89	(0.60, 1.32)	0.56	0.62	(0.36, 1.08)	0.09

Note. CI = confidence interval.
Odds ratio represents change in odds of *d*-AMPH choice per 5-point increase in Total SS and 2-point increase in each of the subscores.

Table 5
Effects of sensation seeking and d-AMPH subjective effects

	Males (n=16)			Females (n=21)		
SS Scale	β	95% CI	*p*	β	95% CI	*p*
Drug Effect						
Total	0.51	(-1.18, 2.21)	0.52	-0.27	(-2.16, 1.61)	0.76
Experience Seeking	-0.33	(-2.66, 1.98)	0.76	-1.13	(-3.96, 1.70)	0.41
Disinhibition	0.52	(-0.90, 1.95)	0.44	0.04	(-1.61, 1.68)	0.96
Thrill and Adventure	0.54	(-2.04, 3.12)	0.66	-0.27	(-2.16, 1.62)	0.77
Boredom Susceptibility	0.54	(-1.24, 2.32)	0.52	0.02	(-1.85, 1.90)	0.98
Good Effect						
Total	0.24	(-1.28, 1.76)	0.74	-0.36	(-2.37, 1.64)	0.71
Experience Seeking	-0.72	(-2.71, 1.26)	0.45	-0.60	(-3.64, 2.44)	0.68
Disinhibition	0.40	(-0.82, 1.61)	0.49	-0.46	(-2.20, 1.28)	0.58
Thrill and Adventure	0.47	(-1.80, 2.74)	0.66	0.27	(-1.76, 2.29)	0.79
Boredom Susceptibility	0.23	(-1.37, 1.82)	0.77	-0.30	(-2.33, 1.72)	0.76
Bad Effect						
Total	-0.85	(-2.06, 0.36)	0.15	0.14	(-0.47, 0.75)	0.63
Experience Seeking	-1.87	(-3.24, -0.50)	0.01	0.12	(-0.81, 1.06)	0.79
Disinhibition	-0.43	(-1.51, 0.65)	0.41	0.04	(-0.49, 0.57)	0.88
Thrill and Adventure	-0.71	(-2.59, 1.18)	0.43	-0.15	(-0.76, 0.46)	0.61
Boredom Susceptibility	-0.19	(-1.56, 1.18)	0.77	0.39	(-0.18, 0.97)	0.16
Like Drug						
Total	1.17	(0.19, 2.15)	0.02	0.16	(-2.48, 2.81)	0.90
Experience Seeking	0.87	(-0.61, 2.36)	0.23	-0.99	(-5.02, 3.03)	0.61
Disinhibition	1.00	(0.24, 1.75)	0.01	0.50	(-1.76, 2.75)	0.65
Thrill and Adventure	1.39	(-0.19, 2.98)	0.08	0.23	(-2.44, 2.90)	0.86
Boredom Susceptibility	0.24	(-1.03, 1.51)	0.69	-0.08	(-2.78, 2.62)	0.95
Stimulant Effect						
Total	-0.43	(-2.32, 1.47)	0.63	0.22	(-1.90, 2.34)	0.83
Experience Seeking	-1.31	(-3.74, 1.11)	0.26	-0.81	(-4.03, 2.41)	0.60
Disinhibition	-0.13	(-1.68, 1.43)	0.86	0.25	(-1.59, 2.10)	0.78
Thrill and Adventure	-0.35	(-3.21, 2.50)	0.79	0.31	(-1.85, 2.48)	0.76
Boredom Susceptibility	0.02	(-2.00, 2.03)	0.99	0.26	(-1.85, 2.37)	0.80

Note. CI = confidence interval.
β represents estimated change in area under the curve per 5-point increase in Total SS and 2-point increase in each of the subscores.

Table 6
Dose-specific relationships between sensation seeking score and d-AMPH subjective effects in males

	Males (n=16)								
	5mg			10mg			20mg		
SS Scale	β	95% CI	*p*	β	95% CI	*p*	β	95% CI	*p*
Drug Effect									
Total	1.11	(-0.46,2.68)	0.15	0.15	(-1.74, 2.04)	0.87	0.29	(-2.45, 3.02)	0.82
Experience Seeking	0.77	(-1.48, 3.03)	0.47	-0.22	(-2.77, 2.33)	0.86	-1.58	(-5.16, 2.00)	0.36
Disinhibition	1.11	(-0.16, 2.39)	0.08	0.15	(-1.45, 1.74)	0.85	0.32	(-1.98, 2.63)	0.77
Thrill and Adventure	1.43	(-0.99, 3.85)	0.22	-0.62	(-3.44, 2.20)	0.64	0.81	(-3.29, 4.91)	0.68
Boredom Suseptibility	0.16	(-1.62, 1.95)	0.84	0.62	(-1.33, 2.56)	0.50	0.85	(-1.98, 3.68)	0.53
Good Effect									
Total	0.83	(-0.99, 2.64)	0.34	0.35	(-0.95, 1.66)	0.57	-0.46	(-3.06, 2.15)	0.71
Experience Seeking	-0.06	(-2.58, 2.45)	0.96	0.13	(-1.64, 1.89)	0.88	-2.24	(-5.46, 0.99)	0.16
Disinhibition	0.93	(-0.49, 2.36)	0.18	0.37	(-0.68, 1.42)	0.46	-0.12	(-2.25, 2.01)	0.91
Thrill and Adventure	1.31	(-1.40, 4.03)	0.32	0.09	(-1.89, 2.07)	0.92	-0.005	(-3.93, 3.92)	1.00
Boredom Suseptibility	0.12	(-1.86, 2.10)	0.90	0.23	(-1.15, 1.61)	0.72	0.33	(-2.42, 3.07)	0.80
Bad Effect									
Total	-0.13	(-0.80, 0.54)	0.69	-1.19	(-2.66, 0.27)	0.10	-1.22	(-3.50, 1.06)	0.27
Experience Seeking	-0.45	(-1.31, 0.42)	0.29	-2.25	(-3.99, -0.52)	0.01	-2.91	(-5.63, -0.18)	0.04
Disinhibition	0.10	(-0.47, 0.67)	0.72	-0.62	(-1.95, 0.72)	0.34	-0.77	(-2.75, 1.21)	0.42
Thrill and Adventure	-0.37	(-1.33, 0.60)	0.43	-1.39	(-3.64, 0.86)	0.20	-0.37	(-3.89, 3.15)	0.82
Boredom Suseptibility	-0.05	(-0.75, 0.66)	0.89	-0.28	(-1.98, 1.42)	0.72	-0.25	(-2.75, 2.26)	0.83
Like Drug									
Total	1.35	(-0.14, 2.84)	0.07	0.98	(-0.59, 2.56)	0.20	1.18	(-0.63, 2.99)	0.18
Experience Seeking	0.63	(-1.56, 2.81)	0.54	1.45	(-0.57, 3.46)	0.14	0.55	(-1.97, 3.06)	0.65
Disinhibition	1.19	(0.05, 2.24)	0.04	0.80	(-0.45, 2.05)	0.19	0.99	(-0.43, 2.42)	0.16
Thrill and Adventure	2.10	(-0.08, 4.29)	0.06	0.82	(-1.62, 3.27)	0.48	1.25	(-1.54, 4.03)	0.35
Boredom Suseptibility	0.19	(-1.60, 1.99)	0.82	-0.03	(-1.81, 1.75)	0.97	0.55	(-1.48, 2.58)	0.57
Stimulant Effect									
Total	0.83	(-0.66, 2.34)	0.25	-1.04	(-3.23, 1.16)	0.33	-1.09	(-4.11, 1.94)	0.45
Experience Seeking	0.95	(-1.08, 2.97)	0.33	-1.62	(-4.51, 1.26)	0.25	-3.27	(-6.90, 0.37)	0.07
Disinhibition	0.72	(-0.49, 1.93)	0.22	-0.47	(-2.30, 1.37)	0.59	-0.63	(-3.12, 1.86)	0.59
Thrill and Adventure	0.90	(-1.39, 3.20)	0.41	-1.64	(-4.90, 1.63)	0.30	-0.32	(-4.95, 4.30)	0.88
Boredom Suseptibility	0.08	(-1.58, 1.75)	0.92	-0.27	(-2.67, 2.12)	0.81	0.24	(-3.02, 3.49)	0.88

Note. CI = confidence interval.
β represents estimated change in area under the curve per 5-point increase in Total SS and 2-point increase in each of the subscores.

Table 7
Dose-specific relationships between sensation seeking score and d-AMPH subjective effects in females

	Females (n=21)								
	5mg			10mg			20mg		
SS Scale	β	95% CI	*p*	β	95% CI	*p*	β	95% CI	*p*
Drug Effect									
Total	-0.21	(-1.32, 0.90)	0.70	-0.63	(-3.15, 1.88)	0.60	0.02	(-2.66, 2.69)	0.99
Experience Seeking	-0.90	(-2.53, 0.73)	0.26	-1.30	(-5.11, 2.50)	0.48	-1.17	(-5.20, 2.86)	0.55
Disinhibition	0.03	(-0.94, 0.99)	0.96	-0.11	(-2.32, 2.09)	0.92	0.19	(-2.13, 2.52)	0.86
Thrill and Adventure	-0.12	(-1.23, 1.00)	0.83	-0.25	(-2.79, 2.28)	0.83	-0.44	(-3.11, 2.23)	0.73
Boredom Suseptibility	-0.04	(-1.14, 1.06)	0.94	-0.60	(-3.09, 1.88)	0.62	0.71	(-1.90, 3.34)	0.57
Good Effect									
Total	0.01	(-1.84, 1.86)	0.99	-0.94	(-3.47, 1.58)	0.44	-0.16	(-2.77, 2.46)	0.90
Experience Seeking	0.26	(-2.54, 3.07)	0.84	-1.51	(-5.33, 2.32)	0.42	-0.57	(-4.52, 3.39)	0.77
Disinhibition	-0.54	(-2.14, 1.05)	0.48	-0.39	(-2.63, 1.84)	0.71	-0.45	(-2.72, 1.82)	0.68
Thrill and Adventure	0.64	(-1.20, 2.48)	0.48	0.07	(-2.52, 2.66)	0.96	0.09	(-2.54, 2.73)	0.94
Boredom Suseptibility	-0.002	(-1.87, 1.86)	1.00	-1.27	(-3.78, 1.24)	0.30	0.36	(-2.27, 2.99)	0.78
Bad Effect									
Total	0.001	(-0.64, 0.64)	0.99	-0.10	(-0.86, 0.66)	0.78	0.53	(-0.56, 1.62)	0.32
Experience Seeking	0.16	(-0.82, 1.14)	0.73	0.24	(-0.91, 1.40)	0.66	-0.04	(-1.76, 1.68)	0.96
Disinhibition	0.08	(-0.48, 0.64)	0.77	-0.61	(-1.19, -0.02)	0.04	0.64	(-0.28, 1.56)	0.16
Thrill and Adventure	-0.24	(-0.87, 0.39)	0.43	-0.06	(-0.82, 0.69)	0.86	-0.15	(-1.27, 0.97)	0.78
Boredom Suseptibility	0.07	(-0.57, 0.70)	0.83	0.50	(-0.21, 1.20)	0.15	0.62	(-0.44, 1.68)	0.24
Like Drug									
Total	0.67	(-1.48, 2.82)	0.52	-0.26	(-3.18, 2.65)	0.85	0.07	(-3.45, 3.61)	0.96
Experience Seeking	-0.13	(-3.46, 3.21)	0.94	-1.64	(-6.04, 2.76)	0.44	-1.22	(-6.60, 4.16)	0.64
Disinhibition	0.26	(-1.60, 2.12)	0.78	0.84	(-1.63, 3.31)	0.48	0.40	(-2.62, 3.42)	0.78
Thrill and Adventure	0.76	(-1.41, 2.93)	0.47	-0.02	(-2.97, 2.93)	0.99	-0.05	(-3.62, 3.52)	0.98
Boredom Suseptibility	0.67	(-1.53, 2.86)	0.53	-1.13	(-4.06, 1.80)	0.43	0.22	(-3.37, 3.82)	0.90
Stimulant Effect									
Total	0.24	(-1.25, 1.72)	0.74	-0.13	(-3.14, 2.89)	0.93	0.55	(-2.10, 3.21)	0.67
Experience Seeking	-0.56	(-2.83, 1.70)	0.61	-1.52	(-6.06, 3.02)	0.49	-0.34	(-4.41, 3.73)	0.86
Disinhibition	0.11	(-1.19, 1.41)	0.86	0.41	(-2.21, 3.03)	0.75	0.25	(-2.08, 2.57)	0.83
Thrill and Adventure	0.42	(-1.08, 1.93)	0.56	0.51	(-2.55, 3.58)	0.73	0.007	(-2.71, 2.73)	1.00
Boredom Suseptibility	0.28	(-1.20, 1.76)	0.70	-0.68	(-3.66, 2.30)	0.64	1.19	(-1.40, 3.78)	0.35

Note. CI = confidence interval.
β represents estimated change in area under the curve per 5-point increase in Total SS and 2-point increase in each of the subscores.

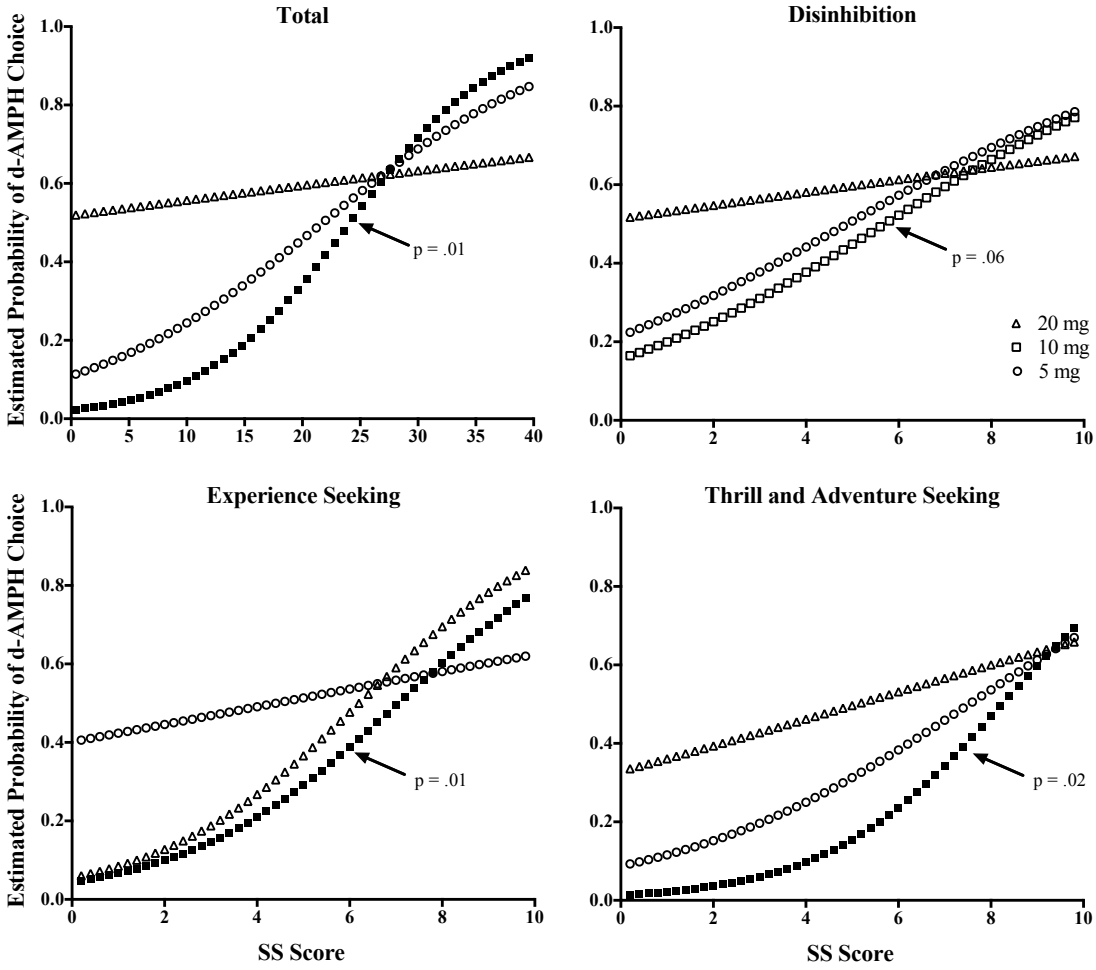

Figure 1. Estimated probability of *d*-AMPH choice in males as a function of SS score.

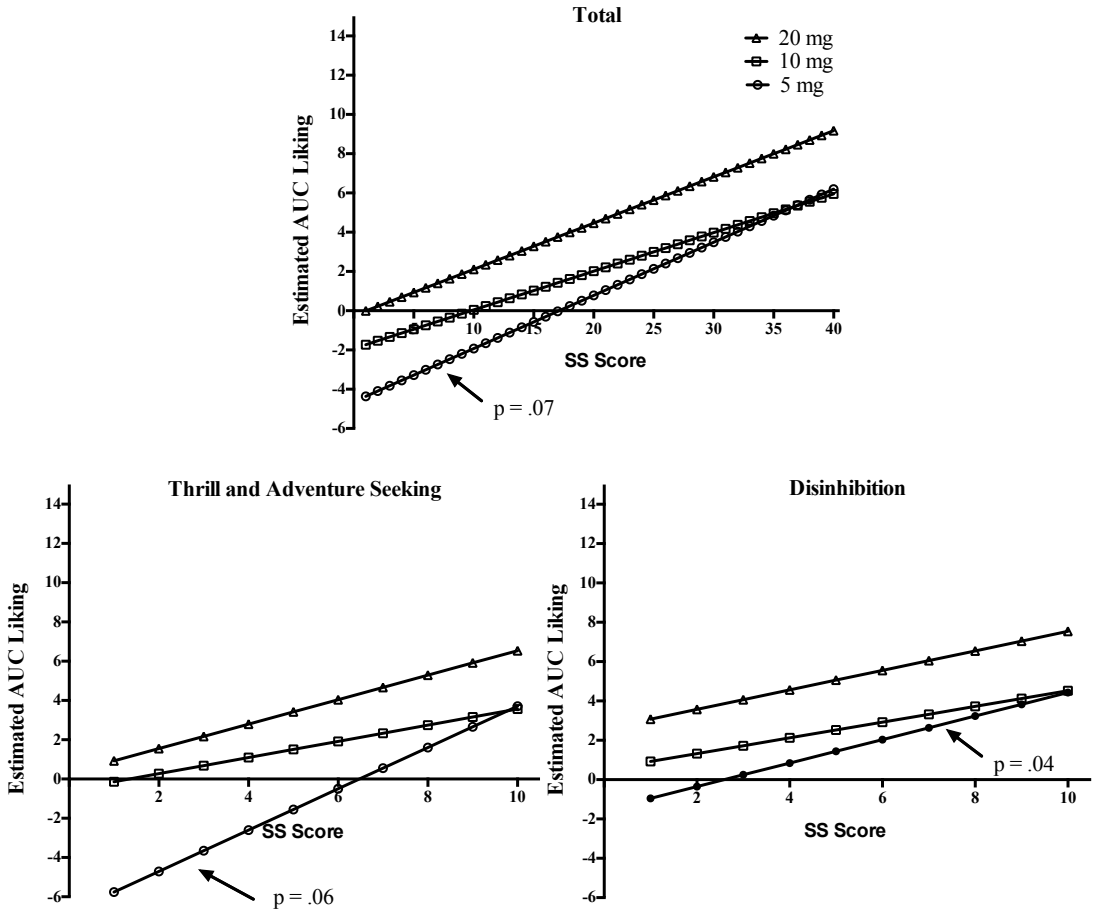

Figure 2. Estimated AUC *d*-AMPH Liking in males as a function of SS score.

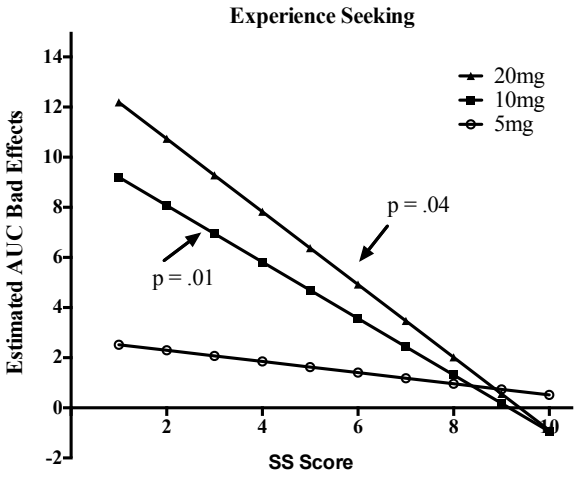

Figure 3. Estimated AUC *d*-AMPH Bad Effects in males as a function of SS score.

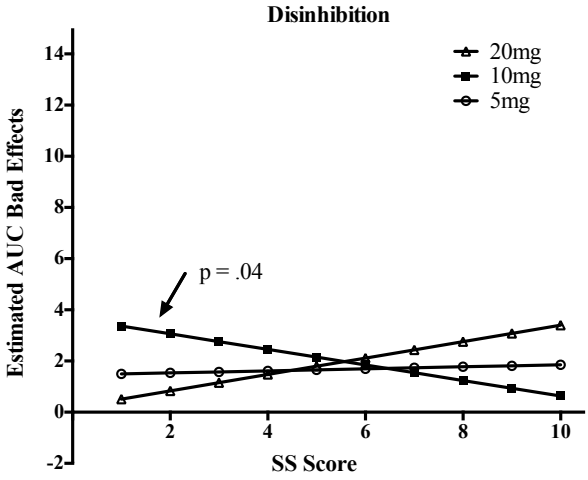

Figure 4. Estimated AUC *d*-AMPH Bad Effects in females as a function of SS score.

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