

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

Holly E.R. Morrell<sup>a</sup>, Lee M. Cohen<sup>b,\*</sup>, Mustafa al'Absi<sup>c</sup>

<sup>a</sup> *University of California, San Francisco, United States*

<sup>b</sup> *Texas Tech University, United States*

<sup>c</sup> *University of Minnesota School of Medicine, United States*

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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).

\* Corresponding author. Texas Tech University, Psychology Department, P.O. Box 42051, Lubbock, TX 79409-2051, United States. Tel.: +1 806 742 3711x236.

E-mail address: [lee.cohen@ttu.edu](mailto:lee.cohen@ttu.edu) (L.M. Cohen).

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).

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