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Depressive symptoms affect changes in nicotine withdrawal and smoking urges throughout smoking cessation treatment: Preliminary results

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Abstract

Background—Individuals who report more depressive symptoms consistently demonstrate higher rates of nicotine dependence and less successful smoking cessation than do individuals who report fewer depressive symptoms. Nicotine withdrawal and smoking urges are two potential factors that may account for the differences observed between these two groups. This study assessed whether elevated depression symptoms among nicotine dependent smokers are associated with changes in withdrawal and urges to smoke when undergoing smoking cessation treatment.

Method—Data on 81 nicotine dependent smokers were collected as part of a smoking cessation randomized trial that compared standard and contingency management treatment across one baseline week and four treatment weeks. Linear mixed model analyses were conducted with high and low depression scores predicting changes in withdrawal and urge ratings from a baseline week and four treatment weeks.

Results—Participants with elevated depression symptoms reported more intense nicotine withdrawal and smoking urges throughout treatment. Further, participants with greater depressive symptoms exhibited an increase in smoking urges at the start of treatment, compared with a gradual decline in urges among participants with fewer depressive symptoms.

Conclusions—Smokers with elevated depressive symptoms experience significantly elevated discomfort during smoking cessation efforts in the form of increased withdrawal and craving. This discomfort has the potential to make quitting smoking more difficult. *Clinical Trial Identifier*: NCT00865254.

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Declaration of Interests

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Keywords

nicotine dependence; affective disorders; smoking cessation; treatment and intervention; withdrawal symptoms; cravings

1. Introduction

A number of pharmacological and behavioral interventions have been shown to be efficacious for smoking cessation across patient populations (e.g., Cahill, Stevens, & Lancaster, 2014; Fiore et al., 2008; Petry & Alessi, 2010); however, the experience of emotional or psychiatric distress among smokers continues to be a chief challenge to those trying to quit (Walsh, Epstein, Munisamy, & King, 2008; Wilhelm, Wedgwood, Niven, & Kay-Lambkin, 2006). Smokers who report being depressed have higher smoking rates, greater nicotine dependence, and increased difficulty quitting (Ziedonis et al., 2008). Depressed individuals also report increased urges in response to smokingrelated cues relative to those with resolved depression diagnoses, and those with no history of depression (Pomerleau et al., 2005; Weinberger, McKee, & George, 2012). However, no studies have systematically examined differential patterns in withdrawal and urges over time in smokers engaged in treatment with high and low levels of depression symptoms. The aim of the present study is to gain a preliminary understanding of these patterns.

Relationships between psychiatric symptoms and nicotine withdrawal patterns have been fairly well established. Leventhal, Ameringer, Osborn, Zvolensky, and Langdon (2013) found that withdrawal symptoms characterized by negative affect are related to smokers' subjective anxiety-related arousal and distress, depressive symptoms, and anhedonia. Another study found that current negative affect mediates between past dysphoria and negative affect, and current smoking urges during abstinence (Leventhal et al., 2013). Further, depressed smokers report increased stress, fewer coping resources, and more physical and psychological symptoms, as well as increased smoking behaviors in the presence of negative affect (Kinnunen, Doherty, Militello, & Garvey, 1996). Despite the literature supporting the relationship between smoking, depression and the effectiveness of quit attempts, there continues to be a need to explore factors that contribute to the relationship between smoking and post-cessation experiences, particularly those that may reduce the effectiveness of smoking cessation.

This study aims to explore whether elevated depression scores among a sample of nicotine dependent smokers assessed prior to a quit attempt predicts patterns of withdrawal and urges throughout treatment for smoking cessation. We hypothesized that greater depressive symptoms at baseline would affect post-cessation patterns of withdrawal and smoking urges throughout smoking treatment. Results that support this hypothesis will indicate the need for a larger-scale study that systematically assesses patterns of depression and smoking experience throughout treatment. The present study will also be used to identify modifications to the design of a future large-scale study.

2. Methods

2.1. Participants

Participants were nicotine dependent cigarette smokers (n = 81) who responded to local newspaper advertisements, flyers, bulletin boards, and electronic bulletin board announcements, and who approached research staff at local health fairs. Informed consent was obtained from all participants, and the study was approved by the Wayne State University Institutional Review Board. Inclusion criteria were: a Fagerström Test of Nicotine Dependence (Heatherton, Kozlowski, Frecker, & Fagerström, 1991) score of 4 or greater (though the scale does not report a standard threshold for nicotine dependence, scores of 3–4 denote “low dependence”; Fagerström, Heatherton, & Kozlowski, 1990), age of 18 or older, and the ability to read and understand English. Exclusion criteria were: severe, uncontrolled psychiatric disorders (e.g. acute suicidality or psychosis), current substance dependence excluding nicotine or caffeine dependence, participation in alternate smoking cessation programs, and being in recovery for pathological gambling (due to the element of chance involved in prize contingency management).

2.2. Procedure

Participants engaged in a controlled trial of contingency management (CM) and standard smoking cessation treatment reported elsewhere (Ledgerwood, Arfken, Petry, & Alessi, 2014). Individuals initially participated in a telephone eligibility screening and were scheduled for an intake assessment if appropriate. During the intake, participants provided written informed consent and completed interview and self-report assessments. Eligible participants then completed the one-week baseline and four-week treatment phases as described below (section 2.4). Participants were requested to attend the clinic twice daily, five days per week, for a period of five weeks (one baseline week, and four weeks of treatment). Unexcused absences were treated as a positive carbon monoxide (CO) reading, unless it was deemed an excused absence (e.g. illness, family emergency).

2.3. Measures

2.3.1. Baseline Characteristics and Inclusion/Exclusion—Gender, age, marital status, education and annual income were collected at intake. To assess exclusion criteria, a brief screen of suicidality, psychosis, and substance use symptoms was adapted using scales from the Structured Clinical Interview for the DSM-IV-TR (First, Spitzer, Gibbon, & Williams, 2002).

2.3.2. Smoking History—At the time of the intake interview, participants were asked about current number of cigarettes typically smoked daily, and periods of abstinence.

2.3.3. Nicotine Dependence—The Fagerström Test of Nicotine Dependence (FTND) is a brief measure of physical dependence to nicotine (Heatherton et al., 1991) and was used as a measure of nicotine dependence in the present study. The FTND does not recommend a standard cut-off for high versus low dependence; however, higher scores indicate greater nicotine dependence, with possible scores ranging from 0–10 (Fagerström et al., 1990).

2.3.4. Beck Depression Inventory, Second Edition (BDI-II)—The BDI-II is a widely used measure of recent depression symptoms (Beck, Steer, & Brown, 1996). It consists of 21 self-report items assessing various symptoms of depression in the preceding two weeks. Depression symptom scores were coded as high or low based on a standard BDI-II clinical significance cut-off of 13, with an average score of 1–13 at baseline categorized as low depression symptoms, and an average score of 14 and above categorized as high depression symptoms. Depression scores were dichotomized as high or low to accommodate the analysis of non-normally distributed data (Delucchi & Bostrom, 2004). The BDI-II was administered at intake, and weekly during the baseline and treatment weeks.

2.3.5. Questionnaire of Smoking Urges-Brief (QSU-B)—The QSU-brief is a 10-item self-report measure that assesses craving to smoke, including positive effects of smoking and perceived benefits in reduction of withdrawal symptoms (Cox, Tiffany, and Christen, 2001). Possible scores range from 10–70. The QSU-B was administered at intake and weekly during the baseline and treatment weeks.

2.3.6. Minnesota Nicotine Withdrawal Scale (MNWS)—The MNWS is an 8-item self-report of nicotine withdrawal symptoms such as anxiety, hunger, and irritability (Cappelleri et al., 2005; Hughes & Hatsukami, 1986). MNWS Total Scores were used to assess withdrawal. Each symptom is rated on a 5-point scale ranging from “no” to “severe” withdrawal symptoms. Possible scores range from 0 to 60. As with the BDI-II and QSU-B, the MNSW was administered at intake, and weekly during the baseline and treatment weeks.

2.3.7. Carbon Monoxide (CO)—Expired CO levels were assessed at intake, twice daily during baseline and treatment using an EC50-MP Micro CO monitor (Bedfont). CO levels of 6 parts per million (ppm) or less were considered “negative”. This standard is consistent with other studies that use a range of 4 ppm to 8 ppm to indicate negative scores (e.g., Corby, Roll, Ledgerwood, & Schuster, 2000; Lamb, Kirby Morral, Galbicka, and Iguchi, 2004). CO levels were used to measure smoking reduction to avoid potential memory and impression-management biases of self-reported measurement of smoking reduction.

2.4. Treatments

During the baseline week, participants provided twice-daily CO samples. The baseline week gave participants an opportunity to prepare for their quit date, which was the first day of the treatment phase. Participants who provided at least five of the 10 total baseline CO samples were randomly assigned to receive either standard care, or one of two prize contingency management (CM) conditions. The treatments are described fully in Ledgerwood et al. (2014) but are summarized briefly here.

Standard care involved intensive monitoring of expired CO readings and brief counseling based on clinical practice guidelines (Fiore et al., 2008). Throughout the four-week treatment period, participants met with the research therapist twice daily, five days per week, to provide CO samples.

For the current analyses, two CM treatment conditions (Traditional Prize CM, and Early-Treatment Enhanced Prize Reinforcement) were combined to create a single CM condition.

In addition to receiving the same CO monitoring and brief counseling procedures described above for standard care, patients in the CM conditions earned chances to win prizes when providing negative expired CO samples during the four-week treatment phase (e.g. Petry & Martin, 2002).

2.5. Analysis

T-tests compared demographic and smoking history between participants with high versus low depression. Primary analyses used linear mixed model analyses, as it is appropriate for longitudinal data that may contain data missing at random. Outcomes were withdrawal (MNWS) and urge ratings (QSU-B) from the baseline week and four treatment weeks. High and low depression scores were based on participant BDI-II scores, and included as a fixed factor. Fixed factors also included treatment condition (CM or standard care), and the interaction between depression symptoms and time. Time-point was the within-subject factor. Analyses examining withdrawal and urges were conducted separately.

Changes in CO levels were also analyzed using linear mixed model analysis to examine whether depression symptom level affected concurrent reductions in smoking throughout treatment. High or low depression score was the independent variable, with condition, week or phase of treatment, and interaction between depression and treatment phase included as fixed factors.

3. Results

3.1. Demographics

The mean participant age was 43.27 (SD = 12.86) years. There were more women (N = 48; 59%) than men (N = 33; 41%), and the majority of participants were African-American (N = 53; 65%). The remainder of the sample identified as European American (N = 25; 31%) and Asian (N = 3; 4%). Most participants were employed (N = 70; 86%) and had greater than a high-school education (N = 61; 75%). The average age of first cigarette use was 16.71 (SD = 3.86) years. The mean number of cigarettes smoked per day, pre-treatment was 16.51 (SD = 8.76), and mean Fagerström score was 6.29 (SD = 1.28), indicating an overall moderate level of nicotine dependence. Eighteen participants (22%) reported high depression scores (M = 18.50, SD = 4.20), and 63 participants (78%) reported low depression scores (M = 5.18, SD = 3.97) at baseline.

Differences in age, gender, education, and baseline cigarette use (including daily cigarette use, and nicotine dependence) were examined to assess group differences based on socio-demographic characteristics. There was a significant difference in age between the high-depression scores group (M = 51.06, SD = 8.17) and low-depression scores group (M = 42.14, SD = 12.51, $p < .05$). No further significant demographic or smoking-related differences were found.

3.2. Nicotine Withdrawal

Linear mixed model analysis revealed main effects of depression scores ($F(1, 74.08)$ = 12.78, $p < .01$) and time ($F(4, 323.85)$ = 10.44, $p < .01$) on nicotine withdrawal symptoms,

but the depression level by time interaction was not significant ($F(4, 323.85) = 1.84$, $p = .12$). Individuals who reported greater depressive symptoms at intake reported greater nicotine withdrawal throughout treatment (see Figure A.1). There was no significant effect of treatment condition on withdrawal ($F(1, 77.74) = .97$, $p = .33$), and no significant condition by time interaction ($F(5, 406.23) = 1.30$, $p = .26$).

3.3. Urges to Smoke

The linear mixed model that assessed differences in patterns of smoking urges between smokers with more depressive symptoms and those with fewer depressive symptoms revealed main effects of depression scores ($F(1, 75.83) = 4.87$, $p < .05$) and time ($F(4, 324.59) = 17.56$, $p < .01$) on smoking urges, and a significant depression score by time interaction ($F(4, 324.59) = 2.90$, $p < .05$). Individuals who reported greater depressive symptoms at intake reported an increase in urges to smoke in the first treatment week before reporting progressive reductions in urges, whereas smokers with fewer depressive symptoms reported reductions in urges from baseline through the final treatment week (see Figure A.2). There was no significant effect of treatment condition on urges ($F(1, 80.06) = .10$, $p = .75$), and no significant interaction effect between condition and time on urges ($F(5, 406.48) = 1.09$, $p = .37$).

3.4. Smoking Reductions

Changes in CO levels throughout treatment are shown in Figure A.3. Linear mixed model analyses with expired CO as the dependent variable revealed no significant effect of depression group on CO levels ($F(1, 82.52) = 1.24$, $p = .27$, and no significant interaction between depression scores and time in predicting changes in CO levels ($F(4, 2877.71) = 1.15$, $p = .33$). There was a significant effect of treatment condition on CO levels ($F(1, 76.51) = 5.57$, $p < .05$) with CM participants providing significantly lower CO levels, but no significant interaction between depression group and treatment condition in predicting CO changes ($F(1, 71.57) = 2.12$, $p = .15$).

4. Discussion

Smokers with greater versus fewer depressive symptoms showed significant differences on withdrawal levels throughout treatment, but the interaction between time and depression scores in predicting withdrawal was not significant. Smokers with greater baseline depression scores reported increased urges to smoke in the first week of treatment, before reporting progressive reductions in urges. Smokers with fewer depressive symptoms at baseline, however, reported more consistent reductions in urges from baseline through the final treatment week.

Elevated withdrawal symptoms and increased urges during smoking cessation treatment have implications for smoking cessation efforts among individuals who report depression. Increased urges and heightened withdrawal may partially account for findings that smokers with more depression experience poorer self-efficacy in quitting smoking (e.g., Cinciripini et al., 2003). This possible mechanism is further supported by research showing that increased self-efficacy to quit, and perceived control over withdrawal symptoms predicts smoking

cessation following treatment (Schnoll et al., 2011). Thus, a smoker's expectations about whether he/she is capable of abstaining in the face of withdrawal and urges may degrade his/her motivation to engage fully in cessation efforts.

Although we found differences between higher and lower depression scores on urges and withdrawal, we did not find differential smoking outcomes (differences in expired CO) between these two groups, which is in contrast with other studies (e.g., Brown et al., 2001). It is likely that mechanisms related to both risk factors and maintaining factors of depression operate in response to negative affective states experienced during withdrawal. Distress tolerance, or the ability to experience and adaptively manage negative psychological states (Simons & Gaher, 2005), is lower in people with depression (Ellis, Vanderlind, & Beevers, 2012; Williams, Thompson, & Andrews, 2013), and related to substance use outcomes (Buckner, Keough, & Schmidt, 2007; Zvolensky, Stewart, Vujanovic, Gavric, & Steeves, 2009). Similarly, those high in discomfort intolerance, defined as the capacity to experience and endure uncomfortable physical sensations (Schmidt & Lerew, 1998), may avoid discomfort as a product of believing they are unable to withstand stress related to a particular event (Hayes & Shenk, 2004; Schmidt, Richey, & Fitzpatrick, 2006). This avoidance and learning response may be useful to target specifically among depressed smokers apt to have learned ineffective coping strategies for managing aversive experiences.

These findings have several clinical implications for the treatment of smokers reporting increased depressive symptoms. Aligned with a negative reinforcement model of relapse, by which lapses to smoking are a means of reducing the negative affect experienced during withdrawal (Baker, Piper, McCarthy, Majeski, & Fiore, 2004), negative mood states related to combined depression and withdrawal likely create a distinct set of aversive experiences during withdrawal for depressed smokers. It may be important for clinicians to assess for psychiatric distress, specifically depressive symptoms, prior to cessation treatment. Smokers who report depression may require intensive treatment tailored specifically to the initial experience of urge and withdrawal immediately following abstinence from smoking.

In particular, a therapeutic focus on acceptance and tolerance has been found to be effective in treating substance dependence for those with co-occuring mood challenges (Brewer, Bowen, Smith, Marlatt, & Potenza, 2010; Dimeff & Linehan, 2008; Linehan et al., 2002). Treatments designed to enhance mindfulness, distress tolerance, and coping may be helpful for depressed smokers, and could be important targets for future research (Brewer, Bowen, Smith, Marlatt, & Potenza, 2010; Brown et al., 2008; Dimeff & Linehan, 2008; Linehan et al., 2002). Similarly, providing depressed smokers with realistic expectations regarding what urges and withdrawal experiences they are likely to face may inoculate some individuals against relapse when these are experienced.

The results of this study should be considered in the context of its limitations. The sample size was relatively small, potentially not allowing the ability to detect the full strength of the relationships between depression scores, time, treatment, and withdrawal and urges, particularly among demographic subgroups of smokers (e.g., gender). The sample was also unevenly split between high and low depression-scoring smokers, with the high-scoring group representing a smaller sample than the low-scoring depression group. Additionally, as

a result of the limited sample size, two separate treatment groups (CM and standard care) were combined to form a single group, which may differ somewhat from standard care more broadly. It is also important to note that, as the present study assessed differences in depression scores, findings are relevant for smokers reporting increased depression symptom scores rather than those reporting diagnoses of Major Depressive Disorder. It will be important to test the present hypotheses in a larger study with a larger and more equally distributed sample to supplement our preliminary clinical implications.

5. Conclusions

The present study provides an important exploration of differential patterns of withdrawal and urges among otherwise healthy, nicotine dependent smokers undergoing smoking cessation interventions, with and without heightened depression symptoms. Our findings reveal important patterns in urges and withdrawal symptoms that occur throughout treatment and have preliminary clinical implications for smokers with elevated depressive symptoms who want to quit. Future investigations into the effects and mechanisms underlying the relationship between depression and abstinence from smoking could provide significant benefits to clinical insight and treatment.

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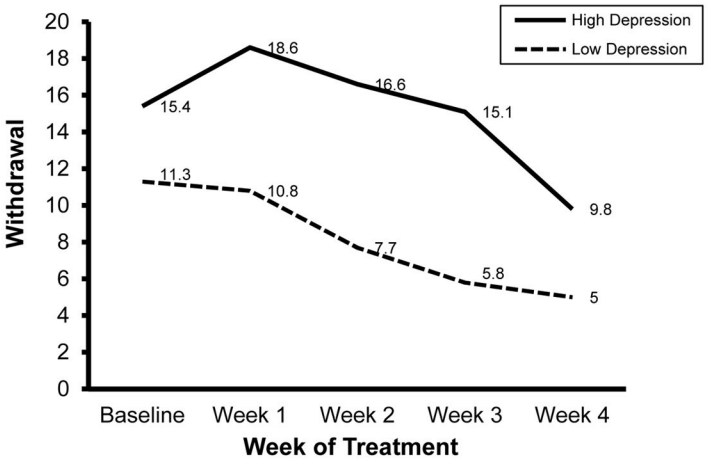
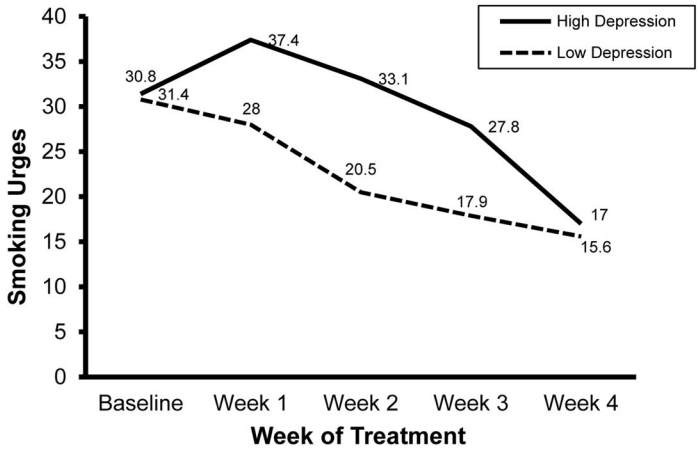
A.1.

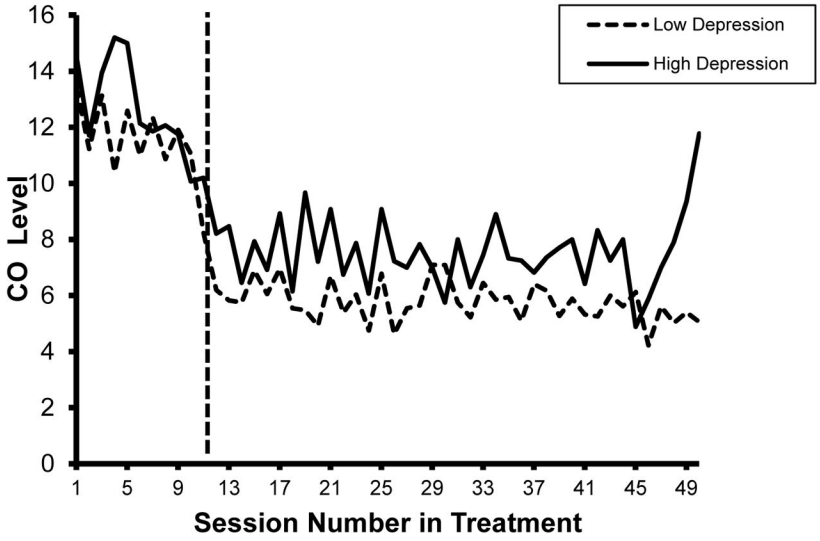


A.2



Note: Depression scores were coded as high or low based on the standard BDI-II clinical significance cut-off of 13. Scores of 1-13 at baseline were categorized as low depression, and scores > 14 were categorized as high depression (Beck et al., 1996).

A.3 Changes in Carbon Monoxide Throughout Treatment



Note: The baseline phase of treatment ended at session 11, and Week 1 of treatment began at session 12.

Figure 1.
Changes in Nicotine Withdrawal and Smoking Urges by High/Low Depression