RESEARCH ARTICLE

Recreational Activities and d-Amphetamine Effects in High and Low Sensation Seekers

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Abstract
This study examined the behavioral effects of d-amphetamine and recreational activities, alone and in combination, in high and low impulsive sensation seekers. Healthy 18-27 year-old participants, scoring in the upper (N=8) or lower (N=8) third of college students on the impulsive sensation-seeking scale of the Zuckerman-Kuhlman Personality Questionnaire, completed eight test days in which sessions were completed before (i.e., baseline) and 60, 120 and 180 minutes after d-amphetamine (0, 10 mg/70 kg) administration. Between sessions, subjects completed recreational activities (movies, music, reading, videogames) identified as high or low in sensation value. Each of four conditions (low and high sensation value activities combined with placebo and active drug) was administered under double-blind conditions on 2 days according to a randomized-block design. Typical stimulant-like cardiovascular and task performance effects were engendered by d-amphetamine; consistent with previous research, the magnitude of drug effects were greater among high sensation seekers. High sensation value activities engendered independent stimulant-like effects on subject ratings. These results suggest that d-amphetamine and high sensation stimulus materials may activate a common neurobiological substrate, likely the mesolimbic dopamine system, and that individual differences in sensation seeking status play a role in vulnerability to stimulant drug abuse.

Recreational Activities and d-Amphetamine Effects in High and Low Sensation Seekers

Substantial evidence has accumulated indicating that sensation-seeking status is linked to individual differences in vulnerability to drug abuse. Adolescents and young adults characterized as high sensation or novelty seekers using personality scales such as the Zuckerman or Cloninger inventories[1,2] are more likely to initiate drug use, begin using at an earlier age, and report greater frequency and amount of drug use compared to their low sensation seeking counterparts[3,4]. Regular drug users and substance abusers score higher on sensation-seeking dimensions than control subjects[5-7]. High sensation seekers in drug treatment also relapse at a greater rate than low sensation seekers[8]. The mechanisms that account for the relationship between sensation-seeking status and drug abuse vulnerability have not been clearly established.

One potential biological factor that may mediate the relationship between sensation seeking status and drug abuse vulnerability is the mesolimbic dopamine system[9]. Much of the evidence suggesting this relationship has come from preclinical studies. The amount of activity rats emit in a novel environment is associated with the locomotor and reinforcing effects of stimulant drugs, such as cocaine and amphetamine, which have a primary mechanism of action on the mesolimbic dopamine pathway[10-12]. These high novelty responding rats have a greater number of dopamine receptors[13,14] and show enhanced release of dopamine following both stimulant drug administration and exposure to novel environments[15-17]. Recent clinical studies suggest that high sensation seekers, based on personality questionnaires, are more sensitive to the behavioral effects of stimulant drugs[18-20], using traditional laboratory measures of abuse liability. Based on these results, it is possible that treatment and prevention strategies that address individual differences in sensation-seeking status and/or mesolimbic dopamine system activity may influence the efficacy in reducing vulnerability and relapse[21].

Similar to drugs of abuse, novel and high sensation value stimulus events, known to function as reinforcers in laboratory models, may activate the mesolimbic dopamine system[22-24]. For example, human volunteers playing a novel video game show enhanced forebrain dopamine activity as measured by positron emission topography[25]. Novel humorous stimulus materials also increase mesolimbic dopamine activity[26]. Given that high sensation value stimulus events and stimulant drugs of abuse affect similar neurobiological systems, it is conceivable that exposure to novel stimulus materials could alter the dopamine-mediated behavioral effects of drugs of abuse. In support of this, preclinical evidence has shown that exposure to novel stimulus materials decreases the rate of amphetamine self-administration in rats[27].

The purpose of the current study was to evaluate the effects of d-amphetamine in high and low sensation seekers participating in activities varying in sensation value in order to test the following hypotheses: 1) high sensation seekers are more sensitive than low sensation seekers to the stimulant effects of d-amphetamine, 2) high sensation activities will engender stimulant-like effects similar to those of d-amphetamine, and high sensation seekers are more sensitive than low sensation seekers to the stimulant effects of high sensation activities, and 3) high sensation activities will reduce the stimulant effects of d-amphetamine to a greater extent in high sensation seekers than in low sensation seekers. The behavioral effects of amphetamine were evaluated

using laboratory measures associated with drug abuse liability.

Method

Participants

Young adult nonsmoking volunteers were recruited from a pool of undergraduates enrolled in Introductory Psychology classes and from the local community. As part of class participation, students completed the Impulsive Sensation-Seeking scale of the Zuckerman-Kuhlman Personality Questionnaire[28]. Those falling in the upper (i.e., high sensation-seekers, $\geq$ 14) or lower (i.e., low sensation seekers, $\leq$ 7) quartile of the distribution of scores from the entire cohort were contacted by telephone and invited to participate in the study. Young adults from the general community meeting these ZKPQ criteria were also contacted. All participants completed a brief telephone interview addressing general medical and legal status, and those reporting good health and occasional stimulant use were invited to participate.

Volunteers were required to attend an initial interview and to complete medical screening and training on separate days. During the initial interview, all details of study participation were discussed. During the medical screen, volunteers completed medical and psychological questionnaires, including locally-developed health and personal history questionnaires, a 17-item drug use questionnaire derived from the Addiction Severity Index[29], the 13-item version of the short form of the Michigan Alcoholism Screening Test[30], the Eysenck Personality Inventory[31], the Addiction Research Center Maturation Scale[32], the Brief Symptom Inventory[33], and the Beck Depression Inventory, short form[34]. Volunteers also completed the Zuckerman Sensation-Seeking Scale (Form V). Blood chemistry, liver function and urinalysis tests were also conducted. Volunteers were excluded from participation if any result indicated that they would be at increased medical risk from the study drug. During training, participants were instructed in the operation of the recreational activities and computer tasks; participants practiced the study tasks until performance was consistent and accurate across consecutive trials.

The final sample consisted of eight high (four female) and eight low (four female) sensation seekers, ages 18 to 27, who had completed 13 to 17 years of education. Two low sensation seekers identified themselves as African-American (1 female), one high sensation seeker identified himself as Asian, and the remaining participants identified themselves as Caucasian. Average drug intake during the preceding month included caffeine (71 $\pm$ 19 mg/day, mean $\pm$ SEM), alcohol (3.8 $\pm$ 0.8 occasions/month of alcohol use, with 4.8 $\pm$ 0.9 and 1.5 $\pm$ 0.3 as the maximum and minimum drinks per occasion) and marijuana (1.7 $\pm$ 1.0 occasions/month). One high and one low sensation seeker reported intermittent tobacco use, and no cocaine or other drug use was reported. Two-tailed t-tests indicated no significant differences in reported drug use as a function of group status, although high sensation seekers reported more caffeine (88 vs. 60 mg/day), alcohol (5.2 vs. 2.2 occasions/month) and marijuana (3.4 vs. 0 occasions/month) use. Low and high sensation seekers differed significantly in total score on the Sensation-Seeking Scale-Form V (17.3 vs. 25.3, $p<.01$), and on the disinhibition (2.5 vs. 6.5, $p<.001$) and boredom susceptibility subscales (2.9 vs. 5.0, $p<.05$). Low sensation seekers were also lower on the thrill and adventure seeking (6.9 vs. 8.0) and experience seeking (5.1 vs. 5.8) scales, but the differences were not statistically significant. The low sensation-seeking group also scored lower on the extraversion scale of the Eysenck Personality Inventory (12.1

vs. 17.1, p<.05) and endorsed fewer impulsivity items on the Addiction Research Center Maturation Scale (0.9 vs. 2.0, p<.05). No other group differences were observed on the screening questionnaires.

The study was reviewed and approved by the University of Kentucky Medical Institutional Review Board, and all participants provided written consent prior to participation. Participants received financial compensation for participation. Compensation included payments for medical screening, training, per diem payments, task earnings, and a bonus for completing all scheduled test days and abstaining from drug use, except alcohol and caffeine, for the duration of the study.

Apparatus

The study was conducted in two separate isolated rooms. One room functioned as the recreational activity room and was equipped with table, chair, and recreational equipment, including cassette player with earphones, a 12-inch color television equipped to display videotapes, and videogame equipment (Super Nintendo). The second room was used for data collection and was equipped with a computer (PowerMac 8600/250, Apple Computer) and 14-inch monitor, blood pressure cuff and recliner. An oscillometric blood pressure machine (Sentry II, NBS Medical) was located outside of the room so that participants were unaware of their blood pressure values.

Procedure

Participants completed eight 4.5-hour test days, each separated by a minimum of 48 hours. Testing occurred at the same time each day. Participants were requested to abstain from the use of any medication, including alcohol, for 24 hours prior to all scheduled days, and to abstain from eating for four hours prior to the start of each test day. At the beginning of each test day, participants completed a field-sobriety test, as well as providing breath (Alco-Sensor III, Intoximeters, Inc.; piCO Carbon Monoxide Monitor, Bedfont Scientific) and urine samples (OnTrack TesTstik Bar, Varian, Inc.), which were tested to verify the absence of drug use (i.e., alcohol, tobacco, cocaine, benzodiazepines, barbiturates, marijuana, amphetamines and opiates). In addition, female urine samples were tested for pregnancy (Clearview HCG II, Unipath, Ltd). Participants then consumed a light snack (2 low-fat breakfast bars, each containing 37 gm and 140 calories, and 177 ml of orange juice containing 90 calories).

After consumption of the snack (5 minutes), participants completed a baseline (i.e., pre-drug) session, after which the test dose was administered. Sessions were repeated 50, 110 and 170 minutes after dose administration. Each session was 30 minutes in duration. Between each session, participants completed scheduled recreational activities. The study used a double-blind, placebo-controlled, randomized block design consisting of 1 between-subject variable (high vs. low sensation-seeking status) and 3 within-subject variables [recreational activity (high vs. low sensation value), dose (0 vs. 10 mg/70 kg d-amphetamine), and time (0, 50, 110 and 170 minutes post dose)].

Session. Each 30-minute session consisted of self-report (Addiction-Research Center Inventory, Profile of Mood States and Visual-Analog Scale items) and performance (Digit-Symbol Substitution Task, Math Stress Reactivity, and Repeated Acquisition of Response Sequences with both Learning and Performance components) tasks presented in the following order during each session:

Visual-Analog Scales (VAS): Participants rated themselves according to adjectives (I feel stimulated, stressed,

sedated, hungry, anxious, light-headed, thirsty, sleepy, sick to my stomach, down, high, and a drug effect, as well as I like the drug effect) by using a mouse to place a cursor mark along a computerized line containing 100 discrete units and anchored on the left by 'Not At All' and on the right by 'Extremely.' Ratings were determined by the number of units between the left endpoint and the location of the mark.

Profile of Mood States (POMS): Participants completed an experimental version of the POMS[35] consisting of 72 adjectives rated along a five point scale, from 'Not at All' to 'Extremely,' yielding scores on eight mood clusters: Anxiety, Depression, Anger, Vigor, Fatigue, Confusion, Friendliness and Elation. Questions were answered by pressing keys one to five on the keyboard.

Addiction Research Center Inventory (ARCI): The 49-item short form of the true-false inventory[36] yielded information on five dimensions: LSD scale, Amphetamine (A) Scale, Benzedrine-Group (BG) Scale, Morphine-Benzedrine Group (MBG) Scale and the Pentobarbital, Chlorpromazine, Alcohol Group (PCAG) Scale. Questions were answered by pressing the T and F keys on the keyboard.

Math Stress Task: This task consisted of three five-minute components. Blood pressure recordings (heart rate, blood pressure) were collected every 60 seconds throughout the three components. Participants, seated in a reclining chair with the blood pressure cuff attached to the nondominant arm above the elbow, rested during the first (pretask) and third (posttask) components, and completed addition problems during the second component. The difficulty of the addition problems (i.e., numbers of digits in the numbers to be added) and the duration of time to enter the sum on the keyboard were systematically manipulated based on participant performance in order to maintain a consistent level of difficulty for all participants, regardless of math ability or drug condition. Changes in cardiovascular activity during math performance (i.e., second component) were examined, as was math task performance rate and accuracy[37,38]. Participants received two cents per correct problem during the task.

Repeated Acquisition of Response Sequences (RA): This task consisted of two components, a learning component that was presented for 180 seconds, and a performance component, presented for 60 seconds. Four buttons on the keypad were active during the task. Participants were required to learn a new 10-response sequence on the four buttons during the learning component, while the sequence remained unchanged during the performance component throughout the study. During both components, when the first correct response in the sequence was emitted, a screen position counter increased from 0 to 1 indicating that the first response had been completed and cueing the need for the second response. A one second time out, during which the screen was blank and button responses were without consequence, immediately followed incorrect responses. The position counter increased as consecutive correct sequence responses were emitted. When the 10^{th} correct response was emitted, a point counter increased by 1 and the position counter reset to 0, cueing the need for the first response in the sequence to be repeated. Participants received two cents per point during both the learning and performance components. Response rates and patterns of correct and incorrect responses throughout the learning and performance components were monitored as indices of drug effects on performance and learning ability[39].

Digit-Symbol Substitution Task (DSST): Nine random 3-row by 3-column

patterns of shaded and empty boxes (one shaded box per row in a randomly-determined column), labeled 1-9 from left to right, were displayed across the top of the screen. A randomly generated number, between one and nine, was displayed in the center of the monitor to cue which of the nine patterns displayed at the top of the screen should be emulated on a particular trial. During each trial, participants were required to press only the keys in a 3-row by 3-column keypad that corresponded to the positions of shaded boxes in the appropriately labeled pattern. Three responses were required per trial (one response in each row, corresponding to the position of the single shaded box in each row), and the third response generated a new random number in the middle of the screen (pattern cue for next trial) and increased a screen counter by one if all three responses in the trial were accurate. Following the completion of 25 trials, a new random pattern of shaded and empty boxes was displayed at the top of the screen. This task was presented for 120 seconds, and participants received one cent per correct trial. Trial rate and accuracy were used in as an index of psychomotor performance[40].

Recreational Activities. Prior to the initiation of the study, 198 volunteers recruited from an Introductory Psychology Course received course credit for rating stimulus materials, including audiotaped music, videogames, clips from videotaped movies, and short articles and excerpted sections from magazines, novels and short stories. Volunteers rated sensation value of a wide range of stimulus materials using a 5-item version of the Perceived Message Sensation Value scale[41]. Items selected for use in the study were among the highest and lowest in perceived sensation value based on this scale.

Between scheduled performance sessions, participants were required to engage in planned recreational activities. Participants completed three of four different activities (i.e., reading, playing videogames, watching videotaped movies, listening to music) between each session, with each activity presented for 5 to 20 minutes. The order and duration of activities was fixed such that all participants participated in the same activities according to the same schedules each day, with only the specific stimulus items varying across days. No item was presented on more than one occasion. On each test day, the content of the stimulus materials were all of either high or low sensation value.

Drug. d-Amphetamine doses (0, 10 mg/70 kg) were prepared in size 00 opaque capsules with lactose filler by the investigational pharmacy at the University of Kentucky.

Statistics. Given the complexity of the research design, the specific hypotheses were tested using planned comparisons of activity (high vs. low sensation value) by time (0, 50, 110 and 170 minutes post dose) interactions for high and low sensation seekers under placebo conditions, as well as dose (0 vs. 10 mg/70 kg) by time interactions for high and low sensation seekers under both low and high sensation value activity conditions using SPSS for Macintosh (v. 11.0). Error terms for the planned comparisons were determined via a 4-way repeated-measures analysis of variance using sensation-seeking status as a between-subject factor, and activity, dose and time as within-subject factors[42].

Composite Variables. In order to limit the number of statistical comparisons and avoid unnecessary inflation of the family-wise Type I error rate, scores on individual variables were standardized and pooled to create composite variables. Five composite self-report variables were created by combining variables shown to be sensitive to drug effects in previous

research. A stimulant variable was established by pooling the standardized scores on the ARCI A scale, the POMS Vigor scale, and the VAS Stimulated item. A sedated variable was created by pooling standardized scores on the ARCI PCAG scale, the POMS Fatigue scale and the VAS Sedated item. Positive and negative mood variables were established by pooling ARCI BG, POMS Friendly and VAS High items and ARCI LSD, POMS Anxiety, Depression, Anger and Confusion and VAS Stressed, Anxious and Down items, respectively. Finally, a positive drug effect variable was created by pooling the ARCI MBG, POMS Elation and VAS Like Drug measures. A composite response rate variable was created by pooling DSST trial rate and RA response rate scores. DSST percent correct and RA index of curvature for incorrect responses were analyzed separately as measures of performance accuracy and learning proficiency, respectively. Similarly, baseline heart rate and mean arterial pressure, as well as change from baseline during math stress task performance, were analyzed as separate variables. These twelve variables were then examined with planned comparisons.

Results

Effects of d-amphetamine

Table 1 presents results of the main effects of dose, and dose by time interactions, from the four-way ANOVA. Amphetamine enhanced task performance (e.g., increased task response rate and enhanced acquisition efficiency on the learning component of the RA task), increased cardiovascular activity (increased heart rate as well as mean arterial pressure) and altered subject reports (e.g., increased stimulated, positive mood and positive drug effect ratings, and decreased ratings on the composite sedated measure) in a manner that was characteristic of psychomotor stimulants. d-Amphetamine had no effect on psychomotor performance accuracy during the DSST task or on math task-induced increases in heart rate or mean arterial pressure.

Table 1: Analysis of variance outcomes associated with the main effects of d-amphetamine, and d-amphetamine by time interactions, on the primary dependent variables.

Dependent Measures	D	A	D x A	SS x D	SS x A	SS x D x A
DSST						
Trial Rate	53.35***		4.15*			
Proportion Correct		3.18*			4.16*	
RA - Acquisition						
Index of Curvature	3.88*					8.01**
Cardiovascular - Resting						
Heart Rate	44.64***					
Systolic	98.41***					
Diastolic	31.27***					
Cardiovascular – Change						
Heart Rate	6.15*					3.60*
Systolic						5.89*

VAS						
Stimulated	6.20*					
Stressed		5.91*			4.22*	
Sedated	5.27*					
Hungry	14.44***					
Anxious	8.81*					
Sleepy	25.44***	6.71*		13.42***	5.45*	
Sick to My Stomach					8.45*	
Down				4.43*		
High	4.64*					
POMS						
Anxiety	10.29**					
Depression				4.92*		
Vigor	50.07***	9.29**				
Fatigue	28.00***					
Confusion	4.56*					9.22**
Friendliness	39.83***	4.37*				
Elation	44.72***	8.68**				
Arousal	58.61***	8.97**				
Total Positive	32.17***	5.79*		4.13*		
ARCI						
PCAG	21.87***	11.17***				
BG	19.74***					
LSD				3.93*		
MBG	26.54***					
A	23.59***					

*: p<.05; **: p<.01; ***: p<.001

High sensation seekers are more sensitive than low sensation seekers to the stimulant effects of d-amphetamine

This hypothesis was examined by testing dose by time interactions separately for low and high sensation seekers under low activity conditions. Significant interactions were observed for high sensation seekers on the stimulated [F(3,42) = 4.06, p<.05], sedated [F(3,42) = 4.61, p<.01], positive mood [F(3,42) = 3.44, p<.05] and positive drug effect [F(3,42) = 6.23, p<.01] variables. Amphetamine decreased sedated and increased stimulated, positive mood and positive drug effect ratings. In contrast, for the low sensation seekers, significant dose x time interactions were observed only on the positive drug effect variable [F(3,42) = 4.15, p<.05]. Baseline heart rate was significantly increased (i.e., dose x time interaction) for both high [F(3,42) = 8.63, p<.01] and low [F(3,42) = 7.00, p<.01] sensation seekers, but MAP was increased in high sensation seekers, only [F(3,42) = 6.05, p<.01]. d-Amphetamine enhanced acquisition efficiency on the RA task [F(3,42) = 3.55, p<.05] in high sensation seekers, only. No

other task performance measures were altered by drug in either high or low sensation seekers. These results are consistent with the hypothesis that d-amphetamine effects were more consistently observed in high sensation seekers than low sensation seekers.

Figure 1 presents the effects of d-amphetamine on ARCI BG and VAS Stimulated ratings separately for high and low sensation seekers in order to characterize the relationship on selected individual measures included in the composite variables. The ARCI BG data were pooled within the composite positive mood variable, and the VAS Stimulated data were pooled within the composite stimulated variable. d-Amphetamine increased BG and stimulated ratings in high-sensation seekers, but not low sensation seekers, relative to both pre-drug baseline and placebo ratings. These results are consistent with the composite variable outcomes that high sensation seekers were more sensitive than low sensation seekers to the stimulant effects of d-amphetamine.

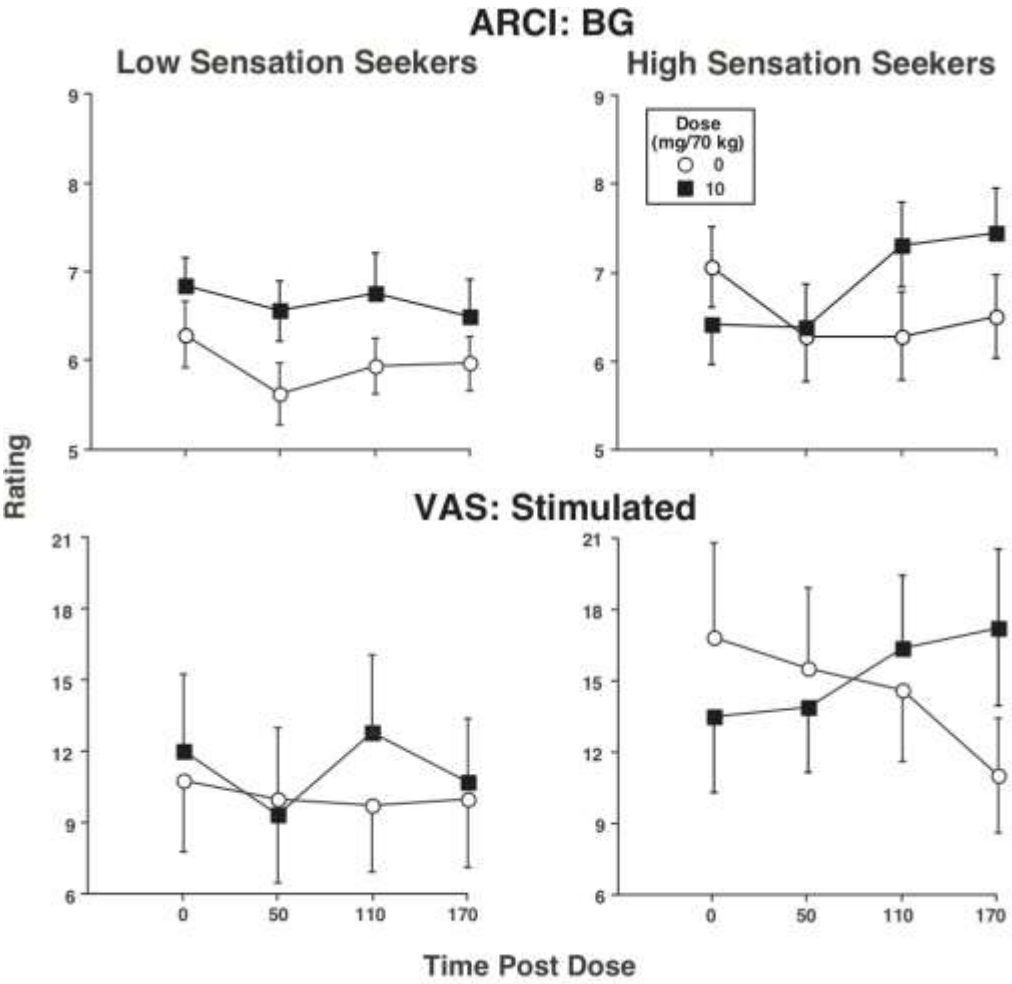

Figure 1

Figure 1: Time-course effects of d-amphetamine on subject ratings of drug effect on the ARCI BG (top row) and VAS stimulated (bottom row) scales for low (left column) and high (right column) sensation seekers. Data points represent the means of 8 participants assessed on four separate occasions, and error bars represent ± 1 SEM.

High sensation activities will engender stimulant-like effects similar to those of d-

amphetamine, and high sensation seekers are more sensitive than low sensation seekers to the stimulant effects of high sensation activities

This hypothesis was examined by testing activity by time interactions separately for low and high sensation seekers under placebo conditions. Significant interactions were observed under placebo conditions for high sensation seekers on the sedated [$F(3,42) = 2.71$, $p<.05$] and positive mood [$F(3,42) = 3.55$, $p<.05$] measures, with sedated scores decreased and positive mood scores increased under high activity conditions. No other significant activity by time interactions were observed for high or low sensation seekers. As such, limited support was obtained for the hypothesis that the effects of high sensation activities were qualitatively similar to those of d-amphetamine on self-report measures, and that these effects were greater in high sensation seekers than low sensation seekers.

Figure 2 presents the effects of activities on VAS Sleepy and ARCI BG ratings separately for high and low sensation seekers. The VAS Sleepy data were pooled within the composite Sedated variable, and the ARCI BG data were pooled within the composite positive mood variable. High sensation seekers reported higher levels of Sleepy than low sensation seekers, and under low sensation-activity conditions, sleepy ratings were increased 50-minutes after dose administration, relative to baseline. High-sensation activities decreased Sleepy ratings in high-sensation seekers, but not low sensation seekers, relative to both pre-drug baseline and placebo ratings. High sensation seeker BG ratings were decreased 50-minutes after dose administration under low sensation-activity conditions. High-sensation activities increased BG ratings in high-sensation seekers, but not low sensation seekers, relative to ratings during low sensation activity conditions. These results are consistent with the composite variable outcomes indicating that high sensation seekers were more sensitive than low sensation seekers to some of the stimulant effects of activities.

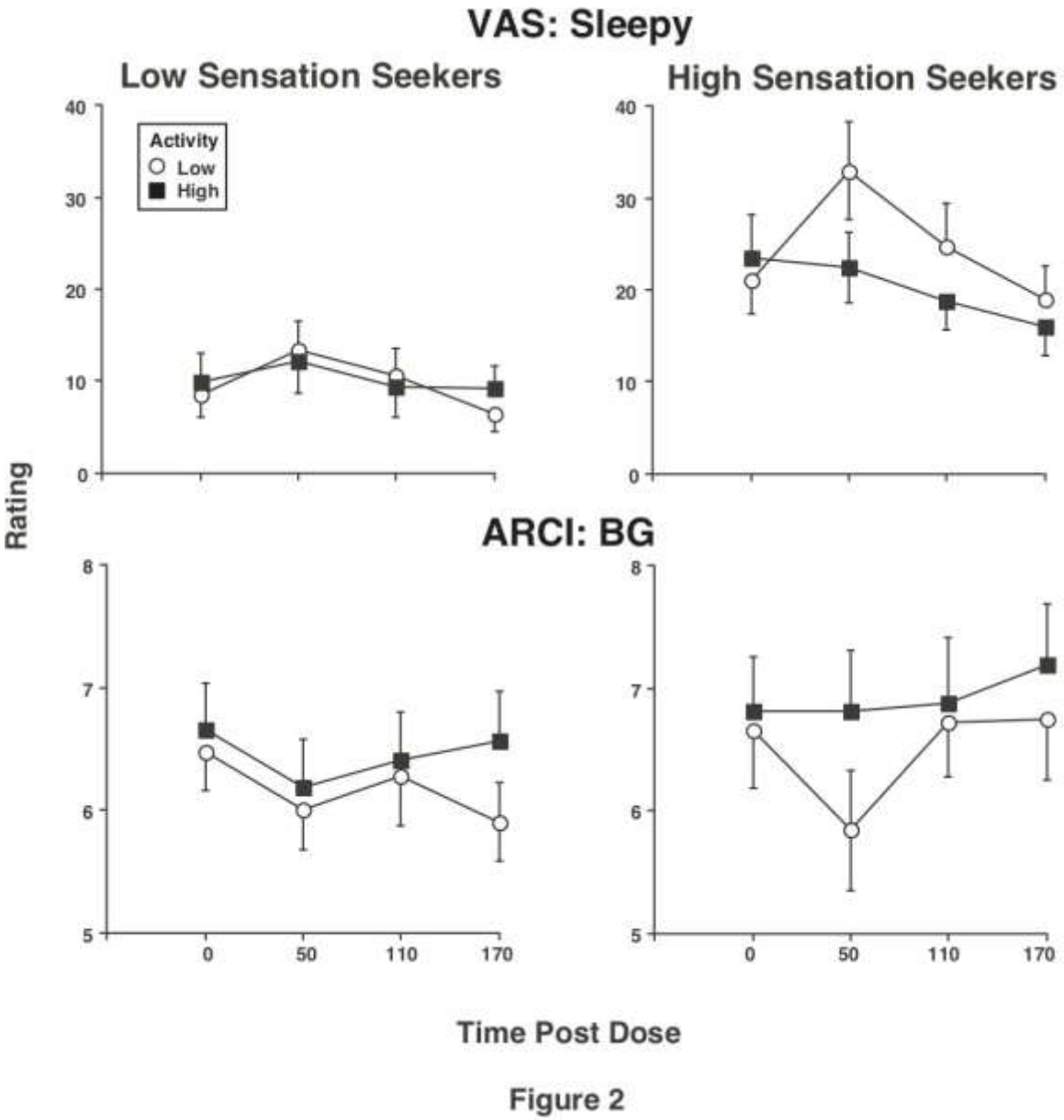

Figure 2: Time-course effects of activity conditions on subject ratings of drug effect on the VAS Sleepy (top row) and ARCI BG (bottom row) scales for low (left column) and high (right column) sensation seekers. Data points represent the means of 8 participants assessed on four separate occasions, and error bars represent ± 1 SEM.

High sensation activities will reduce the stimulant effects of d-amphetamine to a greater extent in high sensation seekers than in low sensation seekers

This hypothesis was examined by testing dose by time interactions separately for low and high sensation seekers under both placebo and active dose conditions. Among the self-report measures, significant dose by time interactions were observed under both low and high sensation activity conditions on stimulated [$F(3,42) = 4.06$, $p<.05$; $F(3,42) = 9.08$, $p<.01$, respectively], positive mood [$F(3,42) = 3.44$, $p<.05$; $F(3,42) = 5.65$, $p<.01$] and positive drug effect [$F(3,42) = 6.23$, $p<.01$; $F(3,42) =$

8.30, p<.01] in high sensation seekers. However, d-amphetamine-induced decreases in sedation under low sensation activity conditions [F(3,42) = 4.61, p<.01] were no longer apparent under high sensation activity conditions. In contrast, for low sensation seekers, significant dose by time effects were only observed on positive drug effects ratings under low sensation activity conditions [F(3,42) = 4.15, p<.05].

Figure 3 presents the effects of d-amphetamine on VAS Like Drug ratings (pooled in the positive drug effect composite variable) by both low and high sensation seekers under low and high sensation activities. Dose-dependent increases in ratings were apparent among high sensation-seekers during the high sensation activity conditions. Increased ratings were observed during both placebo and active dose conditions under low activity conditions. Ratings among low sensation seekers were minimal under all dose and activity conditions.

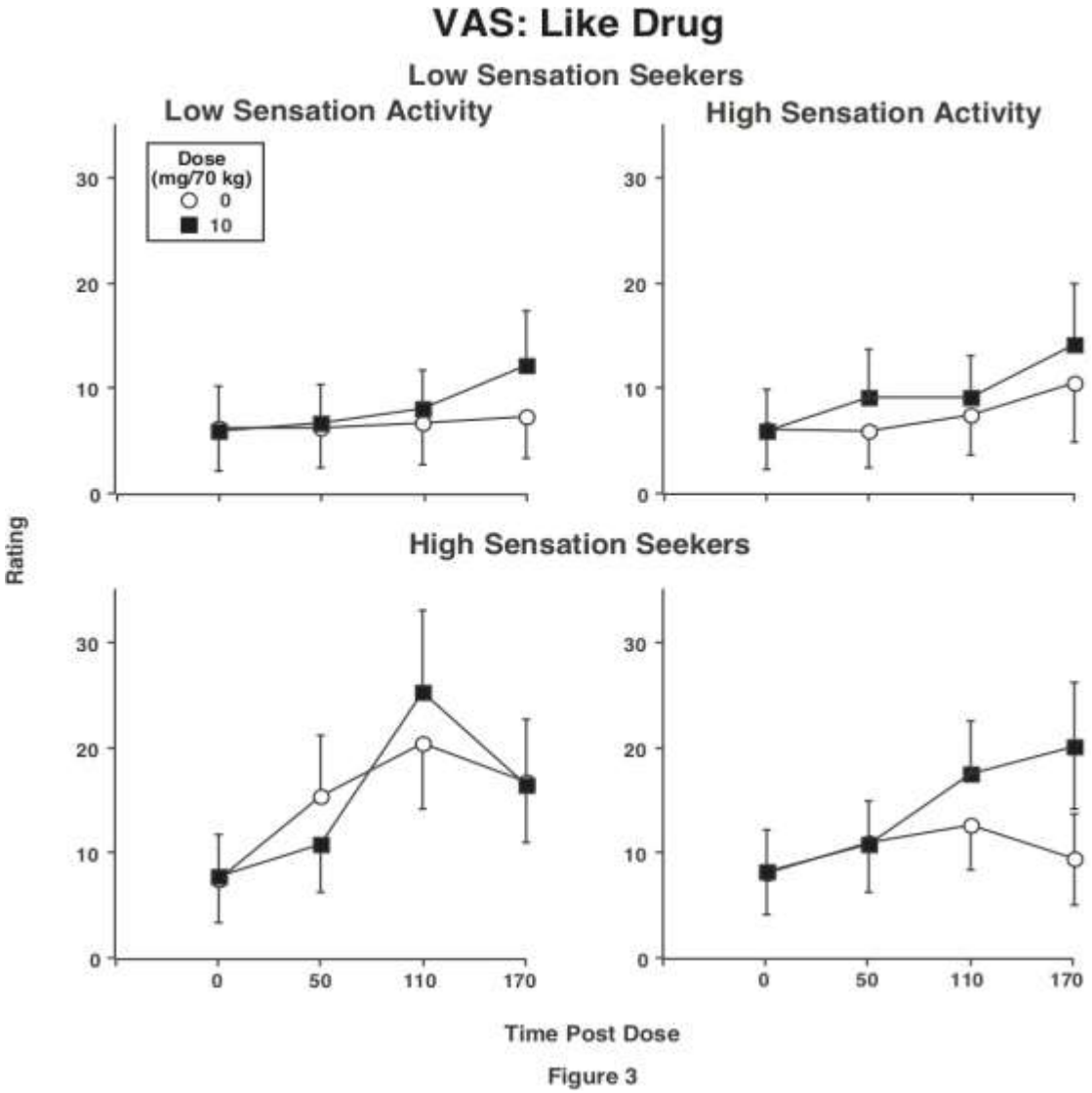

Figure 3: Time-course effects of d-amphetamine on subject ratings of drug effect on the VAS Like Drug scale for low (top row) and high (bottom row) sensation seekers during low (left column) and high (right column) sensation activity conditions. Data points represent the means of 8 participants assessed on two separate occasions, and error bars represent ± 1 SEM.

Among the cardiovascular measures, significant dose by time interactions were also observed during both low and high activity conditions on baseline heart rate [F(3,42) = 8.62 p<.01, F(3,42) = 4.58, p<.01, respectively] and MAP [F(3,42) = 6.05, p<.01, F(3,42) = 7.81, p<.01, respectively] in high sensation seekers. For low sensation seekers, d-amphetamine induced increases in baseline heart rate were observed under both low and high activity conditions [F(3,42) = 7.00, p<.01, F(3,42) = 3.19, p<.05, respectively].

Figure 4 presents the effects of d-amphetamine on mean arterial pressure in both low and high sensation seekers under low and high sensation activities. Dose-dependent increases were apparent among high sensation-seekers during both low and high sensation activity conditions. Baseline differences in mean arterial pressure were apparent among low sensation seekers during both low and high sensation activity conditions, but no dose-related effects were apparent under either condition.

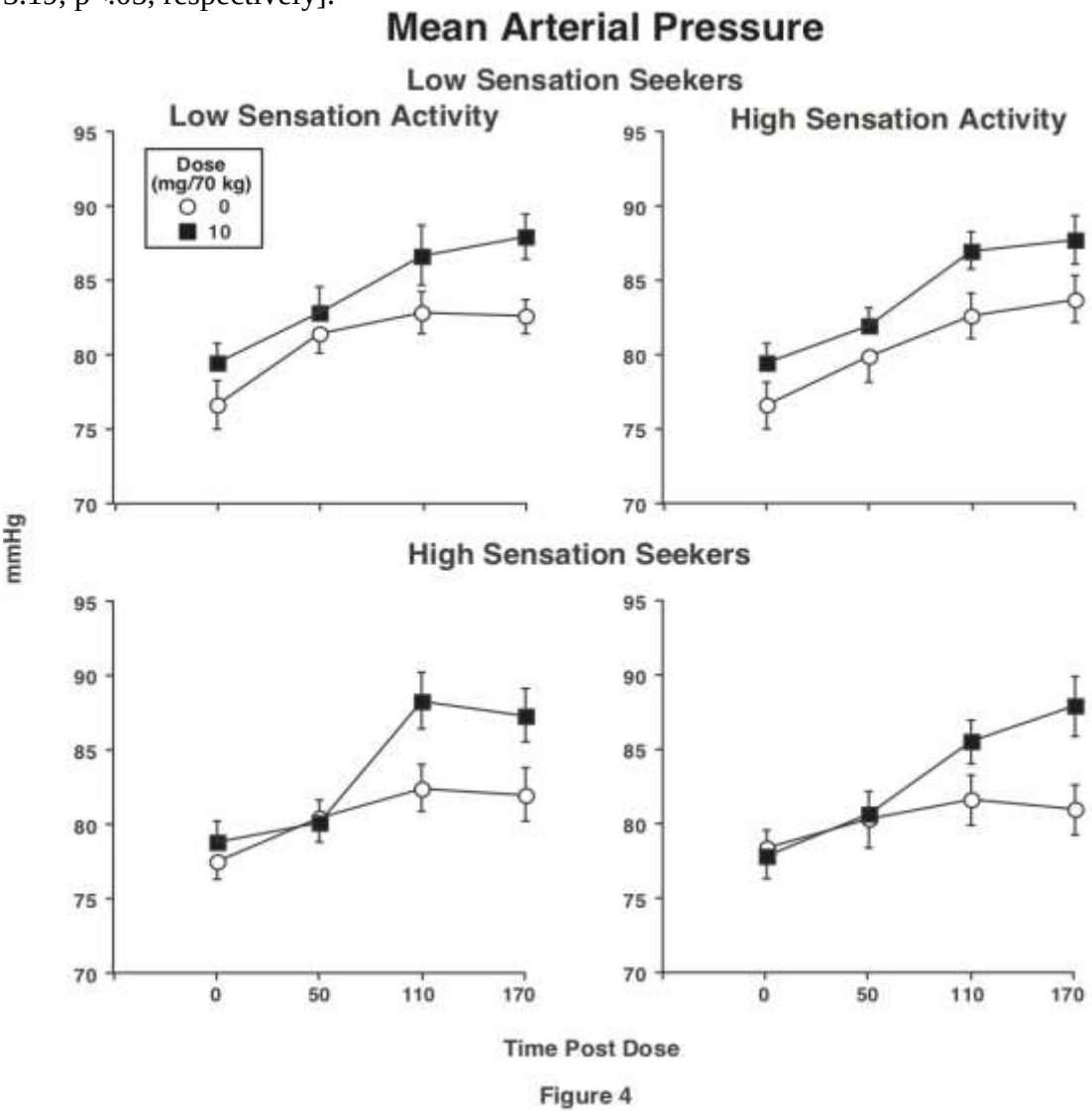

Figure 4: Time-course effects of d-amphetamine on mean arterial blood pressure for low (top row) and high (bottom row) sensation seekers during low (left column) and high (right column) sensation activity conditions. Data points represent the means of 8 participants assessed on two separate occasions, and error bars represent ± 1 SEM.

In the performance measures, d-amphetamine-induced increases in acquisition efficiency during the RA task were observed under low sensation activity conditions, only [$F(3,42) = 3.55$, $p<.05$], for high sensation seekers. In contrast, among low sensation seekers, acquisition efficiency during the RA task was enhanced during high activity conditions [$F(3,42) = 4.10$, $p<.05$], but not during low activity conditions. No other significant drug effects were observed on performance measures in high or low sensation seekers.

Figure 5 presents the effects of d-amphetamine during the learning component of the RA task in both low and high sensation seekers under low and high sensation activities. The index of curvature[43] is a measure of acceleration of errors during a session, with negative values indicate that the number of errors is decelerating across time (i.e., acquisition in occurring). Smaller numbers reflect greater learning efficiency. During low sensation activity conditions, high sensation seekers demonstrated less efficient acquisition across time under placebo conditions. d-Amphetamine decreased this drop in efficiency across time. Under high sensation activity conditions, acquisition efficiency was maintained across time, and d-amphetamine produced no changes in performance. In contrast, low sensation seekers demonstrated less efficient acquisition across time under placebo conditions during high sensation activity conditions, and d-amphetamine reduced this drop in efficiency across time. Under low sensation activity conditions, acquisition efficiency was maintained across time, and d-amphetamine produced no changes in performance. These results suggest that high sensation activities decreased d-amphetamine effects on acquisition efficiency and composite ratings of sedated in high sensation seekers. High sensation activities also decreased d-amphetamine effects on composite ratings of positive drug effect in low sensation seekers. In contrast, d-amphetamine effects on acquisition efficiency in low sensation seekers were apparent only under high sensation activities, but this effect was most likely related to the effects of high-sensation activities on baseline acquisition performance in low sensation seekers. In sum, these data provide little support for the hypothesis that high sensation activities would reduce the stimulant effects of d-amphetamine to a greater extent in high sensation seekers than in low sensation seekers.

Discussion

As expected, stimulant-like effects of d-amphetamine were observed on cardiovascular, task performance and subject rating measures. Exposure to the high sensation stimulus materials also produced stimulant-like effects on the composite positive mood and sedated variables. While the effects of activities were not as robust or widespread as those produced by d-amphetamine, the results are consistent with the notion that d-amphetamine and exposure to high sensation activities involve a common neurobehavioral mechanism likely including, at least in part, the mesolimbic dopamine system[25].

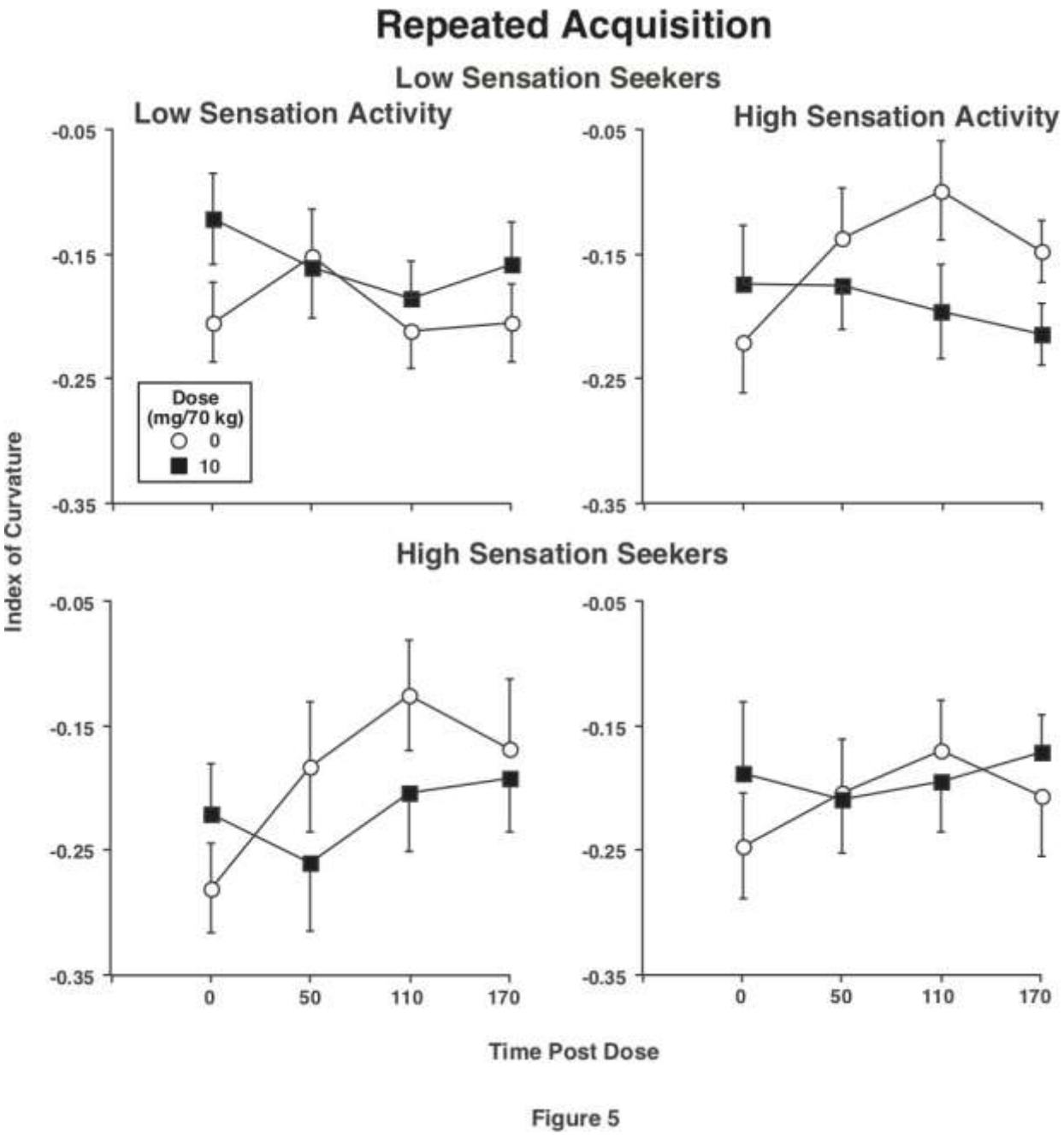

Figure 5: Time-course effects of d-amphetamine on acquisition efficiency (error index of curvature) during the learning component of the RA task for low (top row) and high (bottom row) sensation seekers during low (left column) and high (right column) sensation activity conditions. Data points represent the means of 8 participants assessed on two separate occasions, and error bars represent ± 1 SEM.

It has been hypothesized that the mesolimbic dopamine system may also be involved in determining sensation-seeking status[9,13,14]. An important finding of the current study was that sensation seeking served to moderate the effects of d-amphetamine across a number of dependent measures. Consistent with previous reports showing that high sensation seekers are more sensitive to the effects of stimulant

drugs[18,19], the current study found that high sensation seekers reported greater d-amphetamine effects on the composite sedated, stimulated and positive mood variables, as well as on arterial blood pressure and learning efficiency. These results are consistent with the hypothesis that sensation-seeking status is associated with individual differences in sensitivity to the behavioral effects of psychostimulants.

Given the potential overlapping effects of d-amphetamine, sensation-seeking status and high sensation activities on mesolimbic dopamine system activation, it was hypothesized that drug effects would vary as a function of sensation-seeking status and activity conditions, with high sensation activities reducing the magnitude of drug effects to a greater extent in high sensation seekers than low sensation seekers. No evidence for this hypothesis was obtained. d-Amphetamine effects on composite ratings of sedated were reduced during high-sensation activity conditions in high sensation seekers. However, d-amphetamine effects on composite ratings of positive drug effect were also reduced during high-sensation activity conditions in low sensation seekers, suggesting that the interactions of task conditions with drug effects were not limited to high sensation seekers. Similarly, d-amphetamine effects on acquisition efficiency were reduced during high-sensation activity conditions in high sensation seekers. However, in direct contrast, d-amphetamine effects on acquisition efficiency were increased during low-sensation activity conditions in low sensation seekers. Previous research suggests that the behavioral effects of psychostimulants are most pronounced under conditions in which performance is suboptimal, due to fatigue, boredom, or other adverse conditions[39,44]. It is clear that d-amphetamine effects on acquisition efficiency were observed under conditions in which baseline performance was suboptimal (Figure 5). Amphetamine enhanced acquisition efficiency in high sensation seekers under low sensation activity conditions; acquisition efficiency was diminished across time under placebo conditions during low activity conditions. In contrast, amphetamine enhanced acquisition efficiency in low sensation seekers under high sensation activity conditions, and acquisition efficiency was diminished across time under placebo conditions during high activity conditions. As such, differences in d-amphetamine effects on acquisition efficiency between low and high sensation seekers are most easily understood in terms of performance during placebo sessions.

It is possible to interpret these data using optimal arousal theory[45,46]. This theory postulates that individual differences exist in the level of external stimulation needed to engender an optimal level of arousal and performance. It has been suggested that compared to low sensation seekers, high sensation seekers are under-aroused and therefore require a greater level of external stimulation in order to achieve an optimal level of arousal[47]. Baseline acquisition efficiency on the RA task was consistent with this theory in that suboptimal performance was apparent in high sensation seekers during low sensation activities (i.e., during a suboptimal level of arousal), and during high sensation activity conditions in low sensation seekers (i.e., during an above optimal level of arousal). To the extent that self-report measures of sedation reflect a suboptimal level of arousal, the current results suggest that d-amphetamine increased ratings of sedated only in high sensation seekers under low sensation activity conditions (i.e., under suboptimal arousal). The drug had no effect on sedation in low sensation seekers during either optimal or above-optimal levels of arousal. d-Amphetamine increased high sensation

seeker reports of positive mood and positive drug effects under both low and high sensation. In contrast, no drug-induced changes in positive mood were reported by low sensation seekers under any conditions, and drug-induced reports of positive drug effects occurred only during low sensation activity conditions. These data suggest either that arousal levels remained suboptimal even during the high sensation activity condition in high sensation seekers and thus could be further enhanced by drug, or that the effects of additional arousal (i.e., stimulant drug effects) during an optimal level of arousal are different for high and low sensation seekers (i.e., above-optimal levels of arousal are associated with positive mood in high sensation seekers, only). Furthermore, these results suggest that, like performance, d-amphetamine effects on self-report data may be influenced, in part, by baseline level of arousal.

There are limitations to the present study that merit consideration. First, sample size was small; replication of study results would enhance confidence in study outcomes. Second, in order to avoid the complications associated with interpreting three-way and four-way interactions, the relationships among these variables were examined using a series of planned comparisons. Furthermore, to minimize the number of planned comparisons, composite variables were created by pooling standardized scores from multiple measures. While the specific measures that were pooled to create composite variables were selected based on previous studies of psychostimulant drug effects[48], this analytic approach has not been used previously to examine drug effects. The reliability and validity of the approach will need to be examined in future studies. The generality of the study is also limited by the testing of only two levels of each factor (sensation-seeking status, drug, activity). While the range of sensation-seeking status was maximal (i.e., top and bottom quartiles of the population distribution), the magnitudes of the dose and activity manipulations were modest. Finally, while results indicate that these factors had potent effects on the outcome measures, the small sample size in the present study also limits the generality of the findings.

In summary, this study examined the behavioral effects of d-amphetamine and high sensation activities, alone and in combination, in high and low sensation seekers. Both d-amphetamine and high sensation activities engendered independent stimulant-like effects, although activity effects were not as robust or widespread as those of d-amphetamine. Individual differences in sensation seeking status moderated both the direct effects of d-amphetamine, with high sensation seekers demonstrating greater sensitivity to drug across a range of measures, as well as the interactions between activity and d-amphetamine effects. These results suggest that the sensation level of activities can alter the behavioral effects of d-amphetamine and that these effects vary as a function of sensation-seeking status. These data are consistent with the hypothesis that individual differences in mesolimbic dopamine system activity may influence vulnerability to stimulant drug abuse liability and may be associated with level of arousal.

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