Preliminary evidence of parasympathetic influence on basal heart rate in posttraumatic stress disorder

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Abstract

Objective: Evidence of elevated basal heart rate (HR) in posttraumatic stress disorder (PTSD) has been interpreted in terms of elevated sympathetic cardiac activity, as have possible increased cardiovascular disease risks and outcomes associated with elevated HR. Yet it is well-established that the parasympathetic branch of the autonomic nervous system not only influences HR independently of the sympathetic branch, but makes a greater contribution to HR, including resting HR. Additionally, abnormally low tonic parasympathetic activity on the heart has been implicated in cardiovascular disease and hypertension. This study addressed a potential parasympathetic contribution to elevated basal HR in PTSD. **Methods:** We used a descriptive and subgroup differences approach to investigate relationships between parasympathetic activity and basal HR in 59 adults (50 females) with PTSD, all of whom were participants in a treatment outcome study and assessed prior to exposure to trauma-related script-driven imagery. Consistent with the well-known relationship between parasympathetic activity and HR, we hypothesized that basal respiratory sinus arrhythmia (RSA), a measure of parasympathetic cardiac activity, would be negatively correlated with basal HR. More important, we predicted that pathologically elevated HRs previously associated with PTSD would only characterize a low-RSA subgroup. Potential confounds of age, respiration rate, and aerobic fitness were addressed. **Results:** As predicted, mean HR was 80.5 bpm in the low-RSA tercile group, similar to mean HRs of PTSD groups in prior research and significantly higher than 69 and 65 bpm in the middle- and high-RSA groups, respectively, which are typical of non-PTSD controls. **Conclusion:** These findings suggest that a substantial proportion of those with PTSD may not have elevated basal HRs. Furthermore, among those who do exhibit elevated HR, there may be a parasympathetic contribution that is independent of any sympathetic one. Only measuring both branches at once, ideally with autonomic blockades, can definitively address these issues.
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Introduction

After more than two decades of research [1], evidence is inconsistent for greater baseline cardiac arousal in those with posttraumatic stress disorder (PTSD) compared to those with trauma histories but not PTSD. One concern is that elevated basal heart rate (HR) could be an artifact of anticipatory anxiety or stress associated with laboratory or assessment situations [2]. Buckley and Kaloupek's [3] comprehensive meta-analysis included a separate examination of laboratory studies that minimized anticipatory anxiety or stress, and the elevated basal HR finding remained. However, three of four published studies assessing baseline HR outside of laboratory or medical settings failed to find differences between veterans with PTSD and combat-exposed controls [4–6].

Blanchard [7] first noted that increased basal cardiovascular arousal in PTSD could herald significant health problems and asked, "Are PTSDs in sympathetic overdrive?" Consistent with a wealth of research in humans and nonhuman primates [8], it is thought that negative cardiovascular outcomes associated with elevated basal HR must

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result from pathologically elevated sympathetic nervous system activity [3]. This view reflects a primary focus on the sympathetic branch of the autonomic nervous system (ANS) in the PTSD psychophysiology literature.

There are three major reasons to study parasympathetic contributions to basal HR and cardiovascular health outcomes in PTSD. First, the parasympathetic branch of the ANS influences HR, including resting HR, independently of the sympathetic branch [9]. Second, parasympathetic activity makes a greater contribution to HR than sympathetic activity [10]; the parasympathetic branch exerts a much wider range of cardiac chronotropic control than the sympathetic branch, on the order of 7:1 in humans [11]. Third, abnormally low tonic parasympathetic activity on the heart has been implicated in cardiovascular disease and hypertension, including lethal arrhythmias, atherosclerotic coronary artery disease, congestive heart failure, and sudden death in coronary artery disease (e.g., Refs. [12–20]).

As noted by Beckham et al. [4], abnormally high baseline HR can result from high tonic sympathetic activity, low tonic parasympathetic activity, or both [9]. Only by assessing the contributions of both autonomic branches to basal HR is it possible to uncover the sources of abnormal resting HRs and the mechanisms by which these underlying sources can lead to disease, thus to determine appropriate interventions.

The need to assess both ANS branches in research on basal HR can be clarified by a conceptual framework that adequately captures the autonomic sources of basal HR. The traditional view of the two autonomic branches, as strictly antagonistic and operating along a single dimension of autonomic control, is incorrect. In two classic papers, Berntson et al. [9,11] synthesized decades of research with a model of "autonomic space," constituted by two independent axes, and three different "modes of autonomic control." The modes of control describe how changes in HR are a function of three distinct patterns of activity by the two autonomic branches. In the reciprocal mode of control, often mistaken for the only mode, one branch's activity increases as the other's decreases; in the coactivated mode, both increase together (although the relative increases of each can vary widely and result, for example, in increased, decreased, or unchanged HR); in the uncoupled mode, activity of one branch increases or decreases with no concomitant change in activity of the other. These modes of control explain transient HR changes and changes from one state to another that can be relatively enduring. They can also account for chronic adaptations away from a relatively normative baseline range, as in pathologically elevated resting HR associated with pathology.

Researchers have begun to study parasympathetic tone in PTSD by noninvasively assessing the amplitude of respiratory sinus arrhythmia (RSA), the rhythmic increase and decrease in HR associated with inspiration and expiration. This index of HR variability (HRV) can be quantified using several well-validated methods, each utilizing interbeat interval (IBI) time series data [21]. One method is analysis of spectral power in the relatively high frequency (HF) range above 0.15 Hz, where the parasympathetic but not the sympathetic branch of the ANS can respond to respiration and influence HR, a measure known as HF HRV.

Thus far, samples have been small, and comparisons of basal parasympathetic activity and HR in PTSD versus controls have yielded contradictory results. In two studies with 9 and 14 PTSD patients and 9 and 25 nontraumatized controls, Cohen et al. [22,23] found that PTSD patients had lower mean resting HF HRV and higher mean HR than controls. Sahar et al. [24] compared 14 PTSD patients to 15 traumatized controls and found no differences in basal heart period (HP) or their measure of RSA. Sack et al. [25] used a subgroups comparison approach to study parasympathetic influences on HR activity in 31 PTSD patients. Significant differences were found in mean resting HR between high and low RSA groups (median split of age-adjusted HF HRV) during a relaxation period following script-driven trauma imagery (high RSA, 71.8 bpm; low RSA, 78.3 bpm), although not during a relaxation period immediately preceding trauma imagery.

No studies have specifically focused on parasympathetic involvement in elevated resting HR in PTSD or links between basal HR and cardiovascular disease outcomes in PTSD. Eventually, researchers will investigate sympathetic and parasympathetic involvement in both elevated HR and cardiovascular disease outcomes, and only invasive pharmacological blockade designs can conclusively assess both branches' independent contributions to basal HR [27]. In the meantime, simpler and less invasive studies can address more preliminary pieces of the puzzle.

In the current study, we investigated the relationship of resting cardiac parasympathetic activity to resting HR in PTSD participants in a treatment outcome study. As a measure of resting cardiac parasympathetic activity, we quantified RSA as HF HRV, and we used a subgroups approach that compared baseline HR in low, middle, and high RSA groups. We hypothesized that, consistent with the known inverse relationship between parasympathetic activity and HR in humans [27,28], RSA would be negatively associated with HR. We also hypothesized that pathologically elevated HRs, in the range previously found in PTSD samples compared to non-PTSD controls [3], would only characterize a subgroup of our PTSD sample with relatively low RSA.

Methods

Participants

All participants were part of a PTSD treatment outcome study, recruited via fliers and advertisements posted in the community and clinician referrals. Data for the current study were collected from 59 participants with PTSD, 50 females

and 9 males, before initiation of treatment. This gender distribution likely results from the greater willingness of women to acknowledge posttraumatic distress and seek treatment. Mean age was 35.7 years (S.D.=13.4). Thirty-six (61%) were Caucasian, 10 (17%) African American, 8 (14%) mixed race or self-designated "other" (not Asian American), and 5 (9%) Hispanic. Twenty-seven percent had household incomes under $10,000, 28% $10,000–30,000, and 34% $30,000 or higher. Fifteen percent had high school degrees or equivalent, 38% had completed some college courses, and had 47% undergraduate or graduate degrees. Participants had experienced a variety of traumatic events, most more than one; the following was the only trauma or that most associated with reexperiencing symptoms: child sexual (19) and physical (7) abuse, rape in adolescence (7), motor vehicle or other accidents (11), sexual (4) and physical (6) assault in adulthood, traumatic death of a loved one (3), attempted kidnapping (1), witnessing deaths in a war zone (1).

Exclusion criteria included alcohol or substance dependence within 1 year or abuse within the past 6 months, current or prior psychosis or bipolar disorder, a score of 30 or higher on the Dissociative Experiences Scale (DES) [29,30], any medical condition not stabilized for 6 months, and taking medications that alter cardiac sympathetic or parasympathetic activity. Participants with DES scores greater than 30 were excluded because the treatment study included an exposure-based therapy and dissociation can prevent the emotional engagement required for successful exposure treatment. The only allowed psychiatric medication was lorazepam, given at night for sleep, which no participants used within 24 h of the assessment. Participants were permitted to use caffeine or nicotine on the day of the psychophysiology assessment, provided it was not a deviation from their daily usage. Only caffeine use was assessed. Written informed consent was obtained from all participants, and the study was approved by the Institutional Review Board of Boston University School of Medicine.

PTSD diagnosis was established with the PTSD module of the Structured Interview for DSM-IV Mental Disorders (SCID) [31] and the Clinician Administered PTSD Scale (CAPS) [32]. For the latter, we used the F1/I2 scoring rule, which considers a PTSD symptom present if the frequency of the corresponding CAPS item is rated as 1 or higher and the intensity 2 or higher, plus the S4 scoring rule, which requires that the sum of the frequency and intensity is 4 or higher [33]. We excluded those with total CAPS scores under 50, rather than the 45 total scoring rule, to ensure participants had moderately severe PTSD. Interrater reliability among the five study interviewers was established at study onset, based on 10 CAPS per interviewer, and reassessed at regular intervals to avoid rater drift. Interrater reliability for CAPS diagnosis, based on Cohen's kappa, was very good (kappa=.82; percent agreement=.92) and was excellent for CAPS symptom severity (intraclass correlation coefficient=.96).

Comorbid Axis I diagnoses, assessed with the SCID, included 6 (10%) with current major depression (17 in full and 15 in partial remission) and 7 (12%) with dysthymia; 13 (22%) with generalized anxiety disorder, 7 (12%) with panic disorder, 5 (9%) with social phobia, 5 (9%) with undifferentiated somatoform disorder. Eighteen participants (31%) had past histories of alcohol dependence and 23 (39%) of past abuse; 13 (22%) had histories of past substance dependence and 17 (29%) of past abuse.

Procedure and instruments

Psychometrics

To characterize the sample in terms of anxiety, depression, and dissociative symptoms often associated with PTSD, we include scores on the following questionnaires from the treatment outcome study: Beck Anxiety Inventory (BAI) [34], Beck Depression Inventory (BDI-II) [35], and Dissociative Experiences Scale (DES) [29,30]. Descriptive results are presented in Table 1.

Psychophysiological assessment

Psychophysiological assessment followed self-report measures, which were preceded by the CAPS. Baseline HR and HP data collection immediately preceded a script-driven imagery procedure that included two neutral and two trauma-related scripts. Participants were seated in a comfortable chair. Electrocardiogram (ECG) signals were obtained from two disposable Ag–AgCl electrodes placed on the lowest ribs and respiration rate from a strain gauge respirometer around the chest. Both signals were amplified and digitized with a J&J Engineering I-330 C2 interface (Poulsbo, WA). ECG data were sampled at 500 Hz for detection of r waves and acquisition of IBIs, then transferred to a Pentium II PC. The USE data acquisition software

Table 1
Means and standard deviations of demographic, psychometric, and cardiac indices (*n*=59)

	Mean (S.D.)
Age (years)	35.7 (13.4)
Years since trauma	12.0 (11.8)
CAPS	68.6 (13.2)
BAI	14.8 (8.7)
BDI-II	16.1 (9.7)
DES	14.9 (6.8)
Resting HR	71.5 (11.3)
RSA/HF HRV (ln(ms)^2)	7.51 (1.50)
RMSSD	47.66 (37.94)
LF HRV (ln(ms)^2)	7.13 (1.01)
RSA/HF HRV (ms^2)	2820.7 (4438.8)
LF HRV (ms^2)	1344.5 (1788.5)

RMSSD=square root of the mean of the sum of squared differences of successive IBIs.

(DOS version, J&J) digitized and stored raw IBI and respiration data.

IBI data were transformed into an instantaneous IBI time series, then power spectral densities of the IBI variability were computed by fast Fourier transform (FFT) using commercial software (Nevrokard, Medistar). Consistent with published recommendations for frequency-domain computations of HRV [21], spectral power was partitioned into low-frequency (LF, 0.04–0.15 Hz) and high-frequency (HF, 0.15–0.40 Hz) bands. Natural logarithm transformations were applied to reduce the skewness of the power distributions. RSA was defined as the HRV in the HF band, where spectral power is characterized by a respiratory rhythm [36]. A time domain measure of RSA, the square root of the mean of the sum of the squares of differences between successive adjacent interbeat intervals (RMSSD) was also computed to serve as a validity check on the spectral analyses [21]. For baseline RSA, the last 3 min of the 5-min baseline were used, during which all participants had respiration rates between 0.15 and 0.34 Hz.

Data reduction and statistical analyses

Mean basal HP values were calculated from the same 3-min period used for RSA analyses. For all statistical analyses, we used both HP and HR metrics for cardiac rate. HP was used for neurophysiological and statistical reasons [37,38]. However, since HP is a less intuitive metric than HR, and use of the latter remains standard in PTSD psychophysiology research, we also conducted analyses with HR and used that metric to graphically represent findings.

HF HRV is an imperfect measure of basal parasympathetic tone, as revealed by the gold standard, pharmacological blockade. For analyses of individual differences, HP better predicts blockade-assessed vagal tone; however, RSA measures independently account for additional and unique variance in vagal tone [26,39]. Thus, for noninvasive studies, particularly one assessing parasympathetic contribution to basal HR, RSA as measured by HF HRV is a justifiable index of parasympathetic tone. Importantly, in group-level analyses, RSA is superior to HP as an index of vagal tone [26]. In short, RSA has solid empirical support as a noninvasive index of basal vagal tone when represented as group-level data, not a continuous variable. Therefore, to test our hypotheses, we characterized RSA as tercile membership (normative data on FFT-derived RSA are not available for empirically derived cutoffs).

Basal parasympathetic function is negatively associated with age [40–43] and with respiratory rate [44] and positively associated with tidal volume [45,46]. Consistent with prior work, we accounted for influences and potentially confounding contributions of age and respiratory rate (tidal volume was not measured) to RSA values with methods that incorporated RSA as a continuous variable. We found the expected strong and negative

association of RSA with age ($r=-.49$, $P<.001$), but not a significant relationship between RSA and respiration rate ($r=-.17$, $P=.22$). Thus, residuals from the regression of age on RSA were used to create RSA terciles. In the absence of experimental control over respiration rate, checking for potential confounding influences and using statistical controls is appropriate and has been done in several studies employing other methods for quantifying RSA (e.g., Refs. [39,46]).

There is mixed evidence, depending on samples and methods, that aerobic fitness can be significantly associated with HP and RSA amplitude [47–50]. Not controlling for its potential influence has been noted as a limitation of prior PTSD research on basal autonomic activity [3]. After the study began, we added collection of height, weight, and physical activity data to estimate aerobic fitness and did so for 41 participants. To estimate the maximum volume of oxygen consumed by the body each minute during exercise while breathing air at sea level (i.e., V_{O_2} max), we used the following empirically derived equations [51], where AR is self-reported physical activity (from 0 to 7) and BMI is the body mass index: women, $V_{O_2,max}=44.310-(0.326\times age)-(0.227\times BMI)+(4.471\times AR)-(0.135\times BMI\times AR)$, $R=0.82$, SEE=4.7 ml/kg/min; men, $V_{O_2,max}=55.688-(0.362\times age)-(0.331\times BMI)+(4.310\times AR)-(0.096\times BMI\times AR)$, $R=0.74$, SEE=4.7 ml/kg/min. We found a significant relationship between estimated aerobic fitness and RSA ($r=.56$, $P<.001$), but not when age was controlled in a partial correlation ($r=.21$, $P=.18$), and the strong negative

Table 2

Demographic, psychometric, and cardiac indices in age-adjusted RSA groups ($n=59$)

	Low RSA ($n=20$)	Middle RSA ($n=19$)	High RSA ($n=20$)
Age (years)	35.3 (13.6)	37.1 (15.5)	34.7 (13.3)
Years since trauma	12.1 (12.3)	11.6 (12.8)	12.4 (12.1)
CAPS	68.9 (13.5)	66.5 (12.0)	70.4 (15.2)
BAI	15.5 (8.3)	13.8 (8.8)	15.2 (10.1)
BDI-II	17.6 (10.7)	14.7 (8.7)	16.2 (10.2)
DES	18.5 (5.8)	13.6 (7.4)	13.9 (6.0)
RSA/HF HRV (ln(ms)^2)	6.18 (1.08)	7.65 (0.99)	8.67 (0.80)
RMSSD	23.87 (17.64)	49.52 (45.96)	69.88 (32.95)
LF HRV (ln(ms)^2)	6.39 (1.00)	6.56 (0.89)	7.10 (1.03)
RSA/HF HRV (ms^2)	484.5 (284.2)	2101.0 (1643.3)	5876.3 (5993.2)
LF HRV (ms^2)	934.6 (1028.7)	1019.6 (985.2)	2079.0 (2637.7)
Resting HR[*]	80.0**·***	69.1**	65.7***
	[74.4–86.4]	[64.4–73.9]	[61.5–70.5]

Values are given as means (S.D.), except for resting HR values, which are given as medians [95% CI]. RMSSD=square root of the mean of the sum of squared differences of successive IBIs.

[*] Significant difference in main effects by group, Kruskal–Wallis test, $\chi^2(2)=10.83$, $P<.01$.
[**] Significant difference between groups, $W=225.5$, $P<.01$.
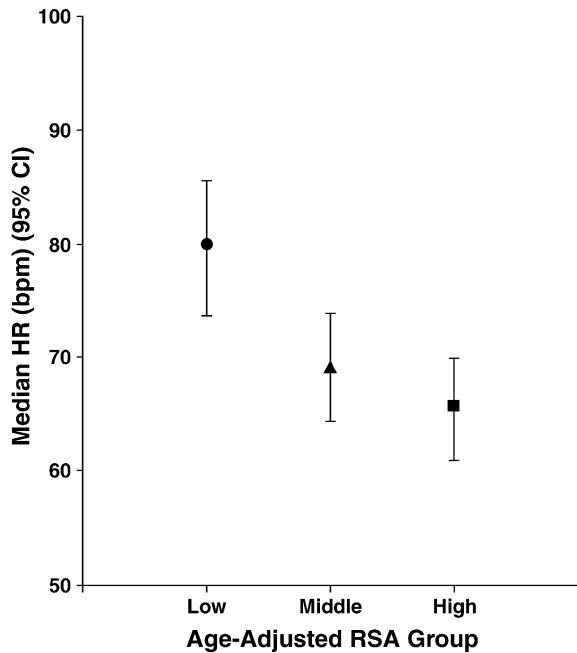[***] Significant difference between groups, $W=214.0$, $P<.01$.

Fig. 1. Median basal HRs for age-adjusted RSA terciles.

would exhibit abnormally short baseline HPs and elevated HRs, we qualitatively compared the HRs of the tercile groups with those of PTSD participants and controls in prior studies. We also used ANOVA and correlations to explore for relationships of RSA, HP, and HR with severities of PTSD symptoms (CAPS).

Results

Sample means and standard deviations on demographics, psychometrics, and cardiac indices are presented in Table 1. Overall, participants suffered from moderately severe PTSD, with mean total symptom severity of 68.6 on the CAPS. In terms of anxiety and depression symptoms, mean scores on Beck measures are consistent with relatively moderate levels of each (according to recommended cutoffs, 34, 35). Consistent with the exclusion of severe dissociation (in the parent treatment outcome study), they exhibited relatively mild dissociation with a mean DES score of 14.9. Mean baseline HP was 859.73 ms (S.D.=136.8), equivalent to a mean HR of 71.5 bpm (S.D.=11.27); mean RSA, uncorrected for age, was 7.00 $\ln(ms)^2$ (S.D.=1.50); and mean LF HRV was 6.68 $\ln(ms)^2$ (S.D.=1.01). Fifty-two percent of participants used caffeine on the assessment day; this was not a deviation from their typical behavior, nor did users and nonusers differ on basal HP or RSA, or their 50% ($\pm$4%) representation in each RSA tercile.

As hypothesized and expected based on well-established relationships between parasympathetic function and basal HR, when we compared the basal HPs and HRs of the three age-adjusted RSA tercile groups via the nonparametric

association between RSA and age remained after controlling for aerobic fitness ($r=-.41$, $P<.01$). Thus, we did not reconduct analyses to control for estimated aerobic fitness.

To test our first hypothesis, that RSA would be positively associated with basal HP and negatively with HR, we used the nonparametric Kruskal–Wallis test followed by pairwise Wilcoxon tests to compare the age-adjusted RSA tercile groups on mean HP. To test our second hypothesis that only the subset of our PTSD sample with relatively low RSA
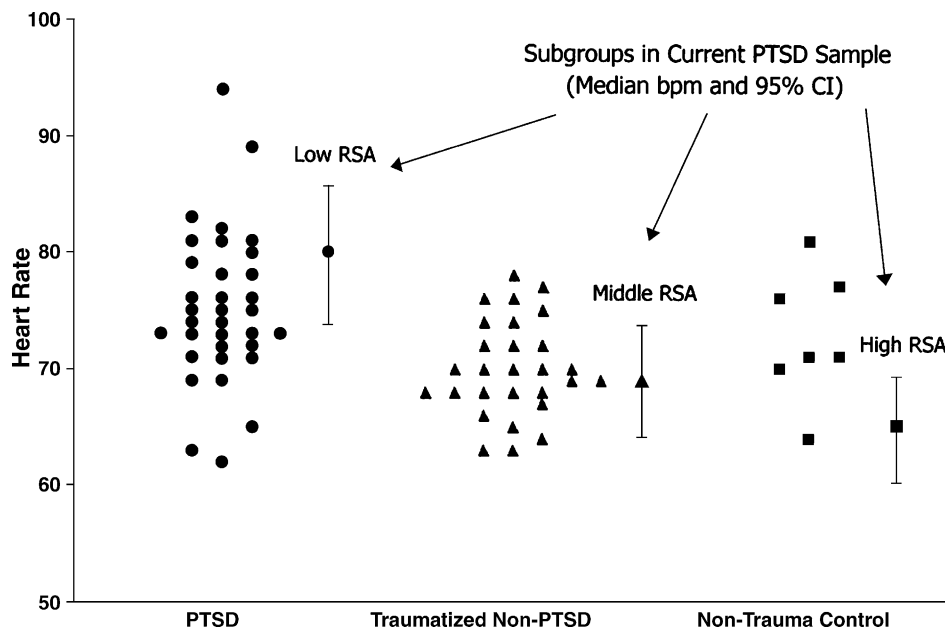

Fig. 2. Mean heart rates as a function of diagnostic group, from individual studies before 2000 group means (reprinted from Buckley and Kaloupek's meta-analytic review [3] and findings from the current study).

Kruskal–Wallis test, there was a significant difference in the main effects by group for HP and HR $[\chi^2(2)=10.83, P=.004]$ (Table 2). Post hoc comparisons of group means with pairwise Wilcoxon tests revealed that mean HP and HR of the lowest adjusted RSA tercile (758 ms or 80.5 bpm) were significantly different from those of the middle group (885 ms or 69.0 bpm) and high group (937 ms or 65.0 bpm). Mean differences between the lowest RSA and the middle and top RSA groups were, respectively, 127 ms or 11.6 bpm (Wilcoxon $P<.01$) and 179 ms or 15.5 bpm (Wilcoxon $P<.01$). Middle and top terciles did not significantly differ from each other ($P=.76$). Fig. 1 depicts HR medians and corresponding 95% exact confidence intervals for the three groups, obtained from the exact Hodges–Lehmann test [52] for nonnormally distributed data (these medians were within 0.7 bpm of the respective means; low RSA, 80.01 bpm; middle RSA, 69.13 bpm; high RSA, 65.70 bpm).

Using Fig. 1 of Buckley and Kaloupek's [3] meta-analytic review, reprinted here as Fig. 2, we qualitatively compared our tercile means to distributions of basal HR data from prior studies of PTSD and traumatized non-PTSD participants. Inspection of Fig. 2 suggests that, confirming our second hypothesis, only our lowest RSA group's mean HR of 80.5 bpm was in the middle range of PTSD subjects and exceeded the entire range of mean HRs of traumatized non-PTSD controls in prior research. Our middle- and high-RSA groups both had HRs (69.0 and 65.0 bpm) in the middle to lower range of traumatized non-PTSD controls in prior studies.

To assess for relationships among demographic variables, PTSD symptom severity, and both basal HP and RSA, we conducted a t test (for gender) and a series of ANCOVAs (with RSA terciles, controlling for age), correlations, and partial correlations. No relationships were found between gender, education, income, or years since the trauma and HP, HR, or age-adjusted RSA tercile membership. Nor were any relationships found between HP, HR, and RSA tercile and total CAPS score or CAPS symptom clusters.

Discussion

Our findings suggest a parasympathetic contribution to basal HR in PTSD. As revealed by RSA subgroup analyses and consistent with our first hypothesis, RSA was highly negatively associated with basal HR (controlling for the significant influence of age). This is expected, based on the axiomatic relationship between basal parasympathetic cardiac activity and basal HR at rest. Nonetheless, because, with few exceptions [4,25], discussions of elevated basal HR in the PTSD psychophysiology literature have focused exclusively on the sympathetic system, it was important to demonstrate this relationship in a PTSD sample.

As noted above, prior studies reporting RSA and HR data in PTSD have employed small samples and group comparisons of PTSD and control samples and yielded inconsistent findings [22-24]. The only prior study addressing subgroup differences in basal RSA and HR within a PTSD sample [25] found significant differences in mean resting HR between those classified as high and low RSA by median split. The current study's comparatively large PTSD sample and thorough assessment procedures provide additional evidence of parasympathetic involvement in basal HR in PTSD.

In support of our second hypothesis, only the lowest RSA group in our study had a mean HR (80.5 bpm) clearly belonging in the range previously found for PTSD samples. In contrast, our high- and middle-RSA subgroups had HRs (69 and 65 bpm) clearly in the middle and lower range of trauma-exposed non-PTSD controls in prior research. The relatively low HRs in the middle- and high-RSA groups are particularly noteworthy and consistent with the high-RSA group HR (71.8 bpm) in Sack et al.'s [25] study. These findings suggest that elevated basal HR is not characteristic of all, or perhaps even most, people suffering from PTSD. Indeed, although participants anticipated exposure to trauma scripts, which should elevate HR and decrease parasympathetic cardiac activity, the middle- and high-RSA groups still exhibited HRs in the middle to lower range of non-PTSD controls in numerous prior studies.

RSA is an imperfect measure of basal parasympathetic tone, as revealed by the gold standard, pharmacological blockade. However, RSA does independently account for additional and unique variance in parasympathetic activity [26,39], and in group-level analyses, RSA is superior to HP as an index of basal vagal tone [26]. Thus, our tercile groups are likely to reflect real differences in basal parasympathetic cardiac activity.

The most serious methodological limitation is not measuring sympathetic cardiac activity. Because the range of control over HR by the parasympathetic branch at rest is so great, even if higher basal HR were caused by increased cardiac sympathetic tone, this relationship could be masked by the observed relationship between basal RSA and basal HR. Only simultaneous measurement of both branches, preferably with autonomic blockade, can rule out such alternative explanations. In addition, measuring both branches could reveal PTSD subtypes characterized by different patterns of the two autonomic branches' contributions to pathologically elevated baseline HR.

Two more characteristics of our assessment procedures warrant comment. Participants were seated, which is associated with lower cardiac parasympathetic activity than the supine position and greater activity than standing, and we did not experimentally control respiratory parameters or assess tidal volume, which can influence RSA and confound inferences about basal parasympathetic cardiac activity from RSA [39,45]. However, by addressing age, respiratory rate, and estimated aerobic fitness, our methodology exceeds in rigor most studies of RSA and HR in clinical populations.

Other findings and limitations of the current study should be noted. Basal HP, HR, and RSA were not associated with

any demographic variables except for age. The lack of relationship between basal HR and years since the trauma differs from meta-analytic findings [3] and may stem from the relative youth of our sample (mean age of 35.7 vs. 40.5 years across prior studies). Other differences between our PTSD sample and those typical in previous studies include its majority female composition, relatively low income, and heterogeneity of trauma types. There is evidence of gender differences in resting HR and RSA [40–43] and a consensus that women generally have higher HRs than men. However, the findings are not consistent in this regard [42,53], and it has been suggested that differences in physical fitness may account for most of the discrepancy [54]. Even with a downward adjustment of 5 bpm (which exceeds the gender difference in most studies that found one) to our sample, the mean low RSA tercile HR would be 75.5 bpm, in the middle range of HRs found in PTSD samples in previous studies [3].

It is unclear whether our participants' low incomes or heterogeneity of traumatic exposures may have influenced our findings, and further research is needed on these issues. Caffeine use was evenly distributed across the tercile groups, and those using and not using caffeine on the assessment day did not differ on basal HR or RSA. Cigarette use, although not assessed, is an unlikely confound because nicotine likely elevates HR via sympathetic rather than parasympathetic activity [55]. Finally, because the sample consisted of participants in a PTSD treatment study, it was shaped by experimenter- and self-selection biases, including exclusion of those with current substance abuse (a common exclusion in PTSD psychophysiology).

Under normal physiological conditions, all humans exhibit an inverse relationship between basal RSA and HR. Thus, sample characteristics are not likely to account for the significant differences between RSA tertile groups. In addition, we are aware of no empirical work to suggest that our sample demographics account for the close correspondence between the actual mean HRs of our low-RSA and middle/high-RSA groups and those previously found in PTSD and control groups. Still, it is important that demographic variables be addressed in future studies.

In summary, the parasympathetic branch of the ANS is known to have an independent and greater influence on basal HR than the sympathetic branch and has been specifically implicated in cardiovascular risk factors, disease processes, and outcomes. These are compelling reasons for investigating parasympathetic contributions to basal HR in PTSD and its possible contribution to cardiovascular disease in this population. These are also compelling reasons for employing individual difference and subgroup methodologies, not just PTSD-versus-control group comparisons. In a sample of 59 predominantly female PTSD participants in a treatment study, we found an expected strong negative relationship between resting HR and RSA and evidence supporting the view that pathologically elevated HR in PTSD may, in part, be associated with low basal para-

sympathetic cardiac activity. Importantly, we did not measure basal sympathetic cardiac activity and cannot know whether sympathetic activity may account for our findings. Nonetheless, our findings suggest the need for more research on contributions of the parasympathetic branch of the ANS to basal HR in PTSD and its possible relationships to pathological HR elevations and cardiovascular disease in this disorder.

Acknowledgments

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