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Distress Intolerance and Smoking Topography in the Context of a Biological Challenge

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Abstract

Introduction: Distress intolerance (DI), one's perceived or behavioral incapacity to withstand distress, is implicated in psychopathology and smoking. This study evaluated the effect of DI on smoking reinforcement in the context of a carbon dioxide (CO₂) biological challenge.

Methods: Adult daily smokers ($n = 90$; 48.9% female) were randomized to receive a single inhalation/breath of 35% CO₂-enriched air ($n = 45$) or compressed room air ($n = 45$). Perceived DI was assessed before the challenge. Smoking reinforcement was examined via average post-challenge puff volume across puffs and at the puff-to-puff level.

Results: Higher DI was associated with an increased average puff volume ($b = -4.7$, $p = .031$). CO₂ produced decreased average puff volume compared with room air ($b = -7.7$, $p = .018$). There was a DI* condition interaction ($f^2 = 0.02$), such that CO₂ decreased average puff volume compared with room air in smokers with higher DI ($b = -13.9$, $t = -3.06$, $p = .003$), but not lower DI. At the puff-to-puff level, there was a significant interaction between DI, condition, and cubic time ($b = 0.0003$, $p = .037$). Specifically, room air produced large initial puff volumes that decreased from puff to puff over the cigarette for high- and low-DI smokers. CO₂ produced persistent flat volumes from puff to puff over the cigarette for higher DI smokers, whereas CO₂ produced puff volumes like that of room air in lower DI smokers.

Discussion: Findings suggest DI heightens smoking reinforcement generally, and in the context of intense cardiorespiratory distress, is associated with stable and persistent smoking. DI is a promising therapeutic target that, if addressed through psychological intervention, may improve cessation outcomes by decreasing smoking reinforcement.

Implications: This study contributes to our understanding of the relationship between DI and smoking reinforcement, via examining these processes in response to acute cardiorespiratory distress. Specifically, we found that smokers who are less tolerant of distress, as opposed to those who are more tolerant, evince a decrease in average puff volume, and consistently low puff-to-puff volume, in response to a biological stressor. These findings suggest that smokers high in DI alter smoking behavior following acute cardiorespiratory distress, perhaps to reduce overstimulation, yet also persist in smoking in a manner that suggests an inability to achieve satiation.

Introduction

Distress intolerance (DI), an individual's perception of or behavioral incapacity to withstand negative emotional or physical distress states,¹ is an etiological and maintenance factor underlying multiple psychological disorders (eg, anxiety disorders, posttraumatic stress disorder, and major depressive disorder) and disorders characterized in part by maladaptive externalizing behaviors (eg, borderline personality disorder, eating disorders, and substance use disorders).² Indeed, DI is implicated in the maintenance of cigarette smoking^{3,4} and is thought to underlie the comorbidity of psychological disorders and smoking.⁵ Theoretically, individuals with higher levels of DI may be more apt to avoid or engage in emotion-focused coping behaviors in response to internal distress cues.^{3,4} Higher DI is related to beliefs that smoking can aid in relieving negative affect⁶ and the tendency to smoke to alleviate negative affect.⁷ Moreover, in the context of acute abstinence-induced distress, higher levels of DI heighten smokers' emotional reactivity to aversive interoceptive cues,^{8–10} which may exacerbate smoking-specific distress (eg, craving, withdrawal severity)^{11,12} and increase risk of smoking lapse¹³ and relapse.^{3,14,15} Thus, DI may serve to negatively reinforce smoking via the temporary amelioration of aversive states.¹⁶ For these reasons, DI has been identified as a promising therapeutic target in smoking cessation interventions^{17,18} and may be particularly relevant to smokers with comorbid psychological symptoms or disorders, given reductions in DI can improve mental health.^{19–22}

It has been posited that through repeated pairing of smoking with acute distress states, smokers with higher DI may learn to associate cigarettes with pleasure (eg, relaxation, escape), which may enhance the incentive salience of cigarettes (ie, excessive motivation for a drug or “wanting”) and produce compulsive use behavior.²³ Style of puffing behavior (ie, topography) has been conceptualized as a behavioral index of incentive motivation or a reinforcing value of smoking (ie, smoking reinforcement).²⁴ DI has been described as vulnerability that is only “activated” in the context of a situational stressor or distress,^{12,13} and the extent to which DI is activated may depend on the *specific type* of stressor or form of distress (eg, nicotine withdrawal, negative mood, anxious arousal). For example, following a 12-hour period of nicotine deprivation, smokers with higher DI take larger average puff volumes during *ad libitum* smoking²⁴ and take more puffs during a smoking task that elicited strong motivation to smoke and competing motivation to abstain.²⁵ In contrast, perceived DI does not appear to be related to smoking reinforcement (ie, average puff volumes) in the context of neutral mood induction or in response to tasks that elicit negative mood, including viewing negative pictures, completing a challenging computer task, or preparing a social speech.²⁴

Anxious arousal (physiological activation and bodily tension: eg, shortness of breath, dizziness, lightheadedness, trembling, shaking) is a primary and relatively unique feature of anxiety psychopathology,^{26,27} and is another distress state that can activate DI and create risk for persistent smoking.^{4,28} Biological challenge paradigms can be used to provide a reliable manipulation of *acute* physiological sensations associated with anxious arousal and panic attacks.²⁹ One of the most widely used procedures is carbon dioxide (CO₂)-enriched air breathing challenges,³⁰ which can be dosed in several ways (eg, altering CO₂ concentration or challenge length) to modify the duration and intensity of the physiological arousal.³⁰ A single vital capacity inhalation of 35% CO₂ gas mixture challenge involves one of the highest exposures but the briefest duration, and phenotypically produces abrupt physiological arousal characteristic of the onset of

naturally occurring panic attacks.³¹ Using this approach, we previously found that 35% CO₂-enriched air, compared with compressed room air, produced significant reductions in average puff volume during *ad libitum* smoking.³² The observed *reduction* in puff volumes following acute physiological arousal may reflect behavioral avoidance, due to high-intensity cardiopulmonary distress produced by CO₂. Importantly, smokers with higher DI respond with greater fear to acute provocation of anxious arousal.^{8,12} Given that DI can “amplify” the negative subjective experience of distress, smokers with elevated DI may be hypersensitive to high-intensity anxious arousal, which may acutely dampen smoking behavior.

Therefore, this study tested the effect of DI on smoking reinforcement measured during *ad libitum* smoking following a biological challenge of 35% CO₂ compared with room air. Smoking reinforcement was indexed by (1) average puff volume and (2) puff-level data to examine variability in puff volume over the course of a single cigarette following the biological challenge. On the basis of findings from the parent study,³² we hypothesized that the 35% CO₂ biological challenge, compared with room air, would reduce average puff volume in smokers with higher DI because of hypersensitivity to the aversive nature of CO₂ exposure. In addition, we hypothesized that smokers with higher DI compared to lower DI who were exposed to 35% CO₂ would demonstrate more persistent puff volumes over the course of a cigarette, which is consistent with efforts to maximize and maintain nicotine exposure.³³

Methods

Participants and Procedures

Participants ($n = 90$; 48.9% female) were adult nontreatment-seeking daily smokers recruited from a large urban city in a southern state in the United States to participate in an experimental study on smoking behavior.³² Inclusion criteria were as follows: (1) 18–65 years of age; (2) daily smoking for at least the past year; (3) smoking an average of at least 10 cigarettes per day; (4) smoking first cigarette of day within at least the first 30 minutes of waking³⁴; and (5) stability of daily cigarette use (ie, had not decreased the number of daily cigarette use by more than half in the past 6 months). Exclusion criteria were as follows: (1) potentially contraindicated medical condition for completion of the biological challenge (eg, cardiovascular disease, chronic obstructive pulmonary disease); (2) limited mental competency and/or the inability to give informed, voluntary, written consent for participation; (3) being currently pregnant or nursing; (4) current (same-day) PRN use of psychotropic medication (eg, benzodiazepines); (5) current suicidal ideation and/or intent assessed via diagnostic assessment; (6) current (past year) non-nicotine substance use disorder or psychotic spectrum disorder; (7) current use of any pharmacotherapy or psychotherapy for smoking cessation; (8) insufficient command of the English language; and (9) self-reported low computer literacy due to the computerized nature of the study assessment and procedures. Participants were not excluded for regular daily use of psychotropic medications (ie, stable at least 3 months).

Baseline Assessment

Smoking history was assessed with the *Smoking History Questionnaire*,³⁵ and tobacco dependence and characteristics of smokers' usual cigarette brand were assessed by the *Fagerström Test for Cigarette Dependence*.³⁴ A biochemical verification of smoking was conducted via *expired carbon monoxide* breath analysis to determine smoking recency. A clinical diagnostic assessment of

past 12-month psychopathology was completed per the *Structured Clinical Interview for DSM-IV-TR Disorders, Non-Patient Version*³⁶ to assess exclusion criteria. Participants then completed an *ad libitum* outdoor smoking trial at a standardized point during the baseline assessment using their own cigarette brand. Next, participants returned inside the laboratory for an adaptation period, during which they completed approximately 60 minutes of self-report assessments (including assessment of DI), which were broken up by two scheduled snack and water breaks (no smoking or caffeine was permitted). The adaptation period was designed to permit the effects of the nicotine to wear off and allow for smoking urges or withdrawal to acutely increase³⁷ before the experimental manipulation. As expected, smoking urges per the *Questionnaire of Smoking Urges-Brief*³⁸ significantly increased during the adaptation period ($M_{\text{change}} = 259.0$, $t = 9.38$, $df = 89$, $p < .001$), which was a large sized-effect ($d = 0.99$).

Experimental Phase

Participants were then randomized to one of two experimental conditions (35% CO₂-enriched air or compressed normal room air) using a computerized randomizer, designed to stratify condition assignment to be equivalent by sex. The participant and research assistant were blinded to experimental condition, and the biological challenge was administered by a separate unblinded researcher. The *biological challenge task* was a single vital capacity breath of CO₂-enriched air mixture or compressed room air. Complete experimental procedures are reported in the original study.³² Briefly, participants were fitted with a respiration band, heart rate monitor, and mask that permitted only mouth breathing. Participants were then informed of the challenge procedures and shown a computerized instructional presentation that informed them how to complete *two* vital capacity breaths and then practiced and followed-along with the instructional prompt. The first vital capacity inhalation was used to clear air from the lungs (on forceful exhale) to prepare for the second vital capacity inhalation (with the manipulated air on randomization). This two-breath combination was completed twice. The first set was used to estimate the vital breath capacity of the participant; the second set for the actual manipulation. Cross-verification of the inhalation volume between the first and second set of breaths was checked for instructional adherence. After practice procedures, a 3-minute neutral adaptation period was observed, after which the biological challenge task was completed. Immediately following the inhalation, a 2-minute recovery period of normal breathing was observed. The manipulation check indicated that CO₂-enriched air (compared with room air) produced significantly larger increases in subjective distress, panic attack symptoms, physiological arousal (heart rate, respiration rate), and peak expired end-tidal partial pressure CO₂ (medium-to-large effects).³² After completion of the biological challenge, participants completed a second outdoor *ad libitum* smoking trial. Finally, participants were provided compensation (\$50) and debriefed regarding the nature of the study and manipulation condition.

Measures

The *Distress Tolerance Scale* (DTS)³⁹ is a self-report assessment of one's perceived ability to experience and endure negative emotional distress states. The 14-item version of the DTS was used, which has been validated in community-recruited cigarette smokers.⁴⁰ Items are answered on five-point Likert-type scales ranging from (1) *strongly agree* to (5) *strongly disagree*. Items are summed, and a mean score is

computed; possible range is 1–5, with higher scores reflecting greater tolerance for distress (lower DI). The DTS items have good psychometric properties, including high internal consistency and appropriate convergence with other self-report ratings of affective distress and regulation,³⁹ including in smoking samples.⁴⁰ In the current sample, item internal consistency was high (Cronbach's $\alpha = .937$).

Smoking reinforcement was assessed before and after the biological challenge during outdoor smoking trials. Participants were told they could have a "smoke break" to smoke one cigarette using the portable *Clinical Research Support System* (CReSS device; Plowshare Technologies, Borgwaldt KC, Inc, Richmond, VA). Participants were oriented to the CReSS device and shown how to use it. The CReSS device has been validated for outdoor use and increases ecological validity.⁴¹ A research assistant accompanied participants outdoors alongside the laboratory for the smoking trial. Participants were instructed to smoke as usual, to avoid distractions while smoking (ie, do not talk to bystanders, use electronic devices), and were given as much time as desired to smoke a single cigarette. Puff topography data were downloaded from the CReSS device after smoking trials. The CReSS device has a sterilized flow meter mouthpiece that is connected to a pressure transducer, which converts pressure into a digital signal that is sampled at 1000 Hz. CReSS computer software transforms the signal to a flow rate (mL/s), from which puff topography data are computed. The reliability and acceptability of use of the portable CReSS device is well documented^{42,43} and the CReSS device is recommended over direct observation.⁴² Consistent with prior studies,²⁴ puff volume (milliliter of smoke taken in during each puff) was used to index smoking reinforcement.

Data Analytic Procedures

Analyses were conducted using Stata v. 14. Smoking reinforcement was examined in two ways: (1) average puff volume and (2) change in puff volumes over smoking trial. In the first model, a linear regression model was constructed to test the main effects of condition and DTS, and the condition $\times$ DTS interaction on average puff volume post-challenge. In the second, multilevel modeling was used to examine the main and interactive effects of condition and DTS on changes in puff volume over number of puffs. Here, puff number was conceptualized as "time." Thus, the multilevel modeling tested involved three primary predictors (condition, DTS, and time) and all interaction terms. The intraclass correlation values for puff-level volumes were above the conservative recommended value of .10 (intraclass correlation = .50, 95% CI = 0.42% to 0.58%). Linear, quadratic, cubic, and hyperbolic effects of time were modeled, and model fit was examined using Akaike information criterion (AIC) and the Bayesian information criterion (BIC). Time (puff number) was mean centered to prevent multicollinearity when using higher-order polynomials.⁴⁴ Random intercepts and slopes were included in all models. Huber-White robust sandwich estimators were used to adjust for heteroskedasticity in the error terms, and an unstructured covariance matrix was specified to allow for each covariance to be uniquely estimated.⁴⁵

Model Building

Average puff volume (during smoking trial 1) was entered as a covarying factor to examine changes in puff volume resulting from the biological challenge. Experimental condition was dummy coded (0 = room air, 1 = CO₂). Participant sex (coded 0 = male, 1 = female) was significantly negatively correlated with average puff volume

during smoking trial 1 ($r = .25$, $p = .016$) and smoking trial 2 ($r = -.22$, $p = .036$); thus, sex was entered as a model covariate. Age, race, body mass index, level of cigarette dependence, cigarettes per day, menthol cigarette use, or smoking recency (expired carbon monoxide parts per million from breath analysis) were not associated with average puff volume during either smoking trial and were therefore not modeled as covariates. In addition, menthol use and race were not related to DTS. Continuous variables were mean centered before model entry. Significance was determined based on p value less than .05.

Data Cleaning

Raw puff-level smoking topography data were examined for range and outliers. Mean and standard deviation are reported as mean $\pm$ SD. The observed range of puffs during *ad libitum* smoking ranged from 7 to 43 (smoking trial 1; 21.3 ± 7.56) and 5 to 43 (smoking trial 2; 21.8 ± 8.92). Because of the small number of datapoints with at least 40 puffs (0.4% smoking trial 1, 1.0% smoking trial 2), those datapoints were dropped from analyses to maintain shape of the data distribution. Outlying values were identified using standard scores, with a criterion of $z = 3.5$ to retain maximum data.⁴⁶ A small number of outlier values were detected (2.1% smoking trial 1; 1.3% smoking trial 2). The outliers were determined to be legitimate high-magnitude values and were recoded as one unit higher than the next lowest nonoutlying value.⁴⁶

Results

Participants ($n = 90$; 48.9% female) were 43.6 ± 9.7 years old and self-reported race as primarily black or African American (61.1%) and white (32.2%). Approximately half completed at least part of college (54.4%), and employment status was primarily reported as full- or part-time (45.6%) and unemployed (35.6%). The sample reported smoking an average of 15.8 ± 5.9 cigarettes per day in the 7 days before the laboratory visit, and scores on the Fagerström Test for Cigarette Dependence were 4.8 ± 1.4 , reflecting moderate levels of tobacco dependence. Average expired carbon monoxide levels at baseline were 24.0 ± 10.9 ppm. Slightly more than half of the sample reported smoking menthol cigarettes (58.9%). In terms of past 12-month psychological disorders, 33.3% of the sample met criteria for a DSM-IV defined Axis I disorder (of which, 46.7% had more than one diagnosis; range 1–4). For complete descriptive information on the sample, see the parent study.³² On average, DTS scores were 3.3 ± 1.0 (observed range 1.2–5.0).

Half of the sample ($n = 45$; 50.0%) was randomized to 35% CO₂ and the other half was randomized to room air. In the parent study, there were no significant demographic or smoking characteristics by experimental condition.

Average Smoking Reinforcement

Results from the multiple regression predicting post-challenge change in average puff volume are displayed in Table 1. The overall model was significant ($F(5,84) = 20.68$, $p < .001$; $R^2 = .55$). In addition, there was a significant main effect of DTS on puff volume, such that higher DI was associated with significantly greater increases in puff volume following the biological challenge regardless of condition ($b = -4.7$, $p = .031$). There was also a small-sized DTS $\times$ condition interaction at a trend level ($b = 5.6$, $p = .060$; $f^2 = 0.02$).

Table 1. Regression Model Predicting Changes in Average Puff Volume

Variable	<i>b</i>	SE	<i>t</i>	<i>p</i>
Sex (female = 1)	−3.1	3.4	−0.93	.355
Puff volume (Pre-Challenge)	0.5	0.1	9.20	<.001
Condition (CO ₂ = 1)	−7.7	3.2	−2.40	.018
DTS	−4.7	2.2	−2.19	.031
Condition $\times$ DTS	−0.01	0.01	−2.18	.060

Continuous variables were mean centered. CO₂ = carbon dioxide; DTS = Distress Tolerance Scale.

Note: High DI (−1SD on the DTS) and low DI (+1SD on the DTS).

Figure 1. Interaction between distress intolerance (DI) and biological challenge on average puff volume. High DI (−1 SD on the Distress Tolerance Scale [DTS]) and low DI (+1 SD on the DTS).

Figure 1 illustrates the model-based estimations of the “simple slopes” (regression lines), showing the relationship between condition and post-challenge puff volume for participants at two levels of DI $\pm$ 1 SD from the mean of DTS. The form of the interaction revealed that 35% CO₂ produced significantly larger reductions in puff volume compared to room air in smokers with higher DI (−1 SD DTS; $b = -13.9$, $t = -3.06$, $p = .003$), but not for those with lower DI (+1 SD DTS; $b = -1.5$, $t = -0.33$, $p = .740$). The Johnson–Neyman technique was used (per recommendations)⁴⁷ to statistically identify points in the range of the continuous moderator variable (DTS) where the effect of the predictor on the criterion variable transitions from being statistically significant to nonsignificant. The Johnson–Neyman technique revealed that the effect of 35% CO₂ on reduced puff volume was significant for smokers with DTS scores less than or equal to 3.53, which included 54.4% of the sample; the conditional effect became stronger as DTS scores decreased.

Puff Level Smoking Reinforcement

Results from the multilevel modeling are presented in Table 2. Comparison of model fit indices indicated that a model with a cubic effect of time best fit the data (lowest AIC and BIC values: linear time [AIC = 17254.1, BIC = 17332.1]; quadratic time [AIC = 17236.8, BIC = 17337.1]; cubic time [AIC = 17217.7, BIC = 17320.3]; hyperbolic time [AIC = 17323.1, BIC = 17378.8]). Results indicated that

Table 2. Results From Puff-Level Analyses

Variable	<i>b</i>	95% CI		SE	<i>z</i>	<i>p</i>
		Lower	Upper			
Linear time	-0.8680	-1.6771	-0.0588	0.4128	-2.10	.036
Quadratic time	0.0053	-0.0240	0.0346	0.0149	0.36	.722
Cubic time	0.0035	0.0011	0.0060	0.0013	2.80	.005
Sex (1 = female)	-3.0417	-9.4358	3.3524	3.2623	-0.93	.351
Average puff volume (Pre-Challenge)	0.5192	0.3023	0.7360	0.1106	4.69	<.001
Condition (1 = CO ₂)	-5.1345	-17.1009	6.8319	6.1054	-0.84	.400
DTS	-2.0256	-10.3138	6.2625	4.2287	-0.48	.632
Condition × DTS	1.2232	-8.5251	10.9714	4.9737	0.25	.806
Linear time × condition	0.1700	-0.9334	1.2733	0.5629	0.30	.763
Linear time × DTS	0.2278	-0.4294	0.8850	0.3353	0.68	.497
Linear time × condition × DTS	-1.0493	-1.9454	-0.1532	0.4572	-2.30	.022
Quadratic time × condition	-0.0207	-0.0576	0.0162	0.0188	-1.10	.271
Quadratic time × DTS	-0.0193	-0.0451	0.0065	0.0132	-1.47	.142
Quadratic time × condition × DTS	0.0096	-0.0309	0.0501	0.0207	0.46	.642
Cubic time × condition	-0.0016	-0.0048	0.0015	0.0016	-1.00	.317
Cubic time × DTS	-0.0014	-0.0037	0.0009	0.0012	-1.16	.247
Cubic time × condition × DTS	0.0034	0.0002	0.0066	0.0016	2.09	.037

Models with statistically significant effects are presented in bold for ease in viewing. Continuous variables were mean centered. CO₂ = carbon dioxide; DTS = Distress Tolerance Scale.

Note: High DI (-1SD on the DTS) and low DI (+1SD on the DTS).

Figure 2. Interaction between distress intolerance (DI) and biological challenge on puff volume trajectory. High DI (-1 SD on the Distress Tolerance Scale [DTS]) and low DI (+1 SD on the DTS).

there was a main effect of cubic time ($b = 0.0035$, $p = .005$). Yet, neither the DTS × cubic time interaction ($p = .247$) and the condition × cubic time interaction ($p = .317$) were significant. However, the cubic time × condition × DTS interaction was significant ($b = 0.0003$,

$p = .037$). See Figure 2. The form of the interaction indicated that 35% CO₂ produced persistent (ie, flat) puff volumes over the course of smoking in smokers with higher DI and produced initial increases in puff volumes, which gradually decreased over the course of smoking in smokers with lower DI. In contrast, room air produced a similar pattern of puff volumes to that observed in smokers lower in DI following CO₂ for smokers with higher and lower DI, except for an additional increase in puff volumes in smokers with higher DI toward the end of the *ad libitum* session.

Discussion

The study provides a novel laboratory model of the relation between DI and smoking reinforcement via comparison of smoking behavior following acute anxious arousal (ie, 35% CO₂) versus a control (ie, no stress) biological challenge. We aimed to extend our previous finding that 35% CO₂ decreases smoking reinforcement compared with room air,³² by considering the role of perceived DI.

We found that regardless of condition, DI is associated with increases in average puff volume during *ad libitum* smoking following the biological challenge. Given that DI is associated with reliance on “quick-fix” coping strategies in the face of emotional and physical distress,^{48,49} larger puff volumes in smokers may demarcate the tendency to smoke to escape, avoid, or cope with distressing states.²⁴ According to negative reinforcement models, individuals learn to associate rapid alleviation of distress with smoking, which may contribute to the maintenance of the reinforcing value of cigarettes. Interestingly, compared with room air, CO₂ decreased puff volume in smokers with higher DI, but not for those with lower DI. Thus, the main effect of DI and interactive effects operate in different ways: DI contributes to increased puff volumes *on average*, but in the context of acute anxious arousal, DI contributes to attenuated puffing behavior. Given that smokers with elevated DI are hypersensitive to acute anxious arousal produced by CO₂ (eg, dry mouth, lightheadedness, racing heart, and suffocation feelings),¹² these

smokers may experience smoke inhalation and the activating effects of nicotine to be particularly aversive following CO₂ exposure and in turn, may compensate by taking smaller puffs to avoid further provocation of distress.³² Here, smaller puff volumes reflect attempts to avoid additional cardiopulmonary distress, which can maintain reliance on cigarettes via negative reinforcement learning. In contrast, in the presence of lower-intensity arousal (ie, room air biological challenge), smokers with elevated DI may be more likely to rely on cigarettes to downregulate mild levels of anxious arousal, thus evidence greater puff volumes that negatively reinforce continued smoking. These findings offer increased specificity to models of negative reinforcement smoking motivation in the context of anxious arousal, specifically,³⁰ relative to other situational states such as nicotine withdrawal or negative mood states.^{24,25}

We also conducted a fine-grained analysis to examine the association between DI and biological challenge response at the puff-to-puff level. Puff volumes over the course of *ad libitum* smoking differed as a function of DI and CO₂ exposure. Regardless of level of DI, inhalation of room air produced large initial puff volumes at the beginning of the cigarette, which gradually declined over the *ad libitum* session. This is a typical pattern of puffing that is thought to reflect initial nicotine loading (ie, early large puff volumes) and subsequent satiation evidenced by decreasing puff volume.⁵⁰ Smokers with higher DI evidenced increased puff volumes toward the end of *ad libitum* smoking, suggesting that they may place higher value on the final puffs of a cigarette and use these puffs as a final opportunity for distress relief or coping. In contrast, 35% CO₂ produced a persistently “flat” shape of puff volumes over the course of the cigarette in smokers with higher DI. Thus, for smokers with higher perceived DI, intense cardiorespiratory arousal may interfere with the ability to achieve satiation, possibly because of the absence of initial nicotine loading while smoking. Consistent (ie, flat) puff volumes during *ad libitum* smoking have previously been documented among smokers with a history of panic attacks and also may reflect a modified smoking pattern aimed at avoiding sudden surges in arousal, including nicotine-induced arousal.³³ Importantly, 35% CO₂ produced persistent and stable puff volumes only for smokers with higher DI, but not for those with lower DI. This finding underscores the importance of considering one’s *perception* of his or her ability to withstand distress in the context of better understanding emotional vulnerabilities for smoking.^{3,51}

There are several limitations to this study. First, although a CO₂ biological challenge is a common anxiety-induction procedure that reliably induces anxious arousal,³⁰ the 35% CO₂ dose produces an intense surge of physiological arousal, as seen in panic attacks.³¹ Thus, these findings may not necessarily generalize to work focused on DI and trait anxiety or lower-intensity anxious states and should not be viewed as necessarily comparable to work specific to negative mood-induced smoking.²⁴ Second, perceived DI was indexed by the DTS, which taps one’s perceived (in)ability to tolerate psychological distress states. We did not consider how one’s perceived inability to tolerate physiological distress or other specific emotional states (eg, frustration, uncertainty) may influence smoking reinforcement. Third, we did not examine one’s actual *ability* to withstand distress in terms of smoking reinforcement (ie, behavioral DI), which may offer unique information about emotional vulnerability and smoking.⁵¹ However, prior work has failed to find an association between behavioral indices of DI and smoking reinforcement,⁵² potentially because behavioral DI is influenced by certain states or conditions,^{53,54} suggesting it may have state like vulnerability and influence.

Fourth, we conceptualized puff topography as a behavioral index of smoking reinforcement,^{24,32} although puff volume can be influenced by individual difference factors not related to smoking intensity. We evaluated numerous individual factors in relation to puff volume and adjusted for those that were relevant (ie, sex). Nevertheless, we cannot rule out the possibility that additional unmeasured factors may influence puff topography. Fifth, the parent study was powered to detect medium-sized interactions, and although consistent with prior work,²⁴ findings here evidenced small-to-medium interaction effects. Finally, participants were recruited from a southern state in the United States, and the resulting sample comprised primarily smokers who were black or African American (61.1%) with low socioeconomic status, and high prevalence of psychopathology. The prevalence of menthol cigarette use was also high (58.9%), and nearly all menthol users were identified as black or African American (89.1%). Although our sample reflects a subgroup of the population that is at particularly high risk for tobacco-related disease,⁵⁵ it may also limit generalizability of findings. Although neither race nor menthol use was related to DI or puff volume in this study, more work is needed in this arena, given the significant dearth of existing studies pertaining to DI⁵⁶ and equivocal results in puff topography.⁵⁷⁻⁵⁹

This study presents novel laboratory evidence that identifies the impact of perceived DI, an identified therapeutic target (ie, mechanism), on smoking reinforcement. Specifically, smokers with higher DI appear to alter smoking behavior following acute cardiorespiratory distress, perhaps to reduce overstimulation, yet also persist in smoking in a manner that suggests an inability to achieve satiation. This type of research approach is aligned with research initiatives in precision medicine,⁶⁰ the National Institutes of Health’s Science of Behavior Change,⁶¹ and experimental therapeutics,⁶² which propel systematic identification of a potential mechanism that can be targeted in tailored treatment to improve physical and mental health outcomes. Indeed, the current findings have direct implications for the development of well-specified smoking cessation interventions for smokers who are at elevated risk for psychopathology (high DI) or with comorbid psychological symptoms or disorders.⁶³ Cognitive and behavioral interventions can be used to increase awareness and tolerance,⁶⁴ which may include uncomfortable physical distress states (ie, interoceptive exposure) and negative emotional distress states. In fact, reductions in perceived DI before a smoking cessation attempt produce improved short-term smoking abstinence.^{17,18} Thus, one’s perception of his or her ability to tolerate distress may be an important precessation treatment target to aid in decreasing the reinforcing value of smoking, especially distress-motivated smoking. When planning exposure-based interventions for smokers, it may be particularly important to tailor the intensity and type of distress induction to understand the unique influence that various distress states have on smoking reinforcement for each individual. Smokers may also benefit from receiving personalized feedback about *how* they smoke in response to certain distress states to help identify internal distress states that enhance the incentive salience of cigarettes.

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Declaration of Interests

The authors declare that there is no conflict of interest.

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