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The association of PTSD with clinic and ambulatory blood pressure in healthy adults

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Abstract

Objective—Posttraumatic stress disorder (PTSD) is associated with incident cardiovascular risk. We tested the association of PTSD with clinic and ambulatory blood pressure (ABP) in a sample of healthy participants, and test ABP reactivity to anxiety as a mechanism by which PTSD may influence BP.

Methods—Participants were originally enrolled during workplace BP screenings at 3 sites; approximately 6 years (SD=1.0) later, they completed 9 clinic BP assessments over 3 visits, 1 week apart. Prior to the 3rd visit, participants were screened for PTSD (33 on the PTSD Checklist-Civilian) and depression (Beck Depression Inventory), then completed 24-hour ABP monitoring with electronic diary assessment of anxiety (0–100) at each awake reading.

Results—Of 440 participants, 92 (21%) screened positive for PTSD. In regression models adjusted for depression and demographic and clinical variables, PTSD was associated with greater mean systolic BP [3.8 mmHg clinic (95% CI: 1.1 to 6.5, $p=0.006$), 3.0 mmHg awake ABP (95% CI: 0.1 to 5.9, $p=0.04$), and a non-significant 2.1 mmHg ABP during sleep, (95% CI: –1.0 to 5.1, $p=0.18$)]. PTSD was associated with greater 24-hour median anxiety ($p<0.001$), and changes in anxiety were positively associated with concurrent systolic ABP ($p<0.001$). ABP reactivity to anxiety was greater in participants with PTSD, which partially explained the association of PTSD with ABP.

Conclusions—PTSD is associated with greater systolic BP, partly because of greater anxiety, and systolic BP reactivity to anxiety, throughout the day. Daily anxiety and related BP reactivity may be targets for interventions to reduce the cardiovascular risk associated with PTSD.

Keywords

PTSD; blood pressure; hypertension; risk factors; prevention; anxiety

Introduction

Posttraumatic stress disorder (PTSD) symptoms are independently associated with incident myocardial infarction¹ and stroke.^{1,2} A meta-analysis (5 studies, N=44,654 followed 3–15 years) found a 62% increased risk of incident cardiac events associated with a positive screen for PTSD.³ Further, PTSD has been associated with hypertension in administrative records of young veterans,^{4,5} and with blood-based measures of endothelial dysfunction⁶ and inflammation in young civilians.⁷

Elevated blood pressure (BP) may be a mechanism by which PTSD increases cardiovascular disease risk, but the association between PTSD and BP is unclear and has been primarily tested in military veterans.^{8–10} Ambulatory blood pressure (ABP) is a better predictor of cardiovascular events than clinic BP^{11,12} and provides an important measure to elucidate the elevated cardiovascular risk associated with PTSD. The few studies that have assessed the association of PTSD with ABP in veterans included relatively small sample sizes ranging from 18–117,^{13–15} and the PTSD-ABP association in the non-veteran civilian population is not known. Across those studies, no consistent picture of PTSD's association with BP has emerged, but no ambulatory study has been powered to detect any but a very large effect (no N > 150 per study). Hypervigilance and hyperarousal in PTSD may produce more frequent and intense anxiety episodes, which may, in turn, produce concomitant increases in BP. PTSD is also associated with sleep disturbances, which may increase BP during sleep.

In the present study, we tested the association of PTSD symptoms with clinic and ambulatory daytime and nocturnal BP in a civilian sample of initially healthy working adult participants in a large, multi-site study of hypertension. We hypothesized that participants who screen positive for PTSD would have elevated clinic and ambulatory BP, and greater acute BP responses to naturally occurring bouts of anxiety [measured using ecological momentary assessment (EMA)].

Methods

Cohort Description

The present study used data from Phase 2 of the multi-site Masked Hypertension Study (P01-HL047540),¹⁶ an investigation of the relationship of BP measured by clinic and ambulatory assessment to cardiovascular target organ damage. The overall NIH-funded program project, of which the Masked Hypertension Study is one component, is titled Psychosocial Factors and Cardiovascular Disease, and has sought to identify how psychosocial factors contribute to intermediate markers such as blood pressure.

Participants were recruited through workplace BP screenings from 2005–2012 at two universities and affiliated medical centers, and a financial investment firm. The study was approved by the Institutional Review Boards of Columbia University Medical Center and Stony Brook University. All participants gave written informed consent to participate. Eligibility for Phase 1 of the study was restricted to employees (at least 17.5 hours/week) aged 21 or older. Excluded from the study were individuals with a screening systolic BP 160 mmHg or diastolic BP 105 mmHg; evidence of secondary hypertension other than a

history of pregnancy-induced hypertension; taking antihypertensive or cardiovascular medications (except statins) or other medications known to affect BP (e.g., steroids, tricyclic antidepressants); any self-reported cardiovascular disease; history of chronic renal disease, liver disease, adrenal disease, or thyroid disease; being pregnant; or reported active substance abuse or a severe psychiatric disorder. Once enrolled in Phase 1, participants remained in the study for Phase 2 even if they did not currently meet Phase 1 inclusion criteria (e.g., in the years between Phase 1 and Phase 2 of the study, 15% of participants initiated antihypertensives but remained eligible).

Procedure

The Masked Hypertension study enrolled participants for its first phase between 2005 and 2012. This manuscript uses data from Phase 2 (2012 to 2016), in which Phase 1 participants were invited to repeat all Phase 1 procedures an average of 6.1 years ($SD=1.0$) later, and also complete a PTSD assessment. Figure S1, Supplemental Digital Content 1, depicts the assessment timeline for Phase 2. The clinic BP of eligible and consented individuals was assessed at each of the first three clinic visits, conducted 1-week apart. Participants were instructed not to eat, smoke, or consume caffeine during the 30 minutes prior to their appointment, and this was confirmed upon arrival. Three manual BP readings were taken by mercury sphygmomanometer 2 minutes apart by a nurse/technician trained according to American Heart Association guidelines, after participants were in the seated position for 5 minutes.

At the end of the third study visit, participants were outfitted with a SpaceLabs 90207 ABP monitor (SpaceLabs; Snoqualmie, WA), programmed to take readings every 30 minutes. They were also fitted with two actigraphy devices (waist and wrist) and provided with a smartphone (Pidion BM-170 smartphone [Bluebird USA, Inc, Englewood Cliffs, NJ]) on which they were asked to answer questions about their thoughts, emotions, and activities immediately after each (awake) BP reading. Participants returned the ABP monitor and smartphone at the end of the 24-hour monitoring period (Visit 4). During a fifth clinic visit (Visit 5), participants completed a comprehensive medical history interview and cardiovascular evaluation. Height and weight were also measured, and used to calculate body mass index (BMI).

Also at Visit 1, participants were given an extensive psychosocial questionnaire battery to complete and asked to return it by Visit 3. Participants were not scheduled for their Visit 5 until the questionnaire had been returned. The psychosocial questionnaire battery included assessments of PTSD and depressive symptoms.

PTSD Assessment

The PTSD Checklist-Civilian version (PCL-C)¹⁷, is a 17-item PTSD screening instrument developed by the National Center for PTSD, and it has been used widely.¹⁸ Participants rate the extent to which they were bothered by each of the 17 *DSM-IV* diagnostic criteria for PTSD in the past month with reference to stressful life experiences. Responses are rated on a scale from 1 ("Not at all") to 5 ("Extremely"). Cronbach's α was 0.91. The PCL-C has excellent sensitivity and specificity for prediction of PTSD clinical diagnosis,^{19,20} We used a

screening cutoff score of 33 (suggested for primary care settings²¹) to classify PTSD (yes/no).

Depression Assessment

Depressive symptoms in the last 2 weeks were assessed using the 21-item Beck Depression Inventory (BDI).²² The BDI has been used for decades, and been shown to have excellent test-retest reliability and construct validity.²³ Cronbach's α in the present study was 0.89.

EMA of Anxiety

Participants rated their anxiety on a 2.5-inch horizontal visual analog scale (VAS, scored 0–100) by responding to the question “Just before [your] BP [was taken], how anxious/tense were you feeling?” using anchors of “Not at all” (0) and “Very much” (100). In a previous study, we estimated the state and trait components of variance in EMA anxiety, as well as the association of a latent variable of 24-hr EMA anxiety with traditional questionnaire based “trait” measures. We estimated that, for a single EMA report of anxiety, the reliability is 0.73. In our sample, 56% of the total reliable variability in EMA anxiety was due to stable trait-like differences between individuals, whereas 38% of the reliable EMA variance was situation-specific. The test-retest correlation over two days of monitoring was 0.90, but the correspondence of EMA anxiety reports with traditional trait questionnaires was poor ($r=0.25$).²⁴ Even so, we tend to view EMA reports as more reflective of participants' true affective experience.²⁵

BP Outcome Measures

The mean of the nine BP readings taken over the three clinic visits (Visits 1–3) was used as the summary measure of clinic BP. For the ABP recordings, we computed mean awake and mean sleep ambulatory systolic and diastolic BP for each participant. The sleep period was determined from the wrist actigraphy (Actiwatch 2, Philips Respironics, Bend, OR) data, processed using the Actiware software (Philips Respironics, Bend, OR) and self-reported sleep/wake times.²⁶ The awake means were treated as missing if the participant had fewer than 14 valid awake readings ($N=1$), and the sleep means were treated as missing when there were fewer than 5 valid sleep readings ($N=31$). Systolic and diastolic BP were analyzed separately.

Analytic Strategy

We tested the hypothesis that participants with PTSD would have higher BP, including: a) clinic BP, b) mean awake ABP, and c) mean sleep ABP, using linear regression, with persons as the unit of analysis. Known demographic correlates of BP (sex, Black race, Hispanic ethnicity, age at Visit 1, BMI at Visit 5) and current use of antihypertensive medications were treated as covariates in all analyses. In addition, we adjusted for depression in all analyses.²⁷ Missing BMI data for 7 participants was handled using multiple imputation.

We next tested the hypothesis that the ABP response to momentary anxiety (assessed by EMA) would be greater for those with vs. without PTSD. Further, we tested whether differences in mean momentary anxiety level over the course of the day, as well as any exaggerated ABP response to momentary anxiety, contributed to the PTSD vs no PTSD

group differences in mean awake ABP. The distribution of anxiety ratings (0 to 100 points) was positively skewed, with person-specific standard deviations highly correlated with person-specific means; these problematic distributional properties (heteroscedasticity) were minimized by transforming the raw scores to their cube root (i.e., $1 \rightarrow 1$, $8 \rightarrow 2$, $27 \rightarrow 3$, $64 \rightarrow 4$, and $100 \rightarrow 4.64$) for analyses.

This second set of hypotheses, concerning the association of momentary anxiety to concurrent ABP and the influence of PTSD on that association, was tested in a multilevel mixed model predicting the individual ABP readings from momentary anxiety ratings and the subject characteristics used in the prior analyses (see Appendix for details of this analysis). All analyses were performed in SAS (version 9.4; Cary, NC).

Role of Funding Source: N/A

Results

Participant Characteristics

A total of 440 Phase 2 participants comprise the analytic sample (Figure 1), and of these, 92 (21%) screened positive for PTSD. The average age at Phase 2 was 52.1 (SD=9.9) years, 38% were male, 6% self-identified as black race, and 14% were Hispanic. Those with vs. without PTSD did not differ significantly on demographic variables or BMI. As expected, BDI scores and mean EMA anxiety during the ABP assessment were significantly higher among those with vs. without PTSD (see Table 1). There were no statistically significant recruitment site differences (all $p > 0.20$) in mean levels of PTSD symptomatology, depression symptomatology, clinic systolic and diastolic blood pressures, mean awake and mean systolic and diastolic ambulatory blood pressure, or mean anxiety score (untransformed or cube root transformed).

PTSD and Clinic BP

PTSD was associated with a 3.5 mmHg greater mean clinic systolic BP in the unadjusted comparison (95% CI: 0.7 to 6.3, $p=0.01$; see Table 1). In the covariate-adjusted model, PTSD was associated with a 3.8 mmHg greater mean clinic systolic BP (95% CI: 1.1 to 6.5, $p=0.006$; see Table 2). Age, male sex, black race, and BMI were also significantly associated with mean clinic systolic BP (all $p < 0.01$). PTSD was not significantly associated with clinic diastolic BP in unadjusted or adjusted analyses (see Table S1, Supplemental Digital Content 2). PCL-C total score was not significantly associated with clinic SBP ($r=0.08$, $p=0.08$) or DBP ($r=0.01$, $p=0.77$).

PTSD and Awake ABP

PTSD was associated with a 3.3 mmHg greater mean awake systolic ABP in the unadjusted comparison (95% CI: 0.6 to 6.0, $p=0.02$). In the fully adjusted model, PTSD was associated with a 3.0 mmHg greater mean awake systolic ABP (95% CI: 0.1 to 5.9, $p=0.04$). Age, male sex, black race, and BMI were also associated with mean awake systolic ABP ($p < 0.01$). PTSD was not associated with mean awake diastolic ABP in unadjusted or adjusted models

(see Table S1, Supplemental Digital Content 2). PCL-C total score was not significantly associated with awake systolic ABP ($r=0.06$, $p=0.18$) or diastolic ABP ($r=0.01$, $p=0.83$).

PTSD and Sleep ABP

PTSD was associated with a 2.1 mmHg greater mean systolic ABP during sleep, but this difference was not statistically significant (95% CI: -0.7 to 5.0 , $p=0.13$). PTSD was unrelated to sleep diastolic ABP (Table S1, Supplemental Digital Content 2). PCL-C total score was not significantly associated with sleep systolic ABP ($r=0.05$, $p=0.27$) or diastolic ABP ($r=-0.01$, $p=0.90$).

PTSD and the Association of Momentary Anxiety with Concurrent ABP

In the full sample, the mean of participants' average EMA anxiety ratings was 17.3 ± 14.6 (the mean of their median anxiety ratings was 13.8 ± 15.8). That is, in response to the prompt "Just before the BP [reading], how Anxious/Tense were you feeling?", participants marked on the horizontal line from "Not at all" and "Very much" in an area which, once converted to an integer that could range from 0 (left endpoint of the line) to 100 (right extreme of the line), corresponded to a 17.3 on average (with a standard deviation of 14.6). After adjustment for PTSD and covariates but no interaction terms, EMA anxiety (cube root) was associated with concurrent systolic ABP ($B=0.87$; 95% CI: $0.58 - 1.16$; $p<0.0001$), indicating that the predicted systolic ABP was 1.75 mmHg higher for an EMA anxiety rating of 27 vs. a rating of 1 (i.e., scores of 3 vs. 1 on the cube root scale). Participants differed significantly in the magnitude of the relationship between their EMA anxiety and concurrent systolic ABP readings (SD of the unstandardized regression coefficients (B) = 1.34; $p<0.0001$). That is, the relationship between EMA anxiety and systolic ABP was between -1.74 and $+3.49$ for 95% of participants.

Next, we included interaction terms in the model to test whether PTSD status could account for some of the between-persons differences in the EMA anxiety $\rightarrow$ ABP association. This provided estimates of the average effects of EMA anxiety on ABP for those with vs. without PTSD. The predicted difference in systolic ABP associated with an anxiety rating of 27 vs. 1 for an individual with PTSD was 2.87 mmHg (95% CI: $1.42 - 4.32$; $p<0.001$) compared to 1.48 mmHg (95% CI: $0.82 - 2.14$; $p<0.001$) for an individual without PTSD. The interaction of PTSD group with EMA anxiety accounted for 9.2% of the between-persons variance in the effect of anxiety on systolic ABP, although the group difference in the average effect of anxiety on ABP did not reach statistical significance ($p=0.098$).

Figure 2 portrays the estimated relationship between momentary ratings of anxiety and concurrent systolic ABP readings for those with vs. without PTSD according to the multilevel mixed model described. The model estimates suggest that 10% (0.33 mmHg) of the overall group difference of 3.2 mmHg is due to those with PTSD being more anxious, 10% (0.31 mmHg) is due to those with PTSD exhibiting a greater increase in systolic ABP for a given change in anxiety.

A similar moderated effect of EMA anxiety ratings on awake diastolic ABP was also found, such that for those with PTSD the predicted increase for an EMA anxiety rating of 27 vs. 1 was 2.18 mmHg (95% CI: $1.20 - 3.16$; $B=1.09$, $p<0.001$), whereas for those without PTSD

the predicted diastolic ABP increase was 1.10 mmHg (95% CI: 0.66 – 1.45; B= 0.55, $p < 0.001$). Again, the ABP response to changes in momentary anxiety was almost twice as large for those with PTSD, compared to those without PTSD, but this difference did not achieve statistical significance ($p=0.06$).

In a sensitivity analysis, we investigated whether any of the other covariates in the model moderated the relationship of EMA anxiety to ABP by testing interaction terms of each covariate with EMA anxiety in the fully adjusted model; none were significant (all $p > 0.15$).

Discussion

This is the first study to systematically assess the association of PTSD with clinic, mean awake, and sleep ABP in a moderately large sample of healthy civilians. We found 3–4 mmHg higher clinic and mean awake systolic BP in participants who screened positive for PTSD, and a non-significant 2.1 mmHg higher mean sleep systolic ABP. We found no significant associations of PTSD with clinic or mean ambulatory diastolic BP.

We previously demonstrated that momentary increases in anxiety are associated with acute increases in systolic ABP and that psychological factors, like self-esteem, can moderate the effect of momentary anxiety on BP.²⁸ In the current study, our *a priori* hypothesis was that PTSD would be associated with higher BP, due in part to participants with PTSD experiencing more anxiety, and a greater BP response to anxiety, throughout the day. The clinical features of PTSD and findings from laboratory studies suggest that PTSD could influence ABP through repeated acute increases caused by autonomic responses to bouts of stress and trauma reminders in daily life.¹⁰ We found that about 20% of the association of PTSD with awake systolic ABP—after adjustment for demographics, BMI, and depression --was indeed accounted for by both the higher level of EMA anxiety reported by those who screened positive for PTSD and the greater increase in systolic ABP associated with any given change in momentary anxiety.

The systolic ABP response to changes in anxiety among those with PTSD was, on average, nearly double that observed among participants without PTSD, causing the predicted systolic ABP difference between groups to increase as anxiety increased. Although laboratory studies have shown exaggerated physiological stress reactivity to trauma reminders and other stressors in participants with PTSD vs without, to our knowledge, this is the first study to test whether PTSD is associated with increased BP response to feelings of anxiety in participants' daily lives. Our findings, along with others in the literature,^{29,30} indicate that taking momentary measures of negative affect into consideration may help to better understand cardiovascular risk in individuals with PTSD.

PTSD and anxiety have been associated with hypertension both cross-sectionally and prospectively.^{4,5,31–33} This study is the strongest evidence to date that PTSD is associated with elevated BP, and it yields support for one mechanism of that association. Chronic feelings of anxiety are thought to lead to chronically elevated BP due in part to the accumulation of momentary BP increases during anxiety provoking circumstances - e.g., in response to perceived threat.³¹ Acute BP elevations are regulated primarily by the autonomic

nervous system as a means to prepare the body for responding to these threats. Systolic BP is particularly responsive under these conditions,^{34,35} and we suspect that this accounts for our findings of a stronger association of PTSD with systolic BP than with diastolic BP. Nevertheless, we also found evidence that diastolic BP is increased during moments of anxiety in both groups and, while only approaching statistical significance, this increase among those with PTSD is nearly twice that for those without PTSD. This study points to an influence of PTSD on both mean level of anxiety and anxiety-induced transient increases in BP that may accumulate over time. Indeed, our finding of an association of PTSD with increased resting clinic BP supports this view.

This study should be interpreted with its limitations in mind. At enrollment, the sample was working and free of existing cardiovascular disease, stage II hypertension, or BP-lowering medication; at the time of PTSD assessment (Phase 2), 15% were taking antihypertensive medication. Thus, these results may not generalize to those with established cardiovascular disease or long-term use of hypertensive medications. Also, the cross-sectional design of the study does not allow for strong causal interpretations, as some physiological stress markers thought to be consequences of psychological disorder have occasionally been shown to precede their psychological “causes” or exist in bidirectional relations with them.^{36,37} Further, although this is the largest study of its kind to date, our statistical power for tests of moderated effects was low. This may explain p values of 0.06–0.10 for some of the very large effects that we observed, such as the apparent interaction of PTSD status and momentary anxiety on ABP parameters,

Another issue is that 21% of the sample scored above the screening cutoff on the PTSD assessment. In a systematic review of 27 studies of PTSD screening in primary care, between 2–39% of participants screened positive, but in most studies the estimate was lower than 20%.³⁸ Also, while we used the gold standard PTSD screening tool, we did not use a clinical interview to determine PTSD status, so we do not know the association of PTSD diagnosis *per se* with BP. That being said, a positive screen for PTSD has been consistently associated with incident CVD risk.³ We also did not document traumatic event exposure, which is necessary for diagnosis of PTSD. However, 90% of the population has been exposed to trauma, suggesting that lack of exposure is rare.³⁹ Indeed, the standard primary care PTSD screening tool does not assess exposure,⁴⁰ and most primary care PTSD studies do not document exposure.³⁸ Finally, *DSM-IV* PTSD symptoms were assessed in the current study, as the investigation was started prior to the publication of *DSM-5*. These limitations notwithstanding, this study provides important new insight into a potential mechanism by which a relatively common psychosocial CVD risk factor may contribute to cardiovascular risk in otherwise healthy people.

Conclusions

These results suggest that PTSD is associated with a moderate increase in systolic BP both in the clinic and in everyday life, and that exaggerated physiological responses to intermittent bouts of anxiety may play a role in causing or maintaining this systolic BP increase. The 3–4 mmHg systolic BP difference associated with PTSD that we observed is

equivalent to 60–80% of the 5 mmHg increase in systolic ABP for smoking vs. non-smoking days.³⁶

Taken together, the direct effect of PTSD on clinic and ambulatory systolic BP, its indirect effect through increased mean levels of anxiety in daily life that are also associated with acute systolic ABP increases, and the synergistic effect of PTSD and momentary anxiety on the magnitude of systolic ABP during periods of high anxiety, suggest a potential causal role of PTSD in increasing BP. However, much of the BP difference due to PTSD remained unexplained in this study. Future research should identify the sources of that variance, and determine whether treating PTSD lowers BP. For now, researchers should focus on daily anxiety and the acute BP response to momentary anxiety as potential intermediate targets for BP reduction in patients who screen positive for PTSD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

EMA	ecological momentary assessment
ABP	ambulatory blood pressure
BP	blood pressure
PTSD	posttraumatic stress disorder

References

1. Sumner JA, Kubzansky LD, Elkind MS, Roberts AL, Agnew-Blais J, Chen Q, Cerdá M, Rexrode KM, Rich-Edwards JW, Spiegelman D. Trauma exposure and posttraumatic stress disorder symptoms predict onset of cardiovascular events in women. *Circulation*. 2015; 132(4):251–259. [PubMed: 26124186]
2. Chen M-H, Pan T-L, Li C-T, Lin W-C, Chen Y-S, Lee Y-C, Tsai S-J, Hsu J-W, Huang K-L, Tsai C-F. Risk of stroke among patients with post-traumatic stress disorder: nationwide longitudinal study. *The British Journal of Psychiatry*. 2015; 206(4):302–307. [PubMed: 25698764]
3. Edmondson D, Kronish IM, Shaffer JA, Falzon L, Burg MM. Posttraumatic stress disorder and risk for coronary heart disease: A meta-analytic review. *Am Heart J*. 2013; 166(5):806–814. [PubMed: 24176435]
4. Cohen BE, Marmar C, Ren L, Bertenthal D, Seal KH. Association of cardiovascular risk factors with mental health diagnoses in Iraq and Afghanistan war veterans using VA health care. *JAMA: The Journal of the American Medical Association*. 2009; 302(5):489–492. [PubMed: 19654382]

5. Burg MM, Brandt C, Buta E, Schwartz J, Bathulapalli H, Dziura J, Edmondson D, Haskell S. Risk for incident hypertension associated with PTSD in military veterans, and the effect of PTSD treatment. *Psychosom Med.* in press.
6. von Känel R, Hepp U, Traber R, Kraemer B, Mica L, Keel M, Mausbach BT, Schnyder U. Measures of endothelial dysfunction in plasma of patients with posttraumatic stress disorder. *Psychiatry Res.* 2008; 158(3):363–373. [PubMed: 18252265]
7. von Känel R, Hepp U, Kraemer B, Traber R, Keel M, Mica L, Schnyder U. Evidence for low-grade systemic proinflammatory activity in patients with posttraumatic stress disorder. *Journal of Psychiatric Research.* 2007; 41(9):744–752. [PubMed: 16901505]
8. Buckley TC, Kaloupek DG. A meta-analytic examination of basal cardiovascular activity in posttraumatic stress disorder. *Psychosomatic Medicine.* 2001; 63(4):585–594. [PubMed: 11485112]
9. Paulus EJ, Argo TR, Egge JA. The impact of posttraumatic stress disorder on blood pressure and heart rate in a veteran population. *Journal of Traumatic Stress.* 2013; 26(1):169–172. [PubMed: 23371434]
10. Pole N. The psychophysiology of posttraumatic stress disorder: a meta-analysis. *Psychological Bulletin.* 2007; 133(5):725–746. [PubMed: 17723027]
11. Conen D, Bamberg F. Noninvasive 24-h ambulatory blood pressure and cardiovascular disease: a systematic review and meta-analysis. *Journal of Hypertension.* 2008; 26(7):1290–1299. [PubMed: 18550999]
12. Siu AL. Screening for high blood pressure in adults: US Preventive Services Task Force recommendation statement screening for high blood pressure in adults. *Annals of Internal Medicine.* 2015; 163(10):778–786. [PubMed: 26458123]
13. Buckley T, Holohan D, Greif J, Bedard M, Suvak M. Twenty-Four-Hour Ambulatory Assessment of Heart Rate and Blood Pressure in Chronic PTSD and Non-PTSD Veterans. *Journal of Traumatic Stress.* 2004; 17(2):163–171. [PubMed: 15141790]
14. Beckham JC, Taft CT, Vrana SR, et al. Ambulatory monitoring and physical health report in Vietnam veterans with and without chronic posttraumatic stress disorder. *Journal of Traumatic Stress.* 2003; 16(4):329–335. [PubMed: 12895015]
15. Muraoka MY, Carlson JG, Chemtob CM. Twenty-four-hour ambulatory blood pressure and heart rate monitoring in combat-related posttraumatic stress disorder. *Journal of Traumatic Stress.* 1998; 11(3):473–484. [PubMed: 9690188]
16. Shimbo D, Newman JD, Schwartz JE. Masked hypertension and prehypertension: diagnostic overlap and interrelationships with left ventricular mass: the masked hypertension study. *American journal of hypertension.* 2012; 25(6):664–671. [PubMed: 22378035]
17. Weathers F, Litz B, Herman D, Huska J, Keane T. The PTSD Checklist (PCL): Reliability, validity, and diagnostic utility. 1993
18. Walker E, Newman E, Dobie D, Ciechanowski P, Katon W. Validation of the PTSD checklist in an HMO sample of women* 1. *Gen Hosp Psychiatry.* 2002; 24(6):375–380. [PubMed: 12490338]
19. Blanchard E, Jones-Alexander J, Buckley T, Forneris C. Psychometric properties of the PTSD Checklist (PCL). *Behaviour Research and Therapy.* 1996; 34(8):669–673. [PubMed: 8870294]
20. Bliese P, Wright K, Adler A, Cabrera O, Castro C, Hoge C. Validating the primary care posttraumatic stress disorder screen and the posttraumatic stress disorder checklist with soldiers returning from combat. *Journal of consulting and clinical psychology.* 2008; 76(2):272–281. [PubMed: 18377123]
21. NCPTSD. Using the PTSD Checklist for DSM-IV (PCL). 2014. <http://www.ptsd.va.gov/professional/pages/assessments/assessment-pdf/PCL-handout.pdf>
22. Beck, AT., Steer, R., Brown, G. The psychological corporation. San Antonio, TX: 1996. Beck depression inventory.
23. Beck Robert A, Aaron T. Psychometric properties of the Beck Depression Inventory: Twenty-five years of evaluation. *Clinical Psychology Review.* 1988; 8(1):77–100.
24. Edmondson D, Shaffer JA, Chaplin WF, Burg MM, Stone AA, Schwartz JE. Trait anxiety and trait anger measured by ecological momentary assessment and their correspondence with traditional trait questionnaires. *Journal of research in personality.* 2013; 47(6):843–852.

25. Solhan MB, Trull TJ, Jahng S, Wood PK. Clinical assessment of affective instability: comparing EMA indices, questionnaire reports, and retrospective recall. *Psychological assessment*. 2009; 21(3):425. [PubMed: 19719353]
26. Booth JN III, Muntner P, Abdalla M, Diaz KM, Viera AJ, Reynolds K, Schwartz JE, Shimbo D. Differences in night-time and daytime ambulatory blood pressure when diurnal periods are defined by self-report, fixed-times, and actigraphy: Improving the Detection of Hypertension study. *Journal of hypertension*. 2016; 34(2):235–243. [PubMed: 26867054]
27. Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB. Posttraumatic stress disorder in the National Comorbidity Survey. *Archives of General Psychiatry*. 1995; 52(12):1048–1060. [PubMed: 7492257]
28. Edmondson D, Arndt J, Alcántara C, Chaplin W, Schwartz JE. Self-esteem and the acute effect of anxiety on ambulatory blood pressure. *Psychosomatic Medicine*. 2015; 77(7):833–841. [PubMed: 26230481]
29. Dennis PA(1), Kimbrel NA, Sherwood A, Calhoun PS, Watkins LL, Dennis MF, Beckham JC. Trauma and autonomic dysregulation: episodic—versus systemic—negative affect underlying cardiovascular risk in posttraumatic stress disorder. *Psychosomatic Medicine*. 2017; 79(5):496–505. [PubMed: 28570433]
30. Dennis PA(1), Dedert EA, Van Voorhees EE, Watkins LL, Hayano J, Calhoun PS, Sherwood A, Dennis MF, Beckham JC. Examining the crux of autonomic dysfunction in posttraumatic stress disorder: whether chronic or situational distress underlies elevated heart rate and attenuated heart rate variability. *Psychosomatic Medicine*. 2016; 78(7):805–809. [PubMed: 27057817]
31. Jonas BS, Franks P, Ingram DD. Are symptoms of anxiety and depression risk factors for hypertension? longitudinal evidence from the National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study. *Archives of family medicine*. 1997; 6(1):43. [PubMed: 9003169]
32. Markovitz J, Matthews KA, Kannel WB, Cobb JL, D'Agostino RB. Psychological predictors of hypertension in the framingham study: Is there tension in hypertension? *JAMA: The Journal of the American Medical Association*. 1993; 270(20):2439–2443. [PubMed: 8230620]
33. Abouzeid M, Kelsall HL, Forbes AB, Sim MR, Creamer MC. Posttraumatic stress disorder and hypertension in Australian veterans of the 1991 Gulf War. *Journal of Psychosomatic Research*. 2012; 72(1):33–38. [PubMed: 22200520]
34. Brondolo E, Rosen RC, Kostis JB, Schwartz JE. Relationship of physical symptoms and mood to perceived and actual blood pressure in hypertensive men: A repeated-measures design. *Psychosomatic medicine*. 1999; 61(3):311–318. [PubMed: 10367611]
35. Schwartz JE, Warren K, Pickering TG. Mood, location and physical position as predictors of ambulatory blood pressure and heart rate: Application of a multi-level random effects model. *Annals of Behavioral Medicine*. 1994
36. Shaffer JA, Edmondson D, Chaplin WF, Schwartz JE, Shimbo D, Burg MM, Rieckmann N, Davidson KW. Directionality of the relationship between depressive symptom dimensions and C-reactive protein in patients with acute coronary syndromes. *Psychosom Med*. 2011; 73(5):370–377. [PubMed: 21636659]
37. Minasian A, Maihofer AX, Baker DG, Nievergelt CM, Geyer MA, Risbrough VB. Association of predeployment heart rate variability with risk of postdeployment posttraumatic stress disorder in active-duty marines. *JAMA psychiatry*. 2015; 72(10):979–986. [PubMed: 26353072]
38. Greene T, Neria Y, Gross R. Prevalence, Detection and Correlates of PTSD in the Primary Care Setting: A Systematic Review. *J Clin Psychol Med Settings*. 2016; 23(2):160–180. [PubMed: 26868222]
39. Kilpatrick DG, Resnick HS, Milanak ME, Miller MW, Keyes KM, Friedman MJ. National estimates of exposure to traumatic events and PTSD prevalence using DSM-IV and DSM-5 criteria. *Journal of Traumatic Stress*. 2013; 26(5):537–547. [PubMed: 24151000]
40. Cameron RP, Gusman D. The primary care PTSD screen (PC-PTSD): development and operating characteristics. *Primary Care Psychiatry*. 2003; 9(1):9–14.

Figure 1. Flowchart of exclusions for deriving the analytic sample

Figure 2. Predicted relationship of systolic ambulatory blood pressure readings to concurrently assessed anxiety, by PTSD group

Figure 2 portrays the estimated relationship between momentary ratings of anxiety on a cube root scale and concurrent systolic ABP readings for those with vs. without PTSD. It illustrates that the difference in predicted systolic ABP for these 2 groups increases as EMA anxiety rating increases. Values in mmHg on vertical lines indicate the predicted systolic ABP difference between participants with vs. without PTSD at the corresponding level of momentary anxiety on the x-axis. From left to right, the vertical lines corresponds to the mean anxiety value in the no PTSD group and the mean anxiety value in the PTSD group. Values in mmHg on horizontal lines indicate the predicted systolic ABP difference between two levels of anxiety within the same PTSD/no PTSD group.

Table 1

Participant characteristics by PTSD status (N=440), with unadjusted group comparisons

	PTSD (N=92)	No PTSD (N=348)	p-value*
Demographics			
Sex, N (%) male	34 (37.0%)	133 (38.2%)	0.90
Black race, N (%)	8 (8.7%)	20 (5.7%)	0.34
Hispanic ethnicity, N (%)	15 (14.3%)	45 (12.9%)	0.40
Age, years (mean $\pm$ sd)	50.4 $\pm$ 10.4	52.5 $\pm$ 9.7	0.071
Clinical			
Body mass index, kg/m ² (mean $\pm$ sd) [†]	28.0 $\pm$ 4.9	27.9 $\pm$ 5.3	0.85
Use of BP lowering meds, N (%)	11 (12.0%)	54 (15.5%)	0.51
Mean clinic SBP (mean $\pm$ sd)	121.3 $\pm$ 13.0	117.8 $\pm$ 12.0	0.014
Mean clinic DBP (mean $\pm$ sd)	76.9 $\pm$ 7.8	76.0 $\pm$ 7.3	0.31
Mean awake ASBP (mean $\pm$ sd)	132.0 $\pm$ 12.8	128.7 $\pm$ 11.6	0.018
Mean awake ADBP (mean $\pm$ sd)	81.0 $\pm$ 9.3	80.0 $\pm$ 8.4	0.30
Mean nighttime ASBP (mean $\pm$ sd)	112.7 $\pm$ 12.9	110.6 $\pm$ 11.3	0.13
Mean nighttime ADBP (mean $\pm$ sd)	64.7 $\pm$ 9.0	64.5 $\pm$ 7.9	0.85
Psychological			
Mean PCL-C PTSD score (mean $\pm$ sd)	41.5 $\pm$ 7.8	22.8 $\pm$ 4.6	--- [‡]
Mean BDI depression score (mean $\pm$ sd)	12.6 $\pm$ 8.0	5.1 $\pm$ 5.0	<0.0001 [#]
Median EMA anxiety score (mean $\pm$ sd)	20.5 $\pm$ 18.0	12.1 $\pm$ 14.7	<0.0001 [#]
Mean EMA anxiety ^(1/3) score (mean $\pm$ sd)	2.42 $\pm$ 0.88	1.96 $\pm$ 0.87	<0.0001

* Based on independent samples t-test or Fisher's exact test, unless otherwise stated.

[†] Multiple imputation was used to handle missing body mass index data for 3 participants with PTSD and 4 participants without PTSD who had not yet completed Visit 5. No imputation was used for 1 participant without PTSD who had fewer than 14 awake ABP readings, 9 participants with PTSD and 22 participants without PTSD who had fewer than 5 sleep ABP readings, and 1 participant without PTSD who had no EMA data due to device malfunction.

[‡] p-value not reported, since groups are defined to have non-overlapping PCL scores.

[#] p-value based on Mann-Whitney test, due to substantial skewness of the distribution.

Estimates of multiple linear regression models predicting mean clinic and ambulatory systolic blood pressure from PTSD status, with adjustment for demographic characteristics, BMI, and depression score

Table 2

Characteristic	Clinic SBP (mm/Hg)		Ambulatory SBP (mm/Hg)			
	B (95% CI)	p	Mean Awake SBP		Mean Sleep SBP	
			B (95% CI)	p	B (95% CI)	p
PTSD (PCL 33), vs PCL<33	3.79 (1.11 – 6.47)	0.006	3.01 (0.14 – 5.88)	0.04	2.06 (–0.96 – 5.09)	0.18
Male sex, women as reference	8.61 (6.59 – 10.63)	<0.0001	6.82 (4.66 – 8.98)	<0.0001	5.05 (2.77 – 7.32)	<0.0001
African American race, non-AA as reference	7.17 (3.22 – 11.13)	0.0004	5.48 (1.26 – 9.71)	0.01	5.88 (1.34 – 10.42)	0.011
Hispanic ethnicity, non-Hispanic as reference	2.04 (–0.86 – 4.94)	0.17	–2.31 (–5.41 – 0.79)	0.14	–2.78 (–6.05 – 0.48)	0.09
Age, per year	0.33 (0.23 – 0.43)	<0.0001	0.20 (0.09 – 0.31)	0.0003	0.16 (0.04 – 0.27)	0.007
BMI, per unit	0.68 (0.49 – 0.87)	<0.0001	0.39 (0.19 – 0.59)	0.0002	0.40 (0.19 – 0.60)	0.0001
Antihypertensive meds, vs none	3.09 (0.29 – 5.89)	0.03	1.52 (–1.48 – 4.51)	0.32	2.61 (–0.48 – 5.71)	0.10
Depression (BDI), per point	0.04 (–0.13 – 0.21)	0.66	0.10 (–0.08 – 0.28)	0.28	0.09 (–0.10 – 0.28)	0.37