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Smoker Reactivity to Cues: Effects on Craving and on Smoking behavior

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Abstract

We assessed craving and smoking in response to smoking-relevant cues. 207 daily smokers viewed images related to one of six cue sets (cigarettes, positive and negative affect, alcohol, smoking prohibitions, and neutral cues) in separate sessions. Compared to neutral cues, cigarette cues significantly increased craving, and positive affect cues significantly decreased craving. When subjects were then allowed to smoke during continuing cue exposure, cues did not affect the likelihood of smoking or the amount smoked (number of cigarettes, number of puffs, puff time, or increased carbon monoxide). However, craving intensity predicted likelihood of smoking, latency to smoke, and amount smoked, with craving increases after cue exposure making significant independent contributions. Some craving effects were curvilinear, suggesting that they are subject to thresholds and might not be observed under some circumstances.

Most theories of smoking emphasize nicotine dependence – and the accompanying need to maintain nicotine levels above some threshold – as the core motivation for smoking (Shadel, Shiffman, Niaura, Nichter, & Abrams, 2000). However, these theories also recognize the importance of particular settings or stimuli for eliciting craving and cueing smoking (Kozlowski & Herman, 1984; Shadel et al., 2000). The role of certain situational stimuli in prompting smoking is reported by smokers on smoking typology questionnaires (Horn & Waingrow, 1967; Ikard, Green, & Horn, 1969) and has also been documented in EMA studies using real-time diaries to track the antecedents of smoking (Shiffman et al., 2002). Even more dramatically, EMA studies of relapse (Shiffman, Paty, Gnys, Kassel, & Hickcox, 1996) have documented the role of such stimuli as triggers for relapse, as well as for temptations to smoke – situations in which craving peaks, even if smokers do not actually smoke (O'Connell & Martin, 1987; Shiffman, 1982; Shiffman, Paty et al., 1996). Such situationally-cued "provoked craving" is thought to be distinct from, and as important as, steady-state "background craving" that arises simply from nicotine deprivation, even in the

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absence of cues (Ferguson & Shiffman, 2009). Craving responses to particular stimuli are thought to develop via conditioning processes arising from repeated pairing of such stimuli with smoking, or possibly with withdrawal (Niaura et al., 1988). Understanding the associations between provocative stimuli, on the one hand, and craving and smoking, on the other, is of theoretical and practical significance.

The role of situational triggers can be observed in the course of ad libitum smoking in uncontrolled observational studies (Shiffman et al., 2002), but observational data are limited by natural and confounding variations in frequency, intensity, and nature of the exposures. Accordingly, researchers have developed controlled laboratory methods for studying smokers' reactions to cues. In the cue reactivity paradigm, smokers are exposed in the laboratory to stimulus cues thought to be associated with smoking, such as the sight and/or smell of cigarettes themselves, and such cigarette cues reliably elicit craving (Carter et al., 2006; Carter & Tiffany, 1999). Individual differences in reactivity have been associated with dependence (Watson, Carpenter, Saladin, Gray, & Upadhyaya, 2010) and greater vulnerability to relapse (Abrams, Monti, Carey, Pinto, & Jacobus, 1988; Niaura, Abrams, Demuth, Pinto, & Monti, 1989), but only inconsistently (Perkins, 2009).

The vast majority of cue reactivity research has been conducted using what Conklin, Robin, Perkins, Salkeld, and McClernon (2008) have characterized as "proximal" cues – that is, cues associated with the act of smoking itself, usually a cigarette. This would be expected to be the cue with the strongest associations, since it is always present prior to and during smoking and has unique sensory characteristics. However, a sole focus on such proximal cues is limited, because it does not explain why smoking and craving (and, especially, relapse) are linked to more "distal" cues, such as alcohol consumption, or affective states (Erblich, Montgomery, & Bovbjerg, 2009; Tiffany & Drobes, 1990), which are not inherently part of the act of smoking, nor uniquely associated with it. A few studies have examined the role of distal cues in the cue reactivity paradigm. For example, Conklin (2008) demonstrated that distal environmental cues (e.g., pictures of a bar) elicited cigarette craving. Negative affect also seems to increase craving (Payne, Schare, Levis, & Colletti, 1991; Tiffany & Drobes, 1990), but affective cues are often confounded with smoking cues, making it hard to evaluate their distinct contribution (though, see Elash, Tiffany, & Vrana, 1995; Perkins, Karelitz, Conklin, Sayette, & Giedgowd, 2010). In this study, we examine smokers' craving responses to a range of cues, including several distal cues that are presented on their own, without any reference to smoking or craving.

One important distal smoking cue is alcohol. Smoking is closely associated with alcohol. People who drink are more likely to smoke, and drinking is associated with smoking in global questionnaire reports (Shiffman & Balabanis, 1995), laboratory studies (Burton & Tiffany, 1997; Sayette, Martin, Wertz, Perrott, & Peters, 2005), EMA analyses of real-world smoking (Piasecki, McCarthy, Fiore, & Baker, 2008; Shiffman et al., 2002), and EMA analyses of relapse episodes (Shiffman, Paty et al., 1996). Tiffany and Hakenewerth (1991) showed that alcohol cues increased cigarette craving. However, their "alcohol" cues also contained explicit smoking cues and prompts to experience craving. Erblich, Montgomery, & Bovbjerg (2009) showed that alcohol imagery cues, devoid of smoking cues, increase

cigarette cravings. In this study, we assessed reactivity to alcohol-specific cues in the absence of specific proximal smoking cues.

Internal cues such as affect – particularly negative affect – are also thought to affect smoking and craving. Negative-affect smoking is the most frequently endorsed smoking pattern (Gilbert, Sharpe, Ramanaiah, Detwiler, & Anderson, 2000), but laboratory studies have not been consistent in reporting increased smoking or craving in response to negative affect (Perkins et al., 2010; Tiffany & Drobes, 1990). Although EMA studies do not find consistent relationships between negative affect and smoking (Shiffman et al., 2002), they do find a consistent relationship with relapse (Shiffman, Paty et al., 1996; Shiffman & Waters, 2004). The expected effect of positive affect is less clear. Smoking in positive affect situations has been observed in young, light smokers (Hedeker, Mermelstein, Berbaum, & Cambell, 2009), but may not be present in established smokers. Baker, Morse, and Sherman (1987) have suggested that craving is associated with positive mood during ad lib smoking (in contrast to deprivation), and EMA studies suggest that craving is associated with positive affect (Dunbar, Scharf, Kirchner, & Shiffman, 2010). Since nicotine enhances the reinforcement value of other stimuli (Caggiula, Donny, Palmatier, Chaudhri, & Sved, 2009), smoking when feeling good may be particularly rewarding, perhaps establishing a link to craving and smoking. On the other hand, if smoking is specifically linked to negative affect, positive affect might actually diminish craving.

An increasingly common - and possibly increasingly important – cue environment that has not been studied is the smoking-prohibited environment. Smoking bans are increasingly pervasive, covering public transportation, workplaces, medical facilities, restaurants and bars, and even some outdoor venues and smokers' own homes (McMillen, Winnickoff, Klein, & Weitzman, 2003). The effect of these smoking-restricted settings on craving is not known, but hypotheses run in both directions. On the one hand, such settings are disassociated from smoking, so they might suppress rather than incite craving. On the other hand, being associated with involuntary abstinence, and coming just before craving relief (e.g., when the person leaves the restricted environment to smoke), they may come to be associated with craving, and may elicit craving in the laboratory. To assess these effects, the present study included a set of stimuli associated with cues for smoking prohibited contexts (e.g., "no smoking" signs).

Thus, the present study included five stimuli: smoking cues, alcohol cues, negative and positive affect cues, and smoking-prohibited cues. Additionally, to control for non-specific reactivity, we included a neutral cue of smoking-irrelevant stimuli matched to the active cues, similar to controls described in previous studies (e.g., see Carter & Tiffany, 1999).

The cue reactivity paradigm has been criticized for limiting its focus to craving elicited by cues, without examining increases in smoking itself. Perkins (2009) argues that our ultimate interest is in smoking behavior, not craving, and Tiffany (1990) has argued that smoking is only tenuously linked to craving, making Perkins' critique all the more telling. The few studies that *have* examined immediate smoking in response to cue exposure generally show increases in smoking. Studies suggest that smoking-related cues prompt shorter latency to smoke (e.g., Droungas, Ehrman, Childress, & O'Brien, 1995; Herman & Polivy, 1984;

Payne et al., 1991) and greater cigarette consumption (Hogarth, Dickinsion, & Duka, 2009; Morgan, Davies, & Willner, 1999; Perkins, Epstein, Grobe, & Fonte, 1994), including changes in smoking topography (e.g., number and duration of puffs; Payne et al., 1991; Rikard-Figueroa & Zeichner, 1985).

In this study, we include assessment of the effects of cues on smoking as well as craving, assessing whether individuals smoke, how soon they initiate smoking, and how much they smoke. The amount of smoking is measured both behaviorally (puffs, puff time) and biochemically (carbon monoxide [CO] increase). Besides testing whether cues elicit smoking, assessing smoking also provides an opportunity to test the relationship between craving and smoking in a controlled context. This is important, as some authors have questioned whether craving is related to or predicts smoking (Tiffany, 1990). Further, in the context of a cue-exposure paradigm, we can test the presumed pathway running from cues to craving to smoking.

We hypothesized that smoking cues, alcohol cues, and both positive and negative affect cues would increase craving, while we considered that smoking prohibited cues might either increase or decrease craving. We expected that cues would have similar effects on smoking, causing subjects to smoke sooner and more intensely. We also hypothesized that craving would predict smoking, and that cue effects on smoking would be mediated by their effects on craving.

In the context of the overall reactivity study, we also evaluated whether gender and race moderate cue reactivity effects. Perkins (1996) has suggested that women's smoking is less motivated by nicotine, and speculated that their smoking is more motivated and controlled by response to environmental cues. One previous large reactivity study (Shiffman et al., 2003) found no gender differences in reactivity to a smoking cue, but the study lacked a neutral cue as a control, and did not test other potential cues. Women tend to report more negative affect smoking on smoking typology questionnaires (Pomerleau, Berman, Gritz, Marks, & Goeters, 1994), suggesting that women might be more reactive to negative affect cues.

Studies have documented substantially different patterns of smoking among European-American (EA) and African-American (AA) smokers (Royce, Hymowitz, Corbett, Hartwell, & Orlandi, 1993), but differences in cue reactivity have not been assessed. Accordingly, we assessed differences in reactivity profiles between AA and EA smokers. Finally, we also examined differences between light and heavy smokers, in part to relate the current study to the larger cue reactivity literature, which has tended to use samples of relatively heavy smokers.

Method

Sample

Subjects were 207 adult daily smokers recruited for a non-treatment study. Subjects had to be at least 21 years old (M = 41, SD = 11), have been smoking for at least 3 years (M = 26, SD = 11), be smoking daily at a self-reported rate of 5–30 cigarettes per day (CPD; M = 16,

SD = 6.5), and not be intending to quit smoking within 3 months. We deliberately over-sampled AA smokers to comprise 39% of the sample; data were weighted to reflect the population representation of AA smokers. Women comprised 43% of subjects. Subjects reported consuming an average of 7.84 (*Mdn* = 4, *SD* = 10.37) alcohol-containing drinks per week; 23% reported no drinking, either on questionnaire assessment, or during three weeks of EMA monitoring. Subjects were paid $135 for this part of the study (they also engaged in other procedures not relevant to the present analyses). Subjects completed informed consent and the study was approved by the University of Pittsburgh Institutional Review Board.

Procedures

Cue exposure occurred over six separate sessions, one cue type per session, with at least one day between sessions. Previous studies (LaRowe, Saladin, Carpenter, & Upadhyaya, 2007) have shown that cue effects are consistent over multiple administrations. Order of cue presentation was randomized to ensure that each cue was equally likely to appear in each session and also equally likely to be preceded and followed by every other cue, with the exception that, by design, neutral and smoking cues were slightly more likely to be adjacent (approximately 30% of the time vs. 20% of the time for other pairings), to mirror past studies in which these are typically the only cues presented.

All sessions were identical in structure and timing, shown in Figure 1. To roughly equate subjects for smoking satiety, subjects were instructed to smoke as much as they wished prior to presenting for the session, at which time they were asked how long ago they had last smoked. Subjects then entered a 30-minute abstinence period while they completed questionnaires. They were told that they would be allowed to smoke later in the session. To encourage attention to the cues, they were told they would be tested on the cues they saw. To begin the session, subjects were seated in the exposure chamber: a simple room approximately 90 ft^2 or more with a chair, desk, TV monitor, audio speakers, and video camera and microphone. The cues were presented as still images on a TV monitor. To avoid unintended cueing by research staff or intrusion of social influences, procedures in the exposure chamber were automated: a pre-recorded DVD provided all subject instructions at the appropriate times, presented the appropriate cue images, and cued subjects when to complete questionnaires. As described further below, automated instructions also indicated when subjects could smoke by making subjects aware of cigarettes (and lighter and ashtray) that had been placed in a closed desk drawer in the exposure chamber. Research assistants were not in the room during cue exposure, but monitored the session from a control room with video and audio feed, and could hear and speak to the subject as needed. Research assistants were blind to cue condition and could not see the cues as they were being presented. The sessions were video-recorded for later review and analysis.

The session proceeded as follows (Figure 1). After a 2-minute acclimation period and pre-cue craving and affect ratings, a 3-minute initial cue exposure period ensued. (In pilot testing, craving effects seemed to peak at about 3 minutes.) Cue images were displayed on a 20-inch monitor, with each image seen for 6 seconds. After a post-exposure assessment, subjects were told they could smoke, and could access two cigarettes of their own brand in the desk drawer. The cues continued to be displayed during the 15-minute free-smoking

period. Heishman, Saha, and Singleton (2004) and Heishman, Lee, Taylor, and Singleton (2010) have shown that cue-induced craving persists for at least 15 minutes, and we also observed this in pilot testing. After a final assessment, the session was terminated.

Cues

Each cue set consisted of 30 different digital images displayed in a pre-randomized order (same order for all subjects) for 6 seconds each. Thus, each image was displayed once during the 3-minute primary cue exposure, and redisplayed 5 times during the 15-minute smoking period. Smoking images were drawn from Gilbert and Rabinovich (1999), Warthen and Tiffany (2009), and original photographs, and showed cigarettes, people smoking, cigarette packs and ashtrays. They did not portray social situations or drinking, and were devoid of other relevant content. Alcohol-related images were drawn from stock photographs and original photographs (iStockPhoto, 2007), and showed alcoholic beverages and hands holding drinks; they did not portray cigarettes or smoking, nor social situations. Negative and positive affect images (separate cue sets) were drawn from the International Affective Picture System (IAPS; Center for the Study of Emotion and Attention, 1999), which reliably influences affect (Lang, Bradley, & Cuthbert, 1995). The images selected did not portray smoking or drinking; some depicted social situations, some of which were negative or violent. Positive and negative affect ratings obtained in this study in response to each cue set are presented below. The smoking prohibited images portrayed no-smoking signs in office, transportation, and other settings, and came from stock photographs (iStockPhoto, 2007). About half the images included the standard “no-smoking” symbol with a diagonal line across a drawing of a cigarette. The neutral stimulus set was drawn from Gilbert and Rabinovich (1999), IAPS (Center for the Study of Emotion and Attention, 1999), and stock photographs (iStockPhoto, 2007), and was constructed to incorporate equally the content domains represented in each of the five active cue sets. Specifically, six images displayed drinks that were clearly non-alcoholic (i.e., matched to the alcohol cue); six displayed prohibitive (e.g., “no parking”) signs (i.e., matched to the smoking prohibited cue); six depicted hands holding neutral objects such as chopsticks or eyeglasses (i.e., matched to the smoking cue); and twelve depicted items such as chairs or clips, selected from IAPS for having affective valence ratings closest to the neutral point of 5 (M = 4.95, SD = 1.06) and low arousal ratings (M = 2.83, SD = 1.90). Pilot testing confirmed that the neutral images did not evoke any of the content contained in the active cues. The images used and the DVDs that display them, along with session instructions, are available from the authors, subject to licensing from the copyright holders. (See the Appendix for specific sources for images.)

Measures

Craving—The brief 10-item QSU (Cox, Tiffany, & Christensen, 2001) was administered 4 times, as shown in Figure 1: We analyzed the difference in ratings made just before cue exposure (A-2) and just after the 3-minute initial exposure, just before the smoking period was initiated (A-3). Subjects marked their QSU responses on a segmented visual-analog scale with 49 segments; thus scores ranged from 1 to 49. The QSU yielded scores for Factor 1 (‘appetitive craving’) and Factor 2 (‘distress-relief craving’); both showed high internal consistency reliability, with average (across administrations) Cronbach α of .97 and .90,

respectively. All the items on the published QSU are scored such that higher scores indicate higher craving. We inserted an additional reverse-scored item to test for fixed response sets: it allowed detection of subjects who were being inattentive and giving the same response to all items; as discussed later, some sessions were invalidated based on this test.

Affect—The Affect Mood Form (Diener & Emmons, 1984) was administered at the same time-points as the craving measure. It yielded separate scores for positive affect (PA) and negative affect (NA). Both PA and NA scales showed high internal consistency reliability, with average (across administrations) Cronbach α of .92 and .88 (PA and NA, respectively).

Smoking measures—After the initial cue exposure and post-cue craving assessments, subjects began a 15-minute free-smoking period during which they were allowed to smoke ad lib. We provided subjects with 2 cigarettes of their own brand. Subjects who did not smoke the cigarettes in-session could take them home; pilot-testing showed that, otherwise, subjects offered cigarettes were inclined to smoke them in the session in order to avoid missing an opportunity for free cigarettes. To equate subjects' awareness of the smoking opportunities across sessions, subjects were informed of the procedures prior to the start of each session.

To avoid the potential reactivity associated with physically instrumenting the subject or the cigarette, subjects were allowed to smoke normally, and smoking topography measures were coded from the video of the session by an independent observer, also blind to cue condition. We coded latency to initiate smoking, and the number and duration of cigarette puffs, which were discerned from the glow of the cigarette as seen in video. Research (Blank, Disharoon, & Eissenberg, 2009) has shown that this method corresponds closely to smoking topography measures derived from specialized topography instruments. If subjects smoked two cigarettes, latency was recorded to the first cigarette, but puff counts and puff time reflected all smoking. Sessions were coded by one of 7 raters. To establish reliability, a randomly-selected set of 21 sessions was cross-coded by all 7 raters. The results demonstrated reliability ($r \geq .95$) for all the topography variables. Exhaled CO was assessed using a Vitalograph Breath CO monitor (Vitalograph Inc., Lenexa, KS) before cue exposure and after the smoking period; CO increases correlated with number of puffs and puff duration (not shown).

Analysis

Dataset creation

Most subjects (n = 201, 97%) completed the full 6-cue series. For subjects who dropped out before completing the full series, we included partial data, so long as their data included the neutral stimulus and at least one other cue (n = 6 partial subjects). Subjects excluded on these criteria (n = 22) did not differ from included subjects in age, gender, race, income, or smoking rate. A few sessions (n = 25) were lost because of equipment malfunction or human error (e.g., the wrong set of images was shown). In addition, 11 cases in which questionnaire responses exhibited aberrant or invalid patterns (e.g., same scores for all items on the QSU, including the reverse-scored item noted earlier) were omitted from the dataset. The analysis

included 1,201 sessions from 207 subjects. Table 1 shows the number of sessions for each cue in the analysis.

Difference scores (pre- to post-cue exposure, i.e., A3-A2 as shown in Figure 1) were used as an index of cue-induced mood changes and craving. Particularly because of extreme response sets, the craving-increase data were highly skewed. A square root transform (preserving the sign of the difference) reduced the skewness and improved model fits, and was used for all analyses.

Statistical analysis

Mixed models (Brown and Prescott, 2006), fit using SAS PROC-MIXED (SAS Institute, Cary, NC), examined effects on craving and continuous smoking parameters (CO, puffs, puff time). After comparing several covariance patterns with an Akaike Information Criterion (AIC), unstructured and variance component (VC) covariance structures were used for modeling between- and within-subject levels, respectively. Stimulus effects represent contrasts between each cue and the neutral cue condition. Except for survival analyses, which had no provision for weighting, the data were weighted by ethnicity to balance the deliberate over-recruitment of AA subjects. (Five subjects that were neither AA nor EA were weighted like EA subjects.) In addition, we reasoned that alcohol cues might be provocative only for those who drink and therefore limited analyses of alcohol cue effects to those who reported drinking.

We also evaluated order and sequence effects. Order refers to which session in the 6-session sequence a cue appeared. There were some order effects, primarily differences between the first session and all others, so all models included session number (order) as a covariate. Sequence effects refers to the sequencing of specific cues; that is, the potential effect of the preceding cue on the current reaction (e.g., whether reactivity to positive affect cues is different if it follows the session with negative affect cues). Sequence effects could not be evaluated in a single model across all cues, because the current cue and preceding cue are not independent (because the current cue could not also be the preceding cue). Accordingly, we assessed separately for each current cue the effect of preceding cues.

We evaluated gender, race, and smoking rate (CPD) as potential moderators of cue effects (i.e., cue x moderator interactions). Race analyses contrasted AA and EA smokers; 5 subjects who did not fit either group were excluded. Smoking rate (CPD) was estimated from average reports of cigarette consumption over a period averaging 60 days, collected via Time-Line Follow-Back (Sobell, Sobell, & Maisto, 1979). CPD was analyzed as a continuous variable. To describe the observed effects, we report data for light smokers versus heavy smokers (split at 16 CPD, which was the mean smoking rate both nationally and in this sample).

Generalized estimating equations (GEE), using a logit link, were used to examine probability of smoking following cue exposure, construed as a dichotomous (smoked, did not smoke) variable. Survival analysis was used to examine latency to smoke following cue exposure; survival analysis takes account of right-censored observations, that is, those subjects who did not smoke at all during the smoking period. Thus, all subjects were

included in the calculations and analysis, even if they did not smoke. Recurrent event models (using Stata *streg;* StataCorp, College Station, TX), with provisions for frailty (the equivalent of random intercept models) were used to analyze time to smoking across the multiple cue sessions (Hosmer, Lemeshow, & May, 2008). We used the Gompertz survival function, on the basis of the best fit (AIC, BIC). We considered quadratic as well as linear functions for craving as a predictor.

Based on the sample sizes in the study, we estimated the power to detect effects in the various outcomes, for main effects of cues and for moderator effects due to dichotomous individual differences (e.g., sex and race). To enable modeling of power, we made simplifying assumptions, positing independence across cues (the data indicated very weak and homogenous correlations across sessions), and equal sample sizes for the individual difference groups (sample sizes were not very far from equal). These assumptions likely lead to some overestimation of power. We modeled moderators as dichotomous categorical variables; as CPD was analyzed as a continuous variable, which would increase power (Kraemer & Thiemann, 1987), our estimates likely underestimate power for CPD as a moderator. For cue effects on craving, the design was estimated to have 80% power to detect a standardized effect size of 0.26 (in *SD* units) for cue main effects, and an effect of 0.26 for interactions. For smoking parameters (number of puffs, puff duration, and CO), which were evaluated on the smaller sample of sessions where smoking occurred, the detectable effect sizes were 0.23 and 0.29. For the probability of smoking, the estimated detectable effect sizes were 0.25 and 0.32, respectively. Using Cohen's (1992) standard rubric for effect sizes, where 0.20 is considered a small effect, 0.50 a medium effect, and 0.80 a large effect, all of these detectable effects are between small and medium effect sizes, closer to small effects. Finally, for survival analyses of time to initiating smoking, detectable hazard ratios (HRs) were $HR = 1.77$ and 3.30, for main effects and interactions, respectively. (There is no Cohen rubric for effect sizes in survival analysis.)

Results

Sessions

Sessions were separated by a median of 3 days (inter-quartile range 3.00). All sessions were held between 8 am and 6 pm. The mean reported time since last cigarette (TSLC) was 66.42 minutes ($SD = 195.01$, median= 20, IQR = 35, excluding one outlier), with a highly skewed distribution (logged for analysis). Reports of longer (log) TSLC were associated higher craving (appetitive: $B = 2.5$, $p < 0.0001$; distress: $B = 0.9$, $p < .0001$) at the time of presentation, as expected. Adjusting for TSLC did not affect outcomes, so we report unadjusted analyses of cue effects.

Affect

The affect data showed order effects. Patterns were complex, but PA showed a weak trend toward being slightly higher prior to cue exposure on the first session, and pre-cue NA tended to decrease over sessions. We controlled for order in all subsequent analyses. There were no carry-over effects; that is, it did not matter which cue had been shown in the session preceding the current one. Table 1 shows mean scores before and after each cue, as well as

the changes in affect following each cue. As intended, the positive affect cue (relative to neutral) significantly increased PA ($p < .0001$) and decreased NA ($p < .0001$). The negative affect cue significantly increased NA ($p < .0001$). The effects of the positive affect cue were consistently greater than those of the negative affect cue. There were no effects of other cues (compared to neutral cue) on mood. There were no interactions with the order of cue presentation.

Craving

As shown in Table 1, subjects reported moderate cravings, both before and after cue exposure. For appetitive craving, (QSU F1) ratings averaged 30.00 (*SD* = 14.88) pre-cue and 32.41 (*SD* = 14.92) post-cue, across all cues. Distress-relief craving (QSU F2) scores were much lower, averaging 15.59 (*SD* = 12.40) pre-cue and 17.41 (*SD* = 13.41) post-cue. Appetitive and distress-relief craving were highly correlated (Pre-cue $r = .70$; Post-cue $r = .67$), but were treated as separate dependent variables. Craving data were subject to order effects; specifically, the first session differed from others. In the first session, pre-cue appetitive craving was 4.06 (*SE* = 0.67) points higher ($p < .0001$) and distress-relief craving was 2.71 (*SE* = 0.45) points higher ($p < .0001$) than other sessions. In addition, in the first session, post-cue change in craving was lower ($p < .01$) for both appetitive ($B = -1.35$, *SE* = 0.46) and distress-relief craving ($B = -1.18$, *SE* = 0.37), relative to all other sessions. We controlled for order main effects in all subsequent analyses. There were no carry-over effects; that is, it did not matter which cue had been shown in the session preceding the current one.

Figure 2 shows changes in craving following cue exposure. All cues, including the neutral cue, resulted in significant increases in craving, though the positive affect cue did not increase distress-relief craving. Compared to the neutral cue, smoking cues significantly increased both appetitive and distress-relief craving. Conversely, positive affect cues significantly decreased appetitive and distress-relief craving relative to neutral cues. There was a trend for negative affect cues to increase distress-relief craving. No other cue changed craving more or less than the neutral cue, in the sample as a whole. Among individuals who drank, the alcohol cues marginally increased appetitive (but not distress-relief) craving ($p < .06$).

Additional craving analyses

We had hypothesized that the smoking prohibited cue could either increase or decrease craving. Thus, we considered whether the null finding could have been the result of effects in opposite directions, increasing craving for some while decreasing it for others. This would have the effect of increasing variance in craving change, compared to other cues. In fact, standard deviation (*SD*) of craving change scores for the smoking prohibited cue set (QSU F1: *SD* = 6.53; QSU F2: *SD* = 4.39) was in line with – and often smaller than – the SDs seen for the other cue sets: smoking (QSU F1: *SD* = 8.05; QSU F2: *SD* = 6.03), negative affect (QSU F1: *SD* = 8.24; QSU F2: *SD* = 6.87), positive affect (QSU F1: *SD* = 6.50; QSU F2: *SD* = 5.51), alcohol (QSU F1: *SD* = 6.16; QSU F2: *SD* = 5.10), and neutral (QSU F1: *SD* = 5.55; QSU F2: *SD* = 5.09).

To examine whether the relative lack of reactivity may have been affected by ceiling effects, which would limit the rise in craving among subjects whose craving was already near the maximum prior to cue exposure, we reanalyzed the data after excluding sessions in the top 10% of pre-cue craving (Total QSU score > 43). The results when excluding this group were essentially unchanged – most relevantly, smoking and positive affect remained the only cues that significantly influenced craving (detail not shown).

Smoking

Subjects smoked during the free-smoking period in 87% of sessions (n = 1040); 21% of these involved 2 cigarettes. Subjects were less likely to smoke (*OR* = 0.66, CI = 0.48 – 0.92) and were slower (by 18.5 seconds) to initiate smoking (*HR* = 0.64; CI = 0.54 – 0.77, by survival analysis) in the first session; this order effect is accounted for in subsequent analyses. The model estimated median latency to smoking at 39.15 seconds, but 10% lit up within 20 seconds, another 10% did not light up until after 3 minutes or more. On average, subjects who smoked took 14.41 (*SD* = 7.23) puffs, puffing for 22.00 (*SD* = 11.82) seconds total, yielding a mean puff duration of 1.59 (*SD* = 0.60) seconds. There were no order effects on number of puffs or puff time.

Table 1 shows the smoking parameters by cue, and Table 2 shows cue effects on smoking outcomes. By logistic regression, there were no variations in the probability of smoking based on which cue was displayed ($p = .89$), nor did cue type influence the likelihood of smoking a second cigarette ($p = .17$). Cues had no effect in survival analyses on progression to smoking (see Table 2, Figure 3). Among those who did smoke, cues had no effect on the number of puffs taken or on total puff time (Puffs: = .28; Puff Time: $p = .47$). CO change trended higher in the positive affect cue when compared to the neutral cue ($B = .65$, $p = .05$).

Smoking and craving

We tested whether craving intensity prior to the smoking period predicted smoking behavior. The analysis revealed substantial relationships, summarized in Table 3. Subjects were more likely to smoke, were more likely to smoke 2 cigarettes (vs. only 1 cigarette), and progressed to smoking more quickly and with greater probability (survival analysis) if their craving immediately prior to smoking was higher (controlling for order and cue). This was true for both appetitive and distress-relief craving. Moreover, as seen in Figures 4, the relationships for latency to smoke were curvilinear for distress-relief craving, such that craving increases at the low end of craving mattered greatly, but the relationship leveled off at higher levels of craving, showing minimal effect of increased craving on smoking behavior. A similar pattern was observed for appetitive craving, but was not significant. A similar pattern was observed for probability of smoking (see Figure 5), although no curvilinear effects were observed for distress-relief craving. In addition, craving immediately prior to smoking was associated with increased probability of smoking 2 cigarettes. However, quadratic effects of craving were less pronounced, and curvilinearity was again not significant for appetitive craving.

Craving levels prior to the smoking period also influenced the intensity of smoking among those who smoked. Higher craving intensity was associated with taking more puffs, puffing

longer, and showing greater increases in exhaled CO (Table 3). As shown in Figure 6, the effects on puffing behavior were curvilinear, accelerating as craving intensity increased. (That is, they showed the opposite pattern from the quadratic effects on initiation of smoking.)

To further explore the relationship between craving just before the free-smoking period (A3 in Figure 1) and subsequent smoking, we decomposed the pre-smoking craving rating into two components: pre-cue craving (as baseline craving, A-2 in Figure 1), which was a function of the subject and setting, and the increase in craving at post-cue (difference between A-3 and A-2), which may reflect the response to cue exposure. (Thus the post-cue (A-3) assessment can be understood as the composite of the subject's craving state pre-cue (A-2) and the change in craving due to any "boost" from the cue exposure.)

Controlling for order and cue, pre-cue (A-2, baseline) appetitive and distress-relief craving ratings were significantly associated with all aspects of smoking: probability of smoking, probability of smoking 2 cigarettes, latency to smoke, number of puffs, time puffing, and increased CO. Over and above this, controlling for order, cue, and pre-cue craving, the increase in craving following cue exposure additionally and significantly predicted almost all smoking parameters (Table 3). The post-cue changes in both appetitive and distress-relief craving incrementally predicted probability of smoking, latency to smoke, puffs and puff time. Change in craving did not predict probability of smoking 2 cigarettes (vs. 1).

Individual difference moderators of cue effects

There were no gender differences or gender-by-cue interactions in either appetitive or distress-relief craving responses to the cues, nor any differences in smoking parameters (likelihood of smoking, latency to smoking, number of puffs, puff duration, or CO boost; details not shown). Compared to EA smokers, AA smokers showed significantly greater increases in distress-relief craving ($p = .009$) and were more likely to smoke ($p = .02$), but had lower cumulative puff duration in the free-smoking period ($p = .002$). These were main effects of race, and not differential effects of cues by race. There were no effects of ethnicity on cue effects or any other variables (details not shown).

There were no significant differences in response to cues based on heaviness of smoking (CPD) in craving response, likelihood of smoking, lighting a second cigarette, number of puffs, puff duration, or CO boost. In survival analyses, we did observe a CPD x cue interaction. However, this was due to variation in how light versus heavy smokers reacted to the neutral cue, rather than variations in reaction to active cues: Compared to heavier smokers (i.e., CPD ≥ 16), lighter smokers (i.e., CPD < 16) were slower to light up specifically after seeing the neutral cue (model-based median latency, in minutes: 0.94 minutes [95% CI: 0.66 – 1.23] vs. 0.53 [0.37 – 0.68], $p < .002$), but reacted similarly across all the active cues (*Mdn* minutes, light vs. heavy smokers; Smoking cue: light smokers, 0.67 minutes [0.47 – 0.86] vs. heavy smokers, 0.56 minutes [0.39 – 0.72]; Alcohol cue: 0.67 [0.47 – 0.87] vs. 0.58 [0.40 – 0.75]; Positive cue: 0.63 [0.45 – 0.82] vs. 0.62 [0.43 – 0.80]; Negative cue: 0.73 [0.51 – 0.95] vs. 0.64 [0.44 – 0.83]; Smoking prohibited cue: 0.72 [0.51 – 0.94] vs. 0.61 [0.43 – 0.79]; all *p*s > .5).

In-session moderators of cue effects

Cue presentation order—We assessed whether the effects of cues were moderated by order of presentation, particularly contrasting the first versus other sessions, which differed in overall cue response. There was no order x cue interaction (detail not shown): cue-specific responses did not vary across sessions.

Pre-cue craving—The main effects of pre-cue craving on smoking were considered above. Here, we consider whether there may have been an interaction between pre-cue craving and cue reactivity; that is, whether subjects with higher or lower pre-cue craving may have reacted differently to cues. With regard to post-cue increases in craving, there were no pre-cue x cue interaction effects (detail not shown). That is, pre-cue appetitive or distress-relief craving did not affect how much the cues subsequently increased either appetitive or distress-relief craving. The absence of interactions with pre-cue craving confirms an absence of ceiling effects, because ceiling effects would preclude subjects with initially high craving from showing increased craving – i.e., would have led to an interaction.

We also examined interaction effects influencing post-cue smoking topography. Pre-exposure distress-relief craving did not interact with cues in any way to influence smoking topography. Nor did pre-cue craving of either type influence the probability of smoking or the latency to smoking. However, there were interactions that influenced how much subjects smoked. Specifically, smokers took more puffs after being exposed to negative affect ($p < .04$) or smoking ($p < .02$) cues (compared to neutral cues) if their pre-cue appetitive craving was higher before exposure. According to model-based estimates, for those low in pre-cue craving (25^{th} percentile) the negative affect cue decreased smoking by 0.64 puffs, compared to the neutral cue; for those at high pre-cue craving (75^{th} percentile), the negative affect cue increased smoking by 0.81 puffs. Similarly, the smoking cue decreased puffing by 0.27 puffs at low levels of pre-cue craving, but increased it by 1.34 puffs at high levels of pre-cue craving.

We also observed that smokers with higher appetitive craving before exposure to the positive affect cues subsequently puffed longer ($p < .03$, compared to neutral, controlling for number of puffs). When pre-cue appetitive craving was low (25^{th} percentile), puffing was essentially unaffected by exposure to the positive affect cue (an increase of 0.26 seconds compared to neutral cue); when pre-cue craving was high (75^{th} percentile), individuals puffed for 1.93 seconds longer after exposure to the positive affect cue.

In all cases, there were no significant interaction effects on change in CO, suggesting that the observed interactions had limited effects on smoke intake.

Time since last cigarette—As reported earlier, TSLC had no main effects on cue reactivity. We further examined potential interactions with cues. There were no interactions moderating craving responses to cues; that is, how long the subject had been without cigarettes did not influence how much their craving increased in response to any of the cues. Nor did TSLC influence the probability of smoking or the latency to smoking following particular cues. However, there were interactions that influenced how much subjects

smoked. TSLC interacted with alcohol cues, such that individuals with longer TSLC took more puffs in the alcohol condition ($p < .0003$) relative to the neutral condition, which showed no effect of TSLC. This effect was also evident when the analysis was limited to drinkers ($p < .002$). The effect was not linear. The number of puffs subjects took decreased relatively steeply (from 16.55 puffs to 14.04 puffs) as TSLC increased from 0 to 15 minutes, but then decreased only very slightly, and non-significantly, with increasing TSLC. These effects were not significant when evaluation was limited to subjects who drank.. There was no significant interaction between TSLC and cues on other smoking topography parameters, total puff duration (controlling for number of puffs) or CO increase, indicating that the observed interactions had limited effects on smoke intake.

We also observed an interaction with TSLC for the number of puffs smokers took after seeing the smoking prohibited cues (compared to neutral; $p < .02$). Again, effects were non-linear. The number of puffs increased with increasing TSLC until TSLC reached 15 minutes (increasing from 12.19 puffs to 14.93 puffs as TSLC went from 0 to 15 minutes); the curve was flat thereafter. There were no interaction effects on total puff duration (controlling for number of puffs) or on CO increase, suggesting that the interactions had limited effects on smoke intake.

Discussion

This study tested minimally-deprived smokers' reactions to a spectrum of visually-presented cues expected to be related to smoking. As in prior studies, "proximal" smoking cues (Conklin et al., 2008) – images of cigarettes and smoking – increased craving. Alcohol cues also seemed to marginally increase appetitive craving, among those who drink, suggesting that these associations developed through experience and conditioning (Niaura et al., 1988). In contrast, positive affect cues actually resulted in reduced craving, while negative affect cues had no, even though they induced emotional distress. A novel set of "smoking prohibited" cues, designed to invoke environments in which smoking is prohibited, had no effects on craving.

Of the cues we tested, the ones that produced the strongest craving response – indeed, the only ones that increased craving in the sample as a whole – were proximal cues (Conklin et al., 2008) that depicted cigarettes and the act of smoking. These cues are the most universally and intimately linked with smoking, so would likely have the strongest conditioned associations that might elicit craving. Though exposure to these cues increased craving on average, the mean increases were modest, with some smokers reporting no increase (30% < 1 point), and some reduced craving (23% dropped > 1 point). This variation in response to cues has previously been observed (e.g., Shiffman et al., 2003), but is unexplained. Perhaps cues obviously intended to provoke craving can sometimes elicit efforts to suppress craving.

We also tested how affective cues influenced craving. The affective cues, derived from a well-validated set of stimuli known to influence affect (Lang et al., 1995), did change affect. The negative affect cues were particularly potent, so it was surprising they did not increase craving. Our study differs from the prior studies that showed mood effects on craving

(Perkins et al., 2010; Tiffany & Drobes, 1990) in several respects (e.g., duration of deprivation, the nature of the affect manipulation, expectations of smoking); it is not clear what accounts for the differences in findings. We saw no moderation by degree of deprivation. Lack of power cannot explain the differences, as this study was considerably larger than the prior studies, and had 80% power (Erdfelder, Faul, & Buchner, 1996) to detect even relatively small differences in craving change (Cohen's $d = 0.20$) across cues – and did so for other cues. The consistent findings from EMA studies (Piasecki, Richardson, & Smith, 2007; Shiffman et al., 2002; Shiffman, Paty, Gwaltney, & Dang, 2004) that negative affect does not influence ad lib smoking make it less surprising that negative affect may have little or no effect on craving, and no effect on ad lib smoking.

We had also expected that increases in positive affect would increase craving, because smokers report craving and smoking in positive affect states (Dunbar et al., 2010) and Baker, Morse, and Sherman (1987) have argued that craving is associated with positive affect during ad lib smoking (vs. abstinence). Contrary to this hypothesis, exposure to positive affect cues (which increased positive affect) was associated with decreased craving relative to a neutral cue (though not relative to baseline: appetitive craving – but not distress-relief craving- increased significantly pre- to post-cue). Perhaps when smokers report associations with distress, they are referring to decrease positive affect rather than increased negative affect; the circumplex model (Russell, 1980) posits that positive and negative affects lie on the same dimension, and are just opposite ends of a single bi-polar dimension. A careful parsing of dimensions of affect may be necessary to disentangle the complex relationship between affect and smoking.

Whereas we observed neither increased craving nor increased smoking after negative-affect induction, others have observed both, but these studies (e.g., Payne et al., 1991) sometimes used manipulations, such as a cognitive performance task, that could introduced other motives for smoking (e.g., for cognitive enhancement). In any case, we used cues that effectively elicited negative affect but did not increase craving or smoking.

Although alcohol and smoking are very tightly linked (Shiffman & Balabanis, 1995), we saw no overall craving response to alcohol cues. However, if conditioned associations due to the pairing of smoking and drinking are the mechanism for reactivity, this link should occur only in smokers who drink. This is what we observed, consistent with this conditioning explanation. In any case, the ability of alcohol cues to elicit craving may in part explain why alcohol plays such a significant role in smoking relapse (Shiffman, Hickcox et al., 1996).

We tested here for the first time the cue effects of stimuli that have become a dominant feature of smokers' lives – signals that smoking is prohibited. Over 75% of US smokers are covered by workplace smoking bans (Bauer, Hyland, Qiang, Craig, & Cummings, 2005), thus spending much of their waking day under restriction. With additional bans in public places and bars and restaurants, the world for smokers is now increasingly divided between smoking-allowed and smoking-prohibited settings. We expected these settings to become conditioned cues for either increased or decreased craving: increased, because they are associated with deprivation, which elicits craving (Sayette, Martin, Wertz, Shiffman, & Perrott, 2001; Tiffany, Cox, & Elash, 2000), or decreased, because craving is generally

reduced when smoking is not possible (Wertz & Sayette, 2001). The data indicated no change in craving. Given the bi-directional hypotheses, the null result might be thought to be due to craving being driven in different directions for different subjects, resulting in no net change. However, this hypothesis would imply an increase in dispersion or variance after exposure to the cues, which was not observed: indeed, the standard deviations for craving change in this condition were lower than or comparable to those in all other cue sets. Thus, we conclude that cues signaling smoking prohibitions have no effect on craving, in either direction. Perhaps smokers have habituated to smoking prohibited cues and environments, but our test is limited by the particular cues used, the sample tested, etc. Further research on non-smoking environments and cues is warranted.

Cue reactivity studies have been criticized for limiting their outcomes to craving, without examining smoking itself (Perkins, 2009). We did assess smoking following cue exposure. Strikingly, cues did not appear to have main effects on any measured aspect of smoking behavior: exposure to specific cues (compared to a neutral cue) was not associated with the probability of smoking, latency to smoke, or amount of smoking (puffs, puff time, number of cigarettes, CO boost) among those who smoked.

This is perhaps the most striking in these data: there was no relationship between exposure to specific cues and smoking, but craving itself had a strong influence on smoking. Craving affected all aspects of smoking assessed in this study: higher craving was associated with increased probability of smoking, faster progression to smoking, increased probability of lighting a second cigarette, taking more puffs, longer puffing, and greater increases in CO. This establishes the relevance of craving to smoking, which has been challenged by some authors (Perkins, 2009; Tiffany, 1990). Importantly, the effects of craving on smoking were often curvilinear. The influence of craving on the probability of smoking and latency to smoking was steepest at lower levels of craving, and then leveled off as craving grew more intense. This is consistent with the relationship observed in EMA studies of craving in the natural environment (Shiffman et al., 2002; Shiffman et al., 2004), which suggested a threshold effect for smoking. This effect is important; it may explain why studies sometimes fail to find a relationship between craving and smoking: the degree of association differs according to the level of craving. Studies in which subjects are at high levels of craving are likely to see no relationship between craving and initiation of smoking, because they are at the flatter end of the craving-smoking curve.

There were also non-linear effects on intensity of smoking, but these were opposite in direction: the influence of craving on puffing behavior was modest at low levels of craving, but accelerated with more intense craving. This suggests a dissociation between the processes controlling initiation of smoking and those controlling puffing once smoking is initiated. It also again suggests that studies of this relationship will yield different results depending on the intensity of craving at which smoking is measured.

Although exposures to specific cues (vs. neutral cues) did not affect smoking behavior, changes in craving during cue exposure did influence smoking. Changes in craving pre- to post-exposure – regardless of cue - had independent, additive effects on behavioral smoking parameters (likelihood, latency, number of puffs and puff duration). It is possible that the

increase in craving during exposure occurred because subjects were anticipating the opportunity to smoke after the initial exposure. However, this effect would be expected to be stronger in later sessions, after subjects had experienced smoking in the lab, and this was not seen. These changes in craving are also unlikely to be due just to the passage of time and increased deprivation, as it seems unlikely that 3 additional minutes of abstinence would have much effect on smokers who have been abstinent for at least 30 minutes and an average of 88 minutes. (Indeed, the average per-minute change in craving is 4–6 times greater [appetitive and distress craving, respectively] during the cue exposure than during the baseline period.) If the change in craving was due to cues, how is it that particular cues had no effects on smoking, but craving increases during exposure reliably affected smoking? This pattern of results suggests that while particular cues did not produce enough of a consistent craving response to influence subsequent smoking across all subjects, smokers' idiosyncratic craving responses to the cues (including the neutral cue) did influence smoking. This suggests that it may be important to explore the effects of personalized cues, taking into account each smoker's idiosyncratic reactions, rather than looking for uniform reactions to a common set of cues (Conklin & Tiffany, 2001).

In any case, in these data, the relevance of craving to smoking is more evident than is the ability of particular cues to influence either craving or smoking. The observed influence of craving on smoking is consistent with models that assume that craving reflects motivational processes that lead to smoking. Some prior studies failed to find associations between craving and smoking, leading some authors (Tiffany & Drobes, 1990) to conclude that craving is not related to smoking. In this study, craving does indeed precede and predict smoking. We also examined several individual differences that could potentially moderate cue reactivity. Perkins (1996) has proposed that female smoking is more driven by cues, which led to the hypothesis that women would demonstrate more cue reactivity. Men and women did not differ in any of their responses to cues, either with respect to craving or smoking, which seems inconsistent with the hypothesis.

As most of the cue reactivity literature has been based on heavier smokers, we also looked for moderation by cigarette consumption, but found no differences in craving or in the likelihood or amount of smoking. We did see some differences in progression to smoking, but these seemed to be driven by lighter smokers progressing more slowly to smoking following the neutral cue, rather than responding differently than heavier smokers to the active cues. These differences in response to the neutral cue were unexpected, and do not represent typical cue-reactivity effects. It may be that heavier smokers attribute smoking relevance to the neutral cues, perhaps because of the study context, or are simply insensitive to context and smoke when given the opportunity, no matter what the circumstance (cf. Herman, 1974).

We did not observe any differences in cue reactivity between AA and EA smokers. We did observe that AA smokers demonstrated greater increases in distress-relief craving, regardless of cues, and were more likely to smoke following cue exposure, again regardless of which cue was shown. While these effects might suggest that AA smokers were more avidly seeking nicotine, AA smokers actually spent less time puffing. As there were no differences in CO boost, however, it appears that EA and AA smokers had similar smoke

intakes. The factors stimulating initiation of smoking, and those controlling its intensity, may differ.

We examined both pre-cue craving and TSLC as potential moderators of cue effects on craving, but found no significant interactions: craving changes were similar regardless of one's pre-cue craving or how long one had gone without smoking. However, these moderators did affect smoking topography after particular cue exposures. Subjects with higher pre-cue appetitive craving took more puffs after negative affect and smoking cues, and puffed longer after positive affect cues. It is not clear why higher baseline craving should increase reactivity to these particular cues and not others, but it could suggest that appetitive craving states increase sensitivity to cues, consistent with incentive-salience theory (Robinson & Berridge, 1993). The moderating effects of TSLC were very complex, and did not follow a coherent pattern. Increases in TSLC of up to 15 minutes (but not longer) led to taking fewer puffs after the alcohol cue, but to increased puffing after the smoking prohibited cues. In no case did these moderator variables influence probability of smoking, latency to smoking, or increases in CO, so these do not seem to be robust effects on smoking, and may be artifactual.

The intensity of craving observed in this study was modest, as were the effects of cue exposure on craving. We studied a range of smokers, including light smokers, under minimal deprivation, perhaps accounting for the modest craving levels. Yet, the mean cigarette consumption in our sample was close to the national average, so might be considered representative. Similarly, the duration of abstinence prior to testing seemed to mirror what smokers typically experience during ad lib smoking: Including the 30 minutes of deprivation we imposed, the typical duration of abstinence was about 50 (median) or 88 (mean) minutes – close to subjects' expected average inter-cigarette interval of about 60 minutes (16 cigarettes in 16 waking hours). Thus, the study arguably represents the typical situation of smokers during ad lib smoking. Moreover, the level of craving observed, though not near the top of the scale, was sufficient to motivate smoking in 87% of the sessions, and even the modest changes in craving during cue exposure were associated with increased probability and intensity of smoking.

That said, more intense cues (e.g., in vivo cues or personalized cues) might be more effective at eliciting cue reactivity. Moreover, real-world settings may be marked by composite cues, combining, for example, alcohol, positive affect, and smoking cues (e.g., at a party), rather than the single cues we used. Like most reactivity studies, we used standardized cues, which could limit the cues' ability to evoke craving, as different smokers may have developed idiosyncratic responses to particular cues; personalized cues may be stronger and more relevant (Conklin, 2006; Conklin & Tiffany, 2001). Importantly, the different cue sets may not have been equally potent – indeed, the affect data showed that the negative affect cues were more powerful at changing mood than were the positive affect cues – so comparisons across cue types may be confounded by the particular stimuli used to represent each. The fact that positive affect cues, which were less potent in changing affect and seemed to be less arousing in IAPS ratings, actually had greater impact on craving further suggest that 'potency' is not a unitary dimension.

This study had other limitations. Our use of multiple stimuli, and multiple cue assessments within each stimulus session could have created demand characteristics, perhaps conveying to subjects that they were supposed to experience craving, and thus perhaps masking differences among stimuli. Repeated assessment could also lead to assessment fatigue, which could introduce noise or bias. However, LaRowe and colleagues (2007) reported no systematic changes in craving across multiple cue exposure sessions, and we similarly did not see progressive changes over time. We did observe that the first session differed from subsequent ones, perhaps because the first session familiarizes subjects with the procedures, allows subjects to discover that they really will be allowed to smoke, and so on. We controlled for these effects.

Our methods of assessing smoking topography relied on visual cues to time puffing, but did not actually measure flow of smoke into the mouth or lungs, as can be done with more sophisticated methods (Creighton, Noble, & Whewell, 1978). However, the visual coding method avoided unnatural interference with smoking behavior, and Blank, Disharoon, and Eissenberg (2009) showed that such observational measures were highly correlated with flow-based measures. Also, in our own data, video-based topography measures correlated with CO.

A subtle but crucial issue that plagues all reactivity studies is the difficulty differentiating specific cue effects from background craving (Sayette et al., 2000). Unavoidably, the context of attending a session at a smoking laboratory, answering questions about smoking, and anticipating being exposed to cues and being allowed to smoke may act as a strong cue in itself, and could overwhelm or mask the specific effects of visual cues.

Our study also had several strengths. It assessed smokers' responses to a range of cues, rather than a single one, and included a neutral control cue. As far as we are aware, this is the largest cue-reactivity study in the literature, with over 200 subjects and over 1,200 reactivity sessions. The size of the study, along with its within-subjects design, allowed for very sensitive analyses capable of detecting small to medium effects, even for moderation relationships. We used well-validated, reliable multi-item assessments of craving. Also, we extended assessment beyond craving to look at smoking behavior, both behaviorally, looking at how quickly people lit up and how much they smoked, and biologically (CO). Our sample also included a wider range of smoking behavior than is usually seen in reactivity studies: while most reactivity studies were done on relatively heavy smokers (Carter & Tiffany, 1999) the subjects in our study smoked as little as 5 CPD, and their average smoking rate approximated the national average (CDC, 2005).

In summary, the study extended the reactivity literature by assessing multiple cues, including a novel smoking prohibited cue, and assessing effects on smoking as well as craving. We confirmed the well-established effect of cigarette cues on craving, but saw no effect of negative affect or smoking prohibited cues on either craving or smoking. Surprisingly, positive affect cues decreased craving, perhaps demonstrating another side of negative-affect smoking. We did not see any effect of cues associated with smoking-prohibited environments, perhaps because smokers have adapted to smoking prohibitions. Cues had virtually no effects on subsequent smoking behavior, but craving intensity and

craving changes during cue exposure both predicted smoking, independent of cues, suggesting that much of the variance in craving was independent of cues or idiosyncratically related to cue exposure. In any case, the data validated the relevance of craving for subsequent smoking, while suggesting a dissociation between cue response and subsequent smoking. Exploration of the mediating processes between cue exposures, craving, and subsequent smoking would also help shed light on how environmental and internal cues influence smoking.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

Abrams DB, Monti PM, Carey KB, Pinto RP, Jacobus SI. Reactivity to smoking cues and relapse: Two studies of discriminant validity. Behavioral Research and Therapy. 1988; 26:225–233.

Baker, TB.; Morse, E.; Sherman, JE. The motivation to use drugs: A psychobiological analysis of urges. In: Rivers, PC., editor. The Nebraska Symposium on Motivation: Alcohol Use and Abuse. Lincoln: University of Nebraska Press; 1987. p. 257-323.

Bauer JE, Hyland A, Qiang L, Craig S, Cummings KM. A longitudinal assessment of the impact of smoke-free worksite policies on tobacco use. American Journal of Public Health. 2005; 95(6):1024–1029. [PubMed: 15914828]

Blank MD, Disharoon S, Eissenberg T. Comparison of methods for measurement of smoking behavior: Mouthpiece-based computerized devices versus direct observation. Nicotine and Tobacco Research. 2009; 11(7):896–903. [PubMed: 19525207]

Brown, H.; Prescott, R. Applied Mixed Models in Medicine. New York: John Wiley & Sons; 2006.

Burton SM, Tiffany ST. The effect of alcohol consumption on craving to smoke. Addiction. 1997; 92(1):15–26. [PubMed: 9060194]

Caggiula AR, Donny EC, Palmatier MI, Chaudhri N, Sved AF. The role of nicotine in smoking: A dual-reinforcement model. Nebraska Symposium on Motivation. 2009; 55:91–109. [PubMed: 19013940]

Carter BL, Robinson JD, Lam CY, Wetter DW, Tsan JY, Day SX. A psychometric evaluation of cigarette stimuli used in a cue reactivity study. Nicotine and Tobacco Research. 2006; 8:361–369. [PubMed: 16801294]

Carter BL, Tiffany ST. Meta-analysis of cue-reactivity in addiction research. Addiction. 1999; 94(3): 327–340. [PubMed: 10605857]

Centers for Disease Control and Prevention (CDC). Cigarette smoking among adults - United States, 2004. MMWR Morbidity and Mortality Weekly Report. 2005; 54:1121–1124. [PubMed: 16280969]

Center for the Study of Emotion and Attention. International Affective Pictures System: Digitized photographs. Gainesville: The Center for Research in Psychophysiology, University of Florida; 1999.

Cohen J. Statistical power analysis. Current Directions in Psychological Science. 1992; 1(3):98–101.

Conklin CA. Environments as cues to smoke: Implications for human extinction-based research and treatment. Experimental and Clinical Psychopharmacology. 2006; 14:12–19. [PubMed: 16503701]

Conklin CA, Robin N, Perkins KA, Salkeld RP, McClernon FJ. Proximal versus distal cues to smoke: The effects of environment on smokers' cue-reactivity. Experimental and Clinical Psychopharmacology. 2008; 16:207–214. [PubMed: 18540780]

Conklin CA, Tiffany S. The impact of imagining personalized versus standardized urge scenarios on cigarette craving and autonomic reactivity. Experimental and Clinical Psychopharmacology. 2001; 9(4):399–408. [PubMed: 11764016]

Cox LS, Tiffany ST, Christensen A. Evaluation of the brief questionnaire of smoking urges (QSU-brief) in laboratory and clinical settings. Nicotine and Tobacco Research. 2001; 3(1):7–16. [PubMed: 11260806]

Creighton, DE.; Noble, MJ.; Whewell, RT. Instruments to measure, record, and duplicate human smoking patterns. In: Thornton, RE., editor. Smoking Behaviour: Physiological and Psychological Influences. Churchill Livingston; 1978. p. 277-288.

Diener E, Emmons RA. The independence of positive and negative affect. Journal of Personality and Social Psychology. 1984; 47(5):1105–1117. [PubMed: 6520704]

Droungas A, Ehrman R, Childress AR, O'Brien CP. Effect of smoking cues and cigarette availability on craving and smoking behavior. Addictive Behaviors. 1995; 20(5):657–673. [PubMed: 8712062]

Dunbar MS, Scharf DM, Kirchner T, Shiffman S. Do smokers crave cigarettes in some smoking situations more than others? Situational correlates of craving when smoking. Nicotine and Tobacco Research. 2010; 12(3):226–234. [PubMed: 20133379]

Elash CA, Tiffany ST, Vrana SR. Manipulation of smoking urges and affect through a brief-imagery procedure: Self-report, psychophysiological, and startle probe responses. Experimental and Clinical Psychopharmacology. 1995; 3(2):156–162.

Erblich J, Montgomery G, Bovbjerg D. Script-guided imagery of social drinking induces both alcohol and cigarette craving in a sample of nicotine-dependent smokers. Addictive Behaviors. 2009; 34:164–170. [PubMed: 18977604]

Erdfelder E, Faul F, Buchner A. GPOWER: A general power analysis program. Behavior Research Methods, Instruments, & Computers. 1996; 28:1–11.

Ferguson SG, Shiffman S. The relevance and treatment of cue-induced cravings in tobacco dependence. Journal of Substance Abuse and Treatment. 2009; 36(3):235–243.

Gilbert, DG.; Rabinovich, NE. International smoking images series with neutral counterparts: Southern Illinois University, Integrative Neuroscience Laboratory, Department of Psychology. 1999.

Gilbert DG, Sharpe JP, Ramanaiah NV, Detwiler FR, Anderson AE. Development of a situation - trait adaptive response (STAR) model-based smoking motivation questionnaire. Personality and Individual Differences. 2000; 29:65–84.

Hedeker D, Mermelstein RJ, Berbaum ML, Cambell RT. Modeling mood variation associated with smoking: An application of a heterogeneous mixed-effects model for analysis of ecological momentary assessment (EMA) data. Addiction. 2009; 104(2):297–307. [PubMed: 19149827]

Heishman SJ, Lee DC, Taylor RC, Singleton EG. Prolonged duration of craving, mood, and autonomic responses elicited by cues and imagery in smokers: Effects of tobacco deprivation and sex. Experimental and Clinical Psychopharmacology. 2010; 18(3):245–256. [PubMed: 20545389]

Heishman SJ, Saha S, Singleton EG. Imagery-induced tobacco craving: Duration and lack of assessment reactivity bias. Psychology of Addictive Behaviors. 2004; 18(3):284–288. [PubMed: 15482084]

Herman CP. External and internal cues as determinants of the smoking behavior of light and heavy smokers. Journal of Personality and Social Psychology. 1974; 30(5):664–672. [PubMed: 4443887]

Herman, CP.; Polivy, J. A boundary model for the regulation of eating. New York: Raven Press; 1984.

Hogarth L, Dickinsion A, Duka D. The associative basis of cue-elicited drug taking in humans. Psychopharmacology. 2009; 208(3):337–51. [PubMed: 19960187]

Horn, D.; Waingrow, S. Smoking behavior change. In: Zagona, SV., editor. Studies and issues in smoking behavior. Tucson: University of Arizona Press; 1967.

Hosmer, JE.; Lemeshow, S.; May, S. Applied survival analysis: Regression modeling to time to event data. New York: Wiley; 2008.

Ikard FF, Green D, Horn D. A scale to differentiate between types of smoking as related to the management of affect. International Journal of the Addictions. 1969; 4:649–659.

iStockPhoto. iStockPhoto website. 2007. http://www.istockphoto.com/index.php

Kozlowski LT, Herman CP. The interaction of psychosocial and biological determinants of tobacco use: More on the Boundary Model. Journal of Applied Social Psychology. 1984; 14:244–256.

Kraemer, HC.; Thiemann, S. How many subjects? Statistical power analysis in research. Newbury Park, CA: Sage; 1987.

Lang, PJ.; Bradley, MM.; Cuthbert, BN. International Affective Picture System (IAPS): Technical manual and affective ratings. Gainesville: University of Florida Center for Research in Psychophysiology; 1995.

LaRowe SD, Saladin ME, Carpenter MJ, Upadhyaya HP. Reactivity to nicotine cues over repeated cue reactivity sessions. Addictive Behaviors. 2007; 32(12):2888–2899. [PubMed: 17537583]

McMillen RC, Winnickoff JP, Klein JD, Weitzman M. US adult attitudes and practices regarding smoking restrictions and child exposure to environmental tobacco smoke: Changes in the social climate from 2000–2001. Pediatrics. 2003; 112:55–60.

Morgan M, Davies G, Willner P. The questionnaire of smoking urges is sensitive to abstinence and exposure to smoking-related cues. Behavioural Pharmacology. 1999; 10:619–626. [PubMed: 10780503]

Niaura R, Abrams DB, Demuth B, Pinto RP, Monti PM. Responses to smoking-related stimuli and early relapse to smoking. Addictive Behaviors. 1989; 14:419–428. [PubMed: 2782124]

Niaura R, Rohsenow DJ, Binkoff JA, Monti PM, Pedraza M, Abrams DB. Relevance of cue reactivity to understanding alcohol and smoking relapse. Journal of Abnormal Psychology. 1988; 97(2):133–152. [PubMed: 3290304]

O'Connell KA, Martin EJ. Highly tempting situations associated with abstinence, temporary lapse, and relapse among participants in smoking cessation programs. Journal of Consulting and Clinical Psychology. 1987; 55:367–371. [PubMed: 3597950]

Payne TJ, Schare ML, Levis DJ, Colletti G. Exposure to smoking-relevant cues: Effects on desire to smoke and topographical components of smoking behavior. Addictive Behaviors. 1991; 16:467–479. [PubMed: 1801570]

Perkins KA. Sex differences in nicotine versus nonnicotine reinforcement as determinants of tobacco smoking. Experimental and Clinical Psychopharmacology. 1996; 4(2):166–177.

Perkins KA. Does smoking cue-induced craving tell us anything important about nicotine dependence? Addiction. 2009; 104(10):1610–1616. [PubMed: 19426293]

Perkins KA, Epstein LH, Grobe J, Fonte C. Tobacco abstinence, smoking cues, and the reinforcing value of smoking. Pharmacology, Biochemistry, and Behavior. 1994; 47(1):107–112.

Perkins KA, Karelitz J, Conklin CA, Sayette M, Giedgowd G. Acute negative affect relief from smoking depends on the affect situation and measure but not on nicotine. Biological Psychiatry. 2010; 67:707–714. [PubMed: 20132927]

Piasecki TM, McCarthy DE, Fiore MC, Baker TB. Alcohol consumption, smoking urge, and the reinforcing effects of cigarettes: An ecological study. Psychology of Addictive Behaviors. 2008; 22:230–239. [PubMed: 18540720]

Piasecki TM, Richardson AE, Smith SM. Self-monitored motives for smoking among college students. Psychology of Addictive Behaviors. 2007; 21(3):328–337. [PubMed: 17874883]

Pomerleau, CS.; Berman, BA.; Gritz, ER.; Marks, JL.; Goeters, S. Why women smoke. In: Watson, RR., editor. Addictive behaviors in women. Totawa, NJ: Humana; 1994. p. 39-70.

Rikard-Figueroa K, Zeichner A. Assessment of smoking urge and its concomitants under an environmental smoking cue manipulation. Addictive Behaviors. 1985; 10(3):249–256. [PubMed: 4083102]

Robinson TE, Berridge KC. The neural basis of drug craving: An incentive-sensitization theory of addiction. Brain Research Reviews. 1993; 18:247–291. [PubMed: 8401595]

Royce JM, Hymowitz N, Corbett K, Hartwell TD, Orlandi MA. Smoking cessation factors among African Americans and Whites. American Journal of Public Health. 1993; 83:220–226. [PubMed: 8427327]

Russell J. A circumplex model of affect. Journal of Personality and Social Psychology. 1980; 37:345–356.

Sayette MA, Martin CS, Wertz JM, Perrott MA, Peters AR. The effects of alcohol on cigarette craving in heavy smokers and tobacco chippers. Psychology of Addictive Behaviors. 2005; 19:263–270. [PubMed: 16187804]

Sayette MA, Martin CS, Wertz JM, Shiffman S, Perrott MA. A multi-dimensional analysis of cue-elicited craving in heavy smokers and tobacco chippers. Addiction. 2001; 96:1419–1432. [PubMed: 11571061]

Sayette MA, Shiffman S, Tiffany ST, Niaura R, Martin CS, Shadel WG. The measurement of drug craving. Addiction. 2000; 95(Supplement 2):S189–S210. [PubMed: 11002914]

Shadel WG, Shiffman S, Niaura R, Nichter M, Abrams DB. Current models of nicotine dependence: What is known and what is needed to advance understanding of tobacco etiology among youth. Drug and Alcohol Dependence. 2000; 59(Supplement 1):S9–S22. [PubMed: 10773435]

Shiffman S. Relapse following smoking cessation: A situational analysis. Journal of Consulting and Clinical Psychology. 1982; 50(1):71–86. [PubMed: 7056922]

Shiffman, S.; Balabanis, M. Association between alcohol and tobacco. In: Ferting, JB.; Allen, JP., editors. Alcohol and Tobacco: From Basic Science to Clinical Practice, NIH Publication 397. Washington, D.C.: United States Department of Health and Human Services; 1995.

Shiffman S, Gwaltney CJ, Balabanis M, Liu KS, Paty JA, Kassel JD, et al. Immediate antecedents of cigarette smoking: An analysis from ecological momentary assessment. Journal of Abnormal Psychology. 2002; 111(4):531–545. [PubMed: 12428767]

Shiffman S, Hickcox M, Paty JA, Gnys M, Kassel JD, Richards T. Progression from a smoking lapse to relapse: prediction from abstinence violation effects, nicotine dependence, and lapse characteristics. Journal of Consulting and Clinical Psychology. 1996; 64:993–1002. [PubMed: 8916628]

Shiffman S, Paty JA, Gnys M, Kassel JD, Hickcox M. First lapses to smoking: Within-subjects analyses of real-time reports. Journal of Consulting and Clinical Psychology. 1996; 64:366–379. [PubMed: 8871421]

Shiffman S, Paty JA, Gwaltney CJ, Dang Q. Immediate antecedents of cigarette smoking: An analysis of unrestricted smoking patterns. Journal of Abnormal Psychology. 2004; 113(1):166–171. [PubMed: 14992670]

Shiffman S, Shadel W, Niaura R, Khayrallah M, Jorenby D, Ryan C, et al. Efficacy of acute administration of nicotine gum in relief of cue-provoked cigarette craving. Psychopharmacology. 2003; 166:343–350. [PubMed: 12601502]

Shiffman S, Waters AJ. Negative affect and smoking lapses: A prospective analysis. Journal of Consulting and Clinical Psychology. 2004; 72:192–201. [PubMed: 15065954]

Sobell, MB.; Sobell, LC.; Maisto, SA. Time-line follow-back assessment method [TLFB]. In: Lettieri, DJ.; Nelson, JE.; Sayers, MA., editors. Alcoholism treatment assessment research instruments. Rockville, MD: NIAA; 1979. p. 167-188.NIAA treatment handbook series 2

StataCorp. Stata Statistical Software: Release 12. College Station, TX: StataCorp LP; 2011.

Tiffany ST. A cognitive model of drug urges and drug use behavior: Role of automatic and non-automatic processes. Psychological Review. 1990; 97:147–168. [PubMed: 2186423]

Tiffany ST, Cox LS, Elash CA. Effects of transdermal nicotine patches on abstinence-induced and cue-elicited craving in cigarette smokers. Journal of Consulting and Clinical Psychology. 2000; 68(2):233–240. [PubMed: 10780123]

Tiffany ST, Drobes DJ. Imagery and smoking urges: The manipulation of affective content. Addictive Behaviors. 1990; 15:531–539. [PubMed: 2075850]

Tiffany ST, Hakenewerth DM. The production of smoking urges through an imagery manipulation: Psychophysiological and verbal manifestations. Addictive Behaviors. 1991; 16:389–400. [PubMed: 1801563]

Warthen M, Tiffany ST. Evaluation of cue reactivity in the natural environment of smokers using Ecological Momentary Assessment. Experimental and Clinical Psychopharmacology. 2009; 17(2): 70–77. [PubMed: 19331483]

Watson N, Carpenter M, Saladin M, Gray K, Upadhyaya H. Evidence for greater cue reactivity among low-dependent vs. high-dependent smokers. Addictive Behaviors. 2010; 35(5):673–677. [PubMed: 20206451]

Wertz J, Sayette MA. Effects of availability on urge responses. Experimental and Clinical Psychopharmacology. 2001; 9:3–13. [PubMed: 11519632]

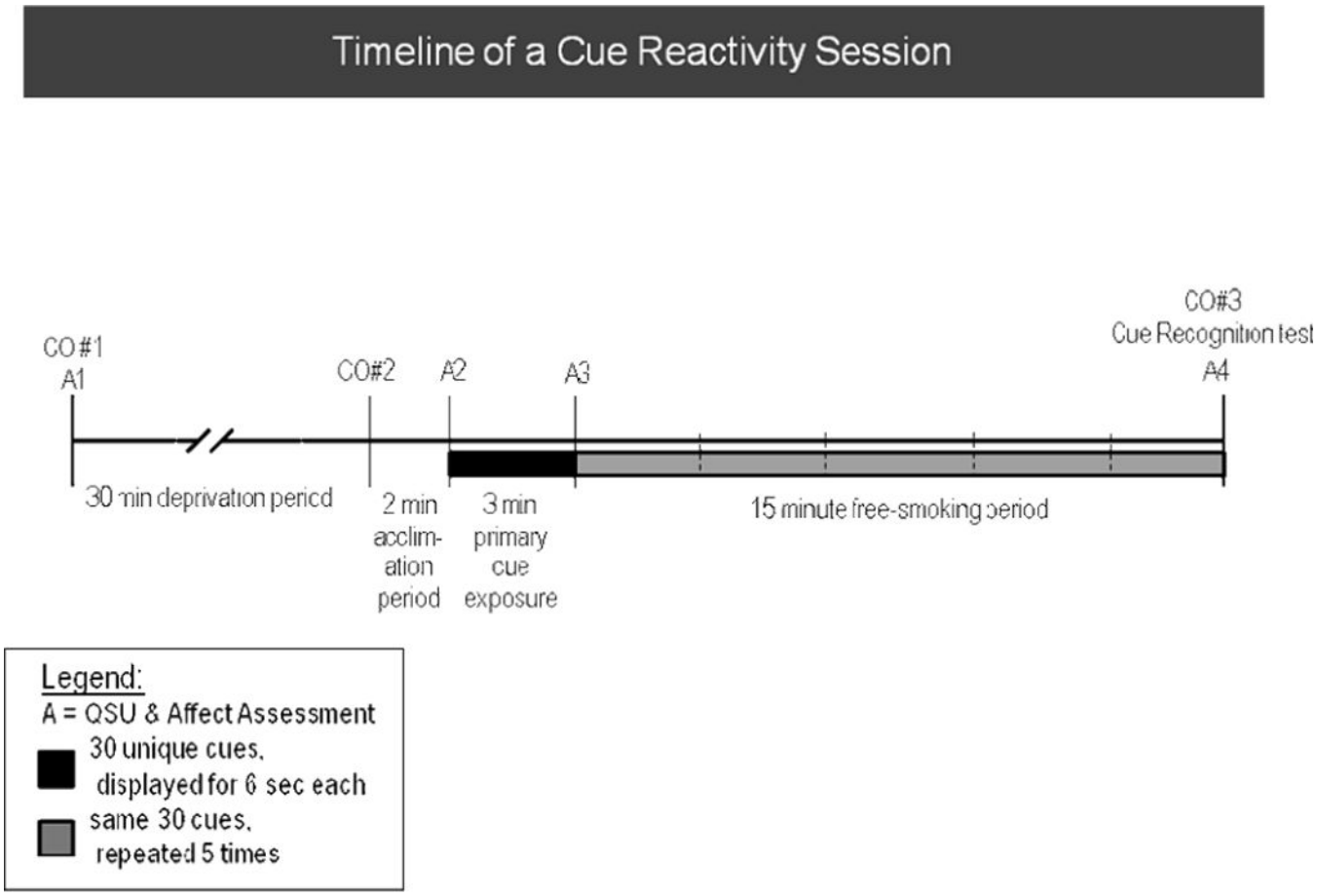


Figure 1.
Timeline of procedure and assessments in cue reactivity sessions.

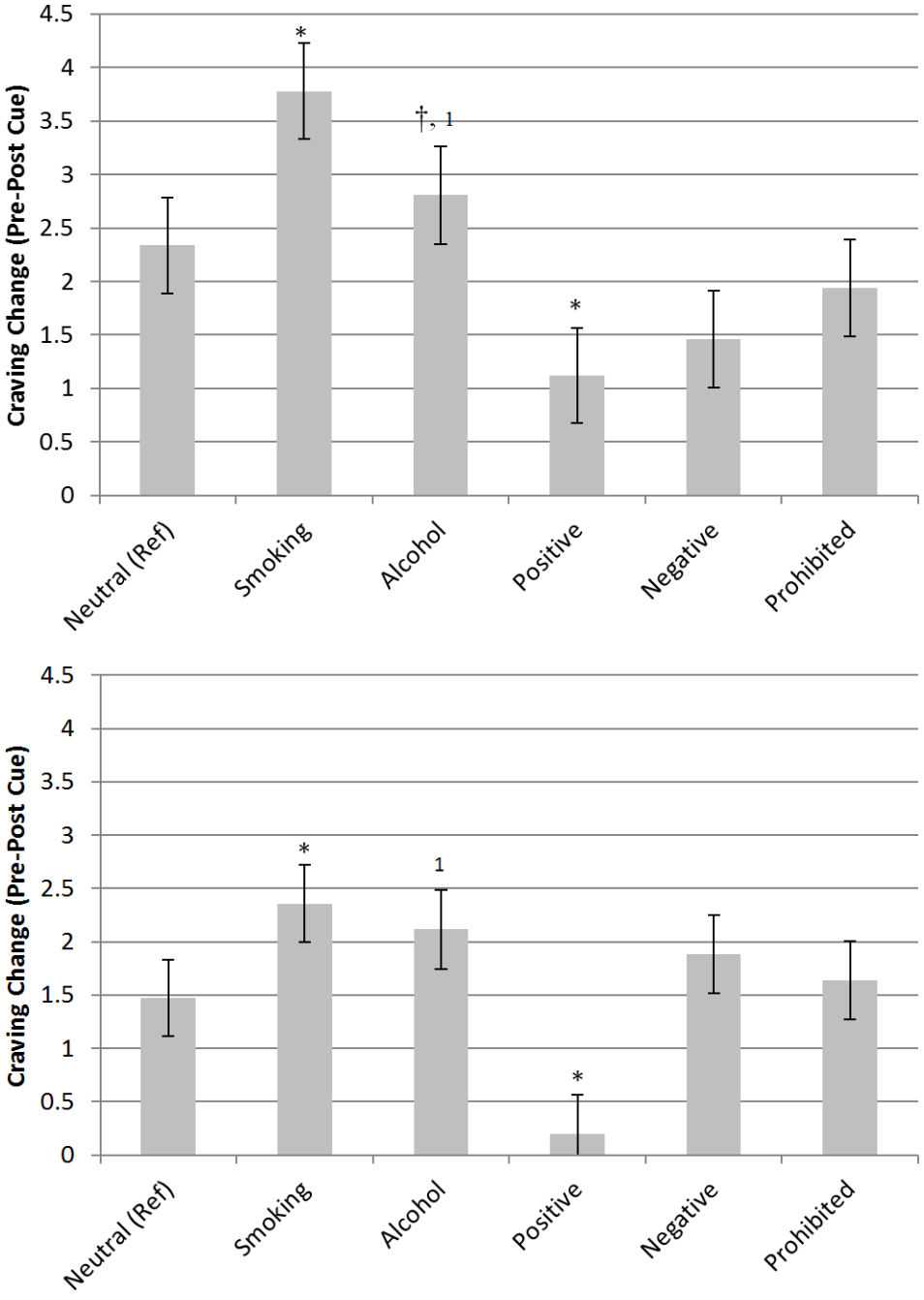


Figure 2.

Change in appetitive craving (A) and distress-relief craving (B) after exposure to each cue. [1]Data for alcohol cue are from subjects who were known to drink. *$p < .05$, †$p < .10$.

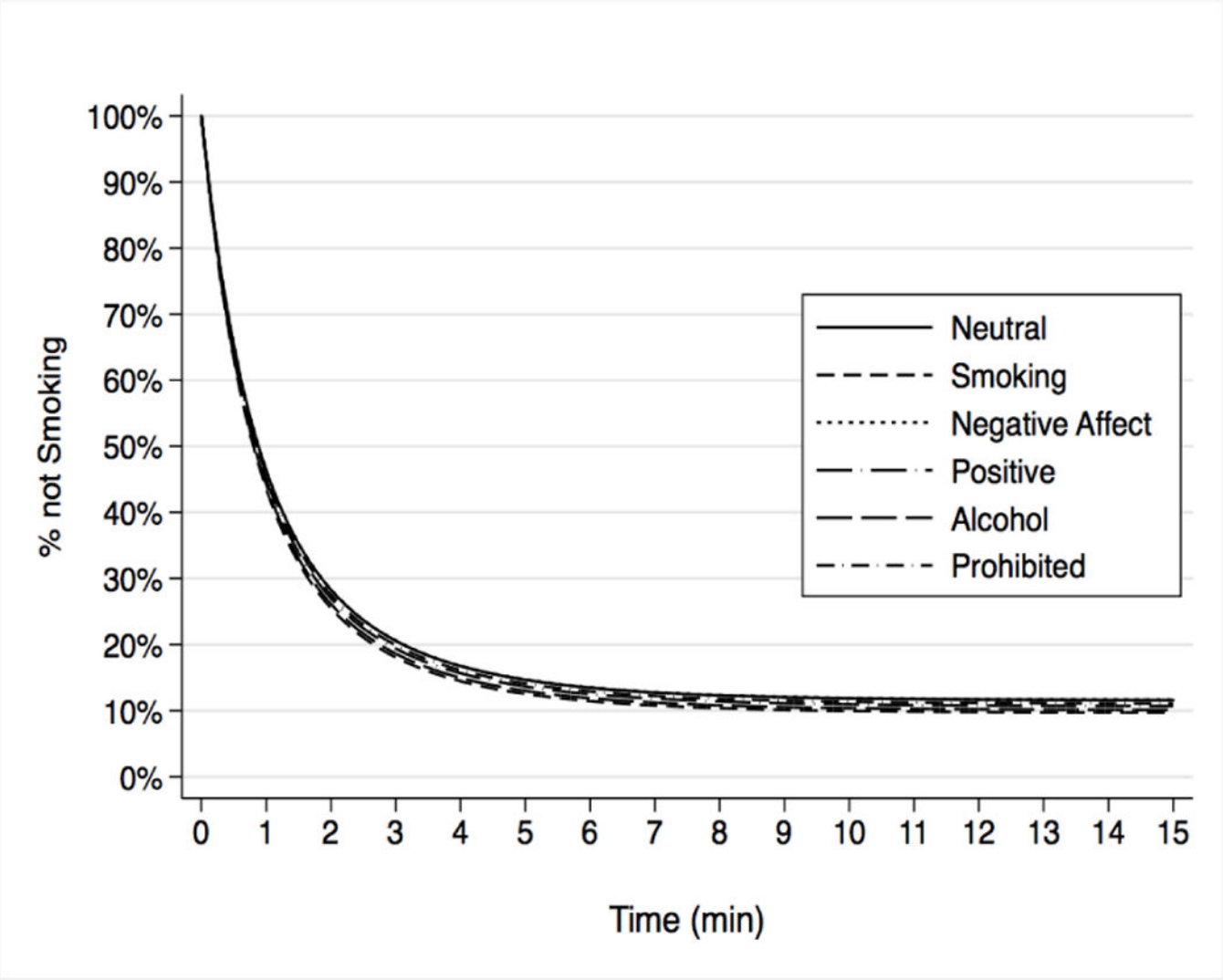
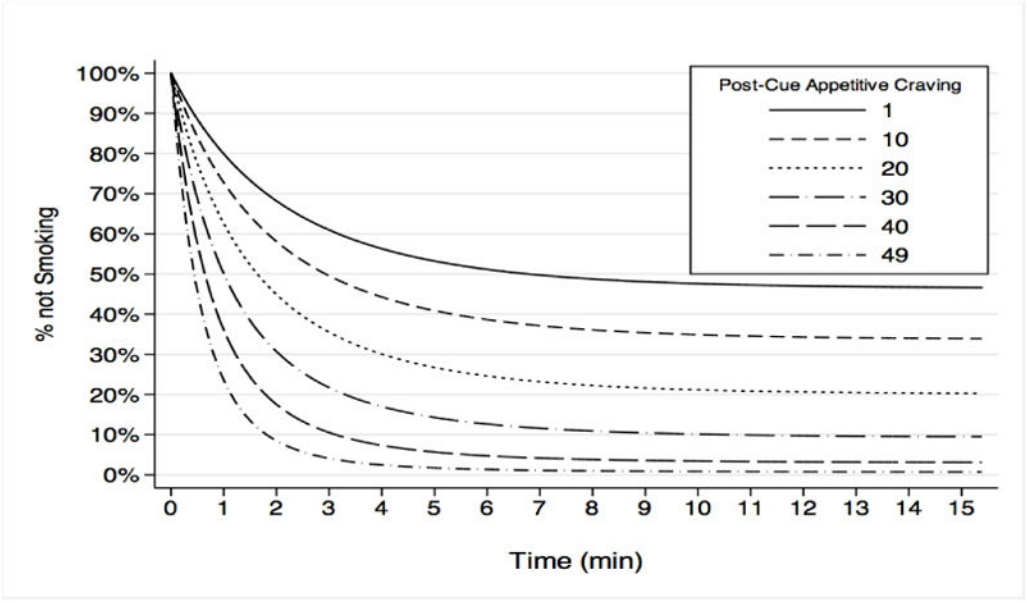


Figure 3.
Survival graphs showing time to smoking after exposure to cues. No significant effect of cues on latency to smoke.

a.



b.

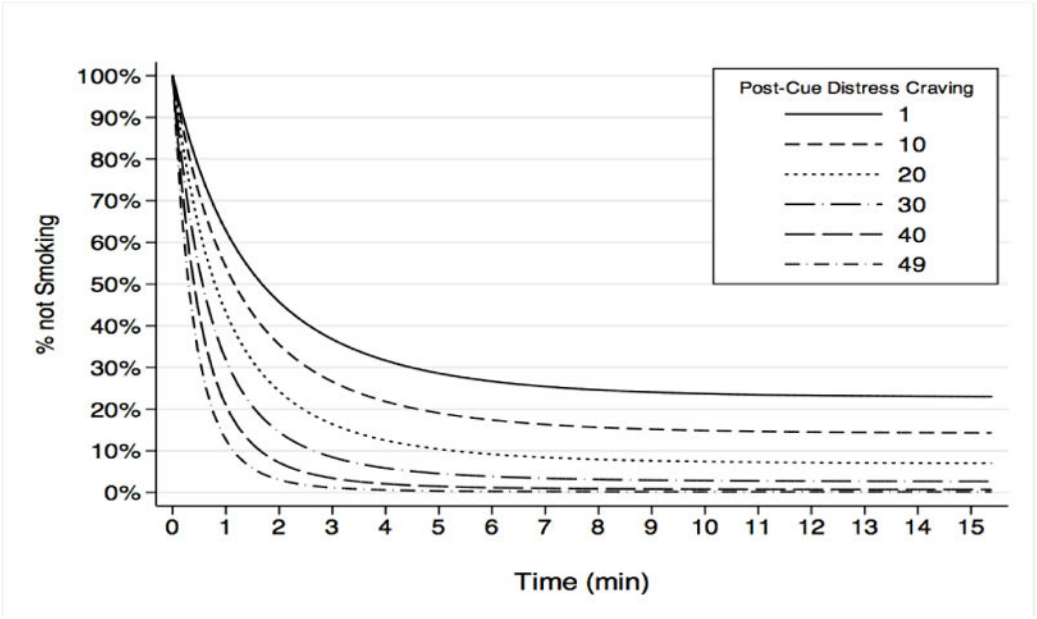


Figure 4.

Survival graphs demonstrating the quadratic effects of appetitive craving (A) and distress-relief craving (B) on latency to smoke. Based on shared-frailty survival analysis with Gompertz function specification. Quadratic term for appetitive craving is non-significant.

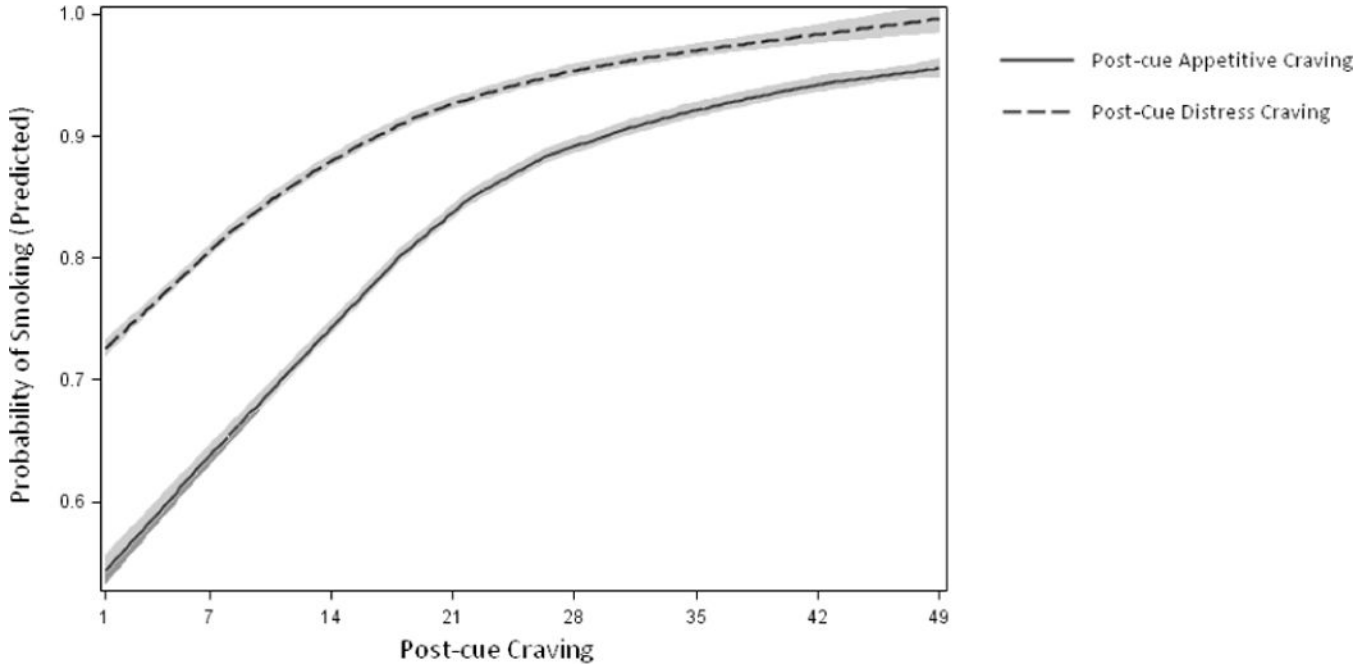
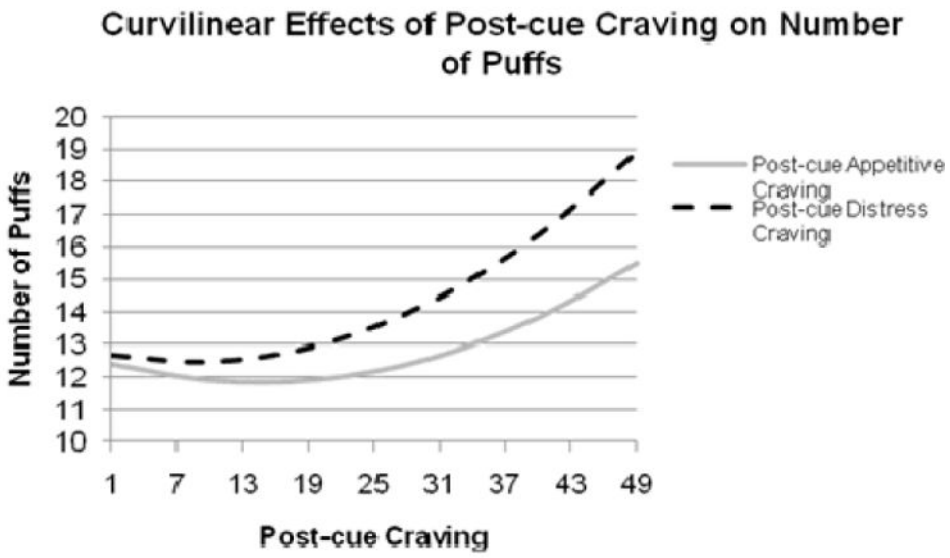


Figure 5.

The association between post-cue craving intensity and probability of smoking. Based on General Estimating Equation logit models with a significant quadratic term for appetitive craving, indicating significant curvature. Quadratic term for distress-relief craving is non-significant. Gray shaded bands represent 95% confidence bands.

a.



b.

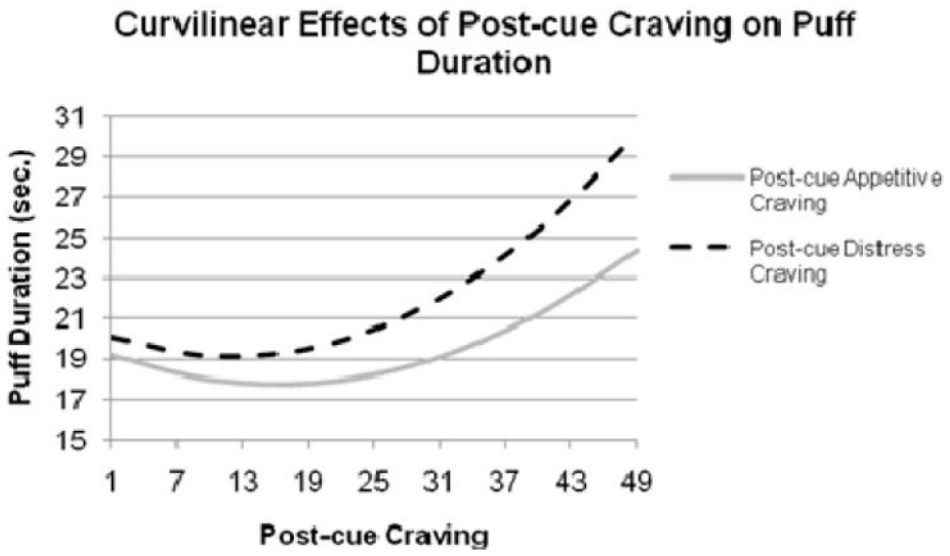


Figure 6.

The association of post-cue craving intensity with number of puffs (A) and total puff time (B). Based on mixed regression models with significant quadratic terms for both appetitive and distress-relief craving.

Table 1

Mood, Craving and Smoking Parameters by Cue

	Neutral *M (SD)*/%	Smoking *M (SD)*/%	Alcohol *M (SD)*/%	Positive *M (SD)*/%	Negative *M (SD)*/%	Smoking prohibited *M (SD)*/%
	n = 207	**n = 201**	**n = 194**	**n = 205**	**n = 196**	**n = 198**
Mood						
NA						
Pre-cue	13.15 (17.64)	13.03 (18.16)	11.58 (17.32)	11.43 (16.67)	11.45 (17.56)	12.23 (17.26)
Post-cue	13.20 (18.10)	13.37 (18.98)	11.57 (15.57)	10.87 (17.00)	18.88 (22.46)	13.21 (18.05)
Change	0.21 (6.18)	0.29 (8.15)	−0.07 (7.66)	−0.85 (6.31)	7.36 (14.38)	0.99 (7.22)
PA						
Pre-cue	63.23 (28.11)	59.53 (29.97)	62.91 (29.59)	62.34 (29.56)	62.73 (29.67)	61.69 (28.74)
Post-cue	60.01 (29.59)	57.85 (30.21)	61.15 (29.63)	64.81 (29.58)	49.73 (32.02)	59.39 (29.58)
Change	−2.56 (8.73)	−1.61 (7.14)	−1.66 (8.06)	3.06 (9.16)	−12.68 (19.44)	−2.07 (9.28)
Craving						
Appetitive craving (QSU Factor 1)						
Pre-cue	29.23 (14.87)	30.18 (14.72)	30.24 (14.70)	30.57 (14.64)	30.75 (15.66)	29.03 (14.76)
Post-cue	31.17 (15.00)	34.02 (14.68)	33.09 (15.01)	31.55 (14.65)	32.91 (15.22)	31.80 (14.92)
Distress-relief craving (QSU Factor 2)						
Pre-cue	14.85 (11.88)	16.30 (13.00)	15.26 (11.93)	15.64 (12.35)	16.07 (12.70)	15.40 (12.66)
Post-cue	16.26 (12.95)	19.08 (14.09)	17.24 (13.08)	16.11 (12.67)	18.66 (13.94)	17.17 (13.60)
Smoking parameters						
% who smoked	85.51	87.56	88.14	86.63	84.62	87.37
% who lit second cigarette[a]	19.77	22.86	21.76	21.02	25.10	16.37
Median latency to smoke (sec)	36.00	36.00	35.50	36.00	37.00	38.00
# of puffs[a]	14.29 (7.02)	14.98 (8.38)	14.46 (7.26)	14.15 (7.56)	14.51 (7.18)	13.89 (6.92)
Total puff time (sec)[a]	20.72 (11.62)	21.73 (12.05)	21.08 (11.82)	21.28 (12.86)	21.82 (12.13)	20.59 (11.88)
CO change (ppm)[a]	3.41 (3.30)	3.59 (3.66)	3.38 (3.81)	3.72 (3.81)	3.56 (3.77)	3.32 (3.96)

Note. NA = Negative Affect. PA = Positive Affect.

[a]Among those who smoked (n=1040 sessions; n=198 participants).

Table 2

Stimulus Effects on Smoking Parameters

	Likelihood of Smoking			Likelihood of Smoking 2 Cigarettes (vs. 1)			Latency to Smoke		
	OR	***95% CI***	***p***	***OR***	***95% CI***	***p***	***Hazard Ratio***	***95% CI***	***p***
Cue									
Neutral (ref)	†			†			†		
Smoking	1.19	0.85 – 1.68	.32	1.33	0.91 – 1.94	.14	1.16	0.94 – 1.44	.18
Alcohol[a]	1.18	0.70 – 1.99	.48	1.20	0.78 – 1.87	.41	1.07	0.82 – 1.38	.63
Positive	1.16	0.83 – 1.62	.38	1.27	0.78 – 2.05	.34	1.12	0.90 – 1.39	.31
Negative	1.01	0.70 – 1.45	.96	1.08	0.66 – 1.77	.76	1.04	0.84 – 1.30	.70
Smoking prohibited	1.07	0.75 – 1.52	.72	0.83	0.53 – 1.27	.39	1.06	0.85 – 1.31	.63

	Smoking Topography								
	Number of puffs[b]			Puff Duration[b]			CO Increase[b]		
	B	*95% CI*	*p*	*B*	*95% CI*	*p*	*B*	*95% CI*	*p*
Cue									
Neutral (ref)	†			†			†		
Smoking	0.42	−0.37 – 1.21	.30	0.58	−0.76 – 1.91	.40	0.14	−0.51 – 0.80	.67
Alcohol[a]	−0.29	−1.48 – 0.90	.58	0.08	−1.37 – 1.52	.76	0.24	−0.43 – 0.91	.65
Positive	0.19	−0.60 – 0.99	.63	1.26	−0.07 – 2.59	.06	0.65	−0.00 – 1.30	.05
Negative	0.14	−0.67 – 0.94	.74	0.83	−0.53 – 2.18	.23	0.17	−0.50 – 0.83	.62
Smoking prohibited	−0.49	−1.30 – 0.31	.23	0.40	−0.95 – 1.76	.56	0.13	−0.54 – 0.79	.71

Note. All models control for session number.

[a] Contrast between alcohol and neutral cue limited to individuals who reported drinking.

[b] Observations limited to individuals who smoked.

† Reference condition.

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Table 3

Effects of Craving on Smoking Parameters

	Appetitive Craving (QSU Factor 1)			**Distress-Relief Craving (QSU Factor 2)**		
Likelihood of Smoking (Logistic Regression)	*OR*	*95% CI*	*p*	*OR*	*95% CI*	*p*
Post-cue craving effects						
Linear	1.06	1.04 – 1.08	<.0001	1.07	1.05 – 1.10	<.0001
Quadratic[a]	1.24	1.08 – 1.43	<.01	1.03	0.91 – 1.19	.59
Decomposition of post-cue craving						
Pre-Cue Craving (univariate)	1.06	1.04 – 1.08	<.0001	1.08	1.06 – 1.10	<.0001
Change in Craving (controlling for pre-cue)	1.13	1.03 – 1.23	<.01	1.11	1.03 – 1.20	<.01
Likelihood of Smoking 2 Cigarettes vs. 1 (Logistic Regression)	*OR*	*95% CI*	*p*	*OR*	*95% CI*	*p*
Post-cue craving effects						
Linear	1.03	1.02 – 1.05	<.0001	1.03	1.01 – 1.05	<.001
Quadratic	1.00	1.00 – 1.00	.07	1.00	1.00 – 1.00	.03
Decomposition of post-cue craving						
Pre-Cue Craving (univariate)	1.04	1.02 – 1.06	<.0001	1.03	1.01 – 1.05	<.001
Change in Craving (controlling for pre-cue)	1.08	0.98 – 1.20	.13	1.04	0.96 – 1.12	.33
Latency to Smoke (Survival Analysis)	*Hazard Ratio*	*95% CI*	*p*	*Hazard Ratio*	*95% CI*	*p*
Post-cue craving effects						
Linear	1.04	1.03 – 1.04	<.0001	1.03	1.02 – 1.04	<.0001
Quadratic	0.99	0.99 – 1.00	.30	0.99	0.99 – 0.99	<.0001
Decomposition of post-cue craving						
Pre-Cue Craving (univariate)	1.03	1.03 – 1.04	<.0001	1.03	1.02 – 1.04	<.0001
Change in Craving (controlling for pre-cue)	1.09	1.04 – 1.13	<.0001	1.05	1.01 – 1.10	<.0001
Smoking Topography (Mixed Regression)[b]	*B*	*95% CI*	*p*	*B*	*95% CI*	*p*
Number of puffs						
Post-cue craving effects						

	Appetitive Craving (QSU Factor 1)			Distress-Relief Craving (QSU Factor 2)		
Linear	0.09	0.06 – 0.12	<.0001	0.11	0.07 – 0.15	<.0001
Quadratic	0.003	0.001 – 0.005	<.01	0.004	0.002 – 0.006	<.001
Decomposition of post-cue craving						
Pre-Cue Craving (univariate)	0.08	0.05 – 0.11	<.0001	0.10	0.06 – 0.14	<.0001
Change in Craving (controlling for pre-cue)	0.28	0.12–0.43	<.001	0.29	0.13 – 0.44	<.001
Puff Duration[c]						
Post-cue craving effects						
Linear	0.15	0.11 – 0.20	<.0001	0.17	0.11 – 0.23	<.0001
Quadratic	0.01	0.003 – 0.010	.0001	0.01	0.004 – 0.012	<.0001
Decomposition of post-cue craving						
Pre-Cue Craving (univariate)	0.13	0.08 – 0.18	<.0001	0.15	0.08 – 0.21	<.0001
Change in Craving (controlling for pre-cue)	0.51	0.25 – 0.77	.0001	0.44	0.18 – 0.70	<.001
CO Increase[d]						
Post-cue craving effects						
Linear	0.03	0.01 – 0.05	<.001	0.04	0.02 – 0.06	<.001
Quadratic	0.001	−0.000 – 0.003	.11	0.00	−0.00 – 0.00	.35
Decomposition of post-cue craving						
Pre-Cue Craving (univariate)	0.03	0.01 – 0.05	<.01	0.05	0.02 – 0.07	<.001
Change in Craving (controlling for pre-cue)	0.12	−0.001 – 0.25	.05	0.03	−0.09 – 0.15	.66

Note. All analyses controlled for session number and stimulus.

[a] Based on log-transformed scores, to compensate for skewness.

[b] Among those who smoked (n = 1040 sessions; n = 198 participants).

[c] Puff duration measured in seconds.

[d] CO=carbon monoxide, exhaled breath, measured in parts per million.