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The effect of anxiety on heart rate variability, depression, and sleep in Chronic Obstructive Pulmonary Disease

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ABSTRACT

Objectives: The current study investigates heart rate variability (HRV) responses to a psychosocial stressor in Chronic Obstructive Pulmonary Disease (COPD) patients, and the potential role of anxiety as a confounding factor in this relationship. Additionally, this study also investigates the influence of anxiety on sleep and depressive symptoms among COPD patients.
Methods: The study utilized a 2 (disease status)×2 (anxiety group) factorial design examining HRV associated with anxiety symptoms and COPD during a standardized acute social stress task. Participants (mean age 59.1 ± 11.2 years; 50% female) completed pulmonary function testing, HRV monitoring, and self-report questionnaires assessing psychological factors. 30 COPD patients were age- and gender-matched with 30 healthy controls.
Results: HRV response to a psychosocial stressor among participants with higher anxiety (both COPD and healthy) reflected autonomic dysregulation in both time and frequency domains that was not evident among non-anxious participants. COPD participants with higher anxiety reported greater symptoms of depression and poorer sleep quality than did COPD participants with low anxiety.
Conclusions: Anxiety is associated with dysregulated HRV response to a psychosocial stressor, but the negative influence of anxiety and COPD on autonomic function did not appear to be additive. Comorbid anxiety in patients with COPD is associated with increased behavioral and psychological symptoms of distress.

Introduction

Anxiety is one of the most common psychiatric symptoms among patients with Chronic Obstructive Pulmonary Disease (COPD) [1–5]. Anxiety associated with COPD may exacerbate physical symptoms such as dyspnea [6,7]. Additionally, patients with both chronic medical illness and comorbid mental illness are more functionally disabled than patients who have either a chronic medical illness or a mental illness alone, and past research has revealed a relationship between psychiatric comorbidity and functional status among patients with COPD [2,3,8–11]. Patients with less psychological distress also will participate more actively in therapies and will subsequently benefit more, leading to enhanced physiological outcomes [3].

Several prior studies suggest that autonomic dysfunction may be more common in COPD patients than among healthy controls, although prior studies do not provide conclusive evidence [12–17]. Volterrani et al. found overall decreased global heart rate variability (HRV), a marker of autonomic dysfunction, in COPD patients compared to healthy controls at rest, during controlled breathing, and during passive orthostatic conditions (indicated by the standard deviation of RR interval) [17]. Stein et al. found decreased high frequency HRV (HF-HRV) in COPD patients compared to healthy controls only during daytime, but not nighttime or during 24-hour recordings. Bedard et al. found reduced HRV in COPD patients compared with healthy controls during daytime, nighttime, and also for 24-hour recordings (measured by low frequency/high frequency (LF/HF) ratio), but no difference in resting HF-HRV when comparing COPD patients to healthy controls [12].

Despite the results indicating decreased HRV in COPD patients, other studies have found increased parasympathetic activity in COPD patients. The majority of these studies investigated the responses to sympathetic or parasympathetic stimuli among COPD patients compared to healthy controls. In the Volterrani et al.'s [17] study, COPD patients demonstrated elevations in standardized HF-HRV at rest and also in response to sympathetic stimuli, indicating increased parasympathetic activity compared to controls. Similarly, Bartels et al. [18] found significantly increased HF modulation of HRV accompanied with decreased LF/HF

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ratio from rest to peak exercise (bicycle ergometry) among patients with COPD but not among healthy controls.

Autonomic dysregulation indexed by decreased HRV may help explain elevated levels of anxiety and depression in COPD patients. Additionally, patients with anxiety disorders and anxiety symptoms, including panic anxiety, generalized anxiety disorder, and panicogenic manipulations, may exhibit reduced HRV [19–30], suggesting that reduced HRV may be a physiological marker linked with clinical anxiety. However, no prior studies of COPD and HRV studies cited above [16–18] have addressed the role of anxiety in the relationship between COPD and autonomic dysregulation.

Although research to date is equivocal regarding the presence of autonomic dysregulation in COPD patients, it is important to determine the degree to which autonomic dysregulation may be a component in the pathophysiology of COPD, contributing to the exacerbation of symptoms (coughing and dyspnea) as well as poor emotion regulation (symptoms of anxiety). This study examined HRV response during an acute psychosocial stress task among COPD patients with and without anxiety compared to healthy controls with and without anxiety. Additionally, psychological variables were examined to compare sleep complaints and depressive symptoms in COPD patients with and without anxiety.

In this study, "autonomic regulation" was operationalized as mean interbeat intervals (mean RR) decreasing in response to a psychosocial stressor, and increasing during a Recovery phase. Any patterns that deviated from this expected response were operationalized as "autonomic dysregulation".

Four groups of participants were included: COPD patients with elevated anxiety (COPD-ANX), COPD patients without anxiety (COPD), healthy individuals with elevated anxiety (HEA-ANX), and healthy individuals without elevated anxiety (HEA).

Three primary hypotheses were evaluated: (1) The COPD-ANX group would exhibit autonomic dysregulation measured by HRV over and above any dysregulation of the other three groups (COPD, HEA, HEA-ANX) in response to a psychosocial stressor; (2) Both anxious groups (COPD-ANX and HEA-ANX) would have elevated state anxiety at baseline and a blunted response of anxiety following a psychological stressor; and (3) The COPD-ANX group would report higher levels of sleep complaints and depressive symptoms compared to the COPD group.

Methods

Participants

Sixty-nine individuals responded to the recruitment efforts and consented to the procedure. However, six individuals were ineligible for the study because group quotas had been met. Of the 63 remaining participants, two individuals completed the study but did not meet criteria for COPD and were excluded from analyses. One individual completed the study but was excluded from analyses due to HRV equipment malfunction. Therefore, 60 participants comprised the final sample, with 15 participants in each of the four experimental groups: COPD, COPD-ANX, HEA, and HEA-ANX.

Participants were recruited from the pulmonary rehabilitation program at Ohio State University (OSU) and from the Columbus metropolitan area. This study was approved by the institutional review board at OSU. All participants with COPD had had a physician diagnosis of COPD for at least 3 months. All diagnostic criteria were consistent with the GOLD standard [31] [indicated by forced expiratory volume in one second/forced vital capacity <.70 (FEV_1/FVC < .70) and FEV_1% predicted <.80].

Participants were excluded if they were pregnant, taking beta-antagonist medication, or had a history of cardiovascular disease. Participants with COPD who were eligible for the study were matched by age (±2 years) and gender to healthy individuals.

Procedure

Following written consent, participants completed the State-Trait Anxiety Inventory — State version to identify high and low anxiety groups (COPD, COPD-ANX, HEA, HEA-ANX). The cut-off score was a standard clinically relevant value of 39 [32]. The target number of individuals in each group was 15, and individuals were deemed ineligible to participate after consenting to the study if the quota for a group had been met. Eligible participants then completed pulmonary function testing and were fitted with HRV monitoring equipment to be worn throughout the remainder of the experimental protocol.

The study was divided into three phases: Baseline, Task, and Recovery, as shown in Fig. 1. At Baseline, all participants completed a packet of self-report questionnaires. Following the questionnaires, participants remained sitting quietly for 5 min to obtain a stable measure of HRV at rest. After quiet sitting, participants read aloud a neutral script about doing laundry. Participants were asked to stop reading the neutral script after 1 min. During the Task phase, participants were exposed to the stressor task. A modified version of the Trier Social Stress Test (TSST) [33] was used for this study.

For the modified TSST, the participant viewed videotaped instructions indicating that the participant would need to deliver a speech on a specified topic, and would be given 2 min to prepare. The participant was informed that the speech would be videotaped and that the speech should be 5 min long. When the taped instructions said "Please take 2 min now to construct your speech", a stopwatch was set for 2 min. After 2 min, the participant stood in front of the video camera, the video camera was switched on, and the participant delivered the speech. If the participant remained silent for more than 20 s during the speaking period, the participant was prompted to continue speaking until the task was terminated.

During the Recovery phase, each participant completed a post-stressor questionnaire of state anxiety. The participant then listened to relaxing music for 20 min.

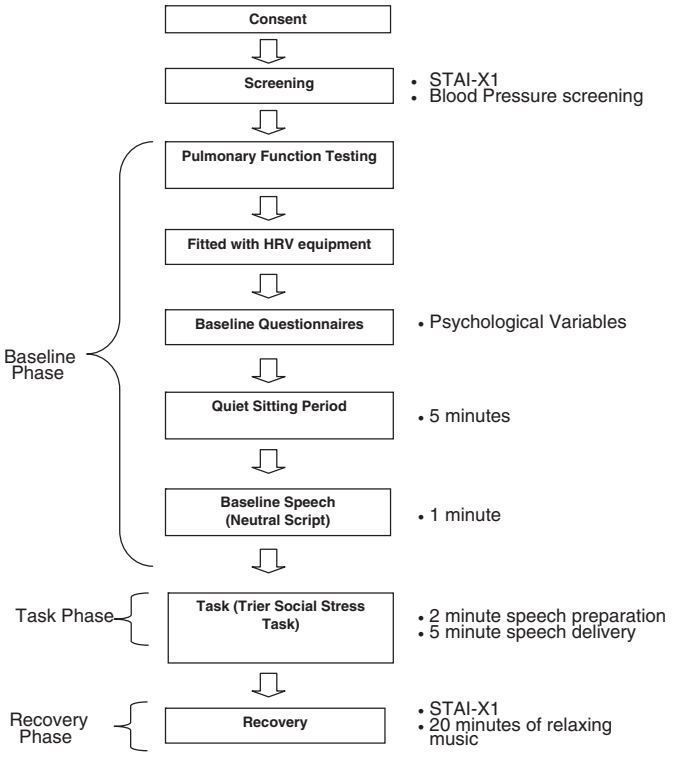

Fig. 1. Study design.

Physiological recording

A Polar S810i Fitness watch (Polar Electro, Finland; www.polar.fi/en/) was used to measure continuous R-to-R intervals using a thoracic band, which transmits and stores IBI at 1000 Hz on a wristwatch. Two previous validation studies [34,35] have compared the S810i with standard ECG recordings during supine rest, walking, and exercise. Both studies concluded that time- and frequency-domain estimates of HRV obtained from IBI time series from the S810i versus a standard ECG system had very good intra-class correlation coefficients and limits of agreement.

The IBI time series for periods of interest were processed using the Kubios HRV Analysis Software (version 2.1; http://kubios.uku.fi/) which calculates HRV parameters in both time and frequency domains per the Task Force Guidelines for HRV [36]. A single experienced rater, blinded to subject group membership, performed the HRV analyses. Within each of the TSST periods (Baseline, Task, Recovery), a single window of 132 to 250 s was selected (avoiding period boundaries) to yield the least amount of artifact correction (piecewise cubic spline interpolation) and trend component removal (smoothness priors) performed by Kubios (i.e., the segment requiring the least amount of adjustment for nonstationarity) [36,37]. A $2\times2\times3$ mixed-factorial ANOVA revealed no significant differences in segment length as a function of disease status [$F(1, 53) = .021$, $p = .886$], anxiety group [$F(1, 53) = .02$, $p = .899$], or phase [$F(2106) = .61$, $p = .544$].

Three outcome measures were calculated from the IBI data within each TSST period. In the time domain, mean IBI (mean RR) and the natural log (ln) transformed value of the standard deviation of the IBI series (SDNN) were calculated. SDNN was used as a measure of global HRV, which has been used in previous studies with COPD patients [17].

As reviewed in the previous studies, in the frequency domain, spectral power estimates are obtained by integrating the autoregressive (AR) power spectrum after factorizing the spectrum into a low-frequency and high-frequency component [36,38]. Because of the fast breakdown of acetylcholine, PNS modulation of the heart is fast and short-lived. Thus, the power in the high-frequency (HF) band (.15–.4 Hz) is dominated by PNS activity. The power in the low-frequency (LF) band (.04–.15 Hz) is considered to reflect joint activation of the PNS and SNS [36]. In the present study, only the vagally mediated HF component was analyzed. The advantages of an AR solution are the smoother spectral components that are independent of pre-specified frequency bands, clear central frequencies of each component, and an accurate estimation of power spectral density even on a small number of (stationary) samples [36]. Furthermore, the central frequency of the HF component has been shown to serve as a surrogate for respiration rate (i.e., frequency in Hz $\times$ 60 = RR) [39], and was calculated here.

Self-report measures included the following assessments of health behavior and psychological distress:

Smoking history

Participants provided detailed information about lifetime duration and amount of cigarettes smoked. Pack-years of smoking (number of packs of cigarettes smoked per day $\times$ number of years smoked this amount) was calculated as a cumulative measure of exposure to smoking.

Sleep

Sleep disturbance has been indicated to affect over 50% of COPD patients, which subsequently diminishes quality of life and increases disease burden [40]. To evaluate sleep disturbance, participants completed the Pittsburgh Sleep Quality Index (PSQI) [41], a self-report questionnaire assessing sleep quality and disturbances over a one-month interval. The scale yields a total score that ranges from 0 to 21, with higher scores indicating more difficulties with sleep. A global score greater than 5 indicates a poor sleeper.

Anxiety

The State-Trait Anxiety Inventory, (STAI-X1) State version [32] is a 20-item measure of state anxiety. Items on the State version include statements such as "I feel upset" and "I am presently worrying over possible misfortunes" rated on a scale of 1 to 4. For all items, respondents indicate how they are feeling at the present moment. The STAI has demonstrated adequate reliability in older adults ($\alpha = .94$; 59). Internal reliability for this sample was excellent (Cronbach's alpha = 0.94).

Depression

The Center for Epidemiological Studies Depression Scale (CESD) [42] is a 20-item measure of symptoms of depression. Respondents rate symptoms of depression during the past week on a 4-point scale. A CESD score of 16 or greater is indicative of depressive symptomatology. The CESD demonstrates internal consistency with $\alpha = .85$. Internal reliability for this sample was excellent (Cronbach's alpha = 0.93).

Pulmonary functioning

Standard pulmonary function testing equipment (Koko Legend Portable Spirometer) was used to determine the volume of expired air, after a maximum inspiration, as well as the flow rate of air. All pulmonary function testing adhered to American Thoracic Society guidelines [43,44]. Common diagnostic measurements include both FEV_1 and FVC, measured in liters. Degree of COPD was characterized for each patient by the percent predicted FEV_1 (according to norms for age, race, sex, and height), and by the ratio FEV_1/FVC.

Data analysis

The current study utilized a 2×2 factorial design to compare the four groups of participants: COPD patients with elevated anxiety (COPD-ANX), COPD patients without anxiety (COPD), healthy individuals with elevated anxiety (HEA-ANX), and healthy individuals without elevated anxiety (HEA). For our first hypothesis, the primary mode of data analysis for HF-HRV and state anxiety was a $2\times2\times3$ (disease status $\times$ anxiety group $\times$ phase) repeated measures ANOVA with disease state (COPD vs. non-COPD) and anxiety group (anxious vs. non-anxious) as between subject variables and phase (Baseline, Task, Recovery) as the within subjects variable. We performed pre-planned trend analyses of the pattern of response among the groups, as Baseline–Task–Recovery paradigms such as the TSST are likely to elicit distinctive patterns of response in HRV [45,46]. Thus, a series of linear and quadratic pre-planned contrasts were performed to characterize responses across groups, as noted in the Introduction. Post-hoc analyses included respiratory frequency (RF) as a covariate for all the HRV analyses.

To control for multiple testing, a sequentially rejective Bonferroni test was used within the RR, SDNN, and HF analyses. This method involves arranging the number of planned comparisons according to p-values, and testing the smallest p-value against alpha (α; 0.05) divided by the number of comparisons (j) within each family. If and only if this comparison was significant, we proceeded to test the next smallest p-value against $\alpha / (j - 1)$.

This method conservatively protects each test performed, and the conditional nature of the procedure leads to a multiplicative, rather than additive compounding of error probability [47].

For the second hypothesis, a 2 (group: COPD, COPD-ANX, HEA, HEA-ANX) $\times$ 2 (phase: Baseline and Recovery) repeated measures ANOVA was conducted for state anxiety with group affiliation as the between subject variables and phase as the within subject variable.

For the third hypothesis, pre-planned tests of group differences in depression and sleep quality were performed. A one-way ANOVA was conducted for pulmonary functioning and psychological variables

Table 1
Demographic characteristics of participants

	COPD (n = 30) M (SD) or N (%)	Healthy (n = 30) M (SD) or N (%)
Age	59.1 (11.24)	59.2 (11.28)
Years of education	14.37 (2.7)	16.0 (3.5)
Years since diagnosis	4.9 (3.5)	–
Income	26,600 (21,500)	31,700 (27,600)
Gender		
Male	15 (50)	15 (50)
Female	15 (50)	15(50)
Race		
CA	17 (56.67)	23 (76.67)***
AA	12 (40)	4 (13.33)
Hispanic	0 (0)	1 (3.33)
Asian	1 (3.33)	2 (6.67)
Marital status		
Single	6 (20.7)	5 (16.7)
Married	10 (34.5)	9 (30)
Divorced/separated	10 (34.5)	13 (43.3)
Widowed	3 (10.3)	3 (10)
Smoking status		
% current smoker	12 (40)	2 (6.7)**
FEV_1	1.45 (0.67)	2.79 (0.81)***
FEV_1%	54.03 (22.11)	94.73 (19.99)***
FVC	2.29 (.094)	3.4 (1.01)***
FVC%	65.40 (20.77)	88.80 (18.10)***
FEV_1/FVC	0.63 (0.15)	0.82 (0.06)***
GOLD criteria		
Stage I	4 (13.3)	
Stage 2	13 (43.3)	
Stage 3	9 (30)	
Stage 4	4 (13.3)	
% use of prescribed medications	30 (100)	22 (73.3)

Abbreviations: COPD = Chronic Obstructive Pulmonary Disease; CA = Caucasian; AA = African American; FEV_1 = Forced Expiratory Volume in one second; and FVC = Forced vital capacity;
Note.
M = Mean.
SD = Standard Deviation.
* p < .05.
** p < .01.
*** p < .001.

evaluating differences within disease status (COPD vs. COPD-ANX) and anxiety group (COPD-ANX vs. HEA-ANX). Post hoc analyses with Tukey's HSD were used to analyze group differences.

Results

Participants were asked to refrain from smoking, consuming alcohol or caffeine, or taking anxiolytic medication 24 h prior to participating in the study to avoid confounding of HRV measurements. Participants with COPD were asked to refrain from taking β2-agonist inhalers 6 h prior to the study to avoid confounding of HRV measurements.

Mean age of participants was 59.1 (±11.2) years (50% female). Participants with COPD presented with moderately severe disease, indicated by a mean FEV_1% predicted of 54.03 (±22.11) and a FEV_1/FVC ratio of 0.63 (±0.15). Additional demographic information and baseline pulmonary function values of the sample are summarized in Table 1.

Participants with COPD (in the COPD and COPD-ANX groups) did not differ from the healthy controls (in the HEA and HEA-ANX groups) with regard to age, gender, marital status, income, or education (p-values ≥ .05). As expected, there were differences in pulmonary functioning among the two groups (p-values < .001). There were also significant racial differences between the groups.

To ensure that changes in heart rate were not due to production of speech during the Task phase, independent t-tests for HRV in both time and frequency domains between the resting baseline and baseline reading task (i.e., the 1-minute script about laundry) revealed no significant differences in mean RR, SDNN, and HF-HRV.

TSST physiological measures[1]

Fig. 2 depicts HRV values in both the time and frequency domain for the four groups across the Baseline, Task, and Recovery phase, plotted separately by disease status. For HF-HRV, three subjects had a single period in which the autoregressive HF-HRV estimate was 0. These three "missing" values were replaced with the group mean for that period (based on the mean of the remaining 14 participants) to avoid having different degrees of freedom across measures (or eliminating those three subjects across all measures).

Mean RR[2]

There was a significant main effect of Task phase on mean RR, characterized by both a quadratic [F_{quad} (1, 56) = 215.42, p < .0001] and a linear [F_{lin} (1, 56) = 47.35, p < .0001] trend, with Recovery having a slower mean IBI than Baseline. As shown in Fig. 2a (with statistics in Table 2), these two trends were consistent across all four groups (COPD, COPD-ANX, HEA, and HEA-ANX).

SDNN[3]

Across all subjects, a significant linear trend [F_{lin} (1, 56) = 14.86, p < .001], but not a significant quadratic trend [F_{quad} (1, 56) = 1.12, p = .295] was present. As evident in Fig. 2b (cf. Table 2), this difference was the result of significant linear trends only in the high anxiety groups (both HEA and COPD).

HF-HRV

Consistent with mean RR, both quadratic [F_{quad} (1, 56) = 7.38, p = .009] and linear [F_{lin} (1, 56) = 19.78, p < .0001] trends were present in the full data set. As seen in Fig. 2c (cf. Table 2), linear effects were more pronounced for both HEA-ANX and COPD-ANX than their non-anxious counterparts.

All pre-planned comparisons continued to be significant after using sequentially rejective Bonferroni test to control for family-wise error within each family of HRV variables (mean RR, SDNN, HF-HRV).

A post-hoc analysis using smoking status and usage of prescribed medications as a covariate was conducted for HRV variables. Both smoking status and number of medications were not statistically significant in all trend analyses for all four groups (p-value ≥ .09).

TSST psychological measures

State anxiety was measured at Baseline and immediately after the Task. Repeated measures ANOVA revealed significant time [F (3, 60) = 18.24, p < .001] and group [F (3, 60) = 2.59, p < .001] effects, and a non-significant interaction [F (3, 60) = 2.59, p = .06]. Tukey's HSD revealed significant differences between the anxious and non-anxious groups (p < .001). Thus, state anxiety increased significantly from Baseline to Task following a psychological stressor in the COPD and HEA group (non-anxious groups), but the COPD-ANX and HEA-ANX groups (anxious groups) had an elevated state anxiety at Baseline and did not show an increase following the psychological stressor (see Fig. 2d).

There were no significant differences between the COPD-ANX and HEA-ANX group in pack-year history and depression (p-values ≥ .1), as shown in Table 3. However, the COPD-ANX group reported lower overall sleep quality [t = 2.74, p = .01] than the HEA-ANX group.

The COPD group and the COPD-ANX group did not differ in disease severity (t = −.10, p = .91), but the COPD group had a higher pack-year history (t = 2.45, p = .02) compared to the COPD-ANX group, as shown in Table 4. The COPD group also exhibited less distress than the COPD-ANX group, with lower scores on the CESD (t = −4.18, p < .001) and lower scores on the PSQI (t = −3.49, p = .002).

Discussion

This study is the first to examine the mediating role of anxiety in the autonomic dysregulation accompanying COPD. Participants with higher anxiety (both COPD and healthy) displayed similar HRV response patterns in both the time (SDNN) and frequency (HF-HRV) domains, that differed significantly from their non-anxious counterparts. These findings suggest that anxiety may function as a confounding factor when characterizing HRV response to a psychosocial stressor.

All four groups displayed strong quadratic trends for mean RR. These differences can also be appreciated visually (see Fig. 2), by examining the strong "overlap" of error bars during the Baseline and Recovery stages (i.e., reflecting similar levels of activity at the group level). For SDNN and HF-HRV, by contrast, only the healthy non-anxious group displayed overlapping error bars for SDNN and HF-HRV. In the other three groups, Recovery values were substantially higher than Baseline values (especially in the case of HF-HRV). This indicates that anxiety (both in COPD and healthy participants) was

[1] There were no significant differences at baseline between groups for any HRV variables.

[2] There were no significant interactions between the trends and disease status or anxiety group for mean RR.

[3] There were no significant interactions between the trends and Disease Status or Anxiety group for SDNN.

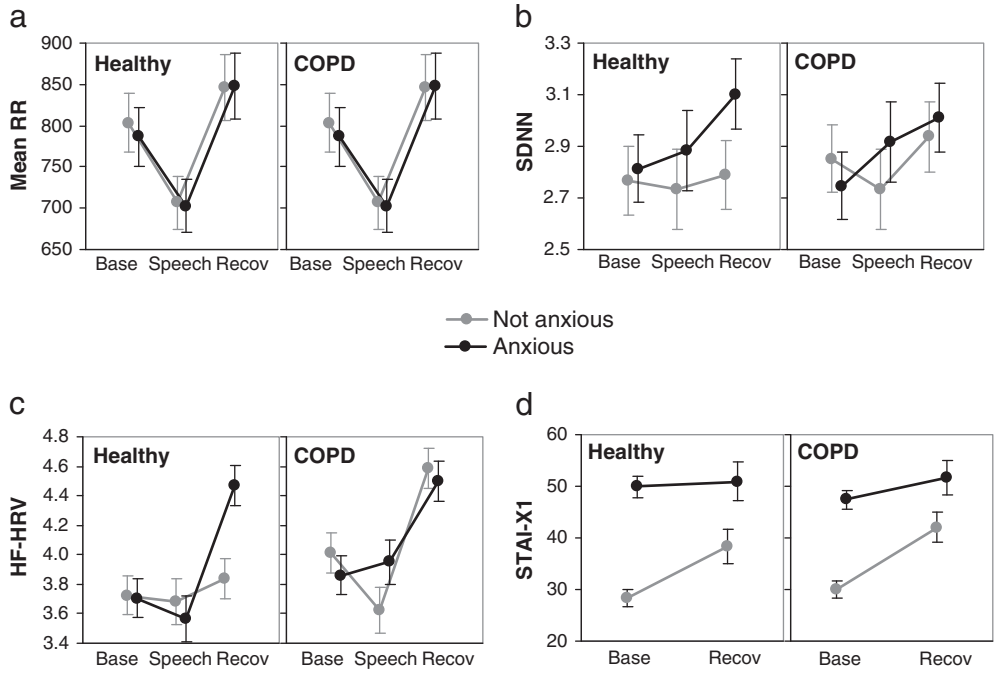

Fig. 2. Dependent measures during the psychosocial stressor task (Baseline, Speech, and Recovery). Abbreviations: Mean RR = mean interbeat intervals (in ms); SDNN = standard deviation of interbeat interval series; HF-HRV = natural ln transformed high frequency value; and STAI-X1 = State-Trait Anxiety Inventory, State version.

associated with a blunted HF-HRV response prior to and after the stressor. This was also confirmed with subjective anxiety measured by the STAI, which indicates that the anxious groups display high anxiety throughout the study and do not change from Baseline to Recovery, whereas the non-anxious groups exhibit increased symptoms of anxiety following the stressor. Thus, the anxious groups show anticipatory anxiety compared to their nonanxious counterparts. This is consistent with the past literature indicating that anxious individuals display a blunted response to stress due to having more anticipatory anxiety at Baseline.

Significant increasing linear trends were consistently present for both SDNN and HF-HRV for only the anxious groups (COPD-ANX and HEA-ANX), but not for the nonanxious groups. These results are consistent with prior research indicating that COPD patients exhibit increased parasympathetic activity in response to sympathetic stimuli when compared to healthy controls [16,17]. Similar patterns were also observed in healthy, anxious individuals. It is possible that past studies investigating HRV in patients with COPD may have included a heterogeneous sample with and without anxiety, and previous studies of HRV in COPD patients may have been affected by the high prevalence of anxiety in this population, as none of the previous studies of HRV in COPD measured anxiety.

Past investigators have suggested that elevated parasympathetic activity in COPD patients may be influenced by breathing against resistance or that obstructed breathing may cause fluctuation in cardiac function in COPD patients [48,49]. Increased parasympathetic activity may be potentiated during dynamic hyperinflation and increased end-expiratory lung volumes [50]. However, the absence of any effect of RF in these data does not support this explanation. This is also supported by the previous studies showing that HRV was not solely influenced by altered breathing pattern [13,17,18,51,52].

Our study did not find decreased global HRV in COPD patients compared to healthy controls, as found in past studies [17]. Inconsistent results across studies may reflect differences in the type of HRV measures and recording procedures used (e.g., utilizing short-term versus long-term HRV recordings). Volterrani et al. [17] found decreased global HRV indexed by the standard deviation of R–R intervals in COPD patients compared to healthy controls, but also found an increased parasympathetic activity in COPD patients in response to sympathetic stimuli and also when utilizing standardized HF-HRV. Bedard et al. [12] found decreased HRV indexed by LF/HF ratio in a 24-hour recording and during daytime and nighttime, but not HF-HRV when comparing COPD patients to healthy controls.

Table 2
Linear and quadratic trend analyses of the three phases (Baseline, Speech, Recovery) of the TSST, separate for each sub-group of 15 subjects. For abbreviations, see Fig. 2 caption

Measure	Group	Anxious	Linear trend		Quadratic trend	
			F (1, 56)	p	F (1, 56)	p
Mean RR	HEA	Not	8.76	.004	64.82	<.0001
		Anx	17.74	<.001	60.90	<.0001
	COPD	Not	2.99	.089	41.21	<.0001
		Anx	23.62	<.001	50.11	<.0001
SDNN	HEA	Not	.07	.787	.14	.710
		Anx	11.31	.001	.36	.550
	COPD	Not	.96	.331	1.72	.196
		Anx	9.57	.003	.09	.766
HF-HRV	HEA	Not	.24	.622	.13	.722
		Anx	10.57	.002	3.04	.086
	COPD	Not	5.90	.018	5.15	.027
		Anx	7.39	.009	.58	.447

Abbreviations: Mean RR = mean interbeat intervals, SDNN = log-transformed standard deviation of normal–normal beats; and HF-HRV = log-transformed High Frequency Value.

Table 3
Psychological variables in the COPD-ANX and HEA-ANX group

	COPD-ANX (n = 15) M (SD)	HEA-ANX (n = 15) M (SD)
Pack year	21.63 (22.36)	9.62 (15.67)
PSQI	12.0 (4.06)	7.8 (4.02)*
CESD	25.73 (11.11)	23.43 (11.56)

Abbreviations: PSQI = Pittsburgh Sleep Quality Index; CESD = The Center for Epidemiological Studies Depression Scale.
* $p < .05$.
** $p < .01$.

Table 4
Pulmonary functioning and psychological variables in the COPD and COPD-ANX group

	COPD (n = 15) M (SD)	COPD-ANX (n = 15) M (SD)
FEV_1	1.31 (0.69)	1.59 (0.63)
FEV_1%	52.4 (26.29)	55.67 (17.78)
FVC	2.06 (1.05)	2.52 (0.78)
FVC%	62.2 (22.83)	68.6 (18.71)
FEV_1/FVC	0.64 (0.14)	0.63 (0.17)
Pack year	44.63 (28.66)	21.63 (22.36)**
PSQI	6.93 (3.47)	12.0 (4.06)**
CESD	11.20 (7.62)	25.73 (11.11)***

Abbreviations: FEV_1 = Forced Expiratory Volume in 1 s; FVC = Forced vital capacity; PSQI = Pittsburgh Sleep Quality Index; and CESD = The Center for Epidemiological Studies Depression Scale.
* $p < .05$.
** $p < .01$.
*** $p < .001$.

Additionally, Bartels et al. [18] did not find decreased HRV in COPD patients at rest compared to healthy controls. It is possible that COPD patients exhibit decreased global HRV during long-term recordings of HRV, but during short-term recordings of HRV, as in this study, COPD patients may exhibit increased HRV compared to healthy controls, especially in response to sympathetic stimulation such as exercise or a stressor.

Because COPD patients with anxiety reported higher levels of clinical depression than COPD patients without anxiety, COPD patients with anxiety may be at higher risk for general distress and disability, regardless of disease severity. It will be important to identify COPD patients experiencing psychological distress and provide appropriate therapeutic interventions such as stress management and cognitive behavioral therapy to reduce distress. Additionally, both COPD patients with and without anxiety reported poor sleep quality, reflected by the PSQI scores greater than 5 for both groups. This indicates that COPD regardless of anxiety affects sleep, and can in turn affect disease management. Thus, insomnia treatment may be necessary to consider for all COPD patients. Based on past research indicating that psychiatric comorbidity decreases functionality among COPD patients [2,3,8–11], treating anxiety may have implications for physical health as well.

This study had several limitations. First, the COPD group in this sample appeared to be relatively high functioning. With the exception of pulmonary functioning, sleep behavior, and pack-year history, behavioral and psychological functioning of COPD patients did not differ from healthy controls. Because most COPD patients in the study were recruited from an outpatient pulmonary rehabilitation program, they may have been relatively active and had greater access to health care resources compared to typical COPD patients.

Second, the absence of HRV differences between the COPD group and the healthy control groups may be due to the long-term use of medications in COPD patients, such as beta-agonist inhalers, beta blocker medication, Ca Channel p blocker, and alpha agonist/blockers. Unfortunately, duration of drug use or use of beta blocker medication, Ca channel p blockers, and alpha agonist/blockers was not measured in this study, although use of beta-agonist inhalers is relatively common among COPD patients. It is common for COPD patients to be treated with cycles of short-term steroids, which may further alter cardiovascular response. Thus, although patients were instructed not to use medication for 24 h prior to participating, patients' prior history of medication use may have influenced outcomes of this investigation. However, past studies have noted that there were no HRV differences in COPD patients using anticholinergic medication or beta agonist medication compared to those not using those medications [12,53,54].

Third, participants completed the Task phase in a standing position, thus it is possible that autonomic changes may have been caused by orthostatic stress. However, the standard protocol for the TSST indicates a standing position, and this issue has been addressed in research literature [54]. While psychosocial stress overlaps with orthostatic stress, research has indicated that the social component (social evaluation) clearly adds to stress. However, we cannot tease apart the extent of HRV changes that were caused by the physiological response from the psychological stressor task.

Finally, our study included participants who were current smokers. While it is true that smoking affects resting HRV, our study focuses on COPD patients, a population that is characterized by high rates of smoking. Thus, it was difficult to exclude patients who were current smokers.

Conclusion

Results of this study indicate that the combined effect of anxiety and COPD did not have a cumulative negative effect on autonomic function, contrary to the original hypothesis. However, an atypical pattern of HRV in response to the stressor task for the COPD-ANX and HEA-ANX compared to their non-anxious counterparts suggests that anxiety may play a mediating role in HRV patterns in response to a stressor. While it is possible that COPD-related stress resembles anxiety in some patients, these data also suggest that autonomic dysfunction may help explain the relatively higher rates of anxiety symptoms among patients with COPD.

Conflict of interest

The authors state that they have no conflict of interest.

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