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Brief Report

Effects of anhedonia on days to relapse among smokers with a history of depression: A brief report

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Abstract

Introduction: Despite the strong co-occurrence between lifetime prevalence of depression and smoking, a history of major depressive disorder (MDD history) does not reliably predict smoking cessation outcomes. However, depression is a heterogeneous syndrome comprising several dimensions (e.g., anhedonia, vegetative symptoms, negative affect), and each symptom expression may differentially influence cessation failure. Measuring proximal depressive dimensions may provide a more reliable way of identifying MDD history smokers most at risk for smoking relapse. Anhedonia, in particular, is a core feature of depression that may increase risk for smoking relapse among MDD history smokers. The primary goal of the present study was to investigate the relation between anhedonia and relapse latency among MDD history smokers following a brief smoking cessation workshop.

Methods: Participants (N = 45, 48.9% female), who were euthymic regular smokers with a history of MDD, were randomized to 1 of 3 treatment groups that all involved participation in a daylong group workshop. Workshops were followed by 48 hr of bioverified abstinence and weekly follow-up visits for 1 month.

Results: Cox proportional hazard modeling was used to evaluate the effect of anhedonia on relapse latency 30 days following quitting smoking. Results showed that higher levels of anhedonia predicted reduced relapse latencies, both with and without prequit depressive symptom severity included in the model.

Discussion: Results suggest that anhedonia may constitute a proximal risk factor identifying depressive history smokers more likely to relapse to smoking.

Introduction

Comorbidity between lifetime prevalence of depression and smoking has been well documented over the past two decades (e.g., Breslau, Novak, & Kessler, 2004; Glassman et al., 1990; Grant, Hasin, & Chou, 2004; Lasser et al., 2000). Despite the strong co-occurrence between depression and smoking, a history of major depressive disorder (MDD history) does not reliably predict smoking outcomes (e.g., Ginsberg, Hall, Reus, & Munoz, 1995; Hitsman, Borrelli, McChargue, Spring, & Niaura, 2003; John, Meyer, Rumpf, & Hapke, 2004). One reason for the inconsistent association between MDD history and cessation failure may be that depression is a heterogeneous syndrome comprising several dimensions (e.g., anhedonia, vegetative symptoms, negative affect; Hasler, Drevets, Manji, & Charney, 2004). Because each depressive dimension may be associated with distinct behavioral, psychological, and biological correlates, only certain dimensions, particularly ones that remain stable between depressive episodes, may influence smoking outcomes among MDD history smokers.

Measuring proximal depressive dimensions may provide a more reliable way to identify MDD history smokers most at risk for smoking relapse. Anhedonia is a unitary depressive phenotype that remains relatively stable between depressive episodes (Clark, Fawcett, Salzar-Grueso, & Fawcett, 1984; Hasler et al., 2004) and that produces significant motivational or self-regulatory deficits. Characterized by a lack of responsivity to appetitive events, anhedonia results, in part, from hypofunction in the mesolimbic dopamine system (Heinz, Schmidt, & Reischies, 1994), which modulates the anticipation and experience of pleasure (Wise, 1982). Nicotine increases both dopamine activity and the reward value of nondrug stimuli (Epping-Jordan, Watkins, Koob, & Markou, 1998), potentially motivating smoking among highly anhedonic individuals. If anhedonic smokers rely on nicotine to bolster their underresponsive reward system, quitting smoking could unmask preexisting reward deficits, prompting return to smoking.

Evidence suggests that smokers high in anhedonia may be particularly sensitive to the secondary reinforcing effects of nicotine in that they require simultaneous administration of

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nicotine to experience increases in positive affect during exposure to a positive mood prompt (Cook, Spring, & McChargue, 2007). Anhedonia might not only decrease positive affective reactions to appetitive events but it might also accelerate the loss of positive affect that follows quitting smoking. The latter effect mediates elevated postquit craving observed among anhedonic smokers (Cook, Spring, McChargue, & Hedeker, 2004), and this in turn could enhance relapse risk. This possibility is underscored by findings of Leventhal, Ramsey, Brown, LaChance, and Kahler (2008) that anhedonic symptoms of depression were associated with increased likelihood of smoking relapse. Results from that study implicate the anhedonic component of depression in cessation failure among smokers lacking a current or past MDD diagnosis. Anhedonia may be a particularly prominent risk for cessation failure among MDD history smokers since their reward deficits are more severe than those in the general population (Clark et al., 1984; Fawcett, Clark, Scheftner, & Hedeker, 1983).

We posit that anhedonia, a stable depressive characteristic, constitutes a risk factor identifying MDD history smokers who are most likely to relapse to smoking. Specifically, the present study investigated the relation between anhedonia and relapse latency among MDD history smokers following a brief smoking cessation workshop. We predicted that smokers with higher levels of anhedonia would relapse more quickly than would those with lower levels of anhedonia.

Method

Participants

The present research was part of a treatment study designed to examine whether adding mood management skills training and rehearsal to smoking cessation skill training would prolong the time that smokers remained abstinent after a bioverified 48-hr period of abstinence. To be eligible, participants ($N = 45$) had to report an interest in quitting smoking and have a history of at least one episode of Structured Clinical Interview for *DSM-IV*-diagnosed major depression. Participants were required to be at least 18 years of age and smoke a minimum of 10 cigarettes daily. Individuals who were currently receiving smoking cessation treatment or were treated for alcohol or other drug use within the past year were excluded from participation as were individuals experiencing a current episode of major depression.

Measures

Axis I disorders

The Structured Clinical Interview for *DSM-IV*, nonpatient version (SCID-NP; Spitzer, Williams, Gibbon, & First, 1992), was administered to assess current Axis I disorders as well as history of depression. Assessors were doctoral level psychology trainees under the supervision of the principal investigator, a licensed clinical psychologist.

Anhedonia

The Fawcett–Clark Pleasure Scale (FCPS; Fawcett et al., 1983) is a 36-item self-report scale that was developed to measure anhedonic features of depression and has been shown to have strong psychometric properties (Fawcett et al. 1983). Respondents rated imagined hedonic reactions to hypothetical pleasurable situations (e.g., "You sit watching a beautiful sunset in an isolated, untouched part of the world"). Scores on the FCPS range between 36 and 180. The FCPS is normally scored such that low scores indicate greater anhedonia. For ease of interpretation, all reported analyses were based on reverse scoring of the FCPS, such that higher scores indicated greater anhedonia (diminished ability to experience pleasure). In addition, the FCPS was standardized ($M = 0$, $SD = 1$) to increase interpretability of the observed effects.

Depression

The Hamilton Depression Rating Scale (HDRS; Hamilton, 1960) is a clinician-rated semistructured interview involving 21 depressive symptoms. The HDRS was administered to assess prequit depressive symptom severity.

Smoking relapse

Smoking status was evaluated at 24- and 48-hr postquit and at four weekly follow-up visits. During each visit, participants reported the number of cigarettes smoked since the previous visit. Participants also provided a breath sample that was analyzed for exhalation carbon monoxide. Those who reported abstinence at the second and fourth weekly follow-up visits also provided saliva samples that were analyzed for cotinine, nicotine's major metabolite. Subjects were judged as nonabstinent if they reported smoking any cigarettes since the quit date, had an ecolyzer value of $\geq$8 ppm carbon monoxide, or had a cotinine value of $\geq$20 ng/ml. If a participant's self-reported abstinence was contradicted by biochemical findings, that participant was considered nonabstinent. Participants were judged to have relapsed if they reported any amount of smoking on 7 consecutive days. Time to relapse was operationalized as the number of consecutive days between the quit day and the day on which the criteria for relapse were met.

Procedure

Following the telephone screening, eligible study candidates were asked to visit the laboratory for assessment. After providing informed consent, participants received a diagnostic interview (SCID-NP) and completed study questionnaires. Participants were randomized to one of three treatments (tryptophan depletion plus mood management and cessation skills training, placebo depletion with mood management and cessation skills training, and cessation skills training alone), each of which involved participation in a 1-day group workshop facilitated by trained therapists (Spring, Pergadia, Richmond, McChargue, & Doran, 2002). Prior to the workshop, all participants ingested capsules and a beverage that contained either placebo or an amino acid mixture that transiently depleted plasma tryptophan and brain serotonin. Workshops focused on training participants in the use of smoking cessation and mood management skills and included an experiential component (negative mood induction via guided imagery) in which skills were practiced. Participants quit smoking immediately following the workshops and returned to the laboratory at 24- and 48-hr postquit for verification of self-reported smoking status. They then returned to the laboratory weekly for 4 weeks to assess smoking status.

Results

Sample characteristics

The mean age of the sample was 41.00 years ($SD = 11.30$) and 48.9% were women. Thirty-six percent identified themselves

as Black, 4.8% as Asian-American, 54% as Caucasian, 2.4% as Latino-American, and 2.8% as multiethnic. Participants smoked an average of 19.42 (*SD* = 7.78) cigarettes/day and smoked for an average of 22.92 years (*SD* = 12.25). Participants' average HDRS score was 4.21 (*SD* = 2.65), suggesting that they were not experiencing clinically significant levels of depression upon entry into the study. Participants' average scores on the FCPS (*M* = 119.17, *SD* = 11.83) were comparable with those reported previously for a clinically depressed population (*M* =122.04, *SD* = 28.44; Fawcett et al., 1983). Although no clinical cutoffs have been specified by the scale's developers, the similarity between our sample's scores and those of depressed patients suggests that many smokers in the study exhibited clinically significant levels of anhedonia. Finally, anhedonia and prequit depressive symptoms were only moderately correlated (r = .38, p = .02), suggesting that the two constructs do not convey redundant information.

Time to relapse

Cox proportional hazard modeling, a survival analysis technique, was used to evaluate the effect of anhedonia on relapse latency 30 days following quitting smoking. The effects of treatment group, number of cigarettes smoked daily at baseline, and age were covaried from the model. The multivariate model that included anhedonia, treatment group, cigarettes smoked, and age significantly predicted time to relapse at 30-day postquit (χ^2 [df = 5] = 15.58, p = .008). Results showed that higher levels of anhedonia predicted reduced relapse latency (Hazard Ratio = 1.55, 95% *CI* = 1.14–1.73); the risk of relapse at any time during the first month postquit increased 55% for every *SD* increase in anhedonia (see Table 1). Finally, anhedonia was dichotomized via median split to plot survival curves for high versus low anhedonic smokers across 30 days following quitting smoking (see Figure 1).

Next, we examined whether anhedonia predicted days to relapse even after covarying prequit depressive symptoms. The multivariate model that included anhedonia, depressive symptoms, treatment group, cigarettes smoked, and age significantly predicted time to relapse at 30-day postquit (χ^2 [df = 6] = 24.99, p < .01). The significant effect of anhedonia on relapse latency persisted even after covarying out prequit depressive symptoms (HR = 1.60, 95% *CI* = 1.30–1.77). Those with higher levels of prequit depressive symptoms were also more likely to report fewer days to relapse (see Table 2). Finally, we removed anhedonia from the model to examine the effects of depressive symptoms on relapse latency independent from anhedonia. The multivariate model that included depressive symptoms, treatment group, cigarettes smoked, and age significantly predicted latency to relapse (χ^2 [df = 5] = 11.69, p = .04). Baseline depressive symptoms were not associated with days to relapse (HR = 1.12, 95% *CI* = 0.95–1.31).

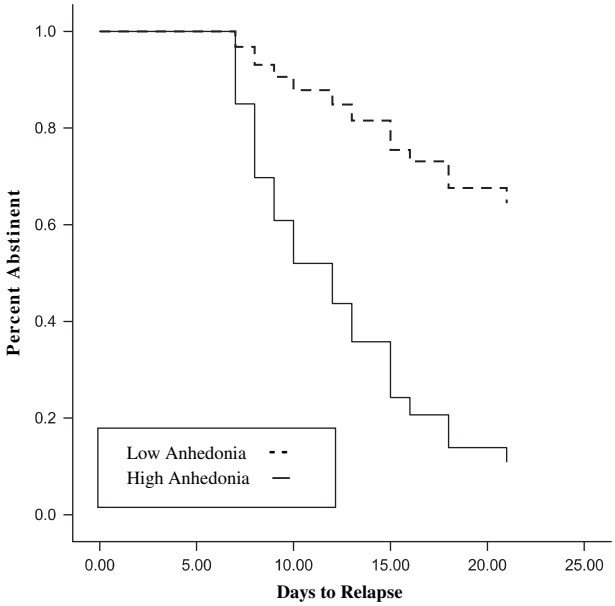

Figure 1. Days to relapse for low versus high anhedonic smokers.

Discussion

Results showed that MDD history smokers characterized by high levels of anhedonia relapsed earlier than those with lower levels of anhedonia. The observed effect of anhedonia on smoking relapse was relatively large when considering the continuous nature of the variable: the effect size represents a 55% increase in the likelihood of relapse across 30-day postquit for every *SD* increase in anhedonia. This effect persisted even after controlling for HDRS, a measure of depressive symptom severity that also predicted reduced relapse latency. Unexpectedly, depressive symptom severity no longer predicted relapse latency when anhedonia was removed from the model. Our findings suggest that there may be relatively little overlap between the two measures in terms of predicting relapse. Perhaps the HDRS, a heterogeneous measure of depression that includes a particularly

Table 1. Results of Cox proportional hazard modeling examining effect of anhedonia on relapse latency 30 days following quitting smoking

Steps	Wald	*p* Value	HR	*CI*
Group	11.77	.01	8.6	(2.52–29.45)
Age	5.36	.02	0.95	(0.91–0.99)
Cigarettes smoked	1.91	.17	0.94	(0.87–1.02)
Anhedonia	6.22	.01	1.55	(1.14–1.73)

Note. Steps refer to order of entry in Cox regression analysis.

Table 2. Results of Cox proportional hazard modeling examining effect of anhedonia and depressive symptoms on relapse latency 30 days following quitting smoking

Steps	Wald	*p* Value	HR	*CI*
Group	14.77	.00	10.86	(3.22–36.68)
Age	5.38	.02	0.95	(0.91–0.99)
Cigarettes smoked	0.57	.45	0.97	(0.90–1.05)
Depressive Symptoms	6.07	.01	1.25	(1.05–1.5)
Anhedonia	10.57	.00	1.60	(1.30–1.77)

Note. Steps refer to order of entry in Cox regression analysis.

strong representation of items assessing physical and neurovegetative symptoms of depression, consists of depressive features that are unrelated to smoking outcomes. Thus, at least in this preliminary research, anhedonia appears to be a stronger predictor of relapse among MDD history smokers than overall depressive symptom severity.

It is interesting to consider the influence of anhedonia on smoking relapse in view of models of substance use motivation. Watkins, Koob, and Markou (2000) review data that suggests that chronic nicotine exposure may produce neuroadaptations that increase an individual's hedonic set point. As such, natural rewards decrease in potency, and increased amounts of nicotine are needed to stimulate reward. After nicotine is withdrawn, the hedonic set point appears to remain high, causing withdrawal-related anhedonia. Functionally, an elevated reward threshold signifies anhedonia: that the person experiences heightened difficulty experiencing pleasure or that stronger rewarding stimuli are required to elicit pleasure. This reward threshold elevation during nicotine withdrawal may be particularly problematic for individuals with preexisting anhedonia associated with depression. The removal of one of the few stimuli (i.e., cigarettes) strong enough to stimulate feelings of pleasure could promote relapse to smoking in attempt to reverse withdrawal-induced dopamine hypofunction.

The study has limitations that should be considered. The findings are correlational in nature, limiting the strength of causal inferences. In addition, since all subjects in this research had a history of depression, we cannot draw inferences regarding the anhedonia–relapse relation outside of coexisting depression. However, anhedonia is a core characteristic of depression (Hasler et al., 2004) that remains high even between depressive episodes (Clark et al., 1984). As such, the effects of blunted reward functioning on smoking outcomes may be especially prominent among those with a depressive diathesis. Overall, our preliminary findings suggest that anhedonia may constitute a proximal risk factor identifying depressive history smokers more likely to relapse to smoking. Further study of anhedonia could be useful for distilling phenotypes that are most sensitive in predicting smoking relapse among depression-prone smokers and among other mental health disorders characterized by anhedonia. The relation between anhedonia and smoking relapse requires additional study with larger more diverse samples before firm conclusions may be drawn.

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Declaration of Interests

None declared.

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