Symptoms of Depression and Smoking Behaviors following Treatment with Transdermal Nicotine Patch

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Abstract

In this study, subscales from the Center for Epidemiologic Studies Depression Scale (CESD), assessed prior to treatment, were examined as predictors of withdrawal, craving, and affect during the first week of abstinence, as well as smoking abstinence during the first week of abstinence and at the end of treatment. The negative affect and somatic features CESD subscales were related to higher levels of nicotine withdrawal. The relationship between the interpersonal disturbance CESD subscale and nicotine withdrawal approached significance. This study suggests the need to examine novel psychological mechanisms that may account for the relationship between depression symptoms and smoking cessation.

Keywords

Smoking Cessation; Depression; CESD; withdrawal

INTRODUCTION

There is an extensive literature concerning the relationship between depression and nicotine dependence, spanning several decades and including epidemiologic studies and clinical trials.[1–2] While the data linking a history of major depression to poor outcomes following nicotine dependence treatment remains equivocal,[3] the association between current depressive symptoms and an inability to quit smoking is more consistent.[4–9]

This research has stimulated investigations into mechanisms that link depressive symptoms to poor nicotine dependence treatment outcomes. Pomerleau and colleagues[10–12] have shown that pre-treatment depressive symptoms increase post-cessation nicotine withdrawal, craving, and psychological distress which, in turn, decrease the individual's ability to maintain abstinence from smoking. However, other studies have failed to replicate this relationship,[4, 13] indicating that the mechanisms linking pre-treatment depression to smoking cessation treatment outcomes remain unresolved.

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Many of these studies have utilized the Center for Epidemiologic Studies Depression Scale (CESD) to measure depressive symptoms. Recently, it has been suggested that investigations of the relationship between smoking outcomes and depression symptoms should consider a broader conceptual view of depression symptoms.[14,15] Consistent with this perspective, researchers have distilled four CESD dimensions: negative affect (e.g., sadness), somatic features (e.g., appetite and sleep disturbance), anhedonia (e.g., lack of positive affect), and interpersonal disturbance (e.g., social difficulties).[16–18] To date, only one study has examined the CESD subscales as predictors of initial cessation reactions in a smoking cessation clinical trial, reporting that only the anehodonia subscale predicted increased withdrawal and relapse.[14] While this study advanced our understanding of the nature of the relationship between depression and smoking, independent replication would support theoretical progress and clinical refinements. Thus, this study sought to examine the relationship between CESD subscales and initial cessation reactions (i.e., withdrawal, craving, and affect) and cessation following treatment with nicotine patch.

METHODS

Study design

A complete description of the trial from which the current data were ascertained can be found in Schnoll et al.[19] To summarize, data were taken from a clinical trial of standard (21mg) vs. high (42mg) dose transdermal nicotine. Participants (n = 87), recruited via media ads, were randomized to eight weeks of two 21mg nicotine patches or one 21mg nicotine patch and a placebo patch. All participants received five behavioral counseling sessions similar to that used in past smoking cessation clinical trials.[20] At a pre-treatment session (week −1), participants completed questionnaires, including the CESD and measures of withdrawal, craving, and affect. The next week (week 0), participants were instructed to quit smoking and initiate the patch. Measures of withdrawal, craving, and affect were again completed at week 1. Smoking cessation was assessed at week 1 and at the end of treatment (week 8) using self-report and breath carbon monoxide (CO).[21] All procedures were approved by the University of Pennsylvania Institutional Review Board and all participants completed an informed consent and HIPAA document prior to enrollment and data collection.

Participants

Study participants were treatment-seeking smokers, age 18–55, self-reported smoking 10 cigarettes/day, and able to communicate in English. To be eligible, participants had to be fast metabolizers of nicotine (i.e., have a ratio of 3′hydroxycotinine [3-HC] to cotinine, the two primary metabolites of nicotine, of .18.[22–24] Participants were excluded if they had a health condition that may increase risk of adverse reactions to the nicotine patch (e.g., uncontrolled hypertension, pregnant), if they were currently using a smoking cessation medication (e.g., varenicline), anti-psychotics, anti-depressants, anxiolytics, or stimulants, if they had a recent history (< 12 months) of substance abuse or dependence, or if they reported a history or a current diagnosis of psychosis, major depression, an anxiety disorder, or bipolar disorder assessed by the MINI International Neuropsychiatric Interview.[25]

Measures

Covariates—Socio-demographic information such as age and gender was collected. *Measured weight (in pounds) was assessed prior to treatment (week −1) and at the end of treatment (week 8).* Smoking characteristics were assessed including level of nicotine dependence using the Fagerström Test for Nicotine Dependence.[26] Saliva was used to determine nicotine metabolism rate (3-HC/cotinine) following procedures described in Dempsey et al.[22]

Initial reactions to nicotine abstinence—Three scales assessed initial reactions to quitting smoking. The Minnesota Nicotine Withdrawal Scale measured withdrawal symptoms associated with quitting smoking (e.g., irritability).[27] The brief Questionnaire of Smoking Urges[28] assessed craving for cigarettes using two subscales (anticipation of reward, relief from negative affect). The Positive and Negative Affect Schedule (PANAS)[29], assessed positive (e.g., enthusiastic) and negative (e.g., distressed) affect.

Depression—The CESD assessed depressive symptoms.[30] In addition to the total score, subscale scores were examined to evaluate unique aspects of depression.[14, 18, 31] The factor structure of the four subscales - negative affect, somatic features, anhedonia, and interpersonal disturbance – has been verified and each subscale has good internal consistency reliability.[14]

Smoking Cessation—Consistent with recommendations[21] and previous studies[19], smoking cessation was defined as self-reported cessation, verified by breath CO (10ppm).[32] Abstinence was assessed at week 1 and week 8. Seven-day point prevalence abstinence was assessed since this is the most common measure in smoking cessation clinical trials. But, 24-hour point prevalence abstinence was also measured since this is the most appropriate point-prevalence measure to use with CO as the form of biochemical verification given the half-life of CO.[21] For both measures, participants were assumed to be smoking if they were lost to follow-up, failed to provide a CO, or had CO levels > 10ppm.

Statistical analysis

The association between the CESD and potential covariates (e.g., sex, age, rate of nicotine metabolism, *change in weight*) was examined using Pearson correlation and analysis of variance. Next, multivariate linear regression was used to evaluate the relationship between pre-treatment depression and week 1 measures of withdrawal, craving, and affect. Separate models were examined for withdrawal, craving, positive affect, and negative affect and for each subscale of the CESD and the total CESD. Week −1 measures of withdrawal, craving, and affect were included in the models to control for pre-treatment values. Gender, rate of nicotine metabolism, and treatment arm allocation were included as covariates[ii]. Lastly, multivariate logistic regression examined the relationship between the CESD subscales and total score and week 1 and 8 cessation rates, controlling for gender, rate of nicotine metabolism, and treatment arm allocation.

RESULTS

Depression and covariates

There were no significant correlations between the CESD summary score, or subscale scores, and participant age, level of education and income, rate of nicotine metabolism, baseline cotinine and cigarettes per day, years of smoking, FTND, number of previous attempts to quit smoking, duration of longest previous quit attempt, gender, marital status, *and weight change from pre-treatment to the end of treatment*.[iii]

Depression and initial reactions to abstinence

There were no significant correlations between the CESD summary score, or subscale scores, and craving and positive and negative affect. Further, the CESD summary score and the CESD anhedonia subscale were not associated with withdrawal (see Table 1). However,

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[ii]There were no significant interaction effects between depression and treatment arm.
[iii]There was no relationship found between withdrawal symptoms and changes in weight across the treatment phase.

the CESD negative affect subscale (β = .25, $\underline{p}$ = .05) and the CESD somatic features subscale (β = .26, $\underline{p}$ = .03) were significantly associated with withdrawal symptoms. The relationship between the CESD interpersonal disturbance and withdrawal symptoms approached significance (β = .18, $\underline{p}$ = .08). The addition of the negative affect subscale and the somatic features subscale to their respective prediction models yielded a significant increase in variance explained in withdrawal (R^2 change = .04, $\underline{p}$ = .05 for negative affect; R^2 change = .04, $\underline{p}$ = .03 for somatic features).

Depression and Abstinence

We found no significant associations between the CESD summary and subscale scores and any measure of smoking cessation at week 1 and week 8.

DISCUSSION

We examined the association between depression, using CESD subscales, and initial withdrawal, craving, and positive and negative affect, as well as smoking cessation, among smokers without a history of psychiatric disorder following treatment with nicotine patch. Overall, the study found limited evidence of an association between pre-treatment depression and initial withdrawal, craving, and affect, and initial or end-of-treatment cessation. Only the association between the negative affect and somatic features CESD subscales and increased withdrawal was found. We discuss these results in the context of previous studies.

First, contrary to numerous studies that have reported pre-treatment depression to be a significant predictor of smoking cessation, including with nicotine replacement therapies (NRTs),[6, 33] we found no evidence of this relationship, even with the CESD subscales. Other studies, however, have also failed to detect a relationship between depression and post-treatment cessation following NRT,[34] indicating that the relationship between depression and the ability to quit smoking is complex. Important smoker (e.g., race or gender) and treatment (e.g., duration of treatment) characteristics may moderate this relationship. Further, differences across studies could not be ruled out as a possible explanation for divergent findings. The scales used to assess depression symptoms, such as the CESD, may also not reflect clinically-meaningful depression that would predict smoking outcomes.

Second, contrary to expectation, we found no relationship between pre-treatment depression symptoms and post-cessation craving and positive and negative affect. Again, while co-factors that moderate this relationship and methodological differences across studies may explain these divergent findings, it is also plausible that craving and affective reactions following cessation do not serve as mechanisms through which depression symptoms influence cessation. Future investigations focused on understanding the association between depression and smoking cessation should consider novel mechanisms such as depression-associated cognitive processes, which have recently received greater attention as predictors of smoking behaviors.[35]

Lastly, our evaluation of the relationship between the CESD subscales and withdrawal indicated that this relationship was confined to the subscales measuring negative affect and somatic features. This finding diverges from Leventhal et al.[14] which found that anhedonia, but not negative affect or somatic features, predicted increased withdrawal symptoms. Dissimilarities across studies in terms of sample composition (fast nicotine metabolizers and no history of major depression vs. heavy alcohol drinkers with possible history of major depression) or treatment (different nicotine patch doses vs. 21mg dose) may explain these differences. Alternatively, this finding is congruent with the suggestion that depression is

weakly associated with smoking behaviors, since these two subscales are thought to represent symptoms that are more generalized to a range of psychological conditions, including anxiety disorders, whereas anhedonia is more specific to depression.[1] The relationship between anxiety symptoms and withdrawal and response to nicotine dependence treatment has been described.[36]

Consideration of study limitations is necessary. First, this study included treatment-seeking smokers who were rigorously screened for medical conditions and were under age 55. Thus, this sample may not represent the US population of smokers or participants in similar studies. Second, measures of depression, withdrawal, craving, and affect may not capture the full dimension of each construct. Third, the sample was relatively small and, thus, the study was under-powered. *Fourth, the present findings may be confined to the use of nicotine replacement therapy and may not generalize to treatment programs involving other medications for nicotine dependence, including bupropion and varenicline.* Lastly, the data were ascertained from a clinical trial of fast nicotine metabolizers who received different doses of transdermal nicotine. While this selection includes 75% of the population of smokers, by definition, and we controlled for treatment arm allocation in the analyses, these are important factors to consider.

This study furthers our understanding of the relationship between depression symptoms and post-treatment smoking behaviors. The results suggest the need to broaden our examination of potential mechanisms linking depression and smoking cessation and encourage further examination of symptoms of psychological distress that may represent broader psychiatric conditions. The more we understand the process of cessation for smokers, the more able we are to refine treatment approaches to improve cessation rates.

Acknowledgments

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TABLE 1

Prediction Models for Depression and Week 1 Withdrawal Symptoms

Model/Predictor	B	95% CI	t	p	F	p
Negative Affect					7.75	<.001
Treatment Arm	.04	−2.21–3.31	.40	.69		
Sex	.08	−1.62–3.96	.84	.41		
NMR	−.16	−8.58–.70	−1.70	.10		
Pre-treatment Withdrawal	.36	.14–.76	2.93	.004		
Negative Affect	.25	.002–1.02	2.00	.05		
Anhedonia					6.61	<.001
Treatment Arm	.05	−2.79–3.58	.53	.60		
Sex	.04	−2.24–3.44	.42	.67		
NMR	−.16	−8.54–.98	−1.58	.12		
Pre-treatment Withdrawal	.53	.39–.93	4.84	<.001		
Anhedonia	−.03	−.78–.60	0.26	.80		
Somatic Features					7.94	<.001
Treatment Arm	.06	−1.91–3.58	.60	.55		
Sex	.05	−2.00–3.45	.53	.60		
NMR	−.15	−8.16–1.09	−1.52	.13		
Pre-treatment Withdrawal	.36	.15–.75	2.98	.004		
Somatic Features	.26	.04–1.09	2.16	.03		
Interpersonal Disturbance					7.52	<.001
Treatment Arm	.05	−2.00–3.54	.55	.58		
Sex	.07	−1.77–3.80	.73	.47		
NMR	−.16	−8.68–.67	−1.71	.09		
Pre-treatment Withdrawal	.46	.32–.82	4.48	<.001		
Interpersonal Disturbance	.18	−.18–3.32	1.79	.08		

Note. NMR = nicotine metabolite ratio, the measure of rate of nicotine metabolism.