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Nicotine Dependence, "Background" and Cue-Induced Craving and Smoking in the Laboratory

Michael S. Dunbar[1], **Saul Shiffman**[1], **Thomas Kirchner**[2], **Hilary Tindle**[3], and **Sarah Scholl**[1]

[1]Smoking Research Group, Department of Psychology, University of Pittsburgh, 130 N. Bellefield Avenue, Suite 510, Pittsburgh, PA 15213, USA

[2]Schroeder Institute for Tobacco Research and Policy Studies, 1724 Massachusetts Avenue NW, Washington, DC 20036, USA

[3]Division of General Internal Medicine, University of Pittsburgh, 230 McKee Place, Suite 600, Pittsburgh, PA 15213, USA

Abstract

Background—Nicotine dependence has been associated with higher "background" craving and smoking, independent of situational cues. Due in part to conceptual and methodological differences across past studies, the relationship between dependence and cue-reactivity (CR; e.g., cue-induced craving and smoking) remains unclear.

Methods—207 daily smokers completed six pictorial CR sessions (smoking, negative affect, positive affect, alcohol, smoking prohibitions, and neutral). Individuals rated craving before (background craving) and after cues, and could smoke following cue exposure. Session videos were coded to assess smoking. Participants completed four nicotine dependence measures. Regression models assessed the relationship of dependence to cue-independent (i.e., pre-cue) and cue-specific (i.e., pre-post cue change for each cue, relative to neutral) craving and smoking (likelihood of smoking, latency to smoke, puff count).

Results—Dependence was associated with background craving and smoking, but did not predict change in craving across the entire sample for any cue. Among alcohol drinkers, dependence was associated with greater increases in craving following the alcohol cue. Only one dependence measure (Wisconsin Inventory of Smoking Dependence Motives) was consistently associated with

Correspondence concerning this article should be addressed to: Michael Dunbar, Department of Psychology, University of Pittsburgh, 130 N. Bellefield Avenue, Suite 510, Pittsburgh, PA 15213, USA; Phone: 412-383-1222; Fax: 412-383-2041; msd13@pitt.edu.

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smoking reactivity (higher likelihood of smoking, shorter latency to smoke, greater puff count) in response to cues.

Conclusion—While related to cue-independent background craving and smoking, dependence is not strongly associated with laboratory cue-induced craving under conditions of minimal deprivation. Dependence measures that incorporate situational influences on smoking correlate with greater cue-provoked smoking. This may suggest independent roles for CR and traditional dependence as determinants of smoking, and highlights the importance of assessing behavioral CR outcomes.

Keywords

Dependence; Cue-reactivity; Craving; Smoking

1. Introduction

Nicotine dependence is the major construct used to explain persistent smoking (Shadel et al., 2000). Traditionally, dependent smoking is conceptualized as being motivated by withdrawal-avoidance, the drive to maintain nicotine levels above a threshold at which withdrawal symptoms may occur (Shadel et al., 2000; Stolerman and Jarvis, 1995). Consistent with this view, individual differences in dependence predict the emergence of nicotine withdrawal (Piper et al., 2008b), and failure to quit smoking (Heatherton et al., 1991; Piper et al., 2004; Shiffman et al., 2004). Individuals with greater dependence are also expected to demonstrate a higher internal drive to smoke (Heatherton et al., 1991; Piasecki et al., 2010; Shiffman et al., 2004), expressed subjectively as more intense craving and behaviorally as heavier cigarette consumption.

Questionnaire-based measures of nicotine dependence have been reliably associated with tonic or *background craving*, the craving that smokers experience irrespective of situational cues (Ferguson and Shiffman, 2009), both in the laboratory (Donny et al., 2008; Payne et al., 1996) and in the real world (Shiffman and Paty, 2006). The relationship with cigarette consumption has been less reliable; for example, Donny et al. (2008) reported a significant but very weak relationship between cigarette consumption and dependence among daily smokers. Also, propensity to smoke has usually been measured in the aggregate as cigarettes consumed per day, which may be influenced by myriad other factors in addition to dependence (Donny and Dierker, 2007), rather than under controlled circumstances. In this study, we assess how dependence relates to the probability of smoking, latency to smoke, and amount of smoking in multiple laboratory sessions when cigarettes are freely available and smoking is allowed.

In addition to background craving, phasic or *cue-induced craving*, craving that arises quickly, in response to situational cues, may also be relevant to dependence. Background and cue-provoked craving appear to be distinct processes (Ferguson and Shiffman, 2009). For example, previous laboratory studies have demonstrated that although active nicotine patch attenuates background craving, it does not appear to reduce cue-induced craving in either *ad libitum* smokers (Tiffany et al., 2000) or among individuals who are attempting to quit (Waters et al., 2004). This suggests that background craving may be more tightly linked

to processes such as regulation of nicotine blood levels, thought to be important to dependence (Benowitz, 2010), compared to cue-induced craving. Thus, while background craving appears to correlate with various features of nicotine dependence (Ferguson and Shiffman, 2009), the relationship between *cue-induced* craving and dependence is less clear.

Most conceptualizations of smoking and relapse recognize that situational cues influence drug craving and use (e.g., Kozlowski and Herman, 1984; Marlatt and Gordon, 1985; Robinson and Berridge, 1993; Tiffany, 1990). Indeed, real-world smoking and relapse are associated with particular environmental contexts (Shiffman et al., 1997a, 2002; Shiffman and Paty, 2006; Shiffman et al., 1996). Similarly, numerous laboratory cue reactivity (CR) studies have demonstrated a relationship between exposure to smoking-relevant cues and craving (see Carter and Tiffany, 1999), although few studies have demonstrated a relationship with subsequent smoking behavior (see Perkins, 2009).

Some models and measures of dependence consider reactivity to cues to be a part of nicotine dependence, albeit in different ways. For example, Tiffany (1990) views response to cues as an important force in dependence, and the Wisconsin Inventory of Smoking Dependence Motives (WISDM) counts cue reactivity towards its overall score for dependence ("Cue Exposure/Associative Processes" subscale; Piper et al., 2004). Conversely, others suggest that dependence is associated with a muted response to cues (Shiffman and Paty, 2006), and the Nicotine Dependence Syndrome Scale (NDSS) considers lower reactivity as an indicator of greater dependence (Shiffman et al., 2004). Cue reactivity also appears to be more closely tied to dependence in positive reinforcement models (Glautier, 2004) than in negative reinforcement models of dependence (Eissenberg, 2004).

The empirical evaluation of these relationships has been complicated by the use of multiple different measures of nicotine dependence, craving, and smoking, and the reliance upon single smoking cues in many CR studies. Different dependence measures correlate only modestly with each other (Japuntich et al., 2009; Piper et al., 2008b), and vary in how or whether they incorporate measures of reactivity. Laboratory reactivity assessments frequently evaluate only those cues explicitly related to cigarettes and smoking as stimuli (Carter and Tiffany, 1999); yet smokers respond to a range of cues (Conklin et al., 2008) that may be relevant to understanding dependence. For example, responses to negative affect cues might be more closely related to dependence, because the repeated cycles of withdrawal and withdrawal-relief that mark dependent smoking may condition negative affect as a cue (Kassel et al., 2003). Conversely, reactivity to cues such as alcohol and positive affect, which are thought to characterize less-dependent smokers (Shiffman et al., 1994; Shiffman and Paty, 2006), might be inversely related to dependence. CR studies have also typically looked only at cue-induced craving (Perkins, 2009), neglecting actual smoking behavior as perhaps the most important outcome.

Consequently, although previous studies have examined the relationship between laboratory CR and dependence, reports have differed substantially in methodology, outcomes, and conclusions. For example, one study reported that more dependent smokers (on the Fagerström Test of Nicotine Dependence [FTND]; Heatherton et al., 1991) showed less cue-induced craving (Watson et al., 2010). Yet, Donny et al. (2008) found no relationship

between CR and dependence (measured via NDSS). Similarly, among young smokers, Carpenter et al. (2014) reported no association between CR and daily vs. occasional smoker status. Another study found that individuals who were less reactive to cues had poorer cessation outcomes, suggesting an inverse relationship between CR and dependence (Powell et al., 2010, 2011). However, most studies that have assessed the relationship between CR and cessation outcomes report no relationship (Perkins, 2012). Thus, while responsiveness to situational cues is thought to play an important role in nicotine dependence and in driving smoking behavior, the extent to which cue-induced craving and smoking in the laboratory correlate with measures of nicotine dependence remains unclear. In summary, previous literature offers a muddled perspective on the relationship between laboratory reactivity and dependence.

The primary goal of this study is to clarify the relationship between nicotine dependence and cue-induced craving and smoking behavior. We examine multiple measures of dependence in relation to both background craving and cue-induced craving, measured in response to multiple smoking-relevant cues, as well as with multiple measures of smoking behavior immediately following cue exposure. The analyses use data from a study in which daily smokers were exposed to five active cues (smoking, alcohol, positive affect, negative affect, and smoking prohibitions) and a neutral cue (Shiffman et al., 2013a). This study found that exposure to smoking cues increased craving, while exposure to positive affect cues decreased craving. Cue exposure did not differentially affect smoking, but smoking was directly related to prior craving. The current analyses examine the main effects of dependence on background craving and smoking, as well as the moderating effects of dependence on cue reactivity.

2. Methods

2.1 Participants

Participants were 207 established daily smokers (5-30 cigarettes per day), who were not trying to quit (Shiffman et al., 2013a). Participant demographics are described in Table 1.

2.2 Nicotine Dependence Measures

The FTND (Heatherton et al., 1991) is a well-established 6-item measure. The NDSS (Shiffman et al., 2004) consists of 19 items scored to derive a total score (NDSS-T) as well as five subscales. The WISDM (Piper et al., 2004) is a multidimensional measure that yields 13 subscale scores and two overarching scores, for Primary Dependence Motives (WISDM-PDM, comprised of the following motives: automaticity of smoking, tolerance, loss of control, and craving) and Secondary Dependence Motives (WISDM-SDM, comprised of the following motives: social goads, affiliative attachment, cognitive enhancement, cue exposure, positive and negative reinforcement, taste, weight control, and behavioral choice; Piper et al., 2008a). The Hooked on Nicotine Checklist (HONC) scale is a 10-item scale intended to assess loss of autonomy over smoking (Wellman et al., 2005). (It is often scored dichotomously; we scored it continuously.) Each of these measures has demonstrated correlations with withdrawal or cessation outcomes (Heatherton et al., 1991; Piper et al., 2004; Shiffman et al., 2004; Wellman et al., 2005). All measures demonstrated moderate to

high internal consistency in this sample (FTND: α=0.51; NDSS-T: α=0.77; WISDM-PDM: α=0.85; WISDM-SDM: α=0.89; HONC: α=0.77). To assess overall dependence, we also derived a composite dependence factor (CDF) that captured the common variance across five scales (FTND, NDSS-T, WISDM-PDM, WISDM-SDM, and HONC), by extracting the first principal component from the correlations across these dependence measures. This factor accounted for 64% of the item variance, and had the only eigenvalue > 0.7.

2.3 Cue Reactivity

CR procedures are described in detail in Shiffman et al. (2013a). Briefly, participants were exposed to five active cue sets consisting of photographic images relating to smoking cues (e.g., cigarettes), alcohol cues (drinks, bars), negative affect (affective images from the International Affective Picture System [IAPS]; Gilbert and Rabinovich, 2003), positive affect (IAPS), and smoking prohibitions (e.g., “no-smoking” signs). In addition, one neutral cue set, depicting irrelevant cues, matched to the active cues (see Shiffman et al., 2013a), was used as a control to isolate specific cue effects. Each cue exposure took place in a different session, in randomized and counterbalanced order over the course of six sessions. Subjects could smoke ad libitum prior to arrival at each session, and reported how recently they had smoked (time since last cigarette; TSLC). Following a 30-minute period of abstinence and a five-minute acclimation period, participants viewed pictures during a three-minute primary cue exposure (30 pictures, each exposed for six seconds), after which they rated craving and were subsequently given the opportunity to smoke. Data were available for 1,201 reactivity sessions.

2.4 Craving

Participants rated craving immediately before and immediately after cue exposure, using the QSU-Brief (Cox et al., 2001), yielding two craving scores: appetitive craving (QSU-Factor 1) and distress-relief craving (QSU-Factor 2). Pre-cue craving scores (“background craving”) and cue-induced craving (the difference in pre-cue and post-cue QSU scores, square root-transformed to reduce skew) were examined.

2.5 Smoking

Following each cue session, participants were allowed to smoke up to two provided cigarettes ad libitum during a 15-minute period, while cue exposure continued (see Shiffman et al., 2013a for a comprehensive description of study procedures). Whether they smoked, when they started smoking, and the number of puffs were coded from subject video recordings (Blank et al., 2009).

2.6 Data Analysis

Dependence measures were standardized to facilitate comparison of effect sizes across scales. We could not include all five dependence measures in a single multivariate analysis, due to multicollinearity and missing data. To mitigate the effect on alpha inflation due to separate tests on five dependence measures across multiple craving and smoking outcomes, we “gated” the tests by first assessing the effect of the CDF, and testing individual

dependence measures only if the CDF test was significant. As a further protection against false positives due to multiplicity, we only interpreted findings at $p < .01$.

All analyses controlled for average cigarettes per day (CPD) and session-specific TSLC (log-transformed), in order to disentangle effects of dependence from those of heaviness of consumption and duration of abstinence. We also controlled for session number to account for potential session order effects. The data were weighted to account for oversampling of African American participants (except for analyses of latency to smoke, which had no provision for weighting).

2.6.1 Dependence and Background Craving and Smoking—We first examined how dependence related to the level of background craving, assessed before cue exposure (i.e., pre-cue craving, reported in each session). These analyses treated the multiple sessions as repeated measures in hierarchical models (i.e., multiple CR sessions nested within participants). For cue-independent effect of craving on smoking, which occurred after cue exposure, analyses controlled for cue type. Analyses of continuous variables (craving and number of puffs) used mixed regression (SAS ProcMixed; SAS Institute, Cary, NC). (For number of puffs, the distribution demonstrated rightward skew; to normalize the distribution, we log-transformed puff counts and conducted separate analyses on transformed puff counts. The pattern of findings was unchanged. Results for untransformed values are presented.) Probability of smoking (smoked, did not smoke) was assessed via generalized estimating equations (GEE), using a logit link, and latency to smoke was analyzed using survival analysis (using Stata streg; StataCorp, College Station, TX) with a provision for shared frailty (Hosmer et al., 2008).

2.6.2 Dependence and Cue-Provoked Craving and Smoking—Further analyses assessed how level of dependence related to changes in craving and smoking as a function of exposure to active cues (accounting for each participant's ‘reactivity’ to the neutral control cue). Each analysis examined a particular active cue (e.g., approximately 200 subject-sessions for each of 5 within-cue analyses), controlling for subjects' response to the neutral cue condition (e.g., number of puffs in response to the neutral cue was included as a covariate in the model assessing the effect of dependence on number of puffs in response to the smoking cue). Analysis for the alcohol cue was limited to those who reported that they consumed alcohol. OLS regression was used to assess cue effects of dependence on craving change and number of puffs taken (among those who smoked). Logistic regression was used for likelihood of smoking. As with other analyses, survival analyses of cue-specific effects examined the participant's latency to smoke in response to each active cue relative to that person's latency following the neutral cue (i.e., each model assessed latency in response to one active cue, in contrast to latency to smoke in the neutral condition). Thus, survival analyses with a provision for shared frailty were used to assess the relationships between dependence and cue-specific effects on latency to smoke.

3. Results

Participants ($n = 207$) were moderate daily smokers (Mean cigarettes per day = 16.01 (±6.03), and exhibited moderate dependence levels, with considerable variability across

dependence measures (see Table 1). Participants also demonstrated variability in pre- to post-cue craving change and smoking across cues (Table 2).

3.1 Dependence and Background Craving and Smoking

3.1.1 Craving—More dependent smokers (indexed by CDF) reported higher background craving on both appetitive ($p < .0001$) and distress relief ($p < .0001$) craving scales prior to cue exposure. All individual measures of dependence, examined separately, were associated with higher background craving (Table 3).

3.1.2 Smoking—More dependent smokers (CDF) were more likely to smoke ($p < .01$) in the CR sessions across all cues (see Table 3). NDSS-T and WISDM-SDM were significantly associated with smoking (increases of 82% and 94%, respectively, in odds of smoking for every 1-*SD* increase). More dependent smokers (CDF) also progressed more quickly to smoking; specifically, a 1-*SD* increase in WISDM-SDM scores was associated with a 25% faster time to initiate smoking across all sessions (*HR* = 1.25, 95% CI [1.09-1.44]). When participants smoked, those with higher CDF took more puffs ($p < .0001$); all dependence measures except FTND were significantly associated with more puffs (see Table 3).

3.2 Dependence and Cue-Provoked Craving and Smoking

3.2.1 Craving—Dependence (CDF) was generally not associated with cue-induced changes in distress-relief nor appetitive craving. The one exception was that, among alcohol drinkers, more dependent smokers demonstrated greater increases in appetitive craving ($p < .0001$) when exposed to alcohol cues. This was seen for NDSS-T, WISDM-PDM, and WISDM-SDM (Table 4).

3.2.2 Smoking Behavior—There was a mixed pattern of associations between dependence and cue-induced smoking. There was no relationship between dependence and probability of smoking in response to smoking cues, positive affect cues, alcohol cues or smoking-prohibited cues. However, CDF was associated with increased probability of smoking in response to the negative affect cue, with specific effects for FTND and WISDM-SDM (see Table 4), which were associated with 181% and 118% increased odds of smoking, respectively, for every 1-*SD* increase in dependence.

Similarly, while dependence was not associated with cue-related changes in latency to smoke in response to the smoking, positive affect, or smoking-prohibited cues, CDF was associated with shorter latency to smoke in response to both the negative affect cue and the alcohol cue (among alcohol drinkers). FTND and WISDM-SDM were significantly associated with reduced latency to smoke in response to the negative affect cue, such that a 1-*SD* increase in dependence was associated with a 33% (FTND) and 28% (WISDM-SDM) faster time to smoke. For the alcohol cue, a 1-*SD* increase in WISDM-SDM was associated with a 28% faster time to smoke (see Table 4).

Among those who smoked, higher CDF was significantly associated with taking more puffs in each of the active cue conditions, relative to neutral. Specifically, higher WISDM-SDM was significantly associated with greater number of puffs in each of the active cue

conditions. In addition, WISDM-PDM was associated with increased puffs in the smoking and positive affect cue conditions (both p values < .01), though multivariate analyses (not shown) reveal that this was attributable to its shared variance with SDM. No other significant relationships between dependence measures and smoking reactivity were observed (see Table 4).

4. Discussion

This study examined the relationship between nicotine dependence, craving, and smoking behavior during laboratory cue exposure among daily smokers. Independent of cues, and controlling for their typical smoking rate and degree of deprivation, more dependent smokers had more intense background craving, were more likely to smoke, moved to smoke more quickly, and took more puffs when they did smoke. This pattern of findings is consistent with those of Donny et al. (2008), as well as with the broad literature on dependence, and validates the psychometric questionnaire measures of dependence tested here. Importantly, these associations were independent of amount smoked, and so confirm that dependence means more than simply heavy smoking. The findings also help to validate behavior in the laboratory as a meaningful reflection of individual differences in dependence.

While the common factor across dependence measures consistently predicted whether one smoked, how quickly one smoked, and how much one smoked, the only scale consistently associated with all three outcomes was the WISDM-SDM. The WISDM-SDM effects were also consistently greater in magnitude (i.e., larger standardized betas) and similar in standard error compared to other scales, suggesting that the observed pattern was not attributable solely to psychometric properties (e.g., higher reliability) of the scale. In this context of modest deprivation, these “secondary” smoking motives related to situational context (Piasecki et al., 2010; Piper et al., 2008a) may actually be more closely linked to smoking behavior than “primary” motives related to withdrawal and craving.

The findings pertaining to whether more dependent smokers also demonstrated greater reactivity to cues were less uniformly positive. In general, dependence was not associated with change in craving due to cue exposure, consistent with findings from Donny et al. (2008). The one exception was that, among those who reported consuming alcohol, higher scores on the NDSS and WISDM (PDM and SDM) were associated with greater change in appetitive craving in response to the alcohol cue. This is consistent with the perspective that cue-specific associations develop through personal experience and conditioning (Niaura et al., 1988). The relationship between drinking and smoking is strong, and strongest among the most dependent individuals (Shiffman and Balabanis, 1995), consistent with the current findings. However, the results seem inconsistent with the finding that less dependent smokers are more likely to cite alcohol as a key trigger of relapse (Shiffman et al., 1997b), and that typically less dependent light (Epstein et al., 2007; Shiffman and Paty, 2006) and intermittent (Shiffman et al., 2012) smokers show particularly strong links between drinking and smoking. Importantly, this exception aside, dependence, as assessed by multiple psychometric scales in this study, was not associated with craving response to cues. It is notable that dependence did not predict increases in withdrawal-related distress craving,

which might have been expected to be linked with exposure to negative affect cues through conditioned association with actual withdrawal in dependent smokers (Niaura et al., 1988). It is not clear whether this indicates that such conditioning does not occur, whether the distress-craving measure does not specifically capture this effect, or whether the cue-reactivity procedure was ineffective at eliciting and capturing this effect.

Similarly, the relationship between dependence and cue-induced smoking was complex. Only one cue – negative affect – made more dependent smokers differentially more likely to smoke, and to progress more quickly to smoking. It is possible that more dependent smokers have a stronger learning history in which negative affect (due to withdrawal) has served as a discriminative cue for reinforcement through negative-affect reduction (Kassel et al., 2003), making this a potent trigger for smoking. More dependent smokers who reported consuming alcohol also demonstrated shorter latencies to smoke in response to the alcohol cue, consistent with a conditioning-history perspective of CR (Niaura et al., 1988).

Although at odds with one previous study, which reported *less* appetitive craving in response to cues among *more* dependent smokers (Watson et al., 2010), the overall finding that cue-induced craving is not related to dependence is largely in agreement with previous research across diverse samples of smokers. This pattern of results was consistent with Donny et al. (2008), despite substantial differences in the nature of Donny et al.'s (2008) sample (heavier smokers), conditions (deprived), and cues (in vivo smoking cue). The current findings are also consistent with two studies that showed no differences in CR among heavy daily smokers compared to very light (Sayette et al., 2001) or non-daily (Shiffman et al., 2013b) smokers, and with a study comparing young daily and occasional smokers (Carpenter et al., 2014). Although more dependent smokers were not consistently more likely to smoke in response to cues, they smoked more heavily (i.e., took more puffs) when they did smoke. Perhaps different processes, extraneous to dependence (e.g., reluctance to smoke in a smoking research facility in a smoke-free university building) may affect the initiation of a cigarette, but not the amount smoked. Notably, only WISDM-SDM was consistently correlated with the amount of smoking following exposure to the active cues, after controlling for smoking in response to the neutral cue. This may reflect the content of the scale, which includes a measure of cue-reactivity, per se (though this sub-scale did not account for the whole effect; data not shown), as well as scales pertaining to smoking in response to social factors and negative and positive affect. Thus, SDM may be particularly sensitive to situational variations in smoking, whereas the other scales may more effectively capture the pharmacologically-based need to smoke when significantly deprived.

In assessing how nicotine dependence relates to laboratory cue reactivity, this study essentially bridged two very different conceptions or types of smoking motives: internal and external factors. Traditional concepts of dependence emphasize an internal and persistent need to smoke in response to declining nicotine levels, implying a minimal role for external cues. In contrast, cue reactivity research invokes cues as determinants of smoking and the drive to smoke (craving). These influences may be complementary rather than contradictory, as suggested by Herman and Kozlowski's (1984) boundary model. The need to maintain nicotine levels may drive a relatively stable range of typical cigarette consumption, independent of situational specifics. Within these broad limits, however, cues may account

for moment-to-moment variations in smoking behavior. This suggests that both factors influence smoking, and that the balance of the two may depend in part upon the smoker's current state of deprivation. It may also vary depending on the type of smoker, with those who do not strive to maintain nicotine levels (e.g., non-daily smokers; Shiffman, 2009) being more influenced by cues, and those who avoid nicotine withdrawal being less influenced by cues (Shiffman and Paty, 2006).

This study had several limitations. Participants were allowed to smoke freely up to 30 minutes before participating in CR sessions; the results might have been different in profoundly deprived smokers. Analyses controlled for CPD and TSLC, which may have resulted in over-control, potentially obscuring variance which may have allowed us to detect relationships between dependence and craving and smoking. However, post-hoc analyses omitting these covariates (not shown) did not suggest that the inclusion of TSLC and CPD obscured the relationship between dependence and outcomes; the magnitude of the effect of dependence on outcomes was largely unchanged across analyses when these covariates were excluded from models. Our sample also consisted of smokers with no intention to quit; results may have differed among individuals who were planning a cessation attempt. In addition, limited effects of cues on craving may have reduced our ability to detect a relationship with dependence. The levels of pre-cue, post-cue, and change in craving observed in this study were relatively modest (Shiffman et al., 2013a), as was the degree of deprivation (one hour on average). Sayette and Tiffany (2013) have suggested that some effects might only emerge when craving is more intense. However, the data demonstrated changes in craving in response to cues, levels of craving sufficient to predict subsequent smoking (with no evidence of ceiling effects for craving) (Shiffman et al., 2013a), and robust relationships between dependence and smoking topography, even after controlling for CPD and minutes of deprivation. In addition, participants demonstrated considerable variability in dependence, in craving, and in smoking, providing an appropriate context in which to observe associations. Another potential limitation is that “background craving,” craving before pictorial cue exposure, was rated in a smoking laboratory setting. As other authors have noted (e.g., Sayette and Tiffany, 2013), the laboratory itself may serve as a smoking cue, potentially prompting individuals to focus on craving and/or to anticipate smoking. However, the modest levels of craving prior to cue exposure suggest that the laboratory itself was not a robust smoking cue. Future CR studies may benefit from assessing baseline or “background craving” in non-laboratory settings. Finally, this study focused on indices of CR craving and smoking; there are many other established CR outcomes (e.g., attentional bias, patterns of brain activation, autonomic responses, etc.) that may have relevance to understanding the complex relationship between CR and nicotine dependence.

This study also had several notable strengths. Our sample size (207 smokers and 1,201 reactivity sessions) provided sufficient power to detect even modest effect sizes (Shiffman et al., 2013a). This sample was larger than any comparable study that has examined the relationship between dependence and cue induced craving. Thus, we were well positioned to detect any relationship between dependence and cue-induced craving, if one existed. In addition, our sample included individuals who smoked as little as five CPD, allowing us to examine this relationship across a broad range of smokers. Finally, we examined a number

of different measures of dependence, two measures of craving, three measures of smoking, and five different cues, allowing for a very comprehensive assessment of the relationships between constructs of interest.

In conclusion, the data show that more dependent smokers consistently demonstrate higher background craving and a greater propensity to smoke, as expected. However, more dependent smokers are generally not more cue-reactive, although higher WISDM-SDM dependence does appear to correlate with increased smoking in response to cues in the laboratory. Future studies should examine the relationship between reactivity to cues, dependence, and actual smoking behavior outside of the laboratory, in order to better understand how CR and dependence may function independently or synergistically to influence smoking behavior, and how laboratory and questionnaire based measures of dependence and CR inform our understanding of smoking behavior in the real world.

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Table 1

Demographics, background craving, and nicotine dependence.

	***M* (*SD*) / % (n=207)**	**Range**
Age	39.87 (11.76)	21 – 70
Male	62.24%	--
Ethnicity		
African American	38.16%	--
Caucasian	59.42%	
Other	2.42%	
Alcohol drinkers	73.17%	--
Cigarettes per day	16.01 (6.03)	5 – 32
Minutes to first cigarette after waking	21.80 (33.86)	0.5 – 200
FTND (0-10 scale)	5.12 (2.03)	0 – 10
NDSS-T (Factor score)	-0.37 (1.06)	-2.71 – 1.94
HONC (0-10 scale)	7.51 (2.25)	1 – 10
WISDM-PDM[a] (1-7 scale)	4.58 (1.27)	1.59 – 7.00
WISDM-SDM[b] (1-7 scale)	4.03 (1.10)	1.18 – 7.00
Background (Pre-Cue) Craving[c] (1-49 scale)		
Appetitive (QSU Factor 1)	29.09 (12.97)	1 - 49
Distress-relief (QSU Factor 2)	14.17 (11.05)	1 - 46
Time since last cigarette[c]	60.07 (102.84)	5 - 630

[a] PDM = Primary Dependence Measures.

[b] SDM = Secondary Dependence Measures.

[c] Values reflect mean of within-subject means across sessions.

Table 2

CR craving and smoking behavior by cue.

	Neutral (control) *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**
Pre-post cue exposure change in craving						
Appetitive craving (QSU Factor 1)	+2.40 (5.55)	+3.84 (8.05)	+2.85 (6.16)	+1.00 (6.50)	+2.16 (8.24)	+2.74 (6.53)
Distress craving (QSU Factor 2)	+1.69 (5.09)	+2.78 (6.03)	+1.98 (5.10)	+0.50 (5.51)	+2.60 (6.87)	+1.66 (4.39)
Smoking parameters						
% who smoked[a]	71.56	74.76	74.57	72.36	71.84	72.53
Median latency to smoke (sec)	36.00	36.00	35.50	36.00	37.00	38.00
Number of puffs[b]	14.44 (7.35)	14.82 (7.48)	14.34 (7.46)	14.17 (7.16)	14.49 (7.21)	13.86 (6.45)

Note.

[a] 96% of individuals smoked in at least 1 session.

[b] Among those who smoked (*n* = 1,040 sessions; *n* = 198 participants).

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Table 3

Effects of dependence on background craving and smoking.

	Craving				*Smoking*					
	Appetitive Craving		**Distress Craving**		**Prob. Smoking**		**Latency to Smoke**		**# of puffs**	
	Beta (SE)	***p***	***Beta (SE)***	***p***	***OR (95% CI)***	***p***	***HR (95% CI)***	***p***	***Beta (SE)***	***p***
Main effects (across all cues)										
CDF	0.41 (0.06)	***	0.45 (0.06)	***	1.88 (1.26 - 2.82)	*	1.29 (1.10 – 1.50)	*	0.27 (0.07)	***
FTND	0.32 (0.07)	***	0.37 (0.07)	***	1.68 (1.09 - 2.59)	‘	1.24 (1.04 – 1.47)	‘	0.01 (0.08)	ns
NDSS-T	0.36 (0.06)	***	0.37 (0.06)	***	1.82 (1.19 - 2.77)	*	1.20 (1.03 – 1.40)	‘	0.18 (0.07)	*
HONC	0.27 (0.06)	***	0.23 (0.07)	**	1.38 (0.97 - 1.96)	ns	1.16 (1.00 – 1.35)	ns	0.20 (0.07)	*
WISDM_PDM	0.29 (0.06)	***	0.30 (0.07)	***	1.42 (0.93 - 2.17)	ns	1.17 (1.00 – 1.36)	ns	0.20 (0.07)	*
WISDM SDM	0.33 (0.06)	***	0.41 (0.06)	***	1.94 (1.24 - 3.02)	*	1.25 (1.09 – 1.44)	*	0.31 (0.06)	***

Note. All analyses are weighted by race to account for oversampling of African American participants, and to control for session number, minutes since last cigarette (log-transformed), and average daily CPD. Smoking analyses also controlled for cue type.

‘ denotes effects that were considered not significant at the designated $p < .01$ criterion level, but were $p < .05$ (i.e., $.05 > p > .01$)

ns denotes non-significant effects ($p > 0.05$)

* $p < .01$,

** $p < .001$,

*** $p < .0001$.

Table 4

Cue-specific effects of dependence on craving and smoking.

	Craving				*Smoking*					
	Appetitive Craving		**Distress Craving**		**Prob. Smoking**		**Latency to Smoke**		**# of puffs**	
	Beta (SE)	***p***	***Beta (SE)***	***p***	***OR (95% CI)***	***p***	***HR (95% CI)***	***p***	***Beta (SE)***	***p***
Cue reactivity, by stimulus (controlling for neutral response)										
Smoking										
CDF	0.10 (0.08)	ns	0.20 (0.08)	ns	1.37 (0.76 - 2.47)	ns	1.26 (1.05 – 1.51)	‘	0.24 (0.07)	*
FTND	--	--	--	--	--	--	--	--	0.16 (0.07)	ns
NDSS-T	--	--	--	--	--	--	--	--	0.12 (0.07)	ns
HONC	--	--	--	--	--	--	--	--	0.16 (0.08)	ns
WISDM_PDM	--	--	--	--	--	--	--	--	0.20 (0.07)	*
WISDM_SDM	--	--	--	--	--	--	--	--	0.21 (0.07)	*
Negative Affect										
CDF	0.01 (0.09)	ns	0.11 (0.08)	ns	2.30 (1.23 - 4.31)	*	1.30 (1.11 – 1.54)	*	0.21 (0.08)	*
FTND	--	--	--	--	2.81 (1.43 - 5.53)	*	1.33 (1.11 – 1.60)	*	0.05 (0.09)	ns
NDSS-T	--	--	--	--	1.54 (0.89 - 2.67)	ns	1.17 (1.00 – 1.37)	ns	0.11 (0.07)	ns
HONC	--	--	--	--	1.41 (0.80 - 2.49)	ns	1.20 (1.02 – 1.42)	‘	0.17 (0.08)	ns
WISDM_PDM	--	--	--	--	1.72 (0.97 - 3.06)	ns	1.17 (0.99 – 1.38)	ns	0.18 (0.08)	ns
WISDM_SDM	--	--	--	--	2.18 (1.23 - 3.86)	*	1.28 (1.11 – 1.49)	**	0.19 (0.07)	*
Positive Affect										
CDF	0.09 (0.07)	ns	0.01 (0.08)	ns	1.67 (0.88 - 3.13)	ns	1.22 (1.02 – 1.47)	‘	0.21 (0.07)	*
FTND	--	--	--	--	--	--	--	--	-0.004 (0.08)	ns
NDSS-T	--	--	--	--	--	--	--	--	0.13 (0.07)	ns
HONC	--	--	--	--	--	--	--	--	0.18 (0.08)	ns
WISDM_PDM	--	--	--	--	--	--	--	--	0.18 (0.07)	*
WISDM_SDM	--	--	--	--	--	--	--	--	0.21 (0.07)	*
Alcohol[a]										
CDF	0.31 (0.08)	***	0.20 (0.09)	ns	1.57 (0.82 - 3.02)	ns	1.28 (1.07 – 1.54)	*	0.27 (0.09)	*
FTND	0.11 (0.08)	--	--	--	--	--	1.26 (1.03 – 1.53)	‘	0.10 (0.09)	ns
NDSS-T	0.23 (0.08)	*	--	--	--	--	1.17 (0.98 – 1.40)	ns	0.17 (0.09)	ns

	Craving				*Smoking*					
	Appetitive Craving		**Distress Craving**		**Prob. Smoking**		**Latency to Smoke**		**# of puffs**	
	Beta (SE)	***p***	***Beta (SE)***	***p***	***OR (95% CI)***	***p***	***HR (95% CI)***	***p***	***Beta (SE)***	***p***
HONC	0.20 (0.08)	--	--	--	--	--	1.15 (0.96 – 1.37)	ns	0.19 (0.09)	ns
WISDM_PDM	0.28 (0.07)	**	--	--	--	--	1.16 (0.97 – 1.39)	ns	0.24 (0.10)	ns
WISDM_SDM	0.33 (0.07)	***	--	--	--	--	1.29 (1.09 – 1.51)	*	0.28 (0.09)	*
Smoking Prohibited										
CDF	0.05 (0.07)	ns	0.07 (0.07)	ns	1.32 (0.73 - 2.40)	ns	1.22 (1.02 – 1.46)	‘	0.18 (0.06)	*
FTND	--	--	--	--	--	--	--	--	0.13 (0.06)	ns
NDSS-T	--	--	--	--	--	--	--	--	0.11 (0.06)	ns
HONC	--	--	--	--	--	--	--	--	0.12 (0.06)	ns
WISDM_PDM	--	--	--	--	--	--	--	--	0.12 (0.06)	ns
WISDM_SDM	--	--	--	--	--	--	--	--	0.18 (0.06)	*

Note. All analyses are weighted by race to account for oversampling of African American participants, and control for session number, minutes since last cigarette (log-transformed), average daily CPD, and response (‘reactivity’) observed in the neutral cue condition.

[a] Among those who drink alcohol.

-- denotes effects not tested due to non-significant effect of dependence principle component factor (CDF)

‘ denotes effects that were considered not significant at the designated $p < .01$ criterion level, but were $p < .05$ (i.e., $.05 > p > .01$)

ns denotes non-significant effects ($p > 0.05$)

* $p < .01$,

** $p < .001$,

*** $p < .0001$.