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The reinforcing, subject-rated, performance, and cardiovascular effects of d-amphetamine: Influence of sensation-seeking status

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Abstract

Individual differences that may contribute to vulnerability to abuse drugs have been identified. Sensation-seeking status has been shown to influence both vulnerability to drug use and response to acute drug administration. The purpose of the present experiment was to examine the reinforcing effects of d-amphetamine in high and low sensation-seeking subjects using a modified progressive-ratio procedure. A battery of subject-rated, performance, and cardiovascular measures was also included to better characterize the effects of d-amphetamine in these groups. Ten high sensation seekers and ten low sensation seekers that were matched for education, age, drug use, height, and weight, first sampled doses of d-amphetamine (0, 8, and 16 mg). In subsequent sessions, subjects were offered the opportunity to work for the sampled dose on a modified progressive-ratio procedure. d-Amphetamine functioned as a reinforcer and produced prototypical stimulant-like effects (e.g., increased subject-ratings of Like Drug, enhanced performance, and increased heart rate). High sensation seekers were more sensitive than low sensation seekers to the reinforcing and some of the subject-rated effects of d-amphetamine. The results of the present experiment extend those of previous findings by demonstrating that the reinforcing effects of d-amphetamine vary as a function of the biologically based sensation-seeking personality trait. These results suggest that increased stimulant drug use and abuse among high sensation seekers may be related, in part, to increased sensitivity to the reinforcing effects of stimulants among these individuals.

Keywords

d-Amphetamine; Sensation-seeking status; Subject-rated effects; Performance effects; Drug reinforcement

1. Introduction

Individual differences that may contribute to vulnerability to abuse drugs have been identified (Kreek, Nielsen, Butelman, & LaForge, 2005; Laviola, Adriani, Terranova, & Gerra, 1999). For example, epidemiological studies demonstrate that comorbid psychiatric conditions, genotype, and alcohol drinking behavior are associated with increased risk for drug use, abuse, and/or dependence (Frisher, Crome, Macleod, Millson, & Croft, 2005;

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Saxon, Oreskovich, & Brkanac, 2005; Substance Abuse and Mental Health Services Administration, 2005). The results of human behavioral pharmacology laboratory-based research mirror these findings in that individuals have been shown to differ in their sensitivity to acute drug effects based on psychiatric diagnosis, genotype, and alcohol drinking behavior (Helmus, Tancer, & Johanson, 2005; Lott, Kim, Cook, & de Wit, 2005; Stoops, Fillmore, Poonacha, Kingery, & Rush, 2003). These differences in response to drug effects may play a role in subsequent drug misuse or abuse (de Wit, 1998).

Personality variables have also been implicated in vulnerability to drug abuse (e.g., White, Lott, & de Wit, 2006). One biologically based personality trait that may contribute to drug abuse vulnerability is sensation seeking, which is characterized by a preference for novel, complex, ambiguous, and/or emotionally intense sensations and experiences and by willingness to take risks for such experiences (Zuckerman, 1994). Sensation-seeking status, or the correlated personality dimension of novelty-seeking status, has been associated with initiation, frequency and amount of drug use, and development of drug abuse and dependence (Brennan, Walfish, & AuBuchon, 1986; Hawkins, Catalano, & Miller, 1992; Huba, Newcomb, & Bentler, 1981; Wills, Duhamel, & Vaccaro, 1995; Wills, Vaccaro, & McNamara, 1994). Results of laboratory studies suggest that high sensation seekers are also more sensitive than low sensation seekers to the acute effects of both stimulant (e.g., d-amphetamine, nicotine) and sedative (e.g., alcohol, diazepam) drugs, including self-report measures that have been associated with the reinforcing effects of drugs (Cheong & Nagoshi, 1999; de Wit, Uhlenhuth, Pierri, & Johanson, 1987; Hutchison, Wood, & Swift, 1999; Kelly et al., submitted for publication, in press; Perkins, Gerlach, Broge, Grobe, & Wilson, 2000; White et al., 2006).

Given previous findings that high sensation seekers are more sensitive to the effects of drugs, the purpose of the present experiment was to further examine the influence of sensation-seeking status on the behavioral effects of d-amphetamine that are related to its abuse potential. Specifically, this experiment was designed to test whether the reinforcing effects of d-amphetamine as measured by a modified progressive-ratio procedure varied as a function of sensation-seeking status, because the reinforcing effects of drugs are the best predictor of the abuse potential of stimulant drugs (Foltin & Fischman, 1991a). The modified progressive-ratio procedure is a measure of the reinforcing efficacy of drugs and is sensitive to drug dose, pharmacological pretreatments, and environmental context (Comer, Walker, & Collins, 2005; Stoops, Lile, Glaser, & Rush, 2005). High sensation seekers who engage in high risk behaviors are known to initiate high-risk drug use at an earlier age than low sensation seekers. By assessing relative sensitivity to the reinforcing effects of drugs, it is possible to determine whether high sensation seekers are also more likely to engage in repeated drug use following initial use and therefore at increased vulnerability to drug abuse and dependence.

2. Materials and methods

2.1. Subjects

Healthy adult volunteers were recruited through advertisements placed on the University of Kentucky campus and in the local community. All volunteers completed a brief telephone interview or an internet-based questionnaire addressing general medical and legal status and completed the Impulsive Sensation-Seeking scale from the Zuckerman-Kuhlman Personality Questionnaire (Zuckerman, Kuhlman, Joireman, Teta, & Kraft, 1993). Respondents who reported good health and occasional stimulant use (e.g., caffeine) with impulsive sensation-seeking scale scores that fell in the upper (i.e., males ≥ 14, females ≥ 13) and lower (i.e., males ≤ 7, females ≤ 6) quartile of scores from a distribution of 2969 college students

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(Zuckerman, personal correspondence) were contacted by telephone and invited to participate in the study.

During an orientation and medical screening day, volunteers completed a battery of medical and psychological questionnaires (e.g., Kelly et al., in press), including the Zuckerman Sensation-Seeking Scale (SSS Form V, Zuckerman, Eysenck, & Eysenck, 1978), as well as blood chemistry, complete blood count with differential, liver function, and urinalysis tests. Volunteers were excluded if they had a history of medical illness (e.g., cardiovascular disease, neurological or psychiatric disorder) or if there was any indication of elevated medical risk associated with administration of the study drug. During two separate training sessions, subjects practiced the study tasks until performance was consistent and accurate across consecutive trials.

Twenty-one subjects completed the 8-day protocol. Data from one male high sensation seeker were excluded from analysis because he failed to respond under any condition on the modified-progressive ratio procedure. The final sample consisted of 10 high (5 female) and 10 low (5 female) impulsive sensation seekers. Low sensation seekers were significantly lower on the total score ($p<0.001$) and on the Thrill and Adventure Seeking ($p=0.05$), Experience Seeking ($p<0.0001$) and Boredom Susceptibility ($p<0.0005$) subscales of the Sensation Seeking Scale (SSS; Form V). Scores on the Disinhibition subscale were not different ($p<0.2$). Groups were not significantly different (two-sample *t*-tests) in age (21.6 vs. 21.7 years for low and high groups, respectively), height, weight (within 20% of their ideal body weight), years of education (14.6 vs. 13.9) or drug use. Alcohol (4.9±2.3 vs. 5.9±3.1 drinks per week) and caffeine (34 vs. 59 mg/day) use was modest for all subjects. Four subjects (1 low sensation seeker) reported intermittent (i.e., less than daily) tobacco use, and two (1 low) reported marijuana use on two or fewer occasions during the month preceding the study. No other drug use was reported (e.g., amphetamines, cocaine). Groups did not differ on any of the questionnaire scores examining personality (e.g., extraversion) or psychiatric symptoms (e.g., depression, ADHD, or conduct disorder).

Subjects earned approximately US$400, including per diem and task earnings, as well as a bonus for completing all scheduled sessions and abstaining from drug use for the duration of the study. There were no group differences in earnings. The study was reviewed and approved by the University of Kentucky Medical Institutional Review Board, and all subjects provided written informed consent.

2.2. Design

A double-blind, placebo-controlled, randomized block design was used to examine the effects of one between-subject variable (high vs. low sensation-seeking status) and two within-subject variables [d-amphetamine dose (0.0, 8.0 and 16.0 mg) and time (0, 60, 120 and 180 minutes post dose)]. After training, each subject completed eight 4.5-h sessions, Monday through Friday, each separated by a minimum of 48 h.

Testing of each of the drug conditions described below consisted of two separate sessions: (1) a sampling session and (2) a self-administration session. Sampling and self-administration sessions were conducted on separate days. Sampling sessions were immediately followed by self-administration sessions on the next experimental session day.

2.2.1. Sampling sessions—Sampling sessions were conducted to acquaint subjects with the effects of each drug dose. After completing a pre-drug assessment consisting of questionnaires and physiological and performance task measures (see below), subjects ingested eight identical capsules and were instructed to pay attention to and make notes about the effects of the drug, because in the next session they would be offered the

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opportunity to respond to receive that drug again. Subjects then completed assessments at hourly intervals for 3 h and recorded individual comments concerning the effects of the drug dose throughout the session.

2.2.2. Self-administration sessions—Self-administration sessions differed from sampling sessions only in that subjects had the opportunity to earn capsules by responding on a modified progressive-ratio procedure (described below). The progressive-ratio procedure was completed immediately following the pre-drug assessment.

2.3. Modified progressive-ratio procedure

The modified progressive-ratio procedure was completed only once after the pre-dose assessment during self-administration sessions. This procedure is a reliable measure of drug reinforcement in humans and has been described previously (Comer, Collins, & Fischman, 1997; Comer, Collins, MacArthur, & Fischman, 1999; Comer et al., 1998; Rush, Essman, Simpson, & Baker, 2001; Stoops, Fillmore, Glaser, & Rush, 2004). Briefly, during each progressive-ratio procedure, subjects were given 8 opportunities to respond on a computer mouse to earn all, or some, of the capsules that were administered during the preceding sampling session (i.e., the previous experimental session). Subjects responded by clicking either a YES or NO presented on a computer screen when asked if they wanted to work for one of the previously sampled capsules. If the subject responded YES, they were then required to click the mouse a predetermined number of times to earn the capsule. To earn the first capsule, subjects were required to click the mouse 25 times. The number of responses required to earn each additional capsule doubled (i.e., 50, 100, 200, 400, 800, 1600, and 3200 responses). If the subject responded NO at any time when they were asked if they wanted to work for one of the capsules administered during the last session, no further opportunities to earn capsules were presented. The procedure lasted 30 min, regardless of the number of capsules earned. This helped to ensure that subjects did not refuse to respond in an attempt to shorten the procedure or the session duration. The dependent measure on this procedure was the break point (i.e., the last ratio completed) and the number of capsules earned.

Subjects ingested all of the capsules they earned after completing the modified progressive-ratio procedure. As described above, each capsule contained 12.5% of the total dose of the test drug administered during the preceding sampling session. After ingesting any capsules earned on the modified progressive-ratio procedure, subjects completed assessments at hourly intervals for three hours. If a subject did not respond for any capsules, he/she still completed the assessments as scheduled.

2.4. Drug

Doses were prepared by the University of Kentucky Investigational Pharmacy in size 00 opaque capsules with lactose filler. Because the modified-progressive ratio procedure consisted of eight ratios, sampling and self-administration doses were divided evenly into eight separate capsules. Thus, for the 8.0 mg dose, each capsule contained 1.0 mg d-amphetamine and for the 16.0 mg dose, each capsule contained 2.0 mg d-amphetamine. Each active dose (8.0 and 16.0 mg) was tested on one occasion and placebo was tested twice.

2.5. Daily schedule

Session start times were fixed for each subject. Subjects were instructed to abstain from medication and alcohol for 24 h prior to all scheduled sessions, and to abstain from eating for 4 h prior to the start of each test day.

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At the beginning of each test day, subjects answered open-ended questions regarding sleep, medication use, eating behavior and health status during the preceding 24 h, and completed field-sobriety, breath (Alco-Sensor III, Intoximeters, Inc. and piCO Carbon Monoxide Monitor, Bedfont Scientific) and urine tests (cocaine, benzodiazepine, barbiturate, marijuana, amphetamine and opiate OnTrack TesTstik Bar, Varian, Inc. and Clearview HCG II, Unipath, Ltd.) to assess drug use and pregnancy. Subjects then consumed a low-fat snack. Assessments were completed before (i.e., time 0) and at hourly intervals for 3 h after dose administration. Each assessment was approximately 35 min in duration.

During each assessment, activities were presented in the following order: a Visual Analog Scale (VAS; see Kelly et al., in press for a description of the items used in this scale), the Profile of Mood States (POMS; McNair, Lorr, & Droppleman, 1971), the Addiction Research Center Inventory (ARCI; Martin, Sloan, Sapira, & Jasinski, 1971), the Digit-Symbol Substitution Task (DSST; McLeod, Griffiths, Bigelow, & Yingling, 1982), a Repeated Acquisition Task (Fischman, 1978; Kelly, Hienz, Zarcone, Wurster, & Brady, 2005), and a Rapid Information Processing Task (RIP; Fillmore, Kelly, & Martin, 2005). Oscillometric heart rate and systolic and diastolic blood pressure were also measured (Sentry II, NBS Medical).

2.6. Data analysis

All results were considered significant at $p=0.05$. Data from the active d-amphetamine doses were analyzed as raw scores. Data from the placebo doses were averaged across the two exposures.

Data from the modified progressive-ratio procedure were analyzed using a mixed-model ANOVA with sensation-seeking status (high and low) as the between-group factor and d-amphetamine dose (0, 8, and 16 mg) as the within-group factor. *F* values from the ANOVA were used to interpret the results.

Data from sampling sessions (e.g., subject-ratings, performance and cardiovascular measures) were analyzed using a linear mixed model with sensation-seeking status (high and low), d-amphetamine dose (0, 8, and 16 mg), and time post-drug (1, 2, and 3 h) as factors. Initial analyses indicated several group differences in pre-drug measures, so the data were re-analyzed using pre-drug performance as a covariate. Significant interactions were analyzed using simple-effects models. During self-administration sessions, subjects ingested varying amounts of drug based on progressive-ratio procedure performance; therefore, subject-rated drug-effect-questionnaire, performance and cardiovascular data from the self-administration sessions were not analyzed statistically.

3. Results

3.1. Modified Progressive-Ratio procedure

Significant main effects of sensation-seeking status ($p=0.03$) and d-amphetamine dose ($p=0.02$) were observed for break point on the Modified Progressive-Ratio Procedure (Fig. 1). In high sensation seekers, break points for the active doses of d-amphetamine were increased relative to low sensation seekers. Similar effects were observed with number of capsules earned with main effects of sensation seeking status ($p=0.05$) and d-amphetamine dose ($p=0.02$). There were no other significant effects detected on this measure.

3.2. Subject rated drug effects

VAS—A significant interaction of sensation-seeking status and d-amphetamine dose (p's<0.04) was observed for subject ratings of Sedated and Anxious from the VAS. Simple

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effects analysis revealed that subject ratings of Sedated were increased for placebo in high sensation seekers relative to low sensation seekers and that subject ratings of Anxious were increased by the high dose of d-amphetamine in high sensation seekers relative to low sensation seekers. A significant interaction of d-amphetamine dose and time (p's<0.04) was observed for subject ratings of Stimulated and Like Drug from the VAS (Fig. 2). Simple effects analyses revealed that subject ratings of Stimulated were increased by the high dose of d-amphetamine relative to placebo at the 2 and 3 h post-drug observation points and that ratings of Like Drug were increased by both active doses of d-amphetamine relative to placebo at the 2 and 3 h post-drug observation points. A significant main effect of sensation-seeking status (p=0.02) was observed for subject ratings of Thirsty from the VAS. A significant main effect of d-amphetamine dose (p's<0.03) was observed for subject ratings of Stressed, Hungry, Thirsty, Sleepy, Sick to Stomach, High, and Feel Drug from the VAS. A significant main effect of time (p's<0.04) was observed for subject ratings of Hungry, Thirsty, and Feel Drug from the VAS.

POMS—A significant interaction of sensation-seeking status and d-amphetamine dose (p's<0.05) was observed for scores on the Anger, Fatigue, and Confusion scales of the POMS. Simple effects analyses revealed that high sensation seekers had higher scores on the Anger scale relative to low sensation seekers at the low dose of d-amphetamine, high sensation seekers had lower scores on the Fatigue scale relative to low sensation seekers at the high dose of d-amphetamine, and high sensation seekers had higher scores on the Confusion scale relative to low sensation seekers at the high dose of d-amphetamine. A significant main effect of d-amphetamine dose (p's<0.03) was observed for scores on the Vigor, Friendliness, Elation, and Arousal scales and Total Positive of the POMS. A significant main effect of time (p's<0.02) was observed for scores on the Elation and Arousal scales and Total Positive of the POMS.

ARCI—A significant interaction of d-amphetamine dose and time (p=0.04) was observed for scores on the MBG scale of the ARCI (Fig. 2). Simple effects analysis revealed that the highest dose of d-amphetamine increased scores on this scale relative to placebo at the 2 and 3 h post-drug observation points. A significant main effect of d-amphetamine dose (p's<0.02) was observed for scores on the PCAG, BG, LSD, and A scales of the ARCI. A significant main effect of time (p=0.04) was also observed for scores on the A scale of the ARCI. There were no other significant effects detected on the ARCI.

DSST—No significant effects were observed on the DSST.

Repeated Acquisition Task—A significant interaction of d-amphetamine dose and sensation-seeking status (p=0.04) was observed for Error Response Rate on the Repeated Acquisition Task. Simple effects analysis revealed that at the low dose of d-amphetamine Error Response Rate decreased in high sensation seekers relative to low sensation seekers. There were no other significant effects detected on the Repeated Acquisition Task.

RIP—A significant interaction of d-amphetamine dose and time (p=0.03) was observed for Proportion of Correct Responses on the RIP. Simple effects analysis revealed that the low dose of d-amphetamine increased Proportion of Correct Responses relative to placebo at the 2 and 3 h post-drug observation points. There were no other significant effects observed on the RIP.

Cardiovascular assessments—A significant interaction of sensation-seeking status and d-amphetamine dose (p=0.04) was observed for Diastolic Blood Pressure. Simple effects analysis revealed that both active doses of d-amphetamine increased Diastolic Blood

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Pressure in high sensation seekers relative to low sensation seekers. A significant main effect of d-amphetamine dose (p's<0.04) was observed for Systolic Blood Pressure and Heart Rate.

4. Discussion

The purpose of the present experiment was to examine the reinforcing, subject-rated, performance and physiological effects of d-amphetamine in high and low sensation-seeking humans. As has been demonstrated in numerous studies, d-amphetamine functioned as a reinforcer (i.e., maintained break points higher than placebo), and produced prototypical stimulant-like behavioral effects (e.g., increased subject ratings of Like Drug, increased heart rate, and enhanced performance) (Comer, Haney, Foltin, & Fischman, 1996; Rush et al., 2001; Stoops et al., 2004).

The results of the present experiment suggest that high sensation seekers are more sensitive to the behavioral effects of d-amphetamine. That is, d-amphetamine engendered greater subject-rated and cardiovascular effects in high sensation seekers than low sensation seekers (e.g., less fatigue and more anxiety following d-amphetamine administration; higher diastolic blood pressure). These findings are concordant with those of previous studies (Hutchison et al., 1999; Kelly et al., submitted for publication, in press; White et al., 2006). In those studies, those high in sensation seeking (or comparable personality dimensions) displayed greater sensitivity to the subject-rated and/or cardiovascular effects of d-amphetamine. The present findings extend the results of previous research by demonstrating that high sensation seekers are also more sensitive to the reinforcing effects of d-amphetamine than low sensation seekers. High sensation seekers who are more likely to engage in high-risk behaviors than low sensation seekers are also more likely to initiate drug use. However, increased sensitivity to the reinforcing effects of d-amphetamine suggests that high sensation seekers may also be more likely to continue use following initial use, and thus are at increased vulnerability to develop drug abuse and dependence, than low sensation seekers (Brennan et al., 1986; Hawkins et al., 1992; Huba et al., 1981; Wills et al., 1995; Wills et al., 1994).

As noted above, the progressive-ratio procedure is a measure of the reinforcing efficacy of drugs or drug doses (Stafford, Le Sage, & Glowa, 1998). Previous research with human subjects has demonstrated that the progressive-ratio procedure is sensitive to the reinforcing effects of a number of drugs including heroin, caffeine, marijuana, pentobarbital, d-amphetamine, and methylphenidate (Comer et al., 1997; Griffiths, Bigelow, & Liebson, 1989; Haney, Comer, Ward, Foltin, & Fischman, 1997; McLeod & Griffiths, 1983; Rush et al., 2001; Stoops et al., 2004). Results from these studies have also demonstrated that the progressive-ratio procedure is sensitive to manipulation of both pharmacological (e.g., dose or pretreatment agent) and environmental (e.g., alternative reinforcers or behavioral requirements following drug administration) variables (Comer et al., 1997, 2005; Stoops et al., 2005). The results of the present experiment serve to extend previous findings in that the modified progressive-ratio procedure is also sensitive to the influence of personality variables on drug-taking behavior.

It is important to note that not all studies have found differences in the sensitivity to acute drug effects as a function of sensation-seeking status (Alessi, Greenwald, & Johanson, 2003; Carrol, Zuckerman, & Vogel, 1982; Corr & Kumari, 2000; de Wit, Uhlenhuth, & Johanson, 1986). The reasons for the discrepancy between those studies and the present experiment are not known, but could be due to the way subjects are recruited for the studies. In the present experiment, sensation-seeking group status was determined by recruiting subjects who scored in the upper and lower quartiles of the general population on the biologically based

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impulsive sensation-seeking scale of the ZKPQ; in contrast, studies examining the relationship between sensation- or novelty-seeking status and drug response among randomly recruited subjects have not consistently found a positive association. Thus, different screening procedures, as well as sample size and the distribution of sensation-seeking scores in the study population (e.g., White et al., 2006), may contribute to discrepant results between studies.

While high sensation seekers displayed greater sensitivity to a number of "negative"subject-rated effects of d-amphetamine (e.g., increased ratings of anxiety on the VAS and increased scores on the Anger and Confusion scales of the POMS) and also had higher break points on the modified progressive-ratio procedure relative to low sensation seekers, one interesting finding is that groups did not differ on a number of subject-rated effects that have been associated with a drug's reinforcing effects (e.g., Like Drug from the VAS, the MBG scale of the ARCI). Previous laboratory studies have reported group differences on such measures (e.g., Hutchison et al., 1999; Kelly et al., in press; Perkins et al., 2000; White et al., 2006). The results of previous research have demonstrated that the reinforcing and subject-rated effects of drugs are not isomorphic (e.g., Chait, 1993; Johanson & Uhlenhuth, 1980; Lamb et al., 1991; Rush et al., 2001; Stoops et al., 2004). The reasons for the discrepancy between verbal report and self-administration behavior are not known, but this finding supports the use of multiple measures to better characterize the reinforcing effects of stimulant drugs (Foltin & Fischman, 1991b).

There are limitations to the current experiment that need to be acknowledged. First, only two active doses of d-amphetamine were tested in the present experiment. Future research should examine a broader dose range in high and low sensation seekers. Second, the response requirements chosen for the modified progressive-ratio procedure may have been too low. That is, high sensation seekers tended to respond maximally for both doses of d-amphetamine in the present study. The use of a higher response requirement might reveal even greater differences between high and low sensation seekers in their response to the reinforcing effects of d-amphetamine. Third, only ten subjects were included in each group. This small sample size may have limited our statistical power, although it is comparable to that of other studies from our group that have found differences between high and low sensation seekers in response to acute drug administration (e.g., Kelly et al., submitted for publication, in press). Fourth, the use of a between subjects design may be seen as a limitation to the present experiment. Although the two groups were matched on a number of variables (e.g., education, age, drug use), it is possible that the differences observed in the present experiment are due to some variable other than sensation-seeking status that was not measured.

In summary, the results of the present experiment suggest that high sensation seekers are more sensitive than low sensation seekers to the reinforcing and some of the subject-rated effects of d-amphetamine. This enhanced sensitivity may contribute to the increased vulnerability of high sensation seekers to drug use, abuse, and dependence (Brennan et al., 1986; Hawkins et al., 1992; Huba et al., 1981; Wills et al., 1995; Wills et al., 1994). Further research is needed, however, to more definitively examine the relationship between sensation-seeking status and acute responses to drugs. It is now clear that the efficacy of drug use prevention and intervention strategies can be enhanced by targeting individuals who are most vulnerable to developing problems and tailoring message content and format based on the characteristics of these individuals (e.g., Palmgreen, Donohew, Lorch, Hoyle, & Stephenson, 2001). The results of research related to the specific aspects of the sensation seeking trait that increase vulnerability to drug use could therefore be used to improve prevention and intervention strategies.

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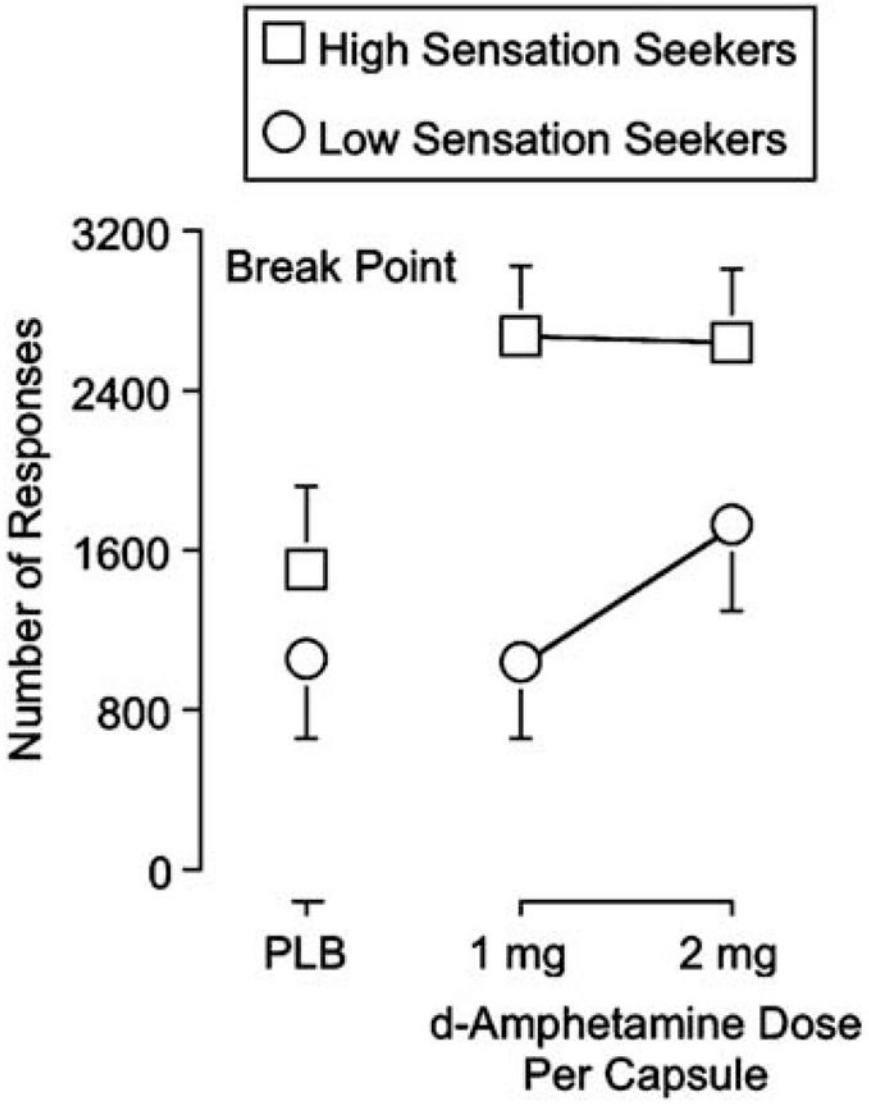

Fig. 1.

Dose–response function for d-amphetamine break point on the Modified Progressive-Ratio Procedure as a function of sensation-seeking status. *X*-axis: d-amphetamine dose per capsule. The total dose sampled was 0 mg d-amphetamine (placebo [PLB]), 8 mg d-amphetamine (1 mg) and 16 mg d-amphetamine (2 mg). The maximum break point was 3200. Brackets indicate ±1 S.E.M. Unidirectional brackets were used for clarity.

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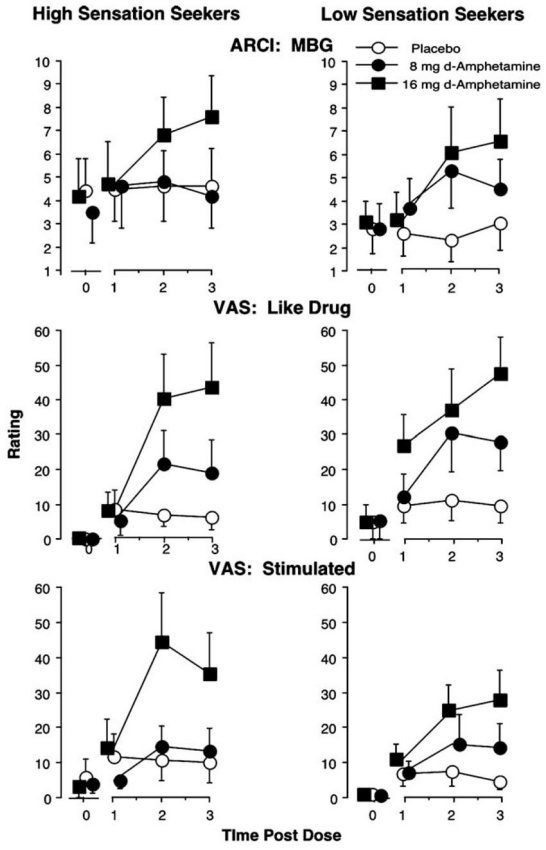

Fig. 2.

Dose– and time–response function for d-amphetamine for the MBG scale of the ARCI and subject-ratings of Like Drug and Stimulated from the VAS as a function of sensation-seeking status. *X*-axis: time in hours. Left panels represent data for high sensation seekers. Right panels represent data for low sensation seekers. Other details are as in Fig. 1.