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Does laboratory cue reactivity correlate with real-world craving and smoking responses to cues?

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ABSTRACT

Background: Laboratory cue reactivity (CR) assessments are used to assess smokers' responses to cues. Likewise, EMA recording is used to characterize real-world response to cues. Understanding the relationship between CR and EMA responses addresses the ecological validity of CR.
Methods: In 190 daily smokers not currently quitting, craving and smoking responses to cues were assessed in laboratory CR and by real-world EMA recording. Separate CR sessions involved 5 smoking-relevant cues (smoking, alcohol, negative affect, positive affect, smoking prohibitions), and a neutral cue. Subjects used EMA to monitor smoking situations for 3 weeks, completing parallel situational assessments (presence of others smoking, alcohol consumption, negative affect, positive affect, and smoking prohibitions, plus current craving) in smoking and non-smoking occasions (averaging 70 and 60 occasions each). Analyses correlated CR craving and smoking cue responses with EMA craving and smoking correlations with similar cues.
Results: Although some cues did not show main effects on average craving or smoking, a wide range of individual differences in response to cues was apparent in both CR and EMA data, providing the necessary context to assess their relationship. Laboratory CR measures of cue response were not correlated with real-world cue responses assessed by EMA. The average correlation was 0.03; none exceeded 0.32. One of 40 correlations examined was significantly greater than 0.
Conclusions: Laboratory CR measures do not correlate with EMA-assessed craving or smoking in response to cues, suggesting that CR measures are not accurate predictors of how smokers react to relevant stimuli in the real world.

1. Introduction

Smoking is motivated and maintained by nicotine (Benowitz, 2008), but smoking and craving are also influenced by situational stimuli (Kozlowski and Herman, 1984). Surveys reliably link smoking and craving to cues such as presence of other smokers and drinking alcohol (McKennell, 1970; Russell et al., 1974). Similarly, studies using electronic diaries show that people were more likely to smoke when seeing others smoking and when drinking, and less likely to smoke when smoking was prohibited (Shiffman et al., 2002, 2014b). The role of situational cues is particularly prominent in relapse (O'Connell and Martin, 1987; Shiffman et al., 1996). These situational linkages are often attributed to conditioned learning due to repeated pairing of smoking with environmental stimuli (Carter and Tiffany, 1999; Niaura et al., 1988). This leads to an emphasis on individual differences, since smokers are likely to differ in smoking patterns and thus in the stimuli they associate with smoking, and might also differ in conditionability (Mineka and Oehlberg, 2008). It also suggests that if individual cue associations could be identified, this might help to individually tailor treatment (Conklin et al., 2010; Drummond, 2000).

Ecological Momentary Assessment (EMA; Shiffman et al., 2008) methods, using electronic diaries to collect detailed real-time data, are increasingly being used to study the effects of cues in

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smokers' real-world settings. However, these methods, while they are considered ecologically valid, rely on smokers' naturalistic exposures to cues in their environment. In contrast, cue reactivity (CR) studies (Carter and Tiffany, 1999; Niaura et al., 1988) attempt to bring cue responses into the laboratory, where they can be manipulated and studied experimentally. As a consequence, CR studies are commonly used to assess the effects of cues on craving and smoking (as well as other drug use; Carter and Tiffany, 1999). However, the degree to which laboratory CR responses predict real-world responses to cues has not been studied. In this paper, we assess the associations between smokers' laboratory CR cue responses and their real-world cue responses, as assessed by EMA.

CR studies (Carter and Tiffany, 1999) expose smokers to stimuli thought to be associated with craving and/or smoking, such as cigarettes themselves, and compare these responses to those elicited by a neutral stimulus. Increases in craving or in the likelihood of smoking are seen as indicators of specific cue reactivity. Cues studied in this way have included cigarette-specific stimuli (termed 'proximal cues' by Conklin et al., 2008), and diverse cues such as positive or negative affect, alcohol cues, etc. ('distal cues'; Conklin et al., 2008). CR effects have been observed both in abstinent smokers (McClernon et al., 2009; Tiffany et al., 2000) and minimally deprived smokers (Bailey et al., 2010), and reactivity seems similar across these conditions (Carter et al., 2009; Franklin et al., 2007). However, individual differences in CR are not consistently linked to smoking cessation outcomes (Perkins, 2012; Powell et al., 2010; Waters et al., 2004), causing some to question its relevance to cessation and treatment (Perkins, 2009).

A key question in the CR field is whether reactivity observed in laboratory settings actually reflects real-world responses to these cues. Such a link would be expected if CR responses reflect participants' condition history (Hogarth et al., 2010; Niaura et al., 1998), and necessary if CR responses are to be used to predict outcome (Perkins, 2012) or to tailor treatment (Conklin, 2006; Drummond, 2000). However, to our knowledge no study has examined the degree to which CR measures predict how smokers react to stimuli in the real world. In this paper, we compare data from previously-published studies examining CR responses observed in the laboratory (Shiffman et al., 2013a) and real-world craving and smoking observed in response to analogous cues in EMA data on the same sample (Shiffman et al., 2014b).

EMA data comparing the presence of cues when subjects are and are not smoking provide estimates of the associations between stimuli and smoking (Paty et al., 1992), and can also be used to assess situational correlates of craving (Dunbar et al., 2010). These EMA data are essentially the real-world analog of laboratory cue-reactivity measures, and thus an apt reference to assess the real-world generalizability of CR assessments.

The primary effects from both the CR and EMA studies have been reported in previous publications. The CR study (Shiffman et al., 2013a) assessed daily smokers' craving and smoking in response to a range of smoking-relevant cues. Craving was increased by exposure to smoking and alcohol cues, and decreased by positive affect; however, negative affect and smoking prohibition cues did not, on average, affect craving. As previously reported, both the probability of smoking and the amount smoked increased in proportion to craving, and in proportion to the observed increases in craving, though not in a cue-specific way (Shiffman et al., 2013a).

Similarly, the data from the EMA study also showed significant cue effects: smoking was associated with situational cues including others smoking and alcohol consumption, and inversely with smoking restrictions (Shiffman et al., 2014b). Negative affect was not associated with smoking, but positive affect showed curvilinear effects. Importantly, there was significant individual variation in response to cues, and when this was taken into account, cues, including affect, were very robust predictors of smoking. Knowing a smoker's affective state at any moment allowed one to predict whether s/he was smoking with 70% accuracy (Shiffman et al., 2015), again demonstrating the importance of individual differences even when average effects in the sample as a whole were not significant.

Our primary papers on the CR (Shiffman et al., 2013a) and EMA (Shiffman et al., 2014b) studies focused on the effects of cues in each paradigm. Here, we aim to directly compare the laboratory CR and real-world EMA responses observed to assess whether CR is an accurate proxy for real-world responses to cues. If so, one would expect the magnitude of reactivity observed for each individual during CR exposure to correlate with that individual's responses in real-world observations. For example, if a particular smoker exhibits a high degree of craving reactivity to smoking cues during the CR sessions, one would similarly expect to see that person's craving be higher when such cues are present in real-world settings.

Note that such individual associations do not rest on there being a shared, common reaction across all smokers. Thus, for example, some smokers may be "negative affect smokers" and others not, with the result that the overall effect of negative mood on smoking is not significant across the whole sample of smokers. Nevertheless, one would expect that the particular individuals who demonstrate negative affect smoking in the CR assessment would show negative affect smoking in the EMA assessment. The validity of such individual assessments even in the absence of group-wide significant effects was illustrated in a previous EMA study. In that study, there was no overall significant relationship between negative mood and smoking (Shiffman et al., 2002). However, within this overall 'null' effect, there were substantial individual differences in the relationship between mood and smoking, and analyses showed that the individual associations predicted which individuals were most vulnerable to relapse (Shiffman et al., 2007). Accordingly, in addition to examining the cues that had group-wise significant effects in each paradigm, we also examine the correlation of individual differences in other cues as well.

For the data to be informative on individual differences, it needs to be demonstrated that each of the measures shows substantial between-subject variation; i.e., that some respond more strongly than others, or even that some respond in one direction (e.g., smoking more when upset) while others respond in the opposite direction (smoking less when upset). The potential for correlation across methods depends on such individual differences; if nearly everyone responds in the same way to a particular cue, individual differences – and correlations – would be minimized. Thus, we precede the analysis of correlations between CR and EMA data with an examination of between-person variation in cue associations within each method.

2. Methods

2.1. Subjects

Subjects were 190 daily smokers who completed both the EMA assessment and the CR assessment (i.e., providing data on the neutral cue and one or more active cues). Volunteers had to be at least 21 years old, smoking 5–30 cigarettes per day, smoking for ≥3 years, at their current rate for ≥3 months, and not planning to quit within a month. Subjects in these analyses averaged 40.19 (±11.58) years old, on timeline follow-back reported smoking an average of 14.98 (±5.89) cigarettes per day, and had Fagerström Test for Nicotine Dependence (FTND; Heatherton et al., 1991) scores averaging 5.18 (±2.03); 60% were female. By design, we oversampled African-American (AA) smokers to comprise 38% of the sample, and weighted observations to rebalance ethnic representation.

2.2. Procedures

2.2.1. Cue reactivity. CR procedures are described in detail in Shiffman et al. (2013a). Briefly, reactivity to five different cues (presented as sets of pictures) was assessed over separate sessions on different days: smoking cues (cigarettes, smoke), smoking-prohibition cues (no-smoking signs and settings), alcohol cues (drinks), negative affect, and positive affect (both via images from the International Affective Pictures