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Effectiveness of a Marijuana Expectancy Manipulation: Piloting the Balanced-Placebo Design for Marijuana

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Abstract

Although alcohol and nicotine administration studies have demonstrated that manipulating subjects' expectancies regarding drug content affects drug response, research with marijuana has not adequately studied drug expectancy effects. The present pilot study was the first to evaluate the credibility and effect of expectancy manipulation on subjective measures and smoking patterns using a marijuana administration balanced-placebo design (BPD). In a 2 × 2 instructional set (told delta-9-tetrahydrocannabinol [THC] vs. told no THC) by drug (smoked marijuana with 2.8% THC vs. placebo) between-subjects design, the authors examined the effect of marijuana expectancy manipulation and the pharmacologic effect on affective and physiologic measures, cigarette ratings, and smoking behavior with 20 marijuana smokers (mean age = 20 years; 25% female). Large main effects of expectancy were found on ratings of cigarette potency, strength, taste, smell, and satisfaction, and observed smoking behavior. Pharmacologic effects were particularly evident for self-reported physical reactions to marijuana and cigarette potency and satisfaction ratings. This study demonstrated the feasibility of the BPD research with marijuana and yielded promising results for future studies examining the independent and combined effects of marijuana pharmacology and expectancies.

Keywords

marijuana; cannabis; placebo; expectancy; drug

Expected effects of drugs are considered important determinants of behavioral and subjective responses to a drug independent of the pharmacological action of that drug (Vogel-Sprott & Fillmore, 1999). A drug-taking situation involves expectations that a particular drug was administered (i.e., stimulus expectancy) and expectancies about the effects or consequences associated with using the drug (i.e., outcome expectancies). The balanced-placebo design (BPD) is the optimal method for separating pharmacological effects from the cognitive expectations of receiving the drug and its effects (Marlatt & Rohsenow, 1980). This 2 × 2

factorial design crosses the substance that is administered to the participant (drug or placebo) with instructions that are given to the participant about the drug content (drug or placebo). Thus, half of the participants are told they are receiving a drug, and half are told they are receiving no drug (i.e., instructional set manipulation). Half of the participants in each of those instructional conditions actually receive the drug and half do not. This improves on the standard placebo-controlled design by allowing a determination of expectancy effects independent of pharmacologic effects and vice versa (Rohsenow & Marlatt, 1981) and the “antiplacebo” effect of the pharmacological action of the drug when expecting no drug (Perkins et al., 2004; Vogel-Sprott & Fillmore, 1999).

Crucial to this design is the credibility of the expectancy manipulation, a factor not usually evaluated in standard placebo-controlled designs (Rohsenow & Marlatt, 1981). Although being told that one may be ingesting a drug may be sufficient to produce drug-related reactions in some cases (Kirsch, 1985), often it is not (Rohsenow & Marlatt, 1981). The magnitude of the placebo or expectancy effect is increased by proximal environmental stimuli consistent with the instructed substance (e.g., smell, appearance of the cigarette), other corroborating sources of information (e.g., pouring from an unopened liquor bottle, false breath alcohol feedback), and distraction from introspection (Rohsenow & Marlatt, 1981). The belief that individuals have about the drug content (stimulus expectancy) activates their outcome expectancies about the effects that the drug is likely to have on them, producing the placebo effects (changes in mood, behavior).

Instructional set manipulations that include all the corroborative information outlined above can influence subjective and objective measures when using the BPD. In alcohol research, the effects of expectancy manipulations predominate over pharmacological effects for consummatory behaviors (e.g., craving and consumption among alcohol-dependent individuals) and interpersonal behaviors including aggression, social anxiety, and sexual arousal, with effects in the small to medium range (Hull & Bond, 1986). For behaviors in the intrapersonal domain such as memory functioning, motor skills, and mood, alcohol consumption had a stronger effect than expectancy (Hull & Bond, 1986; Marlatt & Rohsenow, 1980). In nicotine research, instructional set manipulations using the BPD with denicotinized cigarettes have been shown to affect self-reported anxiety and tension, concentration, smoking urge, ratings of nicotine content, and reinforcing effects of smoking (Juliano & Brandon, 2002; Kelemen & Kaighobadi, 2007; Perkins et al., 2004). These BPD studies have yielded important information on the role that nonpharmacological factors play in the maintenance of alcohol abuse and smoking behavior.

Although a number of marijuana administration studies find effects on behavior when compared to placebo (e.g., Haney et al., 2007; Lane, Cherek, Tcheremissine, Lieving, & Pietras, 2005; Sexton et al., 2000), there is little direct evidence as to the relative roles of expectancy versus pharmacological effects of delta-9-tetrahydrocannabinol (THC). Under usual double-blind conditions, where participants are given no explicit instructions about the drug content, participants are left wondering what they are ingesting, which leads them to search for interoceptive cues (Rohsenow & Marlatt, 1981). This can increase accurate identification of the placebo versus the active drug (Marlatt & Rohsenow, 1980), thus confounding the drug with expectancy. Thus, the double-blind placebo-controlled design does not test for pharmacologic effects unconfounded by the individual's expectancies of receiving that drug.

A few marijuana studies have used an instructional set manipulation. When smoking placebo marijuana, being told that the cigarette was active marijuana had an inhibitory effect on aggressive behavior in provoked users, induced significant subjective effects of intoxication, and influenced smoking behavior in the absence of THC (Alioto, 1974; Cami, Guerra, Ugena,

Segura, & de la Torre, 1991; Chait & Perry, 1992). However, in the Cami et al. (1991) study, administration of marijuana or its placebo was always in the context of alcohol or alcohol placebo administration and thus confounded with alcohol expectancies. In a study with oral THC, participants who expected to receive a cannabinoid reported greater pleasurable effects and desire to consume more than those without this expectancy (Kirk, Doty, & de Wit, 1998). Similarly, subjective effects experienced by marijuana smokers were more influenced by contextual factors such as set and setting than by THC content (Murray, 1986).

This research indicated that manipulating marijuana expectancies is possible and called for a controlled BPD study with smoked marijuana. To set the stage for future fully powered studies, we conducted a pilot marijuana BPD study to evaluate the credibility of the deception and the ability of an instructional set manipulation bolstered by other stimuli to affect subjective measures independently from pharmacologic effects. The credibility of these procedures needed evaluation. We hypothesized main effects for both stimulus expectancy (i.e., instructional set about the presence or absence of THC in the marijuana cigarette) and THC pharmacology (i.e., the presence or absence of 2.8% THC in the marijuana cigarette) on ratings of increased subjective marijuana effects and credibility of the deception (self-report and observed smoking pattern). Because this was a small pilot study, effect size estimates were the focus of the analyses.

Method

Participants

The study was approved by the Institutional Review Board of Brown University. Marijuana smokers ($N = 20$) were recruited from the community through newspaper advertisements and fliers. Telephone and in-person screening ensured that candidates met the following inclusion criteria: native English speakers, 18 to 25 years of age, marijuana use at least once in the past month and at least 10 times in the past 6 months but not more than 4 days per week (to ensure that participants were able to abstain before the lab sessions), no self-report of illicit drug use other than marijuana in the past 30 days, no diagnosis of cannabis dependence in the past 12 months, no history of substance abuse treatment and no intent to quit or receive treatment for cannabis abuse, not pregnant (by urine screen at each visit) or nursing, no major *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.) diagnosis, and no contraindicated medical issues by physical exam by a study physician. Anyone with prior knowledge about the study procedures or contact with study participants (e.g., roommate or close friend) was screened out to avoid potential disclosure about deception used in the study.

Participants were told to abstain from illicit drugs including marijuana prior to their first laboratory session and during the course of the study to rule out potential residual effects. Urine drug (THC, cocaine, benzodiazepines, methamphetamine, and morphine) and pregnancy screens needed to be negative at each session. Participants' first laboratory session was scheduled to allow sufficient time for marijuana to clear out of their system. From the baseline session on, all participants produced negative urine toxicology tests and self-reported abstinence from marijuana outside of the laboratory. Participants were told to refrain from alcohol for 24 hr and caffeine for 1 hr before each session. Breath alcohol level (BAL) was assessed with an Alco-Sensor IV (Intoximeters, Inc., St Louis, MO) to ensure 0.0 BAL at all visits.

Design and Randomization

The study involved a 2×2 randomized factorial design crossing drug administration (2.8% THC or 0% THC) with instructional set (told THC or told placebo). Random assignment was made to one of the following four BPD conditions, balanced on gender: (a) told THC/received

THC, (b) told THC/received placebo, (c) told placebo/received THC, and (d) told placebo/received placebo.

Procedure

Participants completed two individual study sessions, on average 5 days apart: a baseline nonsmoking session and an experimental smoking session. During written informed consent, participants were informed that the study evaluated the effects of marijuana on mood and behavior, and that they would be randomly assigned to smoke either one marijuana cigarette that contained THC or one marijuana placebo cigarette with THC removed. Experimental sessions occurred in a 27.5-ft² ventilated smoking chamber with a Plexiglas wall through which research staff observed participants at all times and communicated by intercom. The participant's computer was connected via a cable to the researcher's monitor, which allowed the experimenter to observe the stimuli presented on the screen and monitor compliance with the study protocol.

At baseline, participants completed a battery of assessment questionnaires, including demographic and substance use questions for descriptive purposes and computer-based tasks. These computerized measures of impulsivity and risk-taking were included to pilot the procedures and will not be reported. Prior to smoking during the second session, participants completed subjective questionnaires, including the Addiction Research Center Inventory (ARCI; Martin, Sloan, Sapira, & Jasinski, 1971), a state measure of affect, and a measure of marijuana withdrawal (described in detail below). Participants then were instructed about which cigarette they were assigned to smoke. The research assistant opened a sealed envelope that specified the instructional condition. Participants in the two told THC conditions were told, "You have been assigned to the condition to smoke an active marijuana cigarette that contains THC. THC is the primary psychoactive cannabinoid that 'gets people high.' The dosage of THC contained in each cigarette is considered to be a moderate dose for the average person. Marijuana cigarettes came from the National Institute of Drug Abuse and marijuana was grown by the government for research purposes. In this condition, we need to test how smoking marijuana will affect your mood, responses, and behavior. Participants in this condition will be compared to others who receive placebo without any THC." Participants in the two told placebo conditions were told, "You have been assigned to the condition to smoke a placebo cigarette. A marijuana placebo cigarette does not contain THC. THC, the active ingredient that gets people high, along with other cannabinoids, was extracted from the cigarettes by the National Institute on Drug Abuse, which provides them for research. Smoking this placebo cigarette will have no effect on your mood and behavior. In this condition, we need to test how people operate in a normal state of consciousness while engaging in all other actions associated with smoking. Participants in this condition will be compared to others who receive marijuana with THC."

Several steps were taken to enhance the credibility of the deception. First, participants in the two "Told THC" conditions provided a saliva sample after they smoked the cigarette. To enhance the validity of the procedure, participants were told that the sample would be sent out for quantitative analysis to verify the amount of THC absorbed in the saliva, but that saliva tests do not yield immediate results so they will not receive feedback on the actual THC levels in the session. Second, to induce a disassociation from the sight and smell of regular marijuana cigarettes and thereby reduce conditioned responses to marijuana, cigarettes in the two told placebo conditions were rolled in an additional piece of purple cigarette paper with a grape aroma prior to the beginning of the experiment (Wachtel, El Sohly, Ross, Ambre, & de Wit, 2002). The need to enhance deception outweighed concern about effects of an additional sheet of paper on smoking.

Postsmoking assessment was designed to capture subjective intoxication at its peak immediately after smoking and over the course of 1 hr when acute effects can still be detected (e.g., Lukas, Mendelson, & Benedikt, 1995). After smoking, participants repeated the self-report subjective measures (ARCI and affect measure), followed by the same computer tasks that they completed during the baseline. Following the last computer task approximately 45 min after the end of smoking, participants completed another ARCI questionnaire, subjective satisfaction and liking ratings, and questions pertaining to the credibility of the instructional set manipulation. Participants who received active marijuana were asked to remain in the laboratory for 4 hr after smoking to allow the acute effects to dissipate and were allowed to watch TV, movies, and read. Before leaving, participants were evaluated for motor signs of intoxication and were required to pass a field sobriety test, then received brief (15 min) informational counseling on the negative consequences of marijuana use. Participants in the deception conditions were fully debriefed regarding the deception following the completion of assessments. Participants were then paid for participation and transported home in a taxi.

Marijuana Administration

Marijuana cigarettes (0% or 2.8% THC) were provided by the National Institute of Drug Abuse, stored frozen in an airtight container, and humidified at room temperature for 24 hr before use. To conceal potential differences in color of placebo marijuana leaves (Chait & Pierri, 1989), all cigarettes were rolled at both ends. A standardized paced puffing procedure (Foltin, Fischman, Pedrosa, & Pearlson, 1987) was used with recorded instructions to “light the cigarette” (30 s), “get ready” (5 s), “inhale” (5 s), “hold smoke in lungs” (10 s), and “exhale.” The interpuff interval was 30 s. Participants smoked until the ash reached a line 10 mm from the butt end that was marked to minimize smoking behavior differences (Herning, Hooker, & Jones, 1986). THC dose selected has been shown to produce moderate behavioral and subjective effects (e.g., Hooker & Jones, 1987; McDonald, Schleifer, Richards, & de Wit, 2003; Wachtel et al., 2002).

Descriptive Measures

The Timeline Followback procedure (TLFB; Babor, Brown, & del Boca, 1990; Dennis, Funk, Godley, Godley, & Waldron, 2004; Sobell & Sobell, 1992) was used to establish a 4-week retrospective marijuana (number of joints smoked) and alcohol use (number of standard drinks) baseline (Stephens, Babor, Kadden, Miller, & the Marijuana Treatment Project Research Group, 2002). The Marijuana History and Smoking questionnaire includes questions about age of onset, number of hours spent smoking per day (Stephens et al., 2002), amount of money spent monthly on marijuana over the past 6 months, tobacco smoking status, and other questions. The Marijuana Withdrawal Checklist (Budney, Moore, Vandrey, & Hughes, 2003; Budney, Novy, & Hughes, 1999) has 15 items ranging from 0 (*not at all*) to 3 (*severe*) with 10 symptoms making up a withdrawal discomfort score (Budney et al., 1999). This measure was administered prior to smoking in the second experimental session to assess for possible withdrawal due to abstinence from marijuana.

Credibility of the Instructional Set Manipulation

These measures were administered after the final ARCI and affect measures. First, several items from the Cigarette Evaluation Scale (Juliano & Brandon, 2002; Rose et al. 2004) as adapted to marijuana administration studies are relevant to the effectiveness of the instructional set: taste, smell, and similarity to marijuana cigarettes usually smoked, scored on 5-point Likert scales ranging from 0 (*not at all*) to 4 (*extremely*). Second, participants rated the potency of the cigarette smoked relative to their usual marijuana cigarettes on a 5-point Likert scale (from 0 = *no effect at all* to 4 = *a very strong effect*; Kirk et al., 1998) and THC content in terms of percentage concentration (scored 1 = *none 0%*, 2 = *low dose < 2%*, 3 = *moderate dose 2%–*

3%, 4 = *high dose* 3%–4%). Third, following the cigarette ratings, participants indicated whether they believed they smoked an active or placebo marijuana cigarette. Fourth, as the very last question, participants were asked on a separate page whether they felt deceived about anything during the experiment using open-ended responses sealed in an envelope for external review (Rohsenow & Bachorowski, 1984). Finally, an objective count of the number of puffs to complete a cigarette served as a behavioral indicator of expectancy set.

Subjective Effects of Marijuana

Affective reactions to marijuana were assessed with several cigarette rating items (Juliano & Brandon, 2002; Kirk et al., 1998), such as cigarette satisfaction (e.g., “It was satisfying”) and liking (e.g., “I liked it” and “it makes me feel better”) scored on 5-point Likert scales ranging from 0 (*not at all*) to 4 (*extremely*). Self-Assessment Manikin (SAM; Bradley & Lang, 1994; Lang, 1995) is a brief, momentary affect measure that includes two pictographic scales: valence (pleasant vs. unpleasant), and arousal (high vs. low), each scored on 5-point Likert scales. This was given before and after smoking to assess changes in affect. Subjective effects of marijuana were determined using the 12-item ARCI—Marijuana (M) scale, which is derived from a 53 true/false item version of the ARCI (Martin et al., 1971) comprising the original 49 statements sensitive to the effects of several drug classes plus 4 items specific to marijuana (Chait, Fischman, & Schuster, 1985). These four items are “I have difficulty in remembering,” “My mouth feels very dry,” “I notice that my heart is beating faster,” and “My thoughts seem to come and go.” The resulting six empirically derived scales consist of the M scale and scales that measure drug-induced euphoria, stimulant-like effects, intellectual efficiency and energy, sedation, dysphoria, and somatic effects.

Data Analysis Plan

To examine the credibility of the instructional set manipulation, we first examined the proportion of participants whose answers regarding the drug they received were congruent with their instructional set. Analyses of variance (ANOVAs) with instructions (told THC vs. told placebo) and drug (received THC vs. received placebo) entered as between-subjects factors were used for the postsmoking cigarette ratings and observed number of puffs. Measures of affect and the ARCI were analyzed with regression analyses, with presmoking ratings entered in the model along with the pharmacologic and expectancy effect terms. Because our goal was to show an effect of group (and not interaction), we used multiple regression rather than ANOVA with repeated measures to capitalize on better statistical power (Stevens, 1992). All tests of statistical significance were conducted with an alpha level set at .05. Measures of effect size are reported using eta squared (η^2 for ANOVAs and sr^2 for regression analyses, with a small effect of $\geq .01$, a medium effect of $\geq .058$, and a large effect of $\geq .137$ (Cohen, 1988). Analyses were conducted using all available data ($N = 20$).

Results

Participant Characteristics

Of the participants, 75% were men and 75% were Caucasian, 20% Asian American, and 5% Hispanic. The mean age of the sample was 20.1 years ($SD = 1.1$). All were currently in college; none had married; 1 participant reported cohabiting. Participants reported using marijuana a mean of 2.2 days a week ($SD = 1.3$) and on 31.8% ($SD = 17.6$) of days prior to baseline. Average ages of marijuana initiation and regular use were 15.6 years ($SD = 1.5$) and 16.7 years ($SD = 0.6$), respectively. Fifty percent of the sample reported smoking approximately 1/16th of an ounce per week, 40% reported smoking less than that amount, and 5% smoked 1/8th of an ounce per week. On average, participants reported feeling high or under the influence of marijuana 3–4 hr on a typical day when they smoked ($SD = 1.1$). The average amount spent on marijuana in this sample was \$134.5 over the past months, ranging from \$20 to \$400 for

all but 1 of the participants who reported not spending any money. The average marijuana withdrawal discomfort score on the Marijuana Withdrawal Checklist at the second session was 3. ($SD = 2.29$), which is not clinically meaningful. Participants reported that during the 4 weeks prior to baseline, they drank on 39.7% ($SD = 15.2$) of possible days and consumed an average of 13.1 drinks ($SD = 7.97$) per week and an average of 4.5 drinks ($SD = 1.8$) per day they drank. Smoking tobacco cigarettes in the past month was reported by 60%, with 25% reporting daily tobacco smoking. The four experimental conditions did not differ significantly on any of these baseline variables ($ps > .19$).

Credibility of the Instructional Set Manipulation

All participants in the told THC/receive placebo group reported receiving THC. Three of five participants in the told placebo/receive THC group reported receiving placebo, whereas the other two indicated that their cigarettes had THC in them. No one in other conditions endorsed any deception. Analyses without the two participants for whom the deception failed produced the same findings for the subjective ratings.

Means and standard deviations for main effects of the experimental manipulations with corresponding effect sizes for dependent measures are presented in Table 1. Results of ANOVAs with the cigarette rating scales indicated that ratings of potency were higher in the told THC conditions than in the told placebo conditions, $F(1, 16) = 14.23, p < .01$, and in the receive THC conditions than in the receive placebo conditions, $F(1, 16) = 42.47, p < .001$. Estimated THC content was greater for the told THC conditions than for the told placebo conditions, $F(1, 16) = 25.0, p < .001$, and for the receive THC conditions than for the receive placebo conditions, $F(1, 16) = 36.0, p < .001$. Significant effects of expectancy but not the drug were seen on the ratings of “It smelled good,” $F(1, 16) = 6.86, p < .05$, and “It tasted good,” $F(1, 16) = 7.45, p < .05$, with higher ratings in the told THC conditions. Taste ratings were higher in the receive THC versus receive placebo conditions, with a large effect, $F(1, 16) = 3.72, p = .07$. There was no significant effect for the subjective rating of how similar the cigarette was to what participants usually smoked (partial $\eta^2 = .02$ for expectancy and $\eta^2 = .10$ for drug). No interaction effects approached significance for any of the cigarette ratings scales.

Participants in the told THC conditions, relative to those in the told placebo conditions, took significantly fewer puffs on the cigarette, $F(1, 16) = 11.53, p < .01$. Because everyone smoked up to the marked 10-mm line (ensuring that drug dose was equivalent across all participants), the difference in the number of puffs therefore reflects the fact that those in told placebo conditions did not inhale as deeply. No drug main or interaction effect approached significance for number of puffs.

Subjective Effects of Marijuana

Ratings of satisfaction were higher in the told THC conditions than in the told placebo conditions, $F(1, 16) = 4.26, p = .06$, and significantly higher in the receive THC conditions than in the receive placebo conditions, $F(1, 16) = 19.0, p < .001$. Only the pharmacological effect of THC was significant for “It made me feel better,” $F(1, 16) = 9.04, p < .01$, and for liking, $F(1, 16) = 20.55, p < .001$, with higher ratings in the receiver THC versus receive placebo conditions; liking ratings were higher in the told THC versus told placebo conditions, with a large effect, $F(1, 16) = 3.19, p = .09$. Interaction effects did not approach significance for any of these ratings.

Results of regression analyses indicated that THC significantly increased subjective ARCI scores of marijuana’s effects, relative to placebo, immediately postsmoking ($B = 3.75, SE = 1.11, p < .01$) and at 45 min after the end of smoking ($B = 4.63, SE = 0.93, p < .001$). THC also

increased ratings on the dysphoria and somatic effects at both time points ($B = 2.9$, $SE = 1.01$, $sr^2 = .24$, $p < .05$; and $B = 3.1$, $SE = 1.08$, $sr^2 = .27$, $p < .05$, respectively) but not on the other ARCI scales. The main and interaction effects of expectancy were not significant.

Stimulus expectancy nonsignificantly decreased self-reported levels of arousal on the SAM at the end of the smoking, with a large size effect ($B = 0.73$, $SE = 0.54$). Only a small pharmacological effect was seen on this scale ($B = -0.41$, $SE = 0.46$). Both of the experimental manipulations had almost no effect on the SAM valence scale ($sr^2 < .01$).

Discussion

This pilot study investigated the effectiveness of a marijuana expectancy manipulation when crossed with actual marijuana administration on the credibility of the deception and on subjective effects associated with marijuana. As such, it is the first step toward demonstrating that the BPD can be adapted for use with marijuana.

Expectancy manipulation was successful for all of the participants in the told THC/receive placebo condition who reported that they indeed smoked active marijuana containing THC. This finding is consistent with results of alcohol and nicotine BPD studies, which indicate that the placebo effect (i.e., successful deception in this condition) is more readily observed as compared with the antiplacebo effect (i.e., successful deception in the told placebo/receive THC condition; e.g., Juliano & Brandon, 2002; Martin & Sayette, 1993). It is likely that the pharmacological effects of this dose of marijuana may have been difficult to conceal. Instructional set effects in alcohol studies have mostly been found with low doses of alcohol (Sayette, Breslin, Wilson, & Rosenblum, 1994). In our effort to standardize smoking administration, participants were asked to smoke the whole cigarette rather than smoking ad lib. Smoking a whole joint on their own in a relatively short time interval may not be that typical for a nondaily nondependent marijuana smoker. In fact, participant ratings of the cigarette as “similar to what is usually smoked” were uniformly low perhaps because of the controlled smoking method or differences in cigarette presentation. Had they smoked less or a less potent cigarette, a greater influence of expectancy may have been revealed.

As hypothesized, we found large statistically significant effects of expectancy and drug manipulation on perceived potency and estimated THC content. Large statistically significant expectancy effects were also observed on the subjective ratings of the cigarette smell, taste, and actual smoking, the latter serving as a behavioral indicator of the credibility of the instructional set manipulation. Participants took seven more puffs to finish their cigarette if told they had placebo versus real marijuana. This indicates that they smoked less deeply when they were told it was placebo, indicating that the expectancy manipulation seemed credible during the time that they were smoking. Several double-blind marijuana administration studies have found that marijuana users titrate their marijuana exposure by inhaling harder as the potency decreases (e.g., Azorlosa, Heishman, Stitzer, & Mahaffey, 1992; Cooper & Haney, in press; Herning et al., 1986). Thus, it appears that both expectancy and pharmacological effects of marijuana can modify smoking behavior, although the latter effect was not found in the context of a BPD.

Despite the small sample size, mostly significant drug manipulation effects with large effect sizes were observed on subjective measures. Expectancy effects on satisfaction and liking ratings, although also large, did not approach statistical significance. Another noteworthy finding is that expectancy manipulation led to reductions in self-reported levels of arousal across both drug conditions with a medium albeit not statistically significant effect size. Because marijuana is believed to reduce arousal and increase pleasure (Schafer & Brown, 1991), the direction of the effect is consistent with college students' endorsed expectancies for

marijuana and with the effect of THC tested in laboratory studies (e.g., Lukas et al., 1995). Pharmacological rather than expectancy set effects were found for ratings of “feel better” and on the ARCI subjective effects scale that mostly assesses the physiological reactions to marijuana.

As expected, there were only main effects for pharmacology and expectancy and no interaction effects, similar to the absence of drug by instructional set expectancy interactions in the alcohol BPD studies (Hull & Bond, 1986). In recent summaries of the alcohol BPD literature (Testa et al., 2006), main effects of expectancy and drug manipulations have been noted, often on the same outcomes (i.e., additive effects), confirming findings from the original meta-analyses of this literature on additive rather than interactive expectancy and pharmacologic effects (Hull & Bond, 1986). Overall, the results provide support for further use of the BPD with marijuana to disentangle expectancy effects from pharmacology.

Limitations

In considering the results of this pilot study, several limitations should be noted. First, the very small sample size in a between-subjects study produces large standard errors and associated large confidence intervals around estimates of effect sizes, necessitating great caution in using such estimates in power analyses (Kraemer, Mintz, Noda, Tinklenberg, & Yesavage, 2006). In this sample, power to detect even a large effect η^2 of .137 was only .40 (Cohen, 1988). In a future fully powered BPD study, adding a within-subjects control by including repeated measures at baseline during nonsmoking conditions and following the drug presentation will increase statistical power and substantially reduce the required sample size because of the control for individual differences (Stevens, 1992). Second, only college students were enrolled, so results may not generalize to noncollege users and to African Americans who did not volunteer for this pilot study. Third, the selected moderate dose of THC could have influenced the credibility of the expectancy manipulation. Other doses in a different population of marijuana users could have produced a somewhat different pattern of results. Although two participants were not deceived, excluding their data from the repeated analyses did not change the results. Analyzing data both ways, with and without such cases in future fully powered studies may allow for a closer inspection of all variables.

BPD in Future Research

Despite some of the limitations of the BPD methodology (e.g., Martin & Sayette, 1993), the potential of this design to yield information of high scientific value and significance to public health is substantial. First, BPD research can significantly contribute to the knowledge base on substance-related behaviors that have high public health impact such as driving under the influence and risky sexual behaviors. For example, many marijuana users perceive driving when high as not dangerous despite the contrary evidence from controlled research (Bates & Blakely, 1999; Kalant, 2004). Coupled with a preexisting expectation that, unlike alcohol, marijuana induces little impairment in driving a car (McCarthy, Lynch, & Pedersen, 2007), these individuals may be more inclined to drive after smoking marijuana. Similarly, although there is correlational evidence of increased sexual risk among marijuana users (Costa, Jessor, Fortenberry, & Donovan, 1996; Fernandez et al., 2004; Shrier, Emans, Woods, & DuRant, 1996), it is unknown whether it is marijuana pharmacology or marijuana expectancies that play a role in individuals' ability to evaluate personal risk in expected involvement in risky sexual practices (e.g., failure to use condoms). Thus, not only is it important to understand whether the pharmacologic effect leads to increases in unsafe sexual practices, but also the potential additive effect of expectancies that may influence what activities are undertaken. Conversely, specific focus on the pharmacologic action of psychoactive drugs such as marijuana independent of the popular cultural beliefs about the drugs has wide-ranging implications for other important behavioral domains (e.g., motivation, affect).

Second, combining the BPD design for an abused substance with the examination of candidate genes for this drug is an important direction in drug research that is likely to be adapted in future studies of genetic risk factors because of increasing demand for narrow phenotypes (e.g., pharmacologic effect of a drug independent of the expectancy effects). Third, a BPD design is also useful when studying comorbid substance abuse or the interactive influence of drugs. For example, given the learned association between alcohol use and cigarette smoking (Rohsenow et al., 1997), the effects of alcohol use on craving for cigarettes may reflect expectancy processes as well as pharmacologic ones. A between-subjects BPD for alcohol administration has been used to disaggregate alcohol stimulus expectancy effects from pharmacological effects of moderate alcohol doses on smoking urges (Sayette, Martin, Wertz, Perrott, & Peters, 2005).

Finally, the BPD methodology could be of significant heuristic value when used with imaging or pharmacological studies. Evidence from these studies reveals that expectancy interacts with the same neurobiological systems as a given medication such as an analgesic, an antiparkinsonian drug, or an antidepressant (Benedetti, Mayberg, Wager, Stohler, & Zubieta, 2005). For example, expectancy of a stimulant drug enhanced the effects of the drug on brain glucose metabolism, with the thalamus mediating this effect (Volkow et al., 2003). With mounting empirical evidence for therapeutic benefits of cannabinoids in pain relief, appetite enhancement, and other medical domains, clearly delineating the degree to which expectancy may contribute to these clinical effects would significantly inform the science and the policy with respect to medical marijuana.

In conclusion, the present results are encouraging in that the BPD may be useful for investigating the degree to which both pharmacological and expectancy effects account for the acute effects of marijuana on a wide range of behavioral domains. Future BPD studies with marijuana should also consider examining outcome expectancies, which are known contributors to individual differences in behavioral response in alcohol and tobacco administration studies. For example, individuals expecting more impairment from alcohol displayed poorer task performance under both alcohol and placebo administrations (Vogel-Sprott & Fillmore, 1999). Outcome expectancies for negative affect reduction also moderated the effect of instructional set on anxiety among smokers who expected nicotine to improve their mood (Juliano & Brandon, 2002). People reporting more positive effects in general from alcohol behaved less aggressively after provocation when they thought they had consumed alcohol (Rohsenow & Bachorowski, 1984). Positive outcome expectancies exerted a significant effect on postdrinking perceptions and behavioral intentions of engaging in unsafe sexual behaviors (Fromme, Katz, & D'Amico, 1997). The examination of self-reported marijuana outcome expectancy as a moderator of instructional set on outcome (e.g., anxiety) can also suggest potential avenues for intervention research. For example, because many users expect marijuana to help relieve tension and anxiety (Schafer & Brown, 1991), these relaxation and tension reduction outcome expectancies may further enhance marijuana's stimulus expectancy effect on reducing anxiety and negative affect in general. Expectancy challenge interventions may be particularly useful with individuals high in these types of beliefs (Copeland & Brandon, 2000; Darkes & Goldman, 1993; Dunn, Lau, & Cruz, 2000). Similarly, behavioral interventions can be employed to help adopt healthy alternative ways of negative symptom management in a range of clinical populations who report increased use of marijuana to cope with a range of negative emotions (e.g., Bonn-Miller, Vujanovic, Feldner, Bernstein, & Zvolensky, 2007). As such, marijuana expectancy may play an important role in the maintenance of marijuana use behavior beyond its immediate acute effects.

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Table 1
Means, Standard Deviations, and Effect Sizes for Main Effects of Expectancy and Drug Manipulations for Credibility and Subjective Measures

Measure	Instructed						Received					
	THC			Placebo			THC			Placebo		
	M	SD	Effect size	M	SD	Effect size	M	SD	Effect size	M	SD	Effect size
Credibility ratings												
Taste	2.03	1.42	.33*	0.80	1.03	.33*	1.83	1.41	.20	1.00	1.25	.20
Smell	2.60	1.07	.30*	1.4	0.97	.30*	2.30	0.95	.10	1.70	1.34	.10
Similar to usual	1.45	1.26	.02	1.10	1.20	.02	1.65	1.16	.10	0.90	1.20	.10
Potency	2.50	1.18	.47**	1.40	1.17	.47**	2.90	0.74	.73***	1.00	0.94	.73***
THC content	1.80	0.63	.61***	0.80	0.92	.61***	1.90	0.57	.69***	0.70	0.82	.69***
Number of puffs	9.70	1.70	.42**	17.0	6.70	.42**	12.8	4.24	.02	13.9	7.67	.02
Subjective effects												
Satisfaction	2.30	1.06	.21	1.40	1.65	.21	2.80	1.13	.54***	0.90	0.99	.54***
Liking	2.45	1.12	.17	1.80	1.23	.17	2.95	0.90	.56***	1.30	0.82	.56***
Makes feel better	1.75	1.23	.05	1.30	1.34	.05	2.25	1.09	.36**	0.80	1.03	.36**
SAM arousal	3.70	0.86	.09 ^a	2.85	1.11	.09 ^a	3.05	0.90	.04	3.50	1.20	.04
ARCI-M scale T1	5.10	3.11	.003 ^a	4.60	3.83	.003 ^a	6.90	3.28	.31**	2.80	2.10	.31**
ARCI-M scale T2	4.60	3.44	.004 ^a	4.10	3.41	.004 ^a	6.80	2.70	.50***	1.90	1.73	.50***

Note. THC = delta-9-tetrahydrocannabinol; SAM = Self-Assessment Manikin; ARCI-M scale = Addiction Research Center Inventory—Marijuana scale; T1 = immediately postsmoking; T2 = 45 min postsmoking.

^aEffect size is indicated as sr^2 from regression analyses controlling for baseline values; all other effects in the table are partial η^2 from two-way (Expected \times Received) analyses of variance.

* $p < .05$.

** $p < .01$.

*** $p < .001$.