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Cue-Elicited Increases in Incentive Salience for Marijuana: Craving, Demand, and Attentional Bias

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Abstract

Background—Incentive salience is a multidimensional construct that includes craving, drug value relative to other reinforcers, and implicit motivation such as attentional bias to drug cues. Laboratory cue reactivity (CR) paradigms have been used to evaluate marijuana incentive salience with measures of craving, but not with behavioral economic measures of marijuana demand or implicit attentional processing tasks.

Methods—This within-subjects study used a new CR paradigm to examine multiple dimensions of marijuana's incentive salience and to compare CR-induced increases in craving and demand. Frequent marijuana users ($N=93$, 34% female) underwent exposure to neutral cues then to lit marijuana cigarettes. Craving, marijuana demand via a marijuana purchase task, and heart rate were assessed after each cue set. A modified Stroop task with cannabis and control words was completed after the marijuana cues as a measure of attentional bias.

Results—Relative to neutral cues, marijuana cues significantly increased subjective craving and demand indices of intensity (i.e., drug consumed at \$0) and $O_{\max}$ (i.e., peak drug expenditure). Elasticity significantly decreased following marijuana cues, reflecting sustained purchase despite price increases. Craving was correlated with demand indices (r 's: 0.23–0.30). Marijuana users

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Contributors

Dr. Metrik designed and conducted the current study with significant contributions by Drs. Kahler, Rohsenow, McGeary, Knopik, and MacKillop. Drs. Metrik and Aston conducted the statistical analyses, and all authors contributed to the analytical approach. Drs. Metrik and Aston wrote the manuscript and all authors contributed to and have approved the final manuscript.

Conflict of Interest

No conflict declared

displayed significant attentional bias for cannabis-related words after marijuana cues. Cue-elicited increases in intensity were associated with greater attentional bias for marijuana words.

Conclusions—Greater incentive salience indexed by subjective, behavioral economic, and implicit measures was observed after marijuana versus neutral cues, supporting multidimensional assessment. The study highlights the utility of a behavioral economic approach in detecting cue-elicited changes in marijuana incentive salience.

Keywords

marijuana; cue reactivity; behavioral economics; attentional bias; incentive salience

1. INTRODUCTION

Drug craving is fundamental to addictive behavior (MacKillop and Monti, 2007; Robinson and Berridge, 1993) such that individuals with a history of using a given substance are vulnerable to strong desire to use the drug in the presence of substance-related cues (Carter and Tiffany, 1999; Niaura et al., 1988). Cue-elicited craving has been extensively studied with alcohol (MacKillop et al., 2010; Monti et al., 2000), tobacco (Niaura et al., 1989; Rohsenow et al., 2007b), cocaine (Rohsenow et al., 2007a), and more recently, with marijuana (Haughey et al., 2008; Lundahl and Greenwald, 2015a; Lundahl and Johanson, 2011). Due to heightened awareness in the field regarding the addiction potential of marijuana (Budney, 2006), emerging cannabis cue-reactivity research may play an important role in the assessment of effects of promising behavioral treatments (Metrik and Ramesh, 2016) and pharmacotherapies for cannabis use disorders (Lundahl and Greenwald, 2015a). Although pertinent to all drugs of abuse, comprehensiveness and precision in assessment of craving are imperative with marijuana, as its steady increase in prevalence use rates, potency, demand, and societal acceptance is unrivaled by other drugs. Toward this end, this study used multidimensional assessment (including subjective, behavioral economic, and implicit measures) to evaluate changes in marijuana incentive salience during a cue reactivity (CR) procedure.

The Incentive Sensitization theory of addiction (Robinson and Berridge, 2001) postulates that individuals learn to associate drugs like marijuana with pleasure, which in turn increases their incentive motivational significance. Rewarding stimuli associated with drug use develop high incentive motivational salience and thus become attractive and “wanted,” eliciting appetitive (i.e., approach) behavior. Exposure to drug-associated versus neutral stimuli (“cues”) is a useful method to produce craving effects in drug users in a laboratory with the goal of assessing a drug’s incentive salience (Carter and Tiffany, 1999).

Cannabis CR studies have examined various dimensions of craving in response to visual pictorial stimuli (Henry et al., 2013; Nickerson et al., 2011; Wölfling et al., 2008), auditory imagery scripts (Singleton et al., 2002), unlit marijuana cigarettes (Gray et al., 2011, 2008), simulated marijuana and marijuana-related paraphernalia (Haughey et al., 2008; McRae-Clark et al., 2011; Schacht et al., 2009), virtual reality environments (Bordnick et al., 2009), or used marijuana paraphernalia supplemented by videotaped marijuana-related imagery (Lundahl and Greenwald, 2015a; Lundahl and Johanson, 2011). Consistent increases in

craving across these studies were observed in terms of subjective urge (Bordnick et al., 2009; Haughey et al., 2008; Lundahl and Greenwald, 2015a; Lundahl and Johanson, 2011; McRae-Clark et al., 2011; Singleton et al., 2002) and arousal, as measured by skin conductance and event-related brain potential (Gray et al., 2011, 2008; Henry et al., 2013; Nickerson et al., 2011; Wölfling et al., 2008). Furthermore, fMRI has been used to confirm that exposure to visual marijuana cues activates multiple brain regions associated with reward, visual response, craving, and relapse (Charboneau et al., 2013; Filbey et al., 2009). In contrast to cannabis-naïve participants, frequent marijuana users display activation in specific brain areas linked with addiction pathology, which has been related to marijuana problem severity (Cousijn et al., 2013a). In addition, there are also significant differences in functional brain connectivity during cue exposure between dependent and non-dependent cannabis users (Filbey and Dunlop, 2014).

Incentive salience can also be indexed by attentional bias to drug-related cues (Field and Cox, 2008), with cannabis dependent individuals exhibiting significant attentional bias for marijuana-related stimuli as measured by a modified Stroop task (Field, 2005). Furthermore, as compared to cannabis users with low levels of craving for marijuana, those with high craving have shown greater attentional bias for marijuana-related words (Field et al., 2004). Regular cannabis users have also demonstrated increased attentional bias to cannabis-related versus neutral cues relative to non-users (Cousijn et al., 2013b; Field et al., 2006), and when under the acute influence of marijuana, relative to placebo (Metrik et al., 2015). High levels of craving are likely related to increases in a drug's incentive salience and attentional bias to drug-related cues (Field, 2005; Field et al., 2004), although findings from one prior marijuana cue-induction study utilizing video and auditory cues did not support this assumption (Eastwood et al., 2010). It is possible, however, that a more robust increase in craving or in demand in response to more salient marijuana cues (e.g., actual lit marijuana cigarette) may be associated with greater attentional bias to marijuana cues on a modified Stroop task.

Drug demand, a behavioral economic index of incentive salience, can be measured by self-reported estimated level of consumption of a substance at a range of prices in a hypothetical purchase task. Analogous to behavioral operant progressive-ratio schedules, purchase tasks offer an efficient mode of evaluating drug demand. Purchase tasks have been psychometrically validated for marijuana (Aston et al., 2015; Collins et al., 2014), alcohol (Murphy and MacKillop, 2006), and tobacco consumption (Jacobs and Bickel, 1999; MacKillop et al., 2008). Moreover, state purchase tasks intended to measure phasic changes in relative drug value have been applied in the context of CR with alcohol (Amlung et al., 2012; MacKillop et al., 2010) and tobacco (Acker and MacKillop, 2013; Hitsman et al., 2008; MacKillop et al., 2012). State increases in craving for a substance effectively increase demand for the drug (Laibson, 2001; MacKillop et al., 2010), potentially resulting in choosing the drug over alternative reinforcers or opting to pay much higher prices to obtain the drug. However, no prior studies have utilized a marijuana CR paradigm to evaluate state changes in marijuana demand with a purchase task.

This within-subjects study was intended to directly examine alterations in incentive salience for marijuana among regular users as a function of acute exposure to marijuana cues with

particularly high salience (i.e., actual lit marijuana cigarettes) using a multidimensional framework. Specifically, we predicted that compared to neutral cues, exposure to and handling of marijuana cues (i.e., sight, smell of a lit cigarette) would increase subjective craving and marijuana demand. We hypothesized that cue-elicited increases in craving and demand would, in turn, predict greater attentional bias to marijuana relative to neutral word stimuli on a Marijuana Stroop Task. Secondary analyses were conducted to examine cue-elicited changes in physiological arousal. Because of evidence of differences in attentional bias for marijuana depending on cannabis dependence (CD) diagnosis (Cousijn et al., 2013b; Field, 2005; Field et al., 2004), we examined CD diagnosis as a predictor of attentional bias to marijuana cues and also of changes in cue-elicited responses on measures of craving and marijuana demand.

2. METHODS

2.1. Participants

Study procedures were approved by the Institutional Review Board of Brown University. Marijuana users recruited from the community met the following inclusion criteria (Metrik et al., 2015): native English speakers, 18 to 44 years of age, non-Hispanic Caucasian (due to additional genetic aims, not reported here), self-reported marijuana use at least two days per week in the past month and at least weekly in the past 6 months, and self-reported ability to abstain from marijuana for 24 hours without withdrawal. Exclusion criteria were: intent to quit or receive treatment for cannabis abuse, pregnancy, nursing, positive urine toxicology screen for drugs other than cannabis, current DSM-IV Axis I affective disorder or panic disorder, psychotic symptoms, or suicidal state assessed by the Structured Clinical Interview for DSM-IV Non-Patient Edition (SCID-IV-NP; First et al., 2002), contraindicated medical issues by physical exam, BMI > 30, and smoking 20+ tobacco cigarettes per day.

Among the 93 participants, 34.4 % ($n = 32$) were female and 14% ($n=13$) met DSM-IV criteria for past year CD. The median annual family income bracket of participants was \$60,000-69,000. Five participants showed inconsistent responding on the marijuana purchase task (MPT) and were excluded from MPT analyses (Amlung et al., 2012; Aston et al., 2015).

2.2. Procedure

Participants were told to abstain from marijuana and tobacco for 15 hours, alcohol for 24 hours, and caffeine for one hour prior to the session. An alveolar carbon monoxide (CO) reading of 6 ppm was used to confirm no recent marijuana or tobacco smoking (Cooper and Haney, 2009; Metrik et al., 2012) with a Bedfont Scientific Smokelyzer®. Tobacco smokers were permitted to smoke a tobacco cigarette following the CO test to prevent nicotine withdrawal. Zero breath alcohol concentration was verified with an Alco-Sensor IV (Intoximeters, Inc., St Louis, MO., USA).

2.3. Cue Reactivity Procedure

All instructions were presented by audiotape. Participants were presented with two inverted opaque covers. Beneath the first cover were the neutral cues (a pencil, an eraser, and a pad of

paper) which were selected to match the number and approximate sizes of the marijuana cues. Marijuana stimuli (a marijuana cigarette rolled at both ends provided by the National Institute on Drug Abuse, a lighter, and a used ashtray) were beneath the second cover. Neutral cues were always presented first to prevent carryover effects from the marijuana cues (Lundahl and Greenwald, 2015b; Monti et al., 1987). Participants were first asked to relax for 4 mins and then were instructed to uncover the neutral cues, view them for 2 mins, then touch the pencil to the eraser, smell it, and continue viewing the cues for 2 mins. After re-covering the neutral cues, participants completed self-report measures of craving and marijuana demand via the MPT and were then instructed to relax for 4 mins. They were subsequently exposed to marijuana cues, whereby participants were instructed to lift the second cover, pick up the cigarette, smell it, and hold it. After 2 mins, participants were asked to light the cigarette without putting it in their mouth, put down the lighter, and hold the lit cigarette in one hand without smoking it, smell it, and look at it. After 2 mins, participants were asked to extinguish the cigarette and re-cover the marijuana cues. An identical set of assessments was then administered followed by the Marijuana Stroop task.

2.4. Baseline Measures

SCID-IV-NP was used to assess for CD and to provide a symptom count for the number of CD symptoms, which included the presence of cannabis withdrawal per DSM-5 criteria. Thus, the possible symptom count ranged from 0-7 (observed range = 0-6). The *Time-Line Follow- Back Interview* (TLFB; Dennis et al., 2004) was used to assess past 60-day number of marijuana, alcohol, and tobacco cigarette use days. The *Marijuana History and Smoking Questionnaire* was used to assess typical marijuana use quantity and questions related to marijuana use patterns (Metrik et al., 2009).

2.5. Experimental Measures

Heart Rate (HR; beats per minute) was recorded prior to the CR task (three consecutive readings) and following the presentation and handling of neutral and marijuana cues (six consecutive readings) via a blood pressure cuff attached to the non-dominant arm (Datascop Accutorr Plus NIBP). The maximum of the readings for each set of cues was used in the final HR analysis.

Subjective marijuana craving was assessed via a 10-item *Marijuana Craving Questionnaire* adapted from a tobacco-smoking urges questionnaire (Tiffany and Drobes, 1991) and validated for use with marijuana (MCQ; Budney et al., 2003). Participants were asked to respond to items according to how they were thinking or feeling “right now,” rated on a 7-point scale (1 = “strongly disagree” to 7 = “strongly agree”), with higher scores indicating greater subjective marijuana craving. Items are averaged to yield a total craving score (possible range 1- 7; observed range 1-6.6). MCQ had high internal reliability at each time point (α .90).

The state version of the *MPT* was used to assess marijuana demand after each set of cues. The MPT assesses how many marijuana hits one would smoke *right now* at 22 prices (\$0 to \$10 per hit; see Aston et al., 2015 for exact prices) if the marijuana available was of average quality and strength, was available only from this source, could not be stockpiled (had to be

consumed), and if no marijuana or drugs were used prior to making choices on this task. Task instructions specified that there were 10 hits of marijuana in a joint and there was no limit on hits or joints (1 joint=1/32nd of an ounce=0.9 grams). Four metrics of marijuana demand were obtained from the MPT: (a) breakpoint (i.e., cost at which consumption is suppressed to zero), (b) intensity of demand (i.e., the amount of drug consumed at \$0), (c) elasticity of demand (i.e., the sensitivity of marijuana consumption to increases in cost), and (d) $O_{\max}$ (i.e., peak expenditure for a drug). Observed values for breakpoint, intensity, and $O_{\max}$ were obtained by directly examining MPT performance. Elasticity of demand was empirically derived using values generated from a nonlinear exponential demand curve model (Hursh and Silberberg, 2008). An R^2 value was generated to reflect the adequacy of the model fit to the data.

The *Marijuana Stroop Task* was used to assess automatic attentional bias to marijuana word stimuli (Field, 2005). The time to respond to the color of a word was assessed over two categories (10 neutral words: e.g., “coast,” “sand,” “hill”; 10 marijuana words: e.g., “cannabis,” “pot,” “joint,” “high”). The words were matched for length and usage frequency. Each word was presented once in each of 4 colors (maximum of 3 seconds), in random blocked order, with 32 words in each category per block, preceded by a practice sequence (20 letter strings: e.g., HHHH). Mean reaction time to respond to the color of a word was measured.

2.6. Data Analysis Plan

Calculations of demand indices were obtained using the following methods. Price elasticity was generated for each cue set (neutral versus marijuana) using the nonlinear exponential demand curve model (Hursh and Silberberg, 2008): $\log_{10} Q = \log_{10} Q_0 + k(e^{-\alpha Q_0 C} - 1)$, where Q =quantity consumed, Q_0 =derived intensity, k =a constant across individuals that denotes the range of the dependent variable (marijuana hits) in logarithmic units, C =the cost of the commodity, and α =elasticity or the rate constant determining the rate of decline in log consumption based on increases in price (i.e., essential value). The overall best-fitting k parameter was determined to be 2 for both cue sets. An R^2 reflected percentage of variance accounted for by the demand equation. Consistent with Jacobs and Bickel (1999) breakpoint consumption was coded as an arbitrarily nonzero value of 0.1 to provide an x-axis intercept of the demand curve that was amenable to logarithmic transformation. Similarly, the initial price (i.e., marijuana at zero cost) was replaced by a value of one cent (i.e., \$.01) to permit the use of the logarithmic transformation in the demand curve model.

Paired samples t -tests were used to examine cue-elicited changes in subjective urge to smoke marijuana, demand indices, and heart rate (HR). Paired samples t -tests were also used to examine attentional interference (average response latency (ms)) by marijuana versus neutral word stimuli on the Marijuana Stroop Task completed once after the presentation of marijuana cues in the CR task. Linear regressions were used to test dummy-coded CD diagnosis as a predictor of cue-elicited changes (change scores between neutral and marijuana cues) in MCQ urge, MPT demand indices, HR, and Stroop response times (ms; change score between marijuana and neutral words). All analyses were conducted using SPSS 22.0 for Windows and GraphPad Prism 6.0.

3. RESULTS

3.1. Preliminary Analyses

Raw MPT data were examined for outliers using standard scores, with a criterion of $Z=3.29$ to retain maximum data. The small number of outliers (1.4% post neutral or marijuana cues) were legitimate high-magnitude values and were recoded one unit higher than the next lowest non-outlying value (Tabachnick and Fidell, 2000). All data were examined for distribution normality. Intensity and $O_{\max}$ were log transformed to correct positive skewness. Descriptive statistics for the sample are presented in Table 1 and dependent variables from the CR task and Marijuana Stroop Task are presented in Table 2.

3.2. Subjective Craving

A paired samples t -test (Table 2) indicated that urge to smoke marijuana on the MCQ significantly increased following marijuana versus neutral cue presentation (paired t ($df=92$) = 8.46, $p < .001$). In the regression analysis, CD diagnosis did not predict cue-elicited increases in urge when tested as a dichotomous ($sr^2 = .01$, $p = .42$) or as a continuous symptom count ($sr^2 < .001$, $p = .93$) measure.

3.3. Marijuana Purchase Task

Figure 1 illustrates the mean number of marijuana hits participants reported they would consume at 22 prices (log-transformed) following exposure to neutral versus marijuana cues. Consumption was highest (approximately 25 hits, observed range 3 to 99 hits) at the lowest price (i.e., when marijuana was free). Marijuana purchase decreased as a function of increasing price in the presence of both types of cues. Figure 2 depicts the expenditure associated with each price. The exponential demand equation provided an excellent fit to the overall demand data for each cue exposure session (post neutral cues $R^2=0.995$; post marijuana cues $R^2=0.996$) and a very good fit to the individual data (post neutral cues median $R^2=0.812$, interquartile range=0.767-0.878; post marijuana cues median $R^2=0.817$, interquartile range=0.763-0.864). As shown in Table 2, demand for marijuana increased following exposure to marijuana versus neutral cues in terms of increases in intensity (paired t ($df = 87$) = 2.84, $p < .01$) and $O_{\max}$ (paired t ($df = 87$) = 3.03, $p < .01$), and decreases in elasticity (paired t ($df = 87$) = 1.97, $p = .05$) but not in breakpoint (paired t ($df = 87$) = 1.45, $p = .15$). In the regression analyses, CD diagnosis did not predict cue-elicited changes in demand when tested as a dichotomous or as a continuous symptom count measure ($sr^2 = .03$, $p = .09$).

3.4. Association between subjective craving and demand

Correlations among the demand variables and urge to smoke marijuana (Table 3) were examined within each of the CR conditions. Cue-elicited craving was significantly correlated with intensity and $O_{\max}$, but not with other demand indices.

3.5. Heart Rate

Paired samples t -tests (Table 2) indicated that there was no significant change in maximum HR after marijuana cues, compared to neutral cues (paired t ($df=92$) = .73, $p = .47$). In the

regression analysis, covarying for the baseline HR score, CD diagnosis predicted change in HR between marijuana and neutral cues at trend level, $B = 3.49$, $SE = 1.81$, $sr^2 = .04$, $p = .06$ indicating relatively greater increase in HR among those with CD. The latter effect became significant when CD diagnosis was tested as a continuous CD symptom count measure, $B = 1.22$, $SE = .50$, $sr^2 = .06$, $p = .01$.

3.6. Marijuana Stroop Task

Paired samples t -tests indicated that participants displayed significant attentional bias by slower color-naming of marijuana versus neutral words ($M_{\text{decrease}} = 31.01$ (72.09), $t(92) = 4.15$, $p < .001$). In the regression analysis with CD diagnosis, there was no significant group difference in attentional bias by CD status when tested as a dichotomous ($sr^2 = .004$, $p = .55$) or as a continuous symptom count measure ($sr^2 = .01$, $p = .25$). Exploratory regression analysis tested cue-elicited changes in subjective urge and demand values (intensity, O_{max}) as predictors of the difference in Stroop response times between marijuana and neutral words. Cue-elicited change in intensity (i.e., consumption at \$0) emerged as the only significant predictor of attentional bias for marijuana versus neutral words on the Stroop Task ($B = 457.25$, $SE = 165.86$, $sr^2 = .08$, $p = .01$).

4. DISCUSSION

This is the first study to utilize a CR paradigm to examine multiple dimensions of marijuana's incentive salience with subjective, behavioral economic, and attentional bias measures in frequent marijuana users. In support of our hypothesis, greater craving and marijuana demand was observed after exposure to marijuana versus neutral cues. Furthermore, cue-elicited increases in intensity of demand predicted greater attentional bias to marijuana versus neutral word cues on the Marijuana Stroop Task.

Utilizing the most salient visual, olfactory, and tactile sensory cues of the actual lit marijuana cigarette, the current marijuana CR paradigm generated a significant increase in subjective craving for marijuana relative to neutral stimuli, consistent with prior marijuana CR studies. While heart rate changes were not significant, physiologic reactivity to drug-related cues are mostly unreliable in other cue-reactivity studies (reviews by Carter and Tiffany, 1999; Rohsenow et al., 1990), including marijuana CR studies (Gray et al., 2011, 2008; Lundahl and Greenwald, 2015a; Lundahl and Johanson, 2011; Nickerson et al., 2011).

To our knowledge, this is the first study that demonstrated the dynamic nature of the relative value of marijuana in relation to cue-elicited craving for marijuana. Similar to alcohol (MacKillop et al., 2010) and tobacco (Acker and MacKillop, 2013; MacKillop et al., 2012) studies, we demonstrated that marijuana cues reliably increased marijuana demand across multiple aspects of relative value including intensity, O_{max} , and elasticity. Demand indices were moderately correlated with subjective craving, sharing 5-9% of variance in intensity and O_{max} , but not significantly associated with the other indices. This provides evidence of related but unique constructs that influence appetitive responding to marijuana cues.

Increases in intensity of demand predicted greater attentional bias to marijuana-related versus neutral word cues on the Marijuana Stroop Task. However, contrary to our

expectations, marijuana urge was not associated with attentional bias. Prior research found an association between subjective craving and attentional bias to marijuana words (Field, 2005; Field et al., 2004), but, similar to our study, findings did not generalize to the only other CR paradigm where urge was experimentally manipulated (Eastwood et al., 2010). This suggests that intensity may be a more proximal behavioral measure of explicit “wanting” of marijuana that underlies implicit changes in attention to marijuana stimuli.

Cannabis dependence diagnostic status did not predict CR responses in terms of changes in self-reported craving and marijuana demand. The lack of variability between the dependent and nondependent users is consistent with another study (Filbey and Dunlop, 2014), which demonstrated CD-related differences in functional connectivity in the reward network but not in regional activation and not in subjective craving response during marijuana CR. Similarly, unlike prior studies that demonstrated greater attentional bias for cannabis words by users with CD as compared to non-dependent users (Cousijn et al., 2013b; Field, 2005), CD status in the current study did not differentiate responses on the Marijuana Stroop Task. It is possible that the experimental design precluded us from replicating these findings as the Marijuana Stroop Task was administered once following the presentation of marijuana cues when marijuana urge was already increased in the entire sample. Because urge for marijuana was relatively high, it is possible that this ceiling effect post CR overrode the hypothesized main effect of CD diagnosis on attentional bias for marijuana cues.

4.1. Limitations

As the sample in the current study was exclusively Caucasian, results may not generalize to racially diverse samples of marijuana users. Furthermore, due to the small subsample of marijuana users with CD, the current research was not sufficiently powered to detect significant group differences, so results may not generalize to studies with higher CD rates. Additionally, the order of cue presentation (neutral cues first) was not counterbalanced to prevent carryover effects (Lundahl and Greenwald, 2015b; Monti et al., 1987; Rohsenow et al., 2001, 2000). However, order effects would only be a threat to the integrity of the design if neutral cues were presented after drug cues (Monti et al., 1987; Sayette and Hufford, 1994).

4.2. Conclusions

Findings from this research demonstrate increased engagement of diverse facets of incentive motivation for reward by marijuana versus neutral cues as evidenced by increases in subjective craving for marijuana and in several dimensions of marijuana demand. In particular, the current findings support the utility of a behavioral economic approach in detecting changes in cue-elicited responding for the first time, suggesting that the state MPT has the potential to aid in discerning alterations in drug “wanting” and relapse liability as a function of subjective drug state. A post-treatment decrease in the motivational salience of marijuana cues, as measured by subjective craving and behavioral-economic indices of marijuana demand, over the course of the abstinence period may have clinical utility. As such, this CR paradigm may be a valid tool for research on behavioral and pharmacotherapeutic approaches to treatment of CD via testing of reinforcement-based

interventions such as contingency management or of medication efficacy in reduction of marijuana demand and subjective craving.

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Highlights

- Marijuana cues increase craving and marijuana demand via behavioral economic measure
- Marijuana demand indices of intensity, $O_{\max}$, and elasticity were affected by cues
- Cue-elicited increases in demand predicted greater attentional bias to marijuana
- Multidimensional assessment detects cue-elicited changes in drug incentive salience

Figure 1.

Demand curves for consumption of marijuana hits following exposure to neutral cues and marijuana cues. The x-axis provides log-transformed price in dollars (\$) and the y-axis provides self-reported consumption in marijuana hits.

Figure 2.

Expenditure curves for purchase of marijuana hits following exposure to neutral cues and marijuana cues. The x-axis provides price in dollars (\$) and the y-axis provides expenditure in dollars (\$). Values are presented in actual units rather than conventional logarithmic units for interpretational clarity.

Table 1

Sample demographics and marijuana use characteristics.

Variable (<i>n</i> = 93)	Mean (<i>SD</i>)
Age	21.4 (4.4)
Years of education	13.8 (1.7)
Percent marijuana use days in the past 60 days	72.5 (21.6)
Times used marijuana on average day	2.1 (1.2)
Number marijuana problems past 90 days	3.7 (3.0)
Percent alcohol use days (<i>n</i> =91)	29.3 (19.4)
Percent smoking tobacco days (<i>n</i> =43)	57.4 (41.0)
Gender	<i>n</i> (%)
<i>Female</i>	32 (34.4)
<i>Male</i>	61 (65.6)
Marijuana ounces used per week	<i>n</i> (%)
<i>Less than 1/16th</i>	9 (9.7)
<i>1/16th</i>	22 (23.7)
<i>1/8th</i>	27 (29.0)
<i>1/4th</i>	14 (15.1)
<i>More than 1/4th</i>	21 (22.6)
DSM-IV cannabis dependence	13 (14%)

Table 2

Comparisons of heart rate, craving, affect, and behavioral economic measures of demand following exposure to neutral versus marijuana cues.

	Neutral Cues		Marijuana Cues		<i>d</i>	<i>p</i>
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>		
Max heart rate	79.17	10.00	78.71	10.29	.07	<i>ns</i>
MCQ	2.59	1.13	3.07	1.33	.88	<0.001
	<i>M</i>	<i>SEM</i>	<i>M</i>	<i>SEM</i>	<i>d</i>	<i>p</i>
Breakpoint	3.99	0.33	4.10	0.34	.15	<i>ns</i>
Elasticity	0.051	0.005	0.048	0.005	.21	<0.05
Intensity	25.42	3.28	25.89	3.25	.30	<0.01
$O_{\max}$	11.19	1.21	12.51	1.38	.32	<0.01
Marijuana Stroop Task						
	Neutral Words		Marijuana Words		<i>d</i>	<i>p</i>
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>		
Mean reaction time (ms)	721.88	174.20	752.89	178.43	.43	<0.001

Note. MCQ = Marijuana Craving Questionnaire. SEM = standard error of the mean. Results are based on paired *t*-test analyses. Intensity and $O_{\max}$ were log-transformed to correct positive skewness but raw means (*SEM*) are shown for ease of interpretation.

Table 3

Correlations between facets of demand and craving after exposure to neutral cues and exposure to marijuana cues.

<i>Demand index</i>	Cue-induced craving	
	Neutral Cues	Marijuana Cues
Intensity	.218 *	.23 *
$O_{\max}$	.278 **	.30 **
Breakpoint	.086	.10
Elasticity	-.133	-.14

Note.

*
 $p < .05$;

**
 $p < .01$;

 $p < .001$.