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Association of Depression Symptom Level with Smoking Urges, Cigarette Withdrawal, and Smoking Reinstatement: A Preliminary Laboratory Study

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Abstract

Background: Cigarette smoking urges, withdrawal, and smoking reinstatement may be especially relevant to **people with elevated depression symptoms who smoke**. This laboratory study aimed to assess relations between depression symptom level and smoking urges for reward and relief, cigarette withdrawal, and smoking reinstatement in people who smoke cigarettes daily during acute abstinence and while smoking as usual. **Methods:** Participants with low ($n=51$) or elevated ($n=29$) baseline depression symptoms underwent two counterbalanced laboratory sessions (i.e., abstinent, non-abstinent). At each session, they completed subjective measures of smoking urges for reward and relief, and withdrawal. They also completed a laboratory smoking reinstatement task measuring whether they would delay smoking and the number of cigarettes smoked. **Results:** The elevated depression symptom group reported significantly higher withdrawal ($p=.01$) and smoked more cigarettes than the low depression symptoms group during the smoking reinstatement task self-administration period at the abstinent session ($p=.04$). Smoking urges for reward and relief were not significantly different by depression symptom group. There were no significant interactions of depression and abstinence with any outcomes. **Conclusions:** As outcomes were measured at both an abstinent and non-abstinent session, findings identify factors for **people with elevated depression symptoms who smoke** which may drive smoking behavior and impede smoking cessation efforts. This study provides evidence that **people with elevated depression symptoms who smoke** may need additional/more

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pharmacological or behavioral smoking cessation aids targeted at reducing withdrawal and number of cigarettes smoked.

Keywords: cigarette smoking, depression symptoms, smoking urge, withdrawal symptoms, smoking reinstatement

1. Introduction

Individuals with elevated depression symptoms (e.g., sadness, irritability, low positive affect, decreased cognitive functioning) are more likely to initiate cigarette smoking, escalate from smoking to meeting criteria for nicotine dependence (Aubin et al., 1996; Weinberger et al., 2017), and to relapse after a quit attempt (Aubin et al., 1996; Cinciripini et al., 2003; Hitsman et al., 1999; Kinnunen et al., 1996; Niaura et al., 2001; Weinberger et al., 2017). As such, it is essential for studies to investigate smoking behavior and predictors of smoking maintenance and relapse (e.g., smoking urges, cigarette withdrawal) in individuals with elevated depression symptoms to inform the development of effective and individualized smoking cessation strategies for this at-risk population. Particularly, studying acute cigarette abstinence in the laboratory may serve as a model of the early phases of a cessation attempt and provide insight into factors that may maintain smoking behavior and prevent cessation success.

Smoking urges—desire and intentions to smoke for pleasure or to relieve negative affect and cigarette withdrawal—are well-studied predictors of smoking maintenance and relapse during a smoking cessation attempt (al'Absi et al., 2004; Allen et al., 2008; Hébert et al., 2021; Killen and Fortmann, 1997). A smoking cessation study found that **people with elevated depression symptoms who smoke** (vs. those with low depression symptoms) experienced more intense smoking urges at the early phases of a cessation attempt and throughout four weeks of smoking cessation treatment (Reid and Ledgerwood, 2016). However, an unassisted cessation study reported no association between depression symptoms and smoking urges at 3-month follow-up (Brodbeck et al., 2014). These prior studies demonstrated mixed results related to depression and smoking urges and they did not differentiate between urges related to positively reinforcing effects of smoking (reward) versus urges related to negatively reinforcing effects of

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smoking (relief) (Cox et al., 2001; Tiffany and Drobes, 1991). For example, a cross-sectional study in lung cancer patients reported that affective symptoms of depression were positively correlated with smoking urges for relief of negative affect and cigarette withdrawal, but there was no relationship between depression symptoms and smoking urges for reward (Walker et al., 2004). This finding suggests that smoking urges for relief of negative affect and cigarette withdrawal may be more relevant to **people with elevated depression symptoms who smoke**, but it would be important to also understand how this relationship may differ by cigarette abstinence.

During periods of abstinence, people who smoke experience cigarette withdrawal symptoms (i.e., seven subjective items: dysphoria/sadness, insomnia, irritability/frustration/anger, anxiety/nervousness, difficulty concentrating, restlessness, and increased appetite), which are powerful motivators of smoking maintenance and relapse (al'Absi et al., 2004; Allen et al., 2008; Budney et al., 2008; Kenford et al., 2002; Piasecki, T. et al., 2003; Piasecki, T.M. et al., 2003) and may be particularly relevant to **people with elevated depression symptoms who smoke**. A cross-sectional study found that higher compared to lower baseline depression symptoms were positively associated with greater withdrawal symptoms at prior quit attempts reported retrospectively (Tsoh et al., 2003). However, other studies did not find significant associations of general baseline depression symptoms and cigarette withdrawal during a cessation attempt (Copeland et al., 2009; Schnoll et al., 2013). One laboratory-based study in **people with elevated baseline depression symptoms who smoke**, found that smoking research cigarettes with varying levels of nicotine following cigarette abstinence associated with greater cigarette withdrawal (Streck et al., 2020). However, this study did not report an effect of depression symptom level on withdrawal when participants smoked their usual brand cigarettes or during periods of non-abstinence (Streck et al., 2020) so these effects may be specific to

smoking cigarettes with reduced nicotine levels during abstinence. Another laboratory-based study reported **people with elevated depression symptoms who smoke** (vs. low depression symptoms) experienced more intense cigarette withdrawal across 3 days of biochemically verified abstinence (Pomerleau et al., 2005), but did not assess withdrawal during non-abstinence.

Smoking reinstatement has been largely investigated by measuring time from ceasing smoking to smoking lapse (i.e., the first instance of smoking during cigarette abstinence) and likelihood of relapse (i.e., resuming regular smoking; Shiffman, 2006). Cessation studies have found that greater baseline depression symptoms significantly associate with earlier lapse and relapse (Fond et al., 2013; Zvolensky et al., 2009), greater number of lapses (Brodbeck et al., 2014), and increased likelihood of relapse after smoking a single cigarette (Muench et al., 2020). Ecological momentary assessment (EMA) studies show that **people with elevated depression symptoms who smoke**, compared to those with low depression symptoms, may also be more sensitive to the effects of stress on smoking lapse risk (Minami et al., 2018). However, Muench and Juliano (2017) did not find a significant association of depression symptoms on smoking reinstatement during a smoking cessation attempt. To the best of our knowledge, no laboratory-based studies have investigated the differences in outcomes of a smoking reinstatement task for those with elevated versus low depression symptoms during experimentally induced abstinence compared to non-abstinence.

Prior studies have found **people with elevated depression symptoms who smoke**, compared to low depression symptoms, may experience greater smoking urges for relief and withdrawal, and may be at higher risk for lapse and relapse during a cessation attempt. Extant work on the role of depression symptoms on smoking urge, withdrawal, and smoking

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reinstatement have been mixed and sparse. Thus, utilizing experimental laboratory methodologies, such as those that allow comparisons of cigarette abstinence with non-abstinence, may be warranted. Additionally, as most smoking lapses tend to occur during early abstinence (Kenford et al., 1994; Shiffman et al., 1997) and specifically within the first few hours of abstinence from smoking (Brown et al., 2005; Hébert et al., 2021), controlled laboratory procedures allow for the investigation of smoking urges, withdrawal, and smoking reinstatement during early acute abstinence. Furthermore, as individuals with elevated depression symptoms may be at risk for poor cessation outcomes, it is important to understand how the relationship of abstinence and these smoking-related variables differ by depression symptom level to help identify abstinence barriers for individuals with elevated depression symptoms.

In this laboratory-based study, individuals who smoke cigarettes daily reported baseline depression symptoms and then completed two counterbalanced experimental sessions (abstinent and non-abstinent). Aim 1 of the study was to investigate whether smoking-relevant factors (i.e., smoking urges, withdrawal, smoking reinstatement) differed by depression symptom level. We hypothesized that across both sessions, **people with elevated depression symptoms who smoke** would report greater smoking urges for reward and relief, cigarette withdrawal symptoms, and would be less likely to delay smoking and smoke more cigarettes in a laboratory analogue smoking reinstatement task compared to **people with low depression symptoms who smoke**. Aim 2 of the study was to investigate whether abstinence effects differed by depression symptom level (elevated vs. low). We hypothesized that cigarette abstinence effects on smoking relevant outcomes would be greater in those with elevated depression symptoms compared to those with low depression symptoms.

2. Methods

2.1 Participants

Non-treatment seeking people who smoke cigarettes daily were recruited from the Los Angeles, California (United States, US) metropolitan area via online advertisements including automated advertisements disseminated by the USC Clinical and Translational Science Institute (CTSI) and word of mouth. To be eligible for the study, participants had to (1) be ≥ 21 years of age; (2) report regular cigarette smoking for at least the past year; (3) currently smoke 5+ cigarettes/day; and (4) be fluent in English. Participants were excluded for (1) meeting diagnostic criteria for lifetime bipolar disorder, current posttraumatic stress disorder, or a current substance use disorder for substances other than nicotine assessed via a structured clinical interview—the Mini International Neuropsychiatric Interview (M.I.N.I.; Sheehan et al., 1998) by a research assistant; (2) an expired breath carbon monoxide (CO) level < 8 ppm at the baseline screening session (Benowitz et al., 2020); (3) current use of nicotine replacement or other medications implicated in smoking cessation (e.g., Chantix, Wellbutrin/Bupropion, Zyban); (4) daily use of non-cigarette tobacco and nicotine products (e.g., e-cigarettes/vaping devices, cigars); (5) current pregnancy or intent to get pregnant; and (6) current detailed plans to cut down or quit smoking.

The initial planned sample size was $N=240$, however, participant accrual was halted prematurely due to the COVID-19 pandemic in March 2020 and results of this study should be considered preliminary and exploratory.

2.2 Procedure

2.2.1 Baseline Session

Potential participants were screened via telephone to determine preliminary eligibility, followed by an in-person baseline session that included informed consent procedures and

additional eligibility screening (e.g., breath CO, M.I.N.I.). Participants then completed measures of demographics, cigarette dependence, and depression symptoms.

2.2.2 Experimental Sessions

Following the baseline session, participants attended two randomized counterbalanced experimental sessions (abstinent and non-abstinent), which took place at the University of Southern California. Experimental sessions were scheduled to start between 11am and 1pm to standardize the abstinence period. See Figure 1 for overview of the experimental sessions. Abstinent and non-abstinent experimental sessions were identical except that (1) participants were instructed to “stop smoking” for 16 hours prior to their abstinent session and to smoke normally prior to their non-abstinent session and (2) participants were administered one of their own cigarettes at the non-abstinent session to standardize for smoking recency.

On arrival at each session, a breath alcohol analysis was conducted to confirm abstinence from alcohol. Participants with a positive breath alcohol analysis were rescheduled ($n=1$). Participants then completed a CO assessment using a Vitalograph breath carbon monoxide monitor. Participants were required to have a CO level ≤ 9 ppm at the abstinent session, and all participants met this requirement. Participants then completed self-report assessments of affect and craving prior to and following smoking one of their own cigarettes (non-abstinent session) or a 5-minute break (abstinent session). In the non-abstinent session, participants also completed self-report measures of cigarette effects following smoking one of their own cigarettes. Participants then completed measures of positive and negative affect, craving and withdrawal, and saliva samples in repeated intervals. Participants then completed a randomized and counterbalanced film clip task (results not reported here) and a smoking reinstatement task. At the end of the second experimental session, participants were debriefed about the study.

2.2.3 Participant Compensation

Participants were paid at the completion of each session they attended and could earn a total of \$225-\$243 for completing the entire study (payment varied based on responses during the smoking reinstatement task). Participants could also earn \$10 for each session that they arrived on time and did not reschedule. This study was approved by the Institutional Review Board at the University of Southern California.

2.3 Measures

REDCap electronic data capture tools hosted at the University of Southern California (Harris et al., 2009) was used to administer baseline session measures.

2.3.1 Baseline Measures

An author-constructed questionnaire assessed demographics (e.g., age, race/ethnicity) and cigarette history (e.g., cigarettes per day, age started smoking). Race/ethnicity and gender were included as planned covariates as a prior study found that females who identify as Non-Hispanic White may have greater abstinence-induced withdrawal than females who identify as Non-Hispanic Black (Pang et al., 2019), and females may have greater abstinence-induced negative affect withdrawal than males (Faulkner et al., 2018; Pang and Leventhal, 2013). The Fagerström Test for Cigarette Dependence (FTCD) is a widely used 6-item self-report measure of cigarette dependence severity with higher scores indicating greater dependence severity (Fagerstrom, 2012; Fagerström, 2003). FTCD was included as a planned covariate due to the association between cigarette dependence and cigarette abstinence effects (Baker et al., 2012; Ben Taleb et al., 2016; Fagerström, 2003; Koob, 2006; Piper et al., 2006; Shiffman et al., 2004).

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The Center for Epidemiologic Studies Depression Scale (CES-D) was used to measure depression symptom levels (Radloff, 1977). This 20-item self-report scale measures the frequency of past week depression symptoms (e.g., dysphoric mood, feelings of guilt and worthlessness, loss of interest, psychomotor retardation, sleep disturbance) on 4-point Likert scale with responses ranging from 0 (*Rarely or none of the time, 0-1 days*) to 3 (*Most or all of the time, 5-7 days*), which are then summed to determine a total score ranging from 0 to 60, with higher scores indicating greater depression symptoms. Participants with a CES-D score ≥ 20 were classified as having an elevated level of depression symptoms (=1) and those with CES-D score < 20 were classified as having a low level of depression symptoms (=0). In a meta-analysis that pooled studies which used the CES-D to screen for major depression, the best trade-off between sensitivity (83%) and specificity (78%) was evidenced by this particular cutoff score (Vilagut et al., 2016).

2.3.2 Experimental Measures

The 10-item Questionnaire for Smoking Urges (QSU; Cox et al., 2001) measured cigarette smoking urges experienced “right now,” with mean scores computed for two separate factors. Factor 1 measured the desire to smoke for pleasure with smoking perceived as rewarding (positively reinforcing effects, e.g., “A cigarette would taste good”); $\alpha_s = .93-.96$. Factor 2 measured the anticipated relief from negative affect and an urgent desire to smoke (negatively reinforcing effects, e.g., “I would control things better if I could smoke”); $\alpha_s = .84-.85$. Responses ranged from 0 (*Strongly Disagree*) to 5 (*Strongly Agree*).

The Minnesota Nicotine Withdrawal Scale (MNWS; Hughes and Hatsukami, 1998; Hughes and Hatsukami, 1986) was used to measure the following cigarette withdrawal symptoms experienced “so far today”: 1) Angry, irritable, frustrated; 2) Anxious, nervous; 3)

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Depressed mood, sad; 4) Difficulty concentrating; 5) Increased appetite, hungry; 6) Restlessness; 7) Insomnia; $\alpha s = .80-.84$. A total mean composite score was computed for items 1-7, with higher scores indicating greater cigarette withdrawal. Responses ranged from 0 (*None*) to 5 (*Severe*).

The smoking reinstatement task is a laboratory analogue of smoking lapse and relapse (McKee, 2009; McKee et al., 2015). Participants were presented the box of cigarettes they brought with them containing 8 of their own cigarettes and their lighter. Participants were monitored through a 1-way mirror and task timing was recorded (e.g., the time from the start of the self-administration period to when the participant smoked their first cigarette). The task began with the delay period, where participants were instructed that they can start smoking at any point over the next 50 minutes, but that for each 5 minutes they delay smoking, they will earn \$0.50 (max: \$5.00). The moment participants started to smoke (or at the end of 50 minutes for those who choose not to smoke), they begin the self-administration period. During the self-administration period, they were told they have a \$4.00 credit, and they can smoke as little or as much as they wish over the next 60 minutes, but each cigarette they light from the 8 in their cigarette box will cost them \$0.50. The maximum amount earned was \$9.00 for not smoking during either portion of the task. Monetary values were based on prior studies (Kahler et al., 2014; Oberleitner et al., 2018; Stevenson et al., 2017). At the end of the self-administration period, participants entered a rest period (i.e., no assessment or smoking). The rest period was 0-60 minutes and was included to standardize the length of the smoking reinstatement task. To summarize, the outcome variables for the smoking reinstatement task were: 1) how long participants delay the opportunity to smoke (range: 0-50 min), and 2) the number of cigarettes smoked during the delay and self-administration period (range: 0-8).

2.4 Data Analysis

2.4.1 Sample Demographics

Preliminary analyses involved comparing sample characteristics in the full sample and by depression symptom group. Independent sample t-tests and chi-square tests were used to evaluate whether depression symptom group differed in continuous and categorical demographic and smoking characteristics, respectively. T-tests and chi-square tests were also conducted to evaluate whether participants who completed the study vs. those who did not complete the study differed by depression symptom group, demographic and smoking characteristics.

2.4.2 Experimental Variables by Abstinence and Depression Symptom Group

General linear mixed models were conducted to test main and interactive effects of depression symptom group and abstinence. Model 1 included depression symptom group, abstinence, and covariates. Model 2 added depression symptom group \times abstinence interaction. Initially, normal multilevel models were examined for the time delay outcome. However, this resulted in non-normally distributed residuals. Therefore, we used a generalized linear mixed model (GLMM: using GENLINMIXED) application of logistic regression to determine whether participants smoked during the delay period (1) or delayed smoking the full 50 minutes (0). Statistical analyses were conducted in SPSS, version 27.

3. Results

3.1 Sample Recruitment

One hundred and forty-one individuals attended an in-person baseline session. Fifty-three potential participants were determined to be ineligible at the baseline session (note: exclusionary groups are not mutually exclusive and participants could be ineligible for more than one reason): 30 were ineligible due to endorsing criteria for one of the exclusionary disorders in the M.I.N.I.

(Sheehan et al., 1998), 26 did not meet the CO inclusion level, and 2 were ineligible due to being unable to complete study tasks. Eighty-eight participants were enrolled in the study and completed the baseline session. Eight participants did not complete any experimental sessions: 2 participants were unable to complete study tasks, 4 were no longer interested, and 2 were lost to follow-up. This left 80 participants included in the analytic sample including 76 participants (male $n=47$; female $n=29$) that completed the study, 2 participants (male $n=1$; female $n=1$) that completed the abstinent session only, and 2 participants (female $n=2$) that completed the non-abstinent session only. See Figure 2 for flow of participants through the study. Participants who completed the study compared to those that did not complete the entire study (i.e., completed one experimental session or no experimental sessions), did not significantly differ by depression symptom group (elevated vs. low), age, sex, race/ethnicity, baseline cigarettes per day, years of regular smoking, or cigarette dependence ($ps > .05$).

3.2 Sample Demographics

Table 1 reports the total sample demographics and cigarette smoking characteristics, overall and by depression symptom group (elevated depression symptoms $n=29$, low depression symptoms $n=51$). There were no significant differences between depression symptom groups for sex, baseline cigarettes per day, number of years of regular cigarette smoking, or cigarette dependence (Table 1). The elevated depression symptom group was significantly younger on average and the depression symptom groups significantly differed in racial/ethnic composition (Table 1). The average CO level at the non-abstinent session (17.44 [$SD=9.07$] ppm) was significantly higher than the average CO level at the abstinent session (4.28 [$SD=1.82$] ppm; $p < .001$).

3.3 Experimental Variables by Depression Symptom Group and Interaction Effects

3.3.1 *Smoking Urges*

Depression symptom group did not significantly associate with smoking urges for reward ($p=.96$; Table 2) nor smoking urges for relief ($p=.74$; Table 2). There was not a significant depression symptom \times abstinence interaction for smoking urges for reward ($p=.31$; Table 2) nor smoking urges for relief ($p=.39$; Table 2).

3.3.2 *Cigarette Withdrawal*

The low depression symptom group reported significantly lower withdrawal compared to the elevated depression symptom group ($p=.01$; Table 2). There was not a significant depression symptom group \times abstinence interaction for withdrawal ($p=.56$; Table 2).

3.3.3 *Smoking Reinstatement*

Whether participants smoked during the delay period or delayed the full 50 minutes did not significantly differ by depression symptom group (odds ratio (OR)[95% confidence interval (CI)] = .76[-0.05, 1.58]), nor was there a significant depression symptom \times abstinence interaction for smoking during the delay period or delaying the full 50 minutes (OR[95%CI] = .003[-1.38, 1.38]).

The low depression symptoms group smoked overall fewer cigarettes than the elevated depression symptoms group during the self-administration period ($p=.04$; Table 2). There was not a significant depression symptom \times abstinence interaction for number of cigarettes smoked during the self-administration period ($p=.20$; Table 2).

4. Discussion

This controlled laboratory-based study investigated the relationship between depression symptom level with smoking urges, cigarette withdrawal, and laboratory analogue smoking reinstatement in a non-treatment seeking sample of people who smoke daily. In accordance with

our hypothesis, we found that cigarette withdrawal was significantly higher in **people with elevated depression symptoms who smoke** compared to those with low depression symptoms. Prior research has shown that elevated depression symptoms associated with greater cigarette withdrawal during a past quit attempt reported retrospectively (Tsoh et al., 2003), measured across 3 days of biochemically verified abstinence (Pomerleau et al., 2005), and in response to reduced nicotine cigarettes (Streck et al., 2020). The current study extends these findings by suggesting that **people with elevated depression symptoms who smoke** may experience elevated withdrawal during periods of both abstinence and non-abstinence. It is possible that, for **people with elevated depression symptoms who smoke**, cigarette withdrawal may be an important factor across the smoking behavior change continuum. For example, **people with elevated depression symptoms who smoke** may be less likely to make a quit attempt due to concern about experiencing withdrawal, and those that do make a smoking cessation attempt may experience intense withdrawal and subsequently, lapse and relapse. Behavioral and pharmacological treatments such as nicotine preloading that focus on reducing withdrawal symptoms (Hajek, 1989; Wadgave and Nagesh, 2016; West and Shiffman, 2001) may be particularly beneficial for **people with elevated depression symptoms who smoke**.

We did not find an association of depression symptom level nor an interaction of depression symptom level and abstinence with the anticipated relief from negative affect and an urgent desire to smoke (i.e., the negatively reinforcing effects of smoking), nor a strong desire to smoke for pleasure with smoking perceived as rewarding (i.e., the positively reinforcing effects of smoking). This result is contrary to prior research that found depression symptoms associate with greater smoking urges for relief of negative affect (Brodbeck et al., 2014; Haas et al., 2004; Walker et al., 2004). **There was a significant main effect of abstinence with smoking urge for**

relief and reward regardless of depression symptom group, which suggests that smoking urge may be an important abstinence target both for individuals with elevated depression symptoms and those with low depression symptoms.

When given the opportunity to smoke, people with elevated depression symptoms who smoke consumed more cigarettes compared to those with low depression symptoms. This finding suggests that during acute cigarette abstinence such as during the early stages of a cessation attempt, people with elevated depression symptoms who smoke, compared to those with low depression symptoms, may be more likely to smoke more cigarettes when given the opportunity to resume smoking. This is somewhat aligned with prior research that people with elevated depression symptoms who smoke experience quicker time to lapse and relapse (Fond et al., 2013; Muench et al., 2020; Zvolensky et al., 2009). However, as participants were smoking as usual, the current findings build on prior work by showing that the likelihood to resume normal smoking is not restricted to a cessation or quit attempt. Elevated depression symptoms may be driving smoking maintenance in naturalistic periods of cigarette abstinence (e.g., following overnight abstinence, prior to the first cigarette of the day).

The results of this study must be taken in context of its limitations. Firstly, the study utilized dichotomized CES-D scores with a cutoff score of 20 to classify elevated versus low baseline depression symptoms, as opposed to a clinical diagnosis. However, a review paper found that both diagnoses of depression and depression symptoms were related to higher prevalence of smoking and greater odds of smoking relapse (Weinberger et al., 2017). Thus, it is important to investigate associations of depression symptom levels in the absence of full diagnosis. Despite not utilizing a clinical diagnosis, these findings provide important information about how depression symptoms influence withdrawal and smoking reinstatement for those who

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have depression symptoms but do not meet criteria for a full diagnosis, and those that do not take medications. This study also utilized a non-treatment seeking sample of people who smoke, and tobacco abstinence was experimentally induced. However, the findings provide important information on depression symptoms and smoking patterns in those who may not be ready or willing to quit, and experimentally induced abstinence has been shown to predict smoking outcomes in a naturalistic quit attempt (Strong et al., 2011), suggesting that these findings may be generalizable outside of the laboratory. We also excluded people who reported daily use of non-cigarette tobacco products. As people with depression have been shown to be more likely to report dual/poly tobacco use than people without depression (Chido-Amajuoyi et al., 2021), the effects of depression on the relevant smoking-related variables in dual/poly users would be an important area for future research. Lastly, since participant accrual was halted due to the COVID-19 pandemic in March 2020, the sample size was smaller than originally planned. While confirmatory power analyses showed that we were adequately powered to detect main effects, it is likely that we were underpowered to detect the planned interaction effects. Thus, results pertaining to the reported non-significant interactions should be considered preliminary and exploratory.

Despite limitations, the study contributes to literature on the relationship between depression symptom levels in relation to smoking urge, withdrawal, and smoking reinstatement in non-treatment seeking people who smoke daily. Strengths of the study include the controlled laboratory-based design and its ability to specifically isolate and compare smoking urges, withdrawal, and smoking reinstatement experienced during non-abstinent and abstinent sessions. The study provides evidence that cigarette withdrawal may be an important smoking-related variable in individuals with elevated depression symptoms who smoke during both abstinence

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and non-abstinence. Thus, individuals with elevated depression symptoms who smoke may need behavioral and pharmacological smoking cessation treatments targeted at reducing withdrawal. We also found that people with elevated depression symptoms who smoke, smoked more cigarettes than individuals with low depression symptoms who smoke, and that those with elevated depression symptoms who smoke showed significant abstinence effects on number of cigarettes smoked. The results show us that people with elevated depression symptoms who smoke, may smoke more cigarettes when given the opportunity to smoke following a period of non-smoking; aligning with previous work that elevated depression symptoms drive greater smoking behavior and those with low depression symptoms may attain better cessation outcomes. Findings highlight the importance of assessing how depression symptom level interacts with smoking maintenance and barriers for quitting in a particularly vulnerable population. The study provides insight into how behavioral and pharmacological smoking cessation treatments may affect people with elevated depression symptoms who smoke and how more efficacious and effective treatments may be developed.

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Conflict of Interest

No conflict declared.

Contributions

CJT and RDP generated the initial idea for the analysis reported in the manuscript and conducted data analysis. CJT wrote the original draft of the manuscript. RDP, MSB, AHW, LMD, and MGK provided critical review and commentary. All authors approved the final manuscript.

Table 2

Associations of depression symptom levels and session type on smoking urges (reward and relief), cigarette withdrawal, and smoking reinstatement.

Variable	Smoking Urges (Reward)				Smoking Urges (Relief)				Cigarette Withdrawal				Smoking Reinstatement (Number of Cigarettes Smoked)			
	Model 1 ^a		Model 2 ^b		Model 1 ^a		Model 2 ^b		Model 1 ^a		Model 2 ^b		Model 1 ^a		Model 2 ^b	
	Estimate (SE)	p	Estimate (SE)	p	Estimate (SE)	p	Estimate (SE)	p	Estimate (SE)	p	Estimate (SE)	p	Estimate (SE)	p	Estimate (SE)	p
Intercept	1.34 (0.35)	<.001	1.22 (0.37)	.01	0.88 (0.14)	<.001	0.55 (0.32)	.09	1.33 ^a (0.25)	<.001	1.30 ^a (0.25)	<.001	1.38 (0.25)	<.001	-1.27 (0.26)	<.001
Age ^c	0.01 (0.01)	.32	-0.01 (0.01)	.31	0.01 (0.01)	.24	-0.01 (0.01)	.24	0.00 (0.01)	.62	-0.00 (0.01)	.61	-0.01 (0.01)	.49	-0.01 (0.01)	.47
Race/Ethnicity	0.25 (0.32)	.40	0.26 (0.32)	.41	0.20 (0.28)	0.30	0.24 (0.28)	.40	0.33 (0.22)	.55	0.33 (0.22)	.50	0.13 (0.23)	.56	0.01 (0.23)	.92
Cigarette Dependence ^c	0.16 (0.07)	.03	0.16 (0.07)	.03	0.26 (0.07)	<.001	0.26 (0.07)	<.001	0.11 (0.05)	.04	0.11 (0.05)	.04	0.06 (0.05)	.27	0.06 (0.05)	.28
Sex	0.02 (0.29)	.94	0.02 (0.29)	.94	-0.15 (0.26)	.57	-0.15 (0.26)	.57	0.12 (0.20)	.53	0.12 (0.20)	.53	-0.07 (0.21)	.72	-0.08 (0.21)	.71
Low Depression	0.01 (0.37)	.92	0.01 (0.37)	.92	0.21 (0.29)	.38	0.03 (0.33)	.93	-0.69 (0.25)	.001	-0.69 (0.25)	.001	-0.48 (0.23)	.04	-0.30 (0.27)	.27
Elevated Depression	REF		REF		REF		REF		REF		REF		REF		REF	
Abstinent Session ^e	2.23 (0.35)	<.001	2.48 (0.38)	<.001	1.87 (0.14)	<.001	1.03 (0.23)	<.001	0.54 (0.17)	<.001	0.54 (0.17)	<.001	0.34 (0.13)	.01	0.55 (0.21)	.01
Non-Abstinent Session	REF		REF		REF		REF		REF		REF		REF		REF	
Age of regular smoking	0.40 (0.39)	.31	-0.40 (0.39)	.31	18.96 (4.52)	<.001	-0.25 (0.29)	.39	18.03 (2.5)	<.001	18.03 (2.5)	<.001	17.03 (2.5)	<.001	17.03 (2.5)	<.001
FTCD ^d	0.39 (0.39)	.31	0.39 (0.39)	.31	4.91 (1.85)	<.001	4.96 (1.88)	<.001	4.83 (1.83)	<.001	4.83 (1.83)	<.001	4.83 (1.83)	<.001	4.83 (1.83)	<.001

^aTotal (N=80), Low Depression Symptoms (n=51), Elevated Depression Symptoms (n=29). ^bTests of differences in sample characteristics by group were conducted with independent samples t-tests for continuous variables and chi-squared tests for categorical variables. ^cOther category included individuals who identified as: Asian (n=3), Middle Eastern (n=2), Multi-Racial (n=5), and Other (n=2) ^dFTCD=Fagerström Test of Cigarette Dependence.

^aModel 1 provides values for main effects of depression symptoms and session type on outcomes. ^bModel 2 provides values for the depression symptom × session type interactions on outcomes. ^cAge and Cigarette Dependence were grand mean centered. ^dRace/Ethnicity coded 0 = Non-Hispanic White, 1 = Other. ^eAbstinent Session manipulation check results.

Figure 1

Experimental Session Timeline

Participant arrives

Session Start	Breath CO & Breathalyzer
-10 mins	Saliva Sample 1
-5 mins	AX1
	Cig/Break
+1 mins	AX2
+5 mins	Saliva Sample 2
+20 mins	Saliva Sample 3
+25 mins	AX3
+35 mins	Saliva Sample 4
+50 mins	Saliva Sample 5
+60 mins	Film Clip Task
+100 mins Smoking Reinstatement Task (110 mins)	Delay Period: 0-50 mins
	Self-Administration: 60 mins
	Rest Period: 0-50 mins
+210 mins Session End	S2: Instructions S3: Debrief

Participant departs

Time points are in relation to the Cig/Break

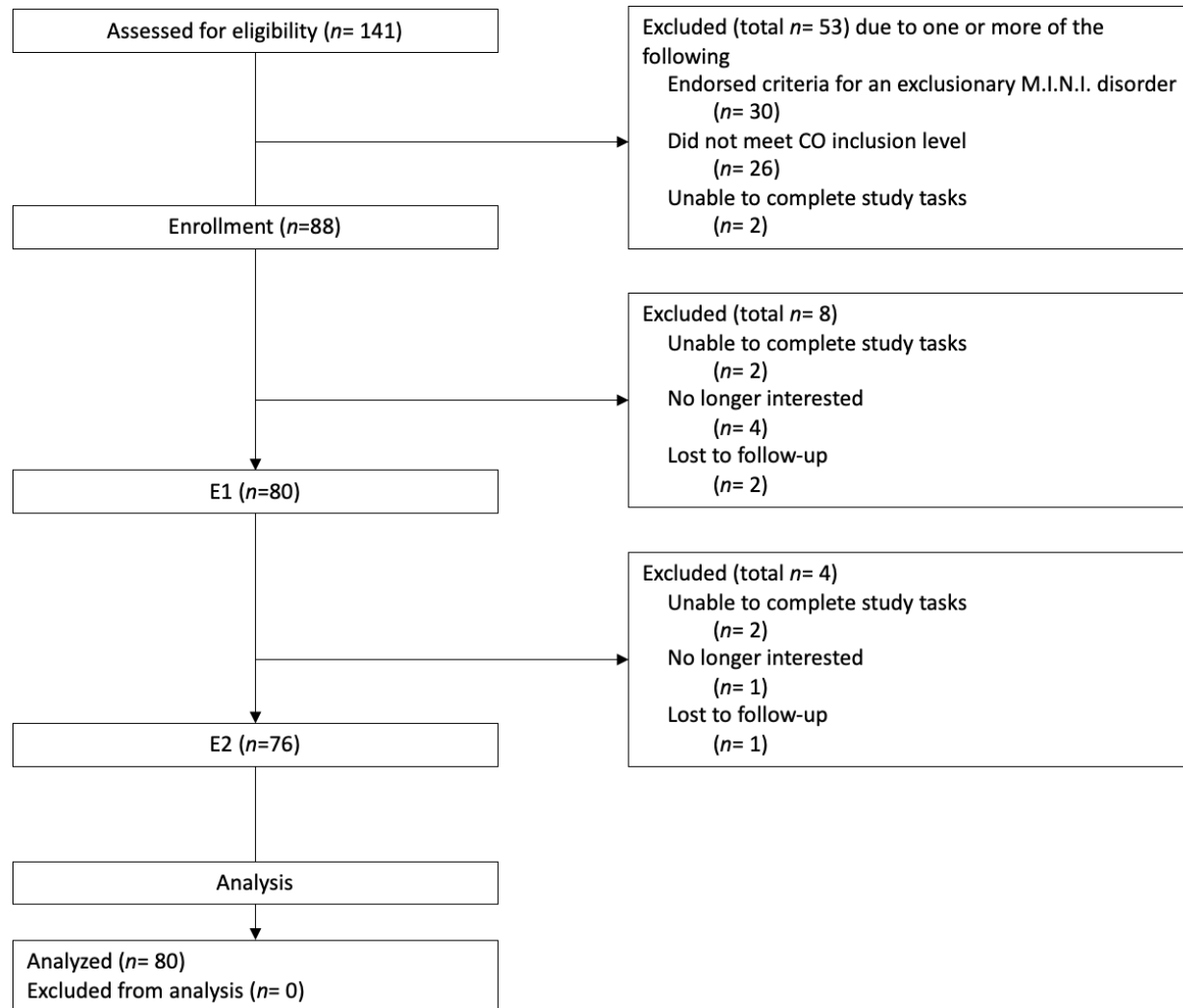
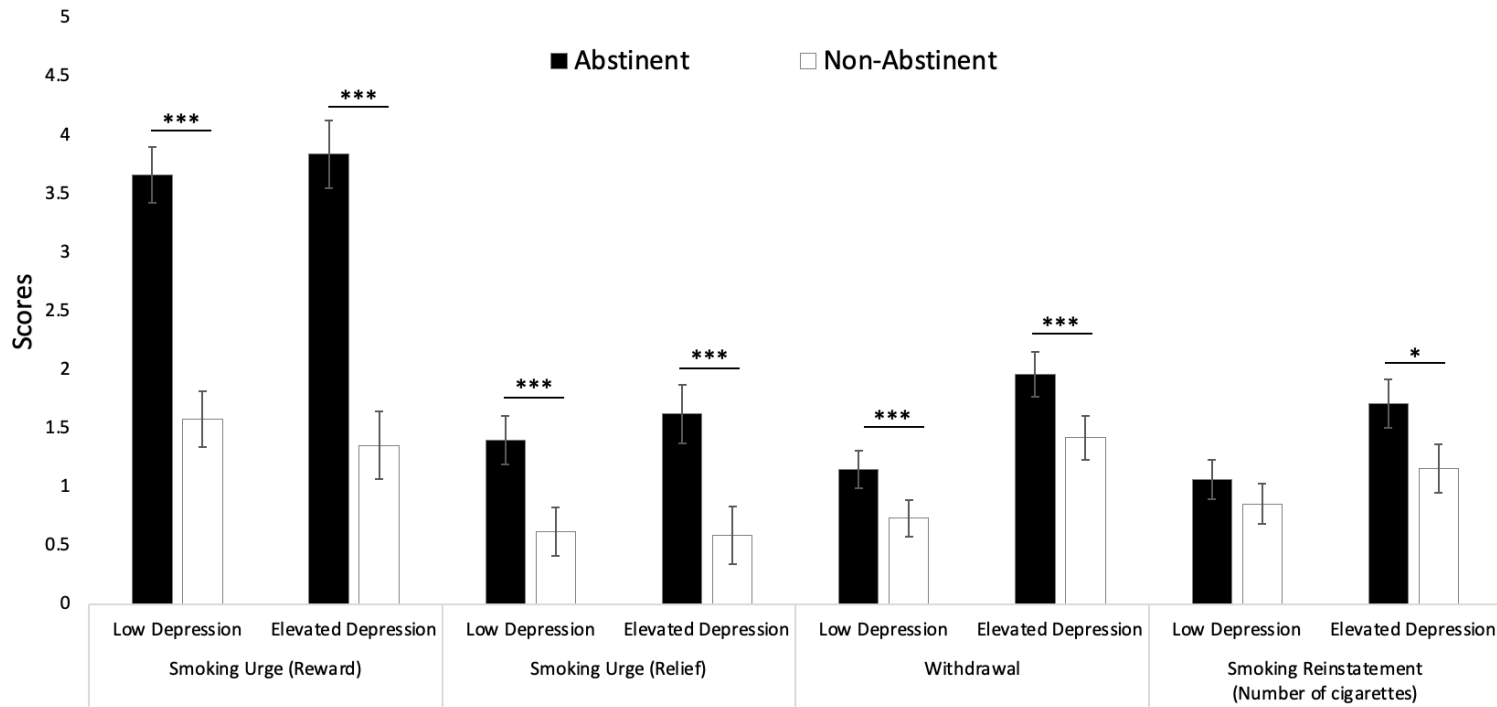
Figure 2*Flow of participants through each state of study*

Figure 3

Pairwise comparison of abstinence effects on smoking urges (reward and relief), withdrawal, and smoking reinstatement (number of cigarettes) by depression symptom group.



Estimated marginal means of smoking urges (reward and relief), withdrawal, and smoking reinstatement (number of cigarettes) at the abstinent and non-abstinent session. * $p < .05$; *** $p < .001$.

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