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Posttraumatic stress disorder, alone or additively with early life adversity, is associated with obesity and cardiometabolic risk

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Abstract

Background and Aims—There is some evidence that posttraumatic stress disorder (PTSD) and early life adversity may influence metabolic outcomes such as obesity, diabetes, and cardiovascular disease. However, whether and how these interact is not clear.

Methods—We analyzed data from a cross-sectional and a longitudinal study to determine how PTSD severity influences obesity, insulin sensitivity, and key measures and biomarkers of cardiovascular risk. We then looked at how PTSD and early life adversity may interact to impact these same outcomes.

Results—PTSD severity is associated with increasing risk of obesity, diabetes, and cardiovascular disease, with higher symptoms correlating with higher values of BMI, leptin, fibrinogen, and blood pressure, and lower values of insulin sensitivity. PTSD and early life adversity have an additive effect on these metabolic outcomes. The longitudinal study confirmed

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findings from the cross sectional study and showed that fat mass, leptin, CRP, ICAM, and TNFR1I were significantly increased with higher PTSD severity during a 2.5 year follow-up period.

Conclusions—Individuals with early life adversity and PTSD are at high risk and should be monitored carefully for obesity, insulin resistance, and cardiometabolic risk.

Key Terms

PTSD; adversity; obesity; cardiac risk

Introduction

Posttraumatic stress disorder (PTSD), a psychological trauma-related disorder, is a relatively common occurrence in veterans, estimated at current rates between 15-19% with lifetime incidence rates of up to 30% [1], and in the general population at about 7.8% [2]. More recently, evidence has accumulated to suggest that PTSD increases the risk of developing metabolic disorders such as type 2 diabetes, dyslipidemia, obesity [3, 4] and cardiovascular diseases [5]. Early life adversity (ELA), which includes emotional, physical, and sexual abuse or neglect before the age of 18, is also known to increase metabolic and cardiovascular disorders [6, 7]. How these two factors, ELA and PTSD, may interact to impact metabolic outcomes is less clear.

Indeed, PTSD has been associated with higher BMI, blood pressure (BP), and MetS (MetS), even when compared to other psychiatric disorders [8]. When PTSD is comorbid with depression, the risk for MetS is drastically increased [9]. However, in a low income population, PTSD still predicted MetS even when depression, demographic factors, and antipsychotic use were controlled [4]. Further, PTSD symptom severity proved to be a predictor of MetS in veterans, controlling for other significant predictors, such as antipsychotic use [3]. Similarly, ELA has been found to increase central obesity and BMI controlling for established adult psychosocial and health behavior risk factors [7, 10]. ELA has also been seen to increase the risk of diabetes, cardiovascular disease, and premature death when controlling for potential confounders [6, 7].

Disrupted activation of the hypothalamic-pituitary-adrenal (HPA) axis and increased activity of the sympathetic nervous system may lead to the metabolic and cardiovascular problems frequently seen in PTSD [11], similar to the proposed mechanisms of dysfunction resulting from ELA [12]. However, whether PTSD and ELA may combine or interact to alter BMI, insulin sensitivity, and hormonal outcomes remains unknown. Here, we performed a cross-sectional and a longitudinal study of a diverse community population to determine how the severity of PTSD symptoms, based on self-report, or probable PTSD (PTSD), may interact with ELA to alter metabolic outcomes and to better define how PTSD may impact biomarkers for adiposity, inflammation and insulin sensitivity to alter risk of diabetes, obesity, and cardiovascular disease.

Methods

Cross-sectional study: study population

We examined 158 adults cross-sectionally. Participants between the ages of 35 and 55 were recruited from the greater Boston area via advertisements to be representative of the general population in terms of socioeconomic status. Participants were White European Americans and Black/African Americans. We excluded individuals with a history of myocardial infarction or stroke, an active diagnosis of diabetes mellitus, active intravenous drug use, hepatitis, cirrhosis, dialysis, long-term steroid use, and/or current treatment for cancer or active infection.

The study was approved by the Institutional Review Board at the Judge Baker Children's Center (JBCC) and Beth Israel Deaconess Medical Center (BIDMC). Written informed consent was obtained from all participants.

Among 158 participants, 55 returned for a follow-up visit 2.5 years after the cross-sectional visit. Follow up sample size was limited by funding constraints. Procedures at the follow-up visit were identical to the cross-sectional visit. Biomarkers and anthropometric data were collected as described previously [7] and in Appendix 1.

Psychosocial data

Information on ELA, probable PTSD (PTSD) and psychosocial measurements was obtained via validated interviews and questionnaires at JBCC. An overall ELA score was created by multiplying the number of ELA×the overall severity of each ELA×the overall chronicity of ELA (chronic/acute) as described previously [7, 10, 13]. PTSD severity scores and subscale scores were measured with the UCLA PTSD scale [14, 15]. For additional information on psychosocial data, see Appendix 2.

Statistical analysis

General characteristics of the study participants according to three categories (Q_1+Q_2 vs. Q_3 vs. Q_4) of PTSD severity scores, with the first two quartiles (Q_1+Q_2) collapsed and then the third (Q_3) and fourth quartiles (Q_4) presented separately, per standard epidemiology practices to correct for the skewedness of the data while still representing the distribution of the scores, were compared using ANOVA or chi-square test and presented as means (or geometric means)±SD or frequency (%). Normality of the distributions was assessed with frequency histograms and the Shapiro-Wilk test. The linear trend was calculated by simple linear regression analysis (continuous variables) or by linear-by-linear association (categorical variables). If there was a significant difference in continuous variables amongst the three groups, a *post-hoc* test using the Bonferroni method was performed for the comparison between two groups amongst three categories. Spearman's correlation analyses were used to compare PTSD severity scores and individual PTSD subscale severity scores with other variables. Cardiometabolic and biomarker values in the three PTSD severity score categories were compared using ANOVA or ANCOVA and presented as means (or geometric means)±SE. Subsequent models were used to test comparisons while controlling

for different potential confounders. For instance, Model 1 was uncorrected, while Model 2 was adjusted for age and gender.

Subsequent analyses were then performed to examine possible interactions between ELA and PTSD. Thus, we divided overall ELA scores as low (T_1+T_2 ; 0–15) or high (T_3 ; 16–156) using the highest tertile point of 16 as a cut-off point. We divided the PTSD severity scores as lower (T_1+T_2 ; 0–10) or higher (T_3 ; 11–57) using the highest tertile point of 11 and combined them with overall adversity scores category to make four categories: both lower ELA and PTSD severity scores (both from the lowest two tertiles); higher ELA (from the highest tertile) and lower PTSD severity scores (from the lowest two tertiles); lower ELA (from the lowest two tertiles) and higher PTSD severity scores (from the highest tertile); and both higher ELA and PTSD severity scores (from the highest tertile of both). Variables were compared according to these categories, and Bonferroni's corrections were made to adjust for six comparisons between the four groups created using the tertiles of PTSD and ELA as described above and are shown in the subscript of the tables. Follow-up variables were also compared according to baseline PTSD severity scores and the combined categories of early adversity and PTSD scores after adjusting their baseline values, age, gender, race, and baseline BMI by using ANCOVA. SPSS version 19.0 (SPSS, IL) was used for the statistical analysis and a two-tailed P value <0.05 was considered statistically significant.

Results

General characteristics of the participants

Mean age of the study population was 45.7 ± 3.5 years. Assuming a PTSD severity score of >38 may represent PTSD, approximately 8.8% ($n=14$) participants in our sample had probable PTSD. Participants with higher PTSD severity scores were less likely to be White European American, well-educated, non-smoking, and insulin-sensitive (Avignon index, SiM) and were more likely to be moderately or severely depressed ($BDI > 21$), obese (elevated BMI and fat mass), and have higher fibrinogen and leptin concentrations compared to those with low PTSD scores. CRP levels show a U-shaped curve where they are highest in those with the highest PTSD severity scores (Table 1).

Correlations between total and subscale PTSD severity scores and anthropometric, nutritional, psychological, and biomarker variables (Table 2)

PTSD severity scores were positively correlated with BMI, fat mass, waist circumference, depression (BDI scores), fibrinogen, and leptin values, whereas they were negatively correlated with insulin sensitivity. The correlations between PTSD subscale severity scores and other variables (fat mass and BDI scores) were similar to that of the total PTSD severity scores. Systolic BP was positively correlated with criteria B subscores (re-experiencing), whereas Avignon index (SiM) was inversely correlated with criteria B and C (avoidance) subscale severity scores. Interestingly, all biomarkers including fibrinogen, CRP, leptin, resistin, PAI-1, and irisin were positively associated with criteria B PTSD severity subscores. Subscale C and D (arousal) subscores were positively correlated with fibrinogen as well as CRP (C) and PAI-1 concentrations (D).

Cardiometabolic and biomarker values vary with PTSD severity (Table 3)

In our multiple linear regression models, BMI showed a positive association with PTSD severity after adjusting for possible confounding factors (P for trend = 0.047, model 6); however, fat mass only showed the same association in an unadjusted model (model 1). Total cholesterol (TC) levels showed a significant increasing trend with PTSD severity after adjusting for socio-demographic variables (P for trend = 0.045, model 4). However, after adjusting for health-related behaviors (smoking, alcohol, and physical activity), this was not significant. Fasting blood glucose (FBG) levels were higher in those with high PTSD scores even when corrected for demographic and health-related behaviors (models 4 and 5) as well as for depression, BMI, and energy intake (model 6). SiM showed a decreasing trend with increasing PTSD severity after adjusting for age and gender (model 2), but was no longer significant after adjusting for race. Higher fibrinogen and CRP concentrations were strongly correlated with high PTSD scores even after correction for all confounders. Leptin showed an increasing trend with PTSD scores after controlling for age and gender; this trend was not observed after controlling for race (model 3). Interactions between race and PTSD severity (race $\times$ PTSD severity) on the categories of BMI, fat mass, and Stumvoll and SiM indices were also detected (P for interaction <0.05 ; Supplementary Table S1).

Effects of combined PTSD and ELA on metabolic outcomes (Table 4)

BMI and fat mass increased across categories as overall ELA and PTSD severity moved from both lower (T_1+T_2) to both higher (T_3) after controlling for age and gender (model 2). Higher TC (after adjusting for all confounders) and FBG levels (after adjusting for demographic and health-related behaviors) were related to the combined highest ELA and PTSD scores, whereas insulin sensitivity indices were lowest in groups with higher ELA and PTSD scores after adjusting for sociodemographic and health-related behaviors. Fibrinogen concentrations increased as ELA and PTSD severity scores increased, even with corrections for demographic and health-related behaviors, depression, BMI, and energy intake. CRP and leptin levels were higher in groups with higher ELA and PTSD severity scores after adjusting for age and gender (model 2), but adjusting for race made this disappear (model 3).

Longitudinal analysis of 55 participants at 2.5 years after the initial visit

For the longitudinal study, participants were grouped as above based on PTSD severity score. Anthropometric, demographic, SES, PTSD scores, and ELA symptoms were not different between participants who returned or did not return for follow-up (all P values were >0.05). The results of the three-group comparison between PTSD groups revealed that both BMI and fat mass were higher in the highest group. BMI increased with increasing PTSD severity after controlling for baseline values in the initial visit ($P=0.027$, ANCOVA, P for trend=0.014). Fat mass was significantly different between the middle and highest PTSD severity groups ($P=0.038$).

Leptin was significantly higher in the highest group ($P=0.008$, P for trend = 0.003). CRP showed a significant positive linear association ($P=0.035$, P for trend=0.013). sICAM-1 also revealed a positive association with PTSD severity ($P=0.028$, P for trend=0.040) as did sTNFR1I ($P=0.002$, P for trend=0.014). CRP and leptin remained significant after further adjusting for age, gender, race, and baseline BMI (P for trend=0.038 CRP, 0.010 leptin).

When patients were grouped into four categories according to ELA and PTSD score (as in Table 4), systolic BP, CRP, leptin, sICAM-1, and sTNFRII showed positive linear associations with higher adversity and PTSD scores after adjusting for their baseline values (P for trend=0.041 systolic BP, 0.030 CRP, 0.002 leptin, 0.007 sICAM-1, 0.025 sTNFRII). Systolic BP and sICAM-1 remained significant after further adjusting for age, gender, race, and baseline BMI (P for trend=0.029 for both).

Discussion

Middle-aged individuals with PTSD and/or ELA appear to be at greater risk and thus should be monitored carefully for obesity, insulin resistance, and cardiometabolic dysfunction. Indeed, these findings suggest underlying increased activity of the sympathetic nervous system and disruption of the HPA axis leading to the metabolic and cardiovascular problems frequently seen in PTSD, as has been previously hypothesized [11]. Approximately 8.8% of our sample would meet criteria for PTSD (score>38 [15]), which is representative of previous studies showing rates of 7.8% [2].

PTSD and/or ELA impact traditional cardiometabolic risk factors

We demonstrate that PTSD severity is associated with anthropometric risk factors for obesity, cardiometabolic disease and diabetes, such as higher BMI, fat mass, and waist circumference (indicating central adiposity). Longitudinally, BMI and fat mass remained significantly increased with PTSD severity at follow-up. These results also point to a higher risk of diabetes in patients with PTSD through increased central adiposity combined with decreased insulin sensitivity and increased cholesterol. Depression symptoms are highly correlated with PTSD severity and may confound these results, but the association between PTSD severity and fasting blood sugar remains significant, independently from potential confounders. Many studies find strong correlations between depression and PTSD, which may stem from common risk factors or vulnerabilities or from one disorder leading to the other [16]. Other studies have found that PTSD symptoms are associated with a future risk of diabetes in a military cohort, and that present diabetes risk was higher in a community population with PTSD [17, 18]. Furthermore, diabetes is worsened, as measured by increased HbA1c, with PTSD symptom severity [19]. Altogether, these support a higher cardiometabolic risk as well as future risk for diabetes with PTSD symptomatology.

PTSD and ELA further showed an additive effect on many of these cardiometabolic risk factors, particularly BMI, fat mass, cholesterol, FBG, and insulin sensitivity. ELA alone has been shown to increase central obesity and BMI as well as the risk of diabetes, cardiovascular disease, and premature death [6, 10]. Because these effects seem to be additive with PTSD, individuals with high levels of ELA and PTSD symptoms should be carefully monitored for cardiometabolic disorders.

PTSD and/or ELA impact adipokines and inflammatory biomarkers

To examine adipokines or biomarkers that may significantly influence the relations between PTSD symptoms alone or in combination with ELA and diabetes, cardiometabolic, and/or obesity risk factors, we examined adipokines, such as leptin, and coagulation or

inflammatory markers, such as fibrinogen and CRP. Leptin is positively correlated with PTSD severity and shows a trend of increasing with PTSD and ELA severity. Although the association between PTSD and leptin was nullified after adjusting for race in the cross-sectional study, our longitudinal follow-up study revealed that there was a significant positive association between PTSD severity and circulating leptin levels even after controlling for race and/or other potential confounders. In prior studies, participants who were subclinical for PTSD showed a correlation between PTSD severity and leptin [20]. These findings, as well as those from our longitudinal study, demonstrate an association between PTSD severity and leptin, indicating that leptin, probably reflecting overall fat mass, is a potentially useful target for long-term follow-up of health-related consequences of PTSD.

In terms of inflammatory biomarkers, we find a U-shaped association between CRP and PTSD severity that remains significant when adjusting for potential confounders including depression and sociodemographic risk factors. In the literature, findings have been varied with CRP. For instance, when depression and demographic variables were controlled in another study, patients with PTSD had lower CRP, in contrast to our findings [21]. Another study found that CRP and sICAM-1, other inflammatory markers, were higher with PTSD, but the difference with CRP disappeared when controlling for depression [22]. Moreover, CRP does appear to increase with combined PTSD and ELA.

Our study also revealed a positive association between PTSD severity score and sICAM-1 and sTNFR2. These results suggest that inflammation is a potential outcome of PTSD. sICAM-1, but not CRP, was the key biomarker associated with PTSD in a study with 238 middle-aged twin pairs [22]. Regarding sICAM-1, an adhesion molecule expressed on endothelial cells as well as immune cells, previous studies have shown positive associations between sICAM-1 and atherosclerosis [23]. This could suggest that populations with PTSD should be followed cautiously for higher risk of atherosclerosis. There are no previous reports on sTNFR2 in relation to PTSD, although one small study has revealed that sTNFR2 was elevated in circulation in patients with depression [24]. Since our longitudinal follow-up analysis did not control for follow-up depression levels (only baseline severity), this result needs to be confirmed in a larger population with detailed information of depression over time.

Most significantly, PTSD severity alone is strongly correlated with fibrinogen, even with correction for depression and demographic and social risk factors. We also observed increasing fibrinogen with additive PTSD and ELA severity that survives corrections for many possible confounders. Similarly, another study reported that patients with a PTSD diagnosis showed higher fibrinogen with baseline stress and induced stress than non-PTSD patients [25]. Fibrinogen has also been predicted by hyperarousal severity and overall PTSD severity in otherwise healthy patients with PTSD [26]. Altogether, these suggest altered coagulation and inflammation with PTSD that may be additive with ELA.

Strengths and Limitations

Limitations include the size of the longitudinal substudy, which was relatively small but of sufficient magnitude to confirm data obtained cross-sectionally. However, this data will

need to be replicated in larger studies. Although the clinical diagnoses of overt PTSD would likely require a score of 38 on the UCLA PTSD index [15], in this population study, we considered PTSD scores as a spectrum and compared people without PTSD (Q_1+Q_2) to those with lower PTSD severity scores (Q_3) and higher PTSD severity scores (Q_4) realizing that some people in the highest category would have subclinical PTSD that may not require treatment. Future longitudinal studies with more participants presenting with PTSD symptoms and ELA will be needed to explore interactions more in-depth, including participants with diagnosed PTSD. Furthermore, although we are confident in reporting these associations in studies done both cross-sectionally and longitudinally, we cannot infer a causal relationship, which would require the performance of a randomized clinical trial. Thus, interventional studies are needed to explore whether these metabolic outcomes may be altered by psychological treatments, further linking these outcomes with this altered psychological state.

Conclusions

Overall, our findings suggest that PTSD symptom severity is linked with significant risk for central obesity and obesity-related problems such as insulin resistance and high cholesterol that can lead to cardiovascular disorders and diabetes. These findings suggest that altered metabolic risk, coagulation, and inflammation in the long-term could play an important role in the development of cardiovascular diseases in traumatized individuals and those with PTSD symptoms. Furthermore, many of these cardiometabolic risk factors show an additive effect with PTSD and ELA. If confirmed, these data suggest that from a clinical standpoint, individuals with ELA and PTSD symptoms should be identified in medical settings and monitored carefully for obesity, insulin resistance, and cardiovascular disease. Whether PTSD symptom-specific treatments alone or in conjunction with therapies aiming at reversing effects of ELA would also improve cardiometabolic risk, coagulation, and inflammation remains to be shown in future randomized clinical trials.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Appendix 1

Anthropometric and biomarker measurements

Bioelectrical impedance analysis was assessed using a Quantum II bioelectrical impedance analyzer (RJL Systems, MI). BMI was calculated as weight/height² (kg/m²) and waist circumference was determined along the superior border of the iliac crest.

Dietary information was assessed by Food Frequency Questionnaire (FFQ; NutritionQuest, CA). Smoking status, alcohol consumption, physical activity, and other sociodemographic variables (e.g. income and education level) were assessed by self-report questionnaires.

Measurement of biomarkers

Venous blood samples were collected after an overnight fast at the Clinical Research Center of BIDMC. Leptin was measured by radioimmunoassay (RIA; Millipore, MA). C-reactive protein (CRP) was measured with the Roche Cobas c311 (Roche Diagnostics, IN). Fasting serum insulin level was measured with Immulite 1000 (Siemens, Germany). Fasting blood glucose, fibrinogen, and lipid profiles were measured by LabCorp (Raritan, NJ). Resistin (Millipore, MI), Irisin (Phoenix Pharmaceuticals, CA), and plasminogen activator inhibitor-1 (PAI-1), sICAM-1, and sTNFR2 (R&D Systems, MN) were measured by ELISA in the Mantzoros lab. Stumvoll [1] and Avignon [2] indices were used to measure insulin sensitivity.

Appendix 2

Methods for psychosocial data

Information on early life adversities, PTSD and psychosocial measurements was obtained via validated interviews and questionnaires at Judge Baker Children's Center (JBCC, Boston, MA, USA). Cumulative adversity occurring before age 18 was assessed using a) the Evaluation of Lifetime Stressors interview assessing trauma exposure, b) the Structured Clinical Interview for Diagnoses Diagnostic and Statistical Manual (DSM) IV-R Non-Patient Version Axis 1 including the Post-Traumatic Stress Disorder module, and c) the Adult Attachment Interview yielding narrative descriptions of childhood adversities. An overall adversity score was created by multiplying the number of childhood adversities $\times$ the overall severity of each childhood adversity $\times$ the overall chronicity of childhood adversity (whether chronic or acute), as done previously [3-5]. Two coders independently reviewed and scored all interviews. The severity of each adversity was assessed using a modified version of DSM-III-R Axis IV scale for children and adolescents. The chronicity of adversity was assessed on a 4-point scale, where a score of 0 was given for no reported events, a score of 1 indicated intermittent or acute events, e.g., death of a grandparent, a score of 2 indicated a chronic situation such as an alcoholic caregiver or poverty that lasted throughout a significant time block, and a score of 3 indicated a mixed event, i.e., acute events occurred in the context of ongoing, chronic adversity.

PTSD severity scores and subscale scores were measured with the UCLA PTSD scale [6]. This instrument assesses trauma-related symptoms based on the DSM-IV criteria for PTSD including intrusion/re-experiencing, avoidance, and hyper-arousal. Subscales of intrusion/re-experiencing (criterion B), avoidance (C), and arousal (D) were assessed following the guidelines for the UCLA PTSD subscales [6]. This measure exhibits good construct validity and has been used among young and middle aged adults [7, 8].

The Beck Depression Inventory (BDI) II was used to assess depressive symptoms of participants. Detailed medical and psychological histories, including psychotropic

medications such as anti-depressants, anti-psychotics, and anxiolytics, were obtained from medical and psychological interviews [9].

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Abbreviations

PTSD	posttraumatic stress disorder
BMI	body mass index
sICAM-1	soluble intercellular adhesion molecule-1
sTNFRII	soluble tumor necrosis factor receptor II
BP	blood pressure
HPA	hypothalamic-pituitary-adrenal
OGTT	oral glucose tolerance test
FBG	fasting blood glucose
BDI	Beck Depression Inventory
BMI	body mass index
WC	waist circumference
SiM	insulin sensitivity
TC	total cholesterol
CRP	c-reactive protein
PAI-1	plasminogen activator inhibitor-1
RIA	radioimmunoassay
ELISA	enzyme-linked immunosorbent assay
OGTT	oral glucose tolerance test
FFQ	food frequency questionnaire

Highlights

- PTSD is correlated with obesity/BMI.
- PTSD is associated with a number of cardiovascular disease and diabetes risk factors in a large sample.
- PTSD and early life adversity act in an additive manner to increase cardiometabolic risk.

General characteristics of the participants and relationship with PTSD severity (split into quartiles [Q₁-Q₄] with the first two quartiles [Q₁+Q₂] collapsed)

Table 1

	All (n = 158)	PTSD severity scores			P value*	P for trend†
		0 [Q ₁ +Q ₂] (n = 81)	1–21 [Q ₃] (n = 37)	22–57 [Q ₄] (n = 40)		
Age (y)	45.7 ± 3.5	46.0 ± 3.7	46.0 ± 3.0	44.9 ± 3.5	0.210	0.122
Gender, male (%)	75 (47.5)	42 (52.5)	20 (54.1)	13 (32.5)	0.080	0.060
Race, white (%)	76 (48.1)	44 (55.7)	21 (58.3)	11 (27.5)	0.007	0.008
Education level, 14 years (%)	88 (55.7)	37 (46.8)	20 (54.1)	31 (83.8)	0.001	<0.001
Income level, below 30,000USD/y (%)	78 (49.4)	33 (46.5)	23 (63.9)	22 (64.7)	0.104	0.052
Smoking status					0.001	<0.001
Current smoker (%)	50 (31.6)	15 (19.2)	12 (32.4)	23 (57.5)		
Ex-smoker (%)	25 (15.8)	13 (16.7)	8 (21.6)	4 (10.0)		
Alcohol drinker (%)	111 (70.3)	58 (75.3)	28 (77.8)	25 (65.8)	0.443	0.340
Regular physical activity (%)	119 (75.3)	61 (76.3)	28 (77.8)	30 (76.9)	0.984	0.914
BDI score, 21 (%)	23 (14.6)	5 (6.5)	4 (11.8)	14 (38.9)	<0.001	<0.001
BMI (kg/m ²)‡	29.4 ± 1.3	28.5 ± 1.3	29.5 ± 1.3	31.3 ± 1.2	0.102	0.034
SBP (mmHg)	122.0 ± 15.8	121.7 ± 15.5	119.9 ± 14.4	124.9 ± 17.5	0.377	0.394
DBP (mmHg)	77.4 ± 10.9	76.7 ± 10.0	76.7 ± 12.2	79.6 ± 11.2	0.350	0.200
Fat mass (%)	30.5 ± 11.3	28.5 ± 10.9 ^a	29.7 ± 11.4	35.0 ± 11.2 ^b	0.014	0.005
Fat mass (kg)	28.2 ± 15.0	25.5 ± 13.6	29.0 ± 17.3	32.7 ± 14.6	0.052	0.015
WC (cm)‡	98.6 ± 1.2	96.4 ± 1.2	99.2 ± 1.2	102.7 ± 1.1	0.178	0.063
TC (mg/dL)‡	175.7 ± 1.2	171.7 ± 1.2	175.4 ± 1.3	184.2 ± 1.2	0.158	0.059
FBG (mg/dL)‡	93.6 ± 1.2	91.9 ± 1.2	94.6 ± 1.2	96.1 ± 1.3	0.452	0.212
Avignon index (SIM)‡	4629.6 ± 2.5	5274.3 ± 2.5	4626.7 ± 2.3	3438.8 ± 2.6	0.119	0.043
Total energy (kcal/day)‡	1893.1 ± 1.7	1787.6 ± 1.6	2002.0 ± 1.7	2016.9 ± 1.7	0.372	0.193
Fibrinogen (mg/dL)‡	276.7 ± 1.3	266.8 ± 1.3 ^a	262.6 ± 1.3 ^a	312.4 ± 1.3 ^b	0.005	0.007
CRP (mg/L)‡	1.3 ± 3.5	1.2 ± 3.8	0.9 ± 3.4 ^a	2.0 ± 2.6 ^b	0.029	0.118
Leptin (ng/mL)‡	14.6 ± 3.4	11.6 ± 3.4 ^a	15.3 ± 3.4	21.8 ± 3.2 ^b	0.030	0.008

	PTSD severity scores				P value [*]	P for trend [†]
	All (n = 158)	0 [Q ₁ +Q ₂] (n = 81)	1-21 [Q ₃] (n = 37)	22-57 [Q ₄] (n = 40)		
Resistin (ng/mL) [‡]	9.4 ± 2.8	10.1 ± 2.3	6.8 ± 3.5	11.0 ± 2.8	0.086	0.953
PAI-1 (ng/mL) [‡]	31.6 ± 9.7	34.6 ± 8.7	15.9 ± 12.7	49.6 ± 8.4	0.085	0.653
Irisin (ng/mL) [‡]	146.1 ± 1.6	145.7 ± 1.6	135.4 ± 1.6	158.7 ± 1.8	0.405	0.524

Data are presented as or means ± SD or frequency (%). BDI, Beck Depression Inventory; BMI, body mass index; CRP, C-reactive protein; DBP, diastolic blood pressure; FBG, fasting blood glucose; PAI-1, plasminogen activator inhibitor-1; PTSD, posttraumatic stress disorder; SBP, systolic blood pressure; TC, total cholesterol; WC, waist circumference.

^{*} By ANOVA or chi-square test.

[†] By simple linear regression analysis (continuous variables) or the linear-by-linear association (categorical variables).

[‡] Values are presented as geometric means ± SD.

^{ab} Means in a row with different letter superscripts differ, P<0.05/3 in a *post-hoc* analysis (Bonferroni).

Table 2
Spearman correlation coefficients (*r*) among PTSD severity scores, PTSD subscale severity scores, anthropometric, nutritional, psychological, and laboratory variables

	PTSD severity (Overall scores)		Criteria severity scores (Intrusion/Re-experiencing)		Criteria C severity scores (Avoidance)		Criteria D severity scores (Arousal)	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
Age	-0.074	0.356	-0.182	0.105	-0.088	0.435	-0.053	0.637
BMI	0.163	0.041	0.153	0.172	0.117	0.298	0.098	0.383
SBP	0.047	0.558	0.223	0.048	0.121	0.289	0.122	0.284
DBP	0.068	0.404	0.188	0.097	0.102	0.370	0.118	0.302
Fat mass (%)	0.247	0.002	0.264	0.020	0.251	0.026	0.265	0.019
Fat mass (kg)	0.213	0.009	0.154	0.179	0.152	0.185	0.154	0.180
WC	0.175	0.031	0.129	0.265	0.119	0.302	0.088	0.449
BDI scores	0.458	<0.001	0.393	<0.001	0.551	<0.001	0.423	<0.001
Total energy	0.107	0.189	-0.046	0.689	0.053	0.644	0.008	0.945
TC	0.148	0.068	0.082	0.469	0.058	0.607	0.102	0.366
FBG	0.079	0.340	0.063	0.582	-0.015	0.893	0.002	0.984
Avignon index (SiM)	-0.190	0.037	-0.280	0.030	-0.258	0.047	-0.236	0.069
Fibrinogen	0.216	0.008	0.280	0.014	0.288	0.011	0.332	0.003
CRP	0.122	0.170	0.304	0.015	0.264	0.035	0.229	0.068
Leptin	0.241	0.003	0.297	0.008	0.170	0.134	0.081	0.479
Resistin	0.028	0.734	0.229	0.042	0.195	0.085	0.105	0.356
PAI-1	0.076	0.351	0.303	0.007	0.199	0.078	0.222	0.049
Irisin	0.070	0.399	0.286	0.012	0.080	0.492	0.084	0.473

BDI, Beck Depression Inventory; BMI, body mass index; CRP, C-reactive protein; DBP, diastolic blood pressure; FBG, fasting blood glucose; PAI-1, plasminogen activator inhibitor-1; PTSD, posttraumatic stress disorder; SBP, systolic blood pressure; TC, total cholesterol; WC, waist circumference.

Table 3

Further analysis of the relationship between PTSD severity and metabolic data, modeling to control for demographic, social risk, and other factors (split into quartiles [Q₁-Q₄] with the first two quartiles [Q₁+Q₂] collapsed)

	PTSD severity scores			P value [*]	P for trend [†]
	0 [Q ₁ +Q ₂] (n = 81)	1-21 [Q ₃] (n = 37)	22-57 [Q ₄] (n = 40)		
BMI (kg/m ²) [‡]					
Model 1	28.5 ± 1.0	29.5 ± 1.0	31.3 ± 1.0	0.102	0.034
Model 2	28.5 ± 1.0	29.6 ± 1.0	30.8 ± 1.0	0.234	0.088
Model 3	28.7 ± 1.0	29.4 ± 1.0	30.3 ± 1.0	0.508	0.245
Model 4	28.2 ± 1.0	29.3 ± 1.0	30.0 ± 1.0	0.437	0.200
Model 5	28.1 ± 1.0	29.9 ± 1.0	31.2 ± 1.0	0.082	0.024
Model 6 [§]	28.0 ± 1.0	30.0 ± 1.0	30.9 ± 1.1	0.139	0.047
Fat mass (%) [‡]					
Model 1	28.5 ± 1.3 ^a	29.7 ± 1.8	35.0 ± 1.8 ^b	0.014	0.005
Model 2	29.1 ± 1.0	30.5 ± 1.4	32.5 ± 1.4	0.151	0.052
Model 3	29.4 ± 1.0	30.3 ± 1.4	31.9 ± 1.4	0.351	0.151
Model 4	28.9 ± 1.1	30.2 ± 1.4	30.3 ± 1.7	0.687	0.429
Model 5	28.1 ± 1.3	30.6 ± 1.5	30.8 ± 1.8	0.247	0.111
Model 6	31.4 ± 1.2	31.6 ± 1.3	31.0 ± 1.4	0.942	0.876
TTC (mg/dL)					
Model 1	171.7 ± 1.0	175.4 ± 1.0	184.2 ± 1.0	0.158	0.059
Model 2	170.7 ± 1.0	175.1 ± 1.0	185.3 ± 1.0	0.088	0.030
Model 3	170.1 ± 1.0 ^a	173.4 ± 1.0	187.8 ± 1.0 ^b	0.034	0.014
Model 4	171.2 ± 1.0	171.6 ± 1.0	189.1 ± 1.0 ^b	0.060	0.045
Model 5	173.5 ± 1.0	172.0 ± 1.0	185.8 ± 1.0	0.278	0.229
Model 6	172.1 ± 1.0	170.7 ± 1.0	188.8 ± 1.0	0.173	0.159
FBG (mg/dL)					
Model 1	91.9 ± 1.0	94.6 ± 1.0	96.1 ± 1.0	0.452	0.212
Model 2	91.4 ± 1.0	94.2 ± 1.0	98.0 ± 1.0	0.188	0.068
Model 3	91.6 ± 1.0	94.2 ± 1.0	97.5 ± 1.0	0.279	0.110

	PTSD severity scores			P value [*]	P for trend [†]
	0 [Q ₁ +Q ₂] (n = 81)	1–21 [Q ₃] (n = 37)	22–57 [Q ₄] (n = 40)		
Model 4	90.8 ± 1.0	95.9 ± 1.0	100.4 ± 1.0	0.077	0.023
Model 5	89.3 ± 1.0	95.9 ± 1.0	100.3 ± 1.0	0.041	0.011
Model 6	90.5 ± 1.0	95.4 ± 1.0	101.4 ± 1.0	0.099	0.031
Avignon index (SIM) [‡]					
Model 1	5274.3 ± 1.1	4626.7 ± 1.2	3438.8 ± 1.2	0.119	0.043
Model 2	5297.9 ± 1.1	4673.8 ± 1.2	3387.2 ± 1.2	0.116	0.043
Model 3	5119.7 ± 1.1	4501.4 ± 1.2	3592.5 ± 1.2	0.262	0.105
Model 4	5374.9 ± 1.1	4631.6 ± 1.2	3619.8 ± 1.2	0.315	0.132
Model 5	5255.7 ± 1.2	4489.1 ± 1.2	3369.7 ± 1.3	0.266	0.101
Model 6	3649.0 ± 1.3	3727.6 ± 1.3	3052.8 ± 1.3	0.779	0.639
Fibrinogen (mg/dL)					
Model 1	266.8 ± 1.0 ^a	262.6 ± 1.0 ^a	312.4 ± 1.0 ^b	0.005	0.007
Model 2	266.4 ± 1.0 ^a	262.0 ± 1.0 ^a	313.6 ± 1.0 ^b	0.004	0.006
Model 3	266.2 ± 1.0 ^a	259.5 ± 1.0 ^a	310.3 ± 1.0 ^b	0.008	0.015
Model 4	267.2 ± 1.0 ^a	254.4 ± 1.0 ^a	316.5 ± 1.1 ^b	0.005	0.030
Model 5	262.2 ± 1.0 ^a	255.8 ± 1.1 ^a	313.3 ± 1.1 ^b	0.010	0.018
Model 6	255.4 ± 1.1 ^a	241.6 ± 1.1 ^a	318.5 ± 1.1 ^b	0.001	0.020
CRP (mg/L)					
Model 1	1.2 ± 1.2	0.9 ± 1.3 ^a	2.0 ± 1.2 ^b	0.029	0.118
Model 2	1.2 ± 1.2	0.9 ± 1.2 ^a	1.9 ± 1.2 ^b	0.041	0.136
Model 3	1.2 ± 1.2	0.9 ± 1.2	1.7 ± 1.2	0.097	0.367
Model 4	1.2 ± 1.2	0.7 ± 1.3	1.4 ± 1.3	0.121	0.965
Model 5	1.1 ± 1.2	0.7 ± 1.3	1.5 ± 1.3	0.089	0.558
Model 6	1.4 ± 1.2 ^a	0.7 ± 1.3 ^b	1.5 ± 1.3	0.023	0.914
Leptin (ng/mL)					
Model 1	11.6 ± 1.1 ^a	15.3 ± 1.2	21.8 ± 1.2 ^b	0.030	0.008
Model 2	12.0 ± 1.1	16.2 ± 1.2	18.3 ± 1.2	0.125	0.046
Model 3	12.2 ± 1.1	16.2 ± 1.2	17.5 ± 1.2	0.222	0.094

	PTSD severity scores			P value [*]	P for trend [†]
	0 [Q ₁ +Q ₂] (n = 81)	1–21 [Q ₃] (n = 37)	22–57 [Q ₄] (n = 40)		
Model 4	12.3 ± 1.2	14.7 ± 1.2	16.1 ± 1.3	0.550	0.280
Model 5	11.5 ± 1.2	15.0 ± 1.2	18.1 ± 1.3	0.248	0.085
Model 6	11.2 ± 1.2	12.8 ± 1.3	16.7 ± 1.3	0.324	0.125

Data are presented as geometric means ± SE. BMI, body mass index; CRP, C-reactive protein; FBG, fasting blood glucose; PTSD, posttraumatic stress disorder; TC, total cholesterol.

^{*} By ANOVA or ANCOVA.

[†] By simple or multiple linear regression analysis.

[‡] Race was not included as a covariate in model 3 to 5 because of the presence of interactions between race and PTSD severity.

[§] BMI was not included as a covariate in model 5.

^{ab} Means in a row with different letter superscripts differ, $P < 0.05/3$ in a *post-hoc* analysis (Bonferroni).

Model 1 was unadjusted.

Model 2 was adjusted for age and gender.

Model 3 was adjusted for age, gender, and race.

Model 4 was adjusted for age, gender, race, education, and income.

Model 5 was adjusted for age, gender, race, education, income, smoking, alcohol, and physical activity.

Model 6 was adjusted for age, gender, race, education, income, smoking, alcohol, physical activity, BDI scores, BMI, and total energy intake.

Table 4

Relationship between PTSD and ELA severity with metabolic factors, modeled to account for demographic, social risk, and other important factors (PTSD and ELA are each split into tertiles [T₁-T₃] with the first two tertiles [T₁+T₂] collapsed for each and described as “lower” and the third tertile [T₃] described as “higher”)

	Adversity/PTSD severity scores				
	Both lower [T ₁ +T ₂] (n = 78)	Adversity higher [T ₃]/PTSD lower [T ₁ +T ₂] (n = 28)	Adversity lower [T ₁ +T ₂]/PTSD higher [T ₃] (n = 26)	Both higher [T ₃] (n = 26)	P value* P for trend [†]
BMI (kg/m ²)					
Model 1	28.5 ± 1.0	28.8 ± 1.0	29.8 ± 1.0	32.6 ± 1.0	0.080 0.016
Model 2	28.6 ± 1.0	28.9 ± 1.0	29.6 ± 1.0	32.0 ± 1.0	0.197 0.046
Model 3	28.9 ± 1.0	28.7 ± 1.0	29.5 ± 1.0	30.8 ± 1.0	0.624 0.262
Model 4	28.5 ± 1.0	28.4 ± 1.0	29.5 ± 1.0	30.0 ± 1.1	0.797 0.348
Model 5	27.5 ± 1.0	29.1 ± 1.0	29.5 ± 1.1	31.0 ± 1.1	0.206 0.057
Model 6 [‡]	27.3 ± 1.0	28.7 ± 1.1	29.1 ± 1.1	31.0 ± 1.1	0.266 0.080
Fat mass (%)					
Model 1	28.1 ± 1.3 ^a	30.3 ± 2.2	32.1 ± 2.2	36.1 ± 2.2 ^b	0.018 0.002
Model 2	28.8 ± 1.0	31.3 ± 1.6	30.6 ± 1.7	33.5 ± 1.7	0.105 0.021
Model 3	29.2 ± 1.0	31.1 ± 1.6	30.5 ± 1.7	32.4 ± 1.7	0.398 0.117
Model 4	28.9 ± 1.1	30.4 ± 1.9	29.3 ± 1.8	30.9 ± 2.0	0.823 0.478
Model 5	27.1 ± 1.3	30.6 ± 1.8	28.3 ± 2.0	31.7 ± 2.0	0.149 0.136
Model 6	30.0 ± 1.2	32.0 ± 1.5	28.7 ± 1.5	32.5 ± 1.6	0.146 0.701
TTC (mg/dL)					
Model 1	168.2 ± 1.0	185.7 ± 1.0	179.5 ± 1.0	185.6 ± 1.0	0.024 0.011
Model 2	168.0 ± 1.0	183.9 ± 1.0	179.0 ± 1.0	186.0 ± 1.0	0.032 0.010
Model 3	166.6 ± 1.0 ^a	185.4 ± 1.0	179.6 ± 1.0	188.1 ± 1.0 ^b	0.010 0.004
Model 4	167.5 ± 1.0	185.5 ± 1.0	178.8 ± 1.0	190.3 ± 1.0	0.035 0.013
Model 5	168.5 ± 1.0	184.5 ± 1.0	177.6 ± 1.0	186.7 ± 1.0	0.162 0.075
Model 6	168.2 ± 1.0	179.3 ± 1.1	177.1 ± 1.1	193.3 ± 1.1	0.152 0.041
FBG (mg/dL)					
Model 1	92.1 ± 1.0	94.0 ± 1.0	98.7 ± 1.0	92.8 ± 1.0	0.460 0.430

Adversity/PTSD severity scores						
	Both lower [T ₁ +T ₂] (n = 78)	Adversity higher [T ₃]/PTSD lower [T ₁ +T ₂] (n = 28)	Adversity lower [T ₁ +T ₂]/PTSD higher [T ₃] (n = 26)	Both higher [T ₃] (n = 26)	P value *	P for trend [†]
Model 2	92.0 ± 1.0	92.8 ± 1.0	99.3 ± 1.0	94.3 ± 1.0	0.360	0.237
Model 3	92.3 ± 1.0	92.6 ± 1.0	99.2 ± 1.0	93.5 ± 1.0	0.427	0.364
Model 4	91.4 ± 1.0	95.8 ± 1.0	100.1 ± 1.0	97.0 ± 1.0	0.263	0.093
Model 5	89.6 ± 1.0	97.6 ± 1.0	100.2 ± 1.0	98.0 ± 1.1	0.100	0.046
Model 6	91.4 ± 1.0	94.7 ± 1.1	99.9 ± 1.1	100.1 ± 1.1	0.296	0.076
Avignon index (SiM)						
Model 1	5624.8 ± 1.1	4419.3 ± 1.2	3394.0 ± 1.2	3297.1 ± 1.2	0.054	0.007
Model 2	5597.5 ± 1.1	4522.5 ± 1.2	3466.7 ± 1.3	3233.8 ± 1.2	0.066	0.008
Model 3	5331.9 ± 1.1	4630.3 ± 1.2	3476.3 ± 1.2	3432.3 ± 1.2	0.182	0.031
Model 4	5545.7 ± 1.1	4215.2 ± 1.3	3471.3 ± 1.3	3420.6 ± 1.3	0.227	0.045
Model 5	5739.9 ± 1.2	4100.7 ± 1.3	3584.6 ± 1.3	2867.5 ± 1.3	0.086	0.023
Model 6	3988.9 ± 1.2	3625.0 ± 1.3	3626.4 ± 1.3	2484.2 ± 1.3	0.435	0.171
Fibrinogen (mg/dL)						
Model 1	260.8 ± 1.0	272.2 ± 1.1	305.0 ± 1.1	305.9 ± 1.1	0.014	0.002
Model 2	262.7 ± 1.0	268.2 ± 1.1	302.3 ± 1.1	305.7 ± 1.1	0.026	0.004
Model 3	263.2 ± 1.0	266.6 ± 1.1	301.2 ± 1.1	298.4 ± 1.1	0.069	0.014
Model 4	264.3 ± 1.0	259.2 ± 1.1	303.1 ± 1.1	296.8 ± 1.1	0.082	0.031
Model 5	255.9 ± 1.0	258.6 ± 1.1	293.2 ± 1.1	310.7 ± 1.1	0.029	0.018
Model 6	252.5 ± 1.1 ^a	239.7 ± 1.1 ^a	287.3 ± 1.1	319.2 ± 1.1 ^b	0.006	0.021
CRP (mg/L)						
Model 1	1.0 ± 1.2	1.5 ± 1.3	1.6 ± 1.3	1.9 ± 1.3	0.084	0.015
Model 2	1.0 ± 1.2	1.5 ± 1.3	1.4 ± 1.3	1.7 ± 1.3	0.176	0.036
Model 3	1.0 ± 1.2	1.4 ± 1.3	1.4 ± 1.3	1.5 ± 1.3	0.486	0.161
Model 4	1.0 ± 1.2	1.4 ± 1.3	1.3 ± 1.3	1.1 ± 1.4	0.786	0.622
Model 5	0.8 ± 1.2	1.4 ± 1.3	1.2 ± 1.4	1.4 ± 1.4	0.332	0.242
Model 6	1.2 ± 1.3	1.3 ± 1.4	1.2 ± 1.4	1.5 ± 1.4	0.876	0.746
Leptin (ng/mL)						
Model 1	11.6 ± 1.1	14.1 ± 1.3	18.6 ± 1.3	23.4 ± 1.3	0.057	0.006
Model 2	12.0 ± 1.1	15.3 ± 1.3	17.3 ± 1.2	19.4 ± 1.3	0.211	0.036

Adversity/PTSD severity scores					
	Both lower [T ₁ +T ₂] (n = 78)	Adversity higher [T ₃]/PTSD lower [T ₁ +T ₂] (n = 28)	Adversity lower [T ₁ +T ₂]/PTSD higher [T ₃] (n = 26)	Both higher [T ₃] (n = 26)	P value* P for trend [†]
Model 3	12.3 ± 1.1	14.9 ± 1.3	17.2 ± 1.2	18.1 ± 1.3	0.405 0.094
Model 4	12.2 ± 1.2	14.3 ± 1.3	17.1 ± 1.3	16.0 ± 1.3	0.631 0.230
Model 5	11.1 ± 1.2	15.2 ± 1.3	18.6 ± 1.3	18.7 ± 1.3	0.237 0.061
Model 6	11.2 ± 1.2	12.1 ± 1.3	16.2 ± 1.3	16.1 ± 1.3	0.465 0.192

Data are presented as geometric means ± SE. High adversity scores: 16; low adversity scores: < 16. High PTSD severity scores: 11; low PTSD severity scores: < 11. BMI, body mass index; CRP, C-reactive protein; FBG, fasting blood glucose; PTSD, posttraumatic stress disorder; TC, total cholesterol.

* By ANOVA or ANCOVA.

[†] By simple or multiple linear regression analysis.

[‡] BMI was not included as a covariate in model 6.

^{ab} Means in a row with different letter superscripts differ, $P < 0.05/6$ in a *post-hoc* analysis (Bonferroni).

Model 1 was unadjusted.

Model 2 was adjusted for age and gender.

Model 3 was adjusted for age, gender, and race.

Model 4 was adjusted for age, gender, race, education, and income.

Model 5 was adjusted for age, gender, race, education, income, smoking, alcohol, and physical activity.

Model 6 was adjusted for age, gender, race, education, income, smoking, alcohol, physical activity, BDI scores, BMI, and total energy intake.