

## Physiological and psychological symptoms and predictors in early nicotine withdrawal

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### Abstract

The present study assessed the structure and intensity of the nicotine withdrawal syndrome in 30 (22 male, 8 female) heavy smokers across three experimental conditions: smoking, brief abstinence (3.5 h), and extended abstinence (18 h). Physiological variables (heart rate and blood pressure) and psychological variables (anxious and depressed mood) were examined in terms of symptom validity and as predictors of nicotine withdrawal intensity. As length of abstinence increased, heart rate and blood pressure decreased, and anxious and depressed mood increased. Only anxious and depressed mood were significant individual predictors of withdrawal intensity. The symptom structure of withdrawal did not change over time as abstinence levels increased; each symptom's contribution to nicotine withdrawal intensity remained stable throughout the first 18 h of abstinence.

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Smoking cessation or a marked reduction in cigarette consumption produces the nicotine withdrawal syndrome, which is composed of symptoms including irritability, sleep disturbance, impatience, hunger, difficulty concentrating, depression, and anxiety (American Psychiatric Association (APA), 2000). Withdrawal is also typically accompanied by physiological changes, such as a decrease in heart rate (al'Absi et al., 2002; Hughes et al., 1994). Many studies suggest that the withdrawal syndrome begins within 1 to 2 days of cessation, peaks within 1 week, and gradually decreases to pre-cessation levels within approximately 4 weeks (Gilbert et al., 2002; Piasecki et al., 1998; Hughes et al., 1994; Hughes, 2007a). Research indicates that the onset of nicotine withdrawal may occur much earlier than originally thought, perhaps within the first 2 to 24 h of abstinence (Hendricks et al., 2006; Hughes et al., 1994; Parrott et al., 1996; Shiffman et al.,

2002). However, surprisingly few studies have examined the temporal progression of the withdrawal syndrome within these first 24 h, thus leaving a significant gap in our understanding of nicotine withdrawal (Hendricks et al., 2006).

Evidence shows that the time course of the withdrawal syndrome may be an important predictor of relapse following a smoking cessation attempt (al'Absi et al., 2004; Piasecki et al., 1998; Piasecki et al., 2000; Piasecki et al., 2003a, 2003b, 2003c). For example, Piasecki and colleagues found that quitters who experienced an escalation in withdrawal severity over time were more likely to relapse than quitters whose symptoms decreased over time (Piasecki et al., 2003a, 2003b, 2003c). These findings suggest that a greater understanding of the time course of withdrawal is warranted, as it may help researchers and clinicians to develop more effective smoking cessation programs by highlighting which symptoms should be targeted most aggressively, and at what point in the cessation process. Such goals necessitate a more complete knowledge of early nicotine withdrawal (i.e., within the first 24 h of smoking cessation), including order of symptom onset and potential symptom stages (Hughes, 2007b).

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Although there are a number of nicotine withdrawal symptoms, anxious and depressed mood were the focus of the present study for several reasons. First, affect regulation models of smoking posit that negative affective states such as anxiety and depression are related to higher rates of relapse during a smoking cessation attempt (Kenford et al., 2002; Shiffman, 2005; Shiffman and Waters, 2004). Studies confirm that individuals with depression find it more difficult to quit smoking, but they fail to elucidate when in the cessation process that depressed mood is most influential (REFS), which is valuable information from a treatment perspective. Second, while there is a growing body of literature that focuses on the relationship between anxiety disorders and cigarette smoking (Morissette et al., 2007; Feldner et al., 2007; Zvolensky and Bernstein, 2005), there is less research on how subclinical anxious mood may impact overall withdrawal severity or how the level of this impact may change as the withdrawal syndrome progresses in its earliest stages. This gap in our understanding of the relationship between anxious mood and nicotine withdrawal continues to exist despite the fact that a majority of smokers report that they smoke to relieve anxiety (Schneider and Houston, 1970). Finally, although studies show that depressed mood is associated with smoking prevalence and difficulty quitting smoking (Cinciripini et al., 2003; Piasecki, 2006), empirical evidence confirming that depressed mood is a valid withdrawal symptom and is related to overall withdrawal severity is somewhat equivocal (Hughes, 2007a; Piper and Curtin, 2006). Therefore, more studies that utilize strong, prospective experimental designs are needed to allow researchers to draw more confident causal conclusions about the potential link between depressed mood and nicotine withdrawal.

Heart rate and blood pressure were also a focus of the current study, because prior research has emphasized the importance of physiological symptoms as components of the nicotine withdrawal syndrome (Gilbert et al., 1998; Hughes et al., 1994; Hughes, Gust et al., 1991; Hughes and Hatsukami, 1986). Data indicate that heart rate decreases by approximately 5 to 10 beats per minute (bpm) (Hughes et al., 1994). This decrease in heart rate appears to begin within the first 48 h of abstinence and continues for two to four weeks following cessation (Hughes et al., 1994; Hughes and Hatsukami, 1986). Thus far, studies examining the effect of withdrawal on blood pressure have produced equivocal results: after reviews of the withdrawal literature, Hughes et al. (1990) concluded that blood pressure either decreased or did not change following abstinence, but Sommesse and Patterson (1995) concluded that blood pressure tends to rise during withdrawal. Clearly, more research in this area is warranted.

The present study was designed to examine the relative contributions of selected physical and psychological symptoms of nicotine withdrawal to self-reported withdrawal intensity during the first 18 h of abstinence utilizing a novel, prospective, experimental design in which abstinence was systematically manipulated and all variables were measured at multiple time points. The primary goals were to confirm the existing understanding of withdrawal symptom validity, and to investigate further the extent to which physiological (heart rate and blood pressure) and psychological (anxiety and depression) withdrawal symptoms differentially predict nicotine withdrawal

intensity during periods of brief abstinence. Accordingly, each participant completed measures of relevant symptomatology during a smoking condition, a brief abstinence condition (3.5 h), and an extended abstinence condition (18 h). Consistent with previous research, the authors predicted that (1) the intensity of the nicotine withdrawal syndrome would increase with length of abstinence, (2) heart rate would decrease with length of abstinence, and (3) symptoms of anxiety and depression would increase with length of abstinence. The authors also hypothesized that blood pressure would decrease with heart rate (hypothesis 2). Finally, the authors hypothesized that (4) the influence of each withdrawal symptom on self-reported experience of overall withdrawal severity would change as length of abstinence increased.

## 1. Materials and methods

### 1.1. Participants

Participants included 30 adults (22 males, 8 females) from a city in the Southwestern United States who were recruited via advertisements posted on a university campus, at a medical center, and at local businesses. Participants were included in the study if they were over 18 years of age, reported smoking more than 16 cigarettes per day, scored at least 4 on the Fagerström Test for Nicotine Dependence (FTND), and had carbon monoxide levels greater than 10 ppm at baseline; otherwise, they were excluded from participation. None of the participants indicated that they were currently trying to quit smoking. All volunteers were compensated with a monetary reward (\$100). The experimental protocol for this study was approved by the Institutional Review Board for the use of Human Subjects at Texas Tech University.

### 1.2. Materials

#### 1.2.1. Verification of smoking status

A Micro Medical Micro Carbon Monoxide (CO) monitor (Lewinston, ME) was used to verify nicotine abstinence in the extended abstinence condition, although measurements of respiratory CO levels were taken in all conditions as points of reference. Carbon monoxide level is an excellent indicator of tobacco use, particularly among heavy smokers, and demonstrates both sensitivity and specificity of about 90% (Society for Research on Nicotine and Tobacco Subcommittee on Biochemical Verification [SRNT SBV], 2002). Typically, a CO level below 10 ppm indicates abstinence during a normal sleep/wake cycle (24 h), although some studies accept CO levels that do not exceed one-half of the baseline CO level (SRNT SBV, 2002).

#### 1.2.2. Nicotine dependence

Nicotine dependence was measured using the Fagerström Test for Nicotine Dependence (FTND; Heatherton et al., 1991), which consists of six items rated either from 0 to 1 or from 0 to 3 (depending on the question) that yield a total score of 10, with higher scores indicating greater nicotine dependence. This measure demonstrates reasonable internal consistency and validity (Colby et al., 2000; Heatherton et al., 1991).

### 1.2.3. Mood

Two self-report questionnaires were used to assess mood: the Profile of Mood States (POMS; McNair et al., 1971) and the Inventory to Diagnose Depression (IDD; Zimmerman et al., 1986). Both measures were included in the current study because they assessed different aspects of depression: the IDD was used to measure baseline levels of depressed mood, whereas the POMS was used to measure acute depressive symptoms.

The IDD is a self-report instrument specifically designed to diagnose Major Depressive Disorder according to DSM-III criteria (Zimmerman et al., 1986). It consists of 22 groups of five statements, each group corresponding with a single symptom of depression (e.g., loss of appetite). Statements are arranged in order of ascending severity, with item scores ranging from 0 (*no disturbance*) to 4 (*the symptom is present and clinically severe*). Studies indicate that the IDD has excellent reliability in both inpatient and normal samples (Zimmerman et al., 1986; Zimmerman and Coryell, 1988).

The POMS contains sixty-five adjectives that describe a series of mood states. Respondents rate the degree to which they have experienced each mood state on a 5-point Likert scale ranging from 0 (*not at all*) to 4 (*extremely*). In the present study, participants were asked to rate the degree to which they experienced each mood state within the past 30 min. The POMS comprises seven subscales, including Tension–Anxiety, Depression–Dejection, Anger–Hostility, Vigor–Activity, Fatigue–Inertia, and Confusion–Bewilderment (Boyle, 1987; McNair et al., 1971). This instrument, particularly the Tension–Anxiety and Depression–Dejection subscales, has been frequently used to assess changes in negative affect associated with the nicotine withdrawal syndrome. Furthermore, research indicates that the POMS exhibits good reliability and validity (Boyle, 1987; Little and Penman, 1989).

### 1.2.4. Nicotine withdrawal

Nicotine withdrawal was assessed using both self-report and physiological measures. Participants rated their withdrawal symptoms on a comprehensive self-report measure that included a list of symptoms derived from: (1) the DSM-IV-TR list of nicotine withdrawal symptoms (APA, 2000), (2) the Tobacco Withdrawal Symptom Checklist (WSC; Hughes and Hatsukami, 1986), and (3) a subjective state scale that has been used in a number of other published studies (al'Absi et al., 2002; al'Absi, Wittmers et al., 2003). Items on this subjective measure included: tension/anxiety, sadness/depression, irritability, anger, difficulty concentrating, restlessness, boredom, confusion, and impatience. Physical symptoms included headache, hunger, tremor, and drowsiness. Additional items measured how calm, content, in control, interested, and cheerful participants felt. For each item on this subjective measure ( $N=24$ ), participants rated the degree to which they experienced each symptom within the previous 30 min on an eight-point Likert scale (0=*not at all*; 7=*very strong*). Total withdrawal score was calculated by taking the sum of all items.

Physical indicators of withdrawal included heart rate and blood pressure. Participants' heart rate and blood pressure were monitored at 30-min intervals using a Dinamap PRO Series 400 monitor (Tampa, FL).

### 1.3. Procedure

Participants contacted the Behavioral Psychopharmacology Laboratory via telephone after reading advertisements posted throughout the university and at strategic locations in the community. Trained graduate students briefly explained the study to potential participants and invited them to complete a short screening interview. During the screening interview, potential participants were assessed for eligibility to participate. If eligible, they received a more detailed description of the study and were asked if they would like to participate. After giving their informed consent to participate, participants completed a demographics questionnaire that consisted of questions regarding gender, age, ethnicity, and smoking habits. Researchers also recorded each participant's heart rate, blood pressure, and respiratory CO level to corroborate self-reported smoking status.

After the screening interview, participants were scheduled to return to the laboratory and complete the first of three experimental conditions: smoking (S), brief abstinence (BA), and extended abstinence (EA). Although participants in the EA condition were still in the early stages of abstinence, it was named EA because the length of abstinence was extended relative to the other two conditions. Each experimental condition began between 12 pm and 2 pm, and the order of experimental conditions was counterbalanced across participants. At the beginning of each session, researchers recorded participants' baseline heart rate, blood pressure, and CO level. In addition, participants completed the FTND, POMS, IDD, and the comprehensive nicotine withdrawal measure before each session. Although the IDD was used as a baseline measure of depressive symptoms, it was administered before each session to check for consistency across experimental conditions.

Following initial measurements, participants in all three conditions watched videos of neutral content (i.e., documentaries) for approximately 4 h. During this time, heart rate and blood pressure were monitored and two self-report measures (the withdrawal measure and the POMS) were completed every 30 min. Participants in the S condition were allowed to smoke prior to and during the session in the laboratory, provided that they informed the researcher each time that they smoked. Participants in the BA condition were allowed to smoke prior to, but not during, the experimental session, and participants in the EA condition were instructed not to smoke 14 h prior to *or* during the session. The baseline CO measurement was used to verify that each participant had not smoked since the night before the EA session. Participants whose CO levels exceeded either 10 ppm or one-half of their baseline CO level were informed that their CO levels were too high to complete the session and were asked to reschedule their EA session. This happened with three participants, all of whom successfully abstained from smoking and completed the EA session on their second attempt.

### 1.4. Statistical analyses

Means and standard deviations were computed for continuous variables, and frequencies were calculate for categorical variables. A series of one-way repeated measures Analyses of

Variance (ANOVAs), followed by post hoc pairwise comparisons using the Tukey correction at  $\alpha=.05$ , were conducted to assess how physical variables, mood state, and withdrawal symptoms changed across the three experimental conditions. Even though these variables were measured five times within each experimental condition (i.e., every 30 min), analyses were conducted on the average value for each condition because this strategy was most consistent with our goal to provide the most accurate representation of overall withdrawal within each condition. These analyses served as both a manipulation check (e.g., did withdrawal intensity increase with abstinence?) and allowed researchers to determine whether withdrawal symptom patterns in the current study replicated those observed in previous studies.

Researchers used hierarchical multiple linear regression to predict nicotine withdrawal, as defined by the last withdrawal measure score of each day, across the three experimental conditions. Therefore, researchers conducted a separate regression analysis for the S condition, the BA condition, and the EA condition. Predictor variables included heart rate, blood pressure, IDD score, POMS-DD score, and POMS-TA score. As mood state (POMS), heart rate, and blood pressure were measured multiple times within each condition, these results were averaged within participants for each condition. Prior to performing the regression analysis, the data were evaluated according to the assumptions of linear regression and were screened for outliers by examining bivariate correlations, scatterplots, normal probability plots, and histograms of standardized residuals.

Each hierarchical regression model consisted of three steps.<sup>1</sup> Average daily heart rate and blood pressure (not including baseline measurements) were entered as a set in the first step because, although physiological variables may be important components of the withdrawal syndrome, the effects of depressive and anxious symptoms above and beyond the effects of physiological variables were of primary interest. Accordingly, IDD and POMS-DD scores were entered as a set in the second step of the analysis, and POMS-TA scores were entered in the third step. Measures of depressive and anxious symptoms were entered as separate blocks because the researchers were most interested in their independent contributions to withdrawal intensity.

## 2. Results

### 2.1. Sample characteristics

The sample for the present study included 22 males (73.3%) and 8 females with a mean age of 27 years ( $SD=10.1$  years). The small number of female participants reflects difficulty obtaining and retaining female participants. Approximately 57% of participants identified themselves as Caucasian, 20% identified themselves as Hispanic, 13% identified themselves as Asian, and 10% identified themselves as “Other.” All participants stated

that they smoked at least 16 cigarettes per day. The majority of participants (78.6%) reported that they did not use any tobacco products other than cigarettes. However, 3.6% of participants used smokeless tobacco products, 10.7% smoked cigars, and 7.1% smoked pipe tobacco in addition to smoking cigarettes. Nicotine dependence was confirmed by the fact that the average FTND score among participants was greater than 4 ( $M=4.6$ ).

### 2.2. Changes in symptoms

Table 1 shows participants' average scores within each experimental condition on the POMS subscales, the IDD, and the withdrawal measure. It also shows average heart rate and blood pressure within each condition. Mean scores that changed significantly in comparison to the previous condition are represented in bold. For example, the mean POMS-TA score in the BA condition was significantly greater than the mean POMS-TA score in the S condition, so the POMS-TA score in the BA condition is shown in bold font.

A one-way repeated measures ANOVA using the Huynh-Feldt correction for violations of sphericity revealed that, as expected (hypothesis 1), nicotine withdrawal intensity significantly increased as length of abstinence increased,  $F(1.7, 48.4)=13.04$ ,  $p<.01$ . Post-hoc pairwise comparisons among average SSS scores for all three experimental conditions showed that withdrawal intensity had already increased significantly within four hours of abstinence,  $F(1, 29)=9.6$ ,  $p<.05$ , and continued to increase through 18 h of abstinence,  $F(1, 29)=7.8$ ,  $p<.01$ .

Consistent with hypothesis 2, heart rate, diastolic blood pressure, and systolic blood pressure all decreased as length of abstinence increased [ $F(2, 58)=20.11$ ,  $p<.001$ ,  $F(2, 58)=4.33$ ,  $p<.05$ , and  $F(2, 58)=7.02$ ,  $p<.01$ , respectively]. Heart rate had significantly decreased within four hours of abstinence [ $F(1, 29)=5.8$ ,  $p<.05$ ], and continued to decrease through 18 h of abstinence [ $F(1, 29)=18.8$ ,  $p<.01$ ]. Systolic and diastolic blood pressure did not significantly decrease until 18 h of abstinence [ $F(1, 29)=7.0$ ,  $p<.05$  and  $F(1, 29)=14.3$ ,  $p<.01$ ].

Table 1

Mean scores and standard deviations of dependent measures according to experimental condition

Measure	Condition			
	S	BA	EA	
Diastolic blood pressure	66.2 (6.8)	64.5 (7.7)	<b>62.5 (6.4)</b>	*
Systolic blood pressure	119.4 (15.6)	118.2 (16.3)	<b>113.6 (13.5)</b>	*
Heart rate	78.9 (12.5)	<b>75.6 (12.1)</b>	<b>68.5 (12.2)</b>	*
Inventory to diagnose depression	9.0 (9.5)	8.7 (9.9)	9.8 (9.7)	
POMS: Depression–Dejection	3 (8.8)	4.2 (9.0)	<b>5.7 (10.7)</b>	*
POMS: Tension–Anxiety	5 (4.3)	<b>7 (5.4)</b>	<b>9.6 (7.9)</b>	*
Subjective State Scale	41.2 (15.7)	<b>51.6 (22.5)</b>	<b>60.2 (26.1)</b>	*

Note. S=smoking condition, BA=brief abstinence condition, and EA=extended abstinence condition; standard deviations are given in parentheses. Mean scores that changed significantly in comparison to the previous experimental condition are represented in bold.

\* $p<.05$  for omnibus  $F$  test.

<sup>1</sup> Each hierarchical regression model initially consisted of four steps. Baseline heart rate and blood pressure were entered as a set in the first step to control for variance due to pre-existing individual differences on these measures. Due to problems with multicollinearity among the baseline and average daily physiological measures, this first step was eliminated.



Table 2  
Hierarchical regression analyses predicting nicotine withdrawal intensity in smoking (S), brief abstinence (BA), and extended abstinence (EA) conditions

Independent variables	S		BA		EA	
	$\Delta R^2$	$R^2$	$\Delta R^2$	$R^2$	$\Delta R^2$	$R^2$
HR, BP	0.09	0.09	0.02	0.02	0.05	0.05
Depressed Mood	0.5***	0.59***	0.42***	0.44**	0.48*	0.53***
Anxious Mood	0.06 <sup>m</sup>	0.65***	0.29***	0.73***	0.20***	0.73***

Note.  $\Delta R^2$ =change in  $R^2$ , HR=heart rate, BP=blood pressure.

<sup>m</sup>marginally significant (.05 <  $p$  < 1.0) \* $p$  < .05. \*\* $p$  < .01. \*\*\* $p$  < .001.

Additional analyses confirmed hypothesis 3: depressed mood (POMS-DD score) and anxious mood (POMS-TA score) both increased as length of abstinence increased [ $F(1.6, 48.7)=3.46$ ,  $p < .05$  and  $F(1.5, 46)=9.65$ ,  $p < .01$ , respectively]. Depressed mood did not increase significantly until 18 h of abstinence [ $F(1, 29)=4.8$ ,  $p < .05$ ], but anxious mood increased within four hours of abstinence [ $F(1, 29)=5.2$ ,  $p < .05$ ]. Anxious mood increased further by 18 h of abstinence,  $F(1, 29)=8.4$ ,  $p < .01$ .

### 2.3. Predictors of nicotine withdrawal intensity

Hierarchical linear regression was used to determine predictors of nicotine withdrawal intensity. Bivariate correlations indicated possible multicollinearity. Specifically, there were positive correlations between average IDD score and average POMS Depression–Dejection (POMS-DD) score ( $r = .62$ ,  $p < .001$ ), between average POMS-DD score and average POMS Tension–Anxiety (POMS-TA) score ( $r = .68$ ,  $p < .0001$ ), and between average IDD score and all POMS subscales except Vigor. Nevertheless, Tolerance values and the Variance Inflation Factor indicated no problems with multicollinearity, and there were no other violations of the assumptions of linear regression.

Regression models for all experimental conditions yielded similar results (Table 2). Average daily heart rate and blood pressure did not significantly predict nicotine withdrawal intensity at any level of abstinence (still smoking, brief abstinence, or extended abstinence). In all cases, depressed mood significantly predicted withdrawal intensity above and beyond the influence of heart rate and blood pressure. Anxious mood also significantly predicted withdrawal intensity above and beyond the effects of heart rate, blood pressure, and depressed mood at all levels of abstinence, except that this effect was marginally significant in the smoking condition ( $p < .06$ ). For all three levels of abstinence, average POMS-DD score was the only significant individual predictor of withdrawal intensity in the second step of the regression model, and POMS-TA score was the only significant individual predictor of withdrawal intensity in the full model (although this effect was marginally significant in the smoking condition,  $p < .06$ ).

## 3. Discussion

It is important to understand the structure of the withdrawal syndrome within the first hours of abstinence, as this is when the onset of the withdrawal syndrome occurs. Understanding which

symptoms are present within this potentially critical period may help researchers and practitioners to develop more effective smoking cessation programs. The current study was designed to evaluate the time course of physiological and psychological symptoms of nicotine withdrawal at two points in time during the first 18 h of abstinence, and to determine whether any symptoms differentially influenced self-reported withdrawal severity over time.

The withdrawal patterns reported in this study coincided with those reported in previous studies that have assessed the withdrawal syndrome during longer periods of abstinence: participants experienced a decrease in heart rate and blood pressure and an increase in anxious and depressed mood as length of abstinence increased. However, most of these changes in symptom levels occurred within the first 4 h of abstinence. Specifically, both blood pressure and heart rate had significantly decreased, while anxious mood had significantly increased within 3 to 4 h of abstinence. Only depressed mood displayed a marginal increase during this time period, but this increase became significant by 18 h of abstinence. These results confirm the importance of evaluating early withdrawal, instead of employing the conventional practice of beginning to evaluate withdrawal after at least 24 h of abstinence (Hendricks et al., 2006; Hughes, 2007b).

The physiological and psychological symptoms of nicotine withdrawal that were measured in the current study accounted for approximately 72% of the variance in withdrawal intensity after 3.5 and 18 h of abstinence. These results suggest that heart rate, blood pressure, trait depression, depressed mood, and anxious mood in combination significantly contribute to an individual's subjective sense of withdrawal intensity. However, mood-related symptoms were much more strongly related to self-reported withdrawal intensity than physiological symptoms, which imply that it may be useful to focus more heavily on relieving anxiety and depression than physiological discomfort during withdrawal (although the latter should by no means be ignored).

Although depressed mood accounted for a significant proportion of the variance in withdrawal intensity in all conditions, an increase in depressed mood corresponded with an increase in withdrawal intensity only *before* anxious mood was included in the regression model. Anxious mood was the sole individual predictor of withdrawal intensity in the full regression model: as anxious mood increased, so did self-reported withdrawal intensity. These results emphasize the role of anxious and depressed mood in the intensity of the withdrawal syndrome, and therefore validate efforts to incorporate treatment for anxiety and depression in smoking cessation programs (e.g., Shiffman et al., 2000). Perhaps alleviating these symptoms can ameliorate the severity of withdrawal, and as a result reduce a smoker's likelihood of early relapse following an attempt to quit smoking. The present findings also suggest that anxious mood may be more strongly related to the subjective experience of withdrawal than depressed mood, and thus indicate that future research should focus on the relationship between anxiety and withdrawal, especially given that studies in this area remain sparse in comparison to studies on depression and withdrawal.

Contrary to initial expectations, the symptom structure of withdrawal did not significantly change as degree of abstinence increased. In other words, the influence of each symptom on nicotine withdrawal intensity did not fluctuate during the onset of the withdrawal syndrome even though individual symptoms demonstrated changes in their own intensity. For example, even though anxious mood significantly increased as length of abstinence increased, its effect on withdrawal intensity remained statistically equivalent across all levels of abstinence. The same was true of the other symptoms that were measured in the current study. This finding implies that treatment during the onset of nicotine withdrawal does not need to be any different than treatment during later stages of withdrawal. However, the present results need to be replicated before such firm conclusions can be made, as it is conceivable that the measures and time points employed in this study were not sensitive enough to detect more minute fluctuations in each symptom's contribution to withdrawal intensity. It is also possible that variables not included in the present analyses might be more likely to fluctuate in importance during the first 18 h of abstinence (e.g., craving).

Although attempts were made to employ rigorous scientific methodology, several factors should be considered when interpreting the results of the present study. First, the current results may be primarily generalizable to male heavy smokers, as 73% of the participants were male, and all were classified as heavy smokers. The small number of female participants in this study precluded gender analyses, but it is conceivable that males and females may demonstrate different patterns of early withdrawal, as might different types of smokers (e.g., social smokers). Second, a portion of our results may be attributable to shared method variance, as we assessed nicotine withdrawal intensity and mood with self-report measures (i.e., the withdrawal measure, POMS, and IDD). However, these measures have been used frequently and have demonstrated good reliability and validity in the smoking literature (e.g., Gilbert et al., 1998; Gilbert et al., 2002; Sommesse and Patterson, 1995). Third, items from the measures of anxious and depressed mood demonstrated some overlap with items on the nicotine withdrawal scale, which may have somewhat inflated the significance of our results. This overlap between withdrawal and negative affect is actually expected, since many withdrawal symptoms are related to negative affect. Therefore, we used a withdrawal measure that included a wide variety of items to capture multiple facets of the withdrawal syndrome, making it unlikely that our results were entirely due to item overlap. Finally, it should be noted that this study was designed to be the first in a series of studies, and therefore provides valuable information on which to build future research.

Future studies should address the concerns listed above by including equal numbers of male and female participants, and by examining patterns of early nicotine withdrawal across different types of smokers. Future research should also include multiple methods of measurement in assessing each construct of interest. For example, researchers might measure anxiety using both self-report and behavioral observations. It may also be helpful to include additional theoretically relevant predictors of withdrawal intensity, such as history of clinically significant anxiety

and depression, number of years as a smoker, gender, and so forth. Furthermore, future studies may want to assess early withdrawal at multiple points during the day (e.g., hourly) to gain a more fine-grained understanding of the progression of the withdrawal syndrome during this potentially critical period. Finally, results from the present study indicate that more research on the relationship between anxious mood and nicotine withdrawal is needed, such as research investigating the mechanisms by which anxious mood affects withdrawal intensity or the most effective treatments for anxious mood during smoking cessation.

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