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A quantitative analysis of subjective, cognitive, and physiological manifestations of the acute tobacco abstinence syndrome

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ABSTRACT

Rationale: Previous studies have documented the *existence* of signs and symptoms of the acute tobacco abstinence syndrome; however, less attention has been paid to quantifying the magnitude of these effects.
Objective: The present study quantified the relative *magnitude* of subjective, cognitive, and physiological manifestations of acute tobacco abstinence.
Method: Smokers ($N = 203$, ≥ 15 cig/day) attended two counterbalanced laboratory sessions, one following 12-h of abstinence and the other following ad-lib smoking. At both sessions, they completed an extensive battery of self-report measures (withdrawal, affect, hunger, craving, subjective attentional bias towards smoking cues), physiological assessments (heart rate, blood pressure, brain EEG), and cognitive performance tasks (psychomotor processing, sustained attention, objective attentional bias).
Results: Abstinence effects were largest for craving, subjective attentional bias, negative affect, overall withdrawal severity, concentration difficulty, hunger, and heart rate. Effects were moderate for positive affect and EEG power. Effects were small, but reliable, for psychomotor speed, sustained attention, and somatic symptoms. Effects on performance-based indices of attentional bias towards smoking-related cues were small and reliable for some indices but not others. Effects were small and inconsistent for blood pressure and EEG frequency. Variation in internal consistency accounted for 33% of the variation in abstinence effect sizes across measures.
Conclusions: There was a wide range of effect sizes both across and within domains, indicating that the acute tobacco abstinence syndrome is not a monotonic phenomenon. These findings may be indicative of the relative magnitudes of signs and symptoms that the average smoker may exhibit during acute abstinence.

1. Introduction

The tobacco abstinence syndrome is considered an important component of tobacco addiction (Baker, Piper, McCarthy, Majeskie, & Fiore, 2004; Koob & Le Moal, 2001), comprising subjective, cognitive, and physiological changes that emerge upon the cessation of tobacco use. These changes cause distress and impairment, can potentially interfere with smoking cessation, and may underlie smoking behavior in smokers not wanting to quit (Hughes, 2006; Shiffman, West, & Gilbert, 2004). Accordingly, this syndrome has attracted considerable scientific and clinical interest.

Tobacco abstinence effects include *DSM-IV* nicotine withdrawal symptoms (APA, 1994), such as irritability, anxiety, restlessness, dysphoria, difficulty concentrating, increased appetite and/or weight gain, sleep disturbance, and decreased heart rate. Tobacco abstinence effects may also may include changes in other subjective states (e.g., cigarette craving, diminished positive affect; al'Absi, Amunrud, & Wittmers, 2002; Sayette, Martin, Wertz, Shiffman, & Perrott, 2001). Tobacco abstinence effects have also been assessed using objective measures, such as electroencephalographic (EEG) deactivation, cognitive performance decrements, and attentional bias towards smoking-related cues (Heishman, 1999; Pickworth, Herning, & Henningfield, 1989; Waters & Sayette, 2006; Dawkins, Powell, West, Powell, & Pickering, 2006). The origins of abstinence effects are multifaceted and may be caused by any or all of the following: (a) nicotine withdrawal (i.e., disruptions of psychobiological homeostasis caused by the removal of nicotine); (b) nicotine offset effects (i.e., dissipation of nicotine's acute pharmacological effects); (c) psychological factors (e.g., expectancies about the effects of abstaining, loss of sensorimotor stimulation); and (d) unmasking effects (e.g., the re-emergence of preexisting dispositions that were suppressed by tobacco use).

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Understanding the tobacco abstinence syndrome is important for several reasons. First, the abstinence syndrome may potentially play an important role in the cessation process (Piasecki, 2006). Treatments that attenuate abstinence effects are among the most effective smoking cessation interventions (USDHHS, 2008) and some studies have reported that the effects of efficacious treatments on smoking cessation outcomes are partially mediated by their influence on abstinence effects (e.g., Ferguson, Shiffman, & Gwaltney, 2006; Piper et al., 2008). Second, among individuals not attempting to quit, signs and symptoms that emerge following brief periods of abstinence (e.g., overnight, tobacco use restriction during work/social events) may maintain day-to-day smoking behavior (Chandra, Shiffman, Scharf, Dang, & Shadel, 2007). Finally, the tobacco abstinence syndrome causes a degree of distress and impairment that may be comparable to levels experienced by patients seeking psychiatric treatment (Hughes, 2006). Thus, the abstinence syndrome is worthy of therapeutic intervention to improve the short-term quality of life among abstinent smokers, irrespective of its influence on smoking outcome. Because it may be a primary target of clinical intervention, understanding the pattern of signs and symptoms of this syndrome is of critical importance.

Numerous studies have documented that statistically significant abstinence effects can be observed for a variety of subjective, cognitive, and physiological measures (for reviews see, Hughes, 2007a,b; Shiffman et al., 2004). Investigations have less frequently characterized the *magnitude* of abstinence effects. This is a notable gap in the literature as understanding the relative magnitudes of specific tobacco abstinence effects may be of use to clinicians and could guide future research into the intensity of abstinence effects. Given that research resources are often limited, data on which measures demonstrate the most robust abstinence effects could inform assessment selection strategies for future studies of tobacco abstinence effects. Research of the impact of candidate treatments or individual difference characteristics (e.g., personality, genetic variation) on the acute abstinence syndrome may be more likely to detect effects when using measures that typically exhibit the largest abstinence effects. In addition, identifying the features that demonstrate the greatest changes induced by abstinence may perhaps inform clinicians as to the typical symptoms that may require the most intensive intervention. It should be noted, however, that the generalization that symptoms with larger abstinence effects require more intensive intervention may not be applicable to certain features of questionable clinical relevance (e.g., abstinence-provoked reductions in heart rate are likely to be the result of nicotine offset effects not requiring treatment). Nonetheless, particular features within a common clinically-relevant domain that are most dramatically exacerbated during abstinence (e.g., anxiety vs. sadness) are likely to require more intensive treatment (to improve short-term quality of life or possibly attenuate relapse risk).

Additionally, extant studies have frequently examined abstinence effects after the first 24 h of abstinence and over the next several weeks (e.g., Hughes & Hatsukami, 1986; McCarthy, Piasecki, Fiore, & Baker, 2006; Piasecki, Jorenby, Smith, Fiore, & Baker, 2003; Shiffman et al., 2006). Relatively few investigations have focused on the first day of abstinence, which is important because a significant number of individuals lapse on their planned quit date (Brown et al., 1998), which could be a function of acute tobacco abstinence symptoms. In addition, acute (but not protracted) abstinence simulates experience in smokers not attempting to quit (e.g., symptoms experienced before the first cigarette of the day).

In the current study, we examined the relative magnitudes of acute smoking abstinence (≥12 h) effects across an extensive battery of subjective, cognitive, and physiological measures. We used a smoking deprivation manipulation,[1] which allowed us to capture the combined effect of pharmacological and non-pharmacological influences on tobacco abstinence. The relatively large sample ($N = 203$) provided adequate power to detect small effect sizes, and allowed us to generate relatively precise effect size estimates. Assessments were administered prospectively in both abstinent and non-abstinent states (order counterbalanced) to neutralize experimental confounds, such as order and practice effects and retrospective recall biases. The sample was comprised of individuals who were not attempting to quit smoking. This is important for understanding the processes that might maintain day-to-day smoking.

In two previous manuscripts, we examined individual difference factors that predict withdrawal effects (i.e., gender, temperament) in this sample (Leventhal, Waters, Boyd, Moolchan, Lerman, et al., 2007; Leventhal, Waters, Boyd, Moolchan, Heishman, et al., 2007). The current report is unique in that it examines effects in the entire sample to describe the relative intensity pattern of signs and symptoms of acute tobacco abstinence. Furthermore, this report describes abstinence effects on some measures not previously reported (e.g., visual dot probe task, EEG data at the electrode level) and scrutinizes internal consistency estimates of abstinence effects.

2. Method

2.1. Participants

Participants were 203 smokers from the Baltimore metropolitan area recruited via newspaper and radio advertisements. The sample was recruited to be balanced on gender (49.8% men, 50.2% women) and race (51.7% black, 48.3% white). On average, participants were 36.7 ($SD = 10.1$) years of age, smoked 22.2 cigarettes/day ($SD = 6.61$), scored 6.47 ($SD = 1.70$) on the Fagerström Test for Nicotine Dependence (FTND; Heatherton, Kozlowski, Frecker, & Fagerström, 1991), and smoked for 19.7 years ($SD = 10.3$). For inclusion in the study, participants had to: be 18 years or older; be a current smoker of at least 15 cigarettes per day; smoke for at least 2 years; smoke a brand of cigarettes that delivers at least 11.0 mg tar and 0.7 mg nicotine as rated by the Federal Trade Commission method; and have a score 3 or higher on the FTND. Participants were excluded if they reported a recent history of certain diseases, including myocardial infarction, angina, heart failure, hypertension, stroke, and diabetes; if they were treated with nicotine replacement products in the past 6 months, or with antidepressants in the past year; if they used any smoking cessation treatments in past 6 months; or if their estimated IQ on the Shipley Institute on Living Scale was less than 78 (Shipley, 1940). Women who were pregnant or nursing were also excluded. The study was approved by the institutional review board of the NIDA-Intramural Research Program.

A total of 858 participants completed the medical screening visit, 337 of whom met inclusion/exclusion criteria. Of these, 209 completed the orientation and two experimental sessions (i.e., abstinent and non-abstinent sessions); however, as noted below, 6 did not meet criteria for biochemical confirmation of smoking.

2.2. Procedure

Following a preliminary telephone screen, eligible participants were invited to attend an in-person medical screening session conducted at NIDA-Intramural Research Program [details on the screening procedure can be found in Leventhal, Waters, Boyd, Moolchan, Lerman, et al. (2007)]. Eligible participants attended a 90-min orientation session followed by two experimental sessions (one while abstinent and one while non-abstinent), lasting 60 min each. The three sessions occurred on different days. Participants were instructed to smoke normally before the first (orientation) session. During the orientation session, participants practiced the cognitive performance tasks for approximately 1 h, which included two 10-min

[1] The literature defines the term *deprivation* to signify experimenter-initiated discontinuation of drug use (Hughes, 2007b). Thus, we use the term *deprivation* to refer to this study's experimental manipulation. We use the term *abstinence* to refer to the psychobiological state induced by any form of tobacco use discontinuation (experimenter-initiated or subject-initiated).