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## Relationship between Negative Affect and Smoking Topography in Heavy Drinking Smokers

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### Abstract

Heavy drinking smokers represent a sizeable subgroup of smokers for whom nicotine deprivation and alcohol use increases the urge to smoke in the laboratory and predicts lapses during smoking cessation. The manner in which individuals smoke a cigarette (i.e. smoking topography) provides a reliable index of smoking intensity and reinforcement, yet the effects of affect on smoking topography have not been thoroughly examined in heavy drinking smokers. The current study examined how affect and nicotine deprivation predict smoking behavior as participants (N=27) smoked one cigarette using a smoking topography device after 12-hrs of nicotine abstinence and after a priming dose of alcohol (target BrAC = 0.06 g/dl). Primary smoking topography measures were puff volume, velocity, duration, and inter-puff interval (IPI). The effect of nicotine deprivation was measured by the Minnesota Nicotine Withdrawal Scale (MNWS) and the Profile of Mood States (POMS). Measures were obtained at baseline (i.e. 12-hrs of nicotine abstinence and pre-alcohol) and 30-minutes after alcohol administration (i.e. peak BrAC). Results revealed post-priming negative affect significantly moderated the trajectories of puff volume, puff duration and IPI ( $p$ 's < 0.05) over the course of the cigarette, such that those with greater negative affect had flatter slopes for volume and duration and increasingly infrequent puffs. Our results suggest that baseline and post-priming negative affect following nicotine deprivation alters smoking patterns and increases nicotine exposure throughout a single cigarette. Future studies need to examine differential amounts of nicotine deprivation on response to alcohol and smoking in heavy drinking smokers.

### Keywords

heavy drinking smokers; smoking topography; nicotine deprivation; negative affect; puff volume; puff duration

### 1. Introduction

Nicotine deprivation results in nicotine withdrawal symptoms including changes in affect and craving for nicotine (Bujarski et al., 2015; Shiffman, 1979). While the prevalence of quit

attempts have increased over the past ten years (CDC, 2011), the most frequent outcome of a quit attempt is relapse (Piasecki, 2006). Both nicotine deprivation and alcohol consumption have been shown to increase smoking urges and decrease the ability to resist smoking (Brown et al., 2013; Kahler et al., 2014). Previous studies have also established a positive association between negative affect and smoking relapse (Baker, Piper, McCarthy, Majeskie, & Fiore, 2004; Shiffman & Waters, 2004). Proposed mechanisms to explain this association include models of negative reinforcement (Baker et al., 2004), affect regulation (Schleicher, Harris, Catley, & Nazir, 2009), and classical conditioning (Brandon, 1994). To further understand these mechanisms, controlled laboratory studies can be used to assess how nicotine deprivation and changes in affect alter smoking behavior. Due to high rates of co-use between alcohol and smoking, and the frequency with which these behaviors occur concurrently, examining heavy drinking smokers as they are engaged in both substances will allow for a greater understanding of the mechanisms perpetuating co-use.

Smoking topography measures are objective and reliable indices of smoking intensity and include the number of puffs taken from a cigarette, puff volume, puff duration, puff velocity and inter-puff interval (IPI) (Lee, Malson, Waters, Moolchan, & Pickworth, 2003; Perkins, Karelitz, Giedgowd, & Conklin, 2012). Smoking topography measures may help elucidate how alcohol consumption in the context of nicotine deprivation and are altering more nuanced aspects of smoking behavior.

Previous studies have examined the effects of nicotine deprivation on smoking behavior including smoking topography, lapse behaviors, and ad libitum smoking (McKee, Weinberger, Shi, Tetrault, & Coppola, 2012; Herscoviv, Rose, & Jarvik, 1985). Some have found that eighteen hours of nicotine abstinence increases the number of cigarettes smoked (McKee et al., 2012). Negative affect and stress induction have been shown to independently increase puff count and lessen the ability to resist smoking (Conklin & Perkins, 2005; McKee et al., 2011). Previous studies of moderate drinkers and smokers have found alcohol administration to cause changes in puff volume (Nil, Buzzi, & Bättig, 1984), and changes in puff count and duration following three hours of nicotine abstinence (King, McNamara, Conrad, & Cao, 2009). This study seeks to extend these findings by testing how affect following overnight nicotine deprivation and alcohol administration predicts intensity of smoking in heavy drinking smokers.

## 2. Methods

### 2.1 Participants

The study was approved by the Institutional Review Board of the University of California, Los Angeles and was conducted in accordance with the Declaration of Helsinki. A community-based sample of heavy drinking smokers was recruited from the Los Angeles area through print and online advertisements. Participants consisted of 27 heavy drinking smokers (66% male, 53% Caucasian) that received a placebo medication as part of a larger study examining the effects of naltrexone, varenicline and their combination on craving for cigarettes and subjective response to alcohol (Ray et al., 2014), along with smoking topography (Roche, Bujarski, Hartwell, Green, & Ray, 2015). Eligible participants were non-treatment seeking daily smokers (10 cigarettes per day) who also met the National

Institute on Alcohol Abuse and Alcoholism (NIAAA, 1995) criteria for heavy drinking ( 14 drinks/week for men and 7 drinks/week for women).

## 2.2 Experimental Procedures

Participants completed a telephone and in-person screening, and a physical examination, to determine eligibility. Inclusion/exclusion criteria are described in detail elsewhere (Ray et al., 2014). Participants were excluded for the medical reasons if their clinical labs were elevated, reported clinically significant alcohol withdrawal, or had a poorly-managed medical illness determined by the study physicians (< 10% of screened participants). During all visits, participants were required to produce a BrAC of 0.000 g/dl on the breathalyzer (Dräger Medical Inc., Telford, PA, USA) and test negative for all drugs except marijuana on a urine toxicology screen. Participants were asked to abstain from alcohol for 24 hours and to abstain from nicotine for 12 hours (nicotine abstinence was verified by expired CO levels of less than 10ppm or below 50% of initial screening value) prior to the experimental session. Immediately following the completion of baseline assessments at the start of the experimental session, participants were given a standardized priming dose of alcohol to reach a target BrAC of 0.060g/dl, calculated using published guidelines (Brick, 2006). Both participants and experimenters were aware that alcohol was being consumed but neither target nor observed BrAC were revealed to participants. Approximately thirty minutes following the alcohol administration (selected based on time to peak target BrAC), participants smoked their first cigarette of the day in the laboratory using a CReSS Pocket smoking topography device (Borgwaldt KC, Inc., Richmond, VA). Participants smoked their own cigarettes and no smoking instructions were given to participants as they smoked. The primary topography measures were puff volume (capacity of each puff in ml), puff velocity (mean flow rate of each puff in ml/s), puff duration (length of each puff in ms), and inter-puff interval (IPI; mean time between each puff in ms). Participants completed various assessments (described below) at baseline, post-alcohol, and post-smoking. Participants were compensated a total of \$140 for completing the study.

## 2.3 Measures

To assess for effects of nicotine deprivation, participants completed the Minnesota Nicotine Withdrawal Scale (MNWS; Toll, O'Malley, McKee, Salovey, & Krishnan-Sarin, 2007), rating nine statements on a 5-point Likert scale ranging from "none" to "severe". Participants also completed the Alcohol Urge Questionnaire (AUQ; Bohn, Krahn, & Staehler, 1995) and Profile of Mood States (POMS; McNair, Lorr, & Droppleman, 1971), where participants rate 40 items on a 4-point Likert scale ranging from "not at all" to "extremely." To reduce the number of statistical tests, positive and negative affect subscales were calculated from the POMS. Nicotine and alcohol dependence measures assessed at the initial screening visit that were tested as covariates included the Fagerström Test of Nicotine Dependence (FTND; Heatherton, Kozlowski, Frecker, & Fagerström, 1991) and Alcohol Dependency Scale (ADS; Skinner & Horn, 1984).

## 2.4 Statistical Analyses

Changes in affect and nicotine withdrawal following alcohol administration were analyzed using dependent t-tests. Smoking topography variables at the single puff level (i.e., puff

volume, velocity, duration and IPI) were analyzed using a series of multilevel models in SAS version 9.4 using proc mixed. The data for puff duration and IPI were positively skewed, therefore these data were log transformed. For each multilevel model, the proportion of the cigarette smoked (cig ratio, computed as current puff number/total puff count) was a level 1 predictor, which was treated as random at the subject level (level 2). Affect variables, nicotine withdrawal, alcohol craving, and alcohol and nicotine dependence were entered at Level 2 and as potential moderators of the cig ratio slope. An unstructured covariance matrix was specified as well as Satterthwaite approximated degrees of freedom. If a significant interaction was observed, alcohol dependence and nicotine dependence were examined as potential covariates in the model. All analyses controlled for baseline affective variables.

### 3. Results

#### 3.1 Sample Characteristics

Mean age of participants was 38.88 years ( $SD = 9.81$ ). On average, participants smoked 14.13 ( $SD = 5.17$ ) cigarettes per day and averaged 20.56 ( $SD = 8.25$ ) drinking days per month and 6.08 ( $SD = 3.32$ ) drinks per drinking day. Participants had a mean FTND score of 4.04 ( $SD = 1.99$ ) indicating low to moderate nicotine dependence. At baseline, participants had an average nicotine withdrawal score of 16.34 ( $SD = 6.36$ ) indicating low to moderate nicotine withdrawal.

#### 3.2 Changes in Affect and Nicotine Withdrawal

Negative affect and positive affect did not significantly change from baseline to the post-alcohol session ( $t(26) = 0.34, 0.64$  respectively;  $p$ 's  $> 0.10$ ). Nicotine withdrawal did not significantly change from pre- to post-alcohol ( $t(26) = -0.79, p = 0.44$ ).

#### 3.3 Smoking Topography

Overall, puff volume and puff duration significantly decreased over the cigarette (Cig Ratio:  $B = -21.94, -0.60$  respectively,  $p$ 's  $< 0.01$ ), while puff velocity and IPI significantly increased over the course of the cigarette (Cig Ratio:  $B = 10.52, 1.30$  respectively,  $p$ 's  $< 0.01$ ). Smoking topography outcomes as predicted by withdrawal and affect presented in Table 1.

**3.3.1 Puff Volume**—Post-alcohol, negative affect significantly moderated the slope of puff volume (Figure 1A; Cig Ratio  $\times$  Negative Affect:  $B = 7.77, t = 2.01, p = 0.05$ ). Additionally, at baseline negative affect had a trending effect in moderating the slope of puff volume ( $B = 7.35, t = 1.93, p = 0.07$ ).

**3.3.2 Puff Velocity**—Negative affect post-alcohol and at baseline did not moderate the slope of puff velocity (Figure 1B; Cig Ratio  $\times$  Negative Affect:  $B = -4.78, t = -1.56, p = 0.13; p = 0.25$  respectively).

**3.3.3 Puff Duration**—Post-alcohol, negative affect significantly moderated the slope of puff duration (Figure 1C; Cig Ratio  $\times$  Negative Affect:  $B = 0.27, t = 2.76, p = 0.01$ ), and this effect was also seen from baseline affect measures ( $B = 0.22, t = 2.13, p = 0.04$ ).

**3.3.4 IPI**—Post-alcohol, negative affect significantly moderated the slope of IPI (Figure 1D; Cig Ratio  $\times$  Negative Affect:  $B = 0.69$ ,  $t = 2.29$ ,  $p = 0.03$ ). At baseline, negative affect had a trending effect in moderating the slope of IPI ( $B = 0.59$ ,  $t = 1.94$ ,  $p = 0.06$ ).

**3.3.5 Positive Affect, Withdrawal, Craving, and Dependence Moderators**—Post-alcohol positive affect, nicotine withdrawal symptoms, and alcohol craving had no moderating effect on any smoking topography measures ( $p$ 's  $> 0.10$ ). Additionally, nicotine dependence and alcohol dependence were not significant moderators of any smoking topography outcome ( $p$ 's  $> 0.10$ ). The moderating effect of post-alcohol negative affect on IPI and duration remained significant when adding alcohol and nicotine dependence as covariates and while the negative affect moderating effect became a trend for puff volume ( $p = 0.09$ ), the effect magnitude was not substantially affected ( $B = 7.77$ , vs.  $B = 7.19$  and  $B = 7.21$  respectively).

## 4. Discussion

The aims of this study were to examine how nicotine deprivation and affect level predict smoking intensity. Consistent with prior studies (Guyatt, Kirkham, Baldry, Dixon, & Cumming, 1989; Kolonen et al., 1992), we found a significant decrease in puff volume and duration over the course of the cigarette, while puff velocity and IPI significantly increased. Additionally, we observed an unexpected finding that the priming dose of alcohol did not alter negative affect or nicotine withdrawal. This could be due to a ceiling effect such that alcohol did not show an effect over and above nicotine deprivation due to already high levels of negative affect and nicotine withdrawal. Negative affect moderated puff volume, duration and IPI trajectories at both baseline and post-alcohol administration time points. Because of these findings, and due to the strong associations between nicotine deprivation and increases in craving and negative affect (Hughes & Hatsukami, 1986; Piasecki, Kenford, Smith, Fiore, & Baker, 1997), we interpreted the moderating effects of negative affect, at baseline and in the context of alcohol priming, on puffing behavior as being primarily driven by nicotine deprivation. This moderating effect is unlikely caused by alcohol craving or withdrawal due to alcohol priming. Individuals with low negative affect had relatively steeper negative slopes among volume and duration, whereas those with high negative affect had relatively flatter slopes. Those with high negative affect also had increasingly more infrequent puffs shown by greater IPI over the course of the cigarette. Considering nicotine withdrawal did not moderate smoking topography, the effect of negative affect could be in part due to non-deprivation trait differences in affect.

Previous studies have suggested individual variation in the sensitivity to alterations in nicotine (Guyatt et al., 1989). Smokers typically regulate their puffing behavior during a single cigarette through decreasing puff volume and duration to account for increasing amounts of nicotine (Guyatt et al., 1989; Kolonen, et al., 1992). Previous studies have found a positive association between nicotine dependence and puff volume (Perkins et al., 2012). Thus, we posit that those with greater negative affect after nicotine deprivation may need more nicotine to extinguish these subjective feelings and exhibit a decreased reactivity to nicotine, demonstrated through increasingly flattened slopes. Alternatively, these increasingly flattened slopes could be due to the perception that smoking is more rewarding,

as previous studies have found smoking to be more rewarding following stress versus relaxation (Ashare et al., 2012). Our results may suggest that elevated negative affect is contributing to a smoking pattern that increases nicotine exposure, which over time could increase the risks for worsening nicotine dependence. These results support previous studies (Zelman, Brandon, Jorenby, & Baker, 1992) regarding the importance of addressing negative affect in smoking cessation counseling.

The present study's strengths include a period of nicotine deprivation that has been shown to increase smoking urge, nicotine reinforcement, and smoking behavior (McKee et al., 2012) a target BrAC of 0.06 g/dl which has been shown to increase craving for cigarettes (Ray et al., 2007), and assessments of affect both pre- and post- alcohol administration. Limitations include a small sample size, participants receiving a placebo medication which may alter their subjective state and/or objective smoking behavior, and the lack of topography measures before deprivation as a comparison.

In sum, we found that negative affect in the context of nicotine deprivation and alcohol administration predicts smoking behavior in the laboratory. A greater understanding of the impact of nicotine withdrawal and affect on smoking behavior can further personalize treatment approaches targeting those who are more likely to experience greater difficulties managing the affective distress accompanying smoking cessation. These findings extend a growing body of literature on the role of affect regulation in smoking behavior (Heinz, Kassel, Berbaum, & Mermelstein, 2010) and how mechanisms of co-use can inform treatment options (Roche, Ray, Yardley, & King, 2016). Future studies should determine how varying amounts of nicotine deprivation moderate the impact of alcohol, and smoking topography, amongst heavy drinking smokers.

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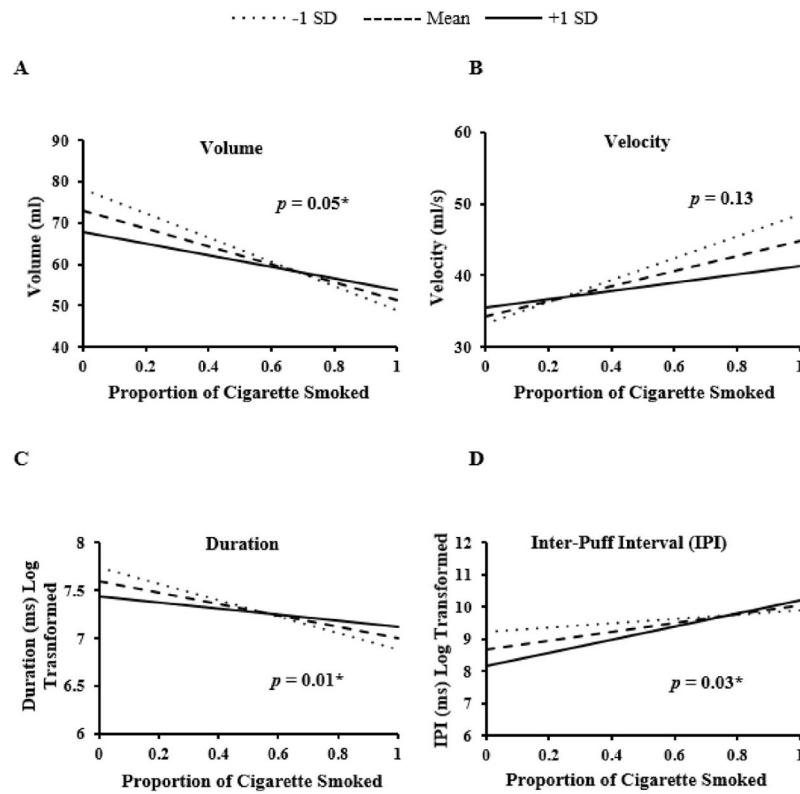
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**Highlights**

- Examined smoking topography in relation to nicotine deprivation.
- Negative affect moderated trajectory of topography over the course of the cigarette.
- Greater negative affect was associated with more stable smoking patterns.
- Nicotine deprivation response influences manner of smoking in heavy drinking smokers.

**Figure 1.**

Puff volume (A), velocity (B), duration (C) and IPI (D) as predicted by negative affect following nicotine deprivation. An asterisk refers to a significant interaction between cig ratio and negative affect over the course of the cigarette.

**Table 1**

Smoking Topography Outcomes as Predicted by Responses to Nicotine Deprivation

Predictor	Volume	Velocity	IPI <sup>‡</sup>	Duration <sup>‡</sup>
<b>MNWS nic. withdrawal</b>				
Withdrawal	0.75	<-0.01	-0.04	<-0.01
Cig Ratio	-28.02 *	8.28	0.29	-0.80 *
Withdrawal * Cig Ratio	0.36	0.13	0.06	0.01
<b>POMS negative affect</b>				
Affect	-5.31	1.14	-0.53 *	-0.15
Cig Ratio	-39.96 *	21.83 *	-0.28	-1.23 *
Affect * Cig Ratio	7.77 *	-4.78	0.69 *	0.27 *
<b>POMS positive affect</b>				
Affect	0.39	-0.50	0.10	0.05
Cig Ratio	-22.52	5.80	1.87	-0.32
Affect * Cig Ratio	0.11	0.86	-0.11	-0.05

*Note:* Data are presented as unstandardized coefficients (B). Cig ratio refers to the proportion of the cigarette smoked. All predictors assessed post-alcohol administration.

<sup>‡</sup>IPI and duration are log transformed

\* indicates significance at p .05