THE EXAMINATION OF THE RELATION BETWEEN PHYSIOLOGICAL AND PSYCHOLOGICAL COMPONENTS OF STRESS REACTIVITY AND RECOVERY IN CIGARETTE SMOKERS

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ABSTRACT OF THE THESIS

The Examination of the Relation between Physiological and Psychological Components of Stress Reactivity and Recovery in Cigarette Smokers

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Cigarette smoking is a major cause of cardiovascular disease, and empirical research suggests that smoking is associated with short and long-term dysregulation of cardiovascular functioning. Adult smokers exhibit blunted heart rate reactivity during stress, and although dysregulated cardiovascular reactivity is associated with long-term consequences, such as morbidity and mortality, less is known about the immediate effects of dysregulated cardiovascular reactivity. Dysregulated reactivity, or a blunted response, may have more immediate effects on an individual's physiological and subjective recovery from stress by slowing recovery. Yet, research examining the relation between the physiological and subjective components of the stress response report equivocal findings, and there is limited research examining this relation in adult daily smokers. Further, individual traits, such as distress intolerance (DI), or the inability to tolerate distress, may moderate the effect of stress reactivity on recovery, in line with a biopsychosocial model. Taken together, variability in reactivity to stress may predict recovery in an individual's physiological arousal and anxious arousal following stress, which may be moderated by individual traits. The current study examined whether dysregulated, or attenuated, physiological reactivity predicted recovery in anxious arousal

and vice versa, and whether DI moderated this relation. Fifty-six adult daily smokers completed a self-report measure of DI, a ten-minute baseline period, followed by a four-minute stressor (i.e., the CO_2 challenge), and a ten-minute recovery period. Heart rate and self-reported anxiety were assessed continuously over the baseline, challenge, and recovery periods. The results of growth curve models indicated significant linear and quadratic effects for heart rate reactivity on recovery in anxiety as well as significant linear and quadratic effects for anxiety reactivity on recovery in heart rate. There was also a significant linear effect of DI on heart rate. These findings suggest that individuals with greater reactivity to stress in one domain showed greater responsivity to stress in the other domain, which was then followed by faster recovery in subjective and physiological arousal. This observed relation may be important for understanding the interplay of cognitive, affective, and physiological processes that maintain smoking or contribute to lapse.

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I. Introduction

According to a recent report by the Centers for Disease Control and Prevention, approximately 15% of U.S. adults report smoking cigarettes (CDC, 2016), and cigarette smoking is a major cause of cardiovascular disease (CVD), including heart disease and stroke. It is estimated that one third of all CVD-related deaths are attributed to smoking (U.S. Department of Health and Human Services, 2014). Experimental research suggests that cigarette smoking, and broader nicotine use, have acute effects on cardiovascular functioning by reliably increasing the activity of the sympathetic branch of the autonomic nervous system (ANS; Grassi et al., 1994; Richards, Stipelman, Bornovalova, Daughters, Sinha, & Lejuez, 2011; Trap-Jensen, 1988; Winniford, 1990). Cigarette smoking as compared to other forms of nicotine delivery, such as the transdermal nicotine patch, appears to be associated with greater increases in heart rate (Benowitz, Hansson, & Jacob, 2002; Parrott & Winder, 1989) and contributes to later cardiovascular risk (Benowitz, 1997). In addition to the effects of cigarette smoking on the sympathetic nervous system, frequent stress also causes repeated activation of an individual's sympathetic nervous system, (Richards et al., 2011; Rohleder & Kirschbaum, 2006; Chrousos & Gold, 1992), contributing to dysregulation of the stress response system and increased cardiovascular risk (Chida & Steptoe, 2010). Therefore, smokers, and in particular in the context of repeated stress, have multiple risk factors that contribute to acute and long-term dysregulation of the stress response placing them at greater risk for CVD-related disorders.

In support of observed dysregulated cardiovascular functioning, adult smokers frequently exhibit attenuated cardiovascular reactivity in response to a stressor. Typically, under acute stress, individuals exhibit cardiovascular reactivity, or an increase in heart rate from its resting state (Turner, 1994). Adult smokers tend to exhibit this anticipated increase in heart rate during

experimental manipulations of stress (Childs and de Wit, 2010; McKee et al., 2011); however, the magnitude of this increase is often reduced compared to non-smokers (Childs and de Wit, 2009). Such group differences were initially observed in women smokers (Girdler, Jamner, Murray, Jarvik, Soles, & Shapiro, 1997) and male smokers (Roy, Steptoe, & Kirschbaum) who exhibited reduced cardiovascular reactivity to a stressor. More recent findings support this observation and demonstrate attenuated cardiovascular reactivity during an acute stressor in both adult smokers (Childs and de Wit, 2009; Ginty et al., 2014) and adolescent smokers (Evans, Greaves-Lord, Euser, Tulen, Franken, & Huizink, 2012).

To date, findings consistently suggest that smokers exhibit reduced heart rate reactivity to acute stress, and a dysregulated cardiovascular response has been associated with negative long-term outcomes. Reduced variability in cardiovascular functioning, such as the difference in resting heart rate and peak heart rate during stress, (Thayer & Lane, 2005) as well as slower heart rate recovery in adults with and without a history of smoking (Dhoble, Brian, Lahr, Allison, & Kopecky, 2014; Thayer & Lane, 2005), is associated with greater morbidity and mortality, and these effects may be compounded by the influence of stress on smoking behavior. In addition to direct implications for cardiovascular health, these cardiovascular effects may also contribute to a forward feeding model of risk whereby a dysregulated stress response, including poor cardiovascular stress reactivity and recovery, increases the likelihood of smoking, thereby further exacerbating risk of smoking.

In direct support of the link between cardiovascular reactivity to stress and smoking, al'Absi and colleagues (2005) reported that smokers with diminished physiological reactivity to an acute stressor exhibited shorter time to lapse within a sample of smokers attempting to quit. Ashare and colleagues (2012) observed similar findings in a sample of adult smokers who

completed a 15-hour abstinence period, and reduced heart rate variability predicted faster time to re-initiate smoking and greater self-reported reinforcement from smoking. These results are aligned with motivational models of substance use suggesting that cigarette smoking may function to reduce stress (Sinha, 2009; Kassel, Stroud, & Paronis, 2003). Indeed, empirical research indicates that stress increases craving for cigarettes (Childs & de Wit, 2010; McKee, Sinha, Weinberger, Sofuoglu, Harrison, Lavery, & Wanzer, 2011) as well as subjective desire to smoke (Childs and de Wit, 2010). Therefore, individual differences in these profiles may have important implications for disentangling the complex relation between stress reactivity and smoking, and understanding this relation may help to reduce the risk for poor health outcomes in smokers.

One initial step in answering this question is to first examine individual differences in reactivity and recovery profiles in order to better understand the interplay of these two important components of the stress response. In particular, dysregulated heart rate reactivity to a stressor has been observed in adult smokers, yet it is unclear how this reactivity affects an individual's recovery from stress. More research is needed to examine how an individual's cardiovascular reactivity, which can be conceptualized as an objective response to stress, impacts his or her subjective arousal, such as changes in self-reported anxiety, to stress, and vice versa. In a non-selected sample, previous research on the stress response examined whether reactivity to stress is comprised of both subjective arousal and physiological arousal (Campbell & Ehlert, 2012; Ursin & Erikson, 2004). This body of research suggests that subjective arousal and physiological arousal may be concordant, discordant, or prospectively related (Levenson, 1988; Mauss, Levenson, McCarter, Wilhelm, & Gross, 2005). However, the results of a recent review (Campbell and Ehlert, 2012) on the cross-sectional and prospective associations of the

components of the stress response were mixed, with approximately twenty-five percent of the studies reporting significant associations between physiological indices of stress reactivity (e.g., cortisol or cardiovascular response) and subjective indices (e.g., self-reports of perceived emotional distress, negative affect, helplessness, or anxiety). The results of one study reviewed suggest that self-reported anxiety was associated with cardiovascular activity during recovery (Gonzalez-Bono et al., 2002). These results were found in a general sample of adults, and the association between subjective arousal and physiological arousal may differ in smokers as compared to non-smokers given observed attenuations in heart rate reactivity (Childs and de Wit, 2009) and prolonged recovery in subjective distress (i.e. jitteriness and restless) in response to a laboratory stressor (Childs and de Wit, 2009). Therefore, dysregulation in one domain of stress reactivity may significantly predict differences in recovery from stress in the other domain within a sample of adult smokers.

In addition to the direct effects of physiological arousal on recovery in subjective arousal, and vice versa, this association may be moderated by personality traits. Within a biopsychosocial model of stress, Blascovich and Tomaka (1996) argue that individual differences in emotion regulation might alter the strength of the relation between the stimulus, stress reactivity, and regulation. Findings from empirical research suggest that hostility and aggression were associated with greater cardiovascular reactivity while neuroticism, anxiety, and negative affect were associated with decreased cardiovascular reactivity and poorer cardiovascular recovery (Campbell & Ehlert, 2012; Chida & Hamer, 2008). Among smokers, distress intolerance (DI), or the inability to tolerate distress, is one candidate personality trait that may exacerbate the effects of stress reactivity on stress recovery. As compared to non-smokers, smokers demonstrate elevations in behavioral DI as indexed by less persistence on the mirror-tracing persistence task

(Quinn, Brandon, & Copeland, 1996), and elevations in DI are prospectively related to various smoking outcomes including less treatment engagement, early lapse, and relapse (Brown et al., 2009; Leyro, Bernstein, Vujanovic, McLeish, & Zvolensky, 2011). Moreover, DI is transdiagnostic, showing relations to both anxiety and mood pathology (Leyro, Zvolensky, & Bernstein, 2010). Theoretically, individuals high in DI are likely to avoid perturbing sensations, which interferes with the ability to develop adaptive regulatory coping strategies. Thus, smokers higher in DI may experience slower recovery from stress. DI has previously been associated with difficulties in emotion regulation (McHugh, Reynolds, Leyro, & Otto, 2013) and smoking to cope with distress (Perkins, Giedgowd, Karelitz, Conklin, & Lerman, 2012), but its association with physiological recovery has yet to be examined. DI may therefore alter the effects of an individual's physiological and subjective response to stress on their cardiovascular and affective recovery, which may ultimately contribute to smoking maintenance.

Given the mixed results of prior research on the associations between physiological and subjective components of stress reactivity, as well as the limited examination of these relations within a population of smokers, there are critical ways to enhance this research base. First, the within-subject effects of physiological reactivity on recovery in subjective, or more specifically anxious arousal, and vice versa, have yet to be examined within smokers. This relation may be particularly important to examine within smokers given the frequently observed dysregulation in cardiovascular response during a stressor (Childs and de Wit, 2009). Due to the limited research investigating the effects of stress reactivity on stress recovery in smokers, it remains unclear as to whether an exaggerated or attenuated stress response is differentially predictive of slower stress recovery. Prior research examining the association between stress reactivity and negative outcomes suggests that large increases in heart rate are associated with future cardiovascular

disease, such as hypertension (Carroll, Lovallo, & Phillips, 2009). Yet there is emerging evidence to suggest that attenuated increases in heart rate during acute stress may also be maladaptive. Reduced cardiovascular reactivity has been associated with faster times to re-initiate smoking and greater self-reported reinforcement from smoking (al'Absi et al., 2006; Ashare et al., 2012). It is therefore unclear whether larger or smaller increases in heart rate are predictive of slower subjective recovery from stress, and vice versa. Further, such a relation may be moderated by distress intolerance, but the potential interactive effects of DI and stress reactivity on recovery have yet to be examined.

The current study seeks to investigate the effects of physiological and subjective stress reactivity on both components of recovery form stress. Specifically, using responses from a sample of adult smokers, the study will first examine 1b) whether physiological reactivity during a stressor predicts differences in the recovery of subjective arousal, or self-reported anxiety. We hypothesize that dysregulated physiological reactivity, as indexed by a change in heart rate during a stressor will predict slower recovery in subjective arousal as indexed by self-reported anxiety. Given that the empirical literature suggests that both increased and decreased reactivity may be predictive of worse outcomes, the study has exploratory aims of examining the reactivity profiles that predict slower recovery in subjective arousal. To investigate reciprocal effects, the study will examine 1b) whether subjective reactivity to a stressor, as indexed by self-reported anxiety, predicts differences in cardiovascular recovery following a stressor. Here, we hypothesize that greater subjective reactivity to a stressor will predict slower cardiovascular recovery. Finally, the study will examine 2) whether the effects of reactivity on recovery in both models, is moderated by distress intolerance, and we hypothesize that greater distress intolerance will predict slower recovery in heart rate and subjective arousal.

II. Method

Sample

Participants were recruited from the greater Burlington, Vermont area. Participants were 56 adults (46.4% female; M_{age} = 29.33, *SD* = 11.92). 91.1% of the final sample identified as Caucasian, 3.6% Black/Non-Hispanic, 3.6% 'other,' and 1.8% as Asian. Participants completed an initial phone screen to determine eligibility based on current frequency and intensity of smoking (i.e., ≥ 15 cigarettes per day). Inclusion criteria included 1) being a daily smoker for at least the past year, 2) being 18 to 65-years-of-age, and 3) willingness to abstain from smoking for 12-hours, which was later confirmed via carbon monoxide (CO) analysis of breath samples (Javors, Hatch, & Lamb, 2005; Morabia, Bernstein, Curtin, & Berode, 2001). Participants were excluded from study participation if 1) they had reduced the number of cigarettes smoked per day by more than half of their normal amount within the past six months, 2) reported a current medical condition (e.g., cardiovascular, endocrine, pulmonary, respiratory, or gastrointestinal illness) that would interfere with the CO_2 administration, 3) a past diagnosis of Panic Disorder, 4) inability to voluntarily consent or difficulty orienting to person, place, and time, 5) pregnancy, 6) current use of nicotine replacement therapy, 7) current substance use dependence, 8) current psychotic symptoms or disorder, 9) current suicidality, 10) any current use of psychotropic medication that could impact the effect of the CO_2 challenge, and 11) prior experience with the CO_2 challenge. Eligible participants were then invited to the laboratory to complete an initial baseline session.

Procedure

The original study design was a 2x2 experimental design intended to examine the effects of Panic Disorder and cigarette withdrawal on panic attack symptoms in adult smokers. During the

experimental session, data on physiological and self-reported anxious arousal was collected. Eligible participants completed two study sessions that are detailed below.

Session One: Upon arrival to the first session, participants completed a written informed consent. Following informed consent, participants completed the Structural Clinical Interview of DSM-IV Disorders (SCID-I/NP; First, Spitzer, Gibbon, & Williams, 2007) to determine a current diagnosis of Panic Disorder and assess for current psychotic symptoms, mood symptoms, and suicidality. Trained graduate assistants conducted all of the semi-structured interviews. Following the SCID-NP, participants completed a medical screening interview and additional baseline measures including the Smoking History Questionnaire (Brown, Lejuez, Kahler, & Strong, 2002) and Distress Tolerance Scale (Simon & Gaher, 2005). Participants also completed a carbon monoxide (CO) analysis of breath to determine current frequency/intensity of smoking and establish a comparison value for participants who were asked to abstain from smoking prior to the second study session.

Session Two: Prior to the second session, participants who were randomized to the smoking deprivation group were asked to abstain from smoking for at least 12-hours prior to the study visit. Participants were also asked to abstain from any other substance use including marijuana, alcohol and prescription medications such as benzodiazepines 24-hours before the study session. Upon arrival to the laboratory for the second session, participants completed a CO analysis of breath to confirm abstinence in the smoking deprivation group. Expired CO levels were assessed using a CO monitor, and smoking deprivation was confirmed at a level of 8-10 ppm or less (Javors et al., 2005; Morabia et al., 2001). Participants in the smoking-as-usual group were asked to smoke one cigarette prior to the experimental procedures in order to standardize time since smoking. Next, physiological recording equipment was attached to the participants and they were

seated in a separate room where they were asked to stay attentive, but relatively still for the duration of the procedure. Participants were then given instructions for the CO_2 challenge. In particular, they were told that they would experience a 10-minute rest period, followed by the challenge period where they would inhale 10% CO_2-enriched air for four minutes, and finally, a 10-minute recovery period (Figure 1). They were also instructed that during the task, they would receive prompts to complete self-report ratings of distress and anxiety. Next, the experimenter attached a nasal canula connected to a portable capnograph to the bottom of the participant's left nostril, which was used to measure continuous levels of end-tidal CO_2 (i.e., CO_2 contained in the exhaled breath), respiration, and heart rate, and a continuous positive airway pressure (CPAP) mask was placed over their nose and mouth, through which both regular room air quality and CO_2 air would be administered. Before leaving the room, the experimenter prompted the participant to complete a rating of self-reported anxiety, cigarette withdrawal, and urge to smoke, which served as the beginning of the baseline period. Participants then completed a 10-minute adaptation time (i.e., baseline) period, which has been established as an adequate pre-experimental baseline for physiological measures in past biological challenge research (Forsyth & Eifert, 1998). Toward the end of this period, (i.e., minute 8), participants were instructed to complete ratings of cigarette withdrawal and urge to smoke, in addition to a rating of anxiety. Next, participants then completed a four-minute challenge period during which they breathed in 10% CO_2-enriched air. Participants were not given any information concerning the CO_2 delivery (onset or offset time points), as is standard protocol for challenge work (Zvolensky & Eifert, 2001). During the challenge, participants were prompted at each minute to complete ratings of their SUDs for anxiety using a visual analog scale. Participants then underwent a ten-minute recovery period during which they were continuously prompted every minute to complete a

SUDs rating. Heart rate was also monitored continuously during the recovery period. At the end of the challenge participants were unhooked from the mask and physiological recording equipment, debriefed, and compensated for their participation.

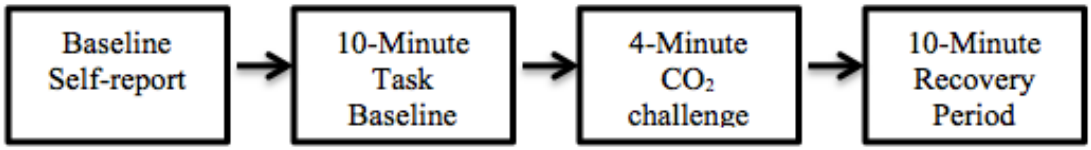

Figure 1. Study Diagram. Heart rate and anxiety were assessed over the 10-minute task baseline, 4-minute challenge, and 10-minute recovery period.

Measures

Demographics and Smoking History-General demographic information was collected, including sex/gender, age, and race/ethnicity. Smoking history was assessed using the **Smoking History Questionnaire** (SHQ; Brown, Lejuez, Kahler, & Strong, 2002). On the SHQ, participants report when they became a regular smoker, any previous quit attempts or periods of abstinence, and the number of cigarettes smoked per day. The SHQ was used to confirm smoking status and eligibility criteria.

Minnesota Nicotine Withdrawal Scale (MWS; Hughes & Hatsukami, 1986) was used to assess symptoms of nicotine withdrawal. Using the MWS, participants rate symptoms of withdrawal based on a 4-point scale from 0 (*not present*) to 3 (*severe*). The MWS was administered at multiple time points throughout the experimental manipulation to examine changes in withdrawal symptom severity throughout the manipulation. Participants completed the MWS prior to setup of the physiological equipment, at the end of the baseline period prior to the CO_2, and at the end of the CO_2 administration. In the current study, participant's MWS score at baseline was included as a covariate in the model to control for the effects of baseline withdrawal

on heart rate and subjective reactivity to a stressor. Internal consistency for the current sample was approximately $\alpha = 0.86$.

Questionnaire of Smoking Urges-Brief (QSU; Cox, Tiffany, & Christen, 2001) was used to assess cigarette craving throughout the study session. The QSU is a 10-item measure consisting of a higher-order craving score and two lower-order craving scores: 1) a stong desire and intention to smoke and 2) anticipation of smoking as a reward. Participants rate items on a 100-point scale (0=*strongly disagree* to 100=*strongly agree*). The measure was used to obtain participants' smoking craving (a) prior to the assessor leaving the room after they had been hooked up to physiological monitoring equipment, (b) directly before the four-minute CO_2-enriched air challenge portion, and (c) directly after the challenge. The current sample evidenced strong levels of internal consistency on global general craving (range of observed α's = .95-.96).

Structural Clinical Interview of DSM-IV Disorders (SCID-I/NP for the DSM-IV; First, Spitzer, Gibbon, & Williams, 2007)- The SCID-I/NP was used to for current and past psychopathology. The principle investigator or a trained research assistant conducted all interviews. Interviews were audio-recorded and a senior level graduate student cross-checked 18.96% of the interviews with an inter-rater agreement of .98 (98% agreement), with no cases of disagreement with regard to PD diagnosis. The interview was used to determine if participants met study inclusion/exclusion criteria related to PD status, history of bipolar or psychotic spectrum illness, or current substance dependence. Adequate reliability of the Axis I SCID has been demonstrated (First et al., 1994).

The Fagerström Test for Cigarette Dependence (FTCD; Fagerström, 2012) was used to assess cigarette dependence. The FTCD has been found to be associated with other indices of dependence, such as cotinine levels, and smoking history (Payne, Smith, McCracken, McSherry,

& Antony, 1994; Pomerleau, Carton, Lutzke, Flessland, & Pomerleau, 1994). It also exhibits high test-retest reliability (Pomerleau, Carton, Lutzke, Flessland, & Pomerleau, 1994). Scores on the FTCD were used to index cigarette dependence and will be included as a covariate in the model to control for the effects of dependence on heart rate and subjective reactivity to a stressor. In the current investigation, this measure was employed to index cigarette dependence ($\alpha = 0.41$ among the present sample). The low internal consistency value for the FTCD is consistent with prior reports (Etter, Vu Duc, & Perneger, 1999).

Distress Tolerance Scale (DTS; Simon & Gaher, 2005) is a 15-item scale that assesses an individual's perception of his/her ability to tolerate distress. The measure assesses an individual's expectations regarding their ability to withstand distress as well as his/her evaluation of the experience of distress (e.g., intensity). In developing the DTS, Simon and Gaher (2005) report one broad domain of distress tolerance that consists of the four sub-factors of 1) tolerance (e.g., "I can't handle feeling distressed or upset," 2) appraisal (e.g., "my feelings of distress or being upset are not acceptable," 3) absorption (e.g., "my feelings of distress are so intense that they completely take over", and 4) regulation (e.g., "I'll do anything to avoid feeling distressed or upset"). Individuals rate the items using a 5-point scale from 1 (*strongly agree*) to 5 (*strongly disagree*). Simon and Gaher (2005) reported consistency in the DTS over a 6-month interval. Internal consistency for the current sample was $\alpha = 0.91$.

Subjective Units of Distress Scale (SUDS; Wolpe, 1958) was used to assess self-reported anxiety throughout the stressor using a visual-analog scale (VAS) ranging from 0 (*no anxiety right now)* to 100 (*extreme anxiety right now*). These ratings were collected before the stressor to assess baseline anxiety, during the stressor, and following the stressor. Ratings were collected at

one-minute intervals. All ratings collected during the 10-minute recovery period were used as the dependent variable.

Cardiovascular Response: A BCI Capnocheck II Handheld Capnograph/Oximeter (Model 8401) manufactured by Smiths Medical was used to capture physiological data, including heart rate. Data was collected at 15-second intervals via a Martel infrared printer (Model MCP8850B). Raw electrocardiogram data were additionally collected with disposable Ag/AgCl electrodes placed in a standard bilateral configuration on the palmar side of each wrist and on the first fingers of the non-dominant hand. Heart rate was collected continuously throughout the procedure, and raw data were used to calculate average heart rate over 15-second intervals. These intervals were then used to calculate mean heart rate at every minute of the baseline period, four-minute stressor, and recovery period.

CO_2 Challenge: The CO_2 challenge is a single four-minute administration of 10% CO_2-enriched air (10% CO_2, 21% O_2, 69% NO_2) (Feldner, Zvolensky, & Schmidt, 2004). During the challenge, 10% CO_2-enriched air is fed through a 2 cm in diameter PVC pipe to a 3 cm in diameter tube connected to a continuous positive airway pressure (CPAP) mask worn by participants. Participants only receive CO_2-enriched air during the challenge portion of the task, and receive regular breathing quality air during the baseline and recovery periods. The CO_2 challenge has commonly been used as a stress-inducing task because it is frequently used to assess how well individuals can manage distress (Brown, Lejuez, Kahler, Strong, & Zvolensky, 2005; Leyro & Zvolensky, 2010). Administration of 10% CO_2 results in significant changes in pre to post $ETCO_2$, increased arousal, and increases in emotional and physical distress (Zvolensky & Eifert, 2001). Performance on the CO_2 challenge appears to be associated with the likelihood of a lapse during a quit attempt for cigarette smokers, greater negative affect on quit day, and greater urges

to smoke on quit day (Abrantes, Strong, Lejuez, Kahler, Carpenter, & Price, 2008). Therefore, the CO_2 challenge appears to reliably induce distress and a stress response in adult smokers, which may be relevant for examining recovery from stress.

III. Data Analytic Strategy

General Approach

Data from all of the participants in the original study were included in the analyses. Since the original study recruited participants with and without a history of panic disorder and participants were randomized to 12 hours of smoking deprivation or to smoke-as-usual, panic disorder status and self-reported cigarette withdrawal symptom severity were included as covariates to account for any differences in heart rate and self-reported anxiety (i.e., SUDs anxiety ratings) related to withdrawal and panic disorder status. Prior to conducting any of the primary analyses, the shape of the recovery profiles for heart rate and SUDs were examined graphically to determine whether there was a potential linear or quadratic effect of time. Additionally, all time invariant predictors were centered, and repeatedly assessed predictor variables were grand-mean centered before completing any longitudinal data analyses.

The indices of heart rate reactivity and reactivity in self-reported anxiety were calculated using two methods supported by research in the area of stress reactivity. Turner (1994) proposed one computational model of reactivity that defines reactivity as a difference score between the peak value during a stressor and the average baseline value, and this model has been used in prior research examining heart rate reactivity (al'Absi et al., 2005; Cacioppo, Uchino, & Berntson, 1994; Evans et al., 2012; Ginty et al., 2015; Roy et al., 1994). However, two common operationalizations of reactivity exist—the observed difference score and the observed residual score. Burt and Obradovic (2013) proposed specific guidelines to use when determining which

index of reactivity to use. First the observed difference score (DS) is determined by the difference between the peak value and the baseline value, with positive scores indicating a greater change. The observed residual score (RS) is determined by the difference between the observed peak value and the expected peak value based on a regression between the observed baseline values and peak values. Larger RS scores indicate that the observed scores are greater than expected and smaller RS scores indicate that the observed scores are smaller than predicted. Further, larger RS scores indicate that an individual may have changed more than expected based on the sample. In this way, the interpretation of the RS score depends on and is restrained to the sample, whereas DS can be compared across samples.

Finally, Burt and Obradovic (2013) provide criteria to use to select DS or RS. These criteria state that the correlation between the baseline value and peak value (i.e., r_{xy}) should be examined as well as the ratio between the variability in the baseline values and the variability in the peak values (i.e., SD(X)/SD(Y), or λ). Next, the correlation coefficient can be compared to the ratio of the variability in baseline and peak. Burt and Obradovic (2013) suggest that RS should be used as a measure of reactivity when the correlation between baseline and peak is less than the ratio between the variability in baseline and peak. This relation would suggest that there is a smaller association between the baseline and peak values for an outcome (i.e., heart rate or self-reported anxiety) and there is a decrease in the observed variability from baseline to peak. Further, this relation suggests that RS is a more reliable measure of reactivity as compared to the observed DS. We will examine the relation between r_{xy} and λ for the DS and RS reactivity scores (please see Results section).

Primary Analyses

Hypothesis 1: Prediction of the recovery in anxious arousal as a function of physiological reactivity to stress, and vice versa.

1a. Dysregulated, or attenuated, cardiovascular reactivity to the CO_2 stressor will predict slower recovery in self-reported anxiety.

1b. Greater reactivity in self-reported anxiety to the CO_2 stressor will predict slower recovery in cardiovascular activity.

Individual growth curve models were conducted in SAS University Edition (SAS® Studio) to examine the primary hypotheses. Models were conducted in a systematic way to determine the significance of the covariates, intercepts, linear and quadratic slopes, and predictor variables on the outcomes of interest. For all of the models examined, the model log likelihood values were compared to determine if there was a significant improvement in each subsequent model.

Model 1: First, a simplified intercepts-only model was examined to determine whether there was a significant fixed intercept (or common starting point) or a random intercept (variable starting point) for heart rate and anxiety during recovery. This model also included the covariates of panic disorder status, withdrawal symptom severity, and an index of cigarette dependence.

Model 2: The next model examined the linear effect of time on heart rate recovery and anxiety recovery to determine whether the recovery profiles were best defined by a linear function. These effects were entered as fixed and random effects to determine whether there was a significant fixed or random slope. This model also included the significant covariates and intercept from the previous model.

Model 3: A similar model was conducted to examine the quadratic effect of time on heart rate and anxiety recovery; this determined whether the recovery profiles were best defined by a

quadratic function as opposed to a linear function, or if the inclusion of a quadratic function in addition to a linear function better defined the rate of the observed recovery profile.

Model 4: The results of the simplified growth curve model indicated whether linear and quadratic effects of time as well as significant covariates (e.g., panic disorder status, withdrawal symptom severity, dependence, etc.) should be retained in the full models. Therefore, the next growth curve model included any significant covariates, a linear and quadratic main effect of time, and predictor variables of interest. This model included the significant covariates, a linear effect of time (i.e., Time), a quadratic effect of time ($Time^2$), and linear and quadratic effects of heart rate reactivity (HRR) (i.e., Time x HRR and $Time^2$ x HRR) on recovery in self-reported anxiety. To examine the reverse model (i.e., hypothesis 1b) we conducted a similar growth curve model with reactivity in self-reported anxiety as the predictor and heart rate as the dependent variable. Again, this model included any significant covariates, a linear (Time) and quadratic ($Time^2$) main effect of time, and linear and quadratic effects of anxiety reactivity (ANXR) (i.e., Time x ANXR and $Time^2$ x ANXR) on recovery in heart rate.

Hypothesis 2: Examination of distress intolerance as a moderator in the relation between stress reactivity and stress recovery.

Model 5: Following the examination of the fourth and final model to test the significance of the effects of physiological reactivity on subjective recovery, and vice versa, a fifth model was conducted to examine the moderating effects of distress intolerance on these relations. The first iteration of this model included significant covariates, a linear effect of time (i.e., Time), a quadratic effect of time ($Time^2$), linear and quadratic effects of heart rate reactivity (i.e., Time x HRR and $Time^2$ x HRR), linear and quadratic effects of distress intolerance (i.e., Time x DI and $Time^2$ x DI), and the interactive effects of time, heart rate reactivity, and distress intolerance

(i.e., Time x HRR x DI and $Time^2$ x HRR x DI) on recovery in self-report anxiety ratings. The reversed model was also conducted to examine the moderating effects of DI on the relation between reactivity in anxiety to stress on recovery in heart rate. This model included the following: significant covariates, a linear effect of time (i.e., Time), a quadratic effect of time ($Time^2$), linear and quadratic effects of anxiety reactivity (i.e., Time x ANXR and $Time^2$ x ANXR), linear and quadratic effects of distress intolerance (i.e., Time x DI and $Time^2$ x DI), and the interactive effects of time, anxiety reactivity, and distress intolerance (i.e., Time x ANXR x DI and $Time^2$ x ANXR x DI) on heart rate recovery.

IV. Results

Manipulation Checks for Laboratory Protocol

Prior to conducting the primary analyses, manipulation checks were conducted to determine that the CO_2 challenge resulted in significant changes in heart rate and self-reported anxiety from pre to post challenge. Similarly, analyses were conducted to examine whether there were any changes in heart rate and self-reported anxiety from the beginning to the end of the recovery period since individual recovery profiles were the primary outcome variable of interest.

To examine whether significant changes occurred in heart rate and anxiety, paired samples t-tests were conducted between pre-challenge (i.e., the last minute of the baseline period) and challenge (i.e., the last minute of the CO_2 challenge) as well as between the end of the challenge (i.e., the last minute of the CO_2 challenge) and the end of the recovery period (i.e., the last minute of recovery). Results of paired samples t-test (Table 1) revealed that there was a significant change in heart rate ($t(45) = 4.08$, $p < .001$) and anxiety ($t(53) = 6.59$, $p < .001$) from pre to post challenge, with increases in both heart rate ($M_{post\ challenge} = 85.34$, SD=11.38) and anxiety ($M_{post\ challenge}$=62.07, SD=33.44). Similar results were observed between the beginning

and end of the recovery period, with significant changes in heart rate ($t(44) = -4.47$, $p < .001$) and anxiety ($t(53) = -7.56$, $p < .001$) from the start to the end of recovery (Table 1). Both heart rate ($M_{post\text{-}recovery}$=79.07, SD=11.92) and anxiety ($M_{post\text{-}recovery}$= 24.09, SD=29.32) appeared to be significantly reduced at the end of the recovery period.

Next, zero-order (or bivariate, as applicable) correlations were computed among baseline and predictor variables. See Table 2 for zero-order correlations among variables. Age was significantly associated with greater cigarette dependence ($r = .49$, $p < .01$) and less distress tolerance (r =-.37, $p < .01$). Cigarette dependence was significantly correlated with cigarettes smoked per day ($r = .56$, $p < .01$), less distress tolerance ($r = -.27$, p =.05), and greater baseline self-reported anxiety ($r = .45$, $p < .01$). Cigarette withdrawal symptoms at baseline were significantly associated with less distress tolerance ($r = -.40$, $p < .01$) and greater baseline self-reported anxiety ($r = .66$, $p < .01$). Distress tolerance was significantly associated with Panic Disorder status ($r = -.28$, p =.04) and greater baseline self-reported anxiety ($r = -.50$, $p < .01$). Baseline heart rate was significantly negatively correlated with anxious reactivity ($r = -0.34$, $p < .01$), and heart rate reactivity was significantly correlated with anxious reactivity ($r = .44$, $p < .01$).

Determining the indices of heart rate reactivity and anxiety reactivity

Prior to conducting any of the proposed analyses, we examined the various associations between the baseline and peak values of heart rate and anxiety as proposed by Burt and Obradovic (2013). For heart rate data, the correlation between baseline heart rate and peak heart rate was 0.68 and the ratio (λ) between the variability in baseline heart rate and variability in peak heart rate was 1.02. For self-reported anxiety, the correlation between baseline and peak anxiety was 0.58 and the ratio (λ) between the variability in baseline anxiety and variability in

peak anxiety was 0.77. For both heart rate and anxiety, the correlation coefficient was greater than the ratio between baseline and peak variability (λ); therefore, these results suggest that the observed residual scores (RS) may be a more reliable index of reactivity than the observed difference scores (DS). For this reason, the observed RS for heart rate and anxiety was used for all of the proposed models[1].

Aim 1a: The effects of physiological reactivity on subjective recovery from stress.

Individual growth curve models were conducted in SAS University Edition (SAS® Studio) to examine whether physiological and subjective reactivity to stress predicted physiological and subjective recovery from stress. These models were conducted in a systematic way to determine whether there was a significant intercept and slope for self-reported anxiety and heart rate, a significant effect of each proposed covariate (i.e., PD status, WD status, CPD, and FTCD), and a significant effect of the predictor variables (i.e., reactivity scores) on recovery. The first model examining recovery in self-reported anxiety tested whether there was a significant starting point, or intercept, for anxiety and whether this intercept was significantly affected by the proposed covariates. The results of the model suggest that there was a significant random intercept for anxiety at the start of recovery (b= 68.29, SE=4.45, $t(50)=15.36$, $p < .01$), indicating significant variability in initial self-reported anxiety (i.e., at the onset of the 10-minute recovery) among participants. In regards to the examination of significant covariates on anxiety during recovery, only age significantly predicted anxiety (b=0.47, SE=0.23, $t(365)=2.03$, $p=0.04$, $d=0.21$).

[1] The observed DS were also examined in the proposed models for exploratory purposes and similar results were observed when using DS. There was not a change in the significant effects observed when using the DS scores.

Next models two and three were examined. Specifically, reduced models, removing non-significant model covariates, were fit to the data to examine whether there was a significant effect of linear and quadratic time on self-reported anxiety. Results indicated a significant linear and quadratic effect on anxiety throughout the 10-minute recovery period. Both time predictors (Time: b=-9.46, SE= 0.84, $t(42)=-11.25$, $p < .01$, $d=3.47$); and Time^2 b= 0.62, SE=0.07, $t(42)=9.10$, $p < .01$, $d=2.81$) significantly contributed to anxiety throughout recovery. These effects were significant when time was entered as a random effect suggesting that there was variability in the change in anxiety recovery among participants. Further, significant linear and quadratic effects of time suggest that there may initially be steeper changes in self-reported anxiety over recovery followed by a deceleration in change.

Model four was conducted to examine the relation between heart rate reactivity during the challenge and self-reported anxiety recovery following a stressor. Results of model fit indicated an improved fit as compared to the model including non-significant covariates. The results also indicated a significant linear effect for heart rate reactivity on recovery in anxiety (Time x HRR; b=-0.75, SE=0.11, $t(296)=-7.01$, $p < .01$, $d=0.81$) and a significant quadratic effect (Time^2 x HRR; b=0.05, SE=0.009, $t(296)=5.80$, $p < .01$, $d=0.67$) supporting hypothesis 1a. There was also a significant effect for the random effect of time in this model, which indicated individual variance in the change in anxiety over time based on an individual's heart rate reactivity. This relation was examined graphically to understand the relation between heart rate reactivity and change in anxiety over time. Figure 1 represents the predicted trajectory for individuals who exhibit low or high heart rate reactivity, and this figure illustrates that greater heart rate reactivity during a challenge predicted greater change in self-reported anxiety during recovery. Further, examination of the observed data indicates that individuals exhibiting heart

rate reactivity scores that are greater than the mean of the sample begin the recovery period with an average self-reported anxiety at a SUDs rating of approximately 74, and those exhibiting heart rate reactivity scores that are below the mean report an average SUDs rating (Figure 2). These initial self-reported anxiety ratings were significantly different ($t(42)=2.84$, $p<.01$). However, by the end of the recovery period those in the high reactivity group report a mean SUDs of 20 and those in the low reactivity report a mean SUDS of 29, which were not significantly different ($t(42)=-1.08$, $p=.28$). Overall, the results of the model suggest that individuals who exhibit greater heart rate reactivity in response to a physiological laboratory stressor may exhibit greater subjective arousal to stress followed by a faster recovery in subjective arousal that eventually resembles the arousal of individuals who exhibited less physiological reactivity to stress.

Aim 1b: The effects of subjective reactivity on physiological recovery from stress.

To examine the next aim, a second model investigating the relation between reactivity in anxiety and physiological recovery was conducted. The first model examined whether there was a significant starting point, i.e., intercept, for heart rate at the beginning of the recovery period and whether there were significant effects of each proposed covariate (i.e., PD status, WD status, CPD, and FTCD) on heart rate. The results suggest that there was a significant random intercept for heart rate at the start of recovery (b=88.29, SE=2.46, $t(40)=35.82$, $p < .01$), suggesting that there was variability in heart rate among participants at the start of recovery. There were no significant effects of the proposed covariates on heart rate.

Next, models two and three were conducted to examine the effect of time on heart rate during recovery. Reduced models were fit to the data to examine whether there was a significant linear and quadratic change in heart rate during recovery. Results indicated a significant decrease in heart rate over time. Both time predictors (Time: b=-1.66, SE= 0.27, $t(42)=-6.20$, $p < .01$,

d=1.91; and Time^2 b=0.10, SE=0.022, *t*(42)=4.50, *p* < .01, *d*=1.39) significantly contributed to heart rate throughout recovery. These effects were significant when time was entered as a random effect suggesting that there was variability in the change in heart rate over time amongst participants. As observed with recovery in self-reported anxiety, the significant linear and quadratic effects of time suggest that there may initially be steeper changes in heart rate over recovery followed by a deceleration in the change in heart rate.

Model four was conducted to examine the relation between reactivity in self-reported anxiety during a challenge and recovery in heart rate following a stressor. Results indicated a significant linear effect for anxiety reactivity on heart rate recovery (Time x ANXR; b =-0.08, SE= 0.010, *t*(302)=-7.65, *p* < .01, *d*=0.88) and a significant quadratic effect (Time^2 x ANXR; b=0.0053, SE=0.001, *t*(302)=6.42, *p* < .01, *d*=0.74) supporting hypothesis 1b. This interaction was examined graphically to understand the relation between reactivity in anxiety and change in heart rate over time. Figure 3 represents the predicted trajectory for individuals who exhibit low versus high reactivity in anxiety. Here, individuals with greater anxious arousal to the challenge experienced greater changes in heart rate during recovery. Despite this effect, probing of differences in heart rate at both the end of the CO_2 challenge (*t*(44)=1.22, *p*=.23) and end of recovery (*t*(43)=-1.6, *p*=.12) revealed no statistically significant differences. However, smokers with greater reactivity evidenced faster recovery (Figure 4).

Aim 2: Examination of distress intolerance as a moderator in the relation between stress reactivity and stress recovery.

In order to examine whether distress intolerance moderated the significant relations observed between stress reactivity and recovery, distress intolerance was added to the final growth curve models for recovery in both heart rate and anxiety. In regards to change in anxiety

over time, there appeared to be a significant linear effect of distress intolerance (Time x DTS; b=1.85, SE=0.94, $t(297)=1.97$, $p=0.05$, $d=0.23$), and the quadratic effect approached significance ($Time^2$ x DTS; b=-0.14, SE=0.08, $t(297)=-1.78$, $p=0.08$). Both the linear and quadratic effects of distress intolerance on recovery in anxiety were examined graphically, and Figure 5 illustrates the predicted trajectory for anxiety as determined by low and high levels of distress intolerance. Further, Figure 6 illustrates the variability in recovery in anxiety for individuals who endorse distress intolerance higher and lower than the sample mean. Together, these results suggest that, individuals who are less tolerant of distress may exhibit faster reductions in anxiety during recovery, but they also exhibit higher ratings of anxiety at the start of recovery, and ultimately, over time, their ratings remain higher than individuals who are more tolerant of distress. Finally, there was not a significant three-way interaction between heart rate reactivity, distress intolerance, and linear or quadratic time ($p > 0.05$).

In regards to recovery in heart rate, there was no significant linear or quadratic effect of distress intolerance on heart rate recovery ($p > 0.05$) and there was not a significant interaction between distress intolerance, reactivity in anxiety, and time on change in heart rate ($p > 0.05$).

V. Discussion

The current study examined the relation between physiological and subjective components of the stress response in daily cigarette smokers in order to better understand how differences in stress reactivity impact recovery. Such a relation may indicate that individual differences in cognitive, affective, and physiological components of the stress response may differentially impact smoking behaviors. To investigate this association, the study first examined whether physiological reactivity to a CO_2 laboratory stressor, as indexed by the residual scores from a linear regression of peak heart rate on baseline heart rate, predicted recovery in the

subjective response to stress, as indexed by self-reported anxiety. The reverse relation was also examined to investigate whether changes in self-reported anxiety during a challenging task predicted recovery in heart rate. The second aim of the study was to examine whether the prospective relations between these two components of the stress response were moderated by individual differences in the ability to tolerate distress. We specifically hypothesized that even when observing greater reactivity in cardiovascular and self-report indices, individuals who are more tolerant of distress may exhibit a faster recovery in both heart rate and anxiety.

The results of the growth curve models conducted to examine the first hypothesis suggest that there was a significant relation between physiological reactivity to stress and subjective recovery from stress in daily smokers. Heart rate reactivity to stress significantly predicted greater linear and quadratic reductions in self-reported anxiety. Specifically, smokers who experienced a greater increase in heart rate from resting to peak experienced greater initial changes in anxiety during recovery that then slowed, as a function of the quadratic effect. Figure 1 illustrates this change over time, with anxiety decreasing, gradually slowing, and then increasing slightly towards a baseline level among smokers with greater heart rate reactivity. Overall, these results suggest that daily smokers who exhibit a greater physiological reactivity to a physiological laboratory stressor may exhibit a greater responsivity to stress that is then followed by substantial reductions in subjective distress. Whereas individuals who are less physiologically reactive may exhibit both a dampened reaction to the stressor as well as slower recovery from stress, with both groups exhibiting equivalent self-reported anxiety at the end of recovery.

Similar results were observed when examining self-reported anxiety reactivity to the challenge task in predicting recovery in heart rate. Again it appears that an increase in anxiety

from resting to peak that is greater than expected is associated with a higher heart rate at the start of recovery and a greater change in heart rate over time. As observed with the subjective ratings of distress, individuals with greater subjective reactivity to stress eventually resemble individuals with less reactivity in that both groups exhibit equivalent heart rate at the end of recovery.

These results add to the limited literature on individual differences in stress reactivity and recovery in adult smokers as well as the prospective relation between physiological and subjective components of stress. Extant research suggests that, as a group, smokers exhibit an attenuated physiological response to stress as compared to never or previous smokers (Childs and de Wit, 2009; Ginty et al., 2014). Smokers also exhibit less of a difference in their physiological response to stress versus control tasks, as compared to non-smokers, who exhibit greater reactivity to stress than a control task (Childs and de Wit, 2009). Further, research examining the longitudinal effects of blunted reactivity to stress suggest that smokers who exhibit reduced physiological reactivity (i.e., plasma cortisol and blood pressure) are more likely to lapse after a quit attempt than those with greater reactivity (al'Absi et al., 2005).

To date, this research has been conducted between smokers and non-smokers, yet these observed differences in the stress response might also be present within smokers. Results of the current study suggest variability in recovery from stress within smokers that may be dependent on their level of reactivity to stress. It appears that individuals who are more reactive to stress in one domain (i.e., physiological or subjective response) exhibit greater recovery from stress in the other domain and over time reach levels of arousal that are equivalent to those of smokers exhibiting less reactivity. These individual differences may have important implications for smoking lapse and maintenance (al'Absi et al., 2005), and smokers who exhibit attenuated reactivity and sustained physiological and subjective arousal levels during recovery may exhibit

worse smoking-related outcomes; whereas greater reactivity to stress may be indicative of an adaptive response to an individual's environment.

In addition to examining individual differences in the stress response within adult smokers, the data also adds to emerging literature on the concordance between physiological and subjective components of the stress response. The results indicate that change in one domain during a stressful task significantly predicts the rate of recovery in the other domain. These results deviate from previous findings that report non-significant associations between the subjective and physiological response to stress. For example, prior research indicates that subjective indices, such as perceived stress or self-reported anxiety, may not be associated with changes in heart rate or cortisol during a social stress task (Campbell & Ehlert, 2012; Cohen et al., 2000; Ditzen et al., 2007).

Although non-significant associations between physiological and subjective stress responses have been reported, alternative evidence supports the significant associations between these components of the stress response. Empirical evidence demonstrates significant associations between perceived stress and cardiac activity during a stressful task (Oldehinkel et al., 2011) and a significant association between negative affect and heart rate during recovery from stress, with poor recovery in one domain associated with poorer recovery in the other (Waugh et al., 2010). Further, Schlotz and colleagues (2008) also found the strongest correlation between subjective measures (i.e., self-reported anxiety) and physiological measures of the stress response (i.e., cortisol) when concordance was examined in a time-lagged manner. In particular they found that changes in subjective responses preceded changes in cortisol response (Schlotz et al., 2008), but not vise versa. Although heart rate was used as an index of physiological reactivity in the current study, the reported findings reflect the association described by Schlotz and

colleagues (2008) in that reactivity in one domain of the stress response significantly predicted rate of recovery in the other domain. Further, the current findings are the first, to our knowledge, to document this relation in smokers. It is possible that this relation may reflect the unique effects of smoking (i.e., nicotine), or other cognitive-affective processes relevant to smoking maintenance, on subjective and physiological stress reactivity in this group. While neither withdrawal status nor psychopathology (i.e., Panic Disorder) significantly predicted differences, cognition and affective processes that play a critical role in emotion regulation (Leventhal & Zvolensky, 2015) may influence the ability to adaptively recover from stress, and identification of the processes that contribute to individual differences in the stress response may have important implications for intervention.

It is also possible that the significant relation between physiological and subjective indices of the stress response may have been observed in the current study due to the intensity of the stressor and the type of arousal examined. Schwerdtfeger and colleagues (2004) suggest that a stressor that elicits a greater stress response may increase the likelihood for observing concordance. The CO_2 challenge has been successfully used to elicit a strong physiological and subjective response (Attwood et al., 2014; Zvolensky, Feldner, Eifert, & Stewart, 2001), and this may have contributed to the observed concordance. Additionally, the use of self-reported anxiety as the subjective measure of distress may be more likely to be associated with physiological changes given the role of physiology in the experience of anxiety (Friedman, 2007).

In addition to examining the prospective association between the physiological and subjective stress responses, the study examined whether distress tolerance moderated the relation. Results of the full growth curve models indicate that distress tolerance did not significantly interact with the reactivity variables to predict recovery in either heart rate or self-

reported anxiety. However distress tolerance did significantly predict a change in self-reported anxiety recovery. Contrary to the predicted relation, greater distress intolerance predicted a greater linear change in anxiety during recovery, yet these individuals still exhibited elevated anxious arousal at the beginning of recovery and maintained higher ratings than those with greater tolerance (Figure 6). This observed relation between distress intolerance and greater self-reported anxiety and change in anxiety may be due to the relation between distress intolerance and negative affectivity. In the current sample, distress intolerance was significantly associated with negative affectivity and Bernstein and colleagues (2009) report a similar significant association. Therefore, individuals with greater levels of distress intolerance may experience the stressor as more arousing, which may be reflected in their greater subjective recovery but not physiological recovery from stress.

When considering these findings, a few limitations should be noted. First, the study did not examine lagged associations between physiological and subjective stress responses (Schlotz et al., 2008), but instead examined the predictive validity of a single index of reactivity on recovery. The study also did not examine reactivity to a control task and did not examine the same relations in a control sample of non-smokers. These limitations make it difficult to explicate whether the observed patterns are unique to stress, per se, or evidence of a general response pattern, and whether these responses are similar or distinct from previously observed relations in non-smokers (Oldehinkel et al., 2011; Schlotz et al., 2008; Waugh et al., 2010). Additionally, the sample size was small which may have affected the ability to detect a three-way interaction between stress reactivity, distress intolerance, and time on recovery as observed by small, but not significant, effect of the quadratic effect of distress tolerance on anxiety recovery.

In conclusion, the current findings suggest that there are individual differences in stress reactivity and recovery within smokers, and differences in reactivity may be predictive of recovery. It appears that adult smokers who exhibit greater reactivity in one domain exhibit greater responsivity to stress in the other domain followed by a faster rate of recovery. This observed relation may be important for understanding processes that maintain smoking or contribute to lapse, and additional research is needed to examine whether individual differences in stress reactivity and recovery differentially predict smoking motives, cigarette dependence, or time to lapse. Future research should also examine the role of cognition and affect in stress responsivity and smoking behavior in order to identify potential mechanisms of change that could be targeted in smoking interventions.

VI. References

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Table 1: Manipulation Checks for Laboratory Paradigm.

	Challenge		
	Pre-Challenge Mean (SD)	**Post-Challenge Mean (SD)**	**Paired Samples T-Test**
Heart Rate$_a$	79.74(11.52)	85.34 (11.38)	$t(45) = 4.08$, $p < .001$
Anxiety$_b$	34.69 (27.36)	62.07 (33.44)	$t(53) = 6.59$, $p < .001$
	Recovery		
	Post-Challenge Mean (SD)	**Post-Recovery Mean (SD)**	**Paired Samples T-Test**
Heart Rate$_a$	85.34 (11.38)	79.07 (11.92)	$t(44) = -4.47$, $p < .001$
Anxiety$_b$	62.07 (33.44)	24.09 (29.32)	$t(53) = -7.56$, $p < .001$

Note: [a]Heart rate averaged over the last minute of the baseline period, the last minute of the CO_2 procedure, and the last minute of the recovery period. [b]*SUDs* = Subjective Units of Distress Scale (Wolpe, 1958) was reported at the last minute of the baseline, immediately post-challenge, and at the end of the recovery period.

Table 2: Zero-Order (or bivariate) correlations among baseline and challenge study variables.

Variable	1	2	3	4	5	6	*M* (SD)
1. Sex	1	.08	.04	.04	-.14	.14	46% Female
2. Age		1	.49**	.26	.06	.16	29.33 (11.92)
3. FTCD			1	.56**	.05	.15	4.00 (1.70)
4. Cigarettes per Day				1	-.16	-.19	19.91 (8.00)
5. Panic Disorder Status					1	.55**	34% PD
6. Negative Affectivity						1	23.45 (8.68)

Variable	7	8	9	10	11	12	*M* (SD)
1. Sex	.16	-.21	-.02	.16	.26	.14	46% Female
2. Age	.19	-.37**	.18	.26	-.27	.04	29.33 (11.92)
3. FTCD	.21	-.27*	.26	.45**	-.22	-.02	4.00 (1.70)
4. Cigarettes per Day	-.03	.12	.02	.12	-.25	-.03	19.91 (8.00)
5. Panic Disorder Status	.08	-.28*	-.003	.17	.13	.08	34% PD
6. Negative Affectivity	.46**	-.67**	-.07	.47**	.14	.31*	23.45 (8.68)

Variable	7	8	9	10	11	12	*M* (SD)
7. Withdrawal SXS	1	-.40**	-.24	.66**	-.13	-.004	7.34 (5.88)
8. Distress Tolerance		1	-.08	-.50**	-.10	-.11	3.60 (.902)
9. BL Heart Rate (HR)			1	<.01	-.05	-.34*	77.97 (11.57)
10. BL Anxiety (SUDS)				1	-.02	-.01	35.24 (25.64)
11. HR Reactivity					1	.44**	-.301 (7.95)
12. Anxiety Reactivity						1	1.09 (27.15)

Note: *$p < .05$, **$p < .01$; *Sex* (0 = *Male*, 1 = *Female*) *Panic Disorder Status (0= NO, 1=PD)*

Table 3. Prediction of the recovery in anxiety from the CO_2 challenge as a function of time and heart rate reactivity.

Dependent Variable: SUDs for Anxiety	b	*SE*	*df*	*t*	*p*
Intercept	63.78	5.34	39	11.84	< .01
HR_RS	2.31	0.44	296	5.28	< .01
Time	-9.46	0.84	42	-11.25	< .01
Time x HR_RS	-0.75	0.11	296	-7.01	< .01
$Time^2$	0.62	0.07	42	9.10	< .01
$Time^2$ x HR_RS	0.05	0.009	296	5.80	< .01

Note: HR_RS – heart rate reactivity to stress was indexed by the residual scores from a linear regression of peak heart rate on baseline heart rate.

Table 4. Prediction of the recovery in heart rate from the CO_2 challenge as a function of time and anxious arousal.

Dependent Variable: Heart Rate	**b**	***SE***	***df***	***t***	***p***
Intercept	85.77	1.67	38	51.30	< .01
ANX_RS	0.24	0.04	302	6.03	< .01
Time	-1.66	0.27	42	-6.20	< .01
Time x ANX_RS	-0.08	0.01	302	-7.65	< .01
$Time^2$	0.10	0.02	42	4.50	< .01
$Time^2$ x ANX_RS	0.005	0.001	302	6.42	< .01

Note: ANX_RS –reactivity in anxiety to stress was indexed by the residual scores from a linear regression of peak anxiety ratings on baseline anxiety ratings.

Table 5. Prediction of the recovery in anxiety from the CO_2 challenge as a function of time, heart rate reactivity and distress intolerance

Dependent Variable: SUDs for Anxiety	b	*SE*	*df*	*t*	*p*
Intercept	63.45	5.55	36	11.42	< .01
HR_RS	2.24	0.46	297	4.87	< .01
DTS	-3.65	4.44	297	-0.82	0.41
HR_RSxDTS	-0.25	0.58	297	-0.43	0.67
Time	-9.38	0.85	40	-11.05	< .01
Time x HR_RS	-0.72	0.11	297	-6.64	< .01
Time x DTS	1.85	0.94	297	1.97	0.05
Time x HR_RS x DTS	0.01	0.14	297	0.08	0.94
$Time^2$	0.62	0.07	40	8.95	< .01
$Time^2$ x HR_RS	0.05	0.01	297	5.50	< .01
$Time^2$ x DTS	-0.14	0.08	297	-1.78	0.08
$Time^2$ x HR_RS x DTS	0.001	0.01	297	0.09	0.93

Note: DTS- Distress Tolerance Scale (Simon & Gaher, 2005)

Table 6. Prediction of the recovery in heart rate from the CO_2 challenge as a function of time, anxious arousal, and distress intolerance.

Dependent Variable: Heart Rate	**b**	***SE***	***df***	***t***	***p***
Intercept	85.86	1.78	36	48.33	< .01
ANX_RS	0.24	0.04	302	5.68	< .01
DTS	0.10	1.29	302	0.08	0.94
ANX_RSxDTS	0.03	0.04	302	0.59	0.60
Time	-1.70	0.28	40	-6.15	< .01
Time x ANX_RS	-0.08	0.01	302	-7.44	< .01
Time x DTS	-0.07	0.31	302	-0.24	0.81
Time x ANX_RS x DTS	-0.006	0.01	302	-0.58	0.56
$Time^2$	0.10	0.02	40	4.52	< .01
$Time^2$ x ANX_RS	0.005	0.001	302	6.20	< .01
$Time^2$ x DTS	0.00004	0.03	302	0.01	0.99
$Time^2$ x ANx_RS x DTS	0.001	0.001	302	0.78	0.43

Note: DTS- Distress Tolerance Scale (Simon & Gaher, 2005)

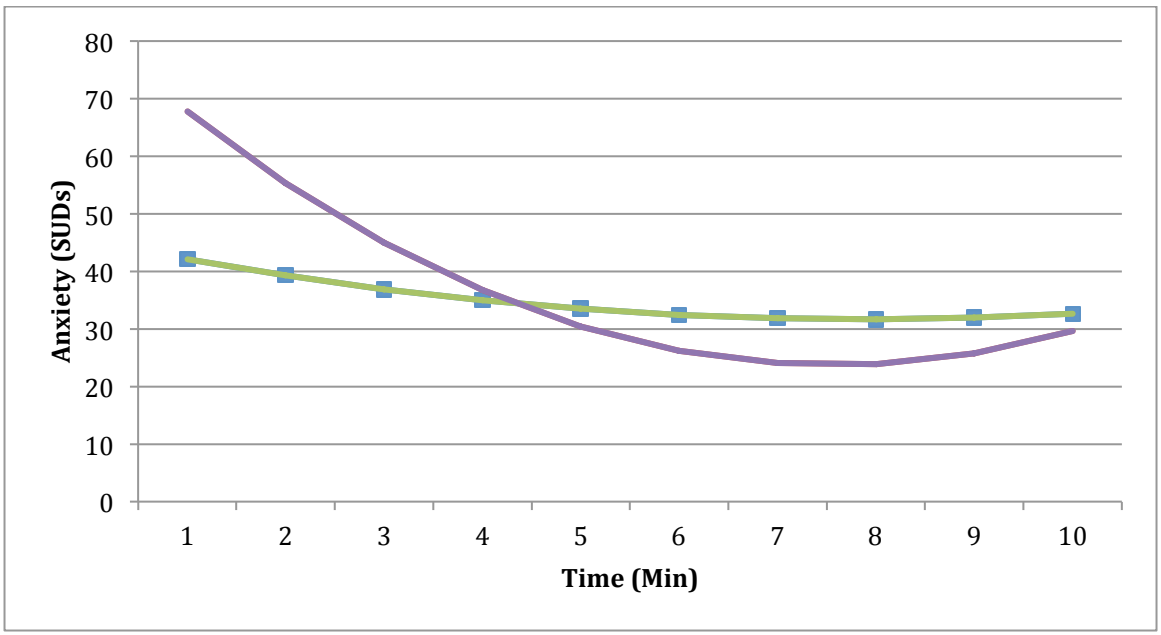

Figure 1. Graphical depiction of the predicted change in anxiety over time as a function of low and high heart rate reactivity (i.e., 1 SD above and below the mean). The purple line represents the trajectory for individuals with greater heart rate reactivity.

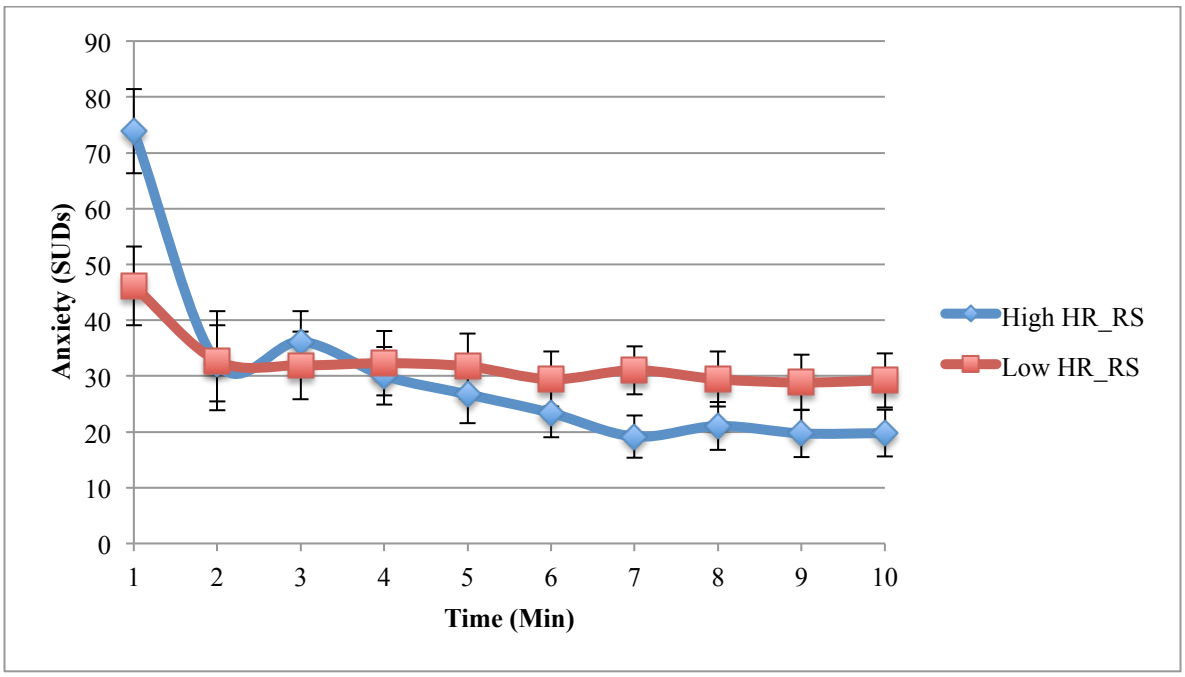

Figure 2. Obtained anxiety ratings plotted over time for individuals above and below the mean of heart rate reactivity scores.

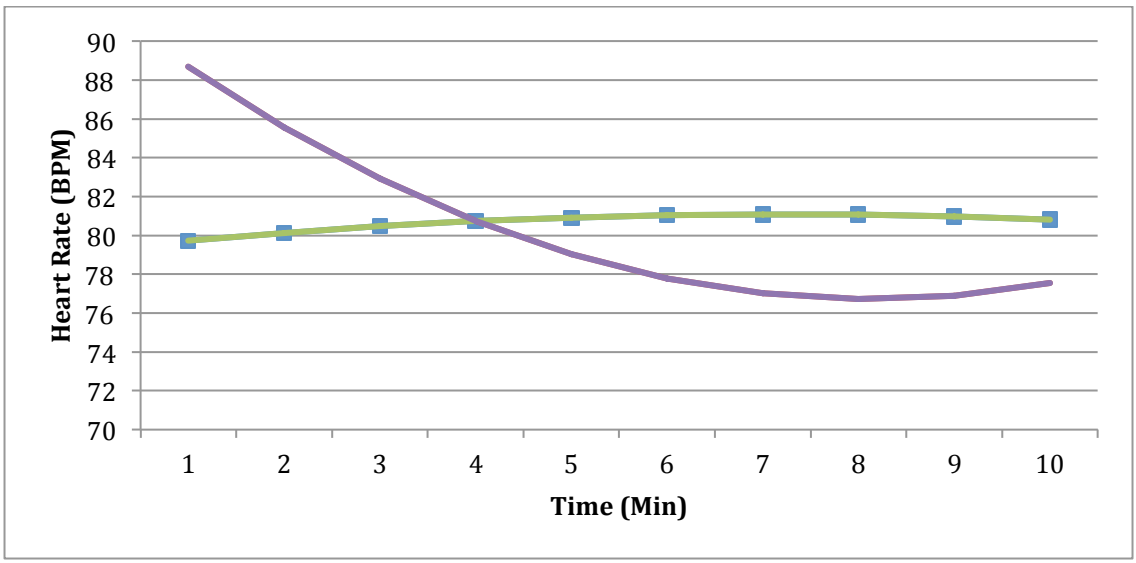

Figure 3. Graphical depiction of the predicted change in heart rate over time as a function of low and high reactivity in anxiety (i.e., 1 SD above and below the mean). The purple line represents the trajectory for individuals with greater reactivity in anxiety.

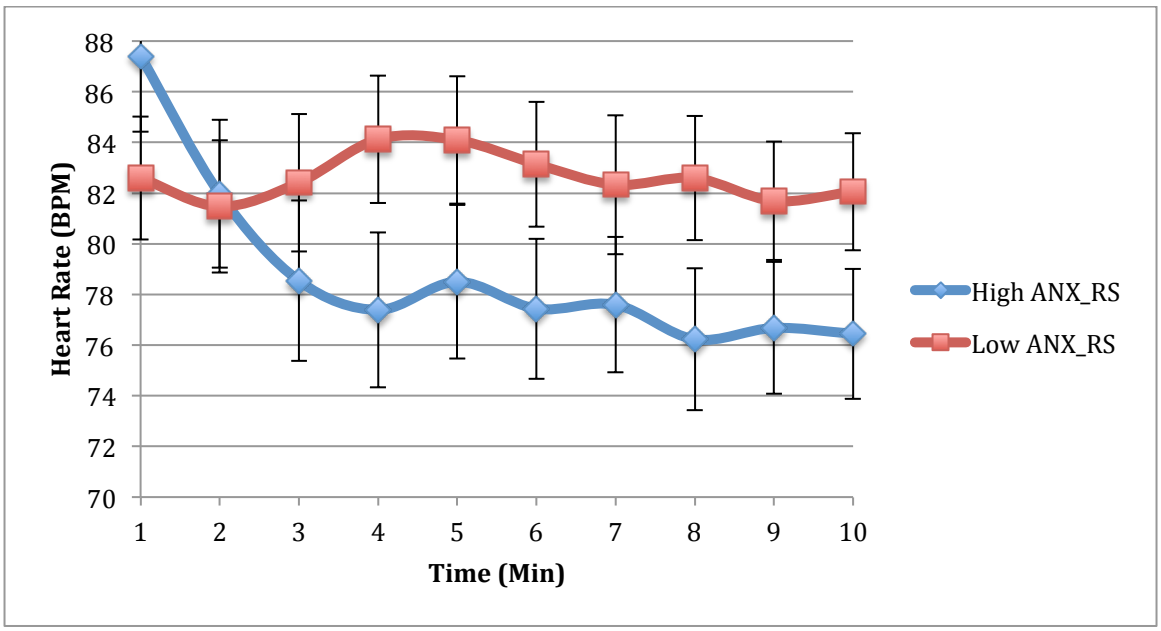

Figure 4. Obtained heart rate data plotted over time for individuals above and below the mean of reactivity in anxiety.

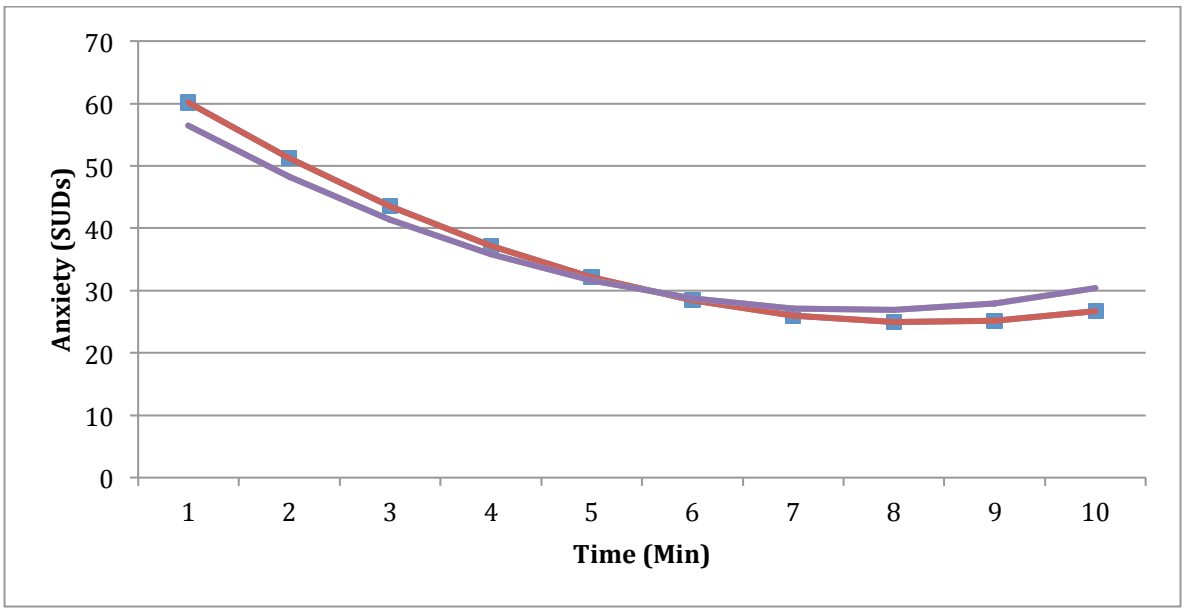

Figure 5. Graphical depiction of the predicted change in anxiety over time as a function of low and high distress tolerance (i.e., 1 SD above and below the mean). The purple line represents the trajectory for individuals with greater distress tolerance.

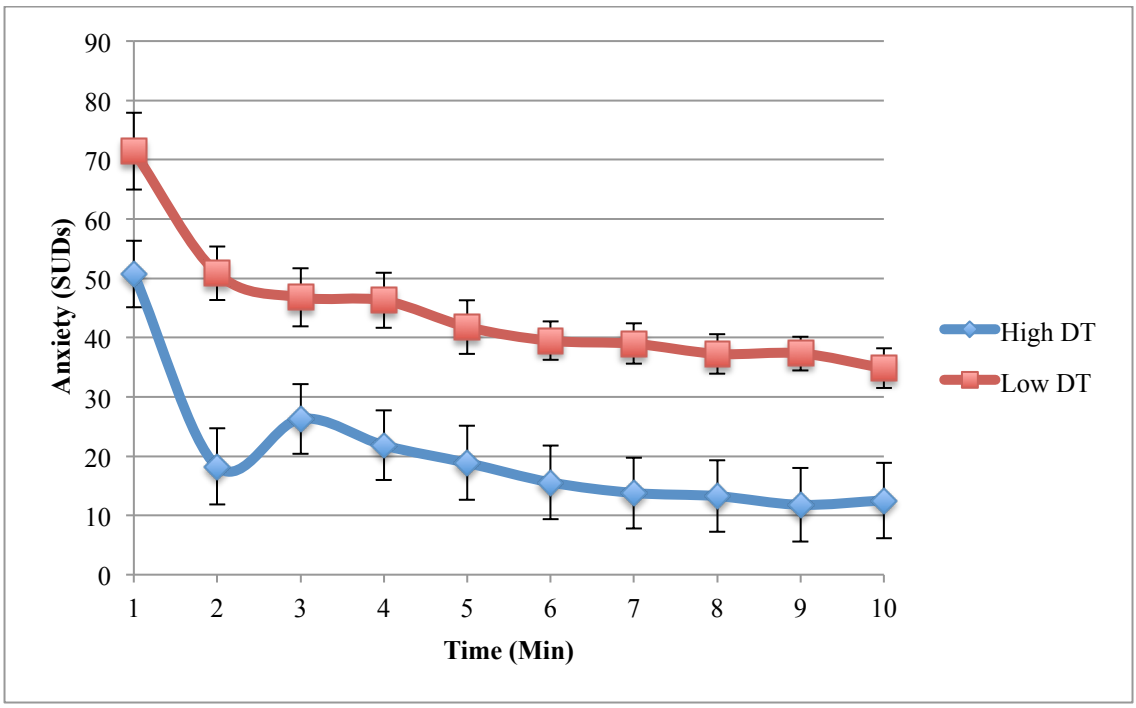

Figure 6. Obtained anxiety ratings plotted over time for individuals above and below the mean of distress intolerance.