Received: 12 July 2019 | Revised: 19 November 2019 | Accepted: 24 November 2019

DOI: 10.1111/psyp.13514

ORIGINAL ARTICLE

PSYCHOPHYSIOLOGY SPR WILEY

The relationship of trauma exposure to heart rate variability during wake and sleep in midlife women

Rebecca C. Thurston[1,2,3] | **Mary Y. Carson**[3] | **Karestan C. Koenen**[4] | **Yuefang Chang**[5] | **Karen A. Matthews**[1,2,3] | **Roland von Känel**[6] | **J. Richard Jennings**[1,3]

[1]Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania

[2]Department of Epidemiology, University of Pittsburgh Graduate School of Public Health, Pittsburgh, Pennsylvania

[3]Department of Psychology, University of Pittsburgh, Pittsburgh, Pennsylvania

[4]Department of Epidemiology, Harvard T. H. Chan School of Public Health, Boston, Massachusetts

[5]Department of Neurosurgery, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania

[6]Department of Consultation-Liaison Psychiatry and Psychosomatic Medicine, University Hospital Zurich, University of Zurich, Zurich, Switzerland

Correspondence
Rebecca C. Thurston, Department of Psychiatry, University of Pittsburgh School of Medicine, 3811 O'Hara St, Pittsburgh, PA 15213.
Email: thurstonrc@upmc.edu

Funding information
National Heart, Lung, and Blood Institute, Grant/Award Number: K24HL123565 and R01HL105647; National Institutes of Health, Grant/Award Number: UL1TR000005

Abstract

Traumatic experiences are common and linked to cardiovascular disease (CVD) risk, yet the mechanisms underlying these relationships is less well understood. Few studies have examined trauma exposure and its relation to autonomic influence over cardiac function, a potential pathway linking trauma exposure to CVD risk. Investigating autonomic influence over cardiac function during both wake and sleep is critical, given particular links of sleep autonomic function to cardiovascular health. Among midlife women, we tested whether trauma exposure would be related to lower high frequency heart rate variability (HF-HRV), an index of vagal influence over cardiac function, during wake and sleep. Three hundred and one nonsmoking midlife women completed physical measures, a 24-hr electrocardiogram, actigraphy sleep measurement, and questionnaires about trauma (Brief Trauma Questionnaire), childhood abuse (Child Trauma Questionnaire [CTQ]), mood, demographics, and medical/psychiatric history. Relations between trauma and HF-HRV were assessed in linear mixed effects models adjusting for covariates (age, race, education, body mass index, blood pressure, psychiatric history, medication use, sleep, mood, childhood abuse history). Results indicated that most women had experienced trauma. Any trauma exposure as well as a greater number of traumatic experiences were associated with lower HF-HRV during wake and particularly during sleep. Relations were not accounted for by covariates. Among midlife women, trauma exposure was related to lower HF-HRV during wake and sleep. Trauma may have an important impact on vagal influence over the heart, particularly during sleep. Decreased vagal influence over cardiac function may be a key mechanism by which trauma is associated with CVD risk.

KEYWORDS

cardiovascular, heart rate variability, middle-age adults, social factors, stress

1 | INTRODUCTION

Traumatic experiences, such as sexual assault, car accidents, and exposure to violence, are common among women living in the United States (U.S.). For example, in a sample of U.S. adult women, lifetime exposure to a traumatic event was 69% (Resnick, Kilpatrick, Dansky, Saunders, & Best, 1993). Further, the prevalence of sexual or physical assault is over 50% among U.S. women (Tjaden & Thoennes, 2000). While trauma exposure is a well-known risk factor for poor mental health across a range of mental health conditions (De Graaf, Bijl, Ravelli, Smit, & Vollebergh, 2002; Kilpatrick et al., 2013), emerging literature indicates that trauma may have implications for physical health, including chronic disease risk.

For example, traumatic events are related to the incidence of negative health outcomes such as type II diabetes (Mooy, de Vries, Grootenhuis, Bouter, & Heine, 2000), cardiovascular disease (CVD) (Sumner et al., 2015), and mortality (Ahmadi et al., 2011). However, the physiologic processes that may underlie links between trauma exposures to chronic disease development are not well understood.

One physiologic pathway by which stress exposure is postulated to increase risk for chronic disease is via alterations in the autonomic nervous system, and particularly vagal withdrawal over cardiac function, which has been linked to chronic conditions such as hypertension, CVD, and obesity (Hillebrand et al., 2013; Thayer, Yamamoto, & Brosschot, 2010). One measure of vagal influence over heart rate is electrocardiogram (ECG)-assessed high frequency heart rate variability (HF-HRV). Several studies have found associations between lower HF-HRV, particularly during sleep, and poor health outcomes (Jarczok, Li, Mauss, Fischer, & Thayer, 2013; Vanoli et al., 1995), although few studies measured HF-HRV during both wake and sleep. Further, some limited data has found a relation between trauma exposure or trauma symptoms and heart rate variability (HRV) (Buckley et al., 2012; Fagundes et al., 2018). However, in other studies this association did not persist over time (e.g., van Ockenburg, 2014). Existing work has key limitations, including a focus on highly specific samples (e.g., bereaved older adults, military veterans) (Dennis et al., 2017; Fagundes et al., 2018), single types of traumatic exposures considered (Buckley et al., 2012; Fagundes et al., 2018), laboratory measurements of HRV during waking hours only (Blechert, Michael, Grossman, Lajtman, & Wilhelm, 2007; Fagundes et al., 2018; van Ockenburg, 2014), and failing to control for factors that may influence HRV (e.g., age, smoking, medication usage) (Norte et al., 2013). Thus, whether traumatic experiences are related to reduced HF-HRV remains an open question.

Several factors are important to consider in relationships between trauma exposure and HRV. Sleep is often disrupted among those exposed to trauma (Kim & Dimsdale, 2007), and poor sleep is linked to lower nocturnal HRV (Stein & Pu, 2012). Vagal influence over cardiac function predominates during the night (Stein & Pu, 2012), and lower nocturnal HRV is particularly predictive of cardiovascular health (Laborde, Mosley, & Thayer, 2017). Thus, considering the role of sleep in any trauma-HRV relationships is critical. Second, childhood abuse can place individuals at increased risk for a range of traumatic experiences over their lifetime (Widom, Czaja, & Dutton, 2008). Notably, childhood abuse has previously been linked to lower HRV (Dale et al., 2009; Stone, Amole, Cyranowski, & Swartz, 2018). Thus, considering the role of childhood abuse in lifetime trauma-HRV relationships is important.

In a well-characterized cohort of midlife women who reported their trauma exposure and underwent 24 hr of ECG monitoring during wake and sleep, we had the opportunity to examine the relation between trauma exposure and HRV. We tested our primary hypothesis that the presence of or a greater number of trauma exposures would be related to lower HF-HRV during both wake and sleep. In exploratory models, we considered individual trauma exposures in relation to HF-HRV, any synergistic relationships of childhood abuse and lifetime trauma exposure in relation to HF-HRV, and a range of potential covariates and confounders in trauma-HRV relationships, including sleep.

2 | METHOD

2.1 | Study sample

Study questions were addressed among women recruited for a study on menopause and cardiovascular health (Thurston et al., 2016). The study sample included 304 women between the ages of 40 and 60. All women were late perimenopausal and postmenopausal (Harlow et al., 2012) and had ≥ 17 hr of valid ECG data. Exclusion criteria included hysterectomy and/or oophorectomy; current smoking; reported heart disease, stroke, or arrhythmia; pregnancy; use of oral or transdermal estrogen or progesterone, gabapentin, insulin, beta blockers, calcium channel blockers, SSRI/SNRI antidepressants within the past 3 months; and currently undergoing chemotherapy. Three women were excluded from all analyses due to missing ECG data and two additional women from sleep models only due to missing sleep ECG, yielding $N = 301$ and $N = 299$ women in models of waking and sleeping HRV, respectively. Women were on average 54 years old. Approximately 72% of the sample was non-Hispanic Caucasian, 22% African American, and 5% other race/ethnicities (Table 1).

2.2 | Design and procedures

After a telephone and in-person screening to determine eligibility, participants came to the study laboratories and height and weight were measured, questionnaires administered, and participants equipped with an ambulatory monitor (VU-AMS, VU University Amsterdam, www.vu-ams.nl, Amsterdam, the Netherlands; (de Geus, Willemsen, Klaver, & van Doornen, 1995; van Dijk et al., 2013; Willemsen, De Geus, Klaver, Van Doornen, & Carroll, 1996) a portable device worn in a pouch around the waist that measures a range of physiologic indices including electrocardiography (ECG, for HRV) and impedance cardiography (for respiration). They wore the device for 24 hr as they went about their daily activities. Procedures were approved by the University of

TABLE 1 Subject characteristics ($N = 301$)

Age, *M* (*SD*; range)	54.1 (4.0; 40.0–60.0)
Race/ethnicity, *N* (%)	
White	217 (72.1)
Black	67 (22.3)
Other race/ethnicity	17 (5.7)
Education, *N* (%)	
High school/some college/vocational	127 (42.2)
College	88 (29.2)
Graduate school	86 (28.6)
BMI, *M* (*SD*; range)	29.0 (6.8; 17.6–64.1)
SBP, mmHg, *M* (*SD*; range)	120.0 (14.4; 93.0–177.5)
DBP, mmHg, *M* (*SD*; range)	70.3 (9.1; 50.0–93.5)
Menopause stage, *N* (%)	
Perimenopausal	49 (16.3)
Postmenopausal	252 (83.7)
Medication use, *N* (%)	
Antidepressants	6 (2)
Inhaled beta agonists	14 (4.7)
Sleep time (actigraphy), min, *M* (*SD*; range)	371.9 (66.2; 157.0–663.7)
Sleep quality (Pittsburgh Sleep Quality Index), *M* (*SD*; range)	5.6 (3.0; 1.0–16.0)

Abbreviations: *M* = mean; *SD* = standard deviation; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; mmHg = millimeters of mercury.

Pittsburgh Institutional Review Board. Participants provided written informed consent.

2.3 | Measures

2.3.1 | Lifetime trauma exposure

Trauma exposure was assessed via the Brief Trauma Questionnaire developed for the Nurses Health Study II (Koenen et al., 2009) and adapted from the Brief Trauma Interview (Schnurr, Lunney, Sengupta, & Spiro, 2005; Schnurr, Spiro, Vielhauer, Findler, & Hamblen, 2002). It is a self-report checklist assessing traumatic events, including car accidents, natural disasters, life threatening illness, being beaten or mugged, unwanted sexual contact, death of a child, sexual harassment, threat of injury or violence, or witnessing a severe injury or death occurring over one's lifetime. As reported by Koenen and colleagues, inter-rater reliability for the presence of Criterion A1 trauma exposure according to the DSM-IV was high (average kappa =0.70 [range 0.74–1.00] for all events except illness [0.60]) (Koenen et al., 2009). The primary exposures we considered were the presence of and number of traumatic experiences. Individual exposures were considered in secondary models.

2.3.2 | Childhood abuse

Childhood abuse and neglect were assessed via the 28-item short form of the CTQ, a validated multi-dimensional scale of childhood abuse and neglect experienced at or before the age of 18 (Bernstein et al., 1994; Scher, Stein, Asmundson, McCreary, & Forde, 2001). The CTQ has strong test-retest reliability (0.79–0.86), internal consistency (Chronbach alpha = 0.74–0.95 across subscales in this investigation), and convergent validity with clinical interview (Bernstein et al., 1994; Scher et al., 2001; Walker et al., 1999). Respondents rate each item on a 5-point scale ranging from 1 (never) to 5 (very often true). Items are summed to yield scores on 5 subscales (emotional abuse, physical abuse, emotional neglect, physical neglect, and sexual abuse) with scores ranging from 5 to 25. CTQ short form clinical cut points validated by Walker et al. have sensitivity and specificity at 0.85 or above relative to clinical interview (Walker et al., 1999). If scoring above the clinical threshold on any one subscale, women are considered to have been exposed to any abuse or neglect.

2.3.3 | Heart rate variability

High frequency heart rate variability was calculated via standard methods (Berntson et al., 1997) from electrocardiograph, sampled via the VU-AMS via three Ag/Ag Cl electrodes in a standard 3-lead configuration. HRV was measured over both sleep and wake for 24 hr. The ECG was sampled at 1000 Hz, and each R wave marker was assessed for artifacts by an artifact detection algorithm (VU-AMS.5fs software) and verified by trained coders. Estimates of HRV were conducted using VU-AMS software using the default 4-min sampling frame, permitting resolution of frequencies as low as 0.05 Hz as well as substantial samples of high frequency variability (Berntson et al., 1997). Intervals with ≥ 10% ectopic beats were eliminated. The interbeat interval event series was resampled at 4 Hz excluding artifactual beats, interpolated, and detrended (convoluted with a smoothness prior matrix) to yield a stationary signal on which a discrete Fourier analysis was performed. High frequency band cutoffs were 0.15–0.40 Hz. Sleep versus wake intervals were classified by the sleep diary completed on the days and nights of monitoring. HF-HRV values were averaged by sleep and wake, with sleep/wake HF power values natural log transformed for analysis. LF-HRV, which reflects mixed vagal and sympathetic influences over heart rate (Reyes del Paso, Langewitz, Mulder, van Roon, & Duschek, 2013), was considered in secondary models. Respiration was measured via thoracic impedance, sampled at 1 KHz via 4 Ag/Ag Cl

electrodes (de Geus et al., 1995; Houtveen, Groot, & de Geus, 2006). Use of thoracic impedance to obtain respiration rate is preferable in the ambulatory setting for participant comfort and data quality (Ernst, Litvack, Lozano, Cacioppo, & Berntson, 1999).

2.3.4 | Covariates

Height was measured via fixed stadiometer and weight via balance beam scale, and BMI was calculated as weight (kg)/height (m^2). Systolic and diastolic blood pressures were the average of the second and third of three seated measurements taken via a Dinamap v100. Demographics, medical history, and health behaviors were assessed by questionnaires. Race/ethnicity was determined in response to "How would you describe your primary racial or ethnic group?" Women reported working day shift or night/rotating shifts (classified as yes/no). Medications were self-reported, with antidepressants (e.g., buproprion, tricyclics), medications impacting the autonomic nervous system (inhaled beta agonists), and sleep medications (hypnotics, melatonin, over the counter sleep aids) considered here. Habitual physical activity was assessed via the International Physical Activity Questionnaire (Lee, Macfarlane, Lam, & Stewart, 2011). Depressive symptoms were assessed via the Center for Epidemiologic Studies Depression Scale (Radloff, 1977) and anxiety via the Spielberger State-Trait Anxiety Inventory (Spielberger, 1983).

Sleep was determined via wrist actigraph (Monk et al., 1994), which participants wore for three days. Data were collected with an Actiwatch-2 (Respironics, Inc., Murrysville, PA) in 1-min epochs and analyzed with the Actiware (Version 6.0.1) software program. Sleep diary data for bedtime and rise time were entered for calculation of sleep-wake variables. Actigraphy variables were total sleep time (TST; difference between actigraphy-defined sleep onset and actigraphy-defined final wake time), wake after sleep onset, (WASO; minutes of wakefulness between actigraphy-defined sleep onset time and actigraphy-defined final wake time) and sleep efficiency (percent of time in bed scored as sleep). Women also completed the Pittsburgh Sleep Quality Index of sleep quality (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989).

2.3.5 | Statistical analyses

Univariable relations between exposures and the outcome HF-HRV were examined via *t* tests, ANOVA, and Spearman correlation coefficients. Relations between abuse or trauma exposure and the HF-HRV time series were tested in mixed effects regression models with a random intercept. Primary models considered both any trauma or the sum of trauma exposures (0, 1–2, ≥3) in relation to HF-HRV in separate models. Exploratory models considered each trauma exposure separately to illuminate any one trauma that was particularly potent. Covariates were selected based upon their association with the outcome at $p < .10$. Interactions between sleep/wake statuses were tested; if a significant interaction was apparent, we examined trauma in relation to wake and sleep HF-HRV separately. Child abuse and lifetime trauma were next considered together in the same model, and interactions between child abuse and lifetime trauma in relation to HF-HRV were also tested. In additional exploratory models, additional covariates were considered (respiration rate, sleep quantity and quality, depressive symptoms, anxiety), interactions by race/ethnicity, as well as the additional outcome of LF-HRV. Analyses were performed with SAS v9.4 (SAS Institute, Cary, NC). Models were two-sided, alpha = 0.05.

3 | RESULTS

Most (59%) women had some type of lifetime trauma exposure, and unwanted sexual contact (22%) was the most common traumatic exposure (Table 2). Considering trauma exposures in relation to HF-HRV, any trauma exposure as well as a greater number of traumatic experiences were associated with lower HF-HRV during wake and sleep (Table 3, Figure 1). When exploring individual exposures, the single most potent exposure was the death of a child, associated with lower HF-HRV during both wake and sleep (Table 4). Relationships between trauma exposure and HF-HRV were significantly modified by sleep/wake status (interactions *p's* < 0.01) such that for most exposures, the relation between

TABLE 2 Prevalence of lifetime trauma exposure

	N (%) yes
Serious car or other accident	53 (17.6)
Major natural or man-made disaster	30 (10.0)
Serious/life-threatening illness	19 (6.3)
Attacked, beaten, or mugged	57 (18.9)
Sexual assault	67 (22.3)
Death of child	19 (6.3)
Workplace sexual harassment	58 (19.3)
Serious injury/threat of injury	40 (13.3)
Witness other's serious injury/death	66 (21.9)
Any trauma exposure	179 (59.5)
Number of trauma exposures	
0	122 (40.5)
1–2	123 (40.9)
≥3	56 (18.6)

trauma and HF-HRV appeared stronger during sleep than during wake.

We conducted several exploratory analyses. As reported previously (Thurston et al., 2017), 44% of the women reported some form of childhood abuse, and 14% of women reported a history of childhood sexual abuse. Women with a history of childhood abuse had an over doubling of the likelihood of any adult trauma exposure (*OR* [95%CI] = 2.72 [1.65–4.49], $p < .0001$, adjusted for race and education) and an over six-fold likelihood of three or more trauma exposures (*OR* [95%CI] = 6.41 [3.12–13.18], $p < .0001$, relative to none, adjusted for race and education). Thus, we explored the relation of childhood abuse to HF-HRV, finding that only a history of childhood sexual abuse was related to lower HF-HRV and only during sleep (*b[SE]* = −0.46 [.17], $p = .007$, covariates age, race, BMI, SBP, education, post-traumatic stress disorder [PTSD] history, autonomic medication use, antidepressant use, menopause stage). No other forms of childhood abuse or neglect (i.e., physical abuse, emotional abuse, neglect) were related to HF-HRV (data not shown). A significant interaction between trauma and childhood sexual abuse ($p = .04$) indicated that women with *both* a history of lifetime trauma exposure and sexual abuse had particularly low HF-HRV during sleep when compared to women with *neither* a history of trauma exposure nor childhood sexual abuse (*b[SE]* = −0.55 [0.19], $p = .004$, adjusted for age, race, BMI, education, SBP, PTSD history, beta agonist medication use, antidepressant use, menopause stage).

TABLE 3 Association between trauma exposure and wake and sleep HF-HRV

	HF-HRV wake	HF-HRV sleep
	B (SE)	***B (SE)***
Any trauma exposure	−0.23 (0.11)**	−0.31 (0.12)**
Number of trauma exposures (relative to none)		
1–2	−20 (0.12)*	−0.25 (0.13)**
≥3	−0.31 (0.15)**	−0.46 (0.17)***

$N = 301$.

Note: Adjusted for age, race, body mass index, education, systolic blood pressure, post-traumatic stress disorder history, menopause stage, beta agonist medication use, antidepressant use. Any exposure and number of trauma exposures considered in separate models.

*$p < .10$; **$p < .05$; ***$p < .01$.

We conducted several additional exploratory analyses. As trauma appeared particularly associated with sleep HF-HRV, we considered relationships between trauma exposure (e.g., any trauma, sum of trauma exposures) and sleep HF-HRV controlling for sleep indices, including actigraphic sleep duration (TST), and continuity (WASO, sleep efficiency), or subjective sleep quality (PSQI scores); findings were largely unchanged (data not shown). Further, we conducted all analyses controlling for respiration rate. Findings were unchanged (data not shown). Moreover, given the potentially important role of depression and anxiety in relations between trauma exposure and HF-HRV, we considered depression or anxiety symptoms as covariates. They were not related to HF-HRV and controlling for them in relations between trauma exposure (any trauma, sum of trauma exposures) and HF-HRV did not change study findings (data not shown). As seven women endorsed a history of PTSD, we repeated analyses excluding these women, and conclusions were unchanged (data not shown). We repeated models of trauma exposure (any trauma, sum of trauma exposures) in relation to HF-HRV excluding

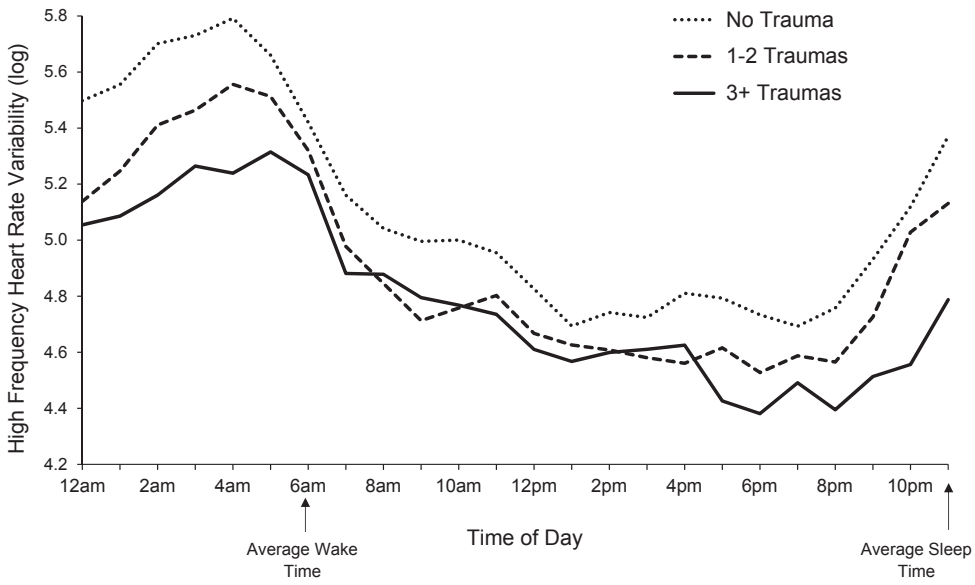

FIGURE 1 HF-HRV over 24 hours by number of trauma exposures. Means adjusted for age, race, body mass index, education, systolic blood pressure, post-traumatic stress disorder history, menopause stage, beta agonist medication use, antidepressant use

TABLE 4 Association between individual trauma exposures and wake and sleep HF-HRV

	HF-HRV wake	HF-HRV sleep
	B (SE)	*B (SE)*
Serious car or other accident	−0.23 (0.14)	−0.33 (0.16)**
Major natural or man-made disaster	0.08 (0.18)	−0.05 (0.20)
Serious/life-threatening illness	0.10 (0.22)	0.28 (0.24)
Attacked, beaten, or mugged	−0.28 (0.14)**	−0.43 (0.15)***
Sexual assault	−0.11 (0.13)	−0.12 (0.14)
Death of child	−0.76 (0.21)***	−0.62 (0.24)***
Workplace sexual harassment	−0.20 (0.14)	−0.15 (0.15)
Serious injury/threat of injury	−0.09 (0.16)	−0.36 (0.18)**
Witness other's serious injury/death	−0.13 (0.13)	−0.31 (0.15)**

$N = 301$.

Note: Adjusted for age, race, body mass index, education, systolic blood pressure, post-traumatic stress disorder history, menopause stage, beta agonist medication use, antidepressant use. Each exposure considered in a separate model.

*$p < .10$; **$p < .05$; ***$p < .01$.

the trauma item related to serious illness; findings remained (data not shown). In additional models, we considered trauma exposure in relation to LF-HRV, which may reflect sympathetic contributions, yet at rest is primarily of vagal origin (Reyes del Paso et al., 2013). A broadly similar pattern of results was observed for relations between trauma exposure and LF-HRV as for relations between lifetime trauma exposure and HF-HRV (data not shown).

4 | DISCUSSION

Among this sample of midlife women, greater lifetime trauma exposure was related to lower vagal influence over cardiac function. Associations were most pronounced during sleep. Moreover, relations were not explained by a range of potential confounders or covariates, including actigraphy-assessed sleep indices. We additionally found that childhood sexual abuse was related to lower HF-HRV during sleep, with women, with both a history of lifetime trauma exposure and childhood sexual abuse showing particularly low sleep HF-HRV. These findings point to the importance of trauma-associated disruption in vagal influences over the heart and suggest a potentially important mechanism by which trauma is associated with CVD risk in women.

Our findings contribute importantly to the extant literature on relations of trauma to autonomic influences on the heart. While some evidence links trauma exposure to HRV, limitations of existing research include a focus on highly specific samples (e.g., bereaved older adults, military veterans) (Dennis et al., 2017; Fagundes et al., 2018), single categories of traumatic exposures (Buckley et al., 2012; Fagundes et al., 2018), laboratory measurements of HRV during waking hours only (Blechert et al., 2007; Fagundes et al., 2018; van Ockenburg, 2014), and failing to control for key factors that may influence HRV (Norte et al., 2013), This study included a large sample of nonsmoking women who underwent 24-hr ECG during both wake and sleep and who were free of clinical CVD. A range of traumatic experiences were assessed and considered. We observed clear and consistent relations between lifetime trauma exposures and reduced vagal influence of the heart. Whereas some exposures (e.g., death of a child [Rostila, Saarela, & Kawachi, 2012]) appeared to be particularly potent exposures, a range of trauma exposures were related to lower HF-HRV. Thus, the general experience of traumatic events, rather than solely a single trauma, appear to be important to HF-HRV. Findings were independent of a range of confounding factors and were somewhat more pronounced during sleep. These findings underscore the importance of trauma exposure, and particularly multiple traumatic exposures, for cardiac vagal control in women.

A greater lifetime trauma exposure burden is most common among women with a history of childhood abuse, often reflecting a lifetime of adversity. Indeed, we found that women with a history of childhood abuse had a greater likelihood of traumatic events over their lifetime. Further, women with a history of childhood sexual abuse had lower sleep HF-HRV. Why only childhood sexual abuse, and not other forms of childhood abuse, were related to HF-HRV is not entirely clear. However, a similar pattern of findings for sexual abuse has been noted in work with other CVD risk indicators (Goodwin & Stein, 2004; Rich-Edwards et al., 2012; Thurston et al., 2014). However, this finding is not universal, with some other work showing associations for emotional or physical abuse with HRV or CVD risk indicators (Stone et al., 2018; Thurston et al., 2017). Notably, childhood sexual abuse may be more precisely recalled than other forms of abuse, may be particularly invasive, or may be a marker for the severity of abuse (Molnar, Buka, & Kessler, 2001; Widom & Morris, 1997). When considered together, adult trauma exposure showed more consistent relations to HF-HRV than childhood abuse, potentially reflecting the greater proximity in time of the adult trauma to the HF-HRV assessment. However, a synergy between childhood and adult trauma was observed, such that women with a history of both childhood sexual abuse and adult trauma exposure had particularly low sleep HF-HRV.

Future work should continue to consider adult and childhood trauma exposure both in relation to autonomic nervous system function.

Although relationships between lifetime trauma exposure and HF-HRV were observed for HF-HRV during both wake and sleep, findings were most pronounced for sleep HF-HRV. Notably, vagal influence over cardiac function predominates during the night (Stein & Pu, 2012), and sleep HRV can be more predictive of cardiovascular health than waking values (Laborde et al., 2017). Although trauma has been linked to poorer sleep (Kim & Dimsdale, 2007), findings were not explained by objectively assessed sleep time, sleep continuity, or even subjective sleep quality. Our findings may suggest a particular susceptibility to disruptions in the nervous system during sleep—a period of repair and restoration. We controlled for PTSD, although did not assess specific symptoms, such as nightmares. The role of PTSD symptoms in these relations should be ascertained in future work. However, our findings indicate important relationships between trauma and nocturnal physiology independent of key sleep characteristics that require further elucidation in the next steps of this work.

The mechanisms that may link trauma to the autonomic nervous system are likely multiple. The autonomic nervous system is well-documented to be sensitive to psychological factors, including symptoms of depression and anxiety. We assessed depression and anxiety symptoms, and these factors did not explain relations between trauma and HF-HRV. Obesity is a common sequela of child abuse (Midei, Matthews, & Bromberger, 2010), and linked to lower HF-HRV (Karason, Molgaard, Wikstrand, & Sjostrom, 1999), yet adiposity did not explain relationships between trauma and HF-HRV. Further, physical activity can increase HF-HRV (Earnest, Lavie, Blair, & Church, 2008). We considered physical activity as a covariate, yet it was not related to HF-HRV, and thus was not included in final models. Future work should consider the role of perseverative cognition in these relationships, as it can perpetuate negative affect after a traumatic event (Zetsche, Ehring, & Ehlers, 2009) and is associated with prolonged reductions in HRV (Ottaviani et al., 2016) including during sleep (Brosschot, Van Dijk, & Thayer, 2007). Finally, neural mechanisms, such as alterations in amygdala structure or function, might be considered in trauma—HRV relations in future work (Thayer, Ahs, Fredrikson, Sollers, & Wager, 2012; Williams et al., 2006).

This study had limitations. Trauma exposures were recalled. These reports may be subject to influences of memory and reporting, particularly underreporting (Widom & Shepard, 1996). We assessed a range of lifetime exposures with an adapted measure used in major cohort studies (NHS II), yet not all possible exposures were assessed. We did not inquire about the timing or duration of the trauma exposures, and therefore their proximity to the HRV assessment or chronicity could not be determined. Multiple potential confounders were assessed and considered, yet residual confounding is a consideration in observational studies. Key psychiatric symptoms were measured and controlled, yet a full diagnostic clinical interview was not performed. Men were not included; therefore, conclusions might not extend to men.

This study had several strengths. Study aims were tested in a well-characterized sample of non-smoking midlife women free of clinical CVD. HRV was assessed with state-of-the-art methods for over 24 hr, including during both wake and sleep, as women went about their daily activities. Child abuse and sleep were assessed and considered here. Multiple possible confounders, modifiers, and mechanisms were considered.

We found that lifetime trauma exposure was related to lower HF-HRV at midlife among women. Given links between reduced vagal influence over the heart and cardiovascular health, these findings point to a potential pathway by which trauma exposure may be associated with greater chronic disease risk later in life. These findings further underscore the importance of assessment of trauma history in routine clinical care. They also point to the potential importance of preventing trauma exposure or mitigating its sequelae for CVD risk reduction.

CONFLICT OF INTEREST

Dr. Thurston consults for Astellas Pharma, Pfizer, and Procter and Gamble. No other authors have conflicts to declare.

ORCID

Rebecca C. Thurston https://orcid.org/0000-0001-6580-1202

REFERENCES

Ahmadi, N., Hajsadeghi, F., Mirshkarlo, H. B., Budoff, M., Yehuda, R., & Ebrahimi, R. (2011). Post-traumatic stress disorder, coronary atherosclerosis, and mortality. *American Journal of Cardiology*, *108*(1), 29–33. https://doi.org/10.1016/j.amjcard.2011.02.340

Bernstein, D. P., Fink, L., Handelsman, L., Foote, J., Lovejoy, M., Wenzel, K., … Ruggiero, J. (1994). Initial reliability and validity of a new retrospective measure of child abuse and neglect. *American Journal of Psychiatry*, *151*(8), 1132–1136. https://doi.org/10.1176/ajp.151.8.1132

Berntson, G. G., Thomas bigger, J., Eckberg, D. L., Grossman, P., Kaufmann, P. G., Malik, M., … Van der molen, M. W. (1997). Heart rate variability: Origins, methods, and interpretive caveats. *Psychophysiology*, *34*(6), 623–648. https://doi.org/10.1111/j.1469-8986.1997.tb02140.x

Blechert, J., Michael, T., Grossman, P., Lajtman, M., & Wilhelm, F. H. (2007). Autonomic and respiratory characteristics of posttraumatic stress disorder and panic disorder. *Psychosomatic Medicine*, *69*(9), 935–943. https://doi.org/10.1097/PSY.0b013e31815a8f6b

Brosschot, J. F., Van Dijk, E., & Thayer, J. F. (2007). Daily worry is related to low heart rate variability during waking and the subsequent nocturnal sleep period. *International Journal of Psychophysiology*, *63*(1), 39–47. https://doi.org/10.1016/j.ijpsycho.2006.07.016

Buckley, T., Stannard, A., Bartrop, R., McKinley, S., Ward, C., Mihailidou, A. S., … Tofler, G. (2012). Effect of early bereavement on heart rate and heart rate variability. *American Journal of Cardiology*, *110*(9), 1378–1383. https://doi.org/10.1016/j.amjcard.2012.06.045

Buysse, D. J., Reynolds, C. F. 3rd, Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The pittsburgh sleep quality index: A new instrument for psychiatric practice and research. *Psychiatry Research*, *28*(2), 193–213. https://doi.org/10.1016/0165-1781(89)90047-4

Dale, L. P., Carroll, L. E., Galen, G., Hayes, J. A., Webb, K. W., & Porges, S. W. (2009). Abuse history is related to autonomic regulation to mild exercise and psychological wellbeing. *Applied Psychophysiology and Biofeedback*, *34*(4), 299–308. https://doi.org/10.1007/s10484-009-9111-4

de Geus, E. J., Willemsen, G. H., Klaver, C. H., & van Doornen, L. J. (1995). Ambulatory measurement of respiratory sinus arrhythmia and respiration rate. *Biological Psychology*, *41*(3), 205–227. https://doi.org/10.1016/0301-0511(95)05137-6

De Graaf, R., Bijl, R. V., Ravelli, A., Smit, F., & Vollebergh, W. A. (2002). Predictors of first incidence of dsm-iii-r psychiatric disorders in the general population: Findings from the netherlands mental health survey and incidence study. *Acta Psychiatrica Scandinavica*, *106*(4), 303–313. https://doi.org/10.1034/j.1600-0447.2002.01397.x

Dennis, P. A., Kimbrel, N. A., Sherwood, A., Calhoun, P. S., Watkins, L. L., Dennis, M. F., & Beckham, J. C. (2017). Trauma and autonomic dysregulation: Episodic-versus systemic-negative affect underlying cardiovascular risk in posttraumatic stress disorder. *Psychosomatic Medicine*, *79*(5), 496–505. https://doi.org/10.1097/psy.0000000000000438

Earnest, C. P., Lavie, C. J., Blair, S. N., & Church, T. S. (2008). Heart rate variability characteristics in sedentary postmenopausal women following six months of exercise training: The drew study. *PLoS ONE*, *3*(6), e2288. https://doi.org/10.1371/journal.pone.0002288

Ernst, J. M., Litvack, D. A., Lozano, D. L., Cacioppo, J. T., & Berntson, G. G. (1999). Impedance pneumography: Noise as signal in impedance cardiography. *Psychophysiology*, *36*(3), 333–338. https://doi.org/10.1017/s0048577299981003

Fagundes, C. P., Murdock, K. W., LeRoy, A., Baameur, F., Thayer, J. F., & Heijnen, C. (2018). Spousal bereavement is associated with more pronounced ex vivo cytokine production and lower heart rate variability: Mechanisms underlying cardiovascular risk? *Psychoneuroendocrinology*, *93*, 65–71. https://doi.org/10.1016/j.psyneuen.2018.04.010

Goodwin, R. D., & Stein, M. B. (2004). Association between childhood trauma and physical disorders among adults in the united states. *Psychological Medicine*, *34*(3), 509–520. https://doi.org/10.1017/s003329170300134x

Harlow, S. D., Gass, M., Hall, J. E., Lobo, R., Maki, P., Rebar, R. W., … de Villiers, T. J. (2012). Executive summary of the stages of reproductive aging workshop + 10: Addressing the unfinished agenda of staging reproductive aging. *Journal of Clinical Endocrinology and Metabolism*, *97*(4), 1159–1168. https://doi.org/10.1210/jc.2011-3362

Hillebrand, S., Gast, K. B., de Mutsert, R., Swenne, C. A., Jukema, J. W., Middeldorp, S., … Dekkers, O. M. (2013). Heart rate variability and first cardiovascular event in populations without known cardiovascular disease: Meta-analysis and dose-response meta-regression. *Europace: European Pacing, Arrhythmias, and Cardiac Electrophysiology*, *15*(5), 742–749. https://doi.org/10.1093/europace/eus341

Houtveen, J. H., Groot, P. F., & de Geus, E. J. (2006). Validation of the thoracic impedance derived respiratory signal using multilevel analysis. *International Journal of Psychophysiology*, *59*(2), 97–106. https://doi.org/10.1016/j.ijpsycho.2005.02.003

Jarczok, M. N., Li, J., Mauss, D., Fischer, J. E., & Thayer, J. F. (2013). Heart rate variability is associated with glycemic status after controlling for components of the metabolic syndrome. *International Journal of Cardiology*, *167*(3), 855–861. https://doi.org/10.1016/j.ijcard.2012.02.002

Karason, K., Molgaard, H., Wikstrand, J., & Sjostrom, L. (1999). Heart rate variability in obesity and the effect of weight loss. *American Journal of Cardiology*, *83*(8), 1242–1247. https://doi.org/10.1016/s0002-9149(99)00066-1

Kilpatrick, D. G., Resnick, H. S., Milanak, M. E., Miller, M. W., Keyes, K. M., & Friedman, M. J. (2013). National estimates of exposure to traumatic events and ptsd prevalence using dsm-iv and dsm-5 criteria. *Journal of Traumatic Stress*, *26*(5), 537–547. https://doi.org/10.1002/jts.21848

Kim, E., & Dimsdale, J. E. (2007). The effect of psychosocial stress on sleep: A review of polysomnographic evidence. *Behavioral Sleep Medicine*, *5*(4), 256–278. https://doi.org/10.1080/15402000701557383

Koenen, K. C., De Vivo, I., Rich-Edwards, J., Smoller, J. W., Wright, R. J., & Purcell, S. M. (2009). Protocol for investigating genetic determinants of posttraumatic stress disorder in women from the nurses' health study ii. *BMC Psychiatry*, *9*, 29. https://doi.org/10.1186/1471-244X-9-29

Laborde, S., Mosley, E., & Thayer, J. F. (2017). Heart rate variability and cardiac vagal tone in psychophysiological research – Recommendations for experiment planning, data analysis, and data reporting. *Frontiers in Psychology*, *8*(213), 1–18. https://doi.org/10.3389/fpsyg.2017.00213

Lee, P. H., Macfarlane, D. J., Lam, T. H., & Stewart, S. M. (2011). Validity of the international physical activity questionnaire short form (ipaq-sf): A systematic review. *International Journal of Behavioral Nutrition and Physical Activity*, *8*, 115. https://doi.org/10.1186/1479-5868-8-115

Midei, A. J., Matthews, K. A., & Bromberger, J. T. (2010). Childhood abuse is associated with adiposity in midlife women: Possible pathways through trait anger and reproductive hormones. *Psychosomatic Medicine*, *72*(2), 215–223. https://doi.org/10.1097/PSY.0b013e3181cb5c24

Molnar, B. E., Buka, S. L., & Kessler, R. C. (2001). Child sexual abuse and subsequent psychopathology: Results from the national comorbidity survey. *American Journal of Public Health*, *91*(5), 753–760. https://doi.org/10.2105/ajph.91.5.753

Monk, T. H., Reynolds, C. F., Kupfer, D. J., Buysse, D. J., Coble, P. A., Hayes, A. J., … Ritenour, A. M. (1994). The pittsburgh sleep diary. *Journal of Sleep Research*, *3*(2), 111–120. https://doi.org/10.1111/j.1365-2869.1994.tb00114.x

Mooy, J. M., de Vries, H., Grootenhuis, P. A., Bouter, L. M., & Heine, R. J. (2000). Major stressful life events in relation to prevalence of undetected type 2 diabetes: The hoorn study. *Diabetes Care*, *23*(2), 197–201. https://doi.org/10.2337/diacare.23.2.197

Norte, C. E., Souza, G. G., Vilete, L., Marques-Portella, C., Coutinho, E. S., Figueira, I., & Volchan, E. (2013). They know their trauma by heart: An assessment of psychophysiological failure to recover in ptsd. *Journal of Affective Disorders*, *150*(1), 136–141. https://doi.org/10.1016/j.jad.2012.11.039

Ottaviani, C., Thayer, J. F., Verkuil, B., Lonigro, A., Medea, B., Couyoumdjian, A., & Brosschot, J. F. (2016). Physiological concomitants of perseverative cognition: A systematic review and meta-analysis. *Psychological Bulletin*, *142*(3), 231–259. https://doi.org/10.1037/bul0000036

Radloff, L. S. (1977). The ces-d scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement*, *1*(3), 385–401. https://doi.org/10.1177/014662167700100306

Resnick, H. S., Kilpatrick, D. G., Dansky, B. S., Saunders, B. E., & Best, C. L. (1993). Prevalence of civilian trauma and posttraumatic stress disorder in a representative national sample of women. *Journal of Consulting and Clinical Psychology*, *61*(6), 984–991. https://doi.org/10.1037/0022-006X.61.6.984

Reyes del Paso, G. A., Langewitz, W., Mulder, L. J., van Roon, A., & Duschek, S. (2013). The utility of low frequency heart rate variability as an index of sympathetic cardiac tone: A review with emphasis on a reanalysis of previous studies. *Psychophysiology*, *50*(5), 477–487. https://doi.org/10.1111/psyp.12027

Rich-Edwards, J. W., Mason, S., Rexrode, K., Spiegelman, D., Hibert, E., Kawachi, I., … Wright, R. J. (2012). Physical and sexual abuse in childhood as predictors of early-onset cardiovascular events in women. *Circulation*, *126*(8), 920–927. https://doi.org/10.1161/CIRCULATIONAHA.111.076877

Rostila, M., Saarela, J., & Kawachi, I. (2012). Mortality in parents following the death of a child: A nationwide follow-up study from sweden. *Journal of Epidemiology and Community Health*, *66*(10), 927–933. https://doi.org/10.1136/jech-2011-200339

Scher, C. D., Stein, M. B., Asmundson, G. J., McCreary, D. R., & Forde, D. R. (2001). The childhood trauma questionnaire in a community sample: Psychometric properties and normative data. *Journal of Traumatic Stress*, *14*(4), 843–857. https://doi.org/10.1023/A:1013058625719

Schnurr, P. P., Lunney, C. A., Sengupta, A., & Spiro, A. III (2005). A longitudinal study of retirement in older male veterans. *Journal of Consulting and Clinical Psychology*, *73*(3), 561–566. https://doi.org/10.1037/0022-006X.73.3.561

Schnurr, P. P., Spiro, A. I., Vielhauer, M. J., Findler, M. N., & Hamblen, J. L. (2002). Trauma in the lives of older men: Findings from the normative aging study. *Journal of Clinical Geropsychology*, *8*, 175–187. https://doi.org/10.1023/A:1015992110544.

Spielberger, C. D. (1983). *Manual for the state-trait anxiety inventory*. Palo Alto: Consulting Psychologists Press.

Stein, P. K., & Pu, Y. (2012). Heart rate variability, sleep and sleep disorders. *Sleep Medicine Reviews*, *16*(1), 47–66. https://doi.org/10.1016/j.smrv.2011.02.005

Stone, L. B., Amole, M. C., Cyranowski, J. M., & Swartz, H. A. (2018). History of childhood emotional abuse predicts lower resting-state high-frequency heart rate variability in depressed women. *Psychiatry Research*, *269*, 681–687. https://doi.org/10.1016/j.psychres.2018.08.106

Sumner, J. A., Kubzansky, L. D., Elkind, M. S. V., Roberts, A. L., Agnew-Blais, J., Chen, Q., … Koenen, K. C. (2015). Trauma exposure and posttraumatic stress disorder symptoms predict onset of cardiovascular events in women. *Circulation*, *132*(4), 251–259. https://doi.org/10.1161/circulationaha.114.014492

Thayer, J. F., Ahs, F., Fredrikson, M., Sollers, J. J. 3rd, & Wager, T. D. (2012). A meta-analysis of heart rate variability and neuroimaging studies: Implications for heart rate variability as a marker of stress and health. *Neuroscience and Biobehavioral Reviews*, *36*(2), 747–756. https://doi.org/10.1016/j.neubiorev.2011.11.009

Thayer, J. F., Yamamoto, S. S., & Brosschot, J. F. (2010). The relationship of autonomic imbalance, heart rate variability and cardiovascular disease risk factors. *International Journal of Cardiology*, *141*(2), 122–131. https://doi.org/10.1016/j.ijcard.2009.09.543

Thurston, R. C., Chang, Y., Barinas-Mitchell, E., Jennings, J. R., Landsittel, D. P., Santoro, N., … Matthews, K. A. (2016). Menopausal hot flashes and carotid intima media thickness among midlife women. *Stroke*, *47*(12), 2910–2915. https://doi.org/10.1161/strokeaha.116.014674

Thurston, R. C., Chang, Y., Barinas-Mitchell, E., von Känel, R., Jennings, J. R., Santoro, N., … Matthews, K. A. (2017). Child abuse and neglect and subclinical cardiovascular disease among midlife women. *Psychosomatic Medicine*, *79*(4), 441–449. https://doi.org/10.1097/PSY.0000000000000400

Thurston, R. C., Chang, Y., Derby, C. A., Bromberger, J. T., Harlow, S. D., Janssen, I., & Matthews, K. A. (2014). Abuse and subclinical cardiovascular disease among midlife women: Findings from the study of women's health across the nation. *Stroke*, *45*(8), 2246–2251. https://doi.org/10.1161/STROKEAHA.114.005928

Tjaden, P., & Thoennes, N. (2000). *Full report of the prevalence, incidence, and consequences of violence against women: Findings from the national violence against women survey*. Rockville, MD: National Criminal Justice Reference Service.

van Dijk, A. E., van Lien, R., van Eijsden, M., Gemke, R. J., Vrijkotte, T. G., & de Geus, E. J. (2013). Measuring cardiac autonomic nervous system (ans) activity in children. *Journal of Visualized Experiments*, *74*, e50073. https://doi.org/10.3791/50073

van Ockenburg, S. L. (2014). Psychological states and physical fates: Studying the role of psychosocial stress in the etiology of cardiovascular disease: A nomotheric versus an idiographic approach. *Acta Psychiatrica Scandinavica*, *131*(1), 40–50.

Vanoli, E., Adamson, P. B., Ba, L., Pinna, G. D., Lazzara, R., & Orr, W. C. (1995). Heart rate variability during specific sleep stages. A comparison of healthy subjects with patients after myocardial infarction. *Circulation*, *91*(7), 1918–1922. https://doi.org/10.1161/01.cir.91.7.1918

Walker, E. A., Gelfand, A., Katon, W. J., Koss, M. P., Von Korff, M., Bernstein, D., & Russo, J. (1999). Adult health status of women with histories of childhood abuse and neglect. *American Journal of Medicine*, *107*(4), 332–339. https://doi.org/10.1016/s0002-9343(99)00235-1

Widom, C. S., Czaja, S. J., & Dutton, M. A. (2008). Childhood victimization and lifetime revictimization. *Child Abuse and Neglect*, *32*(8), 785–796. https://doi.org/10.1016/j.chiabu.2007.12.006

Widom, C. S., & Morris, S. (1997). Accuracy of adult recollections of childhood victimization: Part 2. *Childhood Sexual Abuse. Psychological Assessment*, *9*(1), 34–46.

Widom, C. S., & Shepard, R. L. (1996). Accuracy of adult recollections of childhood victimization: Part I. *Childhood Physical Abuse. Psychological Assessment*, *8*(4), 412–421.

Willemsen, G. H., De Geus, E. J., Klaver, C. H., Van Doornen, L. J., & Carroll, D. (1996). Ambulatory monitoring of the impedance cardiogram. *Psychophysiology*, *33*(2), 184–193. https://doi.org/10.1111/j.1469-8986.1996.tb02122.x

Williams, L. M., Kemp, A. H., Felmingham, K., Barton, M., Olivieri, G., Peduto, A., … Bryant, R. A. (2006). Trauma modulates amygdala and medial prefrontal responses to consciously attended fear.

NeuroImage, *29*(2), 347–357. https://doi.org/10.1016/j.neuroimage.2005.03.047

Zetsche, U., Ehring, T., & Ehlers, A. (2009). The effects of rumination on mood and intrusive memories after exposure to traumatic material: An experimental study. *Journal of Behavior Therapy and Experimental Psychiatry*, *40*(4), 499–514. https://doi.org/10.1016/j.jbtep.2009.07.001

How to cite this article: Thurston RC, Carson MY, Koenen KC, et al. The relationship of trauma exposure to heart rate variability during wake and sleep in midlife women. *Psychophysiology*. 2020;57:e13514. https://doi.org/10.1111/psyp.13514