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Journal

Applied Psychophysiology and Biofeedback, 48(2)

ISSN

1090-0586

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Publication Date

2023-06-01

DOI

10.1007/s10484-023-09580-8

Applied Psychophysiology and Biofeedback
https://doi.org/10.1007/s10484-023-09580-8

Cardiac Vagal Control Among Community Cigarette Smokers with Low to Moderate Depressive Symptoms

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Accepted: 22 January 2023

Abstract
Impairments in cardiac vagal control (CVC) have been independently linked to smoking status and depression and are implicated in self-regulatory processes that may exacerbate depressive symptoms and maintain smoking behavior. Yet, few studies have examined how depressive symptoms, even at low levels, influence CVC reactivity among individuals who smoke. Investigating these relationships may provide novel insights into how depressive symptoms exacerbate existing regulatory vulnerabilities among smokers. This study investigated how depression symptoms affect CVC reactivity as a function of changing situational demands among a community sample of 60 daily adult cigarette smokers. Participants completed a mildly demanding cognitive task while physiological data was recorded. Growth curve modeling was used to examine the main and interactive effects of self-reported depressive symptoms on CVC reactivity over the course of the task. We hypothesized that greater depressive symptoms would be associated with less CVC reactivity, characterized by smaller initial reductions in CVC values and a flatter slope over time. Participants were daily smokers with mild to moderate levels of depression. Final model results, where time was specified as linear and the slope was fixed, showed no significant main or interactive effects of time and depression symptoms on CVC reactivity. Findings suggest that at low to moderate levels, depressive symptom severity is not related to patterns of CVC reactivity among adults who smoke. This is the first study to examine this relationship in this population. Future investigations that examine patterns of CVC reactivity among smokers and non-smokers with more severe depression are needed.

Keywords Cigarette use · Depression · Autonomic regulation · Smoking · Comorbidity

Introduction

Despite declining rates of tobacco use among the general U.S. population, cigarette use remains high among individuals with mental health conditions (Smith et al., 2014). Reducing cigarette use among individuals with co-occurring depression is a particular public health concern given the high prevalence of clinical and sub-clinical depressive symptoms among smokers (Leventhal et al., 2009; Stubbs et al., 2018; Weinberger et al., 2017). Cigarette use and depression symptomatology also appear to exert a bidirectional influence on one another that further complicates their comorbidity (Mathew et al., 2017). Daily cigarette use is associated with an increased risk of the onset and persistence of major depressive disorder (Bakhshaie et al., 2015) and depression severity is associated with greater likelihood of cigarette use and reduced cessation success (Weinberger et al., 2017). However, this relation is not unique to samples meeting diagnostic threshold for major depressive disorder. For example, community smokers with depressive symptoms are more likely to endorse lower self-efficacy in quitting and experience greater quit failure compared to smokers without depressive symptoms (Petroulia et al., 2018). One step toward reducing cigarette use among this population is characterizing how depressive symptoms, even at low levels, may exacerbate existing vulnerabilities that promote smoking behavior and compromise cessation success.

Extensive review articles have documented the adverse effects of nicotine use and cigarette smoke on autonomic nervous system (ANS) functioning including elevated sympathetic activity, reduced parasympathetic activity, and

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Published online: 03 February 2023

overall reduced heart rate variability (Dinas et al., 2013; Middlekauff et al., 2014). These adverse effects appear to result from changes in neural cardiovascular regulation via either the adrenergic effects of nicotine (Cryer et al., 1976; Karakaya et al., 2007; Trap-Jensen et al., 1979) or chronic exposure to particulate matter via smoking (Pope et al., 2002; Stone & Godleski, 1999). Although ongoing work is needed to refine the mechanistic pathways through which smoking leads to ANS impairment, extant work suggests both processes may be at play (Dinas et al., 2013). For example, ANS function appears to incrementally improve upon smoking cessation and initiation of nicotine replacement therapy, as well as upon nicotine replacement termination (Dinas et al., 2013; Middlekauff et al., 2014). The longest follow up period to date, shows consistent ANS improvements at 12-weeks post-cessation (Harte & Meston, 2014). However, whether a full recovery of ANS functioning occurs beyond this timeframe has yet to be explored.

One index of ANS function is cardiac vagal control (CVC). CVC can be measured via heart rate variability in the high frequency range (Berntson et al., 1997; Malik et al., 1996; Pumprla et al., 2002; Shaffer & Ginsberg, 2017), and is thought to reflect the parasympathetic nervous system's predominantly inhibitory influence on the electrical activity of the heart via the vagus nerve (Beauchaine, 2001; Porges, 1995). Having greater CVC is optimal, as it reflects the ANS's ability to *flexibly* shift from rest and arousal states largely produced by the parasympathetic and sympathetic nervous system branches, respectively (Berntson et al., 1993). Greater CVC (i.e., autonomic flexibility) is thought to promote adaptability to changing environmental demands (Porges, 1995) and is associated with higher-order brain functions involved in self-regulation, such as attention regulation and affective information processing (Thayer & Lane, 2000; Thayer et al., 2009). In contrast, reduced autonomic flexibility is associated with forms of diminished self-regulation, such as increased ruminative thinking (Geisler & Kubiak, 2009) and greater difficulty regulating negative emotions (Pu et al., 2010). The ability to successfully quit smoking has also been linked to a myriad of cognitive and emotional self-regulatory processes, including but not limited to, greater distress tolerance, emotion regulation, and task persistence (Brown et al., 2009; Rogers et al., 2018; Szasz et al., 2012). These processes require access to higher-order brain regions (Faulkner et al., 2020) and in turn a well-functioning ANS (Thayer et al., 2009). From this perspective, smoking-related impairments in CVC may correspond with other self-regulatory deficits that directly interfere with one's ability to successfully quit.

Separate work has shown that depression and its symptoms, independent of cigarette use, is also linked to elevated heart rate and reduced parasympathetic activity at rest (Jung et al., 2019). Among individuals with clinically significant depression, depression severity is associated with significantly lower CVC (Agelink et al., 2002; Kemp et al., 2010; Koch et al., 2019). However, studies have also shown that even mild mood disturbances are associated with impaired autonomic activity among various non-clinical samples (Chen et al., 2010; Kogan et al., 2013; Moretta & Messerotti Benvenuti, 2022). For example, among a community sample of elderly male adults, mild depressive symptoms were associated with poor CVC and elevated sympathetic activity (Chen et al., 2010). Separate work among young adults with minimal to low depressive symptoms with familial risk for major depressive disorder also exhibited lower levels of CVC at rest compared to controls with no family history (Moretta & Messerotti Benvenuti, 2022). Such findings highlight the role of other risk factors for depression that may contribute to impairments in autonomic activity even among relatively asymptomatic individuals. Collectively, this work suggests that even low levels of depressive symptoms, and pre-existing risk factors for depression, may contribute to impaired autonomic function. Understanding these relations among smokers with sub-clinical depressive symptoms is further warranted given sub-threshold symptoms can be more prevalent than disorders meeting full diagnostic criteria (Angst et al., 1997) and the presence of sub-threshold symptoms preceding full disorder development later in life (Shankman et al., 2009). Research in this vein also aligns with the missions put forth by widely accepted clinical research frameworks such as RDoC and HiTOP (Insel et al., 2010; Kotov et al., 2017).

Together, the combination of cigarette smoking and depressive symptoms may have a unique negative impact on autonomic function. This may contribute to smokers with depression experiencing greater difficulty quitting via associated self-regulatory impairments central to cessation (Ashare et al., 2012; Mathew et al., 2017). However, evidence for this perspective is limited, given most investigations of CVC in the context of depressive symptoms control for smoking status or exclude individuals who smoke. To our knowledge only one study to date has explicitly sought to clarify the effects of depression and smoking on autonomic function; Harte et al. (2013) found that smokers with major depressive disorder, compared to non-smokers with major depressive disorder, exhibited significantly lower levels of CVC at rest. However, this study did not address the extent to which depressive symptoms is associated with worse autonomic functioning *within* daily cigarette smokers. Moreover, whether depressive symptoms, even at low levels, are associated with in vivo changes in smoker CVC reactivity also remains unclear. Given the high comorbidity between cigarette use and depression symptomatology, as well as evidence for autonomic impairments in both populations, further work is needed to clarify the effects of depressive symptoms on CVC among individuals who smoke.

This study sought to investigate how depressive symptoms affect autonomic flexibility as a function of changing situational demands among a non-clinical community sample of adults who smoke cigarettes daily. Given that autonomic activity is a dynamic (Brooker & Buss, 2010; Miller et al., 2013) rather than a static physiological process, we chose to use growth curve modeling techniques to examine changes in CVC values over the course of a 5-min task. This has the benefit of identifying nuanced effects that depressive symptoms may have on CVC over time that linear models may not detect (Brooker & Buss, 2010). We hypothesized that greater depressive symptoms would be associated with less autonomic flexibility, characterized by smaller initial reductions in CVC values in response to the task, and a flatter slope over time. This is informed by theoretical models suggesting that greater initial vagal withdrawal (i.e., greater CVC) in response to environmental demands reflects greater adaptability and autonomic flexibility (Thayer & Lane, 2000; Thayer et al., 2009). This is also based on empirical work demonstrating the independent and combined effects of smoking and depression symptoms on autonomic function (Agelink et al., 2002; Chen et al., 2010; Dinas et al., 2013; Harte et al., 2013). To our knowledge no studies to date have used growth curve modeling to examine patterns of autonomic activity in adults who smoke cigarettes daily.

Method

Participants

Participants were recruited from the local New Brunswick, New Jersey area via online and community-posted advertisements. Inclusion criteria included being (1) 21–50 years old, (2) smoking at least ten cigarettes per day, (3) computer proficient, and 4) fluent in English. Exclusion criteria included (1) history or presence of bipolar spectrum or psychotic spectrum disorders, (2) current suicidal or homicidal ideation, (3) evidence of current (non-nicotine) substance use disorder, or (4) reported use of a pharmacological aid for smoking cessation and/or active attempts to reduce cigarette use in the past month. Individuals with visual, hearing, or cognitive impairments that would interfere with study participation or provision of informed consent were also excluded, as were those with medical conditions or medications that might increase risk of stress exposure or confound autonomic nervous system reactivity. Our final sample included 60 adults (36.7% female) between the ages of 24–50 (M = 34.43, SD = 7.14) who smoked an average of 14.04 cigarettes daily (SD = 5.00). Participants reported an average BMI of 25.69 (SD = 3.70) and identified as 42.9% White, 37.5% Black or African American, 5.4% Asian, and 14.3% as Other or More than one race.

Procedure

The data reported in this paper were collected as part of a larger study funded by the National Institute on Drug Abuse [R03 DA041556-01A1] examining stress, physiological activity, and subjective and objective smoking factors among daily cigarette smokers. Participants completed an initial screening questionnaire via telephone and eligible participants were scheduled for a single laboratory visit. Prior to the study visit, participants were asked to complete an online battery of self-report questionnaires and asked to refrain from engaging in behavioral activities that might impair physiological activity (i.e., alcohol/substance use for at least 12 h, vigorous physical activity for at least 2 h, etc.).

At the start of the lab visit, participants completed informed consent procedures, a brief interview to confirm eligibility criteria, and a carbon monoxide (CO) breath analysis to verify smoking status (CO > 8 ppm; Javors et al., 2005). Participants were then asked to smoke a cigarette to standardize baseline craving and control for variability in nicotine withdrawal. Participants were then hooked up to the physiological recording equipment and instructed to sit upright in a comfortable chair in front of a computer screen. Participants completed a 5-min (minutes 1–5) baseline physiological recording period during which resting baseline physiological activity was recorded while participants engaged in a low demand cognitive task designed to standardized mental activity (Jennings et al., 1992). Specifically, participants were instructed to look at the computer as a series of different colored rectangles sequentially presented on the screen. The color of the rectangle changed every 10 s (Jennings et al., 1992).

Following baseline, participants completed a 5-min (minutes 6–10) computerized dot-tracking task used previously to examine vagal withdrawal (Muhtadie et al., 2015) and adapted from (Alvarez & Franconeri, 2007). Developed as a visual attention task, dot-tracking requires participants to focus on a cross in the middle of the computer screen as they keep track of moving dots in their peripheral vision. Participants are asked to keep track of a set of yellow dots as they move amongst a larger set of black dots about the screen. After a few seconds, the yellow dots transition to black, blending with the other dots and thereby making them difficult to track. At the end of each trial all dots stop moving and participants use the mouse to identify the initially yellow dots. Participants completed 16 trials of the task, with each trial lasting 14 s, and the number of initially yellow dots to track increasing every 4 trials.

Additional laboratory tasks participants completed as part of the parent study include: a laboratory stress provocation, measures of mood, craving, nicotine withdrawal, and behavioral, biobehavioral, and self-report measures of smoking motivation and reward. The 5-min baseline physiological

recording and 5-min dot-tracking computer task occurred prior to the laboratory stress provocation. This order of study procedures allowed us to examine autonomic measures of interest in the current report without the confounding influence of the stress provocation. To control for time of day, all in-person lab visits were scheduled so that the physiological recordings did not occur until after 12:00 pm. This strategized scheduling was done in attempt to avoid interference due to cortisol awakening response as another component of the parent study involved collection of salivary cortisol samples. In addition, participants were queried at the start of the lab visit, via brief interview, about their past night sleep to ensure they kept to a typical sleep/wake cycle prior to their study visit. At the end of the visit, participants were debriefed and compensated $80. All study procedures were reviewed and approved by the Rutgers University Institutional Review Board.

Measures

Demographics and Smoking Variables

Demographics, including age, biological sex, and body mass index (BMI), were assessed using an author-constructed questionnaire. The Timeline Followback (TLFB) Questionnaire assessed daily cigarette use over the past 28 days (Robinson et al., 2014) and the Fagerström Test for Cigarette Dependence (FTCD) assessed cigarette dependence (Fagerstrom, 2012). The FTCD is a 6-item measure used to quantify cigarette consumption, compulsion to use, and nicotine dependence. The scale includes yes/no items (scored as 1 or 0) and multiple-choice items (scored from 0 to 3). Item scores are summed to give a total score from 0 to 10 with higher scores indicative of greater dependence (Fagerstrom, 2012; Heatherton et al., 1991). In the current investigation, internal consistency for the FTCD scale was $\alpha = 0.31$. The low value observed here is consistent with previous reports for this measure (Etter et al., 1999).

Depression Symptoms

The Inventory of Depression and Anxiety Symptoms (IDAS)—General Depression (IDAS-Dep) subscale was used to compute a depression symptom severity score. The IDAS itself is a 64-item questionnaire designed to assess symptom dimensions of major depression and anxiety disorders in the past two weeks (Watson et al., 2007). The GD subscale is one of two broader subscales within the IDAS that includes 20 items sampled from the seven depressive symptom scales, including lassitude, insomnia, suicidality, appetite loss, appetite gain, ill-temper, and well-being. Items are rated from 1 (Not at all) to 5 (Extremely) and added together to create a GD total sum scale score. The IDAS is a well-validated measure that has demonstrated strong internal consistency and validity across clinical and non-clinical populations (Stasik-O'Brien et al., 2019; Watson et al., 2007, 2008). In the current investigation, the internal consistency for the IDAS-Dep subscale was $\alpha = 0.91$.

Physiological Measures

Electrocardiograph (ECG) data were scored offline in one-minute epochs using Mindware software version 3.1.12 (Mindware Technologies, LTD) and in accordance with standard guidelines (Task Force of the European Society of Cardiology; Malik et al., 1996). Z0 readings from Impedance Cardiography (ICG) data were used to estimate respiration and a R-peak identifying algorithm was used to identify inter-beat interval from ECG data. R-peak detection was based on a low pass filter setting of 0.003 Hz and a high pass filter of 0.42. Data were linearly detrended and a baseline and muscle noise filter were used for signals between 0.25 and 0.40 Hz. Trained research assistants visually inspected the data for additional cleaning, including removal of misplaced R-peaks and insertion of missing R-peaks, with no more than one R-peak estimated within a one-minute segment. We allowed for the removal of up to 15 s of poor-quality data at the beginning or end of a minute-long segment. Insertion of R-peaks was based on estimation from remaining data, RR interval distance from measured and cleaned ECG recording, or by dividing long R-peaks into equal intervals. CVC was measured using heart rate variability data in the high frequency range (HF-HRV) and defined as the natural log of the variance occurring between 0.12 and 0.40 Hz. This frequency band is the default setting in Mindware (Mindware Technologies, LTD, Gahanna, OH), and corresponds with respiratory sinus arrythmia, a reliable, non-invasive index of parasympathetic control of cardiac function (Berntson et al., 1993). Meta-analytic reviews of depression and CVC have identified both frequency (i.e., HF-HRV) and time domain metrics (i.e., RMSSD) as reliable indices for measuring depression-related reductions in CVC (Kemp et al., 2010; Koch et al., 2019). However, unlike HF-HRV, RMSSD is susceptible to positive skewness and requires log transformation, resulting in less precision in the lower and upper tails (Shaffer & Ginsberg, 2017). In addition to HF-HRV having stronger psychometric properties, limited experimental work has examined the relation between CVC measures and clinically relevant smoking outcomes. To our knowledge only one study among non-depressed smokers has examined this relation with HF-HRV as the chosen metric (Ashare et al., 2012). Given this is the first study to examine the effect of depressive symptoms within a smoking sample, we choose to use HF-HRV as our index for CVC as it might allow us to draw more meaningful comparisons to existing experimental work among individuals who smoke.

CVC at rest was indexed as the average CVC value during the 5-min baseline recording. CVC reactivity was indexed using CVC values during the 5-min dot-tracking task. Based on available data from other samples of smokers and non-smokers with and without depressive symptoms, we expected our CVC values to fall within the range of 4.30–6.69 ms^2 (Ashare et al., 2012; Harte et al., 2013; Kogan et al., 2013; Min et al., 2009).

Candidate covariates were selected based on their correlation with the average CVC value for the dot-tracking task. Individual CVC values for each minute of the task were used to examine transient changes in autonomic reactivity using growth curve modeling techniques (see Analytic Strategy). As a mentally demanding task, dot-tracking is an ideal manipulation for examining changes in CVC as a function of cognitive effort and attentional demand, as it reliably induces vagal withdrawal, but does not include any social or emotional cues (Hagan et al., 2017; Human & Mendes, 2018).

Analytic Strategy

General Approach

Sample descriptive characteristics were first examined including data distributions and identification of extreme values. Potential outliers were revisited to ensure validity and z-tests were used to assess skew and kurtosis for non-normally distributed data to be considered for transformation. For medium-sized samples ($50 < n < 300$) the null hypothesis, assuming a normal distribution, is rejected at absolute z-values over 3.29, corresponding with an alpha level of 0.05 (Kim, 2013). Calculated skew and kurtosis z-values showed no significant outliers and each variable's distribution was approximately normal (all $zs < 3.29$). Thus, all data were retained for analyses. Age, sex, cigarettes per day (CPD), body mass index (BMI), respiration rate, and average CVC at rest were selected as candidate covariates based on previous work showing their empirical relationship with autonomic function (Laborde et al., 2017; Shaffer & Ginsberg, 2017). Zero-order bivariate associations between theoretically relevant covariates, predictor, and criterion variables of interest were then assessed. Pearson's correlations were conducted for continuous variables and independent t-tests were conducted for categorical variables. Variables with significant differences between groups at $p < 0.05$ or significant correlations at $r \geq 0.20$ were included as model covariates (Cohen, 1988, 1992). Final model covariates included age, sex, and average CVC at rest (See Table 1 for sample characteristics and bivariate associations).

Models

Individual growth curve models were conducted in the *lme4* R package (Bates et al., 2014) to examine the main and interactive effects of depression symptom severity on autonomic reactivity during the dot-tracking task. Growth curve models included the primary predictor of depression symptom severity (i.e., IDAS-Dep subscale score), time terms (i.e.,

Table 1 Descriptive statistics and correlations for study variables

Variable	M (N)	SD (%)	1	2	3	4	5	6	7	8	9	10	11	12
1.Age	34.43	7.14	–											
2.Sex—F	31	39%	− .01	–										
3.BMI	25.10	3.55	− .08	.09	–									
4.CPD	14.03	5.00	.07	.12	− .15	–								
5.FTCD	3.83	1.46	.36**	− .12	− .15	.40**	–							
6.BL CVC	5.98	1.28	− .37**	.12	.02	− .14	− .14	–						
7.BL HR	70.12	10.14	.11	− .26*	− .16	.11	.20	− .46**	–					
8.IDAS-Dep[a]	40.43	13.10	− .12	− .31	− .04	− .15	− .21	.13	− .07	–				
9.DT CVC	5.98	1.12	− .40**	.06	.02	− .12	− .12	.89**	− .50**	.05	–			
10.DT HR[b]	71.26	9.11	.11	− .27*	− .16	.16	.21	− .43**	.96**	− .04	− 50**	–		
11. BL RR	15.47	3.01	− .20	− .17	.12	− .04	− .02	− .24	.05	.16	− .07	.04	–	
12. DT RR	16.08	3.02	− .29*	− .08	.00	− .11	− .16	− .22	.09	.08	− .14	.00	.58**	–

Sex (1 = Female; 2 = Male); Body Mass Index (BMI); Cigarettes Per Day (CPD); Fagerström Test for Cigarette Dependence (FTCD); Average Baseline Cardiac Vagal Control (BL CVC); Average Baseline Heart Rate (BL HR); Inventory of Depression and Anxiety Symptoms -General Depression Subscale (IDAS-Dep); Average Dot-tracking Cardiac Vagal Control (DT CVC); Average Dot-tracking Heart Rate (DT HR); Average Baseline Respiration Rate (BL RR); Average Dot-tracking Respiration Rate (DT RR)

*$p < .05$. **$p < .01$

Independent samples t-test showed significant differences between males and females on measures of [a]depression [$t(58) = 2.46$, $p = .02$] and [b]average dot-tracking heart rate [$t(58) = 2.09$, $p = .04$]

linear, quadratic, and/or cubic over a 5-min interval), the interaction terms (i.e., time x depression severity), and covariates of age, sex, and average CVC value during the 5-min baseline period. All continuous predictor variables were mean centered and random intercepts were included in all models. Due to limited work examining the effect of depression symptoms on changes in CVC among cigarette smokers, we ran two iterations of each model (i.e., linear, quadratic, and cubic) that included either a fixed or random slope. This resulted in a total of six models.

Model Fit

We used metrics provided by the *performance* R package (Lüdecke et al., 2021) to assess and compare model fit. For each model the *performance* package provides five measures of relative and absolute fit: 1. *Akaike Information Criterion (AIC)* and *2. Bayesion Information Criterion (BIC)* assess which model, among a group of models, has the lowest prediction error when using the fewest possible predictors. Lower AIC/BIC values indicate better model fit relative to higher AIC/BIC values; *3. Bayes Factor (BF)* compares a set of models to a comparator model, where BF values > 1 indicate better model fit relative to the comparator; *4. Marginal and Conditional* R^2 show the proportion of variability in the outcome variable accounted for by the predictor variable(s), with Marginal R^2 reflecting fixed effects and Conditional R^2 reflecting random effects; and *5. Root Mean Squared Error (RMSE)* provides the standard deviation of the error, where lower values indicate better fit (i.e., less error). To assess which model best fit the data across these metrics, the *performance* package assigns each model a composite performance score. This reflects the weighted average of all metrics for each model when comparing multiple models and ranges from 0% (all metrics suggest this model has the worst fit) to 100% (all metrics suggest this model has the best fit).

Results

Sample Characteristics

Table 1. details the sample's descriptive statistics and correlations between study variables. Participants reported an average FTCD score of 3.83 (SD = 1.46), representing low to moderate cigarette dependence (Etter et al., 1999; Fagerstrom, 2012). Participants endorsed an average IDAS-Dep score of 40 (SD = 13.10, range = 20.0–83.0), consistent with minimal depression severity on average and a range capturing minimal to moderately severe symptom severity (Stasik-O'Brien et al., 2019). Average CVC values during the resting baseline and dot-tracking task were 5.98 ms^2 (SD = 1.23) and 5.98 ms^2 (SD = 1.21), respectively. Notably, the average lowest minute value across participants for the dot-tracking period was 5.31 ms^2 (SD = 1.20) and was significantly lower than the average baseline values [$t(59) = 7.52$, $p < 0.001$].

Depressive Symptoms Predicting Changes in Autonomic Reactivity

The growth curve model examining the main and interactive effects of depressive symptoms on CVC reactivity with time specified as linear and the slope as fixed outperformed the corresponding models (see Table 2 for Model Summary and Performance Statistics). Model results showed a significant random intercept for CVC at the start of the task ($b = 5.98$, $p < 0.001$), reflecting significant between-person variability in minute one CVC values. Of the Model's predictors, only average baseline CVC significantly predicted changes in CVC reactivity over the course of the task ($b = 0.77$, $p < 0.001$) such that smokers with higher levels of CVC at rest exhibited greater CVC reactivity during the

Table 2 Model summary and performance statistics examining the effect of depressive symptoms on changes in CVC reactivity during the 5-minute task

Predictors	Estimates	Confidence Interval Lower Limit–Upper Limit	*p*
(Intercept)	6.09	5.28–6.35	< 0.001
Task minute	0.01	− 0.04–0.06	0.79
IDAS-Dep	− 0.01	− 0.02–0.01	0.39
Age	− 0.01	− 0.03–0.01	0.16
BL CVC	0.77	0.66–0.88	< 0.001
Sex—M	− 0.19	− 0.48–0.09	0.19
Task Minute × IDAS-Dep	− 0.00	− 0.00–0.00	0.76
Random effects			
σ2	0.37		
τ00 ID	0.19		
ICC	0.34		
N ID	60		
Observations	300		
Marginal R^2/Conditional R^2	0.64/0.76		
RMSE	0.56		
Sigma	0.61		
AIC|BIC	0.77|0.99		

Cardiac Vagal Control Values for Minutes 6–10 of Dot-tracking task (Task Minute)

Inventory of Depression and Anxiety Symptoms—General Depression Subscale (IDAS-Dep)

Average Baseline Cardiac Vagal Control (BL CVC); Sex (Female = 1, Male = 2); Root Mean Squared Error (RMSE)

Akaike Information Criterion (AIC); Bayesian Information Criterion (BIC)

task. In contrast to our hypothesis, there was no significant main or interactive effects of time and depression symptoms on change in CVC reactivity over time (all $ps > 0.05$). No significant effects for age or sex were observed ($ps > 0.05$).

Discussion

Impairments in autonomic activity have been independently linked to smoking status and depression severity (Agelink et al., 2002; Dinas et al., 2013), and are correlated with self-regulatory processes that may contribute to comorbid depression and smoking (Geisler et al., 2013; Pu et al., 2010). To clarify if depressive symptoms have a unique negative effect on smoker autonomic function, this study examined the moderating role of depression symptoms on cardiac vagal control (CVC) among a non-clinical community sample of daily smokers over the course of a mildly demanding cognitive task. Contrary to expectation, there were no significant main or interactive effects of depression symptoms on smoker CVC reactivity.

Prior work has demonstrated that depression status and severity is negatively associated with reduced CVC activity. For example, when compared to healthy, non-depressed controls, only patients with severe depressive symptoms exhibited significant differences in CVC (Agelink et al., 2002). In contrast, no significant differences in CVC were observed between moderately depressed patients and controls (Agelink et al., 2002). These findings also align with results from a large meta-analytic review of studies among clinically depressed individuals, showing greater depression severity was associated with greater reductions in CVC (Kemp et al., 2010). Despite evidence supporting an inverse relation between depressive symptoms and CVC decrement, our findings suggest that greater depressive symptoms do not worsen CVC amongst community smokers with low to moderate depressive symptoms. One explanation for this may be that smoking-related impairments in autonomic function (Dinas et al., 2013) obfuscate any incremental effects depression symptoms may introduce. However, given our sample evidenced relatively low levels of depression, future work including smokers with more severe depression is needed. Such work can help to discern whether depression severity exacerbates these effects (Harte et al., 2013), or if smoking status, alone, best accounts for reduced autonomic activity among smokers with depression. Similarly, given that prior work has found that depression, regardless of smoking status, is associated with worse CVC (Agelink et al., 2002), future work would benefit from including depressed non-smokers.

Whether certain subtypes of depression or individual differences in other relevant transdiagnostic factors serve as better predictors of autonomic impairment, compared to depression severity alone, also warrants further investigation. Evidence for this perspective comes from studies showing a significant negative relation between rumination and CVC (Carnevali et al., 2018; Woody et al., 2014). However, the link between rumination and CVC has been challenged by separate work showing no relation between these two constructs among a community sample of young adults with and without depressive symptoms (Moretta & Messerotti Benvenuti, 2022). Similarly, another study found that somatic symptoms of depression (i.e., sleep problems and fatigue) were associated with greater CVC reductions compared to cognitive symptoms of depression (i.e., anhedonia, difficulty concentrating; (de Jonge et al., 2007). Although research in this vein appears equivocal, it underscores the need for future investigations that can help tease apart whether (and which) specific subtypes of depression may more reliably predict autonomic impairments.

Consistent with the current investigation, studies examining the relationship between co-occurring psychopathology and autonomic function among other populations with problematic health behaviors have also produced null findings. For example, experimental work among substance using populations have found non-significant associations between the perceived ability to tolerate distress, a transdiagnostic risk factor implicated in substance use, and changes in autonomic activity in response to stress (Paz et al., 2017) and substance cues (Vujanovic et al., 2018). These findings, along with the current study, suggest that elevations in psychological vulnerability and moderate levels of psychopathology, independently, may not meet the threshold necessary to significantly impact autonomic impairment. However, further work is needed to verify if certain cutoffs in psychopathology severity alone, or in combination with other vulnerabilities, reliably correspond with observable changes in autonomic activity across substance and non-substance using populations.

Regardless of the potential compounding effects of psychopathology, smoking-related impairments in autonomic function among individuals who smoke have important clinical implications. Among nicotine-deprived smokers, reduced CVC is associated with shorter time to smoking lapse and greater smoking reward following stress exposure (Ashare et al., 2012). Whether smoking-related impairments in autonomic activity contribute to poor depression outcomes among smokers is less well known. Cohort studies have shown that smokers with depression, compared to non-smokers with depression, are at greater risk for recurrent depressive episodes (Hebert et al., 2011). One possible explanation for this may be that persistent reductions in autonomic function amongst smokers, even in the absence of depressive symptoms, may correspond with other self-regulatory deficits in cognition and affect regulation that indirectly affect depression outcomes. Future work is needed

to further clarify the direct and indirect effects of smoking-related impairments on autonomic activity in depression, smoking, and their comorbidity.

As noted, this study has several limitations. First, the participants in this study were recruited form the community and are not representative of a clinically depressed sample. Although there was a wide range in depressive symptoms across participants (i.e., minimal to moderately severe symptom severity), on average the sample endorsed minimal depressive symptoms. As a result, the non-significant effect of depression symptoms on CVC observed here, may not adequately reflect differences in autonomic function among individuals who smoke with greater depression severity. Second, although the dot-tracking task was chosen given it is void of social and emotional content, it may not have served as a challenging enough task to elicit observable changes in CVC reactivity in a sample with already compromised autonomic activity. However, our findings did show that the average lowest minute across participants for the task did significantly differ from the baseline period. This is consistent with previous investigations using this task among non-smoking, healthy samples (Human & Mendes, 2018; Muhtadie et al., 2015). The inclusion of a non-smoker comparator group in the current investigation would have provided further support for the perspective that our sample of daily smokers simply evidenced reduced CVC reactivity.

Despite these limitations, the current investigation has several notable strengths. First, the lack of social and emotional cues in the dot-tracking task allowed us to explicitly examine changes in autonomic activity as a function of cognitive effort and attentional demand without the influence of confounding factors. Although this limits our ability to draw conclusions about more affect-related changes in ANS dysfunction, theoretical and empirical work suggests that in addition to affect disturbance, cognitive impairment also serves as a unique mechanism linking smoking and depression comorbidity (Mathew et al., 2017). Thus, the use of the cognitive task allowed us to experimentally manipulate aspects of cognitive regulation (i.e., attention, task persistence, etc.) that have been linked to impaired ANS function (Thayer et al., 2009) as well as clinically relevant smoking processes (Szasz et al., 2012). Second, to our knowledge this is the first study to examine the extent to which subclinical depressive symptoms are associated with worse autonomic functioning *within* daily cigarette smokers and whether depressive symptoms are associated with in vivo changes in smoker CVC reactivity. Clarifying the effects of depression symptomatology on autonomic function among individuals who smoke is important given clinical and subclinical levels of depression and smoking status frequently co-occur (Petroulia et al., 2018; Weinberger et al., 2017), as well as evidence for autonomic impairments in both populations (Agelink et al., 2002; Dinas et al., 2013). Third, the use of growth curve modeling to detect the effects of depression symptoms on changes in autonomic activity over time is novel. This allowed for a more nuanced examination of changes in CVC reactivity that occurred over the course of the task. Future study designs that include analytic techniques such as this can further assist in capturing dynamic changes in autonomic activity (Brooker & Buss, 2010; Miller et al., 2013). Although our hypothesis that smokers with greater depressive symptoms would exhibit less autonomic flexibility, compared to smokers with fewer depressive symptoms, was not supported, this investigation adds to a paucity of empirical work seeking to clarify how depressive symptoms, even at low levels, may exacerbate existing physiological vulnerabilities among adults who smoke.

Author Contributions Authors TML and WBM developed the original study design and acquired funding to support data collection. Authors HRB, DLH, EJF, and TML contributed to the literature review and manuscript preparation. Authors HRB and DLH completed statistical analyses. All authors have contributed to and approved the final manuscript.

Funding This work was funded by the National Institute on Drug Abuse (R03 DA041556-01A1) awarded to the last author.

Data Availability Not applicable.

Code Availability Not applicable.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Ethical Approval All study procedures were reviewed and approved by the Rutgers University Institutional Review Board and adhere to the tenets of the Declaration of Helsinki.

Consent to Participate Informed consent was obtained from all individual participants included in this study.

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