Anhedonia and Anxiety Sensitivity: Prospective Relationships to Nicotine Withdrawal Symptoms During Smoking Cessation

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ABSTRACT. Objective: The aim of the present investigation was to explore the main and interactive effects of anhedonic depressive symptoms and anxiety sensitivity in terms of the individual components of nicotine withdrawal symptoms experienced on quit day as well as throughout the initial 14 days of cessation. **Method:** Participants included 65 daily cigarette smokers (38 women; M_{age} = 46.08 years, SD = 9.12) undergoing psychosocial-pharmacological cessation treatment. **Results:** Results indicated that, after controlling for the effects of participant sex and nicotine dependence, anhedonic depression symptoms, but not anxiety sensitivity, significantly predicted quit day levels of mood-based nicotine withdrawal symptoms. Conversely, anxiety sensitivity, but not anhedonic depression symptoms, was significantly related to the change in most nicotine withdrawal symptoms over time. Finally, our results revealed a significant interaction between anxiety sensitivity and anhedonic depression symptoms related to the slope of certain withdrawal symptoms over time. Specifically, among participants with higher levels of anxiety sensitivity, greater levels of anhedonic depression symptoms were related to greater increases in withdrawal symptoms over time for two of the nine anxiety-relevant components of nicotine withdrawal (restlessness and frustration). **Conclusions:** Among high anxiety-sensitivity persons, compared with those low in anxiety sensitivity, anhedonic depression symptoms may be more relevant to the experience of some withdrawal symptoms being more intense and persistent during the early phases of quitting. (*J. Stud. Alcohol Drugs, 74,* 469–478, 2013)

A GROWING BODY OF WORK has focused on the role of depressive symptoms in understanding smoking cessation outcome (e.g., Anda et al., 1990; Brown et al., 2001; Haas et al., 2004). However, the results of more recent studies suggest that a history of major depression may be associated with an increased risk of developing and maintaining more severe nicotine withdrawal symptoms during periods of abstinence, which may contribute to less success in quitting (Borrelli et al., 1996; Covey et al., 1990; Niaura et al., 1999; Pomerleau et al., 2000). Notably, research has documented that nicotine withdrawal symptomatology may be pathognomonic to type of affective vulnerability (Breslau et al., 1992). For example, depressive symptoms are significantly related to emotionally laden nicotine withdrawal symptoms (e.g., depressed mood; Breslau et al., 1992; Pomerleau et al., 2000), whereas anxiety symptoms are significantly associated with hyperarousal (e.g., anxiety, irritability; Breslau et al., 1992; Pomerleau et al., 2000). More recently, studies disassembling the various psychopathologic components of depression symptoms have identified *anhedonia*—defined as the experience of diminished interest, drive, and overall positive affect (Watson et al., 1995)—as a particularly relevant explanatory dimension of depression with regard to certain smoking characteristics (e.g., craving; relapse; see Ameringer and Leventhal, 2010, for a review). Thus, to better isolate the role of depression in nicotine withdrawal, it may be useful to focus on the anhedonic component of depressive symptoms rather than broader, more heterogeneous depressive symptom constructs that incorporate a wide variety of features (e.g., appetite/weight changes, sleep problems, guilt/worthlessness, and/or sadness), because a focus on the latter may obfuscate depression–withdrawal relationships.

Although work on the association between depressive symptoms and nicotine withdrawal symptoms is promising, there is a marked lack of integration of other relevant cognitive-affective risk candidates in elucidating these relations. Thus, it is unclear how depressive symptoms interplay with other cognitive-affective variables known to be related

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to mood vulnerability and may perhaps enhance the risk of experiencing nicotine withdrawal that is exacerbated by depressive symptoms. *Anxiety sensitivity,* defined as the fear of anxiety and internal sensations (McNally, 2002; Reiss and McNally, 1985), is one promising candidate for better understanding the nature of depression-withdrawal symptom relations. Past non-smoking-oriented work has demonstrated that anxiety sensitivity is related to depressive symptoms and disorders (Cox et al., 1999; Otto et al., 1995; Schmidt et al., 2006). Furthermore, a limited, albeit growing, body of work suggests that anxiety sensitivity is retrospectively (Zvolensky et al., 2004) and prospectively (Marshall et al., 2009) associated with greater severity of acute nicotine withdrawal symptoms. Other research has documented that anxiety sensitivity is related to the rate of change in withdrawal symptoms over time (Johnson et al., 2012). However, no work to date has examined how anxiety sensitivity may interact with anhedonic depressive symptoms in predicting withdrawal symptomatology during a quit attempt.

The primary aim of the present investigation was to explore the main and interactive effects of anhedonic depressive symptoms and anxiety sensitivity in terms of the individual components of nicotine withdrawal symptoms experienced on quit day as well as throughout the initial 2 weeks of cessation. Although examining each individual component of withdrawal symptomatology may increase the risk of inflating type I error, the aim of the current investigation was to provide a profile test of which individual characteristics of nicotine withdrawal are most relevant to anxiety sensitivity and to anhedonic depressive symptoms.

Consistent with a pathognomonic typing of affective vulnerability (Breslau et al., 1992), the following hypotheses were proposed. First, it was hypothesized that higher baseline levels of anxiety sensitivity would be associated with (a) a greater intensity of anxiety-related withdrawal symptoms (e.g., anxiety, irritability, restlessness) experienced on quit day and (b) a significantly slower decrease in anxiety-related withdrawal symptoms throughout the initial 2 weeks of cessation. Second, it was hypothesized that higher baseline levels of anhedonic depression symptoms would be associated with (a) a greater intensity of mood-based withdrawal symptoms (e.g., depressed mood) experienced on quit day and (b) a significantly slower decrease in mood-based withdrawal symptoms throughout the initial 2 weeks of cessation. It also was hypothesized that anxiety sensitivity would interplay with anhedonic depression symptoms to exacerbate nicotine withdrawal symptoms.

Specifically, the observed relations between anhedonic depression symptoms and nicotine withdrawal symptoms would be moderated by anxiety sensitivity, such that anhedonic depression symptoms will be more strongly related to the individual components of withdrawal for those with high levels of anxiety sensitivity than for those with low levels of anxiety sensitivity. As mentioned above, individuals who are prone to experiencing anhedonic depression may be more likely to endorse a greater intensity of nicotine withdrawal during periods of smoking deprivation (Borrelli et al., 1996; Covey et al., 1990; Leventhal et al., 2009; Niaura et al., 1999; Pomerleau et al., 2000). Smokers characterized by high levels of anxiety sensitivity (compared with low levels of anxiety sensitivity) may be more reactive to aversive internal cues associated with withdrawal symptomatology, thereby paradoxically driving the affective and drug-state experiences (Zvolensky and Bernstein, 2005).

Thus, anhedonia-driven risk of withdrawal may be amplified for high anxiety-sensitivity smokers who are particularly sensitive to internal affective states that resemble withdrawal symptoms. That is, anhedonic depression and anxiety sensitivity may demonstrate a synergistic effect, such that these two vulnerability factors coalesce to produce a more intense withdrawal experience while a person is quitting smoking.

Method

Measures

Smoking History Questionnaire (SHQ). The SHQ (Brown et al., 2002) is a descriptive, self-report questionnaire used to assess smoking history and pattern. The SHQ includes items pertaining to smoking rate, age at onset of smoking initiation, and years of being a daily smoker. The SHQ has been used successfully in previous studies as a measure of smoking history (e.g., Zvolensky et al., 2004).

Fagerström Test for Nicotine Dependence (FTND). The FTND (Fagerström, 1978; Heatherton et al., 1991) is a six-item scale designed to assess gradations in tobacco dependence (Heatherton et al., 1991). A total score is derived by summing the values of the six items, with higher scores reflecting greater nicotine dependence. The FTND has shown good internal consistency, positive relations with key smoking variables (e.g., saliva cotinine; Heatherton et al., 1991), and high test–retest reliability (Pomerleau et al., 1994). Internal consistency was found to be adequate within the current sample (Cronbach's $\alpha = .75$).

Minnesota Nicotine Withdrawal Scale (MNWS). Nicotine withdrawal symptom severity was assessed daily for the initial 14 days of the cessation attempt using the MNWS (Hughes and Hatsukami, 1986), a reliable and sensitive nine-item scale. Participants were asked to rate daily to what extent they experienced each symptom associated with nicotine withdrawal (i.e., craving, irritability, frustration, anxiety, concentration, restlessness, depression, appetite, and insomnia), using a 4-point Likert-type scale (0 = *not present* to 3 = *severe*). This measure has been used successfully in previous smoking cessation research to capture withdrawal dynamics, including negative affect symptoms (Piasecki et al., 2000). Furthermore, it allows for the assessment of the frequency, duration, severity, and variability of withdrawal

symptoms experienced over time. Indeed, previous work has used the individual components and overall total score of the MNWS to characterize the nature of nicotine withdrawal during cessation (Gray et al., 2010; Heil et al., 2006).

Anxiety Sensitivity Index (ASI). To assess sensitivity to, and discomfort with, anxiety and related internal states, the 16-item ASI (Reiss et al., 1986) was used. The ASI is a self-report measure on which respondents indicate, on a five-point Likert-style scale, the degree to which they fear the potential negative consequences of anxiety-related symptoms and sensations. The ASI is unique from, and demonstrates incremental predictive validity relative to, trait anxiety (McNally, 2002) and negative affectivity (Zvolensky et al., 2005). Based on previous psychometric work using item response theory, the current investigation used 12 of the 16 ASI items, which have demonstrated the strongest capacity to discriminate between, and provide information about, various latent levels of anxiety sensitivity among smokers (Zvolensky et al., 2009). Specifically, the following 12 items were used in the present investigation to calculate the total ASI score: (2 = "When I cannot keep my mind on a task, I worry that I might be going crazy"; 3 = "It scares me when I feel shaky"; 4 = "It scares me when I feel faint"; 6 = "It scares me when my heart beats rapidly"; 8 = "It scares me when I am nauseous"; 10 = "It scares me when I become short of breath"; 11 = "When my stomach is upset, I worry that I might be seriously ill"; 12 = "It scares me when I am unable to keep my mind on a task"; 13 = "Other people notice when I feel shaky"; 14 = "Unusual body sensations scare me"; 15 = "When I am nervous, I worry that I might be mentally ill"; and 16 = "It scares me when I am nervous"). Internal consistency was found to be excellent within the current sample (Cronbach's $\alpha = .90$).

Mood and Anxiety Symptom Questionnaire (MASQ). The MASQ is a 62-item self-report measure of affective symptoms (Watson et al., 1995). Participants indicate how much they have experienced each symptom on a five-point Likert-type scale (1 = *not at all* to 5 = *extremely*). The anhedonic depression subscale (MASQ-AD) measures a loss of interest in life (e.g., "felt nothing was enjoyable") with reverse-keyed items measuring positive affect. Consistent with past work (Zvolensky et al., 2006), only the MASQ-AD subscale was used in the present investigation because it provides a psychometrically sound and empirically specific composite for "pure" depression symptoms (Watson et al., 1995). Internal consistency was found to be excellent within the current sample (Cronbach's $\alpha = .88$).

Participants

Participants included 65 daily cigarette smokers (38 women; $M_{age} = 46.08$ years, $SD = 9.12$) living in the Halifax Regional Municipality in the Canadian province of Nova Scotia. Daily smokers were recruited for participation from among those attending a structured 4-week group Tobacco Intervention Program offered through Addiction Prevention and Treatment Services, Capital District Health Authority. All of those daily smokers participating in the program were invited to participate. Participants reported attaining the following levels of education: 11% had completed junior high school, 42% had completed high school, 33% had completed college (community college or technical schooling), and 14% had completed university (traditional 4-year schooling). With regard to marital/relationship status, 46% of the sample reported being married/cohabiting with a partner, 39% reported being separated/divorced/widowed, and 15% reported being single.

At treatment outset, participants reported smoking an average of 14.25 ($SD = 7.44$) cigarettes per day and endorsed moderate levels of nicotine dependence ($M = 3.66$, $SD = 1.18$), as indexed by the FTND (Fagerström, 1978; Heatherton et al., 1991). Participants reported initiating daily smoking at a mean age of 14.34 years ($SD = 4.14$) and smoking regularly for an average of 28.85 years ($SD = 9.39$). In terms of smoking cessation, participants endorsed an average of 3.22 ($SD = 3.13$) serious lifetime quit attempts and 7.64 ($SD = 16.03$) lifetime quit attempts lasting longer than 12 hours in duration. The average longest lifetime period of smoking abstinence after a quit attempt among participants was 1.05 years ($SD = 1.92$).

Procedure

The present study was a facet of a larger investigation, and, thus, the procedure of the study has been described in detail elsewhere (Zvolensky et al., 2009). Notably, the present study used a smaller sample size than that reported in Zvolensky et al., 2009. Specifically, because we were examining the effects of anxiety sensitivity and anhedonic depression on quit-day withdrawal symptoms as well as the slope of change in symptoms following quit day, the present study included only participants for whom we knew on which day they quit smoking. Conversely, in the larger investigation, all participants were retained in the sample even if we could not identify their exact quit day. During the first session (i.e., information session), participants completed a demographics questionnaire and the SHQ, FTND, MASQ-AD, and ASI. Participants were then enrolled in the smoking cessation program, which consisted of one 90-minute group session per week for 4 weeks. The manualized treatment included both evidence-based behavioral and cognitive strategies and nicotine replacement therapy. During this program, participants selected their own quit date within the 4-week window of treatment. Participants were then instructed to complete the MNWS daily for the initial 14 days of the cessation attempt. Specifically, participants were instructed to rate their overall symptoms of nicotine withdrawal, beginning on quit day, and continuing daily for the first 2 weeks following quit day. Par-

Table 1. Summary of missing data

Day (post-quit)	Missing data *n*	Missing data %
Day 1	0	0.00%
Day 2	4	6.15%
Day 3	4	6.15%
Day 4	4	6.15%
Day 5	4	6.15%
Day 6	5	7.69%
Day 7	5	7.69%
Day 8	10	15.38%
Day 9	10	15.38%
Day 10	11	16.92%
Day 11	14	21.53%
Day 12	17	26.15%
Day 13	20	30.76%
Day 14	16	24.61%

ticipants were given the flexibility of completing their ratings at any point during the day as long as the ratings were made on a daily basis (see Johnson et al., 2012 and Zvolensky et al., 2009, for an expanded discussion of study procedures). Table 1 provides a summary of missing data related to the daily ratings of nicotine withdrawal. As illustrated in Table 3, the percentage of missing data increased steadily from Day 1 (0.00%) through Day 14 (24.61%).

Data analytic strategy

Linear mixed-effects models (LMM, also known as multilevel models, random-coefficient models, etc.), using the mixed-effects module in PASW Statistics 20, were utilized to analyze the present data. Level 1 of the LMM involved the repeated daily assessments of nicotine withdrawal symptoms over the first 14 days starting at the quit date, which were nested within participants (which comprised Level 2 of the analysis). LMM was chosen to perform the present analyses because it (a) includes all participants, regardless of missing data; (b) allows for different numbers of assessments for different subjects; and (c) is the preferred analytic tool for examining longitudinal psychiatric data (Hamer and Simpson, 2009). In the current investigation, nine separate models were run to test the effects of our predictor variables on the criterion variables. The criterion variables were each of the individual components of nicotine withdrawal symptoms (i.e., craving, irritability, frustration, anxiety, concentration, restlessness, depression, appetite, and insomnia), which were assessed daily during the initial 14 days of the cessation attempt. These outcome variables were all continuous; therefore, no linking function was needed for their analysis.

In our analyses, we examined how anxiety sensitivity and anhedonic depression symptoms were related to (a) the quit-day levels (intercept) of the components of nicotine withdrawal and (b) the change (slope) in each component of nicotine withdrawal over time (the first 14 days after quit day). Given our hypothesis that anxiety sensitivity would moderate the relations between anhedonic depression symptoms and the individual symptoms of nicotine withdrawal, the interaction between anxiety sensitivity and anhedonic depression symptoms was included as a central component in the model and therefore was used as a Level 2 predictor of both the intercept and the slope of symptoms over time (as were the main effects for anxiety sensitivity and anhedonic depression symptoms). In addition to the main and interactive effects of anxiety sensitivity and anhedonic depression symptoms, the theoretically relevant variables of nicotine dependence and participant sex were included as potential predictors of the intercept of the individual components of nicotine withdrawal.

In summary, the Level 1 predictors of outcome in our LMM model consisted of the intercept and linear time (linear time was used because a previous investigation using this data set [Johnson et al., 2012] established that the change in nicotine withdrawal symptoms over time in this particular sample was linear). Because time was centered at Assessment 1 (time = 0 for quit day), the intercept in the LMM represented the level of withdrawal symptoms at quit day. The Level 2 predictors of the intercept included the following variables: participant sex, nicotine dependence, anxiety sensitivity, anhedonic depression symptoms, and the interaction of anxiety sensitivity and anhedonic depression symptoms. Our Level 2 predictors of time (the slope of change in symptoms over time) included the following variables: anxiety sensitivity, anhedonic depression symptoms, and the interaction of anxiety sensitivity and anhedonic depression symptoms. All predictors (except time and participant sex) were centered at their means for these analyses.

Results

Quit-day levels of nicotine withdrawal

The means and standard deviations of the predictor and criterion variables at baseline, as well as their correlations, are displayed in Table 2. Anxiety sensitivity was significantly (positively) related to all of the individual withdrawal symptoms except craving and appetite (range of *r*s: .08–.28), whereas anhedonic depression symptoms were significantly (positively) related to all of the individual withdrawal symptoms except craving (range of *r*s: .17–.30). Additionally, consistent with past work (e.g., Zvolensky et al., 2009), anxiety sensitivity and anhedonic depression symptoms were significantly (positively) related to each other ($r = .17$, $p < .01$).

Table 3 provides a summary of regression coefficients for the current analyses. Results of the LMM analyses yielded significant main effects for anhedonic depression symptoms in relation to the following symptoms of nicotine withdrawal (on quit day): anxiety, $b = 0.02$, $t(75) = 2.15$, $p \leq .05$; depres-

Table 2. Descriptive and zero-order relations among our predictors and baseline levels of each withdrawal symptom

Variables	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	Mean or % (*SD*)	Observed range
Predictor variables															
1. Sex	1	.10**	.06	.07*	-.03	-.08*	-.00	-.01	.09*	-.11**	.03	.06	.03	58% (women)	–
2. FTND		1	.10**	.03	.20**	.15**	.10**	.08*	.14**	.03	.04	.05	.02	3.66 (1.18)	1–5
3. ASI			1	.17**	.05	.08*	.12**	.17**	.19**	.13**	.07	.28**	.10**	21.77 (7.68)	9–43
4. MASQ-AD				1	-.05	.17**	.29**	.24**	.18**	.21**	.21**	.30**	.20**	54.58 (12.72)	32–86
Criterion variables															
5. Craving					1	.45**	.36**	.35**	.29**	.32**	.23**	.23**	.14**	1.81 (0.90)	0–3
6. Irritability						1	.76**	.64**	.53**	.57**	.27**	.50**	.31**	1.33 (0.97)	0–3
7. Frustration							1	.68**	.64**	.62**	.17**	.58**	.38**	1.20 (1.00)	0–3
8. Anxiety								1	.70**	.55**	.21**	.60**	.38**	1.22 (1.02)	0–3
9. Concentration									1	.49**	.18**	.63**	.26**	0.89 (0.97)	0–3
10. Restlessness										1	.19**	.51**	.51**	1.36 (0.97)	0–3
11. Appetite											1	.28**	.19**	1.41 (0.99)	0–3
12. Depression												1	.36**	0.81 (0.94)	0–3
13. Insomnia													1	1.08 (1.07)	0–3

Notes: Sex = self-reported participant sex (1 = male; 2 = female); FTND = Fagerström Test for Nicotine Dependence total (Fagerström, 1978) administered at baseline; ASI = Anxiety Sensitivity Index total (Reiss et al., 1986) administered at baseline; MASQ-AD = Mood and Anxiety Symptom Questionnaire–anhedonic depression subscale (Watson et al., 1995) administered at baseline; craving through insomnia = individual components of the Minnesota Nicotine Withdrawal Scale (Hughes and Hatsukami, 1986) administered at baseline.
*$p < .05$; **$p < .01$.

sion, $b = 0.02$, $t(79) = 2.48$, $p \leq .05$; and insomnia, $b = 0.02$, $t(73) = 2.35$, $p \leq .05$. Specifically, participants who reported higher baseline levels of anhedonic depression symptoms had more severe levels of nicotine withdrawal symptoms on quit day. Regarding the other predictors of the intercept (i.e., participant sex, nicotine dependence, anxiety sensitivity, and the interaction term), only nicotine dependence showed significant relationships with quit-day levels of nicotine withdrawal. Nicotine dependence was significantly related to quit-day craving, $b = 0.20$, $t(56) = 2.85$, $p \leq .01$, and frustration, $b = 0.18$, $t(56) = 2.06$, $p \leq .05$, with higher baseline levels of nicotine dependence being associated with more intense craving and frustration on quit day. Thus, although the majority of the studied variables were significantly correlated with outcomes at baseline, only a few specific variables remained significant when examined in the regression analysis (in which the effects of the other variables were controlled).

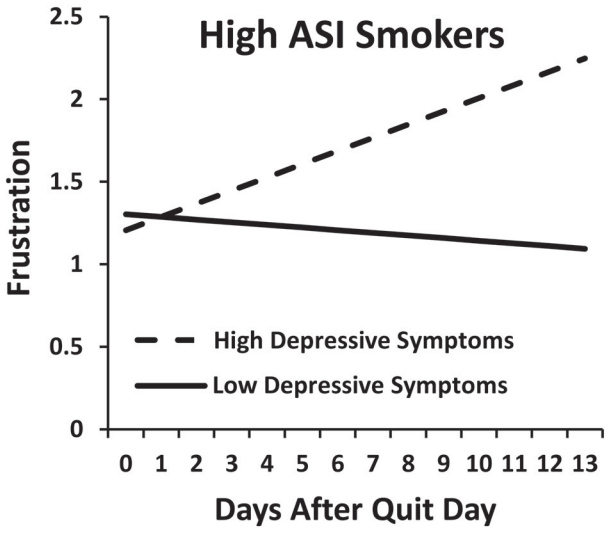
Change in nicotine withdrawal over time

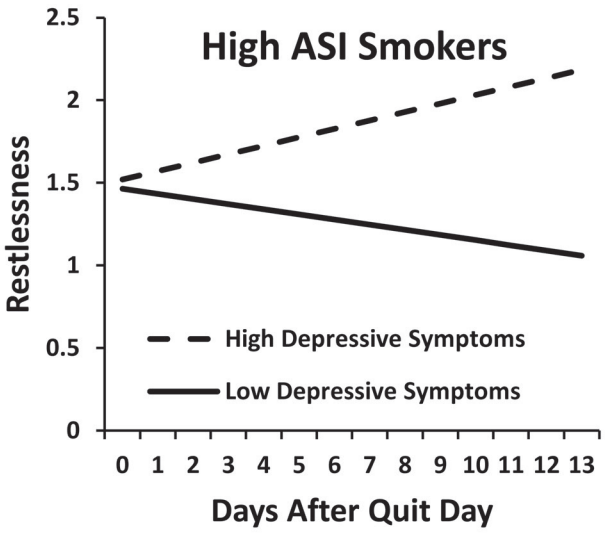
Next, we examined the trajectories of each component of nicotine withdrawal over time. Change in each symptom over time was modeled as linear (days since quit date). The average decrease in symptoms over time was significant only for craving ($b = -0.05$, $p < .001$) and for anxiety ($b = -0.02$, $p < .05$). However, results also indicated that the slope over time of most of the nicotine withdrawal symptoms was related to anxiety sensitivity. Specifically, lower anxiety sensitivity was significantly related to faster rates of decline over time (i.e., there was a significant Time ×Anxiety Sensitivity interaction) in the following symptoms: irritability, $b = 0.004$, $t(67) = 2.15$, $p \leq .05$; frustration, $b = 0.005$, $t(65) = 2.78$, $p \leq .01$; anxiety, $b = 0.003$, $t(68) = 2.21$, $p \leq .05$; restlessness, $b = 0.004$, $t(68) = 3.04$, $p \leq .01$; appetite, $b = 0.003$, $t(71) = 2.47$, $p \leq .05$; depression, $b = 0.004$, $t(70) = 2.86$, $p \leq .01$; and insomnia, $b = 0.003$, $t(68) = 2.31$, $p \leq .05$. Among participants with low anxiety sensitivity (1 *SD* below the mean), most symptoms declined significantly over time: craving, $b = -0.07$, $t(71) = -4.56$, $p < .001$; irritability, $b = -0.04$, $t(62) = -2.43$, $p < .05$; anxiety, $b = -0.06$, $t(63) = -3.83$, $p < .001$; concentration, $b = -0.03$, $t(58) = -2.02$, $p < .05$; restlessness, $b = -0.04$, $t(63) = -2.85$, $p < .01$; appetite, $b = -0.05$, $t(67) = -3.42$, $p < .001$; and insomnia, $b = -0.05$, $t(63) = -3.51$, $p < .001$. However, among participants with high anxiety sensitivity (1 *SD* above the mean), only craving, $b = -0.03$, $t(77) = -2.35$, $p < .05$, declined significantly

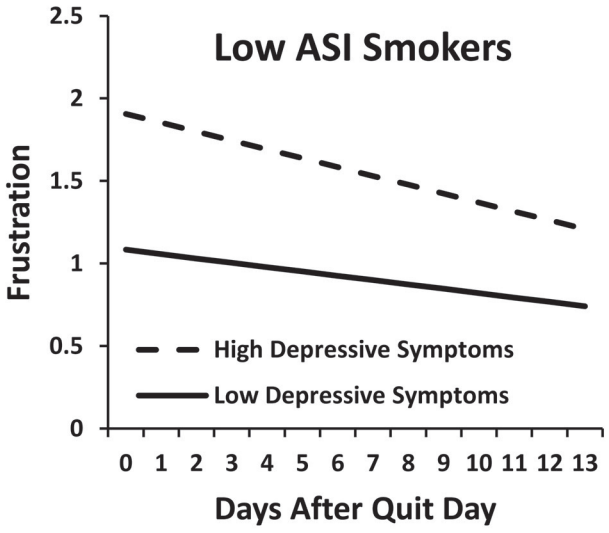
TABLE 3. Regression coefficients for the LMM predicting the nine components of nicotine withdrawal

Variable	Crav. *b*	Irrit. *b*	Frust. *b*	Anx. *b*	Conc. *b*	Restl. *b*	Appet. *b*	Depress. *b*	Insom. *b*
Intercept	1.45***	1.05**	0.71*	0.87*	0.40	1.33***	1.63***	0.51	1.25**
Sex	-0.13	-0.21	-0.01	-0.07	0.14	-0.29	-0.01	0.01	-0.07
FTND	0.20**	0.16	0.18*	0.18	0.18	0.11	-0.02	0.11	0.01
ASI	-0.004	-0.01	-0.02	0.01	0.01	-0.01	-0.02	0.01	-0.02
MASQ-AD	-0.01	0.01	0.01	0.02*	0.004	0.01	0.02	0.02*	0.02*
ASI × MASQ-AD	-0.0001	-0.001	-0.002	0.002	-0.001	-0.001	-0.001	0.0002	-0.001
Time	-0.05***	-0.02	-0.004	-0.02*	-0.02	-0.02	-0.01	0.01	-0.01
Time × ASI	0.002	0.004*	0.005**	0.003*	0.002	0.004**	0.003*	0.004**	0.003*
Time × MASQ-AD	0.0004	0.0005	0.001	0.0001	0.001	0.001	0.0002	0.0000	-0.002*
Time × ASI × MASQ-AD	0.0000	0.0002	0.0003*	-0.0001	0.0002	0.0002*	-0.0001	0.0001	-0.0001

Notes: Time is centered at assessment 1 (i.e., quit day). The other continuous predictors were centered at their mean. LMM = linear mixed-effects models; crav. = craving; irrit. = irritability; frust. = frustration; anx. = anxiety; conc. = concentration; restl. = restlessness; appet. = appetite; depress. = depression; insom. = insomnia; FTND = Fagerström Test for Nicotine Dependence; ASI = Anxiety Sensitivity Index; MASQ-AD = Mood and Anxiety Symptom Questionnaire–anhedonic depression subscale.
*$p \leq .05$; **$p \leq .01$; ***$p \leq .001$.







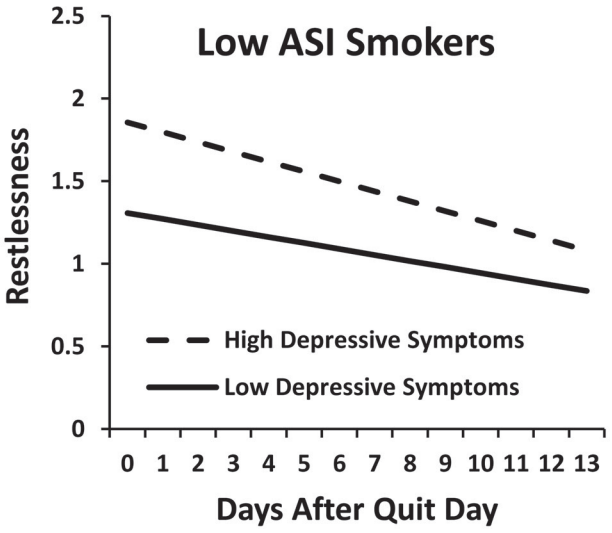


FIGURE 1. Change in frustration over time as a function of the Anxiety Sensitivity Index (ASI) and anhedonic depression symptoms

FIGURE 2. Change in restlessness over time as a function of the Anxiety Sensitivity Index (ASI) and anhedonic depression symptoms

over time, and depression, $b = 0.03$, $t(71) = 2.40$, $p < .05$, increased significantly over time. Results from these analyses also demonstrated that anhedonic depression symptoms were significantly related only to the slope of insomnia over time, $b = -0.002$, $t(62) = -2.22$, $p \leq .05$. Interestingly, higher levels of baseline anhedonic depression symptoms led to decreases in the slope of change in insomnia over time.

Moderating effects of anxiety sensitivity on slopes of withdrawal symptoms over time

Results of our analyses also revealed a significant interaction between anxiety sensitivity and anhedonic depression symptoms with regard to the slope of frustration over time, $b = 0.0003$, $t(58) = 2.45$, $p \leq .05$, and restlessness, $b = 0.0002$, $t(61) = 2.51$, $p \leq .05$. To elucidate the form of the interactions, we used the approach developed by Aiken and West (1991), which involves calculating model-based "simple slopes" (regression lines) for participants who are one standard deviation below the mean on anxiety sensitivity versus one standard deviation above the mean on anxiety sensitivity (Figures 1 and 2). These simple slopes are the regression lines predicted by the LMM model for participants with certain values on an independent variable. They are based on the full LMM model including all participants and are not based on regression calculations for the subset of participants that fall into the category being examined (i.e., the coefficient for those who are 1 *SD* above the mean on anxiety sensitivity is not calculated from those participants who are 1 *SD* above the mean on anxiety sensitivity but from data from the entire sample; Aiken and West, 1991).

These simple slopes take into account the relationships between each independent variable and the outcome at all levels of the other independent variable involved in the interaction. Here, we found that for those with high levels of anxiety sensitivity (1 *SD* above the mean), higher levels of anhedonic depression symptoms were related to greater increases in frustration over time (Figure 1), $b = 0.003$, $t(59) = 2.48$, $p \leq .05$, for the Depression Symptoms × Time interaction, and to greater increases in restlessness over time (Figure 2), $b = 0.004$, $t(61) = 2.49$, $p \leq .05$, for the Depression Symptoms × Time interaction. On the other hand, for those with low levels of anxiety sensitivity (1 *SD* below the mean), anhedonic depression symptoms were not related to the change in either of the withdrawal symptoms over time, $b = -0.001$, $t(59) = -.87$, $p =$ N.S. for the Depression Symptoms × Time interaction on frustration, and $b = -0.001$, $t(61) = -.94$, $p =$ N.S., for the Depression × Time interaction on restlessness.

Discussion

The present study examined the main and interactive effects of anhedonic depressive symptoms and anxiety sensitivity in relation to the individual components of nicotine withdrawal experienced on quit day as well as throughout the initial 2 weeks of cessation. A number of theoretically and clinically important findings were observed.

In terms of main effects, results revealed that higher initial levels of anhedonic depression symptoms were significantly associated with more severe symptoms of anxiety, depression, and insomnia experienced on quit day. This finding is partially consistent with research documenting that depressive symptoms may be most relevant for enhancing the risk of experiencing emotionally laden nicotine withdrawal symptoms (Breslau et al., 1992; Pomerleau et al., 2000). However, our results indicated that anhedonic depression symptoms were significantly related only to the rate of change in insomnia during the initial 2 weeks of cessation. Here, contrary to our hypothesis, higher levels of anhedonic depression symptoms led to decreases in insomnia over time. This pattern of findings suggests that anhedonic depression symptoms are important to understanding mood-based withdrawal symptoms during acute periods of smoking deprivation (e.g., quit day) yet less relevant to understanding the course of these symptoms over time.

Regarding anxiety sensitivity, contrary to our hypothesis, higher initial levels of anxiety sensitivity were not significantly associated with more severe withdrawal symptoms experienced on quit day itself. This finding is consistent with those of Mullane et al. (2008), which failed to find a significant association between anxiety sensitivity and nicotine withdrawal symptoms experienced during the first 2 weeks of cessation. Notably, in that particular study, ratings were averaged across each of the 2 weeks to generate an average score for Week 1 and Week 2, respectively (Mullane et al., 2008).

Yet, as predicted, our results indicated that anxiety sensitivity was significantly related to the slope of all components of nicotine withdrawal, except craving and concentration, over time. Specifically, higher initial levels of anxiety sensitivity were significantly related to increases in the severity of irritability, frustration, anxiety, restlessness, appetite, depression, and insomnia throughout the initial 2 weeks of cessation. Together, these findings highlight anxiety sensitivity as a putative cognitive-based transdiagnostic mechanism underlying the maintenance of certain withdrawal symptoms while quitting smoking. This type of perspective is consistent with previous empirical work demonstrating that smokers high in anxiety sensitivity appear to be hypersensitive to interoceptive sensations—specifically, those related to nicotine withdrawal during the early phases of quitting (e.g., Marshall et al., 2009; Zvolensky et al., 2004). Moreover, our results are in accord with the theoretical and empirically supported prediction that smokers high in anxiety sensitivity lapse to smoking more quickly following a quit attempt (Brown et al., 2001; Zvolensky et al., 2009), perhaps because of their perceptions of nicotine withdrawal symptoms as being more aversive and personally harmful.

Partially consistent with our prediction, the interactive effect of anxiety sensitivity by anhedonic depression symptoms was significantly associated with the rate of change in two anxiety-related withdrawal symptoms (i.e., frustration and restlessness) over time (but this interactive effect was not evident in the seven other items measuring withdrawal symptoms). Inspection of the form of the interaction indicated that it was in accord with the a priori theoretical formulation. That is, anxiety sensitivity significantly moderated the observed relationships between anhedonic depression symptoms and the severity of frustration and restlessness, such that anhedonic depression symptoms were related only to these two components of withdrawal for those persons high, compared with those persons low, in anxiety sensitivity. Moreover, as illustrated in Figures 1 and 2, high anxiety-sensitivity smokers, who also endorsed elevated levels of anhedonic depression symptoms, showed significant increases in frustration and restlessness across the 14 days of cessation.

These findings add to the growing literature suggesting that anxiety sensitivity is a particularly important factor to consider in combination with other emotional vulnerability characteristics (e.g., anhedonia; state anxiety) while quitting smoking. Indeed, this novel pattern of findings highlights the possible clinically relevant interplay between anxiety sensitivity and anhedonic depression symptoms concerning the experience of certain anxiety-related nicotine withdrawal symptoms among daily adult cigarette smokers attempting to quit. Namely, among high anxiety-sensitivity persons, anhedonic depression may be more relevant, compared with those low in anxiety sensitivity, in regard to experiencing symptoms of frustration and restlessness as more intense and persistent during the initial 2 weeks of cessation. That is, there may be a multiplicative effect, such that individuals who tend to experience a diminished capacity to enjoy life and who are fearful of anxiety-related symptoms may experience an increasing overload of cognitive-emotional disturbance and, thus, lack the ability to cope with such feelings in the absence of smoking.

Consistent with this perspective, other work suggests that anxiety sensitivity moderates relations between state anxiety and nicotine withdrawal symptoms while quitting (Johnson et al., 2012). Specifically, state anxiety was more strongly related to the overall experience of nicotine withdrawal symptoms (as opposed to individual symptoms of withdrawal) during the first 2 weeks of cessation among participants characterized by high levels of anxiety sensitivity (Johnson et al., 2012). Such findings may help to explain why high anxiety-sensitivity persons may lapse to smoking more quickly following a quit attempt (Zvolensky et al., 2009), thus pointing to a possible area for psychological intervention.

A number of limitations of the present investigation and points for future direction should be considered. First, the present sample is limited in that it comprises adult smokers who volunteered to participate in smoking cessation treatment. Given that the vast majority of cigarette smokers attempt to quit on their own (70% of smokers; Levy and Friend, 2002), it will be important for researchers to draw from populations other than those included in the present study to rule out potential self-selection bias among persons with these characteristics and therefore to increase the generalizability of these findings.

Second, the study focused primarily on anxiety sensitivity and anhedonic depression symptoms. These emotional factors are naturally only some of many possible emotional risk candidates that may contribute to the development of more severe withdrawal symptoms. Future work could usefully continue to build multi-risk factor models of nicotine withdrawal by incorporating other promising affective-relevant variables, such as emotion dysregulation (e.g., difficulties in the self-regulation of affective states and in self-control over affect-driven behaviors; Carver et al., 1996).

Third, the current findings were based on self-reported acute nicotine withdrawal symptoms assessed once daily during the initial 14 days of the cessation attempt. An important next step in this line of inquiry would be to obtain nicotine withdrawal symptom reports at multiple time points to evaluate the consistency of the present findings throughout the course of individuals' quit attempts. For example, future research would benefit from using an ecological momentary assessment approach to assess nicotine withdrawal symptom severity as it occurs in real time.

Fourth, participants included in the current investigation were given the opportunity to use nicotine replacement therapy during the course of cessation. Therefore, future research may consider examining how the use of nicotine replacement therapy affects the nature and course of the present findings.

Fifth, the current study did not include diagnostic assessments of past or present psychopathology. Such information would be helpful in order to provide a more fine-grained analysis of the psychopathological characteristics of the sample by allowing for the comparison of diagnostic status to anxiety sensitivity and/or anhedonic depression symptoms in relation to the individual components of nicotine withdrawal.

Sixth, as previously explicated, examining each individual component of withdrawal symptomatology may increase the risk of inflating type I error. Yet, the aim of the present investigation was to identify how anxiety sensitivity and anhedonic depression symptoms affect the nature and course of the specific symptoms of nicotine withdrawal. Such knowledge is crucial for developing specialized interventions for smokers characterized by affective vulnerability and/or emotion-based difficulties.

Seventh, withdrawal symptoms were examined throughout the duration of the cessation attempt. It is likely that a portion of the participants returned to smoking at some point during the assessment period. Thus, the administration of

nicotine during smoking lapse/relapse likely affected the expression of withdrawal symptoms.

Finally, the current sample size ($N = 65$) was relatively small. Consequently, using a larger sample size to replicate and extend these findings may be helpful in confirming or challenging our conclusions.

Conclusions

Despite these limitations, the present study helps to clarify how depressive symptoms interplay with other cognitive-affective variables (namely anxiety sensitivity) to exacerbate the experience of nicotine withdrawal and, perhaps, to increase the risk of cessation failure. Such findings serve to conceptually inform the development of specialized intervention strategies for smokers with emotional vulnerability characteristics. Specifically, smokers with elevated levels of anxiety sensitivity, who also suffer from anhedonia, may benefit from intensive cognitive-behavioral strategies (e.g., behavioral activation, interoceptive exposure, cognitive restructuring, and affective regulation strategies) to improve their ability to cope with feelings of frustration and restlessness that may occur in the context of smoking abstinence.

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