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Reactivity to nicotine cues over repeated cue reactivity sessions

Steven D. LaRowe, Ph.D^{1,2}, Michael E. Saladin, Ph.D^{3,4}, Matthew J. Carpenter, Ph.D^{3,5}, and Himanshu P. Upadhyaya, M.B.B.S., M.S^{3,*}

¹ Center for Drug and Alcohol Programs, Dept. of Psychiatry and Behavioral Sciences, Medical University of South Carolina (MUSC), Charleston SC, 29425

² Substance Abuse Treatment Center, Mental Health Service, Ralph H. Johnson, VAMC

³ Division of Clinical Neurosciences, Dept. of Psychiatry and Behavioral Sciences (MUSC)

⁴ Department of Rehabilitation Sciences, College of Health Professions (MUSC)

⁵ Hollings Cancer Center (MUSC)

Abstract

The present study investigated whether reactivity to nicotine-related cues would attenuate across four experimental sessions held one week apart. Participants were nineteen non-treatment seeking, nicotine-dependent males. Cue reactivity sessions were performed in an outpatient research center using in vivo cues consisting of standardized smoking-related paraphernalia (e.g., cigarettes) and neutral comparison paraphernalia (e.g., pencils). Craving ratings were collected before and after both cue presentations while physiological measures (heart rate, skin conductance) were collected before and during the cue presentations. Although craving levels decreased across sessions, smoking-related cues consistently evoked significantly greater increases in craving relative to neutral cues over all four experimental sessions. Skin conductance was higher in response to smoking cues, though this effect was not as robust as that observed for craving. Results suggest that, under the described experimental parameters, craving can be reliably elicited over repeated cue reactivity sessions.

Keywords

Cue reactivity; nicotine; repeated sessions

*Corresponding Author (the work was carried out at the same institution): Department of Psychiatry and Behavioral Sciences, PO Box 250861, Medical University of South Carolina, Charleston SC, 29425, upadhyah@musc.edu, Office Phone: 843-792-5205, Fax: 843-792-0528.

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1. Introduction

While craving occupies a central conceptual role in addictive behaviors research, no consensus has been reached regarding its definition (Pickens & Johanson, 1992). Despite the lack of consensus, one common feature of many definitions of craving is that it is a subjective state of desire with motivational properties that have an important role in the procurement and consumption of drugs (cf., Sayette et al., 2000) as well as relapse to drug use (Childress, McLellan, & O'Brien, 1988; Wise, 1988). The cue reactivity paradigm has been used to systematically study craving (Drobes, Saladin, & Tiffany, 2001; Drummond, Tiffany, Glautier, & Remington, 1995). In a typical cue reactivity study, cues such as drug-related pictures, movies, and/or paraphernalia are presented to participants in a controlled laboratory setting. While numerous response systems have been monitored during cue presentations, the most conceptually important of these responses is subjective craving. Generally, drug-dependent individuals report greater craving in response to cues associated with their drug of choice as compared to neutral cues (Drobes et al., 2001; Drummond et al., 1995). Measures of craving and cue reactivity have been used within the field of addictions research to predict relapse in drug-dependent individuals as well as assess the efficacy of novel pharmacological agents for the treatment of addictions (Carter & Tiffany, 1999; Modesto-Lowe & Kranzler, 1999).

Although numerous theoretical accounts of craving and cue reactivity have been posited, most models postulate a central role for associative learning mechanisms (Childress, Ehrman, Rohsenow, Robbins, & O'Brien, 1992). These models maintain that cues that have been reliably paired with previous drug administration or withdrawal will elicit Pavlovian conditioned reactions when the cues are subsequently encountered. While conditioning models have many similar features, they differ with regard to the nature and form of the conditioned reactions. Appetitively-based models assume that the conditioned reactions are consistent with the rewarding or excitatory effects of the drugs (Stewart, DeWitt, & Eikelboom, 1984; Wise, 1988) whereas aversive or withdrawal-based accounts assume the reactions take the form of withdrawal-like responses (Poulos, Hinson, & Siegel, 1981; Siegel, 1983; Wikler, 1980). Other models suggest that cues may activate both appetitively-based and withdrawal-based mechanisms that in turn contribute to the generation of cravings (Baker, Morse, & Sherman, 1987; Niaura et al., 1988). Despite the differences between these theoretical accounts, all of the models argue that cue-elicited craving and reactivity are important motivators of drug seeking and consumatory behaviors.

If cue-elicited craving and reactivity have a causal role in the maintenance of substance use (among non-treatment seeking individuals), then it should be expected that the response-eliciting properties of substance-paired cues should be maintained over time or across multiple cue reactivity assessments (i.e., if cues don't maintain their potency over time, they aren't likely to have an important role in addictive behavior). This expectation would also be consistent with the aforementioned learning models since active use should sustain the associative learning mechanisms that presumably underlie cue-elicited craving and reactivity. Despite decades of research, relatively few studies have examined cue reactivity over repeated laboratory sessions. A number of 2-session studies have been conducted to assess initial efficacy of various medications for the treatment of cocaine dependence. These

studies have generally found evidence for a reduction in reactivity from the first to the second session (Hersh, Bauer, & Kranzler, 1995; Modesto-Lowe, Burleson, Hersh, Bauer, & Kranzler, 1997; Reid, Mickalian, Delucchi, & Berger, 1999), regardless of whether the medication under study produced any significant effects. However, with only two sessions of cue reactivity, it is difficult to know whether the reduction was the product of acclimation to the novel experimental setting and assessment procedures, or rather a genuine reduction in craving and reactivity in response to the substance cues. Moreover, since these studies had treatment components (i.e. experimental medication), it is possible that the perceived demand characteristics of the study may have led to a reduction in self-reported cravings.

Within the nicotine literature, there have been relatively few studies that have investigated the cue reactivity over repeated sessions. In one such study, Drobos and Tiffany (Drobos & Tiffany, 1997) presented smoking imagery cues and in vivo cues (a confederate smoking) in one session, after which participants either continued to smoke as usual or abstained for 6 hours, then completed a second cue reactivity session. Results suggested that individuals experienced *greater* cue-induced craving in the second session, but since the study had some participants abstain from smoking, it is unclear whether the greater second session craving was a function of this experimental manipulation. Tiffany et al. (Tiffany, Cox, & Elash, 2000) presented in vivo cues (also involving a confederate smoking) in one session, after which participants wore either a nicotine or placebo patch and abstained for 6 hours, then completed a second cue reactivity session. Results indicated increased baseline craving in the second session, but decreased cue-induced craving. Cooney et al. (Cooney, Cooney, Pilkey, Kranzler, & Oncken, 2003) examined alcohol-dependent smokers that participated in two cue reactivity sessions held 48–72 hours apart. All participants were assessed, in a counterbalanced fashion, under conditions of nicotine deprivation (approximately 36 hours of abstinence) and non-deprivation (ad libitum smoking). During both sessions, participants rated their alcohol and nicotine craving in response to alcohol and alcohol-associated imagery. Results indicated that, regardless of nicotine deprivation and cue condition, there was a general reduction in self-reported craving from the first to the second session. Recently, a large 4-session cue reactivity study was completed in which slides depicting nicotine-related cues were presented (Carter et al., 2006). Although slides were rated at the end of the study after participants had already viewed them 4 times, the smoking-related pictures evoked robust cravings. It is important to note, however, that over the course of this earlier multi-session study, participants were either deprived of nicotine for 12 hours, and/or received nicotine nasal spray prior to cue presentation. Thus, it is unclear whether or not these manipulations influenced the maintenance of craving over the 4 sessions.

Taken together, the long-term nature of cue-induced reactivity is unclear. As noted above, a number of cocaine studies have noted first to second session decrements. There are many potential causes for these decrements, including extinction to the cues themselves, a reduction in novelty from the first to second session, or even demand characteristics, since all of the above-cited studies had some form of treatment component. Within the nicotine literature, some multi-session studies exist, but there has typically been some form of between-session manipulation such as nicotine deprivation and/or some form of nicotine replacement during cue reactivity sessions. In contrast to these earlier studies, the present

study assessed reactivity to smoking-related cues over four assessment sessions in nicotine-dependent men who were neither treatment seekers nor deprived of nicotine. This controlled, multi-session methodology not only permitted the assessment of a potential novelty-related decrement in craving and reactivity, but also allowed for evaluation of the potency of smoking related cues over a longer period of time and across a greater number of assessments under non-deprived conditions. It was expected that smoking-related cues would evoke greater cue reactivity (i.e. greater craving and physiological reactivity) relative to neutral cues across all 4 experimental sessions.

2. Methods

2.1 Participants

The present study recruited non-treatment seeking nicotine dependent males between the ages of 18 and 40 who smoked at least 10 cigarettes per day for the past 3 months and who reported experiencing addiction to and craving for cigarettes. All potential participants completed a confidential phone screening to ascertain initial eligibility. Those who qualified and who were interested in participating were invited to an informed consent session at the Department of Psychiatry and Behavioral Sciences at the Medical University of South Carolina (MUSC). Upon completing consent, participants attended additional screening sessions to determine eligibility. Screenings involved SCID-IV administration, as well as a urine drug screen (UDS). Participants were also screened for breath alcohol level (BAL) and carbon monoxide (CO) level. Participants were compensated \$50 for completing the screening. Participants were ineligible if they reported any major axis I psychiatric disorder (e.g., major depression), within the past 30 days, verified by the Structured Clinical Interview for DSM-IV-TR (First, Spitzer, Gibbon, & Williams, 2002). Participants were excluded if they showed evidence of current (within past 30 days) substance use disorders other than nicotine and caffeine, use of psychotropic medication, or use of medication (e.g. beta blockers) that might affect measurement of physiological indices (e.g. heart rate or skin conductance). Medical conditions (e.g., hypertension, arrhythmia) that could affect physiological indices of reactivity were also exclusionary. The current sample was part of a larger study examining gender differences in smoking cue-reactivity. Only males were recruited in this analysis to avoid the potential confound of menstrual cycle effects (Carpenter, Upadhyaya, LaRowe, Saladin, & Brady, 2006). Between April of 2003 and May of 2005, 39 male participants met initial criteria and completed informed consent. Of those, 6 were later found to not meet inclusion/exclusion criteria. Of the remaining 33, 13 did not complete all four sessions and were excluded from the present analysis; another was excluded due to excessive movement during the cue reactivity sessions that interfered with collection of physiological measures. The 19 males who completed all 4 sessions had a mean age of 30.1 ($SD = 6.4$). The sample consisted of 16 Caucasians, 2 African Americans, and 1 Hispanic. Mean daily cigarette use was 19.4 ($SD = 8.8$), and participants had been regular users of cigarettes for an average of 11.7 years ($SD = 6.7$).

2.2 Cues

2.2.1 Smoking Cues—Smoking cues consisted of a pack of the participant's preferred brand of cigarettes and a lighter. Standardized directions were recorded to instruct the

participant in handling the cues and presented over BOSE sound canceling headphones. Cues were initially covered with a box. The participant was signaled to remove the box, and to look at the cues for 15 seconds. Next, participants were instructed to take one cigarette from the pack and hold it between his/her fingers as they normally do while smoking. After 15 seconds, participants were instructed to handle the cigarette and then smell it for 10 seconds. The participants were then instructed to pick up the lighter. Participants were instructed to flick the lighter without actually lighting the cigarette (laboratory regulations prohibited lighting of the cigarettes). After 50 seconds, the participants were instructed to set down the objects and cover them with the box. The instructions and cue handling lasted a total of 90 seconds.

2.2.2 Neutral Cues—Neutral cues consisted of a pack of pencils and an eraser. Participants received identical handling instructions with identical timing. They pulled a pencil from the pack when instructed to do so, and handled the pencil as they would handle a cigarette. The eraser was a standard rubber eraser of dimensions similar to that of a lighter, and participants handled the eraser as they did the lighter, only they were not instructed to “flick” it.

2.2.3 Nature Slides—To mitigate carryover effects associated with multiple stimulus presentations, participants viewed a 10-minute nature show between cue presentations. The slide show consisted of 60 randomly presented nature slides.

2.2.4 Stimulus Presentation—Each participant received both cue types (smoking versus neutral cues) once each session during all four laboratory sessions. In order to control for within-session order effects, stimulus presentation was counterbalanced across sessions. Instructions were recorded digitally using Adobe Audition 1.5, and presented using an IBM-Compatible computer running DMDX stimulus presentation software (Forster & Forster, 2003).

2.3 Self-Report Measures

2.3.1 Questionnaire of Smoking Urges- Brief—The QSU-B (Cox, Tiffany, & Christen, 2001; Forster & Forster, 2003) is a 10 item 7-point Likert-type scale self-report questionnaire for assessment of craving that describes subjective cravings to smoke (Tiffany & Drobes, 1991). The QSU-B total score is calculated by finding the overall mean of all 10 responses (range = 1–7). The QSU has 2 factors. Factor 1 includes items associated with the desire and intention to smoke, and is believed to be associated with the positively reinforcing aspects of tobacco. Factor 2 includes items associated with a desire to smoke in anticipation of relieving negative affect, and is believed to be associated with the negative reinforcing aspects of tobacco (Carter & Tiffany, 1999; Cox et al., 2001; Davies, Willner, & Morgan, 2000).

2.4 Physiological Measures

2.4.1 Heart Rate (HR)—Heart rate sensors were placed on the right mid clavicle bone, left lower rib cage, and non-dominant forearm. Heart rate data were collected using a Coulbourn Lab Linc V series V71–01 Bioamplifier with a low pass filter of 40Hz and a high pass filter

of 8 Hz. Heartbeats were detected with a Coulbourn V21–10 Dual Comparator calibrated to detect the peak of the R-wave within the HR waveform. HR data were stored as interbeat intervals and converted offline into beats per minute (BPM). Data were collected continuously prior to and during cue presentation for 90-seconds. For analysis, data were grouped into 10 second blocks, and means for each block were calculated. Thus, 9 mean values representing 10-second averages were produced for each 90-second segment of data collected at baseline and during cue presentations.

2.4.2 Skin Conductance (SC)—SC data were collected via two sensors placed on the hypothenar eminence of the non-dominant hand. SC data were collected using a Coulbourn Lab Linc V Series V71–23 Isolated Skin Conductance Coupler. Data were stored in arbitrary A/D units and converted to microsiemens (10 μ Siemens per 100 A/D units). Data were log transformed, $\log(\mu\text{Siemens} + 1)$ to normalize the data. As with HR, SC data were grouped into 10-seconds blocks and means for each block were calculated.

2.5 Procedure

Eligible participants were scheduled to attend 4 laboratory assessments, each held approximately one week apart, and completed at the outpatient General Clinical Research Center (GCRC) of MUSC. Sessions commenced between 9:30am and 2:30pm; participants were required to attend at approximately the same time each session (within a 2-hour window). They were also required to bring one pack of their preferred cigarette brand and to smoke one cigarette immediately prior to arriving at the laboratory session. Participants' time of last cigarette smoked was recorded to ensure that it was between 45 and 60 minutes prior to the start of the data acquisition. There was no smoking during the course of the laboratory procedure. Laboratory sessions commenced with a UDS and BAL reading; participants who were positive for any drugs or alcohol were rescheduled and reminded to remain drug free (save for nicotine) prior to laboratory sessions. Once a negative UDS, and BAL of .000 were verified, participants were escorted to the data collection room located in the outpatient unit of the General Clinical Research Center. There, physiological monitoring sensors were attached to collect measures of heart rate and skin conductance.

Prior to cue administration, participants remained in the laboratory to acclimate to their surroundings for a total of 45 minutes. After 30 minutes CO levels were measured. Once complete, 90 seconds of baseline physiological data were collected. Participants then provided pre-cue baseline craving ratings. Next, participants completed the first 90-second presentation and handling of cues, during which physiological measures (i.e. heart rate and skin conductance) were collected continuously. Once the cue presentation was complete, participants provided post-cue ratings. Participants then viewed the slide show depicting nature scenes for 10 minutes. At 8.5 minutes during the nature slide presentation, 90 seconds of baseline physiological data were again collected, followed by pre-cue baseline craving ratings. Once the slide show completed, craving ratings were obtained, and the second cue condition was presented, complete with physiological data collection and post-cue craving ratings.

2.6 Design and Analyses

The multi-session design of the present study provided an opportunity to assess the stability of craving and physiological measures collected at baseline (i.e. pre-cue) and post-cue presentation. In order to assess the stability of these measures across all four sessions, an averaged-measures interclass correlation (ICC) was calculated for each measure prior to the main data analysis procedures.

The design of present study consisted of two within-subjects factors: Session (1 through 4) and Cue Type (Smoking v. Neutral). The dependent variables were: (a) mean craving (QSU-B total score), and (b) the maximum value of the nine 10-sec means for HR and SC (derived from the 90-second data collection periods described above).

Each dependent measure (craving, HR, SC) was analyzed separately, using the General Linear Models (GLM) routine within SPSS 15.0, with Session (4 levels; Sessions 1 through 4) and Cue Type (two levels; Smoking v. Neutral) as fixed effects and Subject as a random effect. Because previous work has suggested that baseline and cue-induced craving may vary differentially across sessions (Tiffany et al., 2000), an initial analysis was conducted to examine baseline values of craving, heart rate, and skin conductance. This provided the opportunity to examine whether baseline craving (i.e. ambient background levels of craving not associated with cue presentations) showed signs of decrements across sessions. Next, the main analysis examined reactivity to cues by assessing post-cue values of craving, heart rate, and skin conductance, with pre-cue baseline values included as covariates. The GLM procedure of SPSS is essentially equivalent to a repeated-measures ANOVA when subject is treated as a random effect, and it provides the added flexibility of treating baseline values as time-varying covariates (e.g. each post-cue craving rating for each cue type within each session has its own respective pre-cue baseline value). Follow-up Bonferroni-corrected t-test comparisons were conducted to further examine the nature of any observed main effects. A planned post-hoc analysis was completed to assess for Cue Type effects within each session separately. This analysis employed Cue Type as a fixed effect, Subject as a random effect, with pre-cue baseline values entered as covariates.

3. Results

3.1 Craving

Means and standard errors for baseline and post cue cravings for each session are presented in Table 1. Pre-cue baseline craving was stable, $ICC = 0.91$, as were the post-cue scores for the neutral cues, $ICC = 0.79$, and smoking cues, $ICC = 0.88$.

ANOVA results revealed that pre-cue baseline values did not differ with respect to Cue Type ($p = 0.37$). There was an effect for Session, $F(3,54) = 5.25$, $p < 0.01$, with Bonferroni-corrected post-hoc tests indicating that pre-cue baseline craving in Session 1, $M = 3.9$ ($SE = 0.1$), was greater than that for Sessions 2, $M = 3.1$ ($SE = 0.1$), Session 3 = 2.9 ($SE = 0.1$), and Session 4, $M = 3.4$ ($SE = 0.1$), t 's = 4.15, 5.14, 2.83, respectively, all p 's $< .05$.

For baseline-corrected cue-induced (post cue) craving, ANOVA results revealed both a main effect for Session, $F(3,60) = 3.35$, $p < 0.05$, and for Cue Type, $F(1,18) = 9.58$, $p < 0.01$ but

no Cue Type x Session interaction ($p = 0.56$). Post-hoc tests revealed that the mean Session 1 craving, $M = 4.2$ ($SE = 0.1$), was greater than Session 2, $M = 3.6$ ($SE = 0.1$), and Session 3, $M = 3.7$ ($SE = 0.1$), t 's = 4.14 & 3.45, p 's = .01. The mean of Session 4, $M = 3.9$ ($SE = 0.1$) did not differ from that of any other session. Since this session effect was corrected for baseline responding, it follows that the observed decrement in craving to the cues (from session 1 to sessions 2 and 3) was unrelated to (or independent of) variation in baseline responding.

Collapsed across all 4 sessions, mean craving in response to smoking cues, $M = 4.14$ ($SE = 0.1$) was greater than craving in response to neutral cues, $M = 3.56$ ($SE = 0.1$). When QSU-B scores for the neutral and smoking cues were compared within each session, results revealed significant differences within each session (one-tailed, Table 2), with effect sizes (partial η^2) ranging between 0.15 and 0.37. Taken together, these results suggested that smoking cues evoked greater craving than neutral cues across all 4 experimental sessions.

It should be noted that the forgoing data analytic strategy was used to separately analyze the two factors of the QSU. Since the analyses yielded results that paralleled those described above for the QSU total scores, the findings are not presented.

3.2 Heart Rate Results

One participant had missing data for one session and was excluded from the analysis. Means and standard errors are presented in Table 1. Pre-cue baseline HR was stable, $ICC = 0.84$, as were the post scores for the neutral cues, $ICC = 0.78$, and smoking cues, $ICC = 0.85$. Pre-cue baseline values showed no effects for Session ($p = 0.74$) or Cue Type ($p = 0.34$). For baseline corrected cue-induced HR reactivity, no effects for Session ($p = 0.83$) or Cue Type ($p = 0.39$) were noted.

3.3 Skin Conductance Results

Due to equipment errors, 3 participants had missing data from at least one session and were excluded from the analysis. For the remaining participants, means and standard errors of the log-transformed SC scores are presented in Table 1. Pre-cue baseline SC was stable, $ICC = 0.87$, as were the post-cue scores for the neutral cues, $ICC = .81$, and smoking cues, $ICC = 0.78$.

ANOVA findings for pre-cue baseline SC revealed no effect for Session ($p = 0.68$) or Cue Type ($p = 0.63$). For baseline-corrected cue-induced SC, there was no effect for Session ($p = 0.22$), nor was the Session by Cue Type interaction significant ($p = 0.74$). A main effect for Cue Type was observed, $F(1, 15) = 9.68$, $p = 0.01$. The mean baseline-corrected score for smoking cues, $M = 0.88$, $SE = 0.02$, was greater than that for neutral cues, $M = 0.82$, $SE = 0.02$. In contrast to the findings for craving ratings, however, the main effect for Cue Type was only apparent when taking into account the data from all four sessions; significant differences were not found when the data from each session were analyzed separately (one-tailed, Table 2).

4. Discussion

While the present study yielded evidence of a modest decrement in craving overall (after Session 1), craving in response to smoking cues was greater than craving in response to neutral cues across all four sessions. Had the present study failed to produce evidence of sustained craving in response to smoking cues relative to neutral cues, it would have significantly challenged the notion that craving has an important role in ongoing risk of relapse. Since sustained differential cue reactivity was observed, the study results are not only consistent with a putative causal role for craving in addictive behavior but are also consistent with conditioning models that would expect cues to remain potent elicitors of craving in persons who have not quit smoking (i.e., non-treatment seekers).

While skin conductance was generally higher for smoking cues, the effect was not as robust as that for craving. This apparent discrepancy between cue-elicited craving and cue-elicited physiological reactivity is not uncommon (Carter & Tiffany, 1999). In their meta-analysis on cue reactivity, Carter and Tiffany (1999) speculate that cue-elicited craving may be more robust than cue-elicited physiological reactivity because craving ratings might reflect a specific response to cues, whereas physiological responses may be influenced by general physiological processes as well as the cues themselves. These researchers also suggest that demand characteristics may lead to greater craving as well (i.e., smokers report more craving because this is consistent with what smokers usually do). Thus, while the present study's recruitment of non-treatment seekers may have served to reduce the demand to report lower cue-induced cravings *across* sessions, there may still have been a perceived demand to report greater craving to smoking cues *within* sessions.

While the absence of heart rate reactivity to the cues was somewhat unexpected, it has been previously noted that heart rate and skin conductance do not always show convergent findings in cue reactivity studies (Conklin & Tiffany, 2001; Drobles & Tiffany, 1997). Perhaps the nature of the cue task itself made it difficult to detect effects for heart rate. Indeed, in response to *in vivo* cues, Drobles and Tiffany found evidence for increased skin conductance, but not heart rate, but observed the reverse pattern for imagery cues (Drobles & Tiffany, 1997). While the present *in vivo* task provided standardized instructions, participants manipulated the cues on their own and the timing of cue presentation was not as precise as if cues had been presented automatically. Thus, cue-related differences in heart rate could have been obscured by movement, or individual differences in the timing of when participants oriented to the cues.

The results suggested that both pre-cue baseline craving and baseline-corrected cue-induced craving decreased, regardless of cue type, following the initial cue reactivity session (with relatively little reduction occurring thereafter). Since there was no treatment manipulation in the present study, this reduction in craving cannot be attributed to treatment-related demand characteristics. Thus, this pattern of data may be indicative of a first session "novelty" effect. The evidence for the effects of novelty is not only consistent with previous cue reactivity studies (Hersh et al., 1995; Modesto-Lowe et al., 1997; Reid et al., 1999), but also previous psychophysiology studies as well (Davis & Cowles, 1988; Hartmann et al., 1995; LaRowe, Kline, & Patrick, 2004), which often show reduced reactivity from the first to the

second laboratory visit. Although it is not known for certain why this occurs, researchers speculate that the milieu of the psychophysiological experiment, which invariably involves the somewhat intrusive placement of sensors by a nearly complete stranger, may account for some of the higher levels of physiological reactivity that is commonly observed in initial laboratory sessions (Ney & Gale, 1988). The novelty of a cue reactivity experiment may also account for greater first-session ratings of craving as well.

The present results have two main implications for future studies of cue reactivity. Firstly, craving is a relatively stable and reliable phenomenon. Secondly, craving persists over multiple (i.e. more than two) sessions in individuals who are non-deprived active smokers. Although these findings may come as little surprise to researchers and clinicians who work with smokers and other addicts, it is nevertheless important to establish “common sense” notions empirically. Having an empirical understanding of how craving manifests in active smokers provides a useful point of comparison for studies that investigate how craving manifests in those undergoing treatment or in those receiving novel anti-craving agents. It would be interesting to see, within the current experimental parameters, if those undergoing treatment would show persistent cue-induced craving over multiple sessions as well, and this remains a viable topic for a future study of cue reactivity.

A limitation of the present study included the use of only male participants, though as noted above, females were purposefully omitted from this initial report in order to avoid the potential confounds of menstrual effects on craving and physiology (Carpenter et al., 2006). Another potential limitation of the present study is the strength and salience of the cues themselves. The observed increase in craving evoked by the smoking cues was modest (QSU-B scores changed by approximately one point on a seven-point scale), with effect sizes falling short of what is typically observed (Carter & Tiffany, 1999). Participants may have experienced more pronounced craving (which might have been more susceptible to extinction) if the cigarettes had been lit (Upadhyaya, Drobos, & Thomas, 2004), or if cues had been presented using virtual reality technology (Lee, Lim, Wiederhold, & Graham, 2005), or if participants had undergone a period of nicotine deprivation over several hours or even days. It is also important to note the limitation of sample size. While the present results indicated no significant interaction between Session and Cue Type, the pattern of effect sizes appeared to decrease across sessions. Thus, while differences in craving in response to smoking and neutral cues were significantly different across all four sessions, it is possible that evidence of diminished cue-induced craving may have been observed had the sample been larger, or had participants attended more than 4 sessions. Despite these limitations, the present study's use of a four-session, within-subjects design that controlled for deprivation level and treatment demand characteristics provides an empirical demonstration of sustained potency of smoking cues within a standardized, laboratory-based, cue reactivity protocol.

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Table 1

Baseline and post-cue means (M) and standard errors (SE) for QSU-B ratings and range-corrected skin conductance values

	Session	Neutral				Smoking			
		Baseline		Post Cue		Baseline		Post Cue	
		M	SE	M	SE	M	SE	M	SE
QSU-B	1	3.9	0.3	4.1	0.3	3.9	0.3	4.8	0.3
	2	3.3	0.3	3.3	0.4	3.0	0.4	3.7	0.5
	3	2.8	0.3	3.1	0.3	3.0	0.3	3.9	0.3
	4	3.4	0.4	3.8	0.4	3.2	0.4	4.1	0.4
HR ¹	1	78.1	2.5	78.8	2.66	76.2	2.4	78.2	2.4
	2	78.4	2.1	78.5	1.78	76.3	2.3	80.1	1.8
	3	75.7	2.3	79.1	2.11	76.1	2.4	78.4	1.97
	4	78.4	2.3	80.7	2.08	78.3	2.5	80.8	1.9
SC ²	1	0.67	0.09	0.81	0.09	0.80	0.07	0.94	0.09
	2	0.72	0.10	0.86	0.10	0.67	0.07	0.90	0.08
	3	0.67	0.08	0.83	0.08	0.64	0.07	0.88	0.07
	4	0.67	0.08	0.79	0.08	0.65	0.09	0.83	0.08

¹ Maximum HR response within 90-second segment of data collection, units are Beats per Minute (BPM).

² Maximum SC response within 90-second segment of data collection, units are log(μ Siemens + 1).

Table 2
Results of within-session comparisons of baseline-corrected means for craving and skin conductance

Session	Neutral		Smoking		F^b	< p	η^2	p
	M^a	SE	M	SE				
QSU-B	1	4.11	0.16	4.82	0.16	10.09	0.01	0.37
	2	3.27	0.13	3.77	0.13	6.90	0.05	0.29
	3	3.13	0.21	3.83	0.21	5.51	0.05	0.25
	4	3.71	0.16	4.12	0.16	3.10	0.05	0.15
SC	1	0.86	0.04	0.94	0.04	2.05	0.09	0.12
	2	0.83	0.03	0.92	0.03	3.08	0.06	0.18
	3	0.81	0.03	0.86	0.03	1.73	0.11	0.11
	4	0.76	0.02	0.80	0.02	0.86	0.19	0.06

^a Estimated means, SEs, and partial

η^2 produced by each respective within-session analyses.

^b Degrees of freedom are 1,18 for QSU and 1,14 for SC. P values are one-tailed.