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An experimental test of the effect of acute anxious arousal and anxiety sensitivity on negative reinforcement smoking

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Abstract

Introduction: Although anxiety sensitivity has been reliably associated with smoking-anxiety comorbidity, there has not been a test of whether this construct moderates the effect of acute anxious arousal on actual smoking behavior. The present study utilized an experimental design to test the moderating role of anxiety sensitivity on laboratory-induced anxious arousal in terms of smoking urges and topography (puff style).

Method: Participants were adult daily smokers (n=90; M_{age}=43.6 SD =9.7); average 15.8 cigarettes per day). A between-subjects design was used; participants were randomly assigned to complete a biological challenge procedure consisting of either a single vital capacity inhalation of 35% carbon dioxide (CO_2)-enriched air mixture or compressed room air. Smoking urges and smoking topography (puff behavior) were assessed before and after the challenge.

Results: Results revealed a significant interaction between anxiety sensitivity and experimental condition (b=–9.96, p=0.014), such that high anxiety sensitive smokers exposed to 35% CO_2-enriched air reported significantly lower levels of smoking urges, relative to low anxiety sensitive smokers; the conditional effect of anxiety sensitivity was not observed for the room air condition. There were no significant interaction effects of experimental manipulation by anxiety sensitivity for any of the smoking topography outcomes.

Discussion: The present results suggest for smokers with higher levels of anxiety sensitivity, the acute experience of anxious arousal is related to decreased subjective smoking urges. These data invite future research to explore the reasons for dampened smoking urges, including cardiorespiratory symptom severity.

Keywords

Puff topography, biological challenge, panic, smoking motivation

Data suggest that anxiety sensitivity, defined as the extent to which individuals believe anxiety and anxiety-related sensations have harmful consequences (Reiss and McNally, 1985), is a key cognitive-affective mechanism that underlies the link between anxiety and smoking (Leventhal and Zvolensky, 2015). Anxiety sensitivity is a risk factor for the acquisition and maintenance of psychopathology, primarily anxiety and mood disorders (Olatunji and Wolitzky-Taylor, 2009). The anxiety sensitivity-smoking association is based on negative-reinforcement models of substance use (Zvolensky et al., 2003), as motivation to avoid the experience of discomfort and negative affective is one of the strongest drivers of maladaptive drug use (McCarthy et al., 2010). Thus, in the context of distressing somatic states (e.g. anxious arousal, panic attack), cigarette smokers high in anxiety sensitivity may be especially likely to rely on cigarettes (nicotine) for affect-regulation (Farris et al., 2015b).

Style of puffing behavior (topography) has been used to comprehensively examine factors that may maintain tobacco use and to understand individual aspects of nicotine regulation (Burling et al.,1985; Frederiksen et al., 1977). Puff topography also provides a behavioral index of the reinforcing value of smoking (Perkins et al., 2010). In the context of acute physiological distress (e.g. as seen in panic attacks, acute stress response), it is plausible that anxiety sensitivity could amplify the threatening experience of somatic distress (Marshall et al., 2009; Vujanovic and Zvolensky, 2009), which could result in greater desire to smoke as evidenced by increased smoking urges and altered puffing behavior (e.g. larger puff volumes, longer puff durations, shorter inter-puff intervals). In contrast, high anxiety sensitive individuals may view acute cardiorespiratory distress as highly aversive (McNally, 2002). Thus, when given the opportunity to smoke, these individuals may be distress avoidant and report lower urges to smoke and evidence attenuated puffing behavior. To date, we are aware of only two studies that have examined the role of anxious arousal on smoking craving (Attwood et al., 2014) and subjective nicotine withdrawal symptom severity (Farris et al., 2015c), whereas other investigations have exclusively focused on explicating the nature of anxious responding to physiological provocation among smokers versus non-smokers (Abrams et al., 2008b), or among smokers in nicotine deprivation or not (Abrams et al., 2011; Leyro and Zvolensky, 2013; Vujanovic and Zvolensky, 2009). Of note, these studies have not

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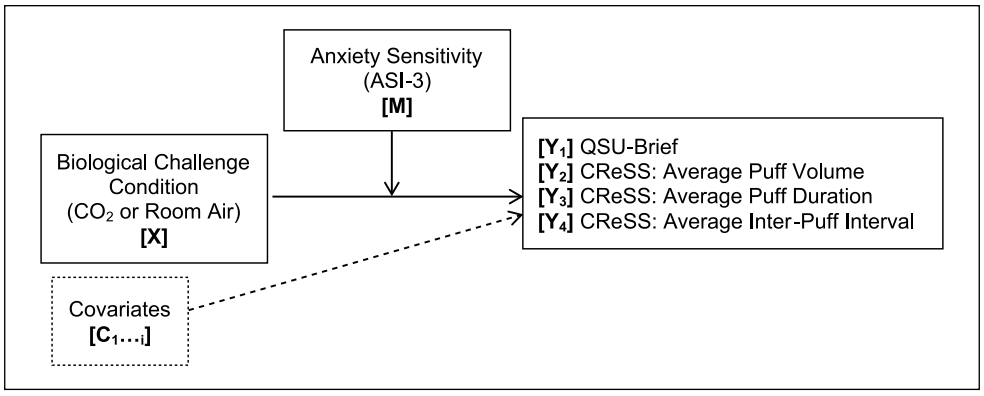

Figure 1. Conceptual model. ASI-3: Anxiety Sensitivity Index-3; CO_2: carbon dioxide; CReSS: Clinical Research Support System; QSU-Brief: Questionnaire of Smoking Urges-Brief.

modeled acute anxious arousal, as they have utilized lower concentrations of carbon dioxide (CO_2) gas for a longer duration which produces prolonged and lower-intensity arousal (Abrams et al., 2008a). Understanding the role of anxiety sensitivity in terms of negative-reinforcement smoking, in the context of acute physiological distress, could further inform and add specificity to integrated theoretical models panic/stress-smoking (Leventhal and Zvolensky, 2015; Sinha, 2001).

Together, the current study utilized a CO_2 biological challenge paradigm (Abrams et al., 2008a) to explore the moderating role of anxiety sensitivity on acute anxious arousal in terms of smoking urges and topography. Figure 1 provides a conceptual model of the study aims. Specifically, the current study utilized a between-subject design of a single vital capacity breath of 35% CO_2-enriched air (counter balanced with 65% O_2) versus compressed room air (normal air composition). This specific CO_2 procedure was used based on the ability of the challenge to produce abrupt somatic arousal (Vickers et al., 2012). A between-subjects design was utilized to help reduce the impact of possible learning-based confounds for the biological challenge and smoking topography tool. Based on the exploratory nature of this investigation, and lack of contextual specificity in existing theoretical models, we aimed to explore how anxiety sensitivity related to smoking urges and topography during ad-lib smoking, following acute induction of physiological distress.

Method and materials

Participants

Adult daily smokers were recruited for a study on "smoking behavior" via flyers posted in community areas and college campuses, newspaper advertisements, webpage announcements (e.g. university website, Craigslist.com), and word-of-mouth. Inclusion criteria for the current study included: (a) being between 18–65 years of age; (b) daily smoking for at least the past year; (c) smoking an average of ⩾10 cigarettes per day; (d) smoking first cigarette of day within at least the first 30 min of waking (⩾2 on the Fagerström Test for Nicotine Dependence (FTND), item 1); and (e) stability of daily cigarette use (i.e. had not decreased the number of daily cigarette use by more than half in the past six months).

Participants were excluded from the current study based on evidence of: (a) potentially contraindicated medical condition with biological challenge (e.g. coronary heart disease, chronic obstructive pulmonary disease); (b) limited mental competency and/or the inability to give informed, voluntary, written consent for participation; (c) being currently pregnant or nursing per self-report; (d) current as needed use of psychotropic medication; (e) current suicidal ideation/intent assessed via diagnostic assessment; (f) current (past year) non-nicotine substance use disorder or psychotic spectrum disorder (i.e. bipolar disorder, psychosis) assessed via diagnostic assessment; (g) current use of any pharmacotherapy or psychotherapy for smoking cessation; (h) insufficient command of the English language; and (i) self-reported low computer literacy due to computerized nature of the study assessment and procedures.

A total of 139 participants were assessed in-person for potential inclusion in the study, of which 40 were excluded due to not meeting the abovementioned inclusion/exclusion criteria. Of the 99 participants randomized as part of the experimental trial, the data from 9 cases were excluded due to: pilot participants (n=3), equipment malfunction (n=2), and invalid self-report data provided at baseline (n=4). Thus, 90 participants (M_{age}=43.6, SD=9.7; 48.9% female) were included in analyses, with equal randomization to experimental condition (n=45; 50% CO_2 condition).

Measures

Baseline assessment. A standardized phone-screening questionnaire was used to collect demographic information (age, gender, race/ethnicity, level of education, income). Mental competency and command of the English language were assessed via caller's understanding of screening questionnaire items. A medical history form (MHF) was used to assess the presence of health conditions and current medication use. Female participants were asked, "Are you currently nursing or pregnant, or expecting to become pregnant in the near future?" in order to assess pregnancy status.

The FTND (Heatherton et al., 1991), a six-item scale that assesses gradations in tobacco dependence, was used to assess the level of physiological dependence on nicotine (range 0–10, with higher scores reflecting higher levels of dependence). The

FTND has adequate internal consistency, positive relations with key smoking variables (e.g. saliva cotinine), and high test-retest reliability (Heatherton et al., 1991; Pomerleau et al., 1994). Respondents were also asked to report on their usual cigarette brand, and indicate specific properties of their preference cigarette (e.g. filtered, menthol). Internal consistency of the FTND items in the current study was α=0.39.

The Smoking History Questionnaire (SHQ; Brown et al., 2002), a 30-item self-report measure, was used to gather information about smoking history in order to establish pattern of cigarette use per eligibility criteria (e.g. daily use).

A carbon monoxide (CO) analysis, using the Vitalograph Breath Co carbon monoxide monitor, was conducted to measure the amount of CO (in parts per million (ppm)) in an expired breath sample, which is an indirect, noninvasive measure of blood carboxyhemoglobin. CO analysis was collected at baseline and 10 min after both within-study smoking trials.

The Timeline Follow-Back Interview (TLFB; Sobell and Sobell, 1992) is a calendar-based assessment of substance use, which was used to document frequency, quantity, and patterns of tobacco, alcohol, and illicit drug use in the past 30 days. This form of data collection has been found to have strong psychometric properties up to 90 days, including excellent inter-rater reliability, test-retest reliability, and strong convergent validity based on collateral interviews (Carey, 1997; Maisto et al., 1982). These data were used, in combination with other assessments, to determine the presence of regular smoking patterns in the past month, and identify use of other substances that might have been contraindicated for study participation. Internal consistency between TLFB days (seven days in past week) was α=0.95.

The Structured Clinical Interview for DSM-IV Disorders-Non-Patient Version (SCID-I/NP; First et al., 2007), a clinician-administered semi-structured diagnostic assessment, was used to assess the presence of past-year psychopathology based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition-Text Revision (DSM-IV-TR) diagnostic guidelines. Diagnostic assessments were conducted by highly-trained post-baccalaureate research assistants. In the current study, all diagnostic assessments were audio-recorded and 100% of cases were supervised by the first author for diagnostic accuracy. A random 20% of recordings were subjected to blinded inter-rater reliability review by a doctoral-level clinical psychology graduate student. No cases of diagnostic disagreement were noted (100% accuracy). The SCID-I/NP was used to characterize the sample and to determine if any psychological exclusionary criteria were met (e.g. psychotic-spectrum or non-nicotine substance use disorders, suicidality).

Pre-challenge measures. The Anxiety Sensitivity Index-3 (ASI-3; Taylor et al., 2007) is an 18-item psychometrically-sound self-report measure in which respondents indicate the extent to which they are concerned about possible negative consequences of anxiety-related symptoms (e.g. "It scares me when my heart beats rapidly"). Responses are rated on a five-point Likert scale ranging from zero (very little) to four (very much) and summed to create a total score (possible range 0–72). The ASI-3 items have strong and improved psychometric properties relative to previous measure items of the construct (Taylor et al., 2007) and have strong documented psychometric properties in daily cigarette smokers, including factor stability, reliability (test-retest, internal consistency), known-group validity, and convergent, discriminant, and predictive validity with key affective and smoking-relevant processes (Farris et al., 2015a). Internal consistency of the ASI-3 items in the current study was α=0.93.

The Positive and Negative Affect Schedule (PANAS; Watson et al., 1988) is a self-report measure that requires participants to rate the extent to which they experience 20 different feelings and emotions (e.g. nervous, interested) based on a Likert scale that ranges from 1 ("Very slightly or not at all") to 5 ("Extremely"). The measure yields two factors (10 items each), negative and positive affect, and has strong documented psychometric properties (Watson et al., 1988). The negative affectivity subscale was utilized as a covariate in analyses. Internal consistency of the PANAS-NA subscales items was α=0.93.

Biological challenge measures

Subjective arousal ratings. Two indices of subjective arousal were utilized immediately before and after the biological challenge. The Subjective Units of Distress Scale (SUDs; Wolpe, 1968) is a self-report measure of the extent to which a respondent is currently experiencing 'distress, discomfort, anxiety, or fear', rated from 0 (none) to 100 (extreme). The Diagnostic Sensations Questionnaire (DSQ; Sanderson et al., 1988) is a 17-item self-report measure of panic attack symptom severity, rated on a three-point Likert-type scale (0=absent to 3=severe). The DSQ was modified for the current study in two ways. First, while not a DSM-defined panic attack sensation, 'headache' was added as an additional symptom, to gauge the extent to which smokers reported pain as a result of the biological challenge. Second, based on pilot testing, the DSQ response options were transformed into a check-box format ("Please CHECK BOX if you are currently experiencing any of the following…") rather than a severity-style Likert-scale. This adaptation was implemented to increase simplicity and decrease time to complete the self-report ratings pre/post biological challenge. This categorical assessment approach was also consistent with the diagnostic procedures for determining the presence/absence of panic attacks symptoms during a panic attack (versus severity; e.g. per the SCID-I/NP informed by the DSM-IV). Thus, the modified-DSQ yielded a symptom count ranging from 0–18 sensations. The SUDs rating and total count on the modified-DSQ were utilized as a check of the manipulation for anxious arousal.

Physiological monitoring. A wireless physiological monitoring device that digitally records data was used to assess heart rate and respiration rate during the three-minute adaptation period (prior to the biological challenge) and two-minute recovery period (after the biological challenge). Data were recorded and displayed using the MP150 BIOPAC Systems bioamplifier (BIOPAC Systems, Inc.) and AcqKnowledge III data acquisition software (version 3.8.2) sampling at 1000 Hz. Data output were used to score average heart rate and respiration rate during recording periods.

End-tidal partial pressure CO_2 in exhaled air ($etpCO_2$). As a manipulation check, $etpCO_2$ was sampled during the breathing challenge using the flow volume sensor (RSS100HR; Hans Rudolph, Inc.). The typical level of expired CO_2 when breathing normal room air is approximately 5.0%. From breathing 35%

CO_2-enriched air, the expected expired CO_2 would be roughly 35.0%, although this value may be higher or lower depending on the depth/duration of the vital capacity breath. The peak etCO_2 level recorded after the manipulated breath was utilized as an additional manipulation check, and to verify that the desired level of CO_2 was administered.

Dependent measures. The Questionnaire of Smoking Urges-Brief (QSU-B; Cox et al., 2001) is a 10-item self-report, psychometrically-sound, assessment of urges for cigarettes. The QSU-B was completed before and after the biological challenge task via pencil/paper. The QSU-B items are rated on a 0–100 scale, with higher ratings indicative of greater agreement with the item. Item responses are scored to yield a total sum score to reflect overall smoking urges. This measure also yields two subscale scores (five items each), which index desire/craving to smoke (e.g. "I have a desire for a cigarette right now"; "If it were possible, I would probably smoke now") and urges to smoke for negative affect relief (e.g. "I could control things better right now if I could smoke"; "Smoking would make me less depressed"). Internal consistency of the QSU-B items was α=0.97 at pre-challenge and α=0.96 at post-challenge.

The Clinical Research Support System (CReSS; Plowshare Technologies, Borgwaldt KC, Inc., Virginia, USA), specifically the portable CReSS pocket device, was used to assess puff topography. The 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 (Blank et al., 2009; Perkins et al., 2012), and is recommended over direct observation (Blank et al., 2009). Puff topography data included: puff volume (volume of smoke taken in during each puff), puff duration (length of time for each puff), and inter-puff interval (amount of time between puffs). Puff level data were averaged to compute mean topography variables for each participant.

Procedure

See Figure 2 for illustration of study procedures. Interested callers responding to study recruitment methods completed a telephone assessment. Potentially eligible participants were informed that the study was about understanding how people smoke in different situations. They were read a standardized script that described the research study, and informed that the in-person visit would last approximately 3–4 h in length. Interested individuals were scheduled for an in-person appointment and instructed to bring their usual brand of cigarettes (at least two full cigarettes) to the appointment. Upon arrival, participants completed a baseline assessment to determine study eligibility, which included a diagnostic assessment (per the SCID-I/NP), clinician-administered TLFB, a series of self-report assessments (including the FTND), and provided a CO analysis of expired breath.

Next, all participants completed an ad-lib smoking trial (#1) at a standardized point during the baseline assessment. Participants were told they could have a 'smoke break' during which they were oriented to the portable CReSS device and shown how to use it. The research assistant accompanied the participant outdoors, alongside the laboratory, and informed the participant that he/she would have the opportunity to smoke one cigarette using the device. The participant was told to smoke as usual, and was given as much time as desired. Next, then participant returned inside the laboratory for an adaptation period which was broken up by two scheduled snack/water breaks (no smoking or caffeine was permitted), during which he/she completed approximately 75 min of self-report assessments (including the ASI-3). The adaptation period was designed to permit the effects of the nicotine to wear off and allow for smoking urges to increase prior to the experimental manipulation. Participants were dismissed if ineligible, or were informed that they had the opportunity to complete the experimental portion of the study (if eligible). Ineligible participants were provided $25 compensation for their time and offered psychiatric or smoking cessation referrals if desired.

Eligible participants completed the biological challenge task. Participants were randomized to one of two experimental conditions (35% CO_2-enriched air or compressed normal room air) using a computerized randomizer, designed to stratify condition assignment to be equivalent by participant sex. The participant and research assistant were blinded to experiential condition. The biological challenge task was a single vital capacity breath of CO_2-enriched air mixture or compressed room air. After completion of the biological challenge, the research assistant instructed the participant that he/she had the opportunity to take another 'smoke break'. The post-challenge ad-lib smoking trial (#2) was completed via identical procedures to the first smoking trial. Afterwards, the research assistant escorted the participant back into the laboratory. The participant was provided compensation ($50), debriefed regarding the nature of the study (and was "unblinded" to the manipulation condition), and was given smoking cessation and/or psychiatric referrals if requested. A final CO breath sample was collected prior to participant dismissal.

Experimental manipulation. Experimental sessions were completed in an 8×10 feet sound attenuated room, with an adjacent (experimenter/control) room. The participant room contained a desk, chair, computer monitor, video camera, and breathing mask apparatus (detailed below). The adjacent experimenter room ("control room") was fitted with a one-way mirror and video recording monitor used to observe the laboratory challenge, an intercom that allowed for communication between the participant and researcher, and a Dell PC desktop computer. The experimenter room also contained two 9 inch (diameter)×51 inch (height) high-pressure steel cylinder gas tanks (Praxair Gas, Inc.) filled with compressed gas (active tank: 35% CO_2, 65% O_2; control tank: 21% O_2, 79% N). Participants were oriented to the participant room, fitted with a respiration band and heart-rate monitor, and then informed of the challenge procedures.

Participants were read instructions by the study principal investigator to standardized expectancies prior to task:

> … to orient you, the mask in front of you connects to a bag filled with gas. This gas, depending on what you are randomly assigned to contains either 35% carbon dioxide–65% oxygen or normal compressed room air. As a reminder, you may

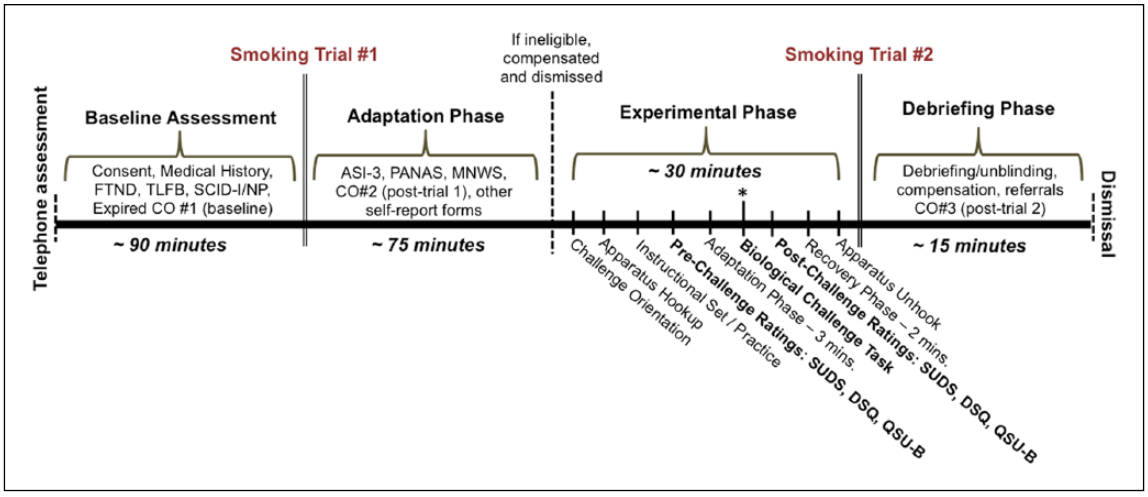

Figure 2. Illustration of study procedures. ASI-3: Anxiety Sensitivity Index-3; CO: carbon monoxide; DSQ: Diagnostic Sensations Questionnaire; FTND: Fagerström Test for Nicotine Dependence; MNWS: Minnesota Nicotine Withdrawal Scale; PANAS: Positive and Negative Affect Schedule; QSU-B: Questionnaire of Smoking Urges-Brief; SCID-I/NP: Structured Clinical Interview for DSM-IV Disorders-Non-Patient Version; SUDs: Subjective Units of Distress Scale; TLFB: Timeline Follow-Back Interview.

> experience various physical feelings such as breathlessness, racing heart, dizziness, dry mouth, feeling sweaty, feeling faint, and the possibility of having a panic attack. You may also notice a difference in taste when you inhale. Taking a breath of these gases is not harmful and has no long-term consequences. Now I will fit you with the mask. You will only be able to breathe from your mouth. Please do not remove the mask.

Before leaving the room, the principal investigator made sure the participant was comfortable and said:

> Now you are ready to learn the breathing task. Turn your attention to the computer monitor in front of you. This will instruct you on how to complete the task. Until it begins, just breathe normally from your mouth. You will only breathe room air during the practice.

Next, participants were shown a computerized instructional presentation. The computerized instructions informed participants how to complete two vital capacity breaths and then allowed practice/follow-along with the instructional prompt. The first vital capacity inhalation was used to clear air from lungs (upon 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. The principal investigator (first author) monitored the participant from the closed-circuit monitor in the adjacent experimenter room during the practice, and communicated via intercom if the participant indicated having questions.

Then, participants were instructed to complete a self-report rating card via pencil/paper. After completion of pre-challenge ratings, participants were instructed to breathe normally and rest until otherwise instructed. This period (timed for 3 min) served as a neutral adaptation period. Following this period, the participants completed the biological challenge task. Immediately following, the participants were instructed to complete the second self-report card (post-challenge ratings), and then completed a recovery period of normal breathing (2 min) before the principal investigator re-entered the room to unmask and unhook the physiological monitoring sensors.

Breathing apparatus. Breathing apparatus and software were engineered and built by Hans Rudolph, Inc. (for specific details of equipment set-up, please contact the corresponding author). Custom software recorded breathing data collected from the tidal flow and CO_2 sensor, and automatically operated the valves that controlled the delivery of test gas versus normal air. The data were sampled and recorded every second. The software also provided a graphical user interface to help the principal investigator monitor the participant and record the selected data.

Power analysis

Prior power calculations were conducted using G*Power 3.1 software application (Faul et al., 2007, 2009). Medium to large effects have been found in smoking topography studies and challenge studies between high and low anxiety sensitive individuals (Perkins et al., 2010; Telch et al., 2011; Zvolensky et al., 2001). Thus, with power set at 0.08 (alpha=0.05, d.f.=1,5), a sample size of 90 would be required (Cohen, 1988).

Data analytic procedures

Analyses were conducted in SAS 9.0. First, data were screened for data entry errors and illogical inconsistencies. Second, the frequency distributions, indices of skewness and kurtosis, and tests of normality were examined to determine the underlying distribution of study variables. Next, the equivalence of the

random assignment based on key baseline characteristics and pre-challenge smoking variables was assessed. Any variables in which groups differed were considered for potential inclusion as model covariates in the primary outcome analyses (e.g. key demographics, psychological disorder comorbidity, level of nicotine dependence, smoking frequency, use of menthol cigarettes).

Manipulation check. To ensure the biological challenge method adequately elicited acute anxious arousal, a series of regression analyses were conducted to examine differences between the experimental groups on four indices: (a) self-reported SUDs; (b) number of panic symptoms reported on the modified-DSQ; (c) average heart rate; and (d) average respiration rate. In each analysis, experimental condition (coded 0=room air; 1=35%-CO_2 enriched air) and the pre-challenge score of the dependence variable were regressed onto the respective post-challenge score.

Analytic overview for test of aims. Four regression models were conducted. Past-week average number of cigarettes per day (per the TLFB) was entered as a covariate, consistent with prior smoking topography studies (Veilleux et al., 2010) and CO_2 studies with smokers (Abrams et al., 2008b, 2011). Additionally, pre-challenge anxiety (SUDs; state-levels of distress) and trait negative affectivity were included as covariates, consistent with other CO_2 studies (Kutz et al., 2010; Richey et al., 2010). These variables were mean-centered prior to entry into the model. The pre-challenge value of the dependent variable was entered in each model (i.e. to test unique changes due to the biological challenge). Experimental condition (dummy coded; 0=room air, 1=CO_2-enriched air) and mean-centered anxiety sensitivity (ASI-3) were entered to test main effects. To test the moderating role of anxiety sensitivity, the interaction term (experimental condition×ASI-3) was entered. Dependent variables included: (a) self-report smoking urges (QSU-B total and subscales); (b) average puff volume; (c) average puff duration; and (d) average inter-puff interval. Analyses were conducted in SAS using the PROC GLM statement (and with 2500 bootstrapped sampling to accommodate non-normal distributions of any outcome variables). Significant interactions were subjected to tests of the simple slopes at high and low values of the moderator (±1 *SD* on the ASI-3), and the form of the interactions were visually plotted to interpret the direction of the effects.

Results

Descriptive overview of sample characteristics

Demographic characteristics, smoking history variables, and psychological factors are reported in Table 1, for the total sample and by experimental condition. Regarding smoking history, the average age of smoking initiation was at age 16.0 (*SD*=6.7) years. Participants indicated smoking for an average of 23.9 years (*SD*=10.2) in duration, and smoked an average of 15.8 (*SD*=5.9) cigarettes per day in the seven-day period prior to the laboratory visit. Based on targeted study sampling, the majority of participants reported smoking the first cigarette of the day with 5 min (56.7%) and moderate levels of nicotine dependence were reported per the FTND (*M*=4.8; *SD*=1.4). Average expired CO levels at baseline were 24.0 ppm (*SD*=10.9). Slightly more than half of the sample reported smoking menthol cigarettes (58.9%).

Average ASI-3 scores in the current sample were 12.7 (*SD*=12.8), with an observed range of 0–50 (18.9% in clinical range with scores ⩾25 per Taylor et al., 2007). 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), which included: posttraumatic stress disorder (11.1%), major depressive disorder (8.9%), specific phobia (8.9%), social anxiety disorder (6.7%), substance use disorder (early/sustained full remission; 5.6%), panic disorder with or without agoraphobia (4.4%), bipolar disorder I or II (full remission; 3.3%), eating disorder (3.3%), dysthymic disorder (2.2%), generalized anxiety disorder (2.2%), and alcohol-use disorder (early/sustained full remission; 2.2%). Additionally, 26.7% of the sample had a lifetime history of panic attacks.

Bivariate associations

See Table 2 for bivariate associations between baseline study variables. Anxiety sensitivity was not associated with participant sex, age, cigarettes per day, level of nicotine dependence, or use of menthol cigarettes. Anxiety sensitivity was significantly and moderately correlated with pre-challenge distress (SUDs and DSQ), trait negative affectivity, and presence of any psychological disorder (r's=0.45–0.61, p's<0.01). Additionally, anxiety sensitivity was correlated at a bivariate level with post-challenge smoking urges (r=0.30, p<0.01) but not the puff topography variables. Post-challenge smoking urges were not significantly correlated with the smoking topography variables. Average post-challenge puff volume and duration were correlated (r=0.64, p<0.01), and both were correlated with average post-challenge inter-puff interval (r's=0.23–0.32, p's<0.05). Additionally, average number of cigarettes smoked per day was correlated with post-challenge smoking urges (r=0.35, p<0.01), but not smoking topography variables. Level of nicotine dependence (FTND) was significantly associated with shorter inter-puff intervals (r=0.23, p<0.05). Participant sex, age, race, and use of menthol cigarettes were not associated with any outcome variables.

Randomization check

Experimental groups were compared in terms of baseline smoking and affective characteristics (Table 1). Chi-square and t-test analyses indicated no statistically significant group differences on any of the examined baseline characteristics. As denoted in Table 3, there were significant group differences on pre-challenges levels of subjective distress (SUDs), thus this variable was adjusted for in all main analyses. By controlling for this variable, the unique effects of anxiety sensitivity above state-levels of distress were also tested.

Manipulation check

Means and *SD*s for all manipulation check variables are presented in Table 3, by experimental condition. SUDs, modified-DSQ, heart rate, and expired etpCO_2 were non-normally distributed, thus a 'negbin' (negative binomial) distribution statement was used in SAS.

Table 1. Sample demographics, smoking and psychological history.

	Total (*n*=90)		**CO_2-enriched air** (*n*=45)		**Room air** (*n*=45)		X^2 or *t*
	Mean/*n*	SD/%	Mean/*n*	SD/%	Mean/*n*	SD/%	
Demographics							
Sex							
Male	46	51.1	23	51.1	23	51.1	0.00
Female	44	48.9	22	48.9	22	48.9	
Age	43.6	9.7	42.5	9.4	44.7	9.9	1.08
Race							
White	29	32.2	16	35.6	13	28.9	0.47
Black	55	61.1	26	57.8	29	64.4	
Other	6	6.7	3	6.7	3	6.7	
Education							
High school or less	41	45.6	23	51.1	18	40.0	1.12
At least part college	49	54.4	22	48.9	27	60.0	
Marital status							
Never married	44	48.9	25	55.6	19	42.2	3.92
Divorced/separated	32	35.6	15	33.3	17	37.8	
Married	9	10.0	2	4.4	7	15.6	
Widowed	5	5.6	3	6.7	2	4.4	
Employment status							
Full-time	23	25.6	13	28.9	10	22.2	1.46
Part-time	18	20.0	7	15.6	11	24.4	
Unemployed	32	35.6	17	37.8	15	33.3	
Other	17	18.9	8	17.8	9	20.0	
Smoking history							
Age smoke initiation	16.0	6.7	15.0	4.4	17.0	8.3	1.48
Years/smoker	23.9	10.2	23.3	10.4	24.4	10.1	0.54
Cigarettes per day	15.8	5.9	16.1	6.4	15.5	5.3	–0.52
FTND total score	4.8	1.4	4.7	1.5	4.9	1.3	0.81
Expired CO at BL	24.0	10.9	24.7	11.5	23.3	10.3	–0.62
Expired CO after 1st cigarette	29.2	14.0	29.1	11.1	27.4	11.2	–0.72
FTND item 1							
Within 5 min	51	56.7	27	60.0	24	53.3	0.41
Greater 5 min	39	43.3	18	40.0	21	46.7	
Menthol cigarettes							
Yes	53	58.9	24	53.3	29	64.4	1.15
No	37	41.1	21	46.7	16	35.6	
Psychological history							
Psychological Dx							
Yes	30	33.3	19	42.2	11	24.4	3.20
No	60	66.7	26	57.8	34	75.6	
History/panic attack							
Yes	24	26.7	14	31.1	10	22.2	0.91
No	66	73.3	31	68.9	35	77.8	

BL: Baseline; CO: carbon monoxide; CO_2: carbon dioxide; DX: Disorder; FTND: Fagerström Test for Nicotine Dependence.

Subjective distress and panic attack symptoms. After adjusting for pre-challenge levels of SUDs, the dummy-coded experimental condition variable was significantly predictive of post-challenge SUDs (b=0.72, p=0.013), such that participants exposed to CO_2-enriched air reported significantly higher post-challenge SUDs relative to those exposed to room air condition (Cohen's d=0.53). After adjusting for the number of pre-challenge panic attack symptoms (per the DSQ), the dummy-coded experimental condition variable was significantly predictive of post-challenge DSQ (b=1.13, p<0.0001); participants exposed to CO_2-enriched air reported significantly more post-challenge symptoms on the DSQ relative to those exposed to room air (Cohen's d=1.00).

Heart rate and respiration rate. After adjusting for heart rate during the adaptation phase, the dummy-coded experimental

Table 2. Bivariate associations between anxiety sensitivity and baseline characteristics.

Variable	2.	3.	4.	5.	6.	7.	8.	9.	10.
1. Anxiety sensitivity	0.09	–0.03	0.04	0.07	0.06	0.54*	0.61*	0.45*	0.49*
2. Sex (female)	–	–0.19	–0.05	–0.15	0.05	0.11	0.07	0.01	0.01
3. Age		–	0.16	–0.07	–0.11	–0.15	–0.24**	–0.25**	–0.12
4. Race (white)			–	0.19	–0.46*	0.06	0.13	–0.06	0.10
5. BL cigarettes/day				–	–0.16	0.14	0.11	0.07	–0.01
6. Menthol cigarette (yes)					–	0.06	–0.17	0.11	0.09
7. Any Disorder (yes)						–	0.47*	0.36*	0.37*
8. BL negative affect							–	0.31*	0.45*
9. Pre-SUDS								–	0.64*
10. Pre-DSQ									–

BL: Baseline; DSQ: Diagnostic Sensations Questionnaire; SUDs: Subjective Units of Distress Scale.
Pre-DSQ refers to pre-challenge number of panic attacks symptoms, pre-SUDS refers to pre-challenge levels of subjective distress. Anxiety sensitivity: Anxiety Sensitivity Index-3 (total score); Sex (0=male; 1=female); Race (0=non-white; 1=white); Menthol cigarette (0=no; 1=yes); Any disorder (0=no psychological disorder; 1=past-year psychological disorder); BL negative affect: Baseline negative affectivity per the Positive and Negative Affect Schedule (negative affect subscale).
*p<0.01; **p<0.05.

Table 3. Means and standard deviations (*SD*s) for manipulation check variables.

Variable	Room air		CO_2	
	Mean	*SD*	Mean	*SD*
SUDs pre-challenge[a]	15.09	23.09	33.27	29.83
SUDs post-challenge	18.09	24.07	42.58	31.92
DSQ pre-challenge	0.40	0.99	0.91	1.55
DSQ post-challenge	0.56	0.56	2.38	2.37
HR pre-challenge	89.38	27.90	94.29	33.61
HR post-challenge	88.33	27.55	105.28	37.47
RES pre-challenge	17.84	1.14	17.70	1.30
RES post-challenge	17.85	0.96	18.27	1.17
Expired etpCO_2	7.51	1.87	42.95	7.93

DSQ: Diagnostic Symptom Questionnaire; Expired etpCO_2: expired end-tidal peak CO_2; HR: heart rate; RES: respiration rate; SUDs: Subjective Units of Distress Scale.
The DSQ was modified (number of panic attack symptoms).
[a]Pre-manipulation group differences were observed on this variable.

condition variable significantly predicted increased heart rate during the recovery phase (b=0.14, p=0.002), such that heart rate was significantly higher following exposure to CO_2-enriched air condition relative to the room air condition (Cohen's d=0.68; large-sized effect). After adjusting for average respiration rate during the adaptation phase, dummy-coded experimental condition variable was significantly predictive of average respiration rate during the recovery phase (b=0.47, p<0.038), such that respiration rate significantly increased following exposure to CO_2-enriched air relative to the room air (Cohen's d=0.76).

Expired etpCO_2. Expired etp$CO_2$was only sampled once (after manipulated breath), thus PROC TTEST was used in SAS. The Satterthwaite degrees of freedom were used to adjust for unequal group variances. Here, mean expired etpCO_2 values significantly differed by experimental condition (t=–29.17, p<0.0001), with higher values recorded in the CO_2-enriched air relative to room air condition.

Test of main and interaction effects

In all models, covariates included (mean-centered) pre-challenge SUDs, trait negative affectivity (per PANAS-NA), average cigarettes per day (per TLFB), and pre-challenge value of the outcome.[1] The main effects included the dummy-coded condition variable and mean-centered ASI-3. The interaction term (ASI-3×condition) was also entered to examine conditional effects. PROC GLM with bootstrapping was used in SAS to adjust for non-normal distribution of outcome variables.

Smoking urges (QSU-B). After adjusting for model covariates, results indicated a significant main effect of the dummy-coded experimental condition variable on post-challenge QSU-B (b=–81.26, p=0.048), indicating that exposure to CO_2 (relative to room air) resulted in lower post-challenge smoking urges. The size of the effect was small to medium (Cohen's d=−0.45). See Table 4 for presentation of results. There was a non-significant main effect of anxiety sensitivity (b=3.15, p=0.363). The effect of the interaction (Condition x ASI-3) was significant (b=–9.96, p=0.014). The size of the effect was medium (Cohen's d=−0.56). Test of the simple slopes revealed a significant effect for the experimental manipulation when anxiety sensitivity was high (b=−208.99, p=0.011), but not low (b=46.47, p=0.30). Specifically, the form of the interaction was such that high anxiety sensitive smokers exposed to CO_2-enriched air reported significantly lower levels of smoking urges, relative to low anxiety sensitive smokers. In contrast, anxiety sensitivity did not differentially affect smoking urges for those exposed to the room air condition.

Post-hoc tests were conducted to examine the QSU-B subscales (QSU-Craving/Desire and QSU-Negative affect relief). Consistent with finding from the total score, the interaction term was significant for both subscales (see Figure 3 for plots of the interaction effects). For QSU-Desire, the interaction was significant (b=−5.20, standard error (*SE*)=2.26; confidence interval $(CI)_{95\%}$=–9.81, –0.85; z=−2.30; p=0.021; Cohen's d=−0.53). Test of the simple slopes indicated that the effect of the CO_2 condition on QSU-Craving/Desire (but not room air) was conditionally significant when anxiety sensitivity was high (b=−53.20, p=0.027), but not low (b=13.50, p=0.628). For QSU-Negative Affect relief,

Table 4. Results for main and interaction effects for smoking urges.

Predictor	*b*	SE	CI low	CI high	Z value	*p*
Intercept	93.10	40.12	7.19	163.27	2.32	0.020
CPD	1.66	2.80	−4.14	6.95	0.59	0.555
Trait negative affect	6.99	4.24	−1.43	15.35	1.65	0.099
Pre-challenge SUDs	0.03	0.88	−1.80	1.73	0.04	0.968
Pre-challenge QSU	0.81	0.09	0.63	0.99	8.66	0.000
Condition	−81.26	40.99	−164.18	−4.25	−1.98	0.048
ASI-3	3.15	3.46	−4.10	9.27	0.91	0.363
Condition×ASI-3	−9.96	4.07	−17.93	−2.08	−2.45	0.014

ASI-3: Anxiety Sensitivity Index-3; CI: confidence interval; CPD: cigarettes per day; QSU: Questionnaire of Smoking Urges; SE: standard error; SUDs: Subjective Units of Distress Scale.

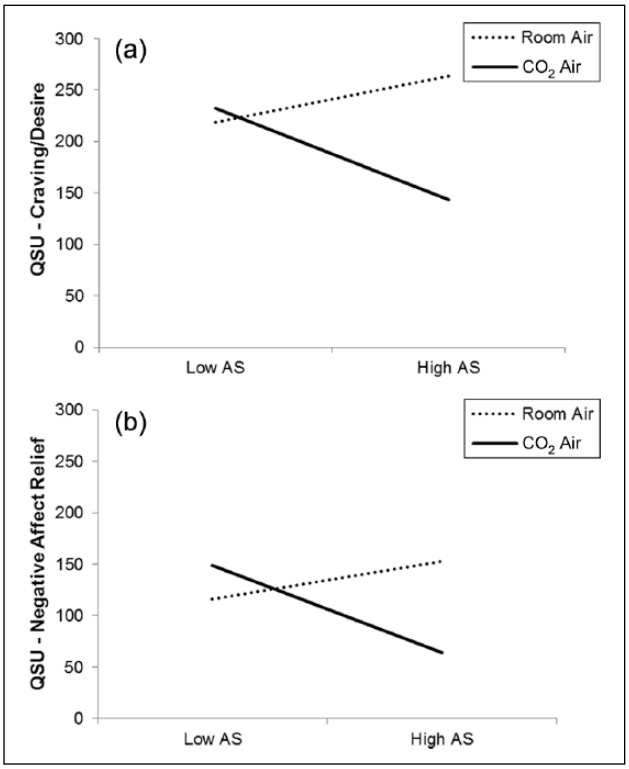

Figure 3. Interaction of experimental condition and anxiety sensitivity in predicting smoking urges: (a) interaction for Questionnaire of Smoking Urges (QSU)-Craving/Desire subscale; (b) interaction for QSU-Negative Affect relief subscale. AS: Anxiety Sensitivity; CO_2: carbon dioxide.

the interaction was significant (b=−4.79, SE=1.97; $CI_{95\%}$=−8.69, –0.95; z=–2.42; p=0.015; Cohen's d=−0.55). Test of the simple slopes similarly indicated that the conditional effect of CO_2 exposure (but not room air) on QSU-Negative Affect relief was significant when anxiety sensitivity was high (b=−89.21, p=0.027) but not low (b=−33.46, p=0.119).

Smoking topography. Results from regression models are presented in Table 5. With regard to average puff volume, there was a significant main effect for dummy-coded experimental condition (b=−8.11, p=0.048; Cohen's d=–0.43), such that CO_2 exposure resulted in reductions in average puff volume. The main effect of anxiety sensitivity and the interaction term were non-significant. For average puff duration, results indicated that there was a trend of significant main effect for dummy-coded experimental condition (b=−144.39, p=0.050; Cohen's d=–0.43), such that exposure to CO_2-enriched air resulted in reductions in average puff duration post-challenge, relative to exposure to room air. There was no significant main effect of anxiety sensitivity, nor was there a significant interaction effect. With regard to average inter-puff interval, regression results indicated no significant main or interactive effects.

Discussion

The current study experimentally examined the effect of acute anxious arousal on negative-reinforcement smoking (smoking urges, average puff volume, average puff duration, and average inter-puff interval), and anxiety sensitivity as a possible cognitive-affective individual difference factor. Regarding smoking urges, findings indicated that the room air condition increased post-challenge smoking urges, relative to 35% CO_2-enriched air. It is possible that the room air condition induced 'mild distress' that motivated a desire to smoke. In contrast, exposure to 35% CO_2-enriched air resulted in significantly lower post-challenge smoking urges immediately following the biological challenge. It is possible that severe acute cardiorespiratory distress during the post-challenge self-report period was aversive (due to intensity of the effects of the CO_2 gas concentration), which caused lower desire to smoke in that moment. Interestingly, Attwood et al. (2014) found that, in a within-subjects test, following 20 min of breathing 7.5% CO_2 (relative to 20 min of room air), there was no main effect of gas condition in terms of post-challenge smoking craving, although higher craving following CO_2 relative to room air was reported when smokers were nicotine-deprived, but not when smokers were non-abstinent. These data further support the dose-response explanation, and suggest that cigarette smoking may only be perceived as negatively reinforcing in the context of lower arousal states or after acute arousal surges have dissipated.

Findings also indicated a significant interactive effect of gas condition and anxiety sensitivity. Specifically, for smokers exposed to the CO_2 condition, highly anxiety-sensitive smokers reported significantly lower self-reported smoking

Table 5. Results for main and interaction effects for smoking topography.

Predictor	*b*	SE	CI low	CI high	Z value	*p*
Outcome: average inter-puff interval (ms)						
Intercept	−240.87	129.85	−2361.99	2033.80	−1.85	0.064
CPD	123.64	68.62	−1.15	266.68	1.80	0.072
Trait negative affect	38.91	72.15	−98.40	184.25	0.54	0.589
Pre-challenge SUDs	−4.71	20.81	−47.02	35.39	−0.23	0.818
Pre-challenge IPI	0.98	0.08	0.82	1.12	12.30	0.000
Condition	−650.96	888.96	−2383.77	1065.73	−0.73	0.465
ASI-3	17.08	44.54	−74.09	101.86	0.38	0.704
Condition×ASI-3	−76.40	55.58	−186.74	39.24	−1.37	0.171
Outcome: average puff volume (mL)						
Intercept	30.71	12.28	0.17	48.42	2.50	0.012
CPD	−0.12	0.26	−0.68	0.40	−0.47	0.639
Trait negative affect	−0.17	0.35	−0.92	0.53	−0.47	0.639
Pre-challenge SUDs	−0.01	0.08	−0.16	0.14	−0.07	0.944
Pre-challenge volume	0.56	0.19	0.31	1.04	3.01	0.003
Condition	−8.11	4.12	−16.82	−0.61	−1.97	0.049
ASI-3	0.06	0.41	−0.71	0.92	0.15	0.883
Condition×AS-3	−0.10	0.34	−0.81	0.54	−0.30	0.764
Outcome: average puff duration (ms)						
Intercept	165.275	123.859	−60.61	414.209	1.33	0.182
CPD	7.645	5.504	−2.343	19.438	1.39	0.165
Trait negative affect	−1.721	4.9	−10.759	8.479	−0.35	0.725
Pre-challenges SUDs	−1.051	1.511	−4.005	1.89	−0.70	0.487
Pre-challenge duration	0.886	0.069	0.752	1.021	12.84	0.000
Condition	−144.393	73.987	−293.164	−3.988	−1.95	0.050
ASI-3	6.679	5.066	−2.994	17.163	1.32	0.187
Condition×ASI-3	−8.734	6.035	−20.943	2.895	−1.45	0.148

ASI-3: Anxiety Sensitivity Index-3; CI: confidence interval; CPD: Cigarettes per day; IPI: Inter-Puff Interval; SE: standard error; SUDs: Subjective Units of Distress Scale.

urges following the challenge, relative to low anxiety-sensitive smokers. Importantly, this same conditional effect of anxiety sensitivity was not seen for smokers exposed to room air. This patterning of effects makes conceptual sense from a 'distress aversion' hypothesis. That is, given high anxiety-sensitive individuals have a greater trait-like propensity towards misinterpreting the meaning of distressing somatic sensations (Reiss et al., 1986), it may be that smokers high in anxiety sensitivity who are exposed to high-concentration CO_2 would respond with decreased urges/desire to smoke, due to fear that smoking may further amplify cardiorespiratory distress (Zvolensky et al., 2003).

Additionally, there was a significant main effect of the biological challenge in terms of post-challenge average puff volume and puff duration, but not average inter-puff interval. Specifically, exposure to 35% CO_2-enriched air condition, relative to room air, produced smaller average puff volumes and shorter puff durations. This set of findings is consistent with results for smoking urges. That is, puffing behavior reflected lower smoking reinforcement after exposure to CO_2-enriched air relative to room air. It is possible that smoking during the second ad-lib period (post-challenge) may have been perceived as aversive for CO_2-exposed smokers, although this was not directly measured. Of note, there was no direct or interactive effect of anxiety sensitivity in terms of any smoking topography outcome. These findings are consistent with a prior study that found a non-significant effect of anxiety sensitivity on smoking reinforcement (per average puff volume) following a negative mood induction task (Perkins et al., 2010). There are a few possible explanations for why anxiety sensitivity may not have been directly or conditionally predictive of smoking topography. First, the physiological effects of 35% CO_2 are transient (Vickers et al., 2012). Thus, it is possible that the effect of the manipulation had dissipated by time participants initiated the second smoking trial, which may not have activated high anxiety-sensitive smokers' concerns about somatic arousal; subsequently, puffing behavior may have not been conditionally affected by this vulnerability trait. Second, it possible that the relatively low/moderate average levels of anxiety sensitivity (per the ASI-3) produced less robust effects on smoking topography than may have otherwise been observed if smokers varied more broadly in this trait factor (i.e. as seen in Perkins et al., 2010). Third, the smoking topography variables were averaged across the cigarette smoked, which may have decreased sensitivity to detect changes in puffing behavior (e.g. Collins et al., 2010). It is possible that high anxiety-sensitive smokers, relative to low, exposed to the CO_2-enriched air may have evidenced greater variability in puff-to-puff behavior during the course of smoking a cigarette. This type of explanation is based on the observation that anxiety symptoms appear to moderate the course of puff behavior during a single cigarette, at least among adolescent smokers (Veilleux et al., 2011). Although not modeled here, future work could build upon the present findings by modeling the role of anxiety sensitivity and other affective vulnerability constructs in terms of puff-level topography. Fourth, it is also

possible that alternative dispositional factors may be more related to smoking topography (e.g. perceived inability to tolerance distress; Perkins et al., 2010), even if the acute effects of the CO_2 manipulation (physiologically and psychologically) had dissipated.

Several study limitations warrant comment. First, the procedures utilized in the current study did not include standardization of smoking behavior prior to the experimental laboratory visit or timing of study appointments (e.g. participants were seen in the morning and afternoon for the experiment). These factors could have affected observable baseline puffing behavior if individuals were already 'satiated' in terms of nicotine. However, based on initial expired CO breath samples (M=24.0 ppm, SD=10.9), data suggest that smokers likely had smoked within the past 12–24 h, thus they were not arriving at the appointment in a state of nicotine deprivation, and may rule-out the possibility that smokers were sated (based on lack of an extremely high mean expired CO value). Further, by design, all participants smoked one cigarette approximately 60–90 min prior to the biological challenge, in an attempt to standardize recency of smoking behavior. Second, while random assignment into experimental condition was utilized, smokers randomized to the CO_2-enriched air condition reported significantly higher levels of pre-challenge subjective distress (SUDs) than those in the room air condition. It could be argued that this pre-manipulation difference confounds findings, however based on the lack of group differences on other pre-challenge measures, consistent patterning of manipulation effects across subjective and physiological measures, medium to large effect sizes, and significant effects above controlling for this variable in all analyses, the effect of this pre-group difference may be negligible. Third, given the specificity of the 35% CO_2 biological challenge to acute physiological arousal/stress (Vickers et al., 2012), the current findings may not similarly generalize to moderate, prolonged levels of anxious arousal (e.g. Attwood et al., 2014) or other (non-physiological) negative mood states (Perkins et al., 2010).

Fourth, participants were not recruited on the basis of level of anxiety sensitivity. The average ASI-3 scores in the current sample were indicative of overall, low to moderate levels of anxiety sensitivity (Taylor et al., 2007). These scores are consistent with ASI-3 scores documented in other samples of smokers (Perkins et al., 2010), especially those smokers without psychopathology (Farris et al., 2015a), but are lower than scores seen in clinical mood/anxiety disordered samples (Farris et al., 2015a; Taylor et al., 2007). Future work may also consider exploring differential effects for the anxiety sensitivity sub-facets (Farris et al., 2015a) or exploring the categorical (taxonic) conceptualizations of anxiety sensitivity (Bernstein et al., 2007). Fifth, while anxiety sensitivity is often considered an amplifier of negative affective states (e.g. Zvolensky et al., 2014a), it is also conceptualized as an underlying explanatory mechanism that accounts for the link between anxious arousal (or affective psychopathology more broadly) and smoking maintenance (Zvolensky et al., 2014b). Thus, it would be warranted to model anxiety sensitivity as a statistical mediator of the effect of the experimental manipulation on smoking reinforcement. Sixth, many individual factors can influence responding to a CO_2 biological challenge, including sleep deprivation (Babson et al., 2009), trauma-exposure (Hawks et al., 2011; Vujanovic et al., 2010), extent of cannabis use (Bonn-Miller and Zvolensky, 2009), exercise (e.g. Esquivel et al., 2012), caffeine use (e.g. Nardi et al., 2007), and among females, menstrual cycle phase (Nillni et al., 2012). These individual difference factors were not considered here, but could meaningfully inform smoking reinforcement post-challenge, thus warrant empirical consideration in future studies. Seventh, a between-subject versus within-subject counterbalanced design was utilized, and model covariates were included. This approach could potentially decrease power and increase the probability of type II error. Finally, the sample was comprised of participants who primarily identified race as Black/African-American (61.1%), reported lower levels of educational attainment (45.6% completed high school or less), high rates of unemployment (35.6%), and the prevalence of menthol cigarette use was high (58.9%). Thus, generalizability may be limited to the studied sample of smokers.

Overall, the present findings empirically document the importance of further exploring the associations between acute anxious arousal and negative-reinforcement smoking, and individual risk factors that may amply risk for smoking maintenance. The current challenge paradigm generated an intense surge in anxious arousal. When considered in the larger context of research on smoking and panic attacks (Piper et al., 2011) and acute stress (Childs and Wit, 2010; McKee et al., 2011), the current findings aid in refinement of integrated models of arousal and smoking (Leventhal and Zvolensky, 2015; Sinha, 2001), and generally inform negative reinforcement models of drug addiction (McCarthy et al., 2010). Specifically, acute subjective and cardiorespiratory distress may be related to immediate decreases in smoking urges and puff behavior (volume, duration), and may be specific to acute respiratory distress versus other types of acute stress (McKee et al., 2011). Thus, the current findings add uniquely to the literature to support the view that smokers alter how they smoke based on acute arousal states. Data also add specificity to negative-reinforcement model of addition by suggesting that the intensity (not just the presence) of physiological arousal may affect smoking motivation and reinforcement. In the context of smoking cessation treatment, the findings suggest that it may be useful to (a) have smokers identify emotional and situational antecedents to smoking behavior, (b) provide psychoeducation about the role of self-regulated puffing behavior as a mechanism for affect-regulation (and how such accommodations may maintain smoking behavior), and (c) teach skills to manage and tolerate acute surges in physiological arousal and negative emotional states, without smoking (or altering smoking style). Additionally, although not directly tested, it is possible that personalized smoking topography data could be usefully summarized to smokers, as a form of tailored feedback regarding one's own smoking behavior. Puffing behavior feedback may be useful for smokers attempting to quit, especially if smoking reduction and or scheduled smoking is part of a smoking cessation intervention. This tactic may increase smokers' awareness of *how* they are smoking and *when* (in what acute context) which would be in addition to monitoring *how much* they are smoking.

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Note

1. Results were unchanged when models were constructed without smoking frequency (cigarettes per day) in the model.

References

Abrams K, Leger K, Schlosser L, et al. (2011) Nicotine withdrawal exacerbates fear reactivity to CO_2-induced bodily sensations among smokers. *Nicotine Tob Res* 13: 1052–1058.

Abrams K, Schruers K, Cosci F, et al. (2008a) Biological challenge procedures used to study co-occurring nicotine dependence and panic disorder. *Addict Behav* 33: 1463–1469.

Abrams K, Zvolensky MJ, Dorflinger L, et al. (2008b) Fear reactivity to bodily sensations among heavy smokers and nonsmokers. *Exp Clin Psychopharmacol* 16: 230–239.

Attwood AS, Ataya AF, Bailey JE, et al. (2014) Effects of 7.5% carbon dioxide inhalation on anxiety and mood in cigarette smokers. *J Psychopharmacol* 28: 763–772.

Babson KA, Feldner MT, Trainor CD, et al. (2009) An experimental investigation of the effects of acute sleep deprivation on panic-relevant biological challenge responding. *Behav Ther* 40: 239–250.

Bernstein A, Zvolensky MJ, Norton PJ, et al. (2007) Taxometric and factor analytic models of anxiety sensitivity: Integrating approaches to latent structural research. *Psychol Assess* 19: 74–87.

Blank MD, Disharoon S and Eissenberg T (2009) Comparison of methods for measurement of smoking behavior: Mouthpiece-based computerized devices versus direct observation. *Nicotine Tob Res* 11: 896–903.

Bonn-Miller MO and Zvolensky MJ (2009) Marijuana use, abuse, and dependence: Evaluation of panic responsivity to biological challenge. *J Psychoactive Drugs* 41: 331–336.

Brown RA, Lejuez CW., Kahler C.W, et al. (2002) Distress tolerance and duration of past smoking cessation attempts. *J Abnorm Psychol* 111: 180–185.

Burling TA, Stitzer ML, Bigelow GE, et al. (1985) Smoking topography and carbon monoxide levels in smokers. *Addict Behav* 10: 319–323.

Carey KB (1997) Reliability and validity of the time-line follow-back interview among psychiatric outpatients: A preliminary report. *Psychol Addict Behav* 11: 26–33.

Childs E and De Wit H (2010) Effects of acute psychosocial stress on cigarette craving and smoking. *Nicotine Tob Res* 12: 449–453.

Cohen J (1988). *Statistical Power Analysis for the Behavioral Sciences*. 2nd ed. Hillsdale, NJ: Lawrence Erlbaum Associates.

Collins CC, Epstein DH, Parzynski CS, et al. (2010) Puffing behavior during the smoking of a single cigarette in tobacco-dependent adolescents. *Nicotine Tob Res* 12: 164–167.

Cox LS, Tiffany ST and Christen AG (2001) Evaluation of the brief questionnaire of smoking urges (QSU-brief) in laboratory and clinical settings. *Nicotine Tob Res* 3: 7–16.

Esquivel G, Dandachi A, Knuts I, et al. (2012) Effects of acute exercise on CO_2-induced fear. *Depress Anxiety* 29: 155–158.

Farris SG, DiBello AM, Allan NP, et al. (2015a) Evaluation of the Anxiety Sensitivity Index–3 among treatment-seeking smokers. *Psychol Assess* 27: 1123–1128.

Farris SG, Leventhal A., Schmidt NB, et al. (2015b) Anxiety sensitivity and pre-cessation smoking processes: Testing the independent and combined mediating effects of negative affect-reduction expectancies and motives. *J Stud Alcohol Drugs* 76: 317–325.

Farris SG, Zvolensky MJ, Otto MW, et al. (2015c) The role of distress intolerance for panic and nicotine withdrawal symptoms during a biological challenge. *J Psychopharmacol* 29: 783–791.

Faul F, Erdfelder E, Buchner A, et al. (2009) Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. *Behav Res Methods* 41: 1149–1160.

Faul F, Erdfelder E, Lang AG, et al. (2007) G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods* 39: 175–191.

First MB, Spitzer RL, Gibbon M, et al. (2007) *Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version. Nonpatient Edition*. New York: Biometrics Research, New York State Psychiatric Institute.

Frederiksen LW, Miller PM and Peterson GL (1977) Topographical components of smoking behavior. *Addict Behav* 2: 55–61.

Hawks E, Blumenthal H, Feldner MT, et al. (2011) An examination of the relation between traumatic event exposure and panic-relevant biological challenge responding among adolescents. *Behav Ther* 42: 427–438.

Heatherton TF, Kozlowski LT, Frecker RC, et al. (1991) The Fagerström Test for Nicotine Dependence: A revision of the Fagerström Tolerance Questionnaire. *Br J Addict* 86: 1119–1127.

Kutz A, Marshall E, Bernstein A, et al. (2010) Evaluating emotional sensitivity and tolerance factors in the prediction of panic-relevant responding to a biological challenge. *J Anxiety Disord* 24: 16–22.

Leventhal AM and Zvolensky MJ (2015) Anxiety, depression, and cigarette smoking: A transdiagnostic vulnerability framework to understanding emotion–smoking comorbidity. *Psychol Bull* 141: 176–212.

Leyro TM and Zvolensky MJ (2013) The interaction of nicotine withdrawal and panic disorder in the prediction of panic-relevant responding to a biological challenge. *Psychol Addict Behav* 27: 90–101.

McCarthy DE, Curtin JJ, Piper ME, et al. (2010) Negative reinforcement: Possible clinical implications of an integrative model. In: Kassel JD (ed) *Substance Abuse and Emotion*. Washington, DC: American Psychological Association, pp.15–42.

McKee SA, Sinha R, Weinberger AH, et al. (2011) Stress decreases the ability to resist smoking and potentiates smoking intensity and reward. *J Psychopharmacol* 25: 490–502.

McNally RJ (2002) Anxiety sensitivity and panic disorder. *Biol Psychiatry* 52: 938–946.

Maisto SA, Sobell LC, Cooper AM, et al. (1982) Comparison of two techniques to obtain retrospective reports of drinking behavior from alcohol abusers. *Addict Behav* 7: 33–38.

Marshall EC, Johnson K, Bergman J, et al. (2009) Anxiety sensitivity and panic reactivity to bodily sensations: Relation to quit-day (acute) nicotine withdrawal symptom severity among daily smokers making a self-guided quit attempt. *Exp Clin Psychopharmacol* 17: 356–364.

Nardi AE, Valença AM, Lopes FL, et al. (2007) Caffeine and 35% carbon dioxide challenge tests in panic disorder. *Hum Psychopharmacol* 22: 231–240.

Nillni YI, Rohan KJ and Zvolensky MJ (2012) The role of menstrual cycle phase and anxiety sensitivity in catastrophic misinterpretation of physical symptoms during a CO_2 challenge. *Arch Womens Ment Health* 15: 413–422.

Olatunji BO and Wolitzky-Taylor KB (2009) Anxiety sensitivity and the anxiety disorders: A meta-analytic review and synthesis. *Psychol Bull* 135: 974–999.

Perkins KA, Karelitz JL, Conklin CA, et al. (2010) Acute negative affect relief from smoking depends on the affect situation and measure but not on nicotine. *Biol Psychiatry* 67: 707–714.

Perkins KA, Karelitz JL, Giedgowd GE, et al. (2012) The reliability of puff topography and subjective responses during ad lib smoking of a single cigarette. *Nicotine Tob Res* 14: 490–494.

Piper ME, Cook JW, Schlam TR, et al. (2011) Anxiety diagnoses in smokers seeking cessation treatment: Relations with tobacco depen-

dence, withdrawal, outcome and response to treatment. *Addiction* 106: 418–427.

Pomerleau CS, Carton SM, Lutzke ML, et al. (1994) Reliability of the Fagerstrom Tolerance Questionnaire and the Fagerstrom Test for Nicotine Dependence. *Addict Behav* 19: 33–39.

Reiss S and McNally RJ (1985) Expectancy model of fear. In: Reiss S and Bootzin RR (eds), *Theoretical Issues in Behavior Therapy*. San Diego, CA: Academic Press, pp.107–121.

Reiss S, Peterson RA, Gursky DM, et al. (1986) Anxiety sensitivity, anxiety frequency, and the prediction of fearfulness. *Behav Res Ther* 24: 1–8.

Richey JA, Schmidt NB, Hofmann SG, et al. (2010) Temporal and structural dynamics of anxiety sensitivity in predicting fearful responding to a 35% CO_2 challenge. *J Anxiety Disord* 24: 423–432.

Sanderson WC, Rapee RM and Barlow DH (1988) Panic induction via inhalation of 5.5% CO_2 enriched air: A single subject analysis of psychological and physiological effects. *Behav Res Ther* 26: 333–335.

Sinha R (2001) How does stress increase risk of drug abuse and relapse?. *Psychopharmacology* 158: 343–359.

Sobell LC and Sobell MB (1992) Timeline follow-back: A technique for assessing self-reported alcohol consumption. In: Litten RZ and Allen JP (eds), *Measuring Alcohol Consumption: Psychosocial and Biochemical Methods*. Totowa, NJ: Humana Press, pp.41–72.

Taylor S, Zvolensky MJ, Cox BJ, et al. (2007) Robust dimensions of anxiety sensitivity: Development and initial validation of the Anxiety Sensitivity Index-3. *Psychol Assess* 19: 176–188.

Telch M, Harrington P, Smits J, et al. (2011). Unexpected arousal, anxiety sensitivity, and their interaction on CO_2-induced panic: Further evidence for the context-sensitivity vulnerability model. *J Anxiety Disord* 25: 645–653.

Veilleux JC, Kassel JD, Heinz AJ, et al. (2011) Predictors and sequelae of smoking topography over the course of a single cigarette in adolescent light smokers. *J Adolesc Health* 48: 176–181.

Vickers K, Jafarpour S, Mofidi A, et al. (2012). The 35% carbon dioxide test in stress and panic research: Overview of effects and integration of findings. *Clin Psychol Rev* 32: 153–164.

Vujanovic AA and Zvolensky MJ (2009) Anxiety sensitivity, acute nicotine withdrawal symptoms, and anxious and fearful responding to bodily sensations: A laboratory test. *Exp Clin Psychopharmacol* 17: 181–190.

Vujanovic AA, Marshall-Berenz EC, Beckham JC, et al. (2010) Posttraumatic stress symptoms and cigarette deprivation in the prediction of anxious responding among trauma-exposed smokers: A laboratory test. *Nicotine Tob Res* 12: 1080–1088.

Watson D, Clark LA and Tellegen A (1988) Development and validation of brief measures of positive and negative affect: The PANAS scales. *J Pers Soc Psychol* 54: 1063–1070.

Wolpe J (1968) Psychotherapy by reciprocal inhibition. *Cond Reflex* 3: 234–240.

Zvolensky MJ, Farris SG, Guillot CR, et al. (2014a) Anxiety sensitivity as an amplifier of subjective and behavioral tobacco abstinence effects. *Drug Alcohol Depend* 142: 224–230.

Zvolensky MJ, Farris SG, Leventhal AM, et al. (2014b) Anxiety sensitivity mediates relations between emotional disorders and smoking. *Psychol Addict Behav* 28: 912–920.

Zvolensky MJ, Feldner M, Eifert G, et al. (2001). Affective style among smokers: Understanding anxiety sensitivity, emotional reactivity and distress tolerance using biological challenge. *Addict Behav* 26: 901–915.

Zvolensky MJ, Schmidt NB and Stewart SH (2003) Panic disorder and smoking. *Clin Psychol Sci Practice* 10: 29–51.