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Brief report
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Is the Effect of Anhedonia on Smoking Cessation Greater for Women Versus Men?

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Abstract

Introduction: Anhedonia has been recognized as a major risk factor for smoking persistence. Potential gender differences in the effect of anhedonia on smoking cessation have not been studied. Using data from a completed clinical trial of maintenance nicotine patch therapy, we hypothesized that gender would moderate the effect of anhedonia on short-term abstinence, such that anhedonic women would be less likely to achieve abstinence.

Methods: Participants (N = 525; 50% female, 48.2% Black/African American, average age: 46 years) received 21 mg/day nicotine patch and four brief behavior counseling sessions over 8 weeks. Participants were classified at baseline using the Snaith–Hamilton Pleasure Scale as anhedonic (scores > 2) or hedonic (scores ≤ 2). Bioverified 7-day point prevalence abstinence was measured at week 8. Using logistic regression analysis, we tested the interaction of anhedonia by gender predicting abstinence, adjusting for age, race, nicotine dependence, and baseline depressive symptomatology.

Results: Seventy participants (13%) were classified as anhedonic. Men were more likely to be anhedonic than women (16.6% vs. 10.2%, p = .03). Contrary to our hypothesis, the interaction of anhedonic status (hedonic vs. anhedonic) by gender was nonsignificant (p = .18). There was a main effect of hedonic capacity, such that anhedonia predicted abstinence, odds ratio = 3.24, 95% confidence interval = 1.39–7.51, p = .006.

Conclusion: Both male and female anhedonic smokers were more likely to be abstinent, which contrasts with prior research indicating that anhedonia is a risk factor for difficulty quitting. This unexpected finding may be explained by a possible selective benefit of nicotine patch therapy, which has been observed in some studies to have antidepressant effects.

Implications: This is the first study to examine whether the association between pretreatment anhedonia and smoking cessation differs by gender. For both women and men, anhedonia was associated with a greater likelihood of abstinence after 8 weeks of treatment with 21 mg/day nicotine patch and behavior counseling. Our findings indicate that the association between anhedonia and smoking cessation is not as clear as has been assumed and may depend in part on the type of treatment delivered.

Introduction

Depression is a well-established risk factor for negative outcomes in smoking cessation.[1] It has been demonstrated that anhedonia, or the absence of positive affect, predicts difficulty quitting above and beyond other dimensions of depression.[2] Anhedonia is also associated with greater withdrawal symptoms and cigarette cravings during a quit attempt.[3,4] Anhedonic smokers may have a heightened bias toward the rewarding value of smoking, which may serve as a primary reinforcing mechanism for smoking behavior.[5]

A special issue of *Nicotine and Tobacco Research* emphasized the importance of evaluating the role of gender in smoking.[6] Given persistent gender differences in depression[7] and smoking cessation,[8] it is important to evaluate whether gender moderates the anhedonia—smoking cessation association. The lack of data in this area is surprising, as women report greater negative affect during acute withdrawal, along with greater overall withdrawal distress and a greater desire to minimize distress through smoking.[9] Higher rates of pretreatment anhedonia have been observed among men,[3] suggesting there could be differences in rates of anhedonia between men and women smokers.

In the current study, we evaluated whether gender modifies the association between baseline hedonic capacity and short-term smoking cessation. Using data from a completed clinical trial of maintenance therapy with nicotine patch, we hypothesized that baseline anhedonia would predict continued smoking, especially among women.

Methods

Participants

Participants were 525 men and women who were at least 18 years of age, smoked at least 10 cigarettes per day, and were interested in smoking cessation (50% female, 48.2% Black/African America, average age: 46 years, and average years smoked: 17 years, range: 3–60 years). Exclusion criteria included current psychosis, mania, or suicidality, as measured using the Mini-International Neuropsychiatric Interview,[10] or any medical condition for which nicotine patch therapy would be contraindicated. There were no inclusionary criteria related to smoking history or exclusionary criteria related to other psychiatric disorders, including alcohol or substance use disorder. Urine pregnancy testing was done for women with child-bearing potential; women who were pregnant, planning a pregnancy, or lactating were excluded. All participants provided written informed consent.

Procedures

The current study used data from a completed randomized controlled trial comparing 8, 24, and 52 weeks of 21 mg/day nicotine patch therapy (clinicaltrials.gov identifier: NCT01047527).[11] Participants were recruited, enrolled, and treated in Chicago, IL, and Philadelphia, PA. Phone screening was conducted to determine initial eligibility before participants attended in-person screening. Eligible participants were enrolled at the baseline visit, where they completed measures and were randomized to treatment. For the current study, data through week 8 were used to equate participants on duration of nicotine patch therapy. Participants completed behavior counseling sessions at prequit (week -2), target quit day (week 0), week 4, and week 8. Participants completed an in-person visit at week 8 for bioverification, using Vitalograph breath monitors, of self-reported abstinence. See Schnoll *et al.*[11] for additional details.

Measures

Anhedonia

The 14-item Snaith–Hamilton Pleasure Scale (SHAPS) was completed at baseline.[12] Each item asks participants to rate the degree to which they would enjoy engaging in a certain pleasurable activity (eg, spending time with friends and family), with four possible responses (definitely agree = 0, agree = 1, disagree = 2, definitely disagree = 3). The possible range of scores was from 0 to 42, consistent with prior studies in which the SHAPS was used as a continuous measure.[13,14] To classify participants as hedonic or anhedonic at baseline, we followed the scoring method devised by Snaith *et al.*[12] Each item response was recoded as hedonic (agree or definitely agree = 0) or anhedonic (disagree or definitely disagree = 1). For this dichotomous measure, scores ranged from 0 to 14. Participants with scores >2 were classified as anhedonic, whereas those with scores ≤2 were classified as hedonic.[12]

Smoking Abstinence

Seven-day bioverified point prevalence abstinence at week 8 was determined by self-reported abstinence (ie, reported smoking 0 cigarettes in the past 7 days) and expired carbon monoxide (CO) of ≤10 parts per million. Participants who reported smoking any cigarettes in the past 7 days or provided a breath CO sample >10 parts per million were classified as continued smokers. An intent-to-treat model was employed, whereby participants who could not be reached or failed to provide a CO sample at week 8 were assumed to be smoking.

Covariates

Demographic Variables

Gender, race, and age were collected at baseline. Due to the small number of minorities other than Blacks/African Americans, race was categorized as white (50.1%) or Black/African American/Minority (49.9%). Race and age were included in the analysis due to their documented relationship to smoking prevalence and cessation rates.[15]

Nicotine Dependence

At baseline, nicotine dependence was measured using the Fägerstrom Test for Nicotine Dependence (FTND), a six-item measure with a possible range of scores from 1 to 10.[16] Nicotine dependence was included as it is a key predictor of long-term cessation.[17]

Inventory of Depressive Symptomatology

Depression were measured using the 30-item Inventory of Depressive Symptomatology (IDS) scale.[18,19] Each item has a four-point response scale ranging from 0 to 3. As only 28 of 30 items are included in the scoring procedure, possible scores range from 0 to 84. Higher scores reflect greater depressive symptomatology over the past 7 days. The IDS has demonstrated validity in nonclinical populations.[18]

Analyses

Preliminary Analyses

Chi-square analysis was used to evaluate the relationship between baseline anhedonia, gender, and abstinence. Analysis of variance was used to compare hedonic capacity (hedonic vs. anhedonic) by gender (women vs. men) groups on continuous race, age, nicotine dependence, depressive symptomology, and continuous anhedonia scores.

Prediction of Short-Term Abstinence

Logistic regression analyses were used to evaluate the interaction of anhedonia by gender in predicting abstinence at week 8. Hedonic capacity (hedonic vs. anhedonic) at baseline, gender, and the hedonic capacity by gender interaction were included in the model. Covariates included race, age, nicotine dependence, and baseline depressive symptomatology. For comparison, the model was rerun using the continuous measure of anhedonia. In a secondary analysis, we evaluated the baseline depressive symptoms by gender interaction predicting abstinence at week 8, along with the main effects and same set of covariates, to determine the extent to which results for anhedonia extended to the broader construct of depression.

Results

Seventy of the 525 participants (13.3%) were classified as anhedonic at baseline. The rate of anhedonia was higher among men (16.6%) than among women (10.2%), $\chi^2(1) = 4.72$, $p = .03$. Abstinence rates did not differ significantly among hedonic capacity by gender groups: hedonic men 30.6%, anhedonic men 39.5%, hedonic women 27.6%, and anhedonic women 44.3% ($p > .05$). As expected, the four groups differed significantly on baseline levels of anhedonia and depressive symptomatology. Groups did not differ significantly on age, race, or degree of nicotine dependence (Table 1).

In the primary logistic regression analysis, the interaction of hedonic capacity (hedonic vs. anhedonic) by gender was not associated with abstinence at week 8 (odds ratio [OR] = 0.48, 95% confidence interval [95% CI] = 0.16–1.43, $p = .187$). However, as shown in Table 2, the main effect of hedonic capacity was statistically significant (OR = 3.23, 95% CI = 1.40–7.5, $p = .006$), such that participants classified as anhedonic at baseline were significantly more likely to be abstinent at week 8. The main effect of nicotine dependence also was statistically significant (OR = 0.84, 95% CI = 0.76–0.93, $p < .001$). As expected, lower scores were associated with a greater likelihood of abstinence. Neither gender, race, age nor baseline depressive symptomatology predicted abstinence (p's > .05). Results of the analysis involving the continuous measure of anhedonia were identical.

In the secondary analysis that was conducted to evaluate the interaction of baseline depressive symptomatology (in place of hedonic capacity) by gender, the interaction and main effects of depressive symptomatology and gender were all statistically nonsignificant (p's > .05). As found in the analyses involving baseline anhedonia (both dichotomous and continuous measures), a lower degree of nicotine dependence predicted abstinence (OR = 0.84, 95% CI = 0.76–0.93, $p = .001$). Age and race were not associated with abstinence in any models (p's > .05).

Discussion

We expected that pretreatment anhedonia would predict inability to achieve short-term smoking cessation, especially among women due to their higher rates of depression[7] and smoking relapse.[8] Our results did not support a modifying influence of gender on the association between pretreatment anhedonia and abstinence. Counter to our expectations, anhedonic participants were three times more likely than hedonic participants to have successfully quit smoking at 8 weeks. This effect of pretreatment anhedonia on abstinence appears to be specific to anhedonia, as baseline depressive symptomatology was unrelated to treatment outcome, consistent with other studies showing that anhedonia is a more robust predictor of smoking behavior.[2] Independent of hedonic capacity, men and women had a comparable likelihood of achieving abstinence.

That anhedonia predicted greater odds of abstinence contrasts with prior studies that have found anhedonia to be a major risk factor for difficulty quitting.[4,20,21] In theory, anhedonic smokers are more likely to relapse because nicotine enhances positive affect[22] and increases the reward value of pleasurable situations.[23] As a result, anhedonic smokers may be more likely to self-administer nicotine and relapse in order to increase their positive affect and receptiveness to experiences.

One possible explanation for the observed association between anhedonia and increased likelihood of short-term abstinence is that anhedonic smokers in this study selectively benefitted from the 21 mg/day nicotine patch therapy. Cook *et al.*[3] observed that administering nicotine replacement therapy (patch and/or lozenge) suppressed abstinence-induced anhedonia (ie, diminished positive affect) and alleviated nicotine withdrawal symptoms during short-term abstinence. Nicotine replacement therapy has been associated with increases in positive affect.[24] While nicotine gum is an effective aid for all smokers, depressed smokers treated with nicotine gum have achieve twice the rate of abstinence compared to those treated with placebo (29.0% vs. 12.5%).[25] Depressed nonsmokers show significant declines during the course of nicotine patch treatment, suggesting that nicotine replacement therapy (and nicotine patch in particular) may have antidepressant-like effects.[25] The extent to which there might be a selective short-term benefit of 21 mg/day nicotine patch for anhedonic smokers and, if so, whether the effect is specific to anhedonia or more broadly related to short-term improvements in other dimensions of depression remains an important question for future research.

Although male smokers in this sample reported higher rates of anhedonia, gender did not moderate the relationship between anhedonia and short-term abstinence. This was surprising, as women have higher rates of depression[7] and are less successful in quit attempts.[8] This is unlikely due to the overrepresentation of male smokers in the anhedonia sample, given that others have previously observed high

Table 1. Sample Characteristics by Gender and Baseline Anhedonia Status

	Men		Women		*p* value
	Hedonic ($n = 216$)	Anhedonic ($n = 43$)	Hedonic ($n = 239$)	Anhedonic ($n = 27$)	
Race (% White)	53.9	50.0	48.5	34.6	.27
Age (years)	45.85 (12.46)	43.81 (11.04)	47.18 (11.74)	48.07 (12.75)	.27
Nicotine dependence	5.29 (1.87)	5.09 (2.20)	4.95 (1.99)	5.37 (2.20)	.28
Depressive symptoms	9.91 (7.20)	11.37 (7.21)	12.30 (8.31)	14.11 (7.29)	.003
Anhedonia	7.17 (4.88)	16.81 (6.42)	6.30 (4.76)	25.04 (10.50)	.001

Values were presented as mean (*SD*) or % of the column sample. Nicotine dependence, depressive symptoms, and anhedonia (continuous) were measured using Fägerstrom Test for Nicotine Dependence, Inventory of Depressive Symptomatology, and Snaith–Hamilton Pleasure Scale, respectively.

Table 2. Logistic Regression Model Predicting Abstinence at Week 8

Variables	Odds ratio	95% confidence interval	Wald χ^2	*p* value
Age	1.02	0.99, 1.03	1.09	.31
Race	0.83	0.55, 1.24	0.86	.35
Nicotine dependence	0.84	0.76, 0.93	11.65	<.001
Depressive symptoms	1.00	0.98, 1.03	0.88	.58
Anhedonic capacity	3.24	1.40, 7.51	7.51	.006
Gender	1.24	0.81, 1.89	0.95	.33
Anhedonic capacity × gender	0.48	0.16, 1.43	1.74	.19

Race (0 = white, 1 = Black/African American), gender (0 = male, 1 = female), and anhedonic capacity (0 = hedonic, 1 = anhedonic). Nicotine dependence, depressive symptoms, and anhedonia (dichotomous) were measured using Fägerstrom Test for Nicotine Dependence, Inventory of Depressive Symptomatology, and Snaith–Hamilton Pleasure Scale, respectively.

rates of prequit anhedonia among male smokers.[3] Nonetheless, no previous studies have explored the potential moderating effect of gender on the relationship between anhedonia and abstinence. Moreover, in the parent trial, gender did not predict long-term abstinence.[11]

There are limitations to this study. First, the sample of anhedonic participants was small (n = 70: 13.3%). However, this rate is comparable to that found by Leventhal *et al*.,[26] suggesting that the rate of anhedonia in the present sample could be reflective of rates of anhedonia among smokers in the general population. Second, although the SHAPS is commonly used to assess anhedonia, particularly among smokers, different measures of anhedonia have not always been shown to be intercorrelated,[14] which may call into question the validity of available scales to accurately measure the construct of anhedonia. Third, the lack of placebo condition made it difficult to draw inferences about the impact of nicotine patch therapy on pretreatment anhedonia or depression more generally. Finally, since hedonic capacity was assessed only at baseline, we were unable to examine changes in anhedonia over the course of treatment.

In conclusion, this is the first study to evaluate whether the association between pretreatment anhedonia and short-term abstinence differs as a function of gender. For both women and men, anhedonia was associated with a greater likelihood of abstinence after 8 weeks of treatment with 21 mg/day nicotine patch and brief behavior counseling. Our findings show that the association of anhedonia and smoking cessation is not as clear as has been assumed, and may depend in part on the type of treatment that is administered. The extent to which certain smoking cessation pharmacotherapies selectively benefit anhedonic smokers deserves attention in future studies.

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Declaration of Interests

BH and RAS receive varenicline and placebo free of charge from Pfizer for use in ongoing National Institutes of Health supported clinical trials. Hitsman has served on a scientific advisory board for Pfizer. RAS reports having provided consultation to Pfizer and GlaxoSmithKline. No other disclosures were reported.

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