Reward and Affective Regulation in Depression-Prone Smokers

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Background: There is a disproportionately high smoking prevalence among individuals who are prone to depression. While depression has been conceptualized as a disorder of dysregulated positive affect and disrupted reward processing, little research has been conducted to determine the role of smoking in these processes among depression-prone smokers.

Methods: Depression-prone smokers (DP+; $n = 34$) and smokers not depression-prone (DP−; $n = 49$) underwent two laboratory sessions, one while smoking abstinent and one while smoking ad libitum, to assess the relative reinforcing value of smoking and reward sensitivity. Using experience sampling methods, participants completed self-report measures of subjective reward, positive affect, and negative affect across 3 days while smoking as usual and 3 days while smoking abstinent.

Results: DP+ were two times more likely to work for cigarette puffs versus money in a progressive ratio, choice task (odds ratio 2.05; 95% confidence interval 1.04 to 4.06, $p = .039$) compared with DP−. Reward sensitivity as measured by the signal detection task did not yield any significant findings. Mixed models regressions revealed a three-way interaction (depression group, smoking phase, and time) for subjective reward, negative affect, and positive affect. For all three of these outcomes, the slopes for DP− and DP+ differed significantly from each other ($ps < .05$) and the effect of smoking (versus abstinence) over time was greater for DP+ than DP− smokers ($ps < .05$).

Conclusions: These findings indicate that the effects of smoking on reward and positive affect regulation are specific to DP+ smokers and highlight novel targets for smoking cessation treatment in this population.

Key Words: Depression, negative affect, positive affect, reward regulation, reward sensitivity, smoking

About 30% to 60% of smokers seeking to enroll in smoking cessation programs have had at least one lifetime episode of major depressive disorder (MDD) (1–5), compared with 15% of the general population (6). Further, half of smokers who enroll in smoking cessation programs have elevated depression symptoms (2,4,7–12). Smokers with a past history of depression and current symptoms of depression (i.e., depression-prone [DP+] smokers) tend to have more difficulty quitting and are at significantly higher risk of relapse than smokers not prone to depression (DP−) (7,13,14).

Negative affect has long been considered a critical factor in smoking maintenance among smokers in general and depression-prone smokers specifically (15,16). To date, smoking cessation interventions for DP+ smokers have focused on the management of negative affect through behavioral and antidepressant therapy with little success (5,17–24). Evidence indicates that targeting negative affect does not significantly improve smoking cessation rates or mitigate negative affect (17,21,23,24) but can exacerbate negative affect and depression symptoms and decrease the likelihood of quitting smoking (25).

While depression has been conceptualized as a disorder of dysregulated positive affect and disrupted reward processing (26), we know little about the role of smoking in these processes among DP+ smokers (24,27). Behavioral economic theory provides a framework to integrate features of depression and the effects of smoking. According to behavioral economic theory, the choice of one rewarding behavior (e.g., smoking) depends on the presence of alternative reinforcers and the reinforcing value of a drug can be enhanced or reduced based on the presence of alternative(s) (28–36). Of relevance, individuals prone to depression have fewer alternative reinforcers (37–39), derive less reward from natural reinforcers in their environment (26,40–45), and as a result, have diminished positive affect (45–48).

In the context of fewer alternative reinforcers, smoking may be an easily available reinforcer with heightened reinforcing value for DP+ smokers (34,49). DP+ smokers are two times more likely to rate smoking as their preferred activity (49), have greater smoking-induced dopamine release (50), and find smoking more reinforcing than DP− smokers (51). Nicotine may also enhance the reinforcement derived from available alternative reinforcers. Preclinical models suggest that nicotine potentiates reward from available reinforcers by increasing the sensitivity of brain reward systems or the ability to experience pleasure (27,52,53), while nicotine withdrawal decreases reward sensitivity (54). In the context of fewer alternative reinforcers, smoking may be a critical reinforcer, while also increasing pleasure derived from available alternative reinforcers.

Research also indicates that nicotine increases positive affect (55–57) and smoking abstinence decreases positive affect, which predicts smoking relapse (24,58–60). Nicotine's effect on positive affect may be especially important for DP+ smokers. Smokers with a history of MDD showed heightened positive affect to a positive mood induction when smoking (27). Although largely ignored, smoking may help regulate positive affect across time, rather than simply managing negative affect for DP+ smokers (48,51,61).

Supported by converging preclinical and clinical evidence, this study sought to provide initial evidence as to whether DP+

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smokers compared with DP− smokers: 1) find smoking more reinforcing relative to other reinforcers; and 2) have greater changes in reward sensitivity, subjective reward from self-selected alternative reinforcers, and affect while smoking as usual versus abstinent. A better understanding of smoking's role among DP+ smokers may shed light on novel smoking cessation treatment targets for these smokers.

Methods and Materials

Study Participants

Cigarette smokers ($n = 83$) were recruited from the community through print advertisements. Interested smokers completed a telephone screen assessing smoking history, depression status, medical and psychiatric conditions, and medication/drug use. Eligible smokers were between the ages of 18 and 65, had smoked at least 10 cigarettes a day for 6 months, and could be classified into one of two depression status groups. DP− included smokers with no past history of major depression and no current depression symptoms. DP+ included smokers with both a past history of major depression and current depression symptoms, a group with disproportionate smoking burden and less success at quitting smoking (14,62). Smokers who had a past history of MDD but no current depression symptoms were excluded, as were smokers with no past history of MDD with current depression.

Past history of major depression was determined by the Inventory to Diagnose Depression-Lifetime (IDD-L) (51,63,64). The IDD-L is a 22-item scale with response options ranging in symptom severity (0 to 4) and an additional question regarding the persistence of the symptom for ≥2 weeks, resulting in a positive or negative history of depression. Current depressive symptoms were defined as a score >16 on the 20-item Center for Epidemiologic Studies Depression Scale (CES-D), which correlates with clinical ratings of depression and has high internal consistency (17,65,66). Both the IDD-L and the CES-D were completed through a semistructured telephone interview by masters-level trained psychologists to prevent ineligible participants from attending an intake visit.

Exclusion criteria included pregnancy; lactation; chronic medical condition; current diagnosis or history of bipolar disorder, schizophrenia, or substance abuse (other than nicotine) (27,51,60,67); and current or recent use of smoking cessation, antidepressant, or antipsychotic medications. The exclusion criteria were assessed via self-report on the telephone screen with an objective assessment of smoking status, medication and drug use, and pregnancy at the intake visit. Participants provided written informed consent to a protocol approved by the University of Pennsylvania's Institutional Review Board. Participants then provided a carbon monoxide (CO) breath sample to verify smoking status and a urine sample for a drug screen (Instant Technologies, Inc., Norfolk, Virginia) and pregnancy. Participants who had a CO <10 ppm or a positive urine drug screen for illicit drugs or psychotropic medication were excluded. The final sample consisted of 34 DP+ smokers and 49 DP− smokers. Table 1 characterizes the groups.

Procedure

Eligible participants completed a baseline assessment of demographics, smoking history, and mood and were scheduled for two morning laboratory assessment sessions. One session was scheduled after overnight smoking abstinence (9 hours) and the second session was scheduled while smoking as usual. The relative reinforcing value of smoking was assessed after smoking abstinence (to ensure motivation to respond), and reward sensitivity was assessed during both smoking abstinence and smoking ad libitum. Participants received $30 compensation for each laboratory visit. Using experience sampling methods, participants then completed measures of subjective reward, positive affect, and negative affect via telephone across 3 days while smoking as usual and 3 days while smoking abstinent. Detailed procedures are described below and depicted in Figure 1.

Laboratory Assessments

A validated smoking choice paradigm permitted the evaluation of the relative reinforcing value of smoking, which is the preference for smoking over other alternatives (67–70). In this

Table 1. Descriptive Characteristics of DP− ($n = 49$) and DP+ ($n = 34$) Smokers at Baseline

Covariate	DP−		DP+		Overall		p Value χ^2_1 *df*; *t* Test
	Mean	SD	Mean	SD	Mean	SD	
Age	41.02	14.17	34.47	13.86	38.34	14.33	.04
Smoking Rate (Cigarettes/Day)	20.10	21.60	18.06	6.99	19.29	17.32	.60
Nicotine Dependence (FTND)	5.61	1.79	5.85	1.58	5.71	1.70	.50
MNWS (Baseline)	8.99	5.56	21.59	7.86	13.98	9.00	<.0001
Positive Affect (PANAS)	35.10	7.29	27.85	7.51	32.13	8.16	<.001
Negative Affect (PANAS)	13.57	3.75	25.11	8.75	18.30	8.47	<.001
Complementary Reinforcers	72.06	41.52	65.59	34.04	69.41	38.54	.46
Substitute Reinforcers	31.65	23.43	20.09	19.53	22.00	31.84	.02
IDD-L	5.83	7.96	40.42	7.12	19.52	18.63	<.0001
CES-D	7.14	5.33	30.61	10.66	16.43	13.94	<.0001
	%	Count	%	Count	%	Count	
Female	27%	(13)	47%	(16)	35%	(29)	.06
Race (White)	37%	(18)	44%	(15)	40%	(14)	.50
Attended College	51%	(25)	53%	(18)	52%	(18)	.90
Married	12%	(6)	18%	(6)	14%	(5)	.50
Employed	53%	(26)	68%	(23)	59%	(20)	.18

CES-D, Center for Epidemiologic Studies Depression Scale; DP+, depression-prone smokers; DP−, smokers not prone to depression; FTND, Fagerstrom Test for Nicotine Dependence; IDD-L, Inventory to Diagnose Depression-Lifetime; MNWS, Minnesota Nicotine Withdrawal Scale; PANAS, Positive and Negative Affect Schedule.