

Cigarette Smoking: Attentional Mediation of Anxiety as a Predictor of Nicotine
Withdrawal Severity

by

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ABSTRACT

Although a majority of cigarette smokers report that they smoke to relieve anxiety, studies examining the anxiolytic properties of smoking have yielded equivocal results. Kassel and colleagues proposed that the anxiolytic effects of nicotine might be mediated by the presence or absence of distracting stimuli. More specifically, Kassel and Shiffman postulated that smoking “constrains smokers’ attention to the most immediate and salient stimuli in their environment—when such stimuli are available.” As a result, smokers are more likely to focus on immediate and distracting stimuli than more distal anxiogenic stimuli, thus reducing anxious mood. Further, smokers who rely more heavily on attentional mediation to relieve anxiety may experience more severe nicotine withdrawal, which may ultimately make it more difficult for them to quit smoking.

The current study was designed to assess the degree to which attentional mediation influences the experience of self-reported nicotine withdrawal severity in a sample of 21 adult heavy smokers. Participants completed the attentional mediation paradigm, as developed by Kassel and Shiffman, and then abstained from smoking for 24 hours. As expected, results indicated that anxiety and withdrawal symptoms increased during abstinence from smoking. However, the primary hypothesis was not supported: smokers who displayed greater reductions in anxiety in the presence of a distracting stimulus did not experience more severe nicotine withdrawal. These findings leave the relationship between anxiety and nicotine withdrawal open to speculation. Implications and directions for future research are discussed.

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CHAPTER 1

INTRODUCTION

Affect regulation theory states that individuals smoke cigarettes to relieve negative affective states, such as anxiety and depression (Carmody, 1992). Even though a majority of smokers report that they smoke to relieve anxiety (Schneider & Houston, 1970), research on the anxiolytic properties of nicotine has generated mixed results (see Morissette, Tull, Gulliver, Kamholtz, & Zimering, 2007). On one hand, a number of studies demonstrate that smoking relieves anxious mood in a variety of contexts. Specifically, Pomerleau, Turk, and Fertig (1982) found that smoking cigarettes significantly relieved anxious mood during an unsolvable anagram task and a cold pressor pain task. Jarvik, Caskey, Rose, Herskovic, and Sadeghpour (1989) sought to replicate and extend Pomerleau et al.'s results by investigating the anxiolytic effects of smoking during an anagram task, a cold pressor task, a white noise condition, and an auditory vigilance task, all of which have been shown to induce anxiety. Again, smoking relieved anxious mood in the anagram task and cold pressor tasks, although the latter effect was only marginally significant. Smoking, however, did not relieve anxious mood in response to white noise or the auditory vigilance task.

The connection between smoking and anxiety relief has also been tested in stressful social interactions. Gilbert and Spielberger (1987) manipulated smoking status among pairs of individuals who were instructed to discuss a topic on which they disagreed. Results from this study demonstrated that, in spite of overall increases in physiological arousal (e.g., heart rate), participants reported less anxiety when allowed to smoke. Gilbert, Robinson, Chamberlin, and Spielberger (1989) moved beyond the realm

of social interaction and examined the anxiety-reducing properties of smoking in response to a stressful movie. They instructed 40 smokers and 40 non-smokers to watch a movie about industrial accidents, which was intended to induce anxiety. Individuals who smoked high-nicotine cigarettes reported significantly smaller increases in anxiety during the movie than individuals in either the low-nicotine or control groups. In a more recent study, researchers examined the anxiolytic properties of smoking and chewing gum in response to a stressful speech task (Britt, Cohen, Collins, & Cohen, 2001). Smokers were told to prepare a speech about their body and physical appearance. Measurements of craving, withdrawal, and anxiety were taken at baseline, after speech preparation but before smoking or chewing gum, after smoking or chewing gum, after the speech itself, and after a 10-minute rest period. Analyses revealed that individuals in the smoking group experienced a significant decrease in anxiety over time, relative to the chewing gum group and a control group.

Although several studies confirm the anxiolytic effects of smoking, others indicate that smoking does not relieve anxiety. For example, Fleming and Lombardo (1987) tested the anxiolytic effects of smoking among 20 female smokers and 20 female non-smokers with a self-reported phobia for rats. The authors instructed participants to approach a large, white rat and rate their anxiety levels at five-foot intervals. Although approaching the rat produced significant increases in anxiety, neither participant smoking status nor being allowed to smoke influenced anxiety levels. Hatch, Bierner, & Fisher (1982) also found that smoking did not relieve anxious mood. They examined the anxiolytic properties of nicotine during a stressful speech task. Participants were randomly assigned to one of three groups: no-smoking, high-nicotine, and low-nicotine.

All participants were then given 10 minutes to mentally prepare a three-minute speech on abortion, after which they delivered the speech. Measures indicated that anxiety increased during the preparation and speech phases of the experiment; however, smoking did not alleviate this anxiety.

In order to reconcile the inconsistent findings in the literature regarding the anxiolytic properties of smoking, Kassel and Shiffman (1997) proposed that attentional processes may mediate the relationship between smoking and anxiety. Specifically, they postulated that smoking “constrains smokers’ attention to the most immediate and salient stimuli in their environment—when such stimuli are available” (p. 360; cf. attention-allocation model of alcohol reinforcement). As a result, smokers are more likely to focus on immediate and distracting stimuli than more distal anxiogenic stimuli, thus reducing anxious mood. Two studies to date have confirmed the hypothesis that smoking relieves anxious mood in minimally deprived smokers in the presence of a distractor, and that this effect cannot be attributed to the behavioral aspects of smoking or the nicotine withdrawal syndrome (Kassel & Shiffman, 1997; Kassel & Unrod, 2000). Only one study (Herbert, Foulds, & Fife-Shaw, 2001) has not supported the attentional mediation hypothesis, but the authors utilized a different anxiety-induction paradigm and tested non-deprived smokers. The latter difference may suggest that attentional mediation is a function of nicotine deprivation level, which in turn implies that there may be a relationship between the effects of attentional mediation and nicotine withdrawal.

Research indicates that approximately 50% of smokers who attempt to quit without pharmacological assistance experience nicotine withdrawal (APA, 1994), although estimates range from 21% (Hughes, Gust, & Pechacek, 1987) to 78% (Hughes

& Hatsukami, 1986). According to the Diagnostic and Statistical Manual of Mental Disorders-IV-Text Revision (DSM-IV-TR; APA, 2000), the nicotine withdrawal syndrome is characterized by the presence of four out of eight of the following symptoms within 24 hours of “abrupt cessation of nicotine use, or reduction in the amount of nicotine used” (p. 266): depressed mood, sleep disturbance, irritability, anxiety, difficulty concentrating, restlessness, decreased heart rate, and increased appetite or weight gain.

The nicotine withdrawal syndrome is often implicated in smoking relapse following a cessation attempt. Perhaps the oldest and most widely held theory (classic psychopharmacologic theory) is that the withdrawal syndrome itself causes relapse. Specifically, individuals resume smoking in order to avoid the physiological and psychological discomfort associated with nicotine withdrawal. Several recent studies have validated classic psychopharmacologic theory and, by extension, have confirmed the importance of understanding what factors may contribute to the nicotine withdrawal syndrome. Specifically, Piasecki and colleagues observed that withdrawal severity, greater symptom volatility, and increases in severity over time were associated with a higher likelihood of relapse (Piasecki et al., 2003a; 2003b; 2003c). The latter result supports earlier findings suggesting that individuals who experience an atypical withdrawal pattern are more likely to relapse (Piasecki et al., 1998; Piasecki et al., 2000).

Given that nicotine withdrawal is likely to predict relapse, it is important to understand what variables may affect the severity of the withdrawal syndrome. One such variable might be degree of attentional mediation. For example, those smokers who rely more heavily on attentional mediation to regulate their anxiety may be more dependent on nicotine, because they have repeatedly used smoking to cope with anxiety. During a

cessation attempt, such smokers might have more difficulty enduring withdrawal-induced anxiety, and therefore experience greater withdrawal severity than individuals who do not rely so heavily on smoking to reduce anxiety. Ultimately, and in accordance with affective regulation theory, these individuals may be more likely to relapse.

The current study was designed to examine the degree to which attentional mediation influences nicotine withdrawal severity. Specifically, each participant completed the standard Kassel-Shiffman attentional mediation paradigm (the non-deprivation phase) and a 24-hour period of abstinence from smoking (the deprivation phase), on two separate occasions. The Kassel-Shiffman attentional mediation paradigm consisted of a baseline period, followed by an anxiety induction task, and later by a distraction task. Participants completed measures of state anxiety, trait anxiety, depression, nicotine dependence, and nicotine withdrawal throughout the experiment. The degree to which attentional mediation influenced anxiety was used to predict nicotine withdrawal severity.

It was hypothesized that (1) the anxiety manipulation would significantly increase anxiety levels; (2) the distraction task would produce a decrease in anxiety levels; (3) withdrawal severity would increase relative to baseline after 24 hours of abstinence from smoking; (4) demographic characteristics such as number of cigarettes smoked per day, number of years as a smoker, and nicotine dependence levels would be positively correlated with withdrawal severity; (5) baseline trait anxiety levels would correlate positively with overall withdrawal severity, such that higher trait anxiety would be associated with more severe withdrawal symptoms; and (6) the degree of anxiety reduction during the non-deprivation phase would be directly related to overall

withdrawal severity following 24 hours of abstinence. Specifically, it was hypothesized that greater anxiety reduction in response to the distraction task would be associated with greater withdrawal severity.

CHAPTER 2

METHOD

Participants

Participants included adult heavy smokers over the age of 18. Based on previous literature, heavy smokers were defined as individuals who had smoked at least 16 cigarettes per day for the past six months, scored at least 4 on the Fagerström Test of Nicotine Dependence (FTND), and had a respiratory carbon monoxide level of at least 10 parts per million (ppm). Participants who reported being diagnosed with an anxiety disorder were excluded from the study, as current clinical anxiety may confound the results of the study.

Power analyses indicated that a sample size of at least 19 participants was needed to have an 80% chance of detecting a truly significant effect. Initially, participants included 25 students and members of the community from Lubbock, Texas and San Diego, California. Four participants did not complete the study, leaving a final sample of 21 individuals (23.8% female). Table 1 and Figures 1 through 3 show baseline descriptive statistics for individuals who did and did not complete the study. It appears that participants who dropped out of the study were younger, smoked fewer cigarettes per day, smoked for fewer total years, and smoked at least 16 cigarettes per day for fewer years than participants who completed the study. They were also less depressed, nicotine dependent, and anxious (both at the trait and state levels). In addition, attritors seemed to experience more withdrawal-like symptoms at baseline and exhibit an *increase* in anxiety following the distraction task. Due to the small number of attritors, there was not enough

statistical power to test differences between individuals who did and did not complete the study.

The final sample of 21 individuals had a mean age of 24 years. Participants primarily identified themselves as Caucasian (76.2%), followed by Hispanic (9.5%), Other (9.5%), and African American (4.8%). All participants reported that they were daily smokers, smoking an average of 19.5 cigarettes per day. At the time of the study, participants had smoked cigarettes for 6.9 years and had smoked at least 16 cigarettes per day for 5.5 years on average. The majority of participants stated that they only smoked cigarettes (71.4%). However, 19% reported that they smoked cigars and 9.5% reported that they used chewing tobacco or snuff in addition to smoking cigarettes. On average, participants reported a mean FTND score of 5.1. None of the participants reported being diagnosed or currently treated for an anxiety disorder. Please see Table 2 for a comprehensive display of sample characteristics.

It should be noted that approximately half ($n = 10$) of the participants were provided with monetary compensation for their participation. A power analysis indicated insufficient power to statistically examine any differences between paid and unpaid participants (there would only be a 19% chance of detecting a true significant difference). However, Table 3 comprises descriptive characteristics of both groups for comparison. Upon visual examination, there appear to be only a few differences between paid and unpaid participants. Specifically, unpaid participants may have experienced more withdrawal-like symptoms at baseline, as well as slightly higher levels of withdrawal symptoms, anxiety, and depression during abstinence. They may also have experienced somewhat less anxiety during the non-deprivation phase.

Materials

Nicotine Dependence. Nicotine dependence was measured using the Fagerström Test for Nicotine Dependence (FTND; Heatherton, Kozlowski, Frecker, & Fagerström, 1991), which is a brief self-report instrument designed to correlate with physiological measures of nicotine tolerance. The FTND 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. The FTND is one of the most frequently used measures of nicotine dependence, and other commonly used measures of the same construct do not display appreciably better psychometric properties (Burling & Burling, 2003; Colby et al., 2000; Etter et al., 1999). This measure demonstrates limited internal consistency because of the heterogeneity of items, with coefficient α s ranging from .61 to .72, and potentially limited content validity relative to DSM-IV criteria for nicotine dependence (Burling & Burling, 2003; Colby, Tiffany, Shiffman, & Niaura, 2000; Etter, Duc, & Perneger, 1999; Haddock, Lando, Klesges, Talcott, & Renaud, 1999; Heatherton et al., 1991; Kozlowski, Porter, Orleans, Pope, & Heatherton, 1994). However, the FTND typically displays good test-retest reliability ($r = .85$; Etter et al., 1999), concurrent validity, and predictive validity (e.g., Burling & Burling, 2003; Kozlowski et al., 1994).

Carbon Monoxide (CO) Level. A BreathCO monitor (model 2900, Vitalograph Inc.) was used to measure participants' level of respiratory carbon monoxide (CO). CO level was used to verify heavy smoking status at baseline and nicotine abstinence during the nicotine deprivation phase of the experiment. 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 hours; SRNT SBV, 2002), although some studies accept CO levels that do not exceed one-half of the baseline CO level (Niaura, 1999).

Nicotine Withdrawal. The Minnesota Nicotine Withdrawal Scale (MNWS; Hughes & Hatsukami, 1986; 2003) is an eight-item self-report measure of withdrawal symptoms. Participants rate the degree to which they experience each symptom on a scale from 0 (*none*) to 4 (*severe*). The items include the seven nicotine dependence criteria specified in the DSM-IV-TR (APA, 2000), plus one item assessing craving for a cigarette. The MNWS is one of the most frequently used measures of nicotine withdrawal, and demonstrates good reliability and validity. Its content has changed slightly over the years according to new empirical evidence and alterations in DSM criteria; therefore, the most current version (Hughes & Hatsukami, 2003) was used in the present study. The authors note that researchers use different rating scales depending on their needs (Hughes & Hatsukami, 2003). Therefore, an eight-point Likert scale (0 = *none* and 7 = *severe*) was used in the current study to increase the likelihood that the data would approach normality and be more appropriate for parametric analyses.

Anxiety. The State-Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, & Lushene, 1970) was used to assess both state and trait levels of anxiety. This self-report instrument comprises two 20-item forms, one measuring state anxiety and one measuring trait anxiety. Participants rate the degree to which each item reflects how they feel at the moment (state form) or in general (trait form) on a four-point Likert scale. Both forms of the STAI demonstrate good to excellent internal consistency (α s range from .86 to .95)

and adequate 30-day test-retest reliability (r_s range from .71 to .75) (Roemer, 2001). The trait form of the STAI demonstrates good convergent validity (i.e., it correlates significantly with other measures of anxiety), it discriminates between anxious and non-anxious samples, and it is sensitive to change in treatment (Roemer, 2001).

The STAI is also one of the most frequently used measures of anxiety in the smoking literature, particularly with regard to attentional mediation (Becoña, Vázquez, & Míguez, 2002; Dalack, Glassman, & Rivelli, 1995; Fleming & Lombardo, 1987; Gilbert et al., 1989; Hall, Muñoz, & Reus, 1994; Hall et al., 1998; Herbert et al., 2001; Jarvik et al., 1989; Juliano & Brandon, 2004; Kassel & Shiffman, 1997; Kassel & Unrod, 1997; Robinson et al., 1995; Takemura, Akenuma, Kikuchi, & Inaba, 1999; Tate, Pomerleau, & Pomerleau, 1993; West et al., 1997). It is a reliable measure of anxiety among different samples of smokers (Cronbach's α averages about .94 for the State Form and .89 for the trait form; Kassel & Shiffman, 1997; Kassel & Unrod, 2000), and using it allowed for a more accurate comparison to data collected by other researchers.

Depression. The CES-D was used to assess depressive symptomatology. It is a brief, structured self-report instrument that was originally designed to measure current symptom levels of depression in epidemiological studies. Respondents rate the frequency of 20 depressive symptoms on a scale from 0 to 3, with higher total scores reflecting higher levels of depressive symptomatology. These depressive symptoms were selected to reflect six domains: depressed mood, guilt and worthlessness, helplessness and hopelessness, psychomotor retardation, loss of appetite, and sleep disturbance. Radloff (1977) found that the CES-D had good internal consistency in community and inpatient psychiatric samples ($\alpha = .85$ and $.90$, respectively). She also found that test-retest

reliabilities ranged from .32 (one year) to .67 (four weeks), with higher reliabilities corresponding with shorter test-retest intervals. Results from the same study indicated that the CES-D was able to discriminate well between psychiatric inpatients and “normals,” with more inpatients scoring above 16 (the authors give no rationale for this particular cutoff point). Finally, the CES-D demonstrated moderate convergent validity, being significantly correlated with clinician ratings of severity ($r = .56$) and the Hamilton Rating Scale for Depression ($r = .44$ to $.69$).

The CES-D has also been used frequently among samples of smokers (Hall, Muñoz, Reus, & Sees, 1993; Killen et al., 1996; Kinnunen, Doherty, Militello, & Garvey, 1996; Koval, Pederson, Mills, McGrady, & Carvajal, 2000; Lerman, Audrain, et al., 1996; Lerman, Caporaso, et al., 1998; Naiura et al., 1999; Piasecki et al., 2000; Tercyak, Goldman, Smith, & Audrain, 2002; Whalen, Jamner, Henker, & Delfino, 2001; Windle & Windle, 2001). Several of these studies suggest that the CES-D demonstrates good internal consistency in both adolescent and adult samples (Cronbach's α ranges from .87 to .90; Lerman, Audrain, et al., 1996; Tercyak et al., 2002; Windle & Windle, 2001).

Procedure

Initial recruitment and screening. Participants were recruited in two ways. First, a smoking demographics form and the FTND were included in the Mass Survey of the Psychology 1300 Subject Pool at Texas Tech University in order to screen for eligible participants. A trained research assistant contacted those individuals who reported smoking 16 cigarettes per day or more for the past six months, had a score of 4 or higher on the FTND, and gave their consent to be contacted for research participation. The researcher explained the purpose of the current study to each individual over the phone,

and then invited him or her to participate. If the individual agreed to participate, he or she was scheduled for the first phase of the experiment. Second, flyers advertising the study were posted around the campuses of Texas Tech University and the University of California at San Diego, and in the community of Lubbock, TX. When potential participants called about the study, they were screened for number of cigarettes smoked per day, length of time smoking, and FTND score. As in the other recruitment procedure, the researcher explained the purpose of the current study to each individual over the phone, and then invited him or her to participate. If the individual agreed to participate, he or she was scheduled for the first phase of the experiment.

Initially, individuals were compensated for participation in one of two ways: (1) they received course credit if they were introductory psychology students, or (2) they were entered into a raffle with a chance to win one of three monetary prizes (two \$50 prizes and one \$75 prize) if they were not students *or* if they were students who had already earned all of their course research credits. Due to the fact that it was extremely difficult to recruit and retain participants, the final 10 participants collected were paid \$100 for successful completion of the study.

Non-deprivation phase. This phase comprised a replication of the attentional mediation paradigm developed by Kassel and Shiffman (1997). All participants were instructed to smoke one of their own cigarettes immediately before entering the laboratory to control for pre-study nicotine levels. After reading and signing an informed-consent agreement, participants' CO levels were measured by the researcher to confirm their smoking status. Next, participants completed a series of self-report baseline measures, including the FTND, MNWS, CES-D, and the state and trait forms of the STAI

(Time 1). Participants then watched a one-hour neutral topic documentary, followed by another anxiety assessment (Time 2). The purpose of asking participants to watch this film was to ensure that all who participated experienced the same period of nicotine deprivation prior to the experimental manipulation. Next, participants were instructed to smoke a cigarette, after which they were informed that in 10 minutes they would have to give a speech on what they liked and disliked about their bodies. Immediately following these instructions, participants rated their anxiety levels again (Time 3). Next, they completed a brief distraction task, followed by one last anxiety assessment (Time 4). During the distraction task, the participants viewed a series of art slides and answered the following four questions: “What do you think of the use of colors in this painting?”, “What do you like best about this painting?”, “What do you like least about this painting?”, and “Is this the kind of painting you would like to own yourself?” Following the last anxiety assessment, participants were informed that they did not have to give a speech, because they were “not in the speech-giving condition.”

Deprivation phase. During this phase, participants were asked to abstain from smoking for 24 hours before their next scheduled visit to the laboratory. According to the literature on nicotine withdrawal and the criteria given in the DSM-IV-TR (APA, 2000), participants should qualify for a diagnosis of nicotine withdrawal after 24 hours of abstinence. Upon arrival to the laboratory, CO measurements were taken to verify self-reported abstinence. If a participant’s CO level indicated that he or she had smoked within the last 24 hours, he or she was told that his or her CO levels were “too high to complete the experiment at this time,” and the researcher scheduled another visit to the laboratory following another 24 hours of abstinence. If a participant’s CO level was

within the appropriate range ($< 10\text{ppm}$ or 50% of his or her baseline CO level), then participants completed the MNWS, the CES-D, and the STAI (Time 5).

CHAPTER 3

RESULTS

Descriptive Statistics

Means and standard deviations were calculated for continuous variables and percentages were calculated for categorical variables. An examination of the descriptive statistics found in Table 4 reveals two minor problems. First, one participant smoked only 10 cigarettes per day, which is below the study cutoff of 16 cigarettes per day. Second, four participants had total FTND scores of 3 and one had a total FTND score of 2, which are below the study cutoff of 4. Unfortunately, these errors were discovered after the conclusion of the study because these participants were not run by the principal investigator. It is unlikely that these individuals created a problem, as all other participants smoked at least 16 cigarettes per day, including those with an FTND score under 4.

Table 4 also provides a summary of the reliability estimates, including Cronbach's α values and mean inter-item correlations (MIICs), for each measure used in the present study. Mean inter-item correlations above .3 were considered acceptable, adequate reliability was defined by a Cronbach's α value greater than .80, and excellent reliability was defined by a Cronbach's α value greater than .90 (Kline, 2005). The CES-D during the non-deprivation phase and the MNWS during both study phases demonstrated adequate reliability ($\alpha = .79$ to $.86$). All other measures demonstrated excellent reliability (α values ranged from $.90$ to $.96$), except for the FTND ($\alpha = .55$, MIIC = $.16$). The FTND's poor psychometric properties may be attributable to the fact that this scale includes a very small number of items (only 6), and estimates of reliability

are typically lower for measures with fewer items (Viswanathan, 2005). As a result, correlations between the FTND and other scales may be attenuated (Viswanathan, 2005).

Correlations

Bivariate correlations among baseline predictor variables and the primary outcome variable (withdrawal severity, defined as total MNWS score during the deprivation phase of the study) were conducted to assess for multicollinearity and to determine which variables would be useful covariates in later analyses (see Table 5). Of note, only two baseline variables were significantly correlated with withdrawal severity during the deprivation phase and therefore used as covariates in subsequent analyses: total withdrawal-like symptoms at baseline (MNWS total score at baseline; $r = .49, p < .03$) and trait anxiety (STAI – Trait Form total score; $r = .50, p < .03$). In other words, more severe withdrawal-like symptoms at baseline and higher levels of trait anxiety were associated with greater withdrawal severity after 24 hours of abstaining from smoking. These relationships are not surprising, given that (1) the same instrument was used to measure withdrawal-like symptoms during non-deprivation and withdrawal severity during deprivation; and (2) one of the hallmark features of nicotine withdrawal is anxiety, which is likely to be further elevated in individuals who already experience a heightened level of trait anxiety. Contrary to Hypothesis 4, no baseline demographic variables were correlated with the severity of nicotine withdrawal.

A high correlation between total number of years smoking and number of years smoking 16 or more cigarettes per day indicated a problem with multicollinearity between these two variables ($r = .98, p < .001$); however, this did not pose a problem, because these two variables were not needed for any additional analyses. Number of

cigarettes smoked per day was positively related to level of nicotine dependence (total FTND score; $r = .63, p < .001$) and negatively related to trait levels of anxiety ($r = -.52, p < .05$), such that smoking more cigarettes per day was associated with greater nicotine dependence and lower levels of trait anxiety. In support of Hypothesis 5, higher trait anxiety was associated with more severe withdrawal symptoms after 24 hours of abstinence from smoking ($r = .50, p < .05$). Higher trait anxiety was also associated with higher state anxiety (STAI – State Form total score; $r = .79, p < .001$), more severe depressed mood at baseline (CES-D total score; $r = .60, p < .01$), and more severe baseline withdrawal-like symptoms ($r = .60, p < .001$). More severe baseline withdrawal-like symptoms were related to higher state anxiety ($r = .55, p < .05$) and more severe depressed mood ($r = .60, p < .001$) at baseline, which suggests that the MNWS successfully tapped into state- and trait-level affective states. Finally, higher levels of baseline state anxiety were related to more severe baseline depressed mood ($r = .79, p < .001$).

Manipulation Checks

Analyses of covariance (ANCOVAs) were performed to test the hypotheses that the anxiety manipulation would produce an increase in anxiety (Hypothesis 1), that the distraction task would produce a decrease in anxiety (Hypothesis 2), and that withdrawal severity would increase following 24 hours of abstinence from smoking (Hypothesis 3). All three hypotheses were supported. An ANCOVA using baseline state anxiety as a covariate revealed that anxiety level significantly increased following the anxiety manipulation (the speech-giving task), $F(1,19) = 7.3, p < .05$. However, it is questionable whether this mean increase (from 33.8 to 35.5) can be considered clinically significant, as

it is merely a 1.7-point change ($SD = 6.8$) on a scale that ranges from 20 to 80 points. Another ANCOVA using baseline state anxiety as a covariate confirmed the hypothesis that anxiety would significantly decrease following the distraction task, $F(1,19) = 3.7, p < .05$. Again, it is debatable whether or not the anxiolytic effects of the distraction task were clinically meaningful, because the mean anxiety level only decreased from 35.5 to 33.1 (mean change = 2.4, $SD = 5.2$). Finally, withdrawal severity significantly increased from the non-deprivation phase ($M = 8.4$) to the deprivation phase ($M = 15.3$) of the study [$t(20) = -5.1, p < .001$].

Additional dependent-samples t-tests were performed to confirm expected changes in CO level, depressed mood, and state anxiety from baseline levels to deprivation levels. Respiratory CO levels significantly decreased from an average of 23.5ppm to an average of 5.1ppm, which corroborates participants' self-report of 24-hour abstinence from cigarettes [$t(20) = 11, p < .001$]. Depressed mood did not significantly change ($M_{\text{non-deprivation}} = 15$ and $M_{\text{deprivation}} = 17.5$), which is not surprising because the CES-D measures depressed mood within the past week and most participants completed the deprivation phase of the study within a few days of completing the non-deprivation phase [$t(20) = -1.3, p > .2$]. However, one should always be cautious when interpreting a statistical null result, given the probability of making a Type II error (i.e., missing a true significant difference). Last, state anxiety significantly increased from baseline ($M = 33.9$) to deprivation (46.8), $t(20) = -4.8, p < .001$.

Regression Analysis

A hierarchical linear regression analysis was used to test the hypothesis that attentional mediation would predict nicotine withdrawal severity after 24 hours of

abstinence from smoking (Hypothesis 6; Table 6). Prior to performing the regression analysis, the data were evaluated according to the assumptions of linear regression (linearity, homoscedasticity, normality of errors, and the absence of multicollinearity), and were screened for outliers and potential influential data points. An examination of bivariate correlations, scatterplots, normal probability plots, and histograms of standardized residuals indicated that there were no violations of the assumptions of linear regression. None of the variables exhibited problems with normality (i.e., values of the skewness index did not exceed 3.0 and values of the kurtosis index did not exceed 10.0; Kline, 2005). Studentized residuals, Cook's Distance values, and leverage values were used to identify outliers that might unduly influence the position of the regression line. Three data points appeared to be potential outliers. These outliers were not deleted from subsequent analyses because the three indicators of outlier status and leverage did not consistently show that they exerted undue influence on the position of the regression line. Furthermore, it was decided that deleting these cases would not justify the reduction in statistical power associated with a smaller sample size.

Two covariates, baseline withdrawal severity and trait anxiety, were entered as the first step in the regression model. Attentional mediation, as defined by the difference between state anxiety after the anxiety manipulation and state anxiety after the distraction task, was entered as the second step in the model. Taken together, the covariates predicated a significant amount of the variance in withdrawal severity ($R^2 = .30, p < .05$); however, neither variable was a significant individual predictor of withdrawal severity. Contrary to Hypothesis 6, attentional mediation of anxiety did not explain a significant proportion of the variance in withdrawal severity above and beyond baseline withdrawal

severity and trait anxiety, $\Delta R^2 = .006$ and $\beta = .08, p > .7$. Further, a simple linear regression analysis indicated that attentional mediation alone did not predict withdrawal severity, $\beta = -.07, p > .7$.

CHAPTER 4

DISCUSSION

Four of the six study hypotheses were supported. First, consistent with Hypotheses 1 and 2, the speech-giving task significantly increased and the distraction task decreased self-reported levels of anxiety. As noted previously, these changes in anxiety were small and therefore may not have been clinically meaningful, even though they were statistically significant. Additionally, consistent with Hypothesis 3, withdrawal severity increased after 24 hours of abstinence from smoking. Finally, consistent with Hypothesis 5, higher trait anxiety was significantly correlated with more severe withdrawal symptoms.

Contrary to expectations, demographic characteristics such as number of cigarettes smoked per day, number of years as a smoker, and nicotine dependence levels were not significantly correlated with withdrawal severity (Hypothesis 4). There are two possible reasons for this. First, there may not have been enough statistical power to detect truly significant correlations. The greatest *a priori* concern appeared to be the probability of making a Type I error (finding a significant difference that is not really there) because of the large number of planned correlations. However, the fact that the correlations in question were all relatively high without reaching statistical significance ($r = -.36, .15,$ and $.22$, respectively) suggested that Type II error may have been the more serious problem. Post hoc power analyses confirmed this suspicion: the chances of detecting a correlation that was significantly different from zero ranged from only 9% to 37% in the present sample. It is likely that these correlations would be significant with a larger

sample size. Second, the poor reliability of the FTND may have attenuated the correlation between nicotine dependence and withdrawal severity.

It should also be noted that the relationship between number of cigarettes per day and withdrawal severity was *not* in the expected direction: individuals who smoked fewer cigarettes per day reported experiencing more severe nicotine withdrawal. It is possible that number of cigarettes per day is not the best indicator of nicotine dependence, which is assumed to correlate positively with withdrawal severity. Given that different types and brands of cigarettes have different levels of nicotine, smoking one cigarette may be equivalent to smoking three or more cigarettes in some cases. Therefore, it would be useful to ask participants in future studies what type of cigarettes that they smoke. It is also possible that individuals who smoke fewer cigarettes have a harder time giving up the cigarettes that they smoke even more so than heavier smokers. Anecdotally, when smokers who wish to quit systematically reduce the number of cigarettes they smoke, often times this is fairly easy task during the initial stages of this process. Reportedly, the reason for this is that the individual realizes that many of the cigarettes they smoke daily are “not necessary.” It is when these individuals have reduced to only the “necessary” cigarettes that this task becomes more difficult.

Another potential explanation is that participants who smoke more cigarettes per day experience less withdrawal than those who smoke fewer cigarettes per day because the former still have higher levels of nicotine in their bloodstream after 24 hours of abstinence. This explanation may be viable; however, studies indicate that it takes approximately 72 to 96 hours for nicotine to leave the bloodstream completely. All smokers were experiencing nicotine withdrawal at 24 hours of abstinence, but it is likely

that all of them still had nicotine in their bloodstream, regardless of how many cigarettes they smoked per day.

The results of the present study also did not support the primary hypothesis that attentional mediation would predict nicotine withdrawal severity after 24 hours of abstinence from smoking cigarettes (Hypothesis 6). One explanation for this finding is that the anxiety-induction task did not produce a large enough increase in anxiety for attentional mediation to be accurately assessed. In other words, a floor effect in the measurement of the change in anxiety may have impaired the ability to measure attentional mediation. Perhaps we see this floor effect because the speech-giving task was not truly effective in increasing anxiety: it produced a statistically significant, but not clinically relevant, rise in anxiety. In previous research, this task has been shown to be very effective at inducing anxiety (Britt et al., 2001; Kassel & Shiffman, 1997; Kassel & Unrod, 2000), but it is possible in this study that research personnel were not convincing in their attempt to make participants believe that they would have to give a speech, or that the research setting itself was too comfortable and non-threatening for participants to feel anxious. In future studies, it would be useful at the end of the study to assess the degree to which participants believed that they would have to give a speech.

It is difficult to attribute the current results to poor abstinence among the participants, as their self-reported abstinence was physiologically verified by respiratory CO levels. Furthermore, participants' abstinence was corroborated by their statistically and clinically significant elevations in withdrawal severity and anxiety during the deprivation phase. It is also unlikely that the non-significant findings are due to a lack of statistical power. Power analyses for the multiple regression analysis indicated that with

21 participants and three predictor variables, there was a 95% chance of detecting a truly significant relationship. Others might argue that the STAI is not the best measure to assess attentional mediation; however, it is the same instrument that was used successfully in the original attentional mediation paradigm (Kassel & Shiffman, 1997; Kassel & Unrod, 2000). Perhaps the MNWS was not a comprehensive enough measure of withdrawal severity, given that it only includes eight items. In the future, researchers may benefit from using multiple measures of the withdrawal construct to avoid mono-operational bias.

It is of course possible that attentional mediation really does not influence withdrawal severity. Replication of the current results is warranted before this explanation can be accepted with confidence. Alternately, it may be that attentional mediation in real-world situations is more strongly predictive of withdrawal severity. Specifically, attentional mediation of anxiety in response to a laboratory stressor may be less salient than in response to personal life-stressors, especially given that the latter are repeatedly associated with smoking over time. Furthermore, it is the real-life stressors that smokers will have to face without the benefit of nicotine when they try to quit smoking. It would be informative to observe attentional mediation in real time as part of an ecological momentary assessment study, perhaps by instructing participants to engage in a specific distraction task each time they feel anxious, and to report their anxiety level before and after the distraction task using a palm pilot.

It is also feasible that the degree to which participants needed, but were unable to, utilize attentional mediation in response to daily stressors during their 24 hours of abstinence affected the relationship between attentional mediation and withdrawal

severity. If participants did not encounter enough anxiety-provoking stressors during abstinence, they may not have needed to use attentional mediation to reduce anxiety. Such an effect might attenuate any relationship between attentional mediation and withdrawal severity. In the future, it would be helpful to ask participants to list the stressors that they experienced during abstinence.

Yet another explanation for the lack of association between attentional mediation and nicotine withdrawal is that distraction may be most effective *while* individuals are actually smoking. This makes sense, given that smoking often serves as a “time out,” wherein smokers remove themselves from a distressing situation for at least a short period of time while they are smoking. When smokers no longer have this option to relieve their anxiety during a quit attempt, their withdrawal severity may be subjectively worse. To test this hypothesis in future studies, attentional medication should be measured when participants are permitted to smoke and complete the distraction task at the same time. It would also be useful to test different types of distraction tasks, particularly ones that smokers commonly employ in their everyday lives. Finally, the current study did not examine the degree to which distractors reduce anxiety in smokers in the absence of nicotine. Future research should investigate any interaction between level of nicotine in the body and type of distractor to determine which distractors might be most effective at reducing anxiety in abstinent smokers.

Although the mechanism by which smoking cigarettes relieves anxiety remains unknown, the results of the present study confirm that anxiety is an important correlate of the nicotine withdrawal syndrome. Specifically, our findings show that both anxiety and withdrawal severity increased after 24 hours of abstinence from nicotine, and that higher

levels of trait anxiety were significantly associated with greater withdrawal severity. Thus, the current study corroborates previous research findings that implicate anxiety reduction as a potentially important component of smoking cessation treatment (Abrams et al., 2003). Indeed, several studies show that anxious smokers are less likely to successfully quit smoking than non-anxious smokers (Ames et al., 2005; Covey, 1999; Becoña, Vázquez, & Míguez, 2002; Takemura, Akanuma, Kikuchi, & Inaba, 1999; Zvolensky, Lejuez, Kahler, & Brown, 2004).

The most appropriate method of relieving anxiety in smokers is not yet clear, and may vary depending on the individual and the source of anxiety. Pharmacological treatment of anxiety may be an effective adjunct to smoking cessation, especially among individuals with a clinically diagnosable anxiety disorder. In addition, standard cognitive-behavioral strategies such as self-monitoring to identify triggers of anxious mood, relaxation training, and coping skills training are likely to be viable treatment options. It is not always feasible in the “real world,” however, to provide a full course of cognitive-behavioral therapy as part of a smoking cessation program. Many smokers’ main resource for smoking cessation is their primary care physician, who does not necessarily have the time or the training for a comprehensive intervention. However, research indicates that routine screening and brief counseling (< 3min.) within emergency rooms increases long-term abstinence rates from 3% (usual care) to 8-11% (Berstein & Becker, 2002). Smoking researchers may be able to improve primary care providers’ effectiveness by developing empirically validated screening questions and brief tailored interventions (e.g., pamphlets emphasizing self-monitoring and outlining coping skills) that target negative affective states such as anxiety.

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Table 1

Baseline Characteristics of Participants who Completed the Study (n = 21) versus Dropouts (n = 4)

	Completed (<i>SD</i>)	Dropped Out (<i>SD</i>)
Age	24.0 (7.4)	20.5 (1.3)
Cigarettes per day	19.5 (4.0)	17.5 (5.0)
Total years smoked	6.9 (7.0)	1.3 (1.2)
Years smoked at least 16 cigarettes per day	5.5 (6.2)	0.7 (.9)
CES-D (Nondeprivation Phase)	20.9 (7.3)	17.3 (3.8)
CO level (Deprivation Phase)	23.5 (8.2)	14.8 (4.2)
FTND	5.1 (1.8)	4.0 (0.8)
MNWS (Nondeprivation Phase)	8.4 (5.8)	10.0 (1.8)
STAI - State Form (Time 1)	33.9 (11.6)	30.0 (10.0)
STAI - State Form (Time 2)	33.8 (8.7)	27.0 (2.0)
STAI - State Form (Time 3)	35.5 (13.1)	34.0 (11.8)
STAI - State Form (Time 4)	33.1 (10.1)	35.7 (13.8)
STAI - Trait Form	39.5 (10.7)	34.7 (8.6)

Note. Time 1 = baseline, Time 2 = after watching documentary, Time 3 = after anxiety induction task, Time 4 = after distraction task, Time 5 = after 24 hours of abstinence from smoking.

Table 2

Demographic Characteristics of Study Sample (N = 21)

	Mean	SD	Range	Skewness	Kurtosis
Age	24.0	7.4	19 - 45	2.2	4.5
Cigarettes per day	19.5	4.0	10 - 30	0.4	2.8
Total years smoked	6.9	7.0	1 - 25	2.2	4.9
Years smoked at least 16 cigarettes per day	5.5	6.2	0.5 - 25	2.3	5.0

Table 3

Mean Sample Characteristics for Paid (n = 10) and Unpaid Participants (n = 11)

	Paid (SD)	Unpaid (SD)
Age	23.1 (8.0)	24.9 (7.1)
Cigarettes per day	19.6 (2.4)	19.4 (5.1)
Total years smoked	6.9 (8.2)	7.0 (6.2)
Years smoked at least 16 cigarettes per day	5.2 (7.2)	5.6 (5.6)
CES-D (Nondeprivation Phase)	14.4 (8.9)	15.6 (6.2)
CO level (Nondeprivation Phase)	22.8 (7.8)	24.1 (8.9)
CO level (Deprivation Phase)	5.2 (2.5)	5.0 (4.0)
FTND	5.5 (2.1)	4.7 (1.6)
MNWS (Nondeprivation Phase)	7.9 (5.8)	8.9 (6.1)

Table 3 Continued

Mean Sample Characteristics for Paid (n = 10) and Unpaid Participants (n = 11)

	Paid (<i>SD</i>)	Unpaid (<i>SD</i>)
MNWS (Deprivation Phase)	13.3 (6.5)	17.2 (6.0)
STAI - State Form (Time 1)	36.3 (12.0)	31.6 (11.4)
STAI - State Form (Time 2)	36.7 (9.2)	31.1 (7.7)
STAI - State Form (Time 3)	39.3 (13.9)	32.0 (11.9)
STAI - State Form (Time 4)	37.8 (9.5)	29.0 (9.0)
STAI - State Form (Time 5)	46.0 (13.7)	47.5 (15.2)
STAI - Trait Form	39.8 (10.5)	39.2 (11.8)

Note. Time 1 = baseline, Time 2 = after watching documentary, Time 3 = after anxiety induction task, Time 4 = after distraction task, Time 5 = after 24 hours of abstinence from smoking.

Table 4

Descriptive Statistics and Reliability Estimates for Testing Instruments

Testing Instrument	Mean	<i>SD</i>	Minimum	Maximum	Skewness	Kurtosis	MIIC	α
CES-D (Nondeprivation Phase)	20.9	7.3	12.0	39.0	1.3	1.7	0.26	0.86
CES-D (Deprivation Phase)	25.1	9.3	13.0	51.0	1.3	2.1	0.33	0.90
FTND	5.1	1.8	2.0	8.0	0.1	-1.3	0.16	0.55
MNWS (Nondeprivation Phase)	8.4	5.8	0.0	18.0	0.2	-1.4	0.34	0.79
MNWS (Deprivation Phase)	15.3	6.4	1.0	27.0	-0.3	0.0	0.39	0.82
STAI - Trait Form	39.5	10.7	25.0	68.0	0.9	0.1	0.37	0.92
STAI - State Form (Time 1)	33.9	11.6	20.0	59.0	0.8	0.1	0.52	0.95
STAI - State Form (Time 2)	33.8	8.7	20.0	51.0	0.5	-0.6	0.30	0.91

Table 4 Continued

Descriptive Statistics and Reliability Estimates for Testing Instruments

Testing Instrument	Mean	<i>SD</i>	Minimum	Maximum	Skewness	Kurtosis	MIIC	α
STAI - State Form (Time 3)	35.5	13.1	20.0	66.0	0.7	-0.2	0.55	0.96
STAI - State Form (Time 4)	33.1	10.1	20.0	52.0	0.2	-1.5	0.41	0.93
STAI - State Form (Time 5)	46.8	14.2	25.0	72.0	0.0	-1.0	0.54	0.96

Note. MIIC = mean inter-item correlation, α = Cronbach's alpha, Time 1 = baseline, Time 2 = after watching documentary, Time 3 = after anxiety induction task, Time 4 = after distraction task, Time 5 = after 24 hours of abstinence from smoking.

Table 5

Bivariate Correlations among Baseline Indicators and Primary Outcome Variable (MNWS)

	1	2	3	4	5	6	7	8	9	10
1. Cigarettes per day	1									
2. Total years smoked	0.15	1								
3. Years smoked at least 16 cpd	0.10	0.98**	1							
4. CES-D (Nondeprivation Phase)	-0.34	-0.09	-0.05	1						
5. CO level (Nondeprivation Phase)	0.63**	-0.02	-0.08	-0.02	1					
6. FTND	0.22	0.10	0.06	-0.31	0.17	1				
7. MNWS (Nondeprivation Phase)	-0.21	0.01	0.01	0.60**	-0.04	-0.28	1			
8. STAI - State Form (Time 1)	-0.36	-0.15	-0.12	-0.79**	0.01	-0.24	0.55*	1		
9. STAI - Trait Form	-0.52*	-0.29	-0.24	0.60**	-0.12	-0.15	0.60**	0.79**	1	
10. MNWS (Deprivation Phase)	-0.36	-0.13	-0.14	0.21	-0.09	-0.21	0.49*	0.18	0.50*	1

Note. cpd = cigarettes per day. * $p < .05$. ** $p < .01$.

Table 6

Results of Regression Analysis Predicting Nicotine Withdrawal Severity After 24 hours of Abstinence from Smoking

Step	Predictor Variables	β	p	ΔR^2	F	p
1	State Anxiety	0.32	ns			
	Baseline Withdrawal Symptoms	0.29	ns	0.30	3.90	< .05
2	State Anxiety	0.36	ns			
	Baseline Withdrawal Symptoms	0.27	ns			
	Attentional Mediation	0.08	ns	0.01	0.14	ns

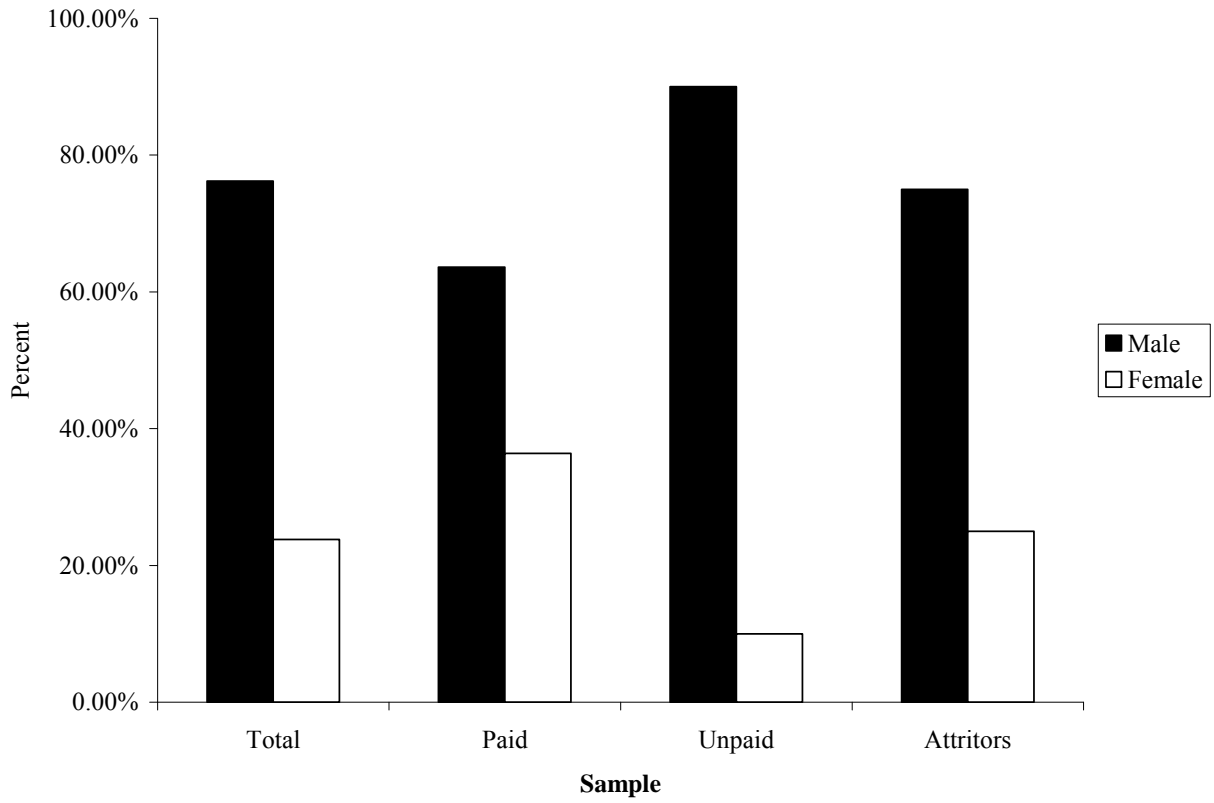
Note. ns = non-significant, β = the regression coefficient, ΔR^2 = the change in variance accounted for by the regression model, F = the F statistic, and p = probability value.

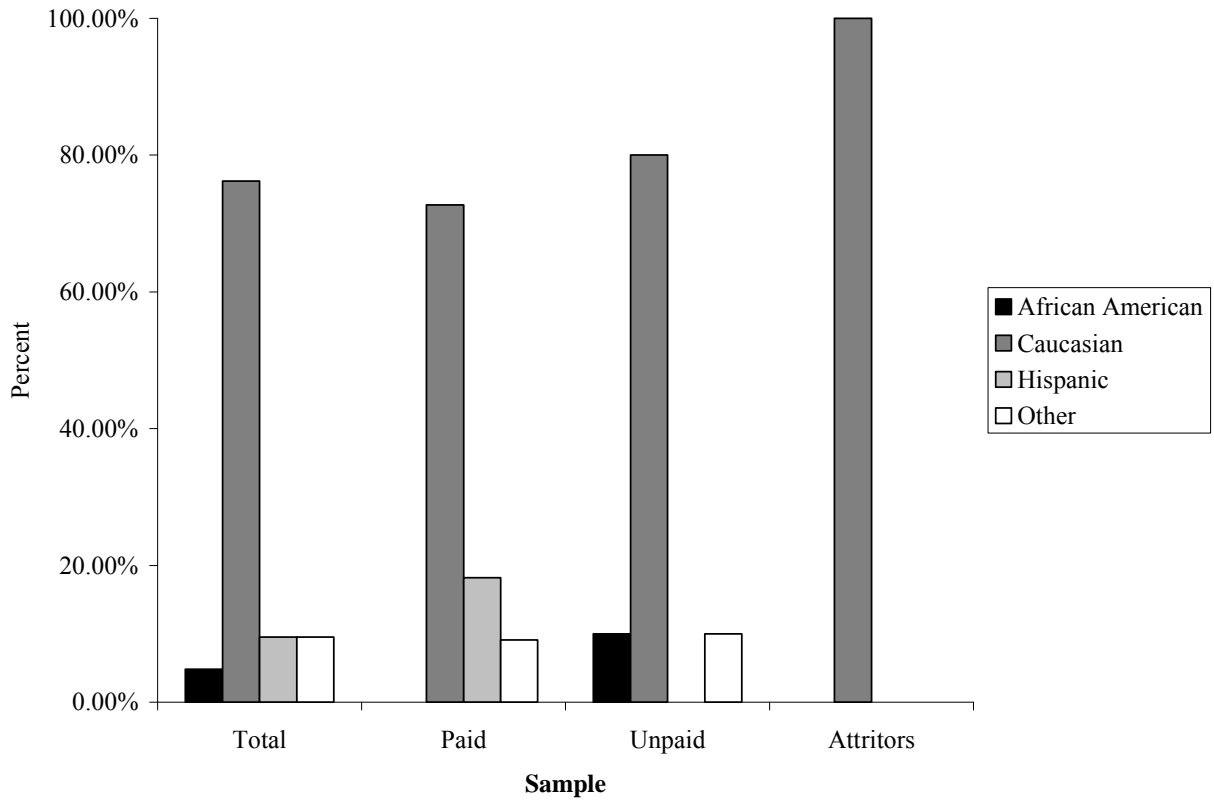
Figure Captions

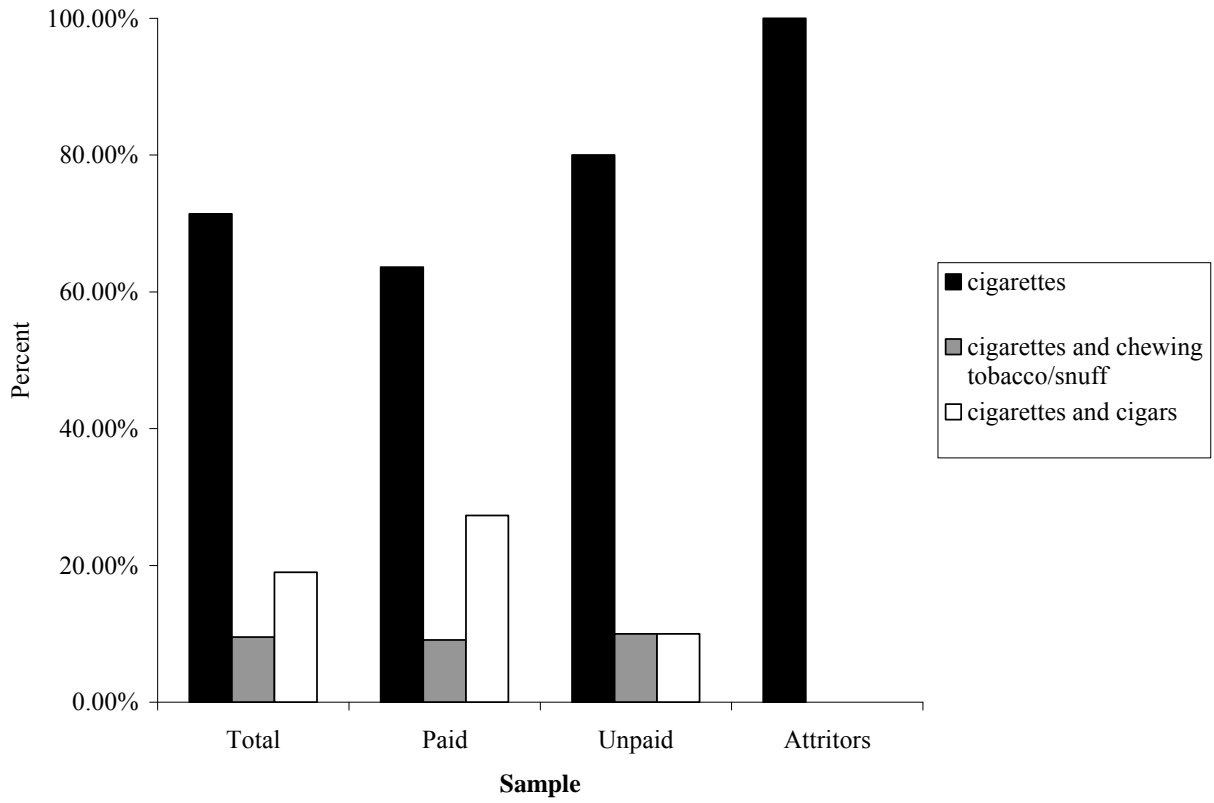
Figure 1. Percentage of male and female participants according to sample.

Figure 2. Ethnicity of participants according to sample.

Figure 3. Types of nicotine-containing products used by participants, according to sample.







APPENDIX

EXTENDED LITERATURE REVIEW

Introduction

Cigarette smoking is considered to be the leading preventable cause of death in the United States (Centers for Disease Control and Prevention [CDC], 2002). It is associated with a number of diseases, including asthma, chronic bronchitis, lung cancer, coronary heart disease, and emphysema, and data suggest that it is responsible for about 438,000 deaths per year (CDC, 2005a; National Institute on Drug Abuse, 2001). Recent statistics indicate that approximately 20.9% of the United States population currently smokes cigarettes (CDC, 2005b). This percentage represents a marked decline in smoking since the 1950s (CDC, 2005c). Nevertheless, cigarette smoking remains a serious public health concern, accounting for an estimated 75.5 billion dollars in health costs and 92 billion dollars in productivity costs per year (CDC, 2005a). Given the serious health-related and economic consequences of cigarette smoking, it is important to understand how and why people quit smoking in the interest of developing effective smoking cessation programs.

The harsh personal and economic costs related to smoking have prompted a significant amount of research over the past 30 years focused on understanding the addictive nature of cigarette smoking in the hopes that new information might help health care professionals to improve smoking prevention and cessation programs.

Although approximately 35% of smokers attempt to quit smoking each year, less than 5% are successful (American Psychiatric Association [APA], 2000). The majority of researchers agree that one of the primary obstacles to successful smoking cessation is nicotine withdrawal (Kassel, Stroud, & Paronis, 2003; Niaura et al., 1999; Robinson et al., 1995; West, 1984). The

advent of Nicotine Replacement Therapy (e.g., nicotine gum, the nicotine patch, etc.) has helped many people deal with withdrawal, and cigarette smoking has steadily decreased in the general population (Hughes, 1993; Office on Smoking and Health, 2002). However, smoking rates remain high among individuals with particularly compelling needs for nicotine, such as the regulation of anxiety and/or anxious mood (L. M. Cohen, personal communication, July 28, 2004; Cohen, McCarthy, Brown, & Myers, 2002; Gilbert & Wesler, 1989; Hall, Muñoz, Reus, & Sees, 1993; Russell, Peto, & Patel, 1974; Warburton, Revell, & Thompson, 1991). This in turn implies that a thorough understanding of the mechanisms underlying the connection between smoking and anxious mood may aid researchers and practitioners in developing more successful smoking prevention and cessation programs.

The Nicotine Withdrawal Syndrome

Definition. According to the Diagnostic and Statistical Manual of Mental Disorders-IV-Text Revision (DSM-IV-TR; APA, 2000), the nicotine withdrawal syndrome is characterized by the presence of four out of eight of the following withdrawal symptoms within 24 hours of “abrupt cessation of nicotine use, or reduction in the amount of nicotine used” (p. 266): depressed mood, sleep disturbance, irritability, anxiety, difficulty concentrating, restlessness, decreased heart rate, and increased appetite or weight gain. Research indicates that approximately 50% of smokers who attempt to quit without pharmacological assistance experience nicotine withdrawal (APA, 1994), although estimates range from 21% (Hughes, Gust, & Pechacek, 1987) to 78% (Hughes & Hatsukami, 1986).

Measurement. The nicotine withdrawal can be measured with a wide variety of instruments whose structures range from visual analog scales to Likert scales. The two most common measures appear to be the Minnesota Withdrawal Scale (MWS; Hughes & Hatsukami,

1986) and the Shiffman-Jarvik Withdrawal Scale (SJWS; Shiffman & Jarvik, 1976). Other scales, such as the Wisconsin Smoking Withdrawal Scale (Welsh et al., 1999), have not been as extensively used or as thoroughly investigated, which casts doubt on their psychometric properties. The SJWS contains symptoms that are no longer considered among the criteria for nicotine withdrawal, and it was developed using an inappropriate application of factor analysis. Therefore, the validity of this measure is suspect. The MWS demonstrates good reliability and validity in a number of samples, but it is also imperfect. Specifically, the form of the MWS has changed over time to mirror changes in the DSM. In addition, researchers have taken great liberty in selecting which items from the MWS they will use, and they have used a multitude of rating scales. For example, the original MWS utilized a 5-point Likert scale, but more recent studies sometimes use an 8-point or 10-point scale. The authors of the scale themselves recommend that researchers use whichever scale best suits their purposes (Hughes & Hatsukami, 2003). As a result of these discrepancies, any observed psychometric properties of the MWS are unlikely to generalize across studies. However, as the most frequently used measure of withdrawal, it is the most accepted measure among tobacco researchers today. In a review of existing withdrawal measures, the Society for Research on Nicotine and Tobacco Work Group on the Assessment of Craving and Withdrawal in Clinical Trials concluded that they could not recommend one measure above all others. Rather, they stated that researchers should use “published and validated measures as far as possible” (Shiffman, West, & Gilbert, 2004).

Symptoms of Nicotine Withdrawal. Multiple studies have confirmed the validity of nicotine withdrawal symptoms, as outlined in the DSM. In one of the earliest comprehensive studies of the withdrawal syndrome, Hughes and Hatsukami (1986) measured craving for tobacco, anxiety, restlessness, headaches, drowsiness, difficulty concentrating, irritability, and

gastrointestinal (GI) disturbances in 50 smokers across four days of abstinence. Although Hughes and Hatsukami assessed the withdrawal syndrome as defined in the DSM-III (APA, 1980), their results validate the current definition of the withdrawal syndrome. Specifically, they found that several symptoms included in the definition of withdrawal at the time increased within approximately 24 hours of abstinence, including craving, difficulty concentrating, anxiety, and restlessness. Additionally, they found that heart rate decreased, but both sleep disturbance and appetite increased (these symptoms were later added to the DSM-IV). Symptoms later excluded from the DSM criteria, such as headache, GI disturbance, and drowsiness, showed no change from baseline to abstinence. It should be noted that these symptoms were consistently observed across self-report measures, behavioral observations, and physiological measures. Despite the strength of these results, several limitations are apparent: (1) 18 of the participants did not completely abstain from smoking, (2) depressed mood was not evaluated, and (3) withdrawal was only assessed across four days, leaving the more long-term effects of smoking cessation unexplored.

Hughes, Gust, Skoog, Keenan, and Fenwick (1991) examined several DSM-III-R (APA, 1987) withdrawal symptoms (craving, irritability, increased appetite/weight gain, restlessness, anxiety, and difficulty concentrating) across 6 months of abstinence using a larger sample size than prior studies. Their results confirmed previous findings, as DSM-III-R symptoms such as anger, impatience, insomnia, and physical complaints (excluding headache) increased within the first week of abstinence. Furthermore, increases in anger, restlessness, impatience, and anxiety were confirmed by independent observers. However, as in Hughes and Hatsukami's (1986) study, not all smokers maintained abstinence for the entire 6 months. On one hand, those who relapse can provide valuable information on the characteristics of successful quitters versus those

who relapse; on the other hand, such attrition limits the sample size and therefore the power of long-term withdrawal analyses. Other limitations of this study include selection bias (participants volunteered to receive free samples of nicotine gum), lack of control groups, lack of physiological measures of withdrawal (e.g., heart rate), and again, the fact that depressed mood was not assessed (even though the authors admitted that this might be a valid symptom of withdrawal).

Hughes (1992) obtained nearly identical results to those described above in a large sample of self-quitters across 2, 7, 14, 30, and 180 days of abstinence. Specifically, his results again validated anxiety, hunger, irritability, restlessness, weight gain, difficulty concentrating, and a decrease in heart rate as symptoms of nicotine withdrawal; however, craving did not increase with abstinence. In addition, Hughes examined depression and found that, while depressed mood did not increase from pre-cessation to post-cessation, it did predict the likelihood of relapse.

As mentioned previously, smokers who attempt to quit smoking often gain weight (Glauser, Glauser, Reidenberg, Rusy, & Tallarida, 1970). Williamson et al. (1991) analyzed data from a 13-year national longitudinal study, and found that male sustained quitters gained 2.8 kg and female sustained quitters gained 3.8 kg on average over the course of the study. This gain was apparent after adjusting for age, race, alcohol use, education level, baseline weight, level of physical activity, and illnesses related to a change in weight. Furthermore, 13.4% of women experienced major weight gain (i.e., more than 13 kg), as compared to 9.8% of men.

One explanation for weight gain following smoking cessation is that nicotine withdrawal increases appetite or hunger. In particular, withdrawal-induced increases in appetite or hunger may precipitate an increase in caloric intake, which in turn may contribute to weight gain.

Gilbert and Pope (1982) observed that smokers ate significantly more snacks during a 24-hour deprivation period than a 24-hour period of ad lib smoking. Males consumed 50% more calories and females consumed 94% more calories in snacks during abstinence, which may explain the fact that other studies have found that women tend to gain more weight than men following smoking cessation (cf. Williamson et al., 1991). Interestingly, both men and women decreased their caloric intake during regular meals by approximately 8%. Additionally, Hughes, Hatsukami, Pickens, & Svikis (1984) found a significant increase in caloric intake across two 96-hour periods of abstinence that were each preceded by two 48-hour periods of ad lib smoking. Although this study only included three participants, its strength lies in the fact that it was an ABAB within-subject design that produced remarkable consistency in symptomatology across abstinence periods.

In line with previous research, Hughes (1992) found that weight gain closely followed a significant increase in hunger among 630 self-quitters across 180 days of abstinence. Specifically, participants showed a significant increase in hunger after 2 days of abstinence and a significant increase in weight after 7 days of abstinence. Both effects continued to be significant after 30 days of abstinence, but by 180 days of abstinence hunger had decreased to baseline levels and weight gain remained stable at about 3.2 pounds above baseline. Hughes et al. (1991) found similar results among heavy smokers enrolled in a smoking cessation program using nicotine gum (they included an experimental control group and a placebo gum group). Overall, hunger and weight gain increased over time with hunger not returning to baseline levels until six months post-cessation and weight gain remained stable at six-month follow-up. Nicotine gum decreased hunger relative to the placebo group, but not weight gain. In an earlier, short-term

study, however, Hughes, Hatsukami, Pickens, Krahn et al. (1984) found that nicotine gum did not relieve withdrawal-related increases in hunger and eating.

Other research has corroborated findings that increased appetite or hunger remains elevated for both long and short periods abstinence. Gilbert et al. (1998; 2002) found that appetite does not return to baseline levels over 31 days of abstinence in both women and men. Tate, Pomerleau, and Pomerleau (1993) found that hunger increased after only 48 hours of withdrawal, although this effect was not reliable across two separate, within-subject withdrawal periods (see also Hatsukami, Hughes, & Pickens, 1985, and Hughes & Hatsukami, 1986). West, Russell, Jarvis, and Feyerabend (1984) also observed an increase in hunger after participants switched to a low-yield (0.1 mg) cigarette for 10 days.

Despite the fact that many studies demonstrate an increase in hunger and weight gain among abstinent smokers, some have failed to find similar effects (Hatsukami, Dahlgren, Zimmerman, & Hughes, 1988). For example, Shiffman et al. (2000) actually found that hunger *decreased* over a 14-day abstinence period, relative to a 2-day baseline period; treatment with bupropion for withdrawal symptoms did not affect hunger ratings.

A significant question remaining regarding nicotine withdrawal and weight gain is why women typically gain more weight than men post-cessation. Perkins, Mitchell, and Epstein (1995) hypothesized that dietary restraint, or “chronic concerns about weight and dieting to attempt to maintain an unreasonably low body weight (p. 373),” which is a characteristic that is more commonly seen in women, may moderate the relationship between smoking cessation and food intake such that women high in dietary restraint are more vulnerable to overeating and weight gain than women low in dietary restraint. Smoking typically enhances feelings of satiety, an effect that may be reversed by smoking cessation. In addition, Epstein, Caggiula, Perkins,

Mitchell, and Dahlgren (as cited in Perkins et al., 1995) observed that individuals high in dietary restraint do not exhibit satiety even after repeated presentations of a food stimulus. Therefore, Perkins and colleagues postulated that women high in dietary restraint who are attempting to quit smoking would experience a reduced satiety response, which in turn may lead to overeating and weight gain.

To address this issue, Perkins et al. examined the satiation response of 20 female smokers (10 high in dietary restraint, HDR; 10 low in dietary restraint, LDR) at baseline and after 16 hours of abstinence. The researchers operationalized satiation as habituation to the salivary response to a food stimulus. In other words, they tested each participant's amount of salivation in response to repeated exposures to food. Results revealed that HDR females showed a greater initial salivary response than LDR females. More importantly, salivary habituation was only attenuated in HDR females, suggesting that women high in dietary restraint exhibit a greater physiological response to food. These results occurred despite the fact that subjective hunger ratings did not differ between groups. Moreover, both the desire to smoke and emotional arousal increased across subsequent food exposure trials in HDR women. The authors posited that HDR women might smoke as a way to cope with elevated levels of craving and emotional arousal that stem from a forbidden desire to eat.

Time Course of Nicotine Withdrawal. Most studies suggest that the withdrawal syndrome begins within 6 to 12 hours of cessation or after a significant reduction in smoking, peaks within one week, and gradually decreases to pre-cessation levels within approximately four weeks (Gilbert et al., 2002; Hughes, 1992; Hughes, Higgins, & Bickel, 1994; Piasecki, Fiore, & Baker, 1998). Some studies suggest an even earlier onset of withdrawal symptoms. For example, Morrell, Cohen, al'Absi, and Emery (2004) used a within-subjects design to measure anxious

mood, depressed mood, changes in heart rate and blood pressure, and overall withdrawal severity across three conditions: smoking (S; participants were allowed to smoke ad lib), brief abstinence (BA; 3 to 4 hours of abstinence), and extended abstinence (EA; 14 to 18 hours of abstinence). Measurements were taken five times within each condition, which typically lasted three to four hours. The results indicated that, consistent with the nicotine withdrawal syndrome, anxious mood, depressed mood, and overall withdrawal severity increased in the BA and EA conditions, relative to the S condition. Also consistent with nicotine withdrawal, heart rate and blood pressure significantly decreased in the BA and EA conditions, as compared to the S condition. Interestingly, Morrell et al. observed that withdrawal severity remained low and stable in the S condition, high and stable in the EA condition, but significantly increased over time in the BA condition. This escalation in withdrawal severity during the first three to four hours of abstinence suggests that the withdrawal syndrome may begin quite soon following smoking cessation.

Although the withdrawal syndrome typically comprises a circumscribed group of symptoms that gradually decreases over time, each withdrawal symptom may display a unique time course (Hughes et al., 1994). Cummings, Giovino, Jaen, and Emrich (1985) performed trend analyses on eight symptoms of withdrawal across 21 days of abstinence. Their results indicated that irritability, feeling sleepy, dizziness, coughing, tightness in the chest, and cravings decreased linearly as a function of time. These findings seem to support a uniform time course for nicotine withdrawal symptoms. However, there are a couple of problems with this study that weaken this interpretation: the authors did not include baseline measurements for pre-post cessation comparison, and the majority of symptoms that they measured are not included in the criteria for nicotine withdrawal in the DSM.

In a more rigorous examination of the time course of nicotine withdrawal, Hughes et al. (1991) found that self-reported anger, anxiety, difficulty concentrating, impatience, and restlessness returned to pre-cessation levels after 30 days of abstinence. However, hunger, craving, and increased weight continued for six months in 69%, 45%, and 42% of quitters, respectively. Similar, although not identical, results were obtained in a sample of self-quitters: anxiety, difficulty concentrating, irritability, restlessness, and heart rate returned to pre-cessation levels within 30 days of smoking cessation. Hunger and weight gain remained elevated, but craving resolved by 180 days post-cessation (Hughes, 1992).

In a more recent pair of studies, Gilbert and colleagues observed that mood disturbance did not resolve after 31 days of abstinence in both men and women (Gilbert et al., 1998; Gilbert et al., 2002). Both studies included a three to five week baseline period and random assignment to either a quit group or a control group. Negative affect was assessed using the Profile of Mood States (POMS; McNair, Lorr, & Droppleman, 1971), in which participants rate the severity of sixty-five adjectives that describe a series of mood states, including Tension-Anxiety, Depression-Dejection, Anger-Hostility, Vigor-Activity, Fatigue-Inertia, and Confusion-Bewilderment (Boyle, 1987; McNair et al., 1971). In both samples, post-cessation increases in tension, depression, and anger did not return to baseline levels within 31 days. Craving and increase in appetite also failed to resolve across the abstinence period. In contrast, physical symptoms (as defined by the Shiffman Withdrawal Questionnaire; Shiffman & Jarvik, 1976) typically decreased within two weeks of abstinence.

Taken together, the results of the few studies that have examined the long-term course of nicotine withdrawal suggest that specific symptoms demonstrate their own time course. In general, craving, depression, hunger/increased appetite, and weight gain appear to remain

elevated at one month to six months following cessation. The courses of anxiety and anger are less clear, as some studies show that they resolve within a month (Hughes et al., 1991; Hughes, 1992) and others do not (Gilbert et al., 1998; Gilbert et al., 2002). Irritability, difficulty concentrating, changes in heart rate, restlessness, and other “physical” symptoms appear to decline within approximately two weeks of abstinence.

In addition to symptom course variability, the nicotine withdrawal syndrome shows between-subject variability. Tate et al. (1993) examined the temporal stability and within-subject consistency of nicotine withdrawal symptoms with strong validity (i.e., irritability, decreased heart rate, anxiety, craving, difficulty concentrating, impatience, restlessness, increased eating, and hunger) in 39 heavy smokers. They assessed these symptoms across two 48-hour abstinence periods, following baseline measurements and separated by a week of normal smoking activity. All symptoms showed excellent temporal stability across two separate abstinence phases, which indicates that these symptoms are reliable components of nicotine withdrawal. However, these symptoms demonstrated within- and between-subject variability, suggesting that quitters may exhibit different withdrawal profiles. A cluster analysis appeared to confirm this hypothesis, with one group of participants experiencing significantly greater irritability, impatience, difficulty concentrating, and anxiety than the other. The authors implied that tailoring treatment components to specific withdrawal profiles might enhance the effectiveness of smoking cessation treatment.

Piasecki et al. (1998) also observed different withdrawal profiles in smokers seeking to quit smoking for 55 days using a nicotine patch. Specifically, they observed three different clusters: smokers in Cluster I experienced a steady reduction in withdrawal symptoms across the entire abstinence period, smokers in Cluster II showed slow improvement in withdrawal

symptoms over the first three weeks of abstinence followed by a resurgence of symptoms, and smokers in Cluster III demonstrated a decrease in withdrawal severity three to six weeks post-cessation, followed by a return to quit-day levels of withdrawal. Piasecki et al. (1998) replicated these results to some extent in another sample, as compared to a placebo group. They also observed similar patterns among unaided quitters, using a broader measure of withdrawal symptomatology and statistically controlling for relapse status (Piasecki et al., 2000). These results suggest that not all quitters experience the prototypical pattern of withdrawal (i.e., a steady decrease in withdrawal symptoms over time), and that a delayed resurgence of withdrawal symptoms in some quitters might account for relapses that occur after weeks, or even months, after cessation.

Moderators of Course. A myriad of individual characteristics have been examined as possible moderators of the relationship between nicotine withdrawal and relapse. These include, but are certainly not limited to, gender, age, expectancy effects, pre-cessation smoking intensity, nicotine dependence, and duration of smoking (Hughes, Higgins, & Hatsukami, 1990). Most studies that address moderators of the withdrawal experience actually do so indirectly by adding one of the variables listed above as a covariate in their analyses. This strategy is based on the assumption that one or more of these variables might account for a significant proportion of the variance in withdrawal, and therefore their influence must be statistically controlled. The majority of these studies do not investigate moderators of the course of withdrawal; rather, they examine moderators of withdrawal severity, which is beyond the scope of the present review. Thus, I focus on a couple of recent, representative articles that summarize what we currently know about possible moderators of the time course of withdrawal.

A common myth in the literature is that gender moderates the course of withdrawal. Specifically, women display poorer smoking cessation outcomes than men (e.g., Wetter et al., 1999), which has led researchers to postulate that women must experience withdrawal differently than their male counterparts. In a recent review of the literature, Perkins (2001) noted that self-reported withdrawal symptoms between men and women are generally equivalent during prospective smoking cessation studies. This evidence suggests that gender may not be a moderator of withdrawal time course; however, this does not exclude the possibility that gender is a moderator of withdrawal severity.

Piasecki, Jorenby, Smith, Fiore, and Baker (2003c) examined predictors of withdrawal severity, linear and quadratic time course, and volatility (i.e., variability over time) in 893 smokers who volunteered for a smoking cessation study at four treatment sites. In the full sample and among lapsed separately (i.e., those who smoked during their cessation attempt), Piasecki et al. found that age, negative affect, and nicotine dependence were positively related to withdrawal severity. In the full sample, lapse status and study site predicted linear trend in withdrawal, while lapse status and age predicted quadratic trend. More importantly, men and younger participants presented with less symptom variability. History of depression, pre-cessation smoking rate, and baseline levels of volatility predicted greater symptom variability. It is notable that (1) gender differences produced only weak withdrawal effects, and (2) few variables predicted the linear course of withdrawal over time. The impact of depression on volatility introduces negative affect as a possible moderator, or even mediator, of the course of withdrawal, a topic which will be addressed in a subsequent domain of the present review.

Craving as a Criterion for Nicotine Withdrawal. The preceding discussion made little mention of nicotine craving, which may be loosely defined as the desire to smoke. Craving was

originally included in the diagnostic criteria for nicotine withdrawal, but was removed as a criterion in the DSM-IV. Researchers continue to debate whether or not craving is a critical symptom of nicotine withdrawal. This is a particularly important issue because it pertains to how nicotine withdrawal should be most accurately measured.

Before considering the utility of craving as a symptom of nicotine withdrawal, it is important to understand how craving is operationalized in the literature. There appear to be two main methods of assessing craving: using a single item or using a multi-item subscale of a withdrawal questionnaire. Despite their differences, which will be explored below, single-item and multi-item instruments are believed to be equally valid (Abrams et al., 2003). Within the single-item approach, there is great variability, ranging from unipolar and bipolar visual analog scales to Likert scales. Furthermore, researchers define craving as desire for a cigarette, craving for a cigarette, urge to smoke, frequency of urge to smoke, and so forth. Others take one or more items (and they are often not clear which) from “validated” withdrawal questionnaires, such as the Minnesota Withdrawal Scale (MWS; Hughes & Hatsukami, 1986).

Those who use multiple-item scales often employ unspecified versions of the craving subscale of Shiffman-Jarvik Withdrawal Scale (Shiffman & Jarvik, 1976). This instrument was originally derived from a 43-item questionnaire developed by Gritz and Jarvik (1973). Shiffman and Jarvik (1976) performed a factor analysis on the measure and determined the existence of four factors, including a seven-item craving factor. The major problem here is that the authors calculated a composite craving score from the items comprising the craving factor. This is a strictly inappropriate application of factor analysis and instead, Hughes and Jarvik should have performed a principle components analysis, from which they could have computed component scores. However, for reasons too time-consuming to address in this paper, further discussion on

this matter will be omitted. Thus, many researchers have used a scale that was derived using inappropriate statistical procedures and is therefore of questionable validity.

Given the wide variety of assessment options, which is best? The Society for Research on Nicotine and Tobacco Work Group on the Assessment of Craving and Withdrawal in Clinical Trials (Shiffman et al., 2004) reviewed both single-item and multi-item measures and concluded that researchers should employ “simple, readily interpretable measures” of craving. This recommendation, coupled with the assertion that both types of measures appear to be equally valid (Abrams et al., 2003), appears to suggest that single-item measures may be the most efficient means of measuring craving.

Hughes (1994) indirectly implied that craving should be removed from the diagnostic criteria because (1) it is not included in the criteria for other withdrawal syndromes (e.g., alcohol, cocaine, etc.), and there are not enough data to determine whether it is more important in nicotine withdrawal than these withdrawal syndromes; and (2) craving per se “does not add substantially to the understanding of these syndromes” (p. 113). He also cited the following as evidence supporting exclusion: smokers still experience craving when they are clearly not in withdrawal, it is uncertain whether craving during withdrawal is reversed by nicotine administration, and craving seems to be influenced by environmental factors in addition to pharmacological ones. The latter two arguments presuppose that withdrawal must be defined as a purely physiological phenomenon; therefore, psychological withdrawal is irrelevant. This is both a narrow and debatable view of withdrawal. The first argument does not specify how long one must remain abstinent for craving to represent a withdrawal symptom. Can we even define when individuals are “clearly not in withdrawal?” To date, researchers have not located the precise

moment at which the withdrawal syndrome begins (and I suspect there is much individual variability). Is it after 24 hours, 48 hours, or perhaps five minutes?

In his defense, Hughes does note that craving is a consistent and reliable consequence of nicotine abstinence, it is relieved by nicotine administration if operationalized appropriately, and it predicts relapse following cessation. I will address each point in turn. Pursuant to the first point, across the 26 studies of nicotine withdrawal since 1970 that have included measures of craving, only six have indicated that craving does not increase with abstinence. Two of these six studies did not include a baseline measurement of craving for comparison (Shiffman & Jarvik, 1976; West, Jarvis et al., 1984); four did not include control groups, two of which were studies of nicotine replacement and partial reduction (Hatsukami et al., 1988; Hughes, Hatsukami, Pickens, & Svikis, 1984; West, Jarvis et al., 1984; West, Russell et al., 1984); and one had only three participants—a visual inspection of the data indicated that increases in craving were likely to be significant with greater power (Hughes, Hatsukami, Pickens, & Svikis, 1984). Hughes (1992) employed the most rigorous methodology and found that craving did not increase relative to baseline, but did decrease over time, especially at 14 and 30 days post-cessation. However, he was examining craving in a sample of self-quitters, which may exhibit different characteristics than smokers who choose to quit via structured cessation programs, or smokers who have no intention to quit but are willing to be abstinent for a few days as part of a research project. Regardless, most studies have found craving to be a reliable consequence of abstinence even though smokers may still experience craving to some degree before cessation.

Hughes's second point is that craving is relieved by nicotine administration if operationalized appropriately. Indeed, a plethora of studies have supported this conclusion. For example, research has shown that nicotine replacement in the form of nicotine gum (Abrams et

al., 2003; Fiore et al., 2000), the transdermal nicotine patch (Abelin, Beuhler, Muller, Vesanen, & Imhof, 1989), clonidine (Glassman, Jackson, Walsh, & Spoose, 1984), and antidepressants such as bupropion (Fiore et al., 2000) are effective in reducing craving during periods of abstinence.

Hughes's (1994) third point which favors inclusion of craving as a symptom of withdrawal is that it reliably predicts relapse. In a study of nicotine gum efficacy, West, Hajek, and Belcher (1989) found that time spent with urges to smoke significantly predicted relapse across three weeks of abstinence, even when the effects of nicotine gum were statistically controlled. Although little has been done with these findings since the study was published, it presents an intriguing hypothesis: perhaps the frequency of cravings is as important as the severity. Indeed, abstainers in the West et al. study reported significantly more time spent with urges to smoke than continuing smokers. Swan, Ward, and Jack (1996) examined predictors of relapse across four weeks of abstinence and found that craving was the single most important predictor of time to relapse. The only study to my knowledge that has failed to implicate craving as a predictor of relapse has already been discussed at some length above: Hughes (1992) found that craving did not predict relapse in self-quitters across 180 days of abstinence, which is not surprising given that craving did not increase following cessation. Again, self-quitters may represent a different population than smokers who choose to use a smoking cessation program.

In general, what conclusions can be drawn about craving? The construct appears to be nebulous at best, defined and measured in multiple ways that all attempt to tap into the desire to smoke. There are reasonable arguments both for and against the inclusion of craving as a criterion for nicotine withdrawal in the DSM. Nevertheless, the weight of any particular argument rests with the individual's definition of withdrawal. Rather than debate the necessity of

craving as a symptom of nicotine withdrawal, I suggest that we examine it in terms of its utility, especially concerning the maintenance of smoking behavior (i.e., does craving serve to maintain smoking behavior, especially when smokers are “clearly not in withdrawal?”). With regard to cessation, it may be beneficial to look at craving as a predictor of relapse (i.e., what variables predict the individual craving response; what variables mediate the relationship between craving and relapse?) and to learn new ways to alleviate it.

Nicotine Withdrawal and Relapse. How does the withdrawal syndrome relate to relapse following smoking cessation? Perhaps the oldest and most widely held theory (viz., classic psychopharmacologic theory) is that the withdrawal syndrome itself causes relapse. Specifically, individuals resume smoking in order to avoid the physiological and psychological discomfort associated with nicotine withdrawal. In essence, this is a behavioral negative reinforcement model in which a behavior (smoking) is reinforced by the removal of an unpleasant stimulus (the withdrawal syndrome). Surprisingly, a review of more than 30 years of smoking research reveals little empirical support for this claim.

The majority of studies that have examined this matter have found that withdrawal does *not* reliably predict relapse. For example, Hughes and Hatsukami (1986) found that intensity of total withdrawal discomfort, as measured by the MWS, was not related to relapse during two days of abstinence. Stitzer & Gross (1988) obtained similar results across a ten-week abstinence period, as did Hughes et al. (1991). According to West et al. (1989), specific withdrawal symptoms (e.g., depressed mood and time spent with urges to smoke) rather than general withdrawal severity during the third and fourth weeks of abstinence predicted relapse. Similarly, Hughes (1992) found that depression alone predicted relapse in self-quitters, and Swan et al. (1996) found that both depression and craving predicted relapse across 28 days of abstinence. It

is important to note that in neither of these studies did total withdrawal severity predict relapse. Kenford et al. (2002) observed that withdrawal severity during the first week of abstinence predicted relapse at six months post-cessation, but this relationship disappeared when negative affect was included in their statistical model. Finally, Cincirpini et al. (2003) found depression to be inversely related to abstinence across six months. Withdrawal was included as a mediator between depression and abstinence in their analyses, but its impact was nonsignificant.

Only recent work by Piasecki and colleagues (Piasecki et al., 1998; Piasecki et al., 2000; Piasecki, Jorenby, Smith, Fiore, & Baker, 2003a, 2003b, 2003c) has demonstrated withdrawal to be a robust predictor of relapse. As mentioned previously, Piasecki et al. (1998; 2000; see *Time Course of Nicotine Withdrawal*) found that withdrawal significantly predicted relapse. Additionally, persons with “atypical” withdrawal features (i.e., an escalation in withdrawal severity over time) were more likely to relapse. Piasecki et al. (2003a, 2003b, 2003c) also examined withdrawal in a double-blind treatment study that included four sites across the United States. In all three studies, they again found withdrawal to be a robust predictor of relapse following smoking cessation. They also found that withdrawal demonstrated a stereotypical course in which symptom severity gradually declined over time when examined at the aggregate level, which is consistent with prior research findings and methodologies. Analyses at the intraindividual level, however, revealed a high degree of variability across participants, with lapsers generally experiencing more severe withdrawal. Specifically, greater withdrawal severity, greater symptom volatility, and increases in severity over time were associated with a higher likelihood of relapse (Piasecki et al., 2003b). The latter result corroborates with earlier findings suggesting that individuals who experience an atypical withdrawal pattern are more likely to

relapse (Piasecki et al., 1998; Piasecki et al., 2000). These results also suggest that facets of withdrawal other than severity, such as volatility, may be useful in predicting relapse.

Why have Piasecki and colleagues consistently found that withdrawal predicts relapse, when almost every other study to date has not? They suggest a couple of reasons. First, whereas the majority of researchers drop smokers who relapse from their studies, Piasecki et al. include them in their analyses. This strategy allows us to see what actually occurs in quitters who relapse, rather than focusing solely on smokers who are able to remain abstinent. Logically, it is likely that successful abstainers represent a different population than lapsers. Second, most previous research has only assessed withdrawal at the aggregate level; therefore, it has ignored both intraindividual fluctuations in withdrawal symptomatology and distinct withdrawal patterns. As Piasecki et al. point out, some withdrawal profiles (i.e., atypical ones) are more predictive of relapse than others. By aggregating across profiles, and therefore including those that are not necessarily predictive of relapse, researchers may have inadvertently diluted the relationship between withdrawal and relapse beyond statistical detection.

There are additional reasons why most studies have not observed withdrawal to predict relapse following smoking cessation. In general, the research is plagued by so many methodological flaws that any results might be the result of systemic Type II error. First, many of these studies are actually treatment studies where participants are typically undergoing some form of pharmacological or psychological cessation therapy. The relationship between withdrawal and relapse is likely to be obscured by treatments directed at alleviating the withdrawal syndrome. Second, instruments measuring the tobacco withdrawal syndrome may reflect poor construct validity, which may in turn compromise the internal validity of the studies. Third, many studies only focus on early withdrawal (i.e., within the first few days of abstinence)

as a predictor of long-term relapse. It is possible that predictors of relapse fluctuate in importance, not just severity, over time.

To summarize, most empirical evidence indicates that nicotine withdrawal does not influence smoking cessation, a finding that contradicts one of the most widely held theories about the causes of relapse. Recently, however, studies aimed at investigating individual withdrawal profiles have found that withdrawal does predict cessation outcomes. In particular, a more severe, escalating, and volatile withdrawal course predicts relapse following cessation.

Cigarette Smoking and Anxious Mood

A preponderance of studies implicate anxiety as an integral component of the nicotine withdrawal syndrome (see review above). The DSM-IV-TR (APA, 2000) lists anxiety as a symptom of the nicotine withdrawal syndrome, but does not operationally define the construct to distinguish between clinical anxiety and anxious mood. One may assume that the DSM is referring to some type of anxious mood that does not necessarily meet criteria for any particular anxiety disorder, such as Generalized Anxiety Disorder. Similarly, many of the smoking studies that include anxiety as a variable assess what can be more correctly termed “anxious mood.” That is, they typically operationalize anxiety as a score on some measure of anxious mood (e.g., the State-Trait Anxiety Inventory; STAI; Spielberger, Gorsuch, & Lushene, 1970) that is not diagnostic of a clinical anxiety disorder as defined by the DSM.

Anxious Mood and the Maintenance of Smoking Behavior. How might anxious mood influence the maintenance of smoking behavior? One explanation is based on the affect regulation model of drug use, which states that individuals smoke to regulate their affective state. With regard to anxiety, this theory states that the anxiolytic effects of smoking negatively reinforce smoking behavior. The anxiety itself may arise from internal sources (e.g., trait

anxiety), from environmental sources (e.g., interpersonal stressors or fear), or as part of the nicotine withdrawal syndrome (i.e., smoking may be maintained by the desire to avoid the nicotine withdrawal syndrome, a hypothesis which is not supported by research, as we have seen).

A number of studies have examined whether smoking does in fact relieve anxiety. While reviewing such studies, it is important to remember that researchers define anxiety (and attempt to produce it) in a variety of ways. Also, it is not always easy to distinguish between the possible anxiety-reducing effects of nicotine or of the actual smoking behavior. Furthermore, even though many smokers report smoking to relieve anxiety, this behavior actually produces symptoms consistent with physiological arousal, a phenomenon referred to as Nesbitt's Paradox (Gilbert, 1979; Robinson et al., 1995).

In order to determine whether individuals smoke to relieve anxiety, it is vital to know if (1) smoking actually reduces anxiety levels, and (2) individuals smoke more during anxiety-provoking situations. Only one study in this domain has focused on anxiety reduction in participants with an existing anxiety disorder, while the remainder assesses changes in anxious mood or stress level in non-clinical samples. Fleming and Lombardo (1987) tested the anxiolytic effects of smoking among 20 female smokers and 20 female non-smokers with a self-reported phobia for rats. The authors instructed participants to approach a large, white rat and rate their anxiety levels at five-foot intervals (they also completed the State Form of the State-Trait Anxiety Inventory at the end of the experiment). All participants held a cigarette in their hand as they approached the rat, but only half of them were actually allowed to smoke this cigarette. Although approaching the rat produced significant increases in anxiety, neither participant smoking status (smoker vs. non-smoker) nor being allowed to smoke influenced anxiety levels.

The authors posited that level of anxiety moderates the anxiolytic effects of smoking, such that smoking is not anxiolytic under conditions of extreme anxiety. However reasonable this hypothesis may seem on a grand scale, its specific applicability to Fleming and Lombardo's study is based primarily on the untestable assumption that their manipulation produced unusually high levels of anxiety.

Hatch, Bierner, & Fisher (1982) also found that smoking does not relieve anxious mood. They examined the anxiolytic properties of nicotine during a stressful speech task. Participants were randomly assigned to one of three groups: no-smoking, high-nicotine, and low-nicotine. All participants were then given 10 minutes to mentally prepare a three-minute speech on abortion, after which they delivered the speech. Measures indicated that anxiety did increase during the preparation and speech phases of the experiment, but that smoking did not alleviate this anxiety.

In contrast to Fleming and Lombardo's and Hatch et al.'s results, several studies demonstrate that smoking does indeed relieve anxious mood in a variety of contexts, including during difficult problem-solving tasks. For example, Pomerleau, Turk, and Fertig (1982) found that smoking significantly relieved anxious mood, as measured by the STAI, in six male participants during an unsolvable anagram task. Additionally, smoking increased participants' pain threshold during a cold pressor pain task, in which each participant immersed his arm in ice water. Jarvik, Caskey, Rose, Herskovic, and Sadeghpour (1989) sought to replicate and extend Pomerleau et al.'s (1982) results by investigating the anxiolytic effects of smoking during an anagram task, a cold pressor task, a white noise condition, and an auditory vigilance task, all of which have been shown to induce anxiety. Again, smoking relieved anxious mood in the anagram task and the cold pressor task, although the latter effect was only marginally significant.

Smoking did not relieve anxious mood in response to white noise or the auditory vigilance task, but insufficient power may be at fault (i.e., there were only eight participants per condition).

The connection between smoking and anxiety relief has also been tested in stressful social interactions. Gilbert and Spielberger (1987) manipulated smoking status (allowed to smoke vs. not allowed to smoke) among pairs of individuals who were instructed to discuss a topic on which they disagreed. Their results demonstrated that, in spite of overall increases in physiological arousal (e.g., heart rate), participants reported less anxiety when allowed to smoke. These results might relate to the fact that smokers often report smoking more in social situations, although more research in this area is needed. Given the high degree of comorbidity between social fears, social phobia, and smoking (Breslau, Novak, & Kessler, 2004; Sonntag, Wittchen, Hofler, Kessler, & Stein, 2000), it might be reasonable to hypothesize that a certain segment of the smoking population experiences elevated levels of social fear, and therefore smokes as a way of coping with that fear.

Gilbert, Robinson, Chamberlin, and Spielberger (1989) moved beyond the realm of social interaction and examined the anxiety-reducing properties of smoking in response to a stressful movie. They instructed 40 smokers and 40 non-smokers to watch a movie about industrial accidents, which was intended to induce anxiety. Before the movie, half of the smokers smoked a high-nicotine cigarette and half smoked a low-nicotine cigarette. Non-smokers puffed on a soda straw to control for the possible effects of smoking behavior alone. Individuals who smoked high-nicotine cigarettes reported significantly smaller increases in anxiety during the movie than individuals in the low-nicotine group or the control group. Furthermore, EEG readings indicated that those who smoked high-nicotine cigarettes experienced decreased brain activity in the right hemisphere only while viewing the stressful movie. Decreased cortical activity is typically

associated with a corresponding decrease in arousal, and the right hemisphere of the brain may be associated with negative affect. Therefore, nicotine's deactivating properties in the right hemisphere might account for the oft-reported relaxing and negative-affect relieving properties of smoking.

Britt, Cohen, Collins, and Cohen (2001) examined the anxiolytic properties of smoking and chewing gum in response to a stressful speech task. Smokers were told that they must prepare a speech about their body and physical appearance. Measurements of craving, withdrawal, and anxiety were taken at baseline, after speech preparation but before smoking or chewing gum, after smoking or chewing gum, after the speech itself, and after a 10-minute rest period. Analyses revealed that individuals in the smoking group experienced a significant decrease in anxiety over time, relative to the chewing gum group and a control group.

More recent research suggests that attentional processes may mediate the relationship between smoking and anxiolysis. Specifically, Kassel and Shiffman (1997) postulated that smoking "constrains smokers' attention to the most immediate and salient stimuli in their environment—when such stimuli are available" (p. 360; cf. attention-allocation model of alcohol reinforcement). As a result, smokers are more likely to focus on immediate and distracting stimuli than more distal anxiogenic stimuli, thus reducing anxious mood. Two studies to date have confirmed the hypothesis that smoking relieves anxious mood in minimally deprived smokers in the presence of a distractor, and that this effect cannot be attributed to the behavioral aspects of smoking or the nicotine withdrawal syndrome (Kassel & Shiffman, 1997; Kassel & Unrod, 2000). In contrast, Herbert, Foulds, and Fife-Shaw (2001) demonstrated that attentional processes in non-deprived smokers did not mediate the anxiolytic effects of nicotine. These findings suggest that attentional mediation may only occur under certain conditions, such as

when smokers are only minimally deprived. We must also keep in mind that these studies induced anxious mood in different ways, which may make it difficult to compare their results. Specifically, Kassel and colleagues instructed participants to give a speech about what they liked and disliked about their body, but Herbert et al. informed participants that their behavior and facial expressions would be monitored during a rapid visual information-processing task.

In summary, there is substantial evidence that smoking can relieve anxious mood in a variety of contexts. There is additional evidence to suggest that attentional processes may mediate nicotine's anxiolytic effects such that smoking relieves anxious mood primarily in situations that provide distracting stimuli. Research also demonstrates that smokers do smoke more when experiencing anxious mood. For instance, Rose, Ananda, and Jarvik (1983) found that individuals smoked more in terms of both volume and puffing frequency during an induced stage fright task and a monotonous concentration task compared to a relaxation condition (cf. Epstein, Ossip, Coleman, Hughes, & Whist, 1981). It may be reasonable to infer from such studies that anxious mood is an important factor in maintaining the smoking cycle.

Anxious Mood and Relapse Following Cessation. Most research indicates that anxious mood increases upon smoking cessation (cf. Ames et al. 2005; Kalman, Morrisette, & George, 2005). In fact, only one study (West & Hajek, 1997) to date has found that anxiety does not increase following smoking cessation, however, the researchers failed to measure anxiety levels during the peak (i.e., during the first two to four days) of the nicotine withdrawal syndrome (Wiseman, 1999). Furthermore, a preponderance of smokers report that they smoke in response to experiencing negative affect, including anxiety and stress. Several studies also appear to validate the anxiolytic properties of smoking and the fact that smokers smoke more when anxious or stressed. Such evidence suggests that anxiety, either in the form of an anxiety disorder

or general anxious mood, may in fact be a significant predictor of smoking cessation outcome. Specifically, anxiety may hinder smoking cessation efforts (Covey, 1999).

Two recent studies have evaluated panic disorder and panic attacks as predictors of cessation outcomes. Amering et al. (1999) retrospectively examined the relationship between a DSM-III-R diagnosis of panic disorder and smoking behavior in a sample of 102 adult Austrian outpatients. They found that 72% of participants reported smoking before the onset of panic disorder, which is consistent with most research regarding anxiety disorders and smoking initiation. Over half of these participants (55%) reported that they had reduced smoking and 26% reported that they had stopped smoking as a result of their panic disorder. Nineteen percent reported that they smoked more after developing panic disorder. This research suggests that the presence of panic disorder might actually increase an individual's likelihood of reducing or quitting smoking. However, the results of this study cannot be generalized to persons with other anxiety disorders and they are limited by the fact that the data were purely retrospective.

Zvolensky, Lejuez, Kahler, and Brown (2004) retrospectively observed the opposite pattern among 40 adult smokers, half of which reported a history of panic attacks, but not panic disorder. Results indicated that smokers with panic attacks reported significantly shorter quit attempts and more severe withdrawal symptoms (*viz.*, anxiety, difficulty concentrating, restlessness, and irritability) than those without panic attacks. The most likely reason for the discrepancies between Amering et al.'s (1999) findings and Zvolensky et al.'s (2004) findings is the fact that they sampled different populations (*e.g.*, individuals with diagnosable panic disorder versus individuals who merely reported a history of panic attacks).

Two additional recent studies investigated the link between anxious mood and smoking cessation. Takemura, Akanuma, Kikuchi, and Inaba (1999) examined whether trait anxiety

influenced smoking cessation in over 2,000 male Japanese government employees using a Japanese translation of the STAI. They reported that high trait anxiety did not increase the risk for smoking initiation, but did predict unsuccessful plans to quit smoking. Despite the high level of statistical power in this study because of the large sample size, the results might be limited by retrospective bias and by the cross-sectional design. Furthermore, these findings may only be generalizable to Japanese male adults. Becoña, Vázquez, and Míguez (2002) assessed state anxiety as a correlate of smoking cessation in 214 Spanish adults who volunteered to complete a six-week cessation program. A comparison of smokers who remained abstinent, as well as smokers who resumed smoking within the 12 months following treatment, revealed that those in the latter group experienced significantly more state anxiety at post-treatment (but not pre-treatment). The primary weaknesses of this study are that the authors did not include a control group, and they did not use their data to prospectively predict smoking cessation from state anxiety scores. Therefore, we cannot make inferences about a causal relationship between state anxiety and smoking cessation outcome based on their findings.

Some indirect evidence concerning the impact of anxiety on smoking cessation can be gleaned from smoking cessation treatment studies (Covey, 1999). Cincirpini et al. (1995) studied the effects of buspirone, a medication with anxiolytic properties, on smoking cessation. They discovered that smokers high in self-reported anxiety were not as likely to maintain abstinence compared to smokers low in self-reported anxiety. Studies of bupropion, an antidepressant approved by the FDA for smoking cessation, indicate that this medication relieves a host of withdrawal symptoms (including anxiety) and that quitters who take bupropion are more likely to remain abstinent. David et al. (2003) showed that quitters taking bupropion reported significantly less anxiety than quitters in a placebo control group. Individuals in the former group

were also more likely to remain abstinent at two weeks post-cessation. Despite the apparent link between certain pharmacological treatments for nicotine withdrawal and anxiety reduction, the assumption that anxiolysis is significantly responsible for improved abstinence rates remains speculative at best.

Conclusions

Cigarette smoking is associated with high health and economic costs to the individual, the health care system, and the workforce. Thus, there has been a strong emphasis on smoking prevention and cessation in the U.S. over the past 20 to 30 years. Researchers have spent considerable effort studying what factors might promote smoking initiation and hinder smoking cessation in the hopes that a greater understanding of these variables might improve the efficacy of current prevention and cessation programs. Two factors that may interact to influence smoking behavior are the nicotine withdrawal syndrome and anxiety. As noted earlier, the nicotine withdrawal syndrome comprises a host of physiological and psychological signs and symptoms, including depressed mood, sleep disturbance, irritability, anxiety, difficulty concentrating, restlessness, decreased heart rate, and increased appetite or weight gain. Craving is no longer included as a symptom of nicotine withdrawal in the DSM-IV, but it may be a useful construct in terms of predicting relapse following smoking cessation. Withdrawal symptoms usually appear within hours of abstinence or a significant reduction in nicotine intake, and each may follow its own time course across a period of prolonged abstinence.

With the exception of a few recent studies, most research has contradicted the traditional theory that individuals resume smoking following a cessation attempt in order to relieve the nicotine withdrawal syndrome. Inherent in this theory is the assumption that greater withdrawal severity should be a robust predictor of relapse. The more recent studies indicate that it is the

course of withdrawal (specifically, an escalating and volatile trajectory) rather than the overall severity that predicts relapse.

The literature implicates anxiety in the maintenance of smoking behavior. For example, many smokers cite anxiety relief as their primary reason for smoking, they tend to smoke more in anxiety-provoking situations, and smoking appears to relieve anxiety in a variety of contexts. Additionally, attention may mediate the relationship between smoking and anxiety, such that smoking truly demonstrates anxiolytic properties in the presence of distracting stimuli. Anxiety may also precipitate relapse among quitters, although the research in this area remains somewhat sparse and inconclusive.