Cannabis users' experience of cannabis craving: a test of the cue-reactivity model

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Cannabis users’ experience of cannabis craving:

A test of the cue-reactivity model

by

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Abstract

Despite craving’s emphasis in treatment programs, little research has been conducted that specifically focuses on cannabis craving. Cannabis use, however, is the second most commonly cited reason for entering treatment for substance abuse and dependency. An understanding of how cannabis users experience craving is necessary. The current study compared heavy/daily cannabis users with infrequent users on measures of craving following presentation of cannabis cues. Hypotheses predicted changes in physiological (heart rate, galvanic skin response) and cognitive (simple reaction time, attentional bias) correlates of craving, and increased self-reported craving following cannabis cue exposure. Results found no significant increase in most indicators of craving. Only galvanic skin response was impacted by presentation of drug cues. Findings are inconsistent with previously published work on cannabis craving, suggesting the need for further research.

*Keywords:* Craving, cannabis, cue-reactance, substance
Cannabis users’ experience of cannabis craving: A test of the cue-reactivity model

**Background**

Marijuana (cannabis) is the second most commonly cited reason for seeking drug treatment. Cannabis users represent 17.5% of all those who are in treatment for substance-related problems in the United States (SAMHSA, 2012). Identifying what differentiates problematic from nonproblematic use of the plant is vital as cannabis regulations loosen across the United States. While applied treatment research suggests that craving is an important factor of interest, basic scientific evidence is equivocal regarding the etiology and function of cannabis craving. It is only assumed that craving is a natural consequence of regular and frequent use of the cannabis plant and that it is a distinguishing indicator of problematic use. Moreover, applied research on cannabis craving uses similar paradigms to manipulate craving as those used for other drugs (Singleton et al., 2002; Wolfing et al., 2008). Reliance on similar paradigms assumes that cannabis craving develops and functions the same as other substances of abuse. A better understanding of how cannabis users’ experience of craving aligns and/or differs from current theory is necessary, particularly given that cannabis users do report craving as a major reason for relapse following abstinence and an obstacle in treatment (Budney et al., 2008; Vandrey et al., 2008; McRae et al., 2007; Coffey et al., 2002; Swift, Hall & Teeson, 2001).

**Function of craving in drug abuse**

The role of craving in drug abuse has received increased attention in the research literature due to the new inclusion of craving as a diagnostic criterion for substance-
related disorders in the DSM 5 (American Psychiatric Association, 2014). Nevertheless, defining craving in the drug literature has been a challenge. Most theorists agree that craving differs from thoughts of enjoyment or liking of the effects of a drug in both degree and kind (West, 1987). While craving is occasionally defined as a more severe form of liking or wanting (Kozlowski et al., 1989), dependency and other problems-related to use do not predict differences across users in how well one likes or enjoys the effects of a drug (Volkow et al., 2003). Some definitions of craving emphasize changes in motivational state, where the individual experiences a strong desire to use a drug (Tiffany & Wray, 2012). Experimental and applied research suggests that drug users’ experience of craving is associated with maintenance of use, an increased risk of dependency, and an increased risk of relapse following abstinence from use of the drug (Flannery et al., 2006; Robinson & Berridge, 2003; Everitt, 1997; Pickens and Johanson, 1992; Baker, Morse & Sherman, 1987; Wise, 1988; Ludwig, Wikler & Stark, 1974). The experience of craving a substance seems to represent a shift away from mere enjoyment of the rewarding aspects of use of the drug (pleasurable effects) toward a motivational drive to obtain the drug (Robinson and Berridge, 1993; Wise, 2004).

Despite a substantial body of literature supporting cravings role in drug seeking behavior (for review see Tiffany & Wray, 2012), researchers and clinicians disagree on how best to conceptualize and measure craving (Drobes & Thomas, 1999). Moreover, theoretical inconsistency across measures and assumptions of drug similarity can lead to problems when attempting to cross apply work on craving from one substance to another. For example, the rationale provided by the American Psychiatric Association’s work group responsible for the addition of craving in the newest DSM cited extensive literature
on the role of craving in problematic alcohol and cocaine users (Casteel & Valora, 2010). No work was cited that investigated the role of craving for other drug classes. Clinicians are meant to assume that what is good for the goose is good for the gander when diagnosing drug-related problems.

Studies that rely on an assumption of similar nomothetic principles of drug abuse across substances tend to cite early work demonstrating that similar reports of problems are seen across drug users (Koston et al., 1987; Feingold, & Rounsaville, 1995). This assumption, however, also assumes that those individual symptoms and problems are also similar in both degree and kind across substances and equally indicate problematic use. This assumption is not supported by the literature; individual symptom criteria perform differently across substances in IRT analysis (Gillespie et al., 2007). If craving is understood as a more severe form of liking, or enjoyment of a drug’s effects, and drug’s effects differ across classes, then we have little basis to assume that endorsement of “craving” is analogous when comparing across drug users.

**Theoretical etiology**

Craving is generally thought to develop through a process of behavioral learning and neurobiological stimulation from ingestion of the psychoactive substance (Skinner & Aubin, 2010). When a behavior is followed by reward it is more likely that the behavior will be repeated in the future (Skinner, 1938). Using a substance with pleasurable effects results in reward via the subjective effect of the drug (Berridge, & Robinson, 2003). Through a process of instrumental conditioning, regular use of the rewarding substance will increase motivation for future use of the drug. Moreover, tenants of learning theory can also explain how environmental cues can take on incentive value increasing ones
motivational state to use through a process of Pavlovian conditioning. When environmental variables related to drug use are repeatedly paired with the pleasurable/rewarding effects of use of that drug, those variables (drug cues) will begin to act as conditioned stimuli that can evoke expectation of the anticipated response. When the pleasurable response (e.g., intoxication, euphoria) that would typically follow presentation of drug cues is denied (as one would see if cues are presented and use is restrained), the body goes into an anticipatory appetitive response. The anticipatory response is functionally analogous to an acute state of withdrawal (Verheul, van den Brink, & Geerlings, 1999). Environmental cues associated with use of the drug then motivate future use of the drug through both positive and negative forms of reinforcement.

While enjoyment of the effects of the drug can certainly act as a reinforcer, pleasure and reward are distinct phenomena (Smith, Berridge, & Aldridge, 2011). Not all behaviors that are subjectively pleasurable are craveable. Early research in addiction attributed the craveable nature of drugs to activation of dopamine pathways in the VTA, colloquially referred to as the pleasure pathway. Studies suggested that the subjective pleasurable experience of drug use was due to activation of the dopaminergic system (Wise, 1980; Volkow et al., 1999). Dopamine, however, likely plays a more complicated role in development of motivation to use a drug than simply being the neurotransmitter associated with pleasurable experience. Craving is more than mere liking. More recent work in addiction suggests that mesolimbic dopamine release is associated with increases in attention (Berridge, 2007; Flagel et al., 2011; Schultz, 2013). This new role of dopamine would explain why pathological craving is present in substance abuse,
gambling, and binge eating (Potenza, 2008; Bluential & Gold, 2010), but to a lesser degree with other naturally enjoyable, but less abused, activities. Activation of dopaminergic pathways in the VTA increase attention, thereby increasing attention to environmental stimuli being presented at the time of drug use. By increasing salience of stimuli, dopamine acts to reduce the proximal distance between cues, use of the drug, and the pleasurable effects. Learning, therefore, occurs more rapidly. Dopaminergic activation, by means of increasing attention to cues, facilitates more effective reinforcement.

**Craving and cue-reactivity**

When stimuli in the environment become associated with drug reward through Pavlovian conditioning, the stimuli can then elicit the conditioned response. Expectation of the drug’s effects can be induced even absent of use of the drug itself. This state of expectation that motivates interest in use of the drug is referred to as cue-elicited craving (Drummond, 2000). Presenting environmentally relevant cues and examining whether or not they induce drug-incentive expectation can determine whether or not craving for a drug is present. These tests are referred to as cue-reactivity paradigms. If cues associated with the use of a drug lead to an increase in interest in taking the drug, there is support that classical conditioning has occurred. Studies using cue-based paradigms to test for craving appear frequently in the literature (e.g., Papachristou, Nederkoorn, Giesen, Jansen, 2014; Garland & Howard, 2014; Carpenter et al., 2014; Ray, Hanson & Hanson, 2014). Support for the use of these paradigms comes from neuroimaging studies, which find that drug-related stimuli are able to induce dopamine release in the
mesolimbic VTA even before the experience of pleasure (Duvanchelle et al., 2000). The conditioned stimulus can invoke a conditioned response.

Testing for the presentation of craving using cue-eliciting stimuli rests on the assumption that all forms of drug craving are functionally similar and develop through the same etiology. The paradigm assumes that craving develops through a process of classical and instrumental conditioning, and that the readiness of the user to learn these associations is increased through the pharmacological effects of the drug on VTA dopamine release. If we assume this general framework for development of craving then the paradigm makes specific predictions about what will occur following the presentation of drug-related cues.

In addition to overt thoughts about wanting to use the drug, we would also expect to see changes in attention and autonomic arousal as the user enters into an anticipatory state where they are awaiting pleasure and experiencing acute withdrawal. The body is expecting the pharmacological and subjective effects of drug use when shown cues of the drug. As the body prepares for the drug’s anticipated effects dopamine is released, leading to increased selective attention to reward-sensitive stimuli (Duvanchelle et al., 2000). We would expect users who have been cued to overly attend to drug-relevant stimuli. Moreover, this state of increased selective attention to drug cues should also make it more difficult to attend to stimuli that are not relevant to use of the drug and interfere in completion of cognitive tasks that rely on switching of attention. Indeed, studies on alcohol and cocaine abuse find that attention to drug-related stimuli tends to increase and cognitive flexibility that requires attentional switching tends to decrease (increased perseverance) following the presentation of drug cues (Dunning et al., 2011;
Finally, cues should also increase physiological arousal. Autonomic nervous system (ANS) activity is a major component of emotion (for review see Kreibig, 2010). Craving is experienced as an affective state driven by an appetitive response (Orford, 2001). When primed to anticipate the effects of a drug, which is rewarding, the user is thinking about experiencing pleasure. Imagining drug exposure leads to the affective (emotional) experience of anticipatory pleasure (Marlatt, 1987). Engaging with emotionally evocative materials that signal anticipatory pleasure activates ANS activity. The experience of anticipatory pleasure is associated with increases in overall galvanic skin-conductance response (Bernat et al., 2006; Codispoti et al., 2008; Codispoti & De Cesarei, 2007; Lang et al., 1993) and decreases in heart rate (Bernat et al., 2006; Britton et al., 2006; Codispoti & De Cesarei, 2007; Codispoti et al., 2008; Ritz et al., 2005). Some studies suggest, however, that when anticipatory pleasure is cued through cognitive processes (e.g., imaginally invoked) heart rate instead increases (Fiorito & Simons, 1994; Van Diest et al., 2001).

In addition, neuroadaptation to the effects of the drug establish a threshold of pleasure/homeostasis that the brain anticipates when in a given state (in the presence of drug cues; DiFranza & Wellman, 2005). When anticipated effects are not reached the body goes into a state of withdrawal, which is experienced as irritability or anxiety (Jasova, Bob, & Fedor-Freybergh, 2007). The body invokes a stress response. Therefore, autonomic arousal would also be expected following the presentation of drug-cues as a product of frustration from anticipating but not receiving reward. Autonomic
activation during states of anxiety is primarily a sympathetic response. Anxiety increases
heart rate (Adsett et al., 1962; Eisenberg et al., 1988; Murakami & Ohira, 2007; Robin et
al., 1998; Tugade & Fredrickson, 2004; Van Diest et al., 2006) and increases galvanic
skin response (Blechert et al., 2006; Chan & Lovibond, 1996; Murakami & Ohira, 2007;
Ritz et al., 2000). Drug cues that can invoke an emotional experience of anticipatory
pleasure and/or acute withdrawal-related stress, therefore, should modify heart rate and
overall galvanic skin response.

The cue-reactivity paradigm

Specific predictions that stem from theories of craving can also be tested using the
cue-reactivity paradigm. Cue-elicited craving manipulations with alcohol, nicotine,
cocaine, and heroin all consistently find that when presented with drug-relevant cues
users demonstrate increases in self-reported craving (Hone-Blanchet, Wensing, &
Fecteau, 2014; Carter & Tiffany, 1999; Cepeda-Benito & Tiffany, 1996; Cortese et al.,
2014). These studies also find post-cue changes in attention and increases in autonomic
arousal (Carter & Tiffany, 1999; Cepeda-Benito & Tiffany, 1996). A meta-analysis of 41
cue-reactivity studies found average effect sizes for cue-elicited craving of +.92 (d = .92,
95% CI: .84 – 1.0; Carter & Tiffany, 1999). As would be expected based on VTA
activation, heroin and cocaine users showed the highest level of reactance post cue (+1.18
- +1.29). The lowest reported effect sizes were +.53 for alcohol.

Applications of cue-reactivity research

The cue-reactivity paradigm provides a useful means of studying craving and it’s
correlated phenomena. When applied to specific substances, cue-elicited craving models
can inform the development of psychological interventions, as we see from the alcohol
and nicotine literature. For example, studies using cue-reactance paradigms with cigarette smokers found that presentation of nicotine cues using imagery scripts elicited an increase in self-reported craving, increases in heart rate and galvanic skin-response, and decreases in reaction time responses (Cepeda-Benito & Tiffany, 1996). What followed from this research was the development of interventions that reduced reactivity to nicotine related cues. Exposure-based coping skill techniques for nicotine related cravings, such as urge-surfing, show promise in reducing individuals’ reactivity to smoking related cues that previously induced cigarette craving (Bowen & Marlatt, 2009). Likewise, literature that supports a connection between alcohol-related cue-reactance and craving has also influenced the development of crave management interventions that function by reducing alcohol-related cue-reactivity (e.g., Rohsenow et al., 2002). There is obvious utility of developing craving interventions for substances where cue-induced craving is well understood. Cannabis, however, may not be one of those substances.

**Theoretical issues with cannabis craving**

Craving of cannabis is assumed to develop and function the same as other drugs of abuse. Interventions focused on reducing craving to all drugs, including cannabis, rely on this assumption of similarity in etiology and function. Nevertheless, the dependency risk associated with cannabis is less understood than with other substances of abuse. The assumption that cannabis craving develops and functions similar to other drugs of abuse might not be supported.

The addictive potential of most drugs of abuse is thought to result from properties of the substance acting on the brain’s mesolimbic dopamine system (Wise, 2004; Hyman et al., 2006). This system projects from the ventral tegmental area (VTA) to the ventral
striatum, which is composed of the nucleus accumbens. The generally accepted theory of
the rewarding, and thereby addictive, nature of drugs of abuse is that these substances
enhance synaptic dopamine levels in the ventral striatum. As discussed previously, the
enhancement of dopamine in the VTA is functionally related to both
reward/reinforcement and increased selective attention. Increased synaptic dopamine
levels in the VTA have been found following administration of many drugs of abuse,
including amphetamine (Breier et al., 1997; Drevets et al., 2001), cocaine (Schlaepfer et
al., 1997), alcohol (Boileau et al., 2003), and nicotine (Brody et al., 2004; Novak,
Seeman, & Foll, 2010).

Some work does suggest that cannabis can stimulate striatal dopamine
neurotransmission (Martin-Santos, 2010; Bossong et al., 2009). However, the amount of
increased dopaminergic availability following administration of psychoactive
components of cannabis differs markedly from other drugs of abuse. Whereas
amphetamine, cocaine, alcohol, and nicotine cause 10-30% reductions in dopamine
D2/D3 receptor availability, human administration of THC is only related to decreases of
3.4-3.9% (Bossong et al., 2009). Reductions in receptor availability lead to increases in
striatal dopamine levels, suggesting that the amount of increase in striatal dopamine after
ingestion of THC is less than increases seen for amphetamine, cocaine, alcohol, and
nicotine. Moreover, while high doses of THC can induce small increases in dopamine
release in the VTA, the effect likely occurs indirectly through CBI receptors on glutamate
and GABA neurons (Schlicker & Kathman, 2001; Lupica et al., 2004). Drugs with
higher dependency indices tend to have stronger and more direct effects on the VTA
dopamine pathway (Hyman et al., 2006). Whether or not the increase in dopamine
following use of cannabis is sufficient to lead to craving in its classic sense has not been
determined.

Even if use of cannabis does work on the dopaminergic pleasure pathway, the
effects of cannabis intoxication undermine a purely bio-behavioral etiology for craving of
cannabis. Dopamine’s role in craving development is in increasing attention to cues and
reward for the purposes of increasing reinforcement of drug use. Reinforcement leads to
craving by means of classical and instrumental conditioning. Two important effects of
cannabis’ psychoactive compound Δ-9 THC are decreased sustained and transient
attention (Crean, Crane, & Mason, 2011; Ilan, Smith, & Gevins, 2004) and acute
impairment of several forms of memory (for review see Ranganathan & D’Souza, 2006).
Right dorsolateral prefrontal cortex, (para)hippocampal, and regions of the cerebellum
show evidence of decreased activation during acute intoxication of cannabis, regions
implicated in associative learning. Basic and applied studies demonstrate that
intoxication leads to deficits in associative learning (Eva et al., 2006; Nexter, Roberts,
Garavan, & Hester, 2007; Skosnik et al., 2008). Contextual encoding is also disrupted
during cannabis intoxication (Ranganathan & D’Souza, 2006). If craving develops in
part through behavioral reinforcement than associative learning is critical for being able
to learn the pairing of stimulus and response.

Known neurological intoxication effects of cannabis use are inconsistent with
current theory of the etiology of drug craving. Cannabis users might not “crave” in the
same way that other drug users experience craving. Alternatively, if present, craving for
cannabis might develop through different mechanisms of action then biologically
exacerbated behavioral reinforcement. A test of the applicability of the cue-reactivity paradigm could potentially provide support for either alternative hypothesis.

**Cue-reactivity studies with cannabis**

Cannabis craving is typically studied using the same cue-reactivity paradigms as other drugs of abuse. Nickerson et al. (2011) looked at cue-reactance of cannabis by showing pictures of flower marijuana to cannabis-dependent adolescents. They found that those who were presented with the cue reported higher craving for marijuana than those who were not. Comparable results of increased self-reported craving appear in other studies that employ primarily visual cues (e.g., Lundahl & Johanson, 2011; Wolfling, Flor, & Grusser, 2008). Wolfling et al.’s (2008) study examined physiological responses to visual material associated with cannabis (i.e. pictures of marijuana) among heavy long-term cannabis users. Again, the results showed that visual cues increased self-reported craving, but also found that the cues increased arousal, specifically skin-conductance, among the cannabis users. This result relating cues to arousal did not replicate, however, in another experiment that found increased craving in response to cues (Lundahl & Johanson, 2011). While marijuana-associated pictures consistently increase reports of interest in use, they apparently do not always lead to heightened physiological reactions. The experience of craving reported by marijuana users is not always consistent with theories of craving development.

File-drawer problems and publication bias for significant results (Rosenthal, 1979) also raise questions about the few studies that do suggest that cannabis cues can induce craving in similar ways to other substances of abuse. Nevertheless, limitations in previous cannabis craving studies also might account for modest effect sizes and failures
to find effects. Most studies use pictures and generic paraphernalia as cues. Participants might not use the type of ingestion mechanism presented (e.g., glass pipes), and photographs might not generalize well to real world environmental stimuli. Testing whether cannabis fits with current conceptualizations of craving is imperative if applied work in this vein is going to continue.

**Primary Aims**

The present study tested whether craving could be induced in a sample of non-treatment seeking heavy/daily users of cannabis using a range of cannabis cues. Consistent with theory, if cannabis craving is the result of bio-behavioral processes, then exposure to cues should lead to specific changes in cognition/attention, autonomic arousal, and experience of craving, the current study had three specific hypotheses:

1. Those who use cannabis regularly and are exposed to the experimental cues would show the greatest change in self-reported craving following cue exposure

2. Those who use cannabis regularly and are exposed to the experimental cues would show the greatest change in correlates of craving following cue exposure, specifically:
   2.1. Increased heart rate (HR)
   2.2. Increased galvanic skin response (GSR)
   2.3. Decreased simple reaction time (RT)
   2.4. Increased attentional bias

3. Density of current cannabis use would account for differences in self-reported craving among those exposed to the experimental cues
Methods

Participants

The target population of interest was non-treatment seeking, heavy/daily cannabis users. Infrequent/novice cannabis users were also targeted as part of data collection to act as controls. The choice of infrequent rather than non-users for the control condition was strategic. A history of some cannabis use is relatively normative within the adult population (SAMHSA, 2014). Adults who have chosen not to use cannabis at any point in their lifetime may hold stronger negative views toward cannabis compared to those who have some experience with the plant. Presentation of drug cues among this population might inadvertently activate these negative emotions, which could impact physiological readings (GSR, HR). Therefore, inclusion in the control condition required at least one instance of prior cannabis use. Recruitment was conducted both on and off the university campus. Recruitment of infrequent cannabis users from the community proved unduly burdensome. Therefore, three samples were recruited: one sample of active cannabis users from the community, one sample of active cannabis users from the University at Albany (college student users), and one control sample of college students who infrequently use cannabis. Participants in the community sample were recruited using advertisements placed on community billboards throughout the city and newspaper advertisements. College student participants were recruited from the University at Albany Psychology subject pool. Community participants were paid $20 for their participation and undergraduate participants were compensated with course credit.
Selection of the heavy/daily cannabis user samples. Participants were excluded if they were under the age of 18, not proficient in English, and/or reported using cannabis on average less than four days per week over the past year.

Selection of the infrequent user sample. Participants were excluded if they were under the age of 18, not proficient in English, and/or reported a lifetime history of cannabis use of more than 52 days (less than 1 day per week).

Materials

Experimental Cues:
- Three marijuana-related posters
- Bong
- “Joint” – hand rolled cigarette containing marijuana-scented plant material
- Glass pipe

Control Cues:
- Three neutral posters that did not contain drug references
- Pencil
- Scented candle (unlit)
- Flower figurine

Procedure

Following consent, subjects were sat at an enclosed desk area with a computer. Participants were asked to place their nondominant hand on a stabilizing pillow with elastic straps to hold their arm in place. Heart rate and GSR probes were place on their index, middle, and ring fingers of their nondominant hand. After a 2-3 minute stabilizing
period, initial physiological readings were taken. Participants then completed baseline cognitive tasks and self-report measures as one computerized questionnaire.

Following the completion of all baseline tasks, the researchers then removed a sheet from the wall, which occluded the poster primes during the baseline administration. All other cues were placed on the desk in front of the participant. Subjects were randomly assigned to either be exposed to experimental or control cues. Participants were instructed by the researchers to examine each of the new items and engage with the cues that were placed on the desk in front of them. Physiological readings continued throughout and directly following cue exposure. After examining the cues, participants were asked to complete a time two survey with questions on current craving, perform the same computerized simple reaction time task, and complete a drug stroop task.

**Measures.** The measures used in the present study included questionnaires regarding participants’ history of marijuana use, preferred methods of use, demographics, state craving level, attention, cognitive load, galvanic skin-response, and heart rate.

**Demographics.** Standard demographics were collected and controlled for in final analyses, including age, sex/gender, and race/ethnicity.

**Marijuana use.** Quantity and frequency of self-reported marijuana use were assessed using a Time-Line Follow Back (TLFB) instrument (Duhig, Cavallo, McKee, George, & Krishnan-Srin, 2005; Sobell & Sobell, 1992). Participants were asked to provide information on events such as parties, holidays, school exams, visits from friends, etc. Participants entered these dates into the TLFB calendar and used the calendar to enhance recall of marijuana use over the past 90 days. Density of use was
assessed by asking how many joints/bowls/cones of cannabis were consumed over the past 90 days.

Craving. One multiple item measure and three single item measures were collected to assess self-reported craving.

Marijuana Craving Questionnaire, 12-item short form (MCQ; Heishman et al., 2009). The MCQ is the only known measure of craving that is designed specifically for marijuana. The MCQ measures four factors of craving: compulsivity (inability to control use, e.g., “I need to smoke marijuana now”), emotionality (relief from withdrawal and negative affect, e.g., “I would feel less anxious if I smoked marijuana right now”), expectancy (anticipation of positive outcomes, e.g., “smoking marijuana would make me content”), and purposefulness (planning/intention to use for positive outcomes, e.g., “smoking marijuana would be pleasant right now”). Items are rated using a Likert scale that ranges from 1 ‘strongly disagree’ to 7 ‘strongly agree.’

Reliability for each of the MCQ’s factor scores is within acceptable range for use in non-treatment seeking cannabis users (Heishman et al., 2001, 2009). Reliability of the overall craving score, however, has not been established. A single-item (VAS) measure of state cannabis craving was used to supplement the multi-item instrument, which was used in final analysis as the main self-report dependent variable (as recommended in Drobes & Thomas, 1999).

Visual-analog scale (VAS1,2). Two single-item measures of self-reported craving were assessed using visual-analog scales. Participants were asked to indicate how strong their “current craving for marijuana is” at two time points (pre/post cue) by making a vertical mark along a line that connects to two anchor statements (i.e., “no
craving,” “very strong craving”. Changes in current rating of craving from Time 1 to Time 2 indicated self-reported craving change (VAS₁). At time two, participants were also asked to indicate how much stronger their craving was after viewing the cues compared to when they began the experiment on a scale from “no change” to “10x stronger” (VAS₂). In each VAS the distance between the first anchor and the participant’s mark was converted to a score from 1-100. Concurrent validity has been established in single-item VAS scales for alcohol craving (Bohn, Krahn, & Stachler, 1995).

Choice of inclusion for final analysis of the self-report craving DV was informed by analyzing the correlation between the three measures (MCQ total change, VAS T1/T2 change, VAS self-reported change), and by comparing the predictive utility of each self-report measure against all other DVs. The correlation matrix for the three self-report measures appears in Table 1.

Total MCQ change scores did not significantly correlate with the other two measures of craving, whereas there was a significant association between the two change scores using the VAS (r = .41, p < .001). Therefore, MCQ was not retained for final analysis. Regression analysis, which regressed the remaining DVs on each VAS change score, produced similar F-values (F(1, 106)₁ = 1.98, F(1, 106)₂ = 1.91) for each regression equation. However, neither of these values was statistically significant. Therefore, the main analysis included only the VAS change score that was computed from VAS ratings of current craving taken before and after cue exposure (VAS₁), because it was most consistent with the style of measurement of all other DVs (residualized change score).
**Autonomic Arousal.** Indication of arousal of the autonomic, sympathetic nervous system was measured through readings of galvanic skin-response (GSR) and heart rate (HR).

**Galvanic skin-response** (GSR; Montagu & Coles, 1966). Electrical skin conductance was measured using the NeuLog GSR sensor system (NeuLog, 2011a). The sensor has two probes with finger connectors that are placed on participants’ nondominant hand on the index and ring fingers. Readings of total conductance in Micro Siemens (μS) were taken at a rate of 10 per second for the entire duration of the experiment. Baseline GSR values were computed from the average μS readings recorded starting 2-3 minutes (based on individual orienting response) after beginning the sensor and 1 minute before introducing the cues. Post cue GSR values were computed from the average μS readings recorded starting 2-3 minutes after the presentation of the cues and 1 minute before the end of the experiment.

**Heart rate** (HR; Porges & Byrne, 1992). Heart rate was measured using the NeuLog Heart Rate and Pulse Sensor (NeuLog, 2011b). The sensor consists of an infrared LED transmitter and matched infrared phototransistor receiver (light detector). The sensor was clipped on to the pad of subjects’ pinky finger. Recordings of heart rate were taken in units of Beats Per Minute (BPM) for the entire duration of the experiment. Baseline HR values were computed from the average BPM recorded starting 2-3 minutes after beginning the sensor (based on individual orienting response) and 1 minute before introducing the cues. Post cue HR values were computed from the average BPM recorded starting 2-3 minutes after the presentation of the cues and 1 minute before the end of the experiment.
**Reaction time.** A simple reaction time (RT) computerized task was used to measure changes in cognitive processing time (PEBL Test Battery; Mueller & Piper, 2014). Participants were instructed to use their dominant hand to hit the space bar as soon as they perceived a light flash on the screen. Subjects were given an opportunity to practice responding to the computer-generated stimulus until they understood the nature of the task prior to their baseline reading. Aggregated mean reaction times to stimuli were used as the primary measure for analysis. RTs below 100ms, the necessary minimum processing time for visual stimuli perception, were counted as anticipation errors and excluded (Whelan, 2008).

**Attentional bias/interference.** Attentional bias to drug-related stimuli were measured using a Drug Stroop Task programmed using Python Software. The Drug Stroop Task is a neuropsychological test used to measure reaction time for recognizing the color of drug-related words compared to neutral words that appear on a computer screen (Cox, Fadardi, & Pothos, 2006). Equal numbers of neutral control words and cannabis related nouns are shown. Lists of neutral and control words are matched on complexity, length, and number of syllables. Parameters for the task were set using the original Drug Stroop Program (Field & Franken, 2014). Each individual word appeared in the middle of the computer screen. Participants were asked to click the correct arrow pertaining to the color of the word without thinking about the word. Time was measured in milliseconds (ms). Total reaction time for all marijuana-related words was regressed on total reaction time for all control words. Residualized scores were retained as the primary outcome measure. In an attempt to limit inadvertent priming, the drug stroop task was only shown to participants after cue exposure and as the final task in the study.
Analytic Plan

Data was analyzed using SPSS 20 and R software with the statistics package (R Core Team, 2013). Choice of analysis was guided by research design and by the experiment’s main hypotheses. The 2 x 3 x 5 experimental design initially suggested the use of either a single MANOVA to test the association between group and condition on all dependent variables (DVs), a series of two-way analyses of variance (ANOVAs) to test the impact of both group and condition on each individual DV, or individual one-way ANOVAs. MANOVA was not chosen apriori due to the high theoretical correlation between each of the dependent variables of interest (Tabachnick & Fidell, 2007). One-way ANOVAs were chosen over two-way ANOVAs, due to the specific nature of the research hypotheses. Significance of the overall F-tests, main effects, and interaction terms within the full two-way model would not address the questions of interest. Follow-up analysis of simple-main effects and contrasts within each of the two-way ANOVAs would be required to answer the research question. For parsimony, a series of independent t-tests and one-way ANOVAs, which directly test the research question, were chosen instead.

Hypotheses 1:

*Those who use cannabis regularly and are exposed to the experimental cues will show the greatest change in self-reported craving following cue exposure*

Hypothesis 2:

*Those who use cannabis regularly and are exposed to the experimental cues will show the greatest change in correlates of craving following cue exposure*

Two findings would need to be present to uphold hypotheses 1 and 2. First, results would need to demonstrate that heavy/daily cannabis users who were exposed to
the experimental cues experienced a greater increase in craving and its theoretical correlates compared to heavy/daily users exposed to control cues. Second, results would also need to demonstrate that heavy/daily cannabis users exposed to the cannabis cues experienced a greater increase in craving and its theoretical correlates compared to infrequent users who were exposed to the same cues.

To test the first requirement, independent t-tests were computed using only the samples of heavy/daily cannabis users. These t-tests compared changes in each of the DVs of interest between cue conditions. For each, test condition (experimental, control) was used as the independent variable (IV). Self-reported craving (VAS) was used as the primary DV to assess hypothesis 1. Galvanic skin response (GSR), heart rate (HR), simple reaction time (RT), and Attentional Bias (bias) were each individually tested to assess hypothesis 2.

To test the second requirement, a series of one-way ANOVAs were computed only among those exposed to the experimental cue. The ANOVAs compared average changes in each of the DVs between the three sample groups. Planned contrasts compared 1. all heavy/daily cannabis users (community and students) with infrequent users (students), and 2. Heavy/daily student users with infrequent student users. The first contrast directly tested the element of hypotheses 1 and 2 that predicted that heavy/daily cannabis users should experience greater indications of craving compared to infrequent users. The second contrast acted as a pseudo control measure, to ensure that any differences on the DVs of interest were a function of cannabis use status and not recruitment type (community versus student).

Hypothesis 3:
Density of current cannabis use will account for differences in self-reported craving among those exposed to the experimental cues

The third hypothesis was tested by regressing past ninety day use on self-reported craving. The regression analysis only included heavy/daily users who were in the experimental cue condition.

All DVs except attentional bias, which was only sampled at Time 2, were computed using the standardized residuals of the correlation between pre and post cue scores. Using these residual scores ensured that “change scores” from Time 1 to Time 2 (change following cue exposure) were free of the effects of baseline (Wright, 2006). All DVs were standardized prior to computing residual change scores to reduce possible inflation of Time 1/Time 2 correlations (Kraemer & Blasey, 2004). Mean, standard deviations, and skewness for all baseline DVs are reported in Table 2.

Power Analysis. Meta-analytic work suggests that average self-reported effect sizes for drug craving are around .92 (Carter, & Tiffany, 1999). However, physiological indicators of craving have lower, moderate effect sizes (GSR: d = +.40). To ensure that the current study was adequately powered to find the between-groups effects of interest, G*Power 3.1 was used to compute the necessary sample size needed (Faul, Erdfelder, Buchner, & Lang, 2009). Using conventional cut-offs for type I and type II error (b = .80, a = .05), the apriori required sample size to compute a one-way ANOVA between groups for a single dependent variable effect of .92 is n = 20. The apriori required sample size for an effect of .40 is n = 76. These estimates are likely rather liberal, however, as I will be running ANOVAs for each of the dependent variables. After a Bonferroni adjustment (a = .05/# of DVs) apriori alpha level was reset at .01. Power analysis at the more conservative alpha found that 104 participants were needed to have
adequate power to find all of the hypothesized effects of the first two hypotheses. Ns of this size are typical of most cue-reactivity studies (Carter & Tiffany, 1999).

A sensitivity test for a predicted sample size of 26 per cell for the within-groups regression analysis with one predictor suggested that the experimental design would be sensitive to effect sizes greater than $d = .28$, which is consistent with reported craving effect sizes. Incremental increases in use should theoretically account for a large proportion of variance if cannabis craving is an artifact of consistent and frequent use. Moreover, for the association between use and craving to be clinically relevant, it should be moderate to large.

**Results**

**Preliminary Analysis**

**Demographics.** Descriptive analysis of demographics for each sample appears in Table 3. The infrequent user sample was designed to function as a pseudo control against the active student user group, and so group differences between the two student samples were tested using independent t-tests and chi-square tests. Given the nature of the intended samples, significant differences in average age of initiation of cannabis use and average days per week of cannabis use were anticipated and upheld. However, the control sample also differed from the active student user sample in gender ratio, which was not expected. The control sample consisted of 50% male participants and 50% female participants, whereas the active student user sample was overwhelmingly male (84.4%).

It was not unsurprising that one of the active user samples would include a disproportionate percentage of women, given that a greater ratio of men report using
cannabis in the general population (SAMHSA, 2014). Nevertheless, the sample that included community users included a gender ratio that more closely aligned with the control sample, and significantly differed from the college student sample of active users ($\chi^2 (1, n = 74) = 13.14, p < .001$). Previous work suggests that symptoms of dependence, which would potentially include craving, develop at differential rates for men and women (Lynch, 2002). Group differences in the male/female ratio between the control and active student user sample could have potentially impacted group differences between our main DVs of interest. Therefore, all analyses that directly compared across the college student samples initially included gender as a covariate. Inclusion/exclusion of gender did not impact the significance trend in any of the primary analytic tests. Therefore, gender was excluded as a covariate in final analysis to ease the interpretation of main group effects.

Descriptive analysis of demographics of participants by condition appears in Table 4. All participants were randomly assigned to receive either the experimental or control cues (condition). Owing to the nature of random assignment, no demographic differences between conditions were anticipated. Independent t-tests and chi-square tests were used to ensure equal demographic representation. Participants randomly assigned to the control condition did not significantly differ from those assigned to the experimental condition in average age, frequency of cannabis use, age of initiation of cannabis use, male to female ratio, or representative ethnicities.

**Analysis of Assumptions.** The analytic plan called for the use of two parametric tests (one-way ANOVA, independent t-test). All parametric tests rely on an assumption that data is sampled from a normally distributed population. ANOVA and the independent-t are typically robust to minor violations of assumptions of normality.
(Harwell et al., 1992). However, when groups have different sample size it is critical that the assumption of homogeneity of variance is met. Specifically, when the group with the largest sample size also has the largest variance and assumptions have not been met, type II error risk increases. When the group with the largest sample size has the smallest variance and assumptions have not been met, type I error risk increases (Glass, Peckham, & Saunders, 1972). Sample sizes across groups and conditions were not even. Therefore, all variables included in final analysis were tested to ensure that their data were normally distributed.

Visual inspection of outliers and tests of skewness and kurtosis revealed that the GSR and past ninety day use variables both showed some positive skew ($S_{GSR} = 1.9$; $S_{90dayUse} = 2.32$), which was adequately corrected for with square-root transformations ($S_{GSR} = .67$; $S_{90dayUse} = .47$). Group comparisons of variance ratios suggested that GSR’s group variance ratios violated the assumption of homogeneity of variance, as the variance ratio of community users compared to both samples of students was greater than 2 ($SD^2_{community} = .07$, $SD^2_{studentheavy} = 2.31$, $SD^2_{studentinfrequent} = 1.44$). However, mean differences were only computed when collapsing across community and student users. The combined heavy/daily user group’s variance ($SD^2_{combined} = 1.1$) was less than 2x the variance of the comparison group ($SD^2_{studentinfrequent} = 1.44$), so no variance transformation was required for final analysis.

All analyses were computed using univariate statistics. Mahalanobis distances (MD) were computed, however, to determine whether any one participant responded consistently deviant from all other subjects across DVs. The Mahalanobis critical value
for five DVs (df = 4) was \( MD_{crit} = 18.47 \). All subjects’ MD’s failed to reach significant
(\( MD_{obt} < 18.47 \)).

**Main Analysis**

**Hypotheses 1 and 2.** Five independent t-tests were used to test mean differences in changes on each of the DVs between participants exposed to the experimental cues and those exposed to the control cues. These tests only included subjects who were recruited as heavy/daily users, but included users from both recruitment populations (community and student). Results for all five tests appear in *Table 5*. Results did not uphold the first hypothesis that heavy/daily users would self-report a greater increase in craving following being exposed to cannabis cues compared to being exposed to control cues. The t-test that analyzed average change in self-reported craving between conditions failed to reach significance (\( t = -.17, 95\% CI: -.57 - +.48; d = .04 \)).

Results partially upheld the second hypothesis that heavy/daily users would experience a greater increase in correlates of craving following being exposed to cannabis cues compared to being exposed to control cues. Heavy/daily cannabis users showed an increase in GSR following cannabis cue exposure (\( M = .32, SD = 1.05 \)), and a decrease in GSR following exposure to the neutral, control cues (\( M = -1.8, SD = .56 \)). The average change in GSR scores from Time 1 to Time 2 was significantly different between conditions (\( t = -2.24, 95\% CI: -.94 - -.05; d = .53 \)). However, changes from Time 1 to Time 2 in HR (\( t = -1.24, 95\% CI: -1.01 - +.17 \)) and RT (\( t = .20, 95\% CI: -.45 - +.56 \)) failed to reach significance, as did differences between conditions in attentional bias (\( t = -1.12, 95\% CI: -.04 - +.01 \)).
Five one-way ANOVAs were used to test whether heavy/daily cannabis users recruited from the community and university both experienced a greater increase in craving and its theoretical correlates following cannabis cue exposure compared to infrequent cannabis users. Hypotheses 1 & 2 only predicted differences between heavy/daily cannabis users and those with little experience with the plant. Therefore, interpretation of the ANOVAs focused on two sets of planned contrasts rather than the overall, omnibus F test. The first contrast tested whether average DV change scores among all heavy/daily cannabis users differed from average change scores on all DVs among the infrequent users. Mean change scores for all heavy/daily users were collapsed across recruitment type (community, student). To ensure that any significant differences found within contrast 1 were not attributable to differences between groups in recruitment population (i.e., the inclusion of community users only in the heavy/daily category), a second planned contrast compared the two student samples (heavy/daily users, infrequent users) on each of the same DVs. Results for all ANOVAs appear in Table 6.

This second set of analyses did not provide support to uphold the first hypothesis that heavy/daily users would experience the greatest increase in self-reported craving compared to infrequent users. After collapsing across recruitment type, heavy/daily users reported no increase in craving following exposure to cannabis cues (M = .00, SD = 1.14). Meanwhile, infrequent users did report an increase in craving (M = .46,SD = 1.23), though the difference between groups did not reach significance ($F(2, 47 = 1.25, p = .30)$. Moreover, heavy/daily users recruited from the community actually reported a decrease in craving from baseline (M = -.19, SD = .67). Though the change failed to reach significance. ($t = -.15, p = .88$).
Results of the additional ANOVAs, which tested each of the correlates of craving as separate DVs, provided some support to partially uphold hypothesis 2. As in the t-tests conducted above, a significant between-subjects effect was found for GSR, but not for HR, RT, or Attentional bias. Results of the first contrast found a significant difference between groups, such that heavy/daily cannabis users experienced a greater increase in GSR following cannabis cue exposure compared to infrequent users ($M_{\text{heavy}} = .32$, $SD_{\text{heavy}} = 1.05$; $M_{\text{infrequent}} = -1.23$, $SD_{\text{infrequent}} = 1.2$). Moreover, results of the second contrast found a significant difference between heavy/daily student users and infrequent student users, which was similar in effect size to the first contrast ($d_{\text{contrast1}} = 1.07$, $d_{\text{contrast2}} = 1.14$). This finding supports the conclusion that differences between user groups are likely attributable to cannabis user categorization and not to recruitment group type (community, student).

**Hypothesis 3.** A single regression equation was used to test whether a linear association exists between density of cannabis use and craving. VAS$_2$ was regressed on past ninety day use (square root transformed). Only heavy/daily users who were randomly assigned to the experimental condition were included in the analysis. No significant linear association was found ($F(1, 34) = .02$, $p = .878$). A scatterplot showing the best prediction line between each variable appears in Figure 1.

In sum, findings were not able to uphold the first hypothesis that heavy/daily users would show an increase in self-reported craving when exposed to cannabis cues, but were able to provide modest support that correlates of craving would be impacted by cannabis cue exposure. Namely, heavy/daily users experienced a significant increase in galvanic skin response when exposed to cannabis cues. However, no changes in heart
rate, reaction time, or attentional bias were found. Finally, hypothesis three was not supported, as past ninety day use did not significantly predict changes in craving.

**Secondary Correlation Analysis**

Pearson product-moment correlation coefficients ($r$) were computed between each dependent variable of interest to provide further context for interpreting the results of the main analysis. Correlations between the baseline dependent variable scores appear in Table 7. Correlations between the residualized change scores of all dependent variables appear in Table 8. Significant associations were found between HR and RT, and the two physiological measures (HR, GSR). Similar associations were present within both the baseline and residualized change measurements.

**Discussion**

The purpose of the current study was to test whether a cue-reactivity paradigm could successfully be applied to non-treatment seeking cannabis users to induce craving. Cue-reactivity is the standard paradigm used in research studies for inducing drug-related craving. For a cue-reactivity paradigm to be successful, craving must be able to be induced by a drug-related cue. These paradigms assume that craving is the consequence of associative and instrumental learning. Use of cannabis, however, impairs associative learning and may not act as a strong reinforcer. Research has been equivocal on whether consistent and frequent use of cannabis can lead to craving in similar ways as other drugs of abuse. The present study, therefore, sought to apply the cue-reactivity paradigm to cannabis in order to test whether exposure to cannabis cues would lead to an increase in craving. The study also sought to test whether physiological and cognitive changes
would be present following cue presentation, which would indicate that associative and instrumental learning had occurred.

**Hypothesis 1**

Results did not provide support for the first hypothesis. Heavy/daily users did not report a significant increase in craving following being exposed to the experimental cues. Trends among the community sample even indicated a possible decrease in self-reported craving. Comparisons with the infrequent, control sample suggested an opposite trend, where infrequent users were reporting greater craving than both groups of heavy/daily users. The effect did not reach statistical significance, possibly due to limited power. This finding is inconsistent with previous published studies that have successfully used cue-reactivity paradigms with cannabis users (Lundahl & Johanson, 2011; Nickerson et al., 2011; Wolfling, Flor, & Grusser, 2008). Given previous positive findings, it is curious that the current sample would show no change and perhaps even a reduction in craving following interaction with drug paraphernalia and other cues. This finding is not, however, inconsistent with neurological research on intoxication effects of cannabis. If cannabis impairs associative learning, then we would not expect that a cannabis cue would develop emotional and motivational salience, and so should not lead to a learned craving response.

**Hypothesis 2**

Results provided partial support for the second hypothesis. Heavy/daily users did show elevations in galvanic skin response (GSR) following exposure to cannabis cues. Consistent with theory, those with little experience with the plant did not show the same increase in GSR. These findings suggest that regular use of cannabis might increase the
emotional salience of cannabis-related paraphernalia. Nevertheless, heavy/daily and infrequent users did not show differences in changes in heart rate (HR), which, if present, would also have indicated emotional reactivity was present. Given the positive correlation between HR and GSR, the fact that differences in HR failed to reach significance raises questions about drawing meaningful inference solely from GSR elevations. Moreover, no differences were found in reaction time (RT) and attentional bias. If a cue has been associated with reward and has taken on incentive value, then we would expect to see changes in attention to those incentive-associated cues. The present study’s results, however, do not support the theory that regular use of cannabis leads to an association between cannabis cues and reward. Taken together, results do not provide a clear answer as to whether cannabis cues can develop emotional salience and incentive value, which would be necessary to indicate that a craving state is occurring.

**Hypothesis 3**

Results did not support the third hypothesis that incremental increases in cannabis use would be associated with increases in reactivity to cues. Heavy/daily cannabis users who were exposed to cannabis cues showed no difference in self-reports of increased craving across levels of use. If cannabis craving develops as a function of associative pairing, then we would expect that more use would equate to more learning. Therefore, a linear association was predicted between use history and experience of craving, which was not upheld. This failure to find an effect is not surprising given the insignificant results found when testing hypothesis one. The third hypothesis focused only on a subset of heavy/daily users, whereas the first hypothesis tested the most discrepant users against one another. If differences in self-reported craving were not present when comparing
novice to heavy users, it would be odd to find a meaningful effect when comparing small incremental differences in heavy/users. The nonsignificant findings, however, could be attributable to a ceiling effect. All participants included in analysis of hypothesis 3 reported using cannabis at least four days per week, every week over the past ninety days. This frequency of use might represent the maximal amount necessary to create a craving effect, where any use beyond that value no longer leads to an effect. Nevertheless, if a craving effect existed that was dependent on frequency/density of use it would have been present in the analysis of hypothesis 1.

**Inconsistency Across Findings**

The apparent inconsistency across results creates challenges for drawing inference. The finding that heavy/daily users showed an increase in GSR following cue exposure might suggest that developing an emotional association between cannabis cues and the intoxication effects of cannabis is in fact possible. The fact that HR did not also change in response to cannabis cues, however, undermines this conclusion. Moreover, even if we assume that an emotional association was created, we do not know whether that emotional response indicates craving. GSR was recorded as an indicator of Sympathetic Nervous System (SNS) activity. All activation of the SNS would lead to an increase in GSR. A range of emotional states are associated with increased SNS activity, and thereby, GSR activity (Kreibig, 2010). Increased GSR might not indicate craving.

The difficulty of interpreting one significant physiological finding is compounded by the failure to find an effect between groups in self-reported craving. One explanation for this apparent mismatch in cognitive and physiological findings could be that users are unconsciously experiencing craving but consciously unaware of the change. Human
beings are notoriously bad at knowing why they do what they do and feel what they feel. Emotions are interpreted cognitively (Schachter & Singer, 1962). Conscious interpretation of emotions is prone to error. Research consistently finds that people regularly misinterpret physiological indications of emotional activation as different emotional states (White, Fishbein, & Rutsein, 1981). For the present study, it might be that heavy/daily cannabis users are experiencing a craving state, but consciously don’t recognize the experience as craving or misattribute it. This assertion fits well with what we see in treatment centers, where users are often unable to identify the catalyst for their most recent relapse.

Nevertheless, the idea that craving might occur at an unconscious level does not fit with previous reports on the function of craving. A proportion of individuals in treatment centers do identify craving, even for cannabis, as a major reason for relapse (Budney et al., 2008; Vandrey et al., 2008; McRae et al., 2007; Coffey et al., 2002; Swift, Hall & Teeson, 2001). To identify craving as problematic relies on one’s ability to consciously be aware that craving has occurred. This research has been used as the basis for including self-reported craving as one criterion in the diagnosis of substance use disorders. Moreover, interventions that target craving rely on the individual’s ability to consciously recognize that craving is present. This does not fit well with assertions that craving might not be a conscious phenomenon. If craving truly does occur at an unconscious level, then it would not be appropriate as a target for cognitive intervention nor as a means of diagnostic assessment.

The question of whether or not individuals are able to consciously recognize the craving state is also blurred by the fact that the literature has yet to adopt a single agreed
upon definition for craving. If scientists differ in their conceptualization of what craving represents, it seems foolish to assume that lay individuals would somehow all agree. By asking participants to rate their experience of craving, we open the definition of “craving” up to individual interpretation. Low bivariate correlations between- and high SDs within - the self-report craving variables might indicate that participants were responding differentially to being asked about craving. This raises obvious questions about the psychometric utility of assessing craving through self-report. It also lends further support to the conclusion that participants in the current study did not experience a cued change in what the field currently refers to as “craving.”

**Implications and Future Research**

The current study’s findings were not consistent with the types of predictions that a cue-reactivity model of craving would make. The results suggest that craving for cannabis might not fit with the universal bio-behavioral model of craving development. This does not mean that craving for cannabis does not occur. On the contrary, clinical research clearly suggests that a large number of cannabis users in treatment report that they experience craving and that it is detrimental to their recovery (Budney et al., 2008; Vandrey et al., 2008). Instead, the results suggest that caution should be heeded before applying cue-reactivity paradigms as a test for cannabis craving interventions. Before we can develop and test interventions that serve to reduce craving, we must be able to measure and define it. The results also call into question the use of self-report measures of cannabis craving.

Given that clinical populations of problematic cannabis users report experiencing craving, future studies should focus on creating an empirically informed definition of
craving for the plant. Work that attempts to understand the function of craving within this population is also necessary. Whether or not the craving state is consciously recognized and labeled as “craving” might be less important than whether or not the emotional experience leads to an increased motivation for use. Future work might consider comparing the impact of cannabis cues on changes in interest or actual changes in future behavior, rather than the unclearly defined notion of craving.

**Limitations**

The present study is the first of its kind to test whether cue-reactivity can be applied to cannabis in a sample of non-treatment seeking cannabis users. The study’s findings are noteworthy because they fail to replicate a growing body of literature that is being used to develop diagnostic schemes and interventions, perhaps prematurely. The study is limited, however, by the lack of control group for the community sample of heavy/daily cannabis users. Student participants were necessary to be able to recruit a pseudo control condition. Therefore, only the responses of the heavy/daily student users were able to be adequately tested for differences that arose as the result of use. Moreover, the difficulty in recruiting novice users and ease of recruitment of heavy/daily users suggest that each population likely differs in their motivations for involvement in cannabis research. In light of current debates on the legalization of cannabis, heavy/daily users might be motivated to engage in this type of research in an attempt to underscore nonproblematic use. Attitudes toward use and beliefs about the addictive potential of cannabis should be controlled for in future studies.
References


Drummond, D. C. (2000). What does cue-reactivity have to offer clinical research? *Addiction, 95*, 129-144


Table 1

Correlation between self-report measures of craving

<table>
<thead>
<tr>
<th></th>
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<th>2</th>
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</thead>
<tbody>
<tr>
<td>1 MCQ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 VAS1</td>
<td>.04</td>
<td></td>
</tr>
<tr>
<td>3 VAS2</td>
<td>-.09</td>
<td>.41**</td>
</tr>
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* = p < .05; ** = p < .01
MCQ = Residualized change in Total MCQ Score from Time 1 to Time 2
VAS1 = Residualized change in VAS rating of current craving from Time 1 to Time 2
VAS2 = Self-reported perceived change in VAS rating of craving
Table 2

Means, SDs, and Skewness for all baseline DVs

<table>
<thead>
<tr>
<th></th>
<th>M (SD)</th>
<th>Range</th>
<th>Skew</th>
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<tbody>
<tr>
<td>VAS\textsuperscript{T1}</td>
<td>15.74 (19.64)</td>
<td>0 - 81</td>
<td>1.39</td>
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<tr>
<td>GSR\textsuperscript{T1}</td>
<td>2.44 (3.19)</td>
<td>.7 - 9.99</td>
<td>-1.029</td>
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<tr>
<td>HR\textsuperscript{T1}</td>
<td>77.72 (10.94)</td>
<td>54.63 - 110.42</td>
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<tr>
<td>RT\textsuperscript{T1}</td>
<td>355.18 (59.45)</td>
<td>275.79 - 595.59</td>
<td>1.44</td>
</tr>
<tr>
<td>Past-90</td>
<td>30.18 (37.51)</td>
<td>0 - 240</td>
<td>2.318</td>
</tr>
</tbody>
</table>

\textsuperscript{T1} = Baseline self-reported craving using Visual Analogue Scale
\textsuperscript{T1} = Resting Galvanic Skin Response in Micro Siemens (\(\mu\)S)
\textsuperscript{T1} = Resting heart rate in Beats per Minute (BPM)
\textsuperscript{T1} = Baseline Simple Reaction Time
Past-90 = Total cannabis use over past ninety days (joints/bowls/cones)
Table 3

Demographics by sample
(N – 104)

<table>
<thead>
<tr>
<th></th>
<th>Community (n =42)</th>
<th>College - Active Users (n = 32)</th>
<th>College - Infrequent Users (n = 30)</th>
<th>Significant Difference Between College Samples</th>
<th>Total N = 104</th>
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</tr>
<tr>
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<td>18.75</td>
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<td>18-28</td>
<td>18-21</td>
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</tr>
</tbody>
</table>

**First Use Cannabis (Age)**

|                          |                 |                               |                                   |                                               |              |
|--------------------------|                 |                               |                                   |                                               |              |
| Mean                     | 15.71           | 15.16                         | 17.35                             | p < .05                                       |              |
| SD                       | 3.56            | 1.68                          | 1.49                              |                                               |              |
| Range                    | 10-25           | 12-18                         | 13-21                             |                                               |              |

**Days/Week Cannabis Use**

|                          |                 |                               |                                   |                                               |              |
|--------------------------|                 |                               |                                   |                                               |              |
| Mean                     | 5.36            | 4.41                          | 0.1                               |                                               |              |
| SD                       | 2.85            | 2.66                          | 0.3                               |                                               |              |
| Range                    | 0-7             | 0-7                           | 0-1                               |                                               |              |

**Gender**

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<th>n</th>
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<th>n</th>
<th>%</th>
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<th>%</th>
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**Ethnicity**

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Table 4

Demographics by condition (N = 104)

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<th>Significant difference between conditions</th>
<th>Total</th>
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<td>18-62</td>
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<td>4</td>
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<td>Other</td>
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<td>Multiple Ethnicities</td>
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<td>2</td>
<td></td>
<td>3</td>
</tr>
</tbody>
</table>
Table 5

Main effects of condition among heavy/daily cannabis users

| Variable | Experimental (n = 36) | | | | | | Control (n = 38) | | | | | | | | | | Independent t-test |
|----------|----------------------|-----------------|----------------|----------------|----------------|----------------|----------------|----------------|-------------------|
|          | M (SD)               | M (SD)          | Residual Change | M (SD)         | M (SD)         | M (SD)         | M (SD)         | M (SD)         | t                 | 95% CI          | d               |
| VAS      | 15.29 (15.38)        | 17.68 (19.14)   | .00 (1.14)      | 27.03 (24.42)  | 9.35 (24.61)   | -.04 (.96)     | -.17           | -.57 - +.48    | .04               |
| GSR      | 1.52 (3.85)          | 4.06 (2.36)     | .32 (1.05)      | 3.14 (2.99)    | 3.87 (3.21)    | -1.8 (.56)     | -2.24*         | -.94 - -.05     | .53               |
| HR       | 77.11 (11.18)        | 76.68 (19.14)   | .15 (1.15)      | 78.31 (12.12)  | 76.27 (11.23)  | -.26 (1.07)    | -1.42          | -1.01 - +.17    | .33               |
| RT       | 348.61 (38.34)       | 365.67 (51.64)  | .07 (1.15)      | 359.25 (82.81) | 375.73 (73.04) | .12 (.82)      | .20            | -.45 - +.56     | .05               |
| Bias     | -                    | 1.02 (.05)      | -              |               | 1.00 (.05)     | -              | -1.12          | -.04 - +.01     | .26               |

* = p < .05

VAS = Self-reported craving using Visual Analogue Scale
GSR = Galvanic Skin Response in Micro Siemens (μS)
HR = Heart rate in Beats per Minute (BPM)
RT = Simple Reaction Time
Bias = Attentional bias in Drug Stroop Task

Note: Time 1 and Time 2 reported as raw scores; residual change reported as standardized scores
Table 6
Differences between user groups following cannabis cue exposure

<table>
<thead>
<tr>
<th>Variable</th>
<th>Community (Heavy/Daily) (n = 21)</th>
<th>Student (Heavy/Daily) (n = 15)</th>
<th>All Heavy/Daily (n = 36)</th>
<th>Student (Infrequent) (n = 13)</th>
<th>Omnibus</th>
<th>ANOVA Contrast Analysis (d)</th>
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</thead>
<tbody>
<tr>
<td>VAS</td>
<td>-.19 (.67)</td>
<td>.31 (1.63)</td>
<td>.00 (1.14)</td>
<td>.46 (1.23)</td>
<td>1.25</td>
<td>.28</td>
</tr>
<tr>
<td>GSR</td>
<td>.11 (.27)</td>
<td>.56 (1.52)</td>
<td>.32 (1.05)</td>
<td>-1.23 (1.2)</td>
<td>4.58*</td>
<td>1.07**</td>
</tr>
<tr>
<td>HR</td>
<td>.54 (.97)</td>
<td>-.25 (1.22)</td>
<td>.15 (1.15)</td>
<td>-.15 (1.11)</td>
<td>2.14</td>
<td>.18</td>
</tr>
<tr>
<td>RT</td>
<td>-.12 (1.24)</td>
<td>.36 (.96)</td>
<td>.07 (1.15)</td>
<td>-.49 (1.12)</td>
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<td>.38</td>
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<tr>
<td>Bias</td>
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<td>1.01 (.04)</td>
<td>1.02 (.05)</td>
<td>1.00 (.04)</td>
<td>0.42</td>
<td>.24</td>
</tr>
</tbody>
</table>

* = p < .05

VAS = Self-reported craving using Visual Analogue Scale
GSR = Galvanic Skin Response in Micro Siemens (μS)
HR = Heart rate in Beats per Minute (BPM)
RT = Simple Reaction Time
Bias = Attentional bias in Drug Stroop Task

Note: Time 1 and Time 2 reported as raw scores; residual change reported as standardized scores
Table 7

Bivariate correlations between baseline DV scores

<table>
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<tr>
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<th>1</th>
<th>2</th>
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</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>VAS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>GSR</td>
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<td>3</td>
<td>HR</td>
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<td>.26*</td>
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<td>4</td>
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<td>.08</td>
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</tbody>
</table>

* = p < .05

VAS = Self-reported craving using Visual Analogue Scale
GSR = Galvanic Skin Response in Micro Siemens (μS)
HR = Heart rate in Beats per Minute (BPM)
RT = Simple Reaction Time
Table 8

Bivariate correlations between residualized change scores

<table>
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<tr>
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<th>1</th>
<th>2</th>
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<tr>
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<tr>
<td>GSR</td>
<td>-.15</td>
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<tr>
<td>HR</td>
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<tr>
<td>RT</td>
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<td>.08</td>
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<tr>
<td>Bias</td>
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</table>

* = p < .05
VAS = Self-reported craving using Visual Analogue Scale
GSR = Galvanic Skin Response in Micro Siemens (μS)
HR = Heart rate in Beats per Minute (BPM)
RT = Simple Reaction Time
Bias = Attentional bias in Drug Stroop Task
^Time 2 score
Figure 1. Scatterplot of craving change regressed on density of use

\[ y = 0.0128x - 0.081 \]

\[ R^2 = 0.0008 \]