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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 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.

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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, 2015; 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, 2015). 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.

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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, 2015; 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, 2015; 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, 18–44 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 h 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 h, alcohol for 24 h, 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).