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Nicotine dependence, "background" and cue-induced craving and smoking in the laboratory

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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 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.

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

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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., 1996, 1997a, 2002; Shiffman and Paty, 2006;). 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 toward 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.

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.

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.