THE ROLE OF DISTRESS INTOLERANCE AND VAGAL FUNCTION IN

ATTENTIONAL BIAS AMONG DAILY SMOKERS

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ABSTRACT OF THE DISSERTATION

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Theoretical frameworks on motivation of substance use posit that affective and cognitive vulnerabilities reinforce daily smokers to continue using cigarette as a means of affect regulation. Synthesizing extant literature on cognitive affective vulnerability and the role of cardiac vagal functioning in affective-cognitive regulation in substance use, the current study aimed to examine the role of distress intolerance (DI) and vagal function in attentional bias (AB) toward motivationally relevant cigarette cues among daily cigarette smokers. Forty-eight eligible daily cigarette smokers completed a set of self-report indices as well as behavioral and computerized tasks to assess DI and AB. Vagal tone and flexibility were indexed by respiratory sinus arrhythmia collected during both rest and a cognitively demanding task. The results showed that DI, indexed by persistence in the mirror tracing task, was associated with AB toward cigarette cues among daily smokers, partially confirming study hypothesis. Contrary to our study hypothesis, DI was not associated with indices of cardiac vagal function, which did not demonstrate significant relations with AB toward cigarette cues. Finally, no significant indirect effect of DI on AB through vagal tone or flexibility was observed. Taken together, these findings suggest that smokers high in DI, as indexed by the mirror tracing persistence, may be more prone to allocate attention to cigarette related cues. Implications regarding smoking maintenance are discussed.

Keywords: distress intolerance, attentional bias, vagal function, cigarette smoking

DEDICATION

To my parents, Jeongyeol Yang and Myungsook Kim, my husband, Youngrok, my brothers, Sikyoon and Siijoon, my two dogs, Haneul and Eunbi, and my cat, Morgan. It is with your unconditional love and endless support that I have been able to accomplish this feat.

Thank you – I love you.

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Introduction

Cigarette smoking is the leading preventable cause of disability, disease and death in the United States (US Department of Health and Human Services, 2014). Promising changes in smoking behavior have been observed among cigarette smokers including decreased prevalence (from 20.9% in 2005 to 13.7% in 2018, US Department of Health and Human Services, 2020a) as well as decreased mean number of cigarettes per day ([CPD], from 16.7 CPD in 2005 to 14.1 CPD in 2016, Jamal et al., 2018). In terms of severity of smoking, trends have indicated declines in moderate (20-29 CPD from 34.9% to 28.4%) and heavy smoking (≥ 30 CPD from 12.7% to 7.5%) but increases in light (1-9 CPD from 16.4% to 25.0%) and moderately light smoking (10-19 CPD from 36.0% to 39.0%, Jamal et al., 2018). However, significant discrepancies in smoking prevalence still remain. For example, the prevalence of cigarette smoking among those with greater psychological distress in the past 30 days (e.g., nervousness, restlessness, worthlessness, and hopelessness) remains high (35.8%) compared to those lower in emotional distress (14.7%, Jamal et al., 2018). Also, the proportion of decline in smoking from 2005 to 2015 is significantly different between daily smokers with versus without psychological distress (3.2% versus 31.0% decline, Centers for Disease Control and Prevention, 2015). Such discrepancies may be explained by psychological vulnerabilities (e.g., distress intolerance, Leventhal & Zvolensky, 2015) that may increase emotional distress over time, leading smokers to rely on smoking as a means of affect management.

Recent theoretical models of smoking and psychopathology comorbidity suggest that reactive emotional vulnerabilities likely play a role in elevated emotional distress among extant smokers, in part, due to their contribution to difficulty in managing psychological distress (Leventhal & Zvolensky, 2015). Distress intolerance (DI), the perceived inability to withstand psychological or physical distress (Leyro et al., 2010), is one such vulnerability suggested to play an affect modulatory role in maintaining smoking behavior. Specifically, by amplifying the affect enhancing effects of smoking (i.e., negative reinforcement), DI is posited to reinforce the anticipatory effects of cigarette (e.g., relief of distress) over time which, in turn, maintains smoking (Leventhal & Zvolensky, 2015).

In support of the theoretical value in developing smoking interventions that increase the ability to tolerate distress (Brown et al., 2008; Brown et al., 2018; Farris et al., 2016), a large body of cross-sectional and prospective work suggests its relation to smoking maintenance and cessation. For example, higher self-reported DI is associated with greater negative reinforcement smoking cognitions (Leyro et al., 2008), more years of being a regular smoker, greater nicotine dependence (Leyro et al., 2011; Schlam et al., 2020), heavier smoking after 12-hours of nicotine deprivation (Bold et al., 2013), and greater nicotine withdrawal symptoms after a biological challenge (Farris et al., 2015). Moreover, DI predicts higher lapse and greater negative affect upon cessation (Abrantes et al., 2008) and one-week post-cessation attempt (Schlam et al., 2020), as well as greater risk of early lapse following quit attempts (Brown et al., 2009; Cameron et al., 2013; Schlam et al., 2020), among daily smokers motivated to quit.

The relevance of DI to cigarette craving is also evident. For example, in an experimental study of heavy drinking smokers receiving a pharmacological smoking intervention, a behavioral index of DI was associated with greater increase in alcohol-induced cigarette craving and less craving reduction following cigarette smoking (Lim et al., 2018). While less work has examined mechanisms explaining the association between DI and smoking, it has been proposed that cognitive-affective processes such as perceived salience of smoking to relieve negative affect is reinforced over time (Baker et al., 2004), leading to reliance on smoking to manage emotional distress (Leventhal & Zvolensky, 2015).

In this way, for daily smokers higher in DI, compared to those lower in DI, cigarettes may possess greater perceived incentive value. One means by which to examine this is via biased cognitive processing of cigarette cues (i.e., attentional bias), which has been found to interfere with quit attempts. Attentional bias (AB) refers to the selective processing of information congruent to one's internal states or based on perceptual salience compared to neutral, internally-irrelevant, or perceptually less salient stimuli (e.g., mood, MacLeod et al., 1986; substance-related, Field & Cox, 2008).

Both theoretical and empirical evidence suggest that smokers higher in DI are more prone to selectively process cigarette-related stimuli due to their increased motivation to smoke in order to immediately terminate uncomfortable states. Specifically, cigarette cues ('reward-related cue') obtain incentive salience, causing conditioned ('learned') neural motivational responses, i.e., 'wanting,' over time, while initial hedonic, i.e., 'liking' responses to cigarette decreases (Berridge, 2007; Berridge & Robinson, 2016) as posited in the incentive-sensitization theory (Berridge & Robinson, 2016; Robinson & Berridge, 1993). In turn, cigarette cues elicit a conditioned appetitive motivational state, 'craving,' that is linked to consequent smoking behaviors (e.g., lapse) through biased attentional allocation (i.e., AB) to cigarette cues (Franken, 2003). Thus, AB toward cigarette cues may interfere with goal-oriented or context-relevant coping behaviors (e.g., quitting, staying abstinent) by drawing one's cognitive resources to goal-irrelevant cues that are congruent to their internal states of distress (e.g., relief of craving or emotional distress, Derryberry & Reed, 2002; Garland et al., 2012).

Biased attentional allocation toward cigarette cues is evident among both current and former smokers (Masiero et al., 2019) and even among other competing appetitive stimuli (Correa & Brandon, 2016). Further, empirical evidence shows that AB toward cigarette cues was prospectively linked to increased craving and shorter latency to smoking (Droungas et al., 1995) and early lapse during a 24-hour (Janes et al., 2010) or 1-week quit attempt (Powell et al., 2010). Moreover, evidence shows that AB can be alleviated by manipulating the anticipatory reinforcing effect of nicotine (Robinson et al., 2016).

Together, evidence suggests that cognitive resources among smokers higher in DI may be primarily and selectively recruited to process cigarette-related information due to their incentive salience (Berridge & Robinson, 2016; Robinson & Berridge, 1993). While there is a paucity of research investigating the direct relation between DI and AB toward cigarette cues, several studies suggest the association between DI and AB may be relevant to smoking maintenance. For example, in a nonclinical young adult population, DI predicts greater AB towards internally congruent (i.e., threat and dysphoric) stimuli following a laboratory stressor (Macatee et al., 2018). The only study, to our knowledge, that has begun to unpack these relations in smokers found that the way smokers react toward thoughts and feelings about cigarette craving (i.e., reappraisal, acceptance, and suppression) significantly affected their ability to both control attention (i.e., AB toward cigarette cues) and persist during behavioral DI tasks (Szasz et al., 2012).

Taken together, DI may amplify the incentive salience of cigarette cues, thus, automatically drawing one's attention to smoking cues as a preparatory action to manage their emotional distress. As a result, AB to cigarettes elicited by motivation to immediately terminate distress (i.e., DI) may contribute to risk of lapse under emotional distress, rather than utilization of alternative effective coping skills to regulate emotional states (Leventhal & Zvolensky, 2015). Yet, cognitive-affective regulatory strategies may in part contribute to biological factors associated with the ability to appropriately recruit cognitive-emotional resources, such as cardiac vagal function.

The cardiac vagal system is regarded as an integrated neural feedback system, which connects the central nervous system and parasympathetic nervous system and is controlled by tonic inhibitory control of the prefrontal cortex (Smith et al., 2017; Thayer et al., 2012; Thayer et al., 2009; Thayer & Lane, 2007). The neurovisceral integration model (Thayer & Lane, 2000) posits that the vagal system, whose activity is commonly indexed by respiratory sinus arrhythmia (RSA), is critical in self-regulation such that it plays a regulatory role in attention and emotion processing, thereby predicting one's response tendency to uncertainty and threat in their external environment.

Relevant indices, such as vagal tone (resting RSA) and vagal flexibility (degree of RSA alterations or vagal withdrawal/reactivity), have been linked to performance on tasks requiring higher cognitive modulation under emotional influence (Muhtadie et al., 2014; Thayer et al., 2009). In particular, both higher vagal tone and flexibility are linked to adaptive top-down (Thayer et al., 2012) and bottom-up cognitive modulation of affective stimuli (Park & Thayer, 2014; Park et al., 2012), including appropriate emotion regulation (Thayer & Koenig, 2019) and perception of one's social environment leading to appropriate behavioral execution (Muhtadie et al., 2014). Also, dysregulation of cardiac vagal functioning (i.e., lower vagal tone/flexibility, high in sympathetic functioning) is linked to a variety of mood and anxiety pathology (e.g., trait anxiety, Ramírez et al., 2015), as well as the inability to control intrusive thoughts (Friedman, 2007; Gillie et al., 2015; Moon et al., 2013), and borderline personality disorder (Chapman et al., 2011; Gratz et al., 2006; Koenig et al., 2016). There is also emerging evidence that targeting these processes (e.g., increasing RSA by resonance paced breathing, Mather & Thayer, 2018) leads to decreases in state anxiety and trauma symptoms (Paul & Garg, 2012; Tan et al., 2011).

While the link between DI and vagal function is yet to be elucidated, smokers higher in DI may display greater vagal dysfunction compared to those lower in DI, given the association between vagal dysfunction and emotional modulation. Specifically, smokers with a dispositional propensity to avoid both perceived and experiential distress may demonstrate a limited physiological capacity to execute goal-directed behaviors. For example, avoidance may become an automated learned response to distress, leading to amplification of sensitivity to potential threat in the environment. Given the evidence supporting the association between vagal dysfunction and DI accounted by difficulties in emotion regulation (Leventhal & Zvolensky, 2015; Thayer & Koenig, 2019), smokers high in DI may be more likely to show vagal dysfunction. In turn, vagal dysfunction may lead to difficulty recruiting cognitive resources to execute context-appropriate responses (e.g., Thayer & Lane, 2000). Consequently, this may contribute to cognitive processing of information associated with the immediate alleviation of emotional distress (e.g., AB toward cigarette cues) by inhibiting processing of other goal-relevant information. Thus, impaired cardiac vagal function may explain why smokers lower in DI have difficulty persisting in goal-directed behavior (e.g., quit attempts). Aligned with this hypothesis, both vagal dysregulation and AB toward cigarette cues have been observed among daily smokers.

In addition to theoretically diminished vagal control in smokers due to elevations in DI, examination of these processes may be particularly relevant in daily smokers given cardiac vagal dysregulation is associated with both short- and long-term smoking (Bodin et al., 2017; Hayano et al., 1990; Leyro et al., 2019; Tsuji et al., 1996). For example, daily smokers evidence acute decreases in vagal tone immediately after smoking and long-term decreases in vagal tone in both controlled laboratory (Hayano et al., 1990) and daily living settings (Bodin et al., 2017). Further, vagal control has been proposed as a biological vulnerability in smoking maintenance, impeding cessation. For example, low levels of both resting RSA and RSA reactivity to emotional stimuli has been linked to unfavorable smoking outcomes, including shorter latency to smoke following a stressor (Ashare et al., 2012) and higher number of cigarettes smoked following a cessation attempt at the follow-up (Libby et al., 2012). These findings suggest that vagal function may serve as an individual difference variable with important implications for affective processes of smoking, its maintenance, and lapse.

Evidence shows vagal dysfunction is linked to greater attentional dyscontrol in both cognitively (e.g., Ramírez et al., 2015) and emotionally challenging situations (e.g., Gillie et al., 2015) and may contribute to AB; a perspective that is aligned with the neurovisceral integration model (Thayer & Lane, 2007). For example, lower vagal tone, as compared to higher vagal tone, predict AB towards threat stimuli (e.g., fearful faces, Park et al., 2012; fearful scenes, Ruiz-Padial et al., 2017) despite low perceptual salience, suggesting difficulty in inhibiting AB (Park & Thayer, 2014; Park et al., 2013). These findings demonstrate that vagal function is related to adaptive top-down (e.g., successful attentional inhibition to fearful face stimuli, (Thayer et al., 2012; Thayer & Koenig, 2019) and bottom-up cognitive modulation of affective stimuli (e.g., attentional engagement to and disengagement from stimuli, Park & Thayer, 2014; Park et al., 2013). Although literature on substance use implies similar observation (e.g., the link between AB toward alcohol cues and RSA cue reactivity, Garland et al., 2012), little work has explicitly examined the direct association between AB and vagal function among smokers.

Synthesizing previous findings and theories, smokers with higher DI may display greater AB toward cigarette cues, a relation which may, in part, be explained by vagal dysfunction. These processes have implications for smoking cessation literature such that these individuals may be at a greater risk of craving and relapse under emotional distress, thus, leading to greater nicotine dependence and poor cessation outcomes. While extant DI interventions focus on the idea that exposure will lead to a change in how individuals 'appraise' distress (e.g., Macatee & Cougle, 2015), promising results targeting DI have been reported in studies combining exposure and acceptance-based treatment to reduce avoidance of cessation related distress (Brown et al., 2008; Brown et al., 2018; Brown et al., 2013). This suggests that there is room to expand our current understanding of mechanisms underlying the relation between DI and smoking. An integrative investigation including examination of cognitive-affective and biological factors may provide preliminary data to explore potential mechanisms underlying the association between DI and affective processes of smoking.

The current study seeks to integrate previous findings on psychological (i.e., DI) and biological vulnerabilities (i.e., vagal function) contributing to automatized implicit smoking processes, i.e., AB, among daily smokers. The aim of the current study is to examine the relation between DI, vagal function, and AB toward cigarette cues, and the indirect effect of DI on AB through vagal dysfunction among daily smokers. The main study hypotheses are: (1) Smokers with higher DI, compared to those with lower DI, will display greater (1a) vagal dysfunction, indexed by vagal tone and vagal flexibility, and (1b) AB toward cigarette cues; (2) greater vagal dysfunction will be associated with greater AB; (3) the relation between DI and AB will be mediated by vagal dysfunction (Figure 1).

Methods

Participants

Participants were daily smokers (*N*=50; 32% female, Mean age=34.16, SD age=7.85, Range age=19-50) recruited through local advertising on community bulletin boards and online forums. Ethnic and racial breakdown was as follows: 14% Hispanic, 56% Caucasian, 28% African-American, 6% Asian, 6% more than one race, 2% other, and 2% unknown. Inclusion criteria were; 1) ≥ 5 cigarette per day (CPD) for the past one year; 2) 19-50 years old; 3) normal or corrected-to-normal color vision; 4) fluent in English; 5) ability to work with computer; 6) verification of smoking status via carbon monoxide (CO) analysis of breath sample > 8 ppm (Javors et al., 2005). The current CPD level was based on the recent report suggesting both moderate and heavy smoking is on the decline and that many newer smokers are not proceeding to moderate (20-29 CPD) or heavy use (≥30 CPD) (Centers for Disease Control and Prevention, 2014; US Department of Health and Human Services, 2014, 2020b). Exclusion criteria included; 1) non-daily smoking; 2) ≥ 35 body mass index; 3) evidence of current or past alcohol or other substance use disorder; 4) use of any smoking cessation aids or medication; 5) use of other tobacco or nicotine products (e.g., marijuana) for regular use; 6) current or past psychotic or manic symptoms indicative of bipolar or schizophrenia spectrum disorders; 7) current suicidal or homicidal ideation; 8) inability to provide written informed consent; 9) visual or hearing impairments that interfere with the completion of computerized tasks; 10) medical condition or medication use that may impact index of physiological parameters.

Measures

Fagerström Test for Cigarette Dependence (FTCD; Fagerström, 2012; Heatherton et al., 1991) is a 6-item self-report scale assessing continuous levels of cigarette dependence. Despite low internal consistency (α = .61; Heatherton et al., 1991), its test-retest reliability is high (Pomerleau et al., 1994) and it is positively correlated with key smoking variables such as saliva cotinine (Heatherton et al., 1991; Payne et al., 1994). In the current investigation, the FTCD was employed to index nicotine dependence (α= .57 in the current sample).

Smoking History Questionnaire (SHQ; Brown et al., 2002) is a 30-item measure assessing self-reported smoking history and pattern. The SHQ includes items pertaining to smoking rate, age of onset of smoking initiation, and years of being a daily smoker. The SHQ has been reliably used as a measure of smoking history (Zvolensky et al., 2004). In this study, we used the items asking about duration, quantity of current smoking, and other tobacco use.

The *Timeline Followback* is a method of assessing substance use and requires participants to retrospectively estimate their daily substance and alcohol use (Sobell & Sobell, 1992, 1995). For the purposes of our study, past 28-day cigarette, alcohol, and marijuana use was assessed (Sobell et al., 1996).

The Positive and Negative Affect Scale (PANAS) is a 20-item self-report index of current, state level, mood (i.e., negative and positive affect). Participants used a 5-point scale (1 = *very slightly or not at all* to 5 = *extremely*) to indicate how they were currently (i.e., today) feeling (e.g. “enthusiastic”) or how they felt in the past few weeks. This measure exhibits high internal consistency, as well as convergent and discriminant validity (Watson et al., 1988). We used PANAS to assess current mood during the lab session to control baseline negative affect. Specifically, negative affect assessed following the baseline smoking will be used as a model covariate.

Distress Intolerance Index (DII) includes 10 items (e.g. “I can’t bear disturbing feelings”) rated on a five point Likert-type scale (0=*very little* to 4=*very much* for question 1, 1 = *strongly agree* to 5 = *strongly disagree* for questions 2-7, and 1 = *absent* to 5 = *very strong* for questions 8-10) to assess individual differences in perceived capacity to withstand and tolerate general somatic and psychological distress (McHugh & Otto, 2011). DII is composed of 1 item from Anxiety Sensitivity Index (Peterson & Reiss, 1992), 6 items from Distress Tolerance Scale (Simons & Gaher, 2005) and 3 items from Frustration Discomfort Scale (Harrington, 2005). In the current study, DII was scored with 10 items from concordant aforementioned scales. The DII demonstrates strong internal consistency reliability and concurrent validity, and evidence for construct validity (McHugh & Otto, 2011) ($\alpha = .89$ in the current sample).

The *Breath Holding Task* is a behavioral assessment of physical DI. Participants were instructed to inhale as deeply as possible and then exhale once a full breath was achieved. At the completion of the exhalation, the participants, again, breathed in as deeply as possible and, this time, were prompted to hold their breath as long as they can (Asmundson & Stein, 1994). Duration of breath holding was recorded. Participants repeated this task for two times and the second trial was considered as main trial. Pre- and post-ratings of distress were collected by two items asking subjective unit of distress and physiological sensations. This task has been frequently used as measure of physical distress intolerance (Brown et al., 2009; Hajek et al., 1987), with shorter durations of breath-holding indicating greater intolerance of physical distress. Its test-retest reliability has been reported high (Sütterlin et al., 2013). In the current investigation, duration of the breath holding from the main trial was used to index behavioral DI.

The *Mirror Tracing Persistence Task – Computerized Version* (MTPT-C; Strong et al., 2003) is a behavioral assessment that measures an individual's ability to persist a difficult and frustrating computer task. In this task, participants traced a red dot along the shape of lines (practice trial) and a star (main trial) using a computer mouse. In order to make the task difficult and frustrating, the movement of the computer mouse and the cursor was reversed such that they moved in opposite directions of one another (e.g., when the mouse was moved left, the cursor moved right, Brandon et al., 2003). If participants failed to move the mouse or moved the mouse outside the lines of the shape, a loud buzzer sounded through the headphone, and the trial started from the beginning. Following two practice trials with shape of lines to ensure that participants understood the task, the main trial with a star figure began. In the main trial, participants were allowed to opt to terminate the task at any time. Although not aware of a time limit, participants were given up to 300 seconds to complete the task. The latency to termination of the task from the main trial was used as an index of behavioral DI. MTPT-C was run on Macromedia Projector software. Pre- and post-ratings of distress were collected using the items on irritability, frustration, anxiety, difficulty concentrating, urge to smoke, and bodily discomfort.

Plain Vanilla Task (Jennings et al., 1992) is a task which requires participants to pay attention to colored rectangles that appear on the computer screen for 10 seconds at a time. This task demands attention, but is not exhaustive. Therefore, it is a validated method of ensuring that participants are relatively relaxed, yet focused, in order to standardize ‘baseline’ physiological measurements. This is often used rather than having a free sitting baseline period during which participants simply sit still in order to attempt to control for confounds that may occur due to individual differences in internal states between participants (e.g., ruminating about an event, thinking about an interaction, worrying about what will come next). Vagal tone was measured during this period. The Plain Vanilla Task was run on E-Prime 2.0 software.

Dot Tracking Task (Cavanagh & Alvarez, 2005) was used to manipulate participants’ attentional demands. In this task, participants were presented with 12 gray dots on the computer screen at the start of each trial. A subset of dots (targets; either 2, 3, or 4) flashed yellow, and then once again turned black, and all dots began to move at random around the screen. Participants were instructed to follow the target dots using their peripheral vision amongst the distractors while fixing their eye gaze on the fixation cross in the middle of the screen. At the end of each trial, participants selected target dots. The trials increased in difficulty (i.e., the number of targets), over the course of 5 minutes, after which the task self-terminated. Though typically employed in studies of visual cognition, due to its cognitive demands, the Dot Tracking Task has been used to invoke changes in respiratory sinus arrhythmia (RSA) such that a change between the baseline and the task reflects vagal flexibility (Muhtadie et al., 2014). In the current study, vagal flexibility was indexed by the change between 5-minute mean RSA during the Plain Vanilla Task and the lowest 1-minute RSA value during the Dot Tracking Task (Hagan et al., 2017). The Dot Tracking Task was run on Matlab R2016b software.

A modified *Attention Bias (AB) Task* was designed to assess AB. The AB task was a computerized reaction time dot-probe task utilizing pictorial stimuli. Participants were asked to respond to probes appearing on the either left or right side of the computer screen followed by presentation of a pair of pictures. Stimuli used for the current AB task were selected from the International Smoking Image Series (ISIS; Gilbert & Rabinovich, 1999) and the International Affective Picture System (IAPS; Lang et al., 2008). Appendix A presents the full description of stimuli selection, stimuli used in the current AB task and the summary of valence, arousal, and urge ratings from IAPS and ISIS. Two indices of AB were computed to assess AB toward cigarette cues: (1) traditional bias score (MacLeod & Mathews, 1988) and (2) trial-level bias score (Zvielli et al., 2015). While the traditional bias score reflects AB across trials, the trial-level bias score reflects the temporal fluctuation and variability of attentional allocation trial-by-trial. Specifically, trial-level bias scores incorporate temporal dynamics of AB through a series of subtraction of neighbored trials' reaction times and can be computed in five ways (e.g., toward, away, variability). For the current investigation, we chose to use the trial-level toward bias score because it assesses tendency to allocate attention toward cues trial-by-trial. The trial-level toward bias score is consistent with the theoretical framework of the current study, i.e., propensity to allocate attention toward cigarette cues due to its incentive salience because they are motivationally relevant (Baker et al., 2004; Berridge & Robinson, 2016). Details regarding computation of the AB indices are presented following a description on AB data reduction later in Methods.

AB task design: In total, there were 174 trials, of which were five practice trials, five buffer trials, 144 experimental trials (i.e., four cycles of a pool of 36 pairs of smoking [S] and matched non-smoking neutral [N] images [S-N], and a pool of 20 filler trials (i.e., four times of five pairs of neutral images [NT-NT]). The AB task began with an instruction on the AB task that was followed by five practice trials (i.e., practice session). After completion of a practice session, a second instruction appeared to ensure that the participants understood the AB task fully. Following the second instruction, the experimental session began followed by the five buffer trials. In the experimental session, a set of 36 S-N and 5 NT-NT pairs were repeated four times. Each trial begun via presentation of a fixation cross lasting 500 ms, followed by a 500 ms presentation of either S-N or NT-NT pairs on the screen; participants responded to the location of the target probe, either right or left side of the screen, using the keyboard immediately after a pair of pictures disappeared. In order to maximize the AB effect by increasing task demand, a distractor probe (one dot) appeared simultaneously on the opposite location of where the target probe (two dots) appeared (e.g., Garland et al., 2012). The intertrial interval randomly varied (i.e., 500ms or 1500ms) in order to avoid prediction of stimuli presentation. The interstimulus interval was 250 ms. The picture presentation order was randomized across participants. For the S and N images, the number of presentation was fixed to 9 in each cell of 2 x 2 condition (location [right vs left] x congruency [congruent vs incongruent]). In the congruent condition, the target probe replaced the S image while the target probe replaced the N image in the incongruent condition. Please see Figure 3 for the schematic presentation of an experimental trial.

AB task setup: The AB task was run and the data was acquired using the E-Prime 2.0 software (Psychology Software Tools, Pittsburgh, PA). Stimuli were presented on a 21.5-in. LED monitor (Dell E2216H), at a screen resolution of 1,920 x 1,080 pixels (60

Hz refresh rate). Responses were recorded using a keyboard by pressing either ‘f (left)’ or ‘j (right)’ keys according to the location of target probe presentation. In order to remove any extra attentinoal load when participants enter their responses, the keys on the keyboard were indicated with each of red (‘f’ key for left) and green (‘j’ key for right) colors. All of the pictorial stimuli including target probe (two dots) and distractor (one dot) were presented on black backgrounds. The size (40%(W) x 37%(H)) and the position (25%(X) x 50%(Y)) of the pictorial stimuli were fixed in the property settings of the E-Prime 2.0 software. Distance between participants’ forehead and the screen was ~45cm (*M*=45.30, *SD*=1.38, *Range*=42 to 51).

Cardiac Vagal Indices

Beat-to-beat variability in heart rate in the 0.12-0.40 Hz range (Task Force of the European Society of Cardiology, 1996), corresponding with respiration was utilized as an index of cardiac vagal activity. The current study utilized two indices of cardiac vagal function (i.e., vagal tone and vagal flexibility). First, the vagal tone was defined by the RSA, a proxy of high frequency heart rate variability, collected during the Plain Vanilla Task. Second, the vagal flexibility was defined by the degree of RSA change observed between the Plain Vanilla Task and the Dot Tracking Task (Muhtadie et al., 2014). The lowest RSA value during the Dot Tracking task at the individual level was used to compute the vagal flexibility as it theoretically reflects the highest attentional demand participants experienced.

General Experimental Setup

The experimental session was conducted in a room with a white noise machine on in the hallway. All of the computerized tasks were conducted on the operating system of

Microsoft Windows 10 Pro (64-bit, Intel Core i5-7500) with the graphic card of AMD Radeon R5 430, installed on OptiPlex 3050 Desktop (Dell Inc). Responses were recorded using a keyboard and mouse.

Procedures

G*Power software, version 3.1.0 (Faul et al., 2009), was used to determine the sample size. Sample size of 60 would be adequate based on the primary hypothesis to provide a power of 0.80 to detect a medium effect size (f^2=.196, [R^2 change/1-cumulative R^2]) via multiple regression analyses with up to five covariates (i.e., age, sex, body mass index, cigarette dependence, and negative affect) and the three main predictors (i.e., DI, vagal tone and flexibility) with an alpha set at .05. Our analyses with recruited N=50 was underpowered to detect effects, given the terminated recruitment following stay at home orders associated with COVID-19. Thus, effect sizes are reported for observed trending effects in order to inform future research as recommended (Nieminen et al., 2013).

The current study was part of a larger investigation aiming to examine the role of cognitive, affective, and physiological vulnerabilities in attentional bias to smoking cues and smoking reward among daily smokers. The full study protocol is described in this section, focusing on the procedures relevant to the current study aims.

Following a brief phone screen, eligible participants consented to complete an online survey, were asked to complete a 1-hour questionnaire online, and scheduled for their laboratory visit. The online survey included questionnaires assessing demographic characteristics, cigarette dependence, perceived distress intolerance, emotion regulation, and psychopathology. Eligible participants received detailed instructions of behaviors to avoid in the 24-hours prior that may confound physiological assessment (e.g., vigorous physical activity, substance use). Upon the arrival, participants completed informed consent and were provided with the information about the study. Eligibility criteria was rechecked including verification of smoking status via CO analysis of breath sample (>8ppm, Javors et al., 2005). Next, participants completed self-reports asking about demographic information, past one-month substance use including cigarette, marijuana, and alcohol, other substance use, and smoking pattern and history. Following the completion of self-reports, participants were asked to smoke a cigarette of their usual brand in a designated smoking room designed to directly ventilate to the outdoors before the procedure began in order to standardize withdrawal status (Ferguson & Shiffman, 2009; Shiffman, 2009). Next, participants completed self-report measure on state affect to assess baseline negative affect. Then, participants completed two behavioral DI tasks including the breath holding task and mirror tracing task in a counterbalanced manner. Then, participants were attached to physiological sensors to continuously measure heart rate, respiration, and heart rate variability throughout the study. Acknowledge Software and wireless MP150 Data Acquisition Systems (BIOPAC Systems Inc) were used to obtain continuous measures of electrocardiography, and respiration rate, derived from impedance cardiography. Following a 5-minute period where participants were asked to stay relaxed but alert, participants completed computerized tasks including the plain vanilla task and dot tracking task, as well as first AB task (see Figure 2). Following the first AB task, which was the outcome variable of the current study, participants were randomized to one of two stress manipulation conditions in accord with the study protocol to examine the additional aims on the relation between emotion and smoking reward. Thus, the AB task used for the current investigation was not affected by the mood manipulation protocol. Participants completed a series of behavioral tasks, questionnaires, and a smoking task while attached to physiological sensors according to the full study protocol in the following order: (i) mood manipulation a, (ii) second AB task, (iii) mood manipulation b, (iv) third AB task, (v) mood manipulation c, and then (vi) smoking analog task. The full protocol of the study lasted approximately 3.5 hours and participants were compensated up to $76.

Data Reduction

Physiological Data Processing

ECG data were scored offline in one-minute epochs, in accord with Task Force guidelines (1996), using Mindware (Mindware Technologies, LTD) software, version 3.1.2, which allows for visual inspection and editing of data. Respiration was estimated from cardiac impedance data (i.e., dz/dt). The interbeat interval series was derived by a peak identification algorithm to identify R-peaks, and the software employed an automated Minimum Artifact Deviation and Maximum Expected Deviation (MAD/MED) check algorithm (Berntson et al., 1990). Data were first linearly detrended to remove any high frequency noise (Ernst et al., 1999), using a Hamming window function, and were decomposed using Fast Fourier Transformation to quantify heart period power spectrum data within specific frequency bands. A Baseline and muscle noise filter was used account for noise signals occurring between 0.25 and 0.40 Hz. R-peak detection was based on a default low-pass filter setting of 0.003 Hz and a high pass filter of 0.42 Hz. High frequency heart rate variability was defined as the natural log of the variance occurring between 0.12 and 0.40 Hz, which is the default setting selected by Mindware (Mindware Technologies, LTD, Gahanna, OH), corresponding with RSA. Following automatic scoring in Mindware, each epoch underwent additional cleaning, based on expert committee report guidelines put forth for detecting QRS complexes (Berntson et al., 1997), via visual inspection. This included removal of misplaced R-peaks and insertion of missing R-peaks, based on RR interval distance from measured and cleaned ECG recording, estimation from remaining data, or by splitting long R-peaks into equal intervals. No more than two R-peaks was permitted to be estimated within a one-minute epoch. Within minute segments, we allowed for the removal of up to 10 seconds (i.e., 20%) of data with signal quality too poor to be scored reliably, occurring either at the beginning or end of a segment. Epochs with poor quality segments that were either more than 10s in duration or occurred in the middle of a segment were not scored and, thus, removed.

Data Reduction of Attentional Bias Task

The raw AB data went through four initial data reduction steps following commonly used procedures (Beevers et al., 2019; Zvielli et al., 2015). First, trials for practice, buffer, and filler (NT-NT) were removed. Second, among the 144 S-N trials, inaccurate responses were removed. At the sample level, the total of 186 trials (2.58%) were removed and, at the individual level, 2.58% of trials were removed at average (M=3.72 trials, SD=12.56, *Range*=0 to 83). Third, the trials with reaction time equal to or less than 200ms and equal to or more than 1,500ms were removed. At this step, the total 130 trials (1.85%) were removed at the sample level and, at the individual level, 2.32% of trials were removed at average (M=2.60 trials, SD=6.35, *Range*=0 to 28). Lastly, trials with outlier reaction time (i.e., 3SD) were removed from each of congruent and incongruent conditions. At this final step of data reduction, the total 103 trials (1.50%)

were removed at the sample level and, at the individual level, 1.47% of data were removed at average (*M*=2.06 trials, *SD*=1.20, *Range*=0 to 4). This initial cleaning procedure led to a removal of 5.82% data at the sample level in total sample (N=50).

Computation of AB index

Following the initial data reduction, the traditional bias score and trial-level toward bias scores were computed as recommended (Rodebaugh et al., 2016; Zvielli et al., 2015). For convenience, the term 'trial-level bias score' will be used in the rest of this paper referring to the trial-level toward bias score. In order to compute the indices of AB, an R package itrak (https://github.com/ jashu/itrak, Beevers et al., 2019) was used. To compute the trial-level bias score, the "nearest" method was used as stated in Zvielli's study (Zvielli et al., 2015). The average of a series of subtracted trial-level values (i.e., incongruent trial – neighbored congruent trial) that are greater than 0ms construes the trial-level toward bias score. That is, the reaction time difference greater than 0ms reflects the propensity to allocate greater attention toward cigarette cues, as indexed by a greater response latency to incongruent conditions. The traditional bias score was computed by subtracting mean congruent trial reaction times from mean incongruent trial reaction times (MacLeod & Mathews, 1988). For each AB index, greater values reflect greater AB. In order to illustrate the difference between these two AB indices, the visual comparison between raw reaction time data and two computed AB indices is presented as an example in Appendix A (Figure 1 and 2).

Reliability was computed for each AB index following the procedures of Schmukle (2005) for the traditional bias score and Zvielli (2015) for the trial-level bias score. Specifically, the split half reliability of the traditional bias score was obtained by a correlation between the bias scores obtained from the random split trials (arbitrarily numbered even and odd trials). The reliability of the trial-level bias score was tested through the association between trial-level bias scores from the first half and the second half of the task. The reliability of the traditional bias score was very low (*Spearman's rho* = .10, *p* = ns) while the reliability of the trial-level bias score was very high (*Spearman's rho* = .83, $p < .001$). Such observed reliability is consistent with extant literature showing low reliability in the traditional bias score and high reliability in the trial-level bias scores (Beevers et al., 2019; Zvielli et al., 2015).

Data Analysis

All of the analyses were conducted utilizing packages in RStudio (RStudio Team, 2016) on R (R Core Team, 2013) with tidyverse package (Wickham et al., 2019) to facilitate processing and visualization of data. Descriptive analyses were conducted using JASP 0.9.2 (JASP Team, 2019) and Psych package (Revelle, 2018). Following normality tests of each of study variables, visual inspection of residual plots was conducted between the standardized residuals and the predicted values of study variables to ensure that the data meets normality assumption for regression models as recommended (Pituch & Stevens, 2016). Next, zero order correlations among predictor (self-report and behavioral DI measures), proposed mediators (vagal tone and flexibility), criterion variable (AB), and potential covariates (i.e., age, sex, body mass index, cigarette dependence, and negative affect after the baseline smoking) were conducted.

Next, the main study hypotheses were tested. The main study hypotheses were: (H1) Higher DI, compared to lower DI, will be associated with (H1a, path α) greater vagal dysfunction (i.e., lower vagal tone and flexibility), and (H1b, total effect) greater

AB; (H2, path β) lower vagal indices will be associated with greater AB; (H3, α * β) the relation between DI and AB will be mediated by each of two vagal indices (i.e., vagal tone and flexibility). In order to test H1 and H2, a series of regression analyses was performed by controlling for aforementioned covariates. The significance of regression coefficients in the models testing H1 and H2 (i.e., paths α 's, β 's, and total effect) does not preclude examination of the indirect effect of DI on our outcome variable as the significance of those coefficients is not a necessary condition to examine the indirect effect (Hayes, 2009). Moreover, Kenny and Judd (2013) have shown that the power to test the indirect effect (α * β) is greater than the tests of either the total effect or direct effects. Therefore, in order to test H3, a series of mediation analysis were conducted by entering vagal tone and vagal flexibility as a mediator of the indirect effect of DI (X) on AB (Y). Instead of running parallel mediation, a series of simple mediation analyses were conducted due to a limited power in the current sample as a result of the termination of further recruitment. We decided to enter each indices of DI as a predictor in the analysis models because the intra class correlation revealed heterogeneity of DI measures in the current study indicating that use of composite DI score would not be appropriate (*intra class correlation* = .02, p = ns).

The mediation analyses were carried out utilizing the Mediation package (Tingley et al., 2014) to test for direct, indirect, and total effect. Here, direct effect refers to the effect of predictor on outcome variable after controlling for the mediator. And total effect stands for the sum of direct and indirect effect (Figure 1). Regarding the determination of statistical significance of indirect and direct effect, a Quasi-Bayesian confidence interval was used, which was shown to reduce Type 1 error in small samples between 20 to 80, compared to conventional bootstrapping methods (Koopman et al., 2015). The effect size was calculated for observed trending effects using the equation (1) (Nieminen et al., 2013):

$$\text{Effect Size (ES)} = (SD_X)(\text{effect}) / (SD_Y) \quad (1)$$

, where SD_X refers to the standard deviation of independent variable, effect refers to the unstandardized regression coefficients, and SD_Y refers to the standard deviation of dependent variable. The interpretation of ES was made based on Cohen's guideline (i.e., .01 small, .09 medium, .25 large, Cohen, 1988).

Results

Participants

Demographics

Of the 50 participants recruited, a final sample of 48 participants (29.2% women (n=14); M_{age} = 33.96, SD_{age} = 7.95) was included in data analyses. Of those excluded (*n* = 2), one participant was excluded due to their body mass index being over 35 and one participant was excluded due to a medical condition deeming them ineligible. Sample characteristics are shown in Table 1. Our sample was racially and ethnically diverse, with 12.5% identifying as Hispanic/Latinx, 54.2% identifying as Caucasian, 29.2% as African American, 6.3% as Asian, 2.1% as other, 6.3% as biracial, and 2.1% unknown (Table 1).

Smoking Status and Other Tobacco/Substance Use

The sample met for moderate levels of cigarette dependence as indexed by the FTCD (*M*=5.88, *SD*=1.83, *range* 0-10; Fagerström, 2012, Table 1). The average onset of regular smoking was 18.85 years (*SD*=4.94, *range* 10-31) and the average years of regular smoking was 15.56 years (*SD*=8.21, *range* 4-35). Participants reported smoking an average of 13.92 cigarettes per day (*SD*=5.01, *range* 7.25-24.93) in the past 28 days. Other tobacco and substance use are presented in Table 2.

Manipulation Check

A manipulation check was conducted to ensure that the DI tasks (i.e., mirror tracing and breath holding) elicited significant increases in psychological and physical distress. Paired samples t-tests were conducted between pre- and post-task ratings (Table 3a and 3b). Significant differences in pre- and post-task ratings were observed, indicating the behavioral DI tasks were effective in increasing distress, although, in the breath holding task, the post-subjective unit of distress was not significantly different from the pre-rating. Next, we additionally conducted manipulation checks to ensure that the dot tracking task elicited vagal withdrawal (Table 3c). A significant difference between vagal tone and vagal withdrawal indexed by the lowest respiratory sinus arrhythmia value during the dot tracking task was observed indicating that the dot tracking task elicited significant vagal withdrawal.

Reaction Time Difference by AB task Design Within Individual

A series of paired t-tests were performed to examine the reaction time difference by the nature of AB study design (Table 4). Within individuals, a significant difference in reaction time in the intertrial interval pair was found in the incongruent condition but not in the congruent condition. These results indicate that it took a significantly longer time to disengage from an initially attended task-irrelevant stimuli (i.e., smoking cue) and then reorient to a task-relevant stimuli (i.e., target probe) in the incongruent trials when the intertrial interval was 1500ms; however, no differences between target probe location were observed in both conditions. Together, the results showed that the current AB task was valid as the reaction times were not significantly affected by the nature of AB task.

Zero Order Correlations

Table 5 displays the correlations between study variables. Sex and age were significantly associated with several study variables. Specifically, compared to females, males reported significantly greater perceived DI indexed by distress intolerance index while demonstrating lower behavioral DI indexed by persistence in the breath holding task. The traditional bias score showed a significant association with sex such that males demonstrated less AB. Next, in regard to the association between age and study variables, vagal tone was the only variable that was significantly associated with age such that lower vagal tone was observed among older participants. Finally, participants higher in perceived DI reported greater negative affect after the baseline smoking. Next, there was a significant association between DI and AB indices. Specifically, behavioral DI indexed by persistence in the mirror tracing showed a significant association with the traditional and trial-level bias scores. No significant association was observed between perceived DI and breath holding persistence, and indices of AB. Neither vagal tone or vagal flexibility was significantly associated with the indices of AB.

Mediation Results

A series of mediation models were planned for the examination of the indirect effect of DI, indexed by both behavioral indices of DI (i.e., mirror tracing and breath holding persistence) and perceived DI, on AB toward cigarette cues through vagal indices (vagal tone and vagal flexibility). Tables 6, 7, and 8 present results of the mediation analyses by each predictor with regression coefficients for paths α and β, direct effect, indirect effect, and total effect with the Quasi-Bayesian confidence intervals (CI). The regression model with the path β refers to the so-called full model with the mediator. In each mediation model, age, sex, body mass index, cigarette dependence, and state negative affect were entered as covariates.

Mediation Results with Mirror Tracing Persistence as a Predictor

In the first two models examining DI as indexed by mirror tracing persistence and the traditional bias score with vagal tone or flexibility as mediators, paths α and β were not significant in each model (Table 6a, see model fit). The coefficients of path α and path β were not significant. There was a trending relation in the path α, in an unexpected direction, in the model examining the relation between DI and vagal tone (effect size = -0.26). The direct and total effects of mirror tracing persistence on the traditional bias score were nonsignificant as was the indirect effect of mirror tracing persistence on the traditional bias score through vagal tone or flexibility (Table 6a).

The next two models examining DI as indexed by mirror tracing persistence and the trial-level bias score with vagal tone or flexibility as mediators revealed that both the regression models of path α and β were not significant (Table 6b, see model fit). The coefficients of paths α and β were not significant. There was a trending relation in the path α, in an unexpected direction, in the model examining the relation between DI and vagal tone (effect size = -0.26). In the model with vagal tone as a mediator, a significant and trend level relation for mirror tracing persistence on the trial-level bias score was found for the total and direct effects, respectively. As for the model with vagal flexibility as a mediator, significant relations for mirror tracing persistence on the trial-level bias score were found for the total and direct effects. No significant indirect effect of mirror tracing persistence on the trial-level bias score via vagal tone or flexibility was observed (Table 6b).

Mediation Results with Breath Holding Persistence as a Predictor

In the first two models examining DI as indexed by breath holding persistence and the traditional bias score with vagal tone or flexibility as mediators, both the regression models of path α and path β were not significant (Table 7, see model fit). The coefficients of path α and path β were not significant. The direct and total effects of breath holding persistence on the traditional bias score were nonsignificant nor was the indirect effect of breath holding persistence on the traditional bias score through vagal tone or flexibility (Table 7a).

The next two models examining DI as indexed by breath holding persistence and the trial-level bias score with vagal tone or flexibility as mediators revealed that both the regression models of path α and path β were not significant (Table 7b, see model fit). The coefficients of path α and path β were not significant. There was a trending relation in the path β, in an unexpected direction, in the model examining the relation between vagal tone and the trial-level bias score (effect size = 0.28). The direct and total effects of the breath holding persistence on the trial-level bias score were not significant nor was the indirect effect of the breath holding persistence on the trial-level bias score via vagal tone or flexibility (Table 7b)

Mediation Results with Distress Intolerance Index as a Predictor

In the first two models examining perceived DI as indexed by distress intolerance index and the traditional bias score with vagal tone or flexibility as mediators, neither paths α or β were significant (Table 8a, see model fit). The coefficients of paths α and β were not significant. The direct and total effect of the perceived DI on the traditional bias score were not significant nor was the indirect effect of perceived DI on the traditional bias score through vagal tone or flexibility (Table 8a).

Finally, the last two models examining perceived DI and the trial-level bias score with vagal tone or flexibility as mediators revealed that both the regression models of paths α and β were not significant (Table 8b, see model fit). The coefficients of paths α and β were not significant. There was a trending relation in the path β, in an unexpected direction, in the model examining the relation between vagal tone and the trial-level bias score (effect size = 0.28). Neither the direct or total effects were significant. No significant indirect effect of the perceived DI on the trial-level bias score via vagal tone or flexibility was observed (Table 8b).

Discussion

The current study aimed to examine the role of distress intolerance (DI) and vagal function in attentional bias (AB) toward motivationally relevant cigarette cues among daily cigarette smokers. A multi-method approach was implemented in order to examine DI in accord with documentation indicating that various indices may index different processes (Leyro et al., 2010; McHugh et al., 2011; Veilleux, 2019). The results showed that DI indexed by persistence in the mirror tracing task predicted AB toward cigarette cues indexed by the trial-level bias score, but not the traditional bias score, such that smokers who terminated the task earlier demonstrated greater AB at the trial level. This relation was not observed between other indices of DI and AB. Further, contrary to our study hypothesis, indices of DI were not associated with cardiac vagal indices and vagal indices were not associated with AB. Altogether, these results partially supported the hypothesis 1b whereas the current results did not support the hypotheses 1a, 2, and 3. There were trending relations, in an unexpected direction with large effect sizes, between greater DI indexed by mirror tracing persistence and higher vagal tone and between higher vagal tone and greater AB indexed by the trial-level bias score.

Contrary to our hypotheses neither behavioral nor self-report indices of DI were related to vagal tone or vagal flexibility and there was a trending relation between mirror tracing persistence and vagal tone in an unexpected direction. The current results were surprising given the existing evidence on the link between vagal functioning and trait- (e.g., emotion dysregulation, Williams et al., 2015) and state-level measures (e.g., performance on tasks requiring higher cognitive and emotional demand, Muhtadie et al., 2014; Thayer et al., 2009) in healthy populations. However, more recent literature has failed to document significant relations between indices of vagal function and measures of DI among individuals with substance use. For example, behavioral and self-report indices of DI were not significantly associated with a change in vagal activity in response to stressor (Paz et al., 2017) or substance cue (Vujanovic et al., 2018) which is more consistent with our null findings. More replication of null findings between DI and vagal activity would supplement current findings.

We found that DI, as indexed by mirror tracing persistence, significantly predicted one of our indices of AB. Specifically, daily smokers who persisted for a shorter period of time on the mirror tracing task took a longer time to respond to incongruent versus congruent trials as indexed by the trial-level bias score. However, persistence in the mirror tracing task was not related to our other index of AB, the traditional bias score, and no other relations between other DI indices and AB were observed. Although some prior work has examined the relations between DI and AB among daily smokers (Szasz et al., 2012) and non-clinical sample (Macatee et al., 2018), this is the first to our knowledge to provide preliminary evidence on the direct link between DI and AB toward cigarette cues among daily smokers. This is particularly important given the significant impact of ability to self-control under distress on subsequent cognitive, physiological, and behavioral outcomes (Leventhal & Zvolensky, 2015; Veilleux, 2019; Vujanovic et al., 2018). As cigarette cues become motivationally salient (Robinson et al., 2016), for smokers who are less able to persist in a distressing task, a desire to avoid distress may amplify the salience of cigarette cues, thereby, allocating increased cognitive resources to cigarette cues (i.e., AB). AB and subsequent reliance on smoking as a means to manage distress might reinforce avoidance of distress by increasing conditioned appetitive motivational state, craving.

It is notable that there was no association between other indices of DI and AB. These null findings may be consistent with extant theory and empirical work suggesting various indices appear to differ based on domain of distress indexed (Leyro et al., 2010; McHugh & Otto, 2011) and method employed (Dang et al., 2020). One explanation of our observed finding is shared measurement method (i.e., cognitive demand in this case) involved in both the mirror tracing task and AB. The current findings add to the body of literature showing that various indices of DI may reflect unique constructs, wherein perceived and physical DI may be less relevant to implicit cognitive bias to cigarette cues among daily smokers.

Another consideration regarding our null findings are questions regarding the validity of AB indices including low internal consistency (Christiansen et al., 2015; Drobes et al., 2019; Field & Cox, 2008). However, in an effort to increase the validity of our task, the current AB task implemented multiple methods (i.e., adding distractors, filler trials, and varying intertrial interval) to maximize AB toward cigarette cues (Garland et al., 2012; Szasz et al., 2012; Vujanovic et al., 2016). Further, a novel trial-level bias score with high internal consistency (i.e., reliability) was utilized to quantify AB toward cigarette cues, in addition to the traditional bias score. With the recent evidence on the temporal fluctuations of AB (Mogg et al., 2004), the novel trial-level AB indices demonstrated better reliability and association with measures of substance use (Gladwin, 2017; Zvielli et al., 2015). Consistent with the literature (Beevers et al., 2019; Zvielli et al., 2015), the trial-level bias score demonstrated superior reliability and greater association with some of the study variables in the current study. Thus, we believe that the validity of AB measure in the current study might be less likely to contribute to null findings.

No significant associations between vagal indices and AB were observed while there were a few trending associations between vagal tone and the trial-level AB score in an unexpected direction. These results were surprising as they are inconsistent with extant literature demonstrating significant associations between these variables in other populations. In accord with the neurovisceral integration model, existing evidence showed that lower vagal tone was associated with greater AB toward threat stimuli (Park et al., 2012; Ruiz-Padial et al., 2017), difficulty in attentional control (Ramírez et al., 2015), and aversive feedback (Azam et al., 2018) among healthy college students. There is a robust body of work suggesting smokers evidence lower tone and flexibility (Ashare et al., 2012; Leyro et al., 2019; Thayer et al., 2010; Tsuji et al., 1996), which may generally impede the ability to observe significant associations between study variables and vagal indices in the current study. However, this does not appear to be the case in the current investigation given that the respiratory sinus arrhythmia values in the current sample was comparable to the values among the samples from previous studies. Further, given the observed unexpected trending relations between vagal tone and the trial-level bias score, further replication of our findings is warranted in a larger sample for a better interpretation in the extant theoretical framework. In this way, our null findings in the indirect effect of DI on AB through vagal indices may be better understood.

While caution should be made in interpreting the significant relation between mirror tracing persistence and biased attentional allocation toward cigarette cues given various null findings, several clinical implications are warranted. Smokers persisting shorter in the mirror tracing task might be motivated to immediately avoid and escape from emotional distress, which may interfere with ongoing goal-directed behavior (e.g., smoking cessation, Leventhal & Zvolensky, 2015; Schlam et al., 2020; Veilleux, 2019). AB due to incentive salience of cigarette cues might be amplified by DI and, in turn, reinforce the avoidance of distress among smokers high in DI, which becomes habitual and automatic. Thus, it is possible that intervening upon an increased awareness of a propensity to avoid distress and associated attentional allocation to cigarette cues might be an avenue by which to target smoking behavior (e.g., craving, Marlatt & Gordon, 1985; reduced 7-day cigarette per day, Bowen & Marlatt, 2009; stress reactivity and recovery, Paz et al., 2017). Further, exposure and acceptance-based DI specific interventions have demonstrated decreased smoking-specific avoidance, greater abstinence rate, and higher rate of reengaging in cessation following lapse (Brown et al., 2018; Brown et al., 2013). These results indicate that smokers high in DI may benefit from such DI specific intervention through paying full attention to their implicit bias to cigarette relevant cues and craving, facilitating extinction learning (Hölzel et al., 2011; Treanor, 2011).

There are several limitations in the current study. First, the small sample size (n=48) in the current study inflates the risk of both Type I and Type II error (Vadillo et al., 2016). In order to reach .80 level of power, n of 60 was identified as adequate sample size according to the study hypotheses. However, due to unexpected termination of study recruitment, the current results with small sample size warrant caution in its interpretation as represented in the wide interval of 95% CI for point estimates (Cumming, 2014).

Second, there was no control group in the current study. Adding non-smoking or other substance use control groups would elucidate the specificity of current findings on DI and AB toward cigarette cues. Finally, participants in the current study were spontaneously breathing in a relaxed posture during the physiological data collection. Individual differences in respiratory rate might dissociate vagal tone and respiratory sinus arrhythmia (Grossman & Taylor, 2007; Shaffer & Ginsberg, 2017), indicating that the changes in respiratory sinus arrhythmia no longer reflect vagal activity. However, controlling breathing was not amenable to the current study design as the tasks were non-exercise mental task (Grossman & Taylor, 2007; Houtveen et al., 2002).

Overall, the current study provides initial evidence on the link between DI indexed by persistence in behavioral task and AB toward cigarette cues among daily smokers. To the best of our knowledge, the current investigation is the first to empirically demonstrate the less ability to withstand cognitive distress is associated with greater propensity to automatically process cigarette related stimuli. Our finding adds to the existing smoking literature on the relation between DI and implicit cognitive bias among non-deprived daily smokers. Future studies with larger sample size and DI assessed in a way reflecting contextual factors at both within- (e.g., momentary emotion regulation) and between-person level (e.g., disposition, nicotine deprivation, Roos & Witkiewitz, 2017; Veilleux, 2019) may supplement current findings. A change in vagal activity elicited by both cognitively and affectively taxing task (e.g., stress manipulation) might demonstrate a significant link to AB toward cigarette cues among daily smokers. Lastly, inclusion of other motivationally relevant stimuli with new technology such as eye tracking methods might be helpful to identify the specificity of AB toward cigarette cues compared to other drug or appetitive stimuli.

Tables

Table 1.

Sample Characteristics (*N*=48).

Descriptive summary	Study Sample *N*=48
Sex *n* (%)[a]	14 (29.2%)
Age *M (SD, range)*	33.96 (7.95,19-50)
Race *n* (%)	
Caucasian	26 (54.2%)
African American	14 (29.2%)
Asian	3 (6.3%)
Other	1 (2.1%)
Unknown	1 (2.1%)
More than one race	3 (6.3%)
Ethnicity *n* (%)	
Hispanic/Latinx	6 (12.5%)
Nonhispanic	35 (72.9%)
Unknown	7 (14.6%)
Marital Status *n* (%)	
Single	41 (85.4%)
Married	4 (8.3%)
Widowed	1 (2.1%)
Other	2 (4.2%)
Income *n* (%)	
Less than $5,000	18 (37.5%)
$5,000 through $49,000	21 (43.7%)
$50,000 through $99,000	2 (4.2%)
$100,000 and greater	2 (4.2%)
Missing	5 (10.4%)
BMI *M (SD, range)*	24.77 (3.08, 19.6-31.2)
Smoking Variables *M (SD, range)*	
Age onset of regular smoking	18.85 (4.94, 10-31)
Years of regular smoking	15.56 (8.21, 4-35)
CPD in the past 28 days	13.92 (5.01, 7.25-24.93)
Cigarette Dependence (FTCD)[b]	5.88 (1.83, 0-10)

Note. [a]Female. [b]Two participants' total scores were computed without item 3 (i.e., Which cigarette of the day would you most hate to give up) due to their incorrect responses.

CPD = Cigarette Per Day, FTCD = Fagerstrom Test for Cigarette Dependence

Table 2.

Current Other Tobacco Use and Past 28-day Alcohol and Marijuana Use

Descriptive summary	Female (n=14)	Male (n=34)	Total (N=48)
Current Other Tobacco Use[a] (n, %[1])			
Cigar	1 (7.1%)	6 (17.6%)	7 (14.6%)
Smokeless Tobacco	-	1 (2.9%)	1 (2.1%)
Pipe Tobacco	-	3 (8.8%)	3 (6.3%)
Electronic Cigarette[b]	-	4 (11.8%)	4 (8.3%)
Alcohol[c] (n, %[1])			
Any Alcohol Use	6 (42.9%)	26 (76.5%)	32 (66.7%)
Average Drinks per Drinking Day (M, *SD*)	3.00 (*1.56*)	2.82 (*1.93*)	2.85 (*1.84*)
Binge Drinking[2]	4 (28.6%)	8 (23.5%)	12 (25.0%)
Marijuana[c] (n, %[1])			
Any Marijuana Use	2 (14.3%)	5 (14.7%)	7 (14.6%)
Marijuana Use > 1 Day/Week at Average	1 (7.1%)	3 (8.8%)	4 (8.4%)

Note. [a] Assessed by Smoking History Questionnaire on the lab visit day, [b] Assessed by a separate item on past month electronic cigarette use, [c] Past 28-day use assessed by Timeline Follow Back on the lab visit day; [1] Percentage based on the indicated sample in each column; [2] 4 or more drinks/day for females and 5 or more drinks/day for males. Note that the definition of binge drinking in the current study is slightly different from its definition by National Institute on Alcohol Abuse and Alcoholism (i.e., 4 or more drinks for females and 5 or more drinks for males in about 2 hours) due to the measurement utilized in the current study.

Table 3.

Paired Sample T-Test for Manipulation Check

(a) Mirror Tracing (N=47[1])

Pairs		*M*	*SD*	*t*	*df*	*95% CI [LL, UL]*
Irritability	Pre	6.11	11.75	-6.51***	46	[-23.17, -12.23]
	Post	23.81	21.52			
Frustration	Pre	5.04	9.03	-7.09***	46	[-38.63, -21.54]
	Post	35.13	30.53			
Anxiety	Pre	12.77	19.00	-3.01**	46	[-9.94, -1.97]
	Post	18.72	21.81			
Difficulty Concentrating	Pre	6.23	10.69	-3.67***	46	[-13.01, -3.80]
	Post	14.64	19.30			
Urge to Smoke	Pre	14.06	23.32	-3.64***	46	[-15.31, -4.40]
	Post	23.91	25.55			
Bodily Discomfort	Pre	5.85	9.57	-2.25*	46	[-6.89, -0.39]
	Post	9.49	16.26			

Note. [1] Data of one participant's ratings were missing. * indicates $p < .05$. ** indicates $p < .01$. *** indicates $p < .001$. The scale of each rating is 0 – 100.

(b) Breath Holding (N=47[1])

Pairs		*M*	*SD*	*t*	*df*	*95% CI [LL, UL]*
SUDS	Pre	1.55	1.90	-1.09	46	[-0.60, 0.18]
	Post	1.77	1.84			
Physiological Sensations	Pre	1.19	1.62	-2.44*	46	[-1.11, -0.11]
	Post	1.76	2.31			

Note. [1] Data of one participant's pre-ratings were missing. * indicates $p < .05$. ** indicates $p < .01$. *** indicates $p < .001$. SUDS = Subjective Unit of Distress Scale (0 – 10)

(c) Vagal Indices (N=47[2])

Pairs		*M*	*SD*	*t*	*df*	*95% CI [LL, UL]*
Vagal Indices	Vagal Tone[3]	5.63	1.13	7.16***	46	[0.50, 0.88]
	Raw Vagal Withdrawal[4]	4.97	1.27			

Note. [2] Data of one participant's vagal withdrawal is missing due to technical difficulty encountered during data collection. [3] Average respiratory sinus arrhythmia during the 5-minute Plain Vanilla Task. [4] The raw value of the lowest sinus arrhythmia during the Dot Tracking Task. * indicates *p* < .05. ** indicates *p* < .01. *** indicates *p* < . 001. SUDS = Subjective Unit of Distress Scale (0 – 10)

Table 4.

Paired Sample T-Test for Reaction Time of AB by Intertrial Interval (ITI) and Target Probe Location (N=48)

Condition	Pair	*M*	*SD*	*t*	*df*	*95% CI [LL, UL]*
Congruent	ITI					
	500ms	512.11	108.06	-0.29	47	[-22.08, 16.51]
	1,500ms	514.89	103.11			
	Target Probe Location					
	Left	517.72	103.30	-1.40	47	[-3.72, 20.79]
	Right	509.18	101.13			
Incongruent	ITI					
	500ms	511.59	102.76	-2.94**	47	[-18.63, -3.48]
	1,500ms	522.65	101.70			
	Target Probe Location					
	Left	516.70	105.33	-0.17	47	[-11.51, 9.72]
	Right	517.59	101.91			

Note. * indicates $p < .05$. ** indicates $p < .01$. *** indicates $p < .001$.

Table 5.

Zero-Order Correlations (N=48)

Variable	1	2	3	4	5	6	7	8	9	10	11	*M*	*SD*
1. Sex												29.2%[a]	-
2. Age	.05 [-.23, .33]											33.96	7.95
3. BMI	-.21 [-.47, .08]	-.01 [-.30, .27]										24.77	3.08
4. FTCD	-.20 [-.46, .09]	-.23 [-.48, .06]	.16 [-.13, .43]									5.88	1.83
5. NA	.13 [-.16, .40]	-.19 [-.46, .10]	-.00 [-.29, .29]	.25 [-.04, .50]								5.96	1.59
6. DII	.35* [.07, .57]	-.24 [-.49, .05]	-.08 [-.36, .21]	-.02 [-.30, .27]	.34* [.05, .57]							12.81	7.91
7. BH	.39** [.12, .61]	.19 [-.09, .45]	-.17 [-.43, .12]	-.14 [-.40, .15]	.15 [-.15, .42]	.06 [-.23, .34]						53.39	27.41
8. MT	.26 [-.02, .51]	-.05 [-.33, .24]	.12 [-.17, .39]	.02 [-.26, .30]	.12 [-.18, .39]	.12 [-.17, .39]	.10 [-.19, .37]					160.49	105.52
9. VT	-.08 [-.36, .21]	-.34* [-.57, -.06]	-.02 [-.30, .27]	-.04 [-.32, .25]	-.00 [-.29, .29]	.09 [-.20, .36]	-.09 [-.36, .20]	-.19 [-.45, .10]				5.63	1.13
10. VF	-.07 [-.35, .23]	-.06 [-.34, .23]	.18 [-.11, .45]	.19 [-.11, .45]	.01 [-.28, .30]	.02 [-.27, .30]	.03 [-.26, .32]	-.17 [-.44, .12]	.06 [-.23, .35]			0.69	0.66
11. Traditional Bias Score	-.29* [-.53, -.00]	-.19 [-.45, .09]	-.04 [-.32, .25]	.22 [-.07, .47]	.05 [-.24, .33]	-.01 [-.29, .27]	-.21 [-.46, .08]	-.29* [-.53, -.00]	.08 [-.21, .36]	-.02 [-.30, .27]		3.27	20.18
12. Trial-level Bias Score	-.22 [-.47, .07]	.19 [-.10, .45]	-.12 [-.39, .17]	-.09 [-.37, .20]	-.07 [-.35, .22]	-.03 [-.32, .25]	-.18 [-.44, .11]	-.41** [-.62, -.14]	.18 [-.11, .44]	-.16 [-.43, .13]	.31* [.03, .55]	95.85	54.35

Note. [a] Female (Female was coded with 0 and male with 1). * indicates $p < .05$. ** indicates $p < .01$. Values in square brackets = 95% confidence interval. AB = attentional bias; BH = Breath Holding (duration of breath holding in seconds); BMI = Body Mass Index; DII = Distress Intolerance Index (higher score means greater distress intolerance); FTCD = Fagerstrom Test for Cigarette Dependence; HSI = Heaviness of Smoking Index; MT = Mirror Tracing (persistence in seconds); NA = Negative Affect indexed by PANAS immediately following the baseline smoking; VT = Vagal Tone; VF = Vagal Flexibility

Table 6.

Mediation Results with Mirror Tracing (MT) as a Predictor (N=48)

(a) *Mediation results using traditional bias score as a criterion*

M	Model	B	SE	*t*	*p*	CI (lower)	CI (upper)
VT	MT → Vagal Tone (α)	-0.00+	0.00	-1.75	0.09	-0.01	0.00
	Model Fit: R^2 = 0.20, *df* = 7, 41, *F* = 1.66, *p* = .16						
	Vagal Tone → Traditional Bias Score (β)	-0.38	2.96	-0.13	0.90	-6.37	5.60
	Model Fit: R^2 = 0.19, *df* = 8, 40, *F* = 1.33, *p* = .26						
	Direct Effect						
	MT → Traditional Bias Score	-0.05			0.19	-0.11	0.02
	Total Effect						
	MT → Traditional Bias Score	-0.04			0.13	-0.10	0.01
	Indirect Effect						
	MT → Vagal Tone → Traditional Bias Score	0.00			0.94	-0.03	0.03
VF	MT → Vagal Flexibility (α)	-0.00	0.00	-1.54	0.13	-0.00	0.00
	Model Fit: R^2 = 0.12, *df* = 7, 40, *F* = 0.85, *p* = .54						
	Vagal Flexibility → Traditional Bias Score (β)	-2.55	4.70	-0.54	0.59	-12.10	6.96
	Model Fit: R^2 = 0.19, *df* = 8, 39, *F* = 1.30, *p* = .28						
	Direct Effect						
	MT → Traditional Bias Score	-0.04			0.25	-0.11	0.03
	Total Effect						
	MT → Traditional Bias Score	-0.04			0.26	-0.10	0.03
	Indirect Effect						
	MT → Vagal Flexibility → Traditional Bias Score	-0.00			0.79	-0.03	0.04

(b) *Mediation results using trial-level bias score as a criterion*

M	Model	B	SE	*t*	*p*	CI (lower)	CI (upper)
VT	MT → Vagal Tone (α)	-0.00^{+}	0.00	-1.75	0.09	-0.01	0.00
	Model Fit: R^2 = 0.20, *df* = 7, 41, *F* = 1.66, *p* = .16						
	Vagal Tone → Trial-level Bias Score (β)	9.67	7.63	1.27	0.21	-5.76	25.10
	Model Fit: R^2 = 0.26, *df* = 8, 40, *F* = 1.92, *p* = .09						
	Direct Effect						
	MT → Trial-level Bias Score	-0.15			0.05	-0.31	0.00
	Total Effect						
	MT → Trial-level Bias Score	-0.18*			0.02	-0.35	-0.03
	Indirect Effect						
	MT → Vagal Tone → Trial-level Bias Score	-0.03			0.41	-0.12	0.03
VF	MT → Vagal Flexibility (α)	-0.00	0.00	-1.54	0.13	-0.00	0.00
	Model Fit: R^2 = 0.12, *df* = 7, 40, *F* = 0.85, *p* = .54						
	Vagal Flexibility → Trial-level Bias Score (β)	-18.30	12.20	-1.50	0.14	-43.00	6.37
	Model Fit: R^2 = 0.27, *df* = 8, 39, *F* = 2.00, *p* = .08						
	Direct Effect						
	MT → Trial-level Bias Score	-0.21*			0.02	-0.39	-0.03
	Total Effect						
	MT → Trial-level Bias Score	-0.18*			0.04	-0.36	-0.01
	Indirect Effect						
	MT → Vagal Flexibility → Trial-level Bias Score	0.03			0.33	-0.02	0.11

Note. Covariates entered in all models: Age, Sex (0=female, 1=male), Body Mass Index, Fagerstrom Test for Cigarette Dependence, and State Negative Affect. * indicates $p < .05$. ** indicates $p < .01$. $^{+}$ indicates a trending effect. MT = Mirror Tracing (persistence in seconds); VT = Vagal Tone; VF = Vagal Flexibility

Table 7.

Mediation Results with Breath Holding (BH) as a Predictor (N=48)

(a) *Mediation results using traditional bias score as a criterion*

M	Model	B	SE	*t*	*p*	CI (lower)	CI (upper)
VT	BH → Vagal Tone (α)	0.00	0.01	0.05	0.96	-0.01	0.01
	Model Fit: R^2 = 0.14, *df* = 7, 41, *F* = 1.07, *p* = .40						
	Vagal Tone → Traditional Bias Score (β)	0.77	2.92	0.27	0.79	-5.12	6.67
	Model Fit: R^2 = 0.16, *df* = 8, 40, *F* = 1.03, *p* = .43						
	Direct Effect BH → Traditional Bias Score	-0.07			0.48	-0.27	0.13
	Total Effect BH → Traditional Bias Score	-0.07			0.49	-0.28	0.14
	Indirect Effect BH → Vagal Tone → Traditional Bias Score	0.00			0.99	-0.06	0.06
VF	BH → Vagal Flexibility (α)	0.00	0.00	0.57	0.58	-0.01	0.01
	Model Fit: R^2 = 0.07, *df* = 7, 40, *F* = 0.48, *p* = .82						
	Vagal Flexibility → Traditional Bias Score (β)	-0.97	4.68	-0.21	0.84	-10.40	8.50
	Model Fit: R^2 = 0.16, *df* = 8, 39, *F* = 1.03, *p* = .43						
	Direct Effect BH → Traditional Bias Score	-0.04			0.69	-0.23	0.16
	Total Effect BH → Traditional Bias Score	-0.04			0.69	-0.26	0.18
	Indirect Effect BH → Vagal Flexibility → Traditional Bias Score	-0.00			0.95	-0.10	0.09

(b) *Mediation results using trial-level bias score as a criterion*

M	Model	B	SE	t	p	CI (lower)	CI (upper)
VT	BH → Vagal Tone (α)	0.00	0.01	0.05	0.96	-0.01	0.01
	Model Fit: $R^2 = 0.14$, $df = 7, 41$, $F = 1.07$, $p = .40$						
	Vagal Tone → Trial-level Bias Score (β)	13.70⁺	7.57	1.81	0.08	-1.64	29.00
	Model Fit: $R^2 = 0.21$, $df = 8, 40$, $F = 1.50$, $p = .20$						
	Direct Effect						
	BH → Trial-level Bias Score	-0.37			0.21	-0.95	0.20
	Total Effect						
	BH → Trial-level Bias Score	-0.37			0.25	-1.01	0.27
	Indirect Effect						
	BH → Vagal Tone → Trial-level Bias Score	0.00			0.99	-0.27	0.28
VF	BH → Vagal Flexibility (α)	0.00	0.00	0.57	0.58	-0.01	0.01
	Model Fit: $R^2 = 0.07$, $df = 7, 40$, $F = 0.48$, $p = .82$						
	Vagal Flexibility → Trial-level Bias Score (β)	-9.63	12.80	-0.76	0.46	-35.40	16.20
	Model Fit: $R^2 = 0.16$, $df = 8, 39$, $F = 1.03$, $p = .42$						
	Direct Effect						
	BH → Trial-level Bias Score	-0.33			0.23	-0.85	0.19
	Total Effect						
	BH → Trial-level Bias Score	-0.35			0.23	-0.95	0.21
	Indirect Effect						
	BH → Vagal Flexibility → Trial-level Bias Score	-0.03			0.81	-0.27	0.16

Note. Covariates entered in all models: Age, Sex (0=female, 1=male), Body Mass Index, Fagerstrom Test for Cigarette Dependence, and State Negative Affect. * indicates $p < .05$. ** indicates $p < .01$. $^+$ indicates a trending effect. BH = Breath Holding (duration of breath holding in seconds); VT = Vagal Tone; VF = Vagal Flexibility

Table 8.

Mediation Results with Distress Intolerance Index (DII) as a Predictor (N=48)

(a) *Mediation results using traditional bias score as a criterion*

M	Model	B	SE	*t*	*p*	CI (lower)	CI (upper)
VT	DII → Vagal Tone (α)	0.00	0.02	0.13	0.90	-0.05	0.05
	Model Fit: R^2 = 0.14, *df* = 7, 41, *F* = 1.07, *p* = .39						
	Vagal Tone → Traditional Bias Score (β)	0.74	2.92	0.25	0.80	-5.17	6.65
	Model Fit: R^2 = 0.15, *df* = 8, 40, *F* = 0.99, *p* = .45						
	Direct Effect DII → Traditional Bias Score	0.14			0.75	-0.67	1.00
	Total Effect DII → Traditional Bias Score	0.15			0.75	-0.70	1.00
	Indirect Effect DII → Vagal Tone → Traditional Bias Score	0.00			0.98	-0.18	0.19
VF	DII → Vagal Flexibility (α)	0.01	0.02	0.31	0.76	-0.03	0.04
	Model Fit: R^2 = 0.06, *df* = 7, 40, *F* = 0.44, *p* = .85						
	Vagal Flexibility → Traditional Bias Score (β)	-1.16	4.66	-0.25	0.80	-10.60	8.28
	Model Fit: R^2 = 0.16, *df* = 8, 39, *F* = 1.03, *p* = .43						
	Direct Effect DII → Traditional Bias Score	0.12			0.79	-0.74	1.03
	Total Effect DII → Traditional Bias Score	0.12			0.81	-0.77	1.01
	Indirect Effect DII → Vagal Flexibility → Traditional Bias Score	-0.01			0.96	-0.26	0.24

(b) *Mediation results using trial-level bias score as a criterion*

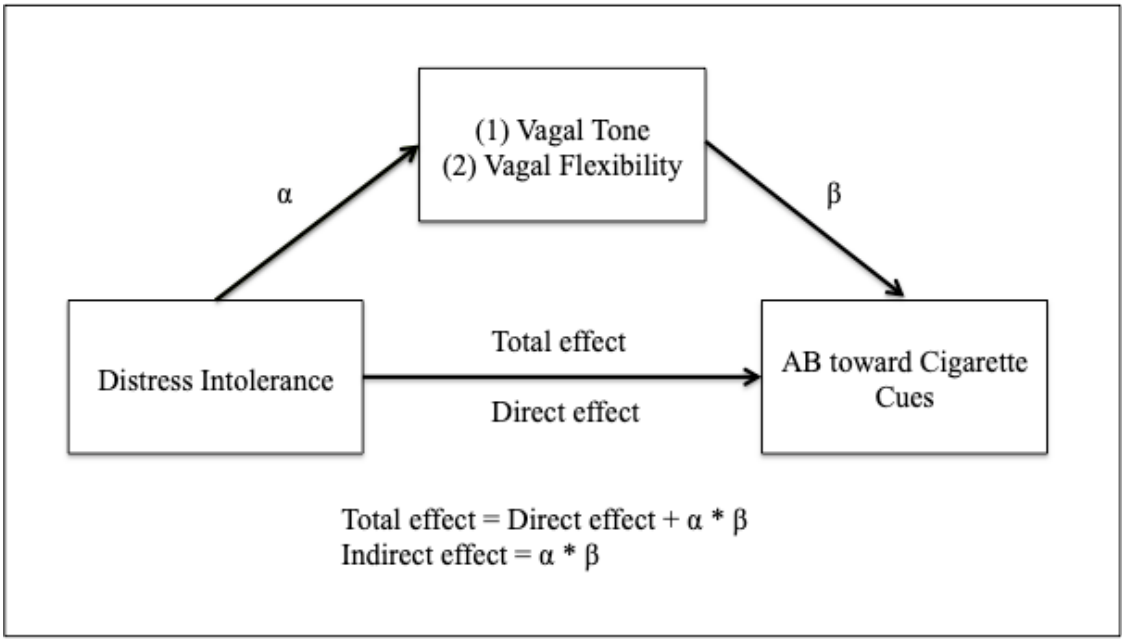
M	Model	B	SE	*t*	*p*	CI (lower)	CI (upper)
VT	DII → Vagal Tone (α)	0.00	0.02	0.13	0.90	-0.05	0.05
	Model Fit: R^2 = 0.14, *df* = 7, 41, *F* = 1.07, *p* = .39						
	Vagal Tone → Trial-level Bias Score (β)	13.50^{+}	7.66	1.76	0.09	-1.99	29.00
	Model Fit: R^2 = 0.20, *df* = 8, 40, *F* = 1.35, *p* = .26						
	Direct Effect						
	DII → Trial-level Bias Score	0.77			0.58	-2.01	3.59
	Total Effect						
	DII → Trial-level Bias Score	0.81			0.57	-2.02	3.73
	Indirect Effect						
	DII → Vagal Tone → Trial-level Bias Score	0.04			0.92	-0.78	0.90
VF	DII → Vagal Flexibility (α)	0.01	0.02	0.31	0.76	-0.03	0.04
	Model Fit: R^2 = 0.06, *df* = 7, 40, *F* = .44, *p* = .85						
	Vagal Flexibility → Trial-level Bias Score (β)	-11.20	12.80	-0.88	0.39	-37.10	14.70
	Model Fit: R^2 = 0.15, *df* = 8, 39, *F* = .97, *p* = .47						
	Direct Effect						
	DII → Trial-level Bias Score	0.83			0.59	-2.08	3.81
	Total Effect						
	DII → Trial-level Bias Score (c)	0.78			0.62	-2.17	3.78
	Indirect Effect						
	DII → Vagal Flexibility → Trial-level Bias Score	-0.05			0.86	-0.73	0.51

Note. Covariates entered in all models: Age, Sex (0=female, 1=male), Body Mass Index, Fagerstrom Test for Cigarette Dependence, and State Negative Affect. * indicates $p <$ .05. ** indicates $p < .01$. $^{+}$ indicates a trending effect. DII = Distress Intolerance Index (higher score means greater distress intolerance); VT = Vagal Tone; VF = Vagal Flexibility

Figures

Figure 1.

Study Model



Note. AB = Attentional Bias.

Figure 2.

Study Flow

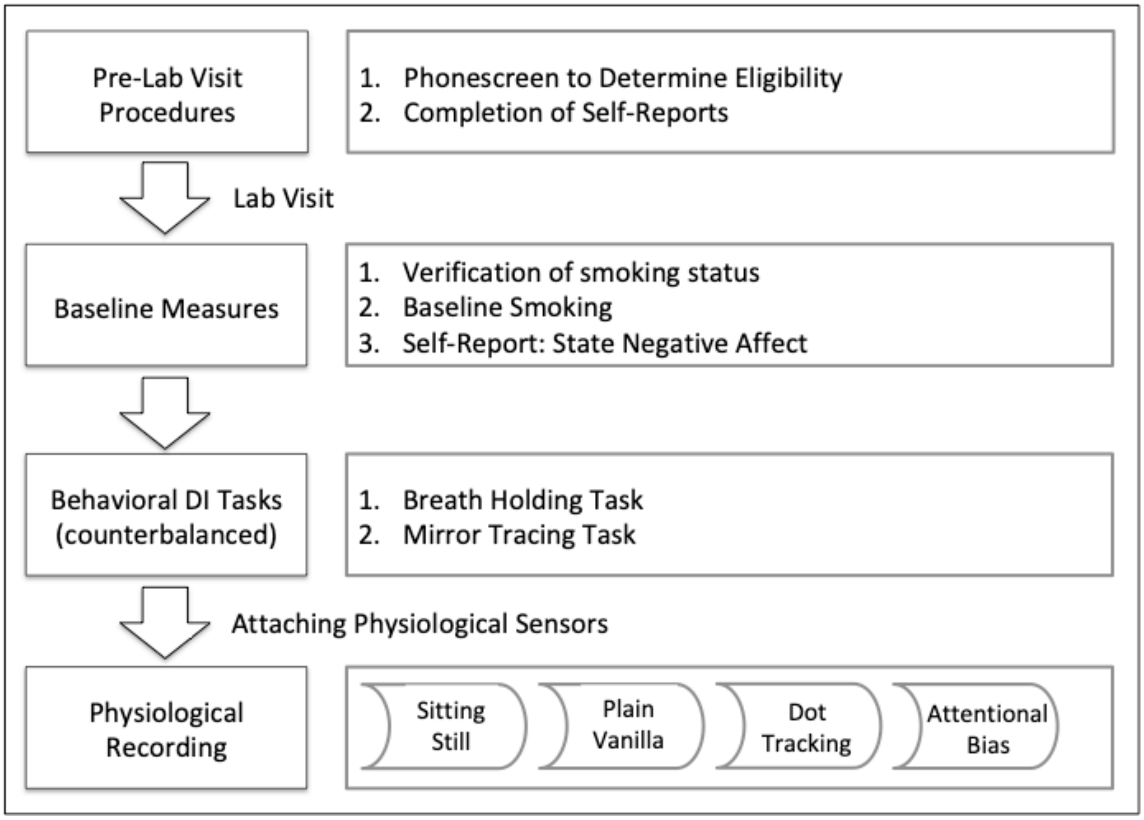
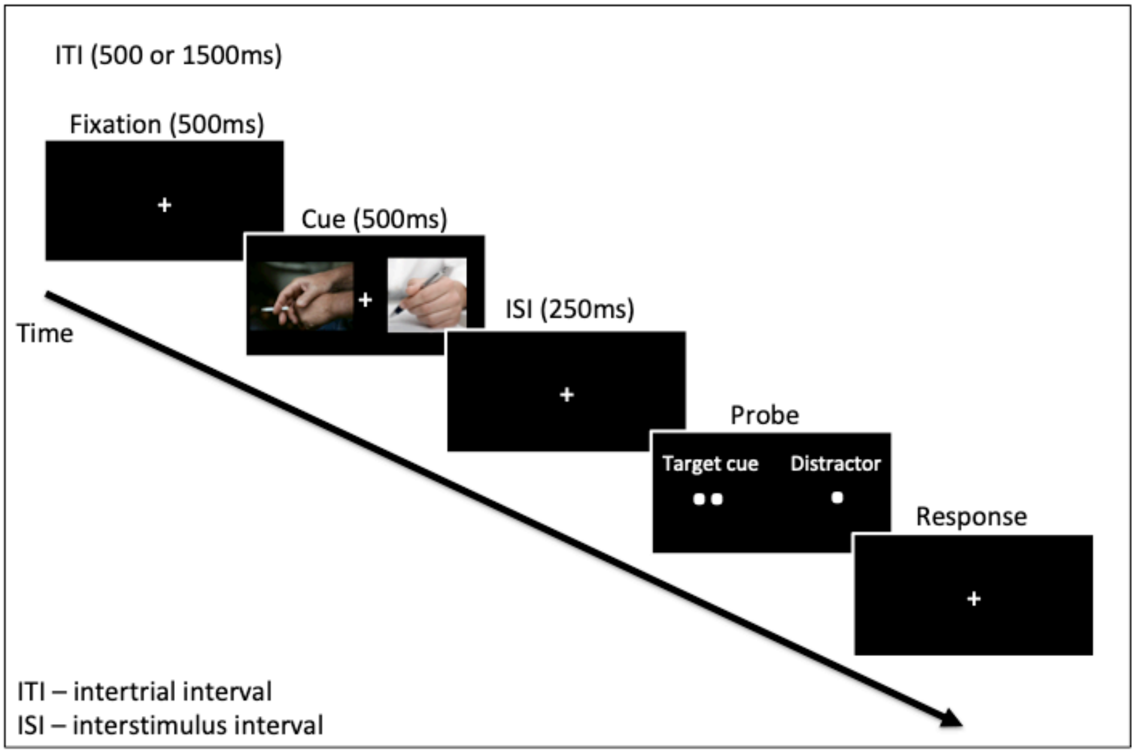


Figure 3.

Schematic Presentation of Experimental Session in Attentional Bias Task



Appendix A

Description of Stimuli in the AB Task

AB Stimuli

There were three pools of pictorial stimuli used in the AB task. First, a pool of 36 pairs of smoking and non-smoking pictures (S-N pairs) was used and presented randomly: Smoking pictures (e.g., individuals or a group of people either smoking or holding a cigarette) paired with non-smoking neutral pictures (e.g., individuals or a group of people holding non-smoking related objects). While the presentation of the pool repeated 4 times in the AB task, the orientation of the stimuli was controlled as either right (presented 2 times) or left orientation (presented 2 times). Second, a pool of 10 pairs of neutral pictures was used for the filler trials (NT-NT pairs), which was designed to keep smoking pictures (S-N pairs) from presenting every trial (Frankland et al., 2016). Five pairs were randomly drawn at each cycle. Lastly, another pool of 10 pairs of neutral pictures was used for the practice and buffer trials, which were randomly drawn for each of practice and buffer trials.

Stimuli Selection

Smoking and matched non-smoking pictures were selected from the International Smoking Image Series (ISIS, Gilbert & Rabinovich, 1999). The ISIS provides a library of smoking and non-smoking neutral pictures (e.g., holding non-smoking objects) based on the ISIS ratings of interest, valence, arousal, and urge to smoke. Smoking pictures that were rated higher than mean urge and interest provided in the ISIS manual were selected. Matched non-smoking pictures were selected by the contents of the smoking pictures in order to pair up with smoking pictures. Each pair of smoking and non-smoking pictures was matched with gender, contents (e.g., a group of people, body part), color, and orientation (e.g., a smoker looking at the right direction). Next, neutral pictures for the filler and practice/buffer trials were selected from the International Affective Picture System (IAPS, Lang et al., 2008). IAPS neutral pictures with moderate valence and low arousal were selected.

Table 1.

Neutral Stimuli Used In Attention Bias Task

(a) Stimuli for the Practice and Buffer Trials

Pair Number	Image Category	Image Number (IAPS)		Valence[1] M (*SD*)	Arousal[2] M (*SD*)
1	Household	7034	7056	4.97 (*0.38*)	3.07 (*0.12*)
2	Person	2381	9210		
3	Person	2850	2870		
4	Person	2102	2104		
5	Person	2210	2221		
6	Household	2980	7038		
7	Person/Abstract	2499	7160		
8	Nature	5120	5500		
9	Household	7003	7009		
10	Household	7052	7055		

(b) Stimuli for the Filler Trials (10 NT-NT Pairs)

Pair Number	Image Category	Image Number (IAPS)		Valence[1] M (*SD*)	Arousal[2] M (*SD*)
1	Nature	5390	5740	5.02 (*0.31*)	2.67 (*0.30*)
2	Nature	5520	5530		
3	Household	7012	7026		
4	Household	7025	7235		
5	Household	7030	7050		
6	Household	7490	7950		
7	Household	7224	7705		
8	Household	7053	7059		
9	Household	7006	7233		
10	Household	7150	7175		

Note. [1] IAPS ratings scored 1-9, where 1 being low pleasure (negative valence) and 9 being high pleasure (positive valence), [2] IAPS ratings scored 1-9, where 1 being low arousal and 9 being high arousal. IAPS = International Affective Picture System (Lang et al., 2008)

Table 2.

Smoking Stimuli and Matched Non-Smoking Stimuli (36 S-N Pairs)

(a) List of Stimuli

Pair Number	Image Category	Image Number (ISIS)	
		Smoking (S)	Non-Smoking (N)
1	Face	Sisis002	Bisis062
2	Face	Sisis011	Bisis054
3	Face	Sisis012	Bisis060
4	Face	Sisis015	Bisis001
5	Face	Sisis016	Bisis018
6	Face	Sisis017	Bisis015
7	Body	Sisis018	Bisis008
8	Body	Sisis020	Bisis034
9	Body	Sisis021	Bisis036
10	Face	Sisis022	Bisis058
11	Body	Sisis024	Bisis053
12	Face	Sisis028	Bisis061
13	People	Sisis029	Bisis002
14	Face	Sisis030	Bisis059
15	Face	Sisis031	Bisis016
16	People	Sisis032	Bisis003
17	Body	Sisis034	Bisis019
18	Body	Sisis035	Bisis010
19	Body	Sisis039	Bisis055
20	Face	Sisis041	Bisis065
21	Face	Sisis042	Bisis051
22	Body	Sisis043	Bisis039
23	Body	Sisis049	Bisis057
24	Face	Sisis051	Bisis063
25	Face	Sisis053	Bisis052
26	Face	Sisis056	Bisis048
27	Body	Sisis059	Bisis056
28	Body	Sisis060	Bisis009
29	Face	Sisis061	Bisis067
30	Face	Sisis062	Bisis017
31	Face	Sisis063	Bisis064
32	Face	Sisis067	Bisis066
33	People	Sisis076	Bisis044
34	Face	Sisis081	Bisis049
35	Face	Sisis082	Bisis050
36	Body	Sisis088	Bisis020

(b) Descriptives of Ratings

Interest[2] M (*SD*)		Valence[1] M (*SD*)		Arousal[1] M (*SD*)		Smoking Urge[2] M (*SD*)	
Smoking	Non-Smoking	Smoking	Non-Smoking	Smoking	Non-Smoking	Smoking	Non-Smoking
3.85 (*0.44*)	2.08 (*0.32*)	5.42 (*0.31*)	5.10 (*0.32*)	3.80 (*0.32*)	2.46 (*0.16*)	5.32 (*0.44*)	2.10 (*0.20*)

Note. [1] ISIS ratings among all smokers, adopted from IAPS ratings system, [2] ISIS ratings among all smokers scored 1-10, where 1 being no interest/no urge to smoke at all and 10 being high level of interest/the strongest urge to smoke. ISIS = International Smoking Image Series (Gilbert & Rabinovich, 1999).

Figure 1.

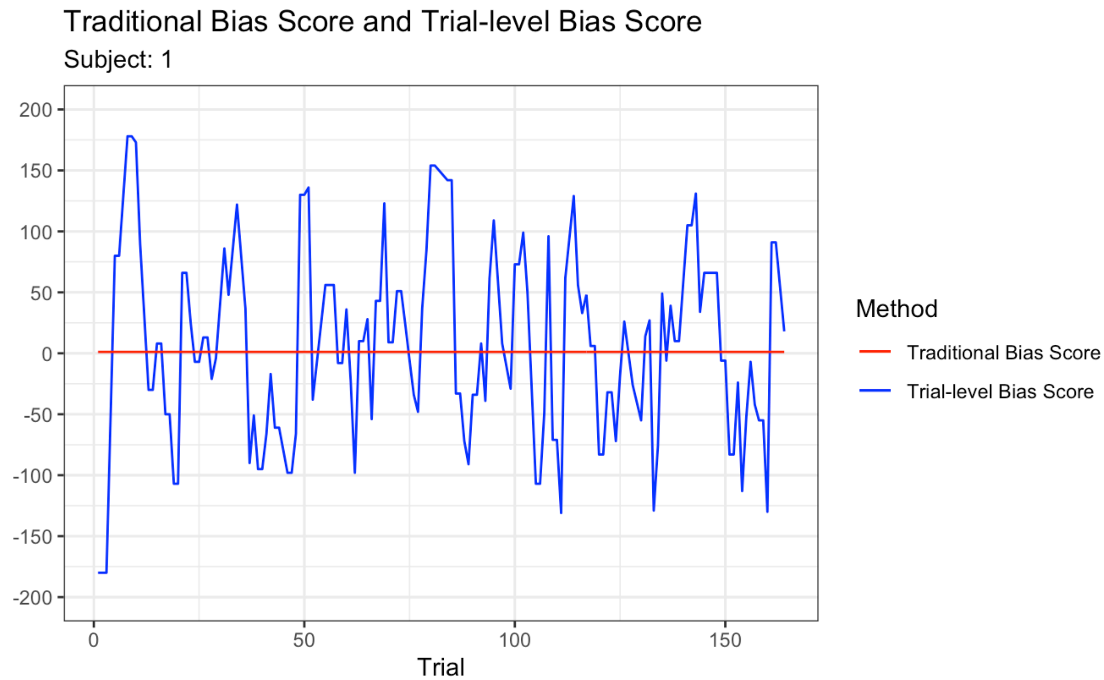
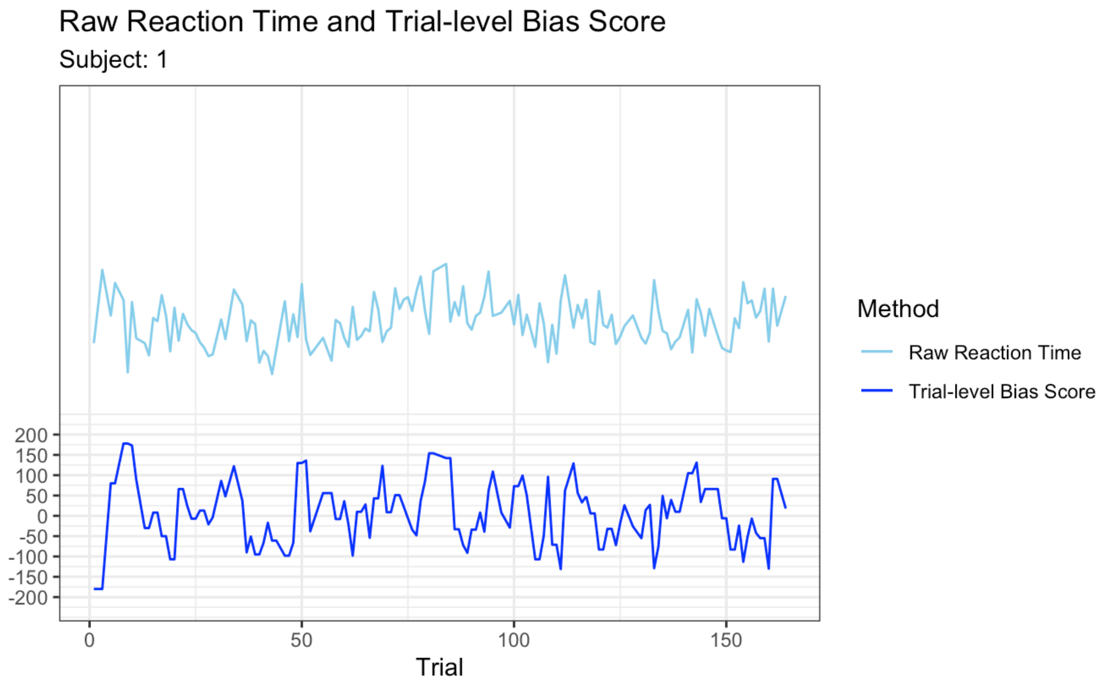

Traditional Bias Score and Trial-level Bias Score
Subject: 1
200
150
100
50
0
-50
-100
-150
-200
0
50
100
150
Trial
Method
Traditional Bias Score
Trial-level Bias Score

Figure 2.


Raw Reaction Time and Trial-level Bias Score
Subject: 1
200
150
100
50
0
-50
-100
-150
-200
0
50
100
150
Trial
Method
Raw Reaction Time
Trial-level Bias Score

Acknowledgment of Previous Publications

None

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