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Assessment of Heart Rate Variability as a Measure of Acute Psychological Stress in Ambulatory Settings

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Assessment of Heart Rate Variability as a Measure of Acute Psychological Stress in Ambulatory Settings

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B.E.,

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2018

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An abstract of

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Abstract

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By Manasvi Sundar

Background

While previous studies have shown that Post Traumatic Stress Disorder (PTSD) is associated with reduced Heart Rate Variability (HRV), most studies are cross sectional in design, limiting the ability to make causal inferences and illustrate temporality of the association. Although HRV is often measured in ambulatory settings, few studies have adjusted for the effect of physical movement on HRV. We sought to examine the relationship between everyday PTSD symptoms severity and HRV, adjusting for physical activity assessed using actigraphy.

Methods

Study participants were male twins from the Vietnam Era Twin Registry. HRV was collected using ambulatory ECG monitoring patch that participants wore for up to 8 days. They also wore an Actiwatch device on their wrist which collected physical activity counts. Daily PTSD symptoms were ascertained using PTSD Checklist for DSM-V (PCL-5). Low Frequency HRV (LF-HRV) and physical activity counts were log transformed and standardized, and PCL score was standardized. Multilevel Models were used to assess the associations between PTSD symptoms and LF-HRV, adjusting for physical activity counts, PTSD diagnosis, and other confounders. In addition to estimating the association among individual participants, between and within twin pair effects were analyzed.

Results

The analytic sample (n = 106) consisted of men with a mean age of 68.0 years (SD = 2.6) and 18.8% of the sample had current or past PTSD. Examining the relationship among individual subjects, daily PTSD symptoms measured by PCL score was significantly associated with lower LF-HRV on a log scale ($p<0.0001$) and the relationship remained significant after adjusting for potential confounders. One standardized unit increase in PCL score was associated with 0.03 decrease in standardized log LF-HRV after adjusting for confounders. The within pair effect for daily PCL score was significantly associated with lower log LF-HRV values in both unadjusted and adjusted models ($p < 0.0001$).

Conclusion

We observed that higher levels of Post Traumatic Stress Disorder (PTSD) symptoms severity recorded everyday was associated with reduced Heart Rate Variability indicating impaired autonomic regulation, controlling for potential confounders, genetic, and familial factors. Furthermore, this relationship was independent of PTSD diagnosis, showing that acute measures of psychological stress account for autonomic dysfunction independent of chronic stress conditions.

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Chapter I: Background

Posttraumatic Stress Disorder (PTSD) is a common psychiatric condition caused by exposure to traumatic events and reflects dysregulation of the stress response system (1). Chronic stress conditions like PTSD could affect cardiovascular health by influencing health behaviors such as diet, smoking, alcohol consumption, physical activity which may in turn increase risk of coronary heart disease (CHD), or result in acute or chronic pathophysiological changes (2). Several studies have found an association between PTSD and increased risk of developing cardiovascular diseases (CVD) and coronary heart disease (CHD). Solter et al reported elevated concentrations of serum lipids associated with combat-related PTSD among veterans, indicating a higher risk for atherosclerosis (2). The study by conducted by Falger et al in a sample of Dutch Resistance veterans indicated a higher prevalence of PTSD and excess CVD risk factors in subjects exposed to high levels of war-related trauma (3). Boscarino and Chang demonstrated that PTSD was specifically related to atrioventricular conduction defects and infarctions (4). However, these early studies were cross-sectional in design, thereby limiting the ability to make causal inferences regarding the findings.

A prospective study of twin veterans from the Vietnam Era Twin Registry conducted by Vaccarino et al indicated that the risk of incident CHD among those with PTSD was more than twice compared to those without PTSD (6). Kubzansky et al found a higher risk of incident CHD among women with PTSD (7). Two studies conducted by Boscarino indicated a higher CVD mortality rate associated with PTSD (8,9). In order to investigate the underlying physiological pathway between PTSD and CHD, more mechanistic research similar like the randomized clinical trial conducted by LoSavio et al is required (11).

In addition, PTSD has been shown to be associated with reduced baroreflex sensitivity and impaired autonomic modulation. Three independent studies conducted by Cohen et al indicated that PTSD is associated with reduced heart rate variability (HRV), which is a measure of beat to beat fluctuation over time, assessed through power spectral analysis (13-15). Hughes et al found that baroreceptor sensitivity is decreased among those with PTSD, suggesting that PTSD is associated with reduced parasympathetic nervous system functioning (16). These findings led to HRV being commonly used as an indicator to examine the association between PTSD and autonomic nervous system (ANS).

HRV can be decomposed into its component discrete frequency bands using power spectral analysis, which consists of ultra low frequency, very low frequency, low frequency, and high frequency bands (14). Previous studies have shown an association of mental stress with both low frequency (LF) and high frequency (HF) HRV (23, 30, 40, 41). Low frequency HRV (LF-HRV) which corresponds to both sympathetic nervous system and parasympathetic nervous system controls of the autonomic function is commonly used to assess the PTSD-HRV relationship. Shah et al showed that among veteran male twins, twins with current PTSD had lower LF-HRV than their brothers without PTSD (23). Findings from Rissling et al indicated that higher PTSD symptoms severity was associated with reduced LF amplitude (24). However, these studies only used a 24 hour ECG recording and therefore were similar to cross sectional studies in design. This calls for a need to conduct longitudinal studies that will be able to account for the inherent baseline differences in HRV among subjects.

Although studies that evaluate HRV use ambulatory monitoring of HRV, most studies did not account for the potential effect of physical movement on HRV. Boyett et al postulated that the amplitude of all frequency bands of HRV are expected to fall during physical activity because

heart rate increases during movement (25). There are several studies that have attempted to study cardiac autonomic responses during varying intensities of exercise and during the post-exercise recovery period (26-28). Understanding this relationship can improve the methodology of controlling for the effects of both momentary physical activity and long term effects of varying intensities of exercise on HRV in ambulatory monitoring settings.

Chapter II: Manuscript

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Abstract

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Study participants were male twins from the Vietnam Era Twin Registry. HRV was collected using ambulatory ECG monitoring patch that participants wore for up to 8 days. They also wore an Actiwatch device on their wrist which collected physical activity counts. Daily PTSD symptoms were ascertained using PTSD Checklist for DSM-V (PCL-5). Low Frequency HRV (LF-HRV) and physical activity counts were log transformed and standardized, and PCL score was standardized. Multilevel Models were used to assess the associations between PTSD symptoms and LF-HRV, adjusting for physical activity counts, PTSD diagnosis, and other confounders. In addition to estimating the association among individual participants, between and within twin pair effects were analyzed.

Results

The analytic sample (n = 106) consisted of men with a mean age of 68.0 years (SD = 2.6) and 18.8% of the sample had current or past PTSD. Examining the relationship among individual subjects, daily PTSD symptoms measured by PCL score was significantly associated with lower LF-HRV on a log scale ($p<0.0001$) and the relationship remained significant after adjusting for potential confounders. One standardized unit increase in PCL score was associated with 0.03 decrease in standardized log LF-HRV after adjusting for confounders. The within pair effect for daily PCL score was significantly associated with lower log LF-HRV values in both unadjusted and adjusted models ($p < 0.0001$).

Conclusion

We observed that higher levels of Post Traumatic Stress Disorder (PTSD) symptoms severity recorded everyday was associated with reduced Heart Rate Variability indicating impaired autonomic regulation, controlling for potential confounders, genetic, and familial factors. Furthermore, this relationship was independent of PTSD diagnosis, showing that acute measures of psychological stress account for autonomic dysfunction independent of chronic stress conditions.

Introduction

Posttraumatic Stress Disorder (PTSD) is a common psychiatric condition caused by exposure to traumatic events and reflects dysregulation of the stress response system (1).While a growing body of literature suggests a link between PTSD and increased risk of developing cardiovascular diseases (CVD) and coronary heart disease (CHD), the underlying pathophysiological mechanisms are largely unknown (2-11). Although early studies were

mostly cross-sectional in design (2-5) ,newer prospective studies have been instrumental in attempting to examine the causality of the association between PTSD and CHD (6-11). In addition, there is a need to conduct mechanistic research to understand the pathways through which PTSD may impact CHD risk (12).

PTSD has been linked to reduced baroreflex sensitivity and impaired autonomic modulation (13-17). Heart Rate Variability (HRV) is a measure of beat-to-beat fluctuations over time and serves as a non-invasive marker of autonomic nervous system (ANS) function (18). Reduced HRV indicates impaired regulatory ANS functions and has been shown to predict cardiac arrhythmia, cardiac mortality, and all-cause mortality (19-22). HRV has been used to assess links between PTSD and ANS functioning. Results from previous studies show that Post Traumatic Stress Disorder (PTSD) is significantly associated with low frequency HRV which corresponds to both sympathetic nervous system and parasympathetic nervous system controls of the autonomic function (23,24). However, these studies are cross-sectional by design, thereby limiting the ability to make causal inferences between PTSD and reduced HRV and illustrate the temporality of the association.

To help overcome this limitation, we can employ a longitudinal study to evaluate the relationship between PTSD and HRV with long-term ambulatory electrocardiogram (ECG) monitoring methodology. It is also vital to recognize that any regular physical movement could potentially influence HRV. It has been shown that there is a pronounced reduction in the frequency domain measures of HRV due to physical movement or activity (25,26). Although there have been conflicting findings about the effect of exercise and its varying intensities on HRV, along with ongoing discussions regarding autonomic changes and pathways of such changes that occur during exercise, it is critical to recognize physical activity as an important

factor that impacts HRV (26-28). Therefore, there is a need to account for physical activity assessed real-time while examining the association between psychosocial stress factors and the autonomic function. However, few studies have evaluated the association between PTSD symptoms and HRV while controlling for potential variations in HRV due to physical activity (24,29,30).

A detailed mechanistic understanding of the association between PTSD and HRV is necessary to potentially improve the quality of life of PTSD patients, and reduce PTSD related morbidity and mortality. Encouraging evidence shows that interventions that alleviate psychiatric symptoms and increase HRV may lower risk of morbidity and mortality (31). Motivated by these studies, we sought to examine if the heart rate variability derived from ambulatory ECG monitoring in veteran male twins is impacted by their self-reported daily PTSD symptoms severity, controlling for physical activity assessed by actigraphy and baseline PTSD diagnosis. We hypothesized that higher levels of self-reported daily PTSD symptoms would be associated with reduced low-frequency HRV.

Methods

Study cohort

Data obtained from Emory Twin Study Follow-up (ETSF) was used in this analysis. This study was a follow-up to the Emory Twins study (ETS), which recruited a sample of 566 twins (283 pairs) from the Vietnam Era Twin (VET) Registry, including monozygotic (MZ) and dizygotic (DZ) twin pairs born between 1946 and 1956. The sample was recruited from two companion studies: the Twins Heart Study and the Stress and Vascular Evaluation in Twins (SAVEIT). The sample consisted of twin pairs discordant for major depression or PTSD, along with control pairs unaffected by both (23,32,33). ETSF included a subset of 124 pairs and 31 single twins

from ETS (279 subjects) recruited for follow-up with an aim of examining if PTSD is related to the worsening of Ischemic Heart Disease measured longitudinally using PET myocardial perfusion imaging. These pairs were either discordant for PTSD or depression.

The data used in this analysis is obtained from an ancillary study which recruited a subset of participants from the ETSF study to conduct ambulatory monitoring of heart rate variability using electrocardiographic monitoring patches for 7 days. The participants also wore actigraphy wristbands for monitoring sleep and physical activity. Clinical data collection and psychometric assessments, including PTSD diagnosis, major depression, depressive symptoms, early life stress, resilience, alcohol and drug abuse, and anger, were conducted at Emory University. All clinical examinations for the twin pairs were conducted together by maintaining similar schedules. Since the data for this study was obtained from an ancillary study, and participants without usable HRV, actigraphy, or covariates data were excluded, including some participants who were missing timestamps marking the start of ECG recording, the analytic sample reduced to 106 participants. The study was approved by the Emory Institutional Review Board, and all twins signed an informed consent.

Measurement of HRV and physical activity

All participants wore an ambulatory ECG monitoring patch (Cardea SOLO) for up to 8 days and was applied by a trained study coordinator on the day of the participants' clinical and psychometric examinations at Emory University. The ECG recording was analyzed to produce frequency domain HRV metrics through previously used and published methodology (34). The power spectrum was integrated over four discrete frequency bands, which consisted of ultra low frequency (ULF, <0.003 Hz), very low frequency (VLF, 0.003 to <0.04 Hz), low frequency (LF, 0.04 to <0.15 Hz), and high frequency (HF, 0.15 to <0.40 Hz). Data was segmented into

5 minute windows that slide by 30 seconds. All participants also wore an Actiwatch Spectrum Pro device (Philips Respironics, Murrysville, PA) on their nondominant wrist for up to 7 days. The device recorded physical activity counts in 30 second epochs and sleep-wake status for each epoch was determined using an actigraphy data scoring algorithm. The activity counts were then averaged over 5 minute windows to match the epochs in HRV data.

Assessment of PTSD and daily PTSD symptoms

Structured Clinical Interview for DSM-IV (SCID) was used to assess lifetime history of PTSD and classify twins as current, past or no history of PTSD at the beginning of the study (35). Diagnosis of other psychiatric disorders, including major depression and a lifetime history of alcohol and of drug abuse, were also obtained using the Structured Clinical Interview for DSM-IV. The Clinician-Administered PTSD Scale for DSM-V (CAPS-5) was used to provide a continuous measurement of current PTSD symptoms throughout the ambulatory monitoring period (36). In addition, the participants recorded a self-rated measure of PTSD symptom severity, the PTSD checklist for DSM-V (PCL-5) on a daily basis throughout the ambulatory monitoring period (37).

Other measurements

Depressive symptoms were assessed at the beginning of the study using the Beck Depression Inventory-II (BDI-II) (38). General occupational and leisure physical activity was measured using the Baecke Questionnaire of Habitual Physical Activity (39). A research nurse or physician assistant obtained the medical history and conducted a physical examination. Hypertension was defined as a measured systolic blood pressure greater than 140 mm Hg or current usage of anti-hypertensive medication. Diabetes was defined as a detected fasting glucose level greater than 126 mg/dl or current usage of anti-diabetic medication. Body Mass

Index (BMI), waist to hip ratio, low density lipoprotein (LDL) cholesterol, High density lipoprotein (HDL) cholesterol, fasting blood glucose level, and other clinical measures were recorded. History of chronic conditions including previous cardiovascular disease, defined as presence of coronary heart disease, myocardial ischemia, revascularization, peripheral vascular disease, or cerebrovascular accident, was determined. Health behaviors including smoking, alcohol consumption, and drug use were recorded. Smoking was classified based on having smoked at least 100 cigarettes in their lifetime.

Statistical Analysis

Participants' demographic and health characteristics were compared based on PTSD status obtained from SCID, the statistical significance of each variable was analyzed by using t test or Wilcoxon test for continuous variables and Fisher's exact test for categorical variables. Multilevel Modeling (MLM) was used to determine the association between daily PTSD symptoms with LF-HRV. MLM is capable of accommodating repeated measures for each participant and data missing at random. LF-HRV and physical activity counts were log transformed and standardized, and PCL scores variable was standardized with a mean of 0 and standard deviation of 1. Unadjusted estimates between daily PTSD symptoms, physical activity, and baseline PTSD diagnosis with log transformed LF-HRV were obtained respectively. For the adjusted analysis, activity counts, Beck depression score, Baecke physical activity score, age, hypertension, diabetes, LDL cholesterol level, Body Mass Index (BMI), history of cardiovascular diseases, and zygosity (monozygotic or dizygotic) were included as covariates. In all the models, a measure of circadian cycle was incorporated by including the hour of day. The participant ID and pair ID were included as random effects while all other dependent variables were included as fixed effects in the models.

Between and within pair analyses were conducted to examine the relationship of HRV with the average values of the dependent variables within twin pairs (between effect) and the difference in dependent variables between twins in a pair (within effect). Between and within pair effects were calculated for daily PCL scores, physical activity counts, and PTSD diagnosis. Adjusted analysis was performed by including the covariates previously mentioned. Only twin pairs which had both brothers included in the analytic sample contributed data to within-pair analysis, while all subjects including unpaired twins contributed to between-pair analysis. All statistical analyses were conducted using SAS 9.4 (SAS Institute).

Results

Participant characteristics

Of the 288 subjects (144 twin pairs) enrolled in the follow-up study, usable HRV and actigraphy data was available for 115 participants. After excluding 9 participants due to missing covariates, there were a total of 106 participants included in this analysis. The mean age of the sample was 68.0 years (SD = 2.6), 10 (9.4%) participants had current PTSD, and 10 participants (9.4%) had past PTSD (Table 1). PCL-5 scores ranged from 0 to 57 with a mean of 4.59 (SD = 9.0) and physical activity counts averaged over five minute windows ranged from 0 to 3731.5 with a mean of 63.27 (SD = 91.9) before standardizing. The mean low-frequency HRV on a log scale was 5.8 ln ms^2 and did not significantly vary among participants based on PTSD status. Participants without current or past PTSD, on average, were more educated ($p = 0.02$) and consumed more alcoholic drinks per week ($p = 0.02$). Participants with current or past PTSD were more likely to have a lifetime history of major depression ($p < 0.0001$), have higher scores on the Beck Depression Scale ($p < 0.01$), and to use antidepressant medication ($p < 0.0001$). They also had higher values of low-density lipoprotein (LDL)

cholesterol ($p = 0.02$). There were no other statistically significant differences in health measures, health behaviors, or medication use based on PTSD status.

Association of PTSD diagnosis and daily PTSD symptoms with Low Frequency HRV

Examining the relationship among individual subjects, daily PTSD symptoms measured by PCL score was significantly associated with lower LF-HRV on a log scale ($p<0.0001$) and the relationship remained significant after adjusting for potential confounders (Table 2). One standardized unit increase in PCL score was associated with 0.03 decrease in standardized log LF-HRV after adjusting for confounders. Past PTSD diagnosis was significantly associated with lower values of log LF-HRV ($p<0.05$), but this association did not persist after adjusting for confounding. In addition, log of physical activity counts obtained from actigraphy and log LF-HRV had an inverse relationship in both unadjusted and adjusted models ($p<0.0001$).

Between and Within pair analysis

The within pair effect for daily PCL score was significantly associated with lower log LF-HRV values in both unadjusted and adjusted models ($p < 0.0001$). While both between and within pair effects of physical activity counts had an inverse relationship with log LF-HRV in unadjusted analyses (p for between pair effect < 0.05, p for within pair effect < 0.0001), only the within pair effect retained statistical significance after adjusting for confounding ($p < 0.0001$). No significant between and within pair associations were found for baseline PTSD diagnosis and log LF-HRV.

Discussion

In this ambulatory monitoring study of Vietnam War veteran twins, we found that daily PTSD symptoms severity measured using PCL-5 scores was associated with reduced low frequency

heart rate variability, independent of PTSD diagnosis and physical activity assessed using actigraphy over a period of 7 days. This association remained significant after controlling for cardiovascular risk factors, depression, and health behaviors. Results from within-pair analysis indicate that the relationship between PCL score and LF-HRV was independent of genetic and familial factors. In addition, we observed that there was a significant inverse relationship between physical activity counts and low frequency heart rate variability.

The findings from this study add to an existing body of evidence that suggest a link between psychosocial stress and reduced HRV (23,30,40,41). Most studies that considered PTSD as an indicator of stress have defined the exposure only by using the diagnosis obtained from administering the Structured Clinical Interview for DSM. Results from an analysis using data from Emory Twins Study showed an association between current PTSD and impaired autonomic modulation in male veteran twins by means of 24-hour HRV (23). We have demonstrated that the relationship between everyday symptoms severity of PTSD and HRV is significant and robust to baseline diagnosis of PTSD. The use of longitudinal data in the form repeated measures over multiple days, our study is a step towards making causal inferences when compared to cross sectional study designs. Our results are consistent with previous findings from Rissling and colleagues that PTSD symptom severity was related to reduction of LF component of HRV (24).

The LF component of HRV is postulated to be reflective of the parasympathetic nervous system and baroreflex sensitivity (42,43). In addition, findings from studies show that those with PTSD had lower BRS as compared to those without PTSD (44,45). Both reduced LF power and lower BRS are indicators of autonomic dysfunction and are associated to cardiovascular morbidity and mortality (46). It is important to note that ambulatory HRV is highly susceptible to

subjects' physical activity and durations of physical movement can cause an acute increase in sympatho-vagal response, regardless of external stressors (47). This is indicated by the inverse relationship between physical activity counts assessed by actigraphy and LF-HRV in our results. However, the relationship between stress and HRV persisted even after accounting for variations in HRV due to physical movement.

There are a number of limitations in this study. First, the sample consisted of middle-aged and mostly White males, limiting generalizability of the findings to people of other demographic groups. Second, although we had controlled for traditional cardiovascular risk factors and previous cardiovascular disease, there may be uncontrolled confounding due to subclinical cardiovascular disease and varying disease pathologies. Finally, respiration, which might affect low frequency heart rate variability, was not included in our analysis (48). Supported by the findings from our study, there are considerable research venues to be explored. Firstly, it would be of interest to examine the effect of other indicators of psychosocial stress on autonomic regulation in an ambulatory setting. These relationships could be evaluated across sleep and wake periods, and utilize more complex correcting factors to account for the effect of physical activity on HRV.

Conclusion

We observed that higher levels of Post Traumatic Stress Disorder (PTSD) symptoms recorded everyday was associated with reduced Heart Rate Variability indicating impaired autonomic regulation. Furthermore, this relationship was independent of PTSD diagnosis, showing that acute measures of psychological stress account for autonomic dysfunction independent of chronic stress conditions. This suggests HRV may also be a useful adjunct in PTSD treatment monitoring. Cardiovascular morbidity and mortality could be reduced by providing measures

of acute stress alleviation and methods of improving autonomic flexibility along with treatments for chronic stress disorders.

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Tables

Table 1. Participant characteristics by PTSD status

Characteristics	All (n=106)	No PTSD (n=86)	Current or past PTSD (n=20)	P value
Age (years), mean (SD)	68.0 (2.6)	68.0 (2.6)	68.1 (2.4)	0.92
Education (years), mean (SD)	14.4 (1.5)	14.5 (1.4)	13.8 (1.5)	0.02
Employed, n (%)	33 (31.1%)	28 (32.6%)	5 (25.0%)	0.60
Smoking (ever), n (%)	72 (67.9%)	56 (65.1%)	16 (80.0%)	0.29
Alcohol (drinks per week), mean (SD)	2.0 (2.5)	2.3 (2.6)	1.0 (2.1)	0.02
History of Cardiovascular Disease, n (%)	8 (7.6%)	6 (7.0%)	2 (10.0%)	0.64
Hypertension, n (%)	55 (51.9%)	46 (46.5%)	9 (45.0%)	0.62
Systolic Blood Pressure (mmHg), mean (SD)	139.3 (19.6)	138.0 (18.5)	144.9 (23.1)	0.16
Diastolic Blood Pressure (mmHg), mean (SD)	78.7 (11.3)	77.8 (10.8)	82.6 (12.8)	0.10
Diabetes, n (%)	24 (22.6%)	17 (19.8%)	7 (35.0%)	0.15
Fasting glucose (mg/dL), mean (SD)	100.2 (16.9)	100.4 (16.3)	99.8 (19.5)	0.89
LDL Cholesterol (mg/dL), mean (SD)	121.9 (34.6)	118.0 (34.6)	138.6 (29.9)	0.02
HDL Cholesterol (mg/dL), mean (SD)	38.7 (11.1)	38.7 (11.4)	38.7 (10.1)	0.81
BMI, mean (SD)	29.5 (4.0)	29.2 (3.6)	30.6 (5.1)	0.52
Waist to Hip ratio, mean (SD)	1.02 (0.06)	1.03 (0.06)	1.00 (0.06)	0.12
Beck Depression Score	5.3 (5.5)	4.2 (4.6)	9.6 (6.8)	0.0004
Baecke Physical Activity Score, mean (SD)	7.9 (1.3)	8.0 (1.3)	7.6 (1.4)	0.17
Lifetime History of Major Depression, n (%)	21 (19.8%)	9 (10.5%)	12 (60.0%)	<0.0001
Medications				
Antidepressant medications, n (%)	18 (17.0%)	6 (7.0%)	12 (60.0%)	<0.0001
Beta blocker medications, n (%)	25 (23.6%)	21 (24.4%)	4 (20.0%)	0.78
Aspirin, n (%)	49 (46.2%)	44 (51.2%)	5 (25.0%)	0.046
ACE-inhibitors, n (%)	28 (26.4%)	23 (26.7%)	5 (25.0%)	0.87
Statin, n (%)	64 (60.4%)	54 (62.8%)	10 (50.0%)	0.32

P values are obtained from t test or Wilcoxon test for continuous variables and Fisher's exact test for categorical variables

Abbreviations: PTSD - Post Traumatic Stress Disorder; LDL – Low Density Lipoprotein; HDL – High Density Lipoprotein, BMI – Body Mass Index; ACE – Angiotensin Converting Enzymes; SD – Standard Deviation

Table 2. Unadjusted and Adjusted associations of daily PTSD symptoms, PTSD diagnosis, and log physical activity with Low Frequency Heart Rate Variability in Individual twins

Dependent Variable	Association with log LF-HRV [a]			
	Unadjusted		Adjusted [†]	
	$\hat{\beta}$	95% CI	$\hat{\beta}$	95% CI
PCL score [a]	-0.03 **	-0.03, -0.02	-0.03 **	-0.03, -0.02
PTSD diagnosis [b]				
Current PTSD	0.04	-0.32, 0.40	0.14	-0.26, 0.55
Past PTSD	-0.42 *	-0.78, -0.06	-0.31	-0.69, 0.07
Log Physical activity counts [a]	-0.06 **	-0.07, -0.06	-0.06 **	-0.07, -0.06

Note: N=106

[a] Log LF-HRV, PCL scores, and Log physical activity counts were standardized to mean of 0 and SD of 1

[b] No PTSD is the referent group

** $p < 0.0001$; * $p < 0.05$

[†] Adjusted for Beck Depression Score, Baecke physical activity score, Age, Hypertension, Smoking, LDL cholesterol, BMI, diabetes, previous cardiovascular disease

Abbreviations: LF-HRV – Low Frequency Heart Rate Variability; PCL – PTSD Checklist; PTSD – Post Traumatic Stress Disorder; CI – Confidence Interval

Table 3. Unadjusted and Adjusted Between-pair and Within-pair Associations of PTSD symptoms, PTSD diagnosis, and Log physical activity with Low Frequency Heart Rate Variability

Dependent Variable	Association with log LF-HRV [a]			
	Unadjusted		Adjusted [†]	
	$\hat{\beta}$	95% CI	$\hat{\beta}$	95% CI
Between-pair effects				
PCL score [a]	-0.02	-0.03, 0.02	0.10	-0.08, 0.29
PTSD diagnosis	-0.08	-0.29, 0.13	-0.15	-0.49, 0.19
Log Physical activity counts [a]	-0.37 *	-0.70, -0.05	-0.49 *	-0.82, -0.17
Within-pair effects				
PCL score [a]	-0.03 **	-0.03, -0.02	-0.03 **	-0.03, -0.02
PTSD diagnosis	-0.002	-0.31, 0.30	-0.06	-0.35, 0.23
Log Physical activity counts [a]	-0.06 **	-0.07, -0.06	-0.06 **	-0.07, -0.06

Note: N=106

[a] Log LF-HRV, PCL scores, and Log physical activity counts were standardized to mean of 0 and SD of 1

[†] Adjusted for Beck Depression Score, Baecke physical activity score, Age, Hypertension, Smoking, LDL cholesterol, BMI, diabetes, previous cardiovascular disease

Abbreviations: LF-HRV – Low Frequency Heart Rate Variability; PCL – PTSD Checklist; PTSD – Post Traumatic Stress Disorder; CI – Confidence Interval

** $p < 0.0001$; * $p < 0.05$

Chapter III: Summary

Post Traumatic Stress Disorder (PTSD) can develop if a person is exposed to a traumatic event and is found to be more prevalent in women compared to men. PTSD and its symptoms are associated with poorer quality of life, and patients often find the disorder to impact their personal and professional relationships. While PTSD is being commonly treated using psychotherapy and trauma-focused therapy, there is growing interest in prevention methods by improving resilience especially among high risk groups such as military personnel and first responders. In addition, there is extensive research to improve pharmacologic methods of treating PTSD.

A significant association between PTSD symptoms severity and reduced Heart Rate Variability found in this analysis indicates an impaired autonomic regulation that is independent of diagnosis of chronic PTSD. Considering that PTSD symptoms can fluctuate over the course of time, similar to several other stress condition, the results of this study places an added importance to alleviate the severity of symptoms to potentially improve health outcomes. This could be done through methods that directly address causes of PTSD, similar to the psychotherapy methods discussed, or by improving autonomic flexibility. Autonomic nervous system functions independent of conscious awareness and some traditional methods of improving autonomic flexibility include breathing techniques, mindfulness, and meditation. Biofeedback has found to be useful in regulating heart rate variability and is a potential commercial treatment option to alleviate stress related autonomic dysregulation.