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PTSD as a Catalyst for the Association between Metabolic Syndrome and Reduced Cortical Thickness

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Abstract

Background—Metabolic syndrome (MetS), defined by a constellation of cardiometabolic pathologies, is highly prevalent among veterans, especially those with posttraumatic stress disorder (PTSD), and poses a major risk for adverse health outcomes, including neurodegeneration and mortality. Given this, we evaluated: (a) the association between MetS and neural integrity, indexed by cortical thickness; (b) the relationship between PTSD and MetS; and (c) if PTSD was associated with cortical thickness indirectly through MetS.

Methods—The sample consisted of 346 US military veterans (89.3% male; 71.4% white) who deployed to Iraq and/or Afghanistan. Neuroimaging data were available for 274 participants.

Results—In whole-brain analyses, MetS was negatively associated with cortical thickness in 2 left and 4 right hemisphere regions: (a) bilateral temporal lobe, including temporal pole, fusiform gyrus, and insula, and extending into occipital cortex (left hemisphere) and orbitofrontal cortex (right hemisphere); (b) bilateral precuneus, posterior cingulate, calcarine, and occipital-parietal cortex; and (c) right rostral anterior cingulate cortex and central sulcus/postcentral gyrus. Path

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Authors Wolf and Sadeh had full access to data and take responsibility for the integrity of the data and accuracy of the data analysis.

models showed that PTSD predicted MetS (β = .19, $p < .001$), which, in turn, was associated with reduced cortical thickness (βs from −.29 to – .43, all $p < .001$).

Conclusions—Results from this young veteran sample provide evidence that PTSD confers risk for cardiometabolic pathology and neurodegeneration and raise concern that this cohort may be aging pre-maturely and at risk for substantial medical and cognitive decline. This highlights the need to identify the molecular mechanisms linking PTSD to MetS and for effective interventions to reduce PTSD-related health comorbidities.

Keywords

metabolic syndrome; cortical thickness; magnetic resonance imaging; posttraumatic stress disorder; structural equation modeling; accelerated aging

Introduction

Metabolic syndrome (MetS) is a constellation of pathogenic cardiometabolic markers that collectively increase risk for cardiovascular disease (1–2), type 2 diabetes (2–3), cancer (4), cognitive decline (5–6), and death (1;7). It is defined by three or more of the following: obesity, high blood pressure, insulin resistance, and dyslipidemia (elevated triglycerides or low high-density lipoprotein) (8–9) and medical consensus is that when these symptoms co-occur, the health consequences are particularly profound (6,10). Stress, including psychological and traumatic stress (11–13), is thought to play a role in the pathogenesis and course of MetS (14–16) and various pathways have been implicated including autonomic dysregulation and cardiovascular reactivity (13;17–18), hypothalamic-pituitary-adrenal (HPA) axis dysregulation (13;16–17;19), oxidative stress (13;19–22), and immune system dysfunction (13;17–19).

Posttraumatic stress disorder (PTSD) has been linked with elevated risk for MetS (23–25). PTSD is defined by severe trauma exposure followed by reliving of the traumatic experience, avoidance of trauma-related stimuli, negative alterations in cognition and mood, and alterations in arousal and reactivity (26). It is prevalent among nearly a quarter of veterans of the conflicts in Iraq and Afghanistan (27), and poses a major public health concern (28) and financial burden (29). Chronic symptoms of PTSD, including emotional and physiological reactivity, blunted positive affect, social isolation, sleep disturbance, hypervigilance, and startle, are thought to induce dysregulation in autonomic arousal (30), HPA axis (31), and immune functioning (32–33), and may also be associated with oxidative stress and premature cellular senescence (34–36). Two recent meta-analyses found that the prevalence of MetS given PTSD was 37–39% (23–24), which was nearly double that of general population controls (23). Longitudinal studies also suggest that PTSD predicts increasing metabolic risk over time (37–38). Thus, MetS may be an important mechanism linking PTSD to a host of associated medical comorbidities, including cardiovascular disease (39–43), type 2 diabetes (44), cognitive decline (45), and pre-mature death (35;39).

MetS features have also been shown to exert widespread effects on the structural integrity of the brain through reduced blood flow which leads to suboptimal vessel perfusion and degeneration of brain tissue (46–47). Obesity is a strong predictor of decreased cortical

thickness, an indicator of gray matter integrity (48–49), and this is most consistently found for temporal, frontal, and parietal regions (50–54). Blood pressure has been negatively associated with cortical thickness (55–56), as have glucose, insulin resistance, and type 2 diabetes (55;57–59). Cholesterol, in contrast, has shown less consistent patterns, with some studies supporting negative associations with cortical thickness (54) and others suggestive of positive associations(55;60). To our knowledge, only one prior study has evaluated the combined effects of the full constellation of MetS markers on cortical thickness. Specifically, Song et al. (61) found that MetS diagnosis was associated with reduced cortical thickness in the left insular, superior parietal, postcentral, entorhinal, and right superior partial cortices in a sample of 86 participants (40 with MetS).

The primary aim of this study was to examine associations between PTSD, MetS, and neural integrity of the cortex in a cohort of veterans deployed to Iraq and/or Afghanistan. We hypothesized that PTSD severity would be associated with greater MetS severity which, in turn, would be associated with reduced cortical thickness in temporal and frontal lobes.

Methods and Materials

Participants

Participants were US Military veterans deployed to Iraq and/or Afghanistan who underwent assessment at the Translational Research Center for TBI and Stress Disorders, a US Department of Veterans Affairs (VA) Rehabilitation Research and Development Traumatic Brain Injury Center of Excellence at VA Boston Healthcare System. Exclusion criteria included history of seizures unrelated to head injury, neurological illness, current psychotic or bipolar disorder, severe depression or anxiety, active homicidal and/or suicidal ideation with intent, cognitive disorder due to general medical condition other than traumatic brain injury (TBI), and unstable psychological diagnosis that would interfere with accurate data collection. Additional MRI exclusion criteria included pregnancy and having a metal implant, shrapnel, aneurysm clip, or pacemaker. MetS-related measures were available for 346 participants. Of these, 89.3% were male and the mean age was 32.48 years (*SD*: 8.95). The majority of the sample (71.4%) reported their race as white; additional self-reported race and ethnicity was 15.6% Hispanic or Latino/a, 7.8% black, 1.7% Asian, 1.2% American Indian. With respect to educational attainment, 34.4% of the sample had earned up to a high school degree or equivalent and an additional 65.0% of the sample engaged in education beyond high school. Whole-brain cortical thickness data were available for a subset of 274 participants, none of whom had a history of moderate or severe TBI. Demographic characteristics for this subgroup were near identical to that of the larger sample, as detailed in Supplementary Results and Supplementary Table 1.

Procedure

Participants provided written informed consent and had early morning fasting blood samples drawn. Two standing and two seated blood pressure readings were taken at one minute intervals and height, weight, and waist-to-hip ratio was measured. Blood samples were processed immediately and shipped the same day to a commercial lab for metabolic panels. A binary MetS variable was computed following the National Cholesterol Education

Program (NCEP) Adult Treatment Panel III recommendations (9) (Table 1), which requires the presence of three or more MetS criteria for the diagnosis. Participants completed diagnostic interviews performed by a PhD-level clinician and underwent MRI scans. The protocol was approved by the relevant institutional review boards.

MRI Acquisition and Processing—Structural imaging scans were completed in a 3-Tesla Siemens TIM TRIO whole-body MRI scanner. Two T1-weighted anatomical scans (voxel size = 1mm3, TR = 2530ms, TE = 3.32ms, FOV = 256×256, # of slices = 176) were acquired and averaged to create a single high contrast-to-noise image. The FreeSurfer v5.1 (http://surfer.nmr.mgh.harvard.edu/) morphometric pipeline was applied, including reconstruction of the cortical mantle and spatial smoothing of 20mm FWHM. Cortical surface models were manually checked slice-by-slice and edited for accuracy. Measurement of cortical thickness was calculated using procedures described previously (49;55;62). See Supplementary Materials for additional MRI processing details.

Measures

PTSD diagnosis and symptom severity was assessed with the Clinician Administered PTSD Scale for DSM-IV (CAPS) (63), the gold-standard PTSD structured diagnostic interview. The CAPS was administered for three time periods: past-month (current PTSD), pre-deployment (if relevant pre-deployment trauma), and post-deployment (worst post-deployment symptoms). The frequency and intensity of symptoms were summed to form a severity score and the highest value of these three assessments was used in analyses as an index of maximum lifetime PTSD severity. Psychiatric diagnoses were reviewed by an expert consensus team.

Data Analysis

Primary analyses modeled MetS using raw lab values and physiological measurements which were submitted to a confirmatory factor analysis (CFA) to form an overall index of the severity of MetS features (i.e., “MetS Severity”). CFA generates latent variables that capture the variance in common across multiple indicators to better reflect an underlying trait, such as an unobserved syndrome. Higher scores on the latent variable reflect greater pathology and co-occurrence of multiple MetS indicators; CFA is preferable from a statistical and ecological validity standpoint to the use of arbitrary diagnostic thresholds. Our model included three lower-order factors to represent MetS components: latent Blood Pressure was indicated (defined) by diastolic and systolic blood pressure measurements; latent Lipid/Obesity was indicated by waist-to-hip ratio, BMI, HDL, and triglycerides; and latent Blood Sugar was indicated by fasting glucose and A1c values. These three factors were specified to load together on a higher-order latent MetS Severity variable, with age and sex included in all analyses as covariates of MetS Severity.[a] All We then extracted factor scores for the higher-order MetS Severity factor, reflecting individual differences in MetS severity, and used those in the whole-brain analyses.

[a]Although BMI and A1c are not components of the NCEP MetS definition, they reflect similar metabolic profiles as do the core MetS criteria and are included here to provide additional indicators of the latent variables. This helps to avoid factor under-identification (i.e., negative *df*). Age and sex were included to identify the higher-order portion of the model (i.e., ensure positive *df* so the regression equations can be solved simultaneously).

Whole-cortex vertex-wise analyses examined associations between MetS severity and cortical thickness using the FreeSurfer general linear model application in Qdec with factor scores on latent MetS entered as the predictor, and age and sex as covariates. The vertex-wise significance threshold was set at $p < .05$. We applied a Monte Carlo simulation with 10,000 iterations to correct for multiple comparisons with a cluster-wise threshold of $p < .001$. We extracted cortical thickness scores from significant clusters for use in subsequent structural equation modeling (SEM).

In each SEM (Figures 2 and 3), maximum PTSD severity was specified to predict latent MetS Severity and latent MetS was specified to predict scores on the cortical thickness clusters with clusters from the right and left hemisphere examined in separate models. Age and sex were included as covariates of MetS Severity and of each cluster and residual covariances among the clusters were estimated. The indirect effects of maximum PTSD severity on each cluster via MetS severity were tested using the 'model indirect' command in Mplus 7.11 (64), which was the software employed for all structural models evaluated (e.g., CFAs and SEMs). Models were evaluated using standard fit indices and guidelines (65) (see Supplementary Materials) by focusing first on overall model fit before evaluating the strength and significance of each path; as such, no *p*-value thresholds were applied.

Results

Prevalence of MetS, Medication Use, and PTSD

The prevalence of MetS in the overall sample was 12.7%; an additional 19.4% had 2 MetS criteria (just short of the diagnostic threshold; see Table 1). A minority of participants was on cholesterol lowering (4.6%), diabetes management (0.6%), or antihypertensive (11.0%) medications; 26.9% were on antidepressants. The prevalence of current PTSD was 61.0% and of lifetime PTSD was 77.2%; the mean maximum PTSD severity across the three assessment time frames was 69.18 (*SD*: 32.72). The prevalence of MetS among those with a lifetime diagnosis of PTSD was 14.3% compared with 7.6% among controls (i.e., those who never met criteria for PTSD). Veterans with a lifetime diagnosis of PTSD met the threshold for a greater number of MetS criteria ($M = 1.12$, $SD = 1.13$) than controls ($M = .84$, $SD = .94$, $p = .027$; see Supplementary Results and also Supplementary Table 2 for an alternative MetS definition).

MetS Severity Latent Variable

The CFA with covariates provided adequate fit to the data (see Supplementary Table 3) with all indicators showing significant associations with their respective lower-order factors at the $p < .001$ level and in the range of $\beta = .41 – .95$ (see Supplementary Figure 1). The three lower-order factors were associated with the higher-order MetS Severity factor at the $p < .001$ level, with the Lipid/Obesity factor showing the strongest association with MetS. Age was positively associated with MetS and women tended to have lower MetS scores (see Supplementary Figure 1).

Cortical Thickness Analyses

The whole-cortex vertex-wise analysis revealed two left and four right hemisphere clusters that survived correction for multiple comparisons wherein cortical thickness was reduced given greater MetS severity (see Table 2 and Figure 1). Bilateral reductions were observed in temporal lobe, including temporal pole, fusiform gyrus, and insula, and extending into occipital cortex (left hemisphere) and orbitofrontal cortex (right hemisphere). Both hemispheres also showed MetS severity-related reductions in portions of precuneus, posterior cingulate, calcarine, and occipital-parietal cortex. Two additional clusters emerged in right hemisphere, the first located in rostral anterior cingulate cortex and the second in central sulcus/postcentral gyrus. Cortical thickness values for these six clusters were extracted and included in the subsequent SEMs. Analyses examining potential confounders of the MetS-cortical thickness associations, including medication use, cigarette and alcohol use, major depression, traumatic brain injury, educational attainment, head size, and an index of inflammation, are described in Supplementary Materials (none altered our primary results).

Structural Equation Models

SEMs were used to test our hypothesis that PTSD severity influences cortical thickness via its association with MetS. The left hemisphere model yielded good fit (Supplementary Table 3) and revealed a significant association between PTSD severity and MetS severity ($\beta = .19$, $p < .001$) and between MetS and both clusters ($\beta = -.43$, $p < .001$ for temporal cluster and $\beta = -.29$, $p = .001$ for precuneus cluster; see Figure 2). The indirect effect of PTSD on left temporal cluster via MetS severity was significant ($\beta = -.08$, $p = .01$) as was the indirect effect on left precuneus cluster ($\beta = -.06$, $p = .02$). The model explained 27% of the variance in temporal cluster and 17% in precuneus. The right hemisphere model also yielded good fit (Supplementary Table 3) and revealed an equivalent PTSD-MetS association as that for left hemisphere and significant associations between MetS and precuneus ($\beta = -.40$, $p < .001$), temporal ($\beta = -.43$, $p < .001$), rostral anterior cingulate cortex ($\beta = -.34$, $p = .001$), and postcentral ($\beta = -.37$, $p = .001$) clusters (see Figure 3). All indirect effects of PTSD on the cortical thickness clusters via MetS severity were significant: precuneus, $\beta = -.08$, $p = .01$; temporal, $\beta = -.08$, $p = .007$; rostral anterior cingulate cortex, $\beta = -.07$, $p = .02$; postcentral, $\beta = -.07$, $p = .02$. The model explained 25% of the variance in precuneus cluster, 32% in temporal, 11% in rostral anterior cingulate cortex, and 14% in postcentral.

Discussion

PTSD is a serious and often disabling condition that affects approximately 23% of veterans of the Iraq and Afghanistan conflicts (27), with an estimated one-third of individuals with PTSD exhibiting chronic symptoms (28;66). Medical comorbidity and pre-mature cognitive decline and mortality are common among those with the disorder (39;43–45). In this sample of returning veterans with a high prevalence of military-related PTSD, we examined associations between PTSD severity, MetS severity, and neural integrity and found PTSD to be associated with both MetS and broad bilateral reductions of cortical thickness, primarily in temporal and parietal regions. That these associations were observed in a relatively young sample, with an average age in their early thirties, is remarkable and underscores the need

for new interventions that target not only the psychiatric features of PTSD, but the co-occurring metabolic and disease processes that are potentiated by PTSD.

The prominence of temporal lobe cortical alterations observed in this sample is consistent with prior studies showing obesity to be associated with decreased microstructural integrity of white matter frontal-temporal tracts (67–68), shorter temporal (and frontal) fiber bundle length (69), decreased cerebral blood flood in temporal and frontal regions (70), decreased functional connectivity in the temporal lobe network (71), and longitudinally associated with temporal lobe atrophy (72). Reduced cortical thickness and other forms of temporal and frontal neurodegeneration may be one mechanism underlying the association between cardiometabolic problems and cognitive decline, including onset of dementing disorders like Alzheimer's disease (70;73–75). Effects observed for parietal regions may bear on research suggesting that parietal cortex atrophy is a prodromal marker for Alzheimer's disease (76): associations between MetS and this region raise questions regarding if MetS contributes to this initial Alzheimer's-related decline in some cases. This is speculative and requires additional research.

This study builds on prior work showing associations between PTSD and reduced cortical thickness in temporal and frontal regions (62;77–79) by suggesting that MetS may be one path to such degeneration. Though precise molecular mechanisms linking the stress of PTSD to MetS are still unknown, various well-known processes are likely involved, including heightened autonomic activity, glucocorticoid activation, immunological dysregulation, and oxidative stress (13;17;80). For example, chronic activation of glucocorticoid pathways secondary to emotional and physiological arousal may yield impaired negative feedback inhibition of the HPA-axis with downstream effects on systemic inflammation (31). This, in turn, may give rise to weight gain and dyslipidemia, which together may provide a pathogenic milieu that leads to MetS (13). Behavioral factors also likely play a role as PTSD has been linked to poor diet and insufficient exercise (81) and these may directly contribute to MetS. Just how psychological symptoms and cardiometabolic processes affect the brain is also not fully understood. One possibility is that they exert epigenetic changes that are expressed in the brain (82–83). A second, emerging possibility based on animal research is that PTSD (84) and MetS components (85–86) (i.e., obesity) might have effects on the integrity of the blood-brain barrier such that it becomes more permeable, which allows inflammation to spread, resulting in neuroinflammation and oxidative stress, and ultimately, cognitive and neuronal decline.

PTSD-related MetS and neurodegeneration may be clinical manifestations of a broader accelerated aging process (30;34–35) wherein normal age-related decline in cellular integrity and function is enhanced due to the cumulative burden of chronic PTSD-related stress. Recent work using DNA methylation data (87) and telomere degradation (88–92) as indices of cellular age provide support for PTSD-related accelerated cellular aging. Emerging research suggests that accelerated aging may be evident even in young adults, coordinated across multiple biological systems, including those implicated in MetS, and predictive of age-dependent abilities such as motoric and cognitive function (93). This highlights the importance of identifying those at risk for accelerated aging as early as possible and developing targeted interventions to prevent, attenuate, or reverse age acceleration and

associated morbidities. To that end, there is preliminary evidence that exercise interventions for PTSD may ameliorate psychological symptoms (94–95) and improve physical fitness and health (94).

Results should be interpreted in light of study limitations. First, these were cross-sectional data and we are unable to draw causal conclusions. Our models were based on hypothesized directional associations, grounded in evidence that PTSD longitudinally predicts MetS (37) and that obesity shows longitudinal associations with neurodegeneration (72). However, reductions in cortical thickness may reflect a risk factor rather than a consequence of MetS and PTSD and/or these variables may exert bidirectional effects on each other. Support for the former idea comes from research suggesting that neuropsychological deficits, including lower IQ, pre-date the development of obesity (96), MetS (97), and PTSD (98), raising the possibility that reduced cortical thickness may similarly pre-date PTSD and MetS. Thus, additional, prospective research is necessary to address this question. Second, generalizability is limited to predominately male military veterans from the conflicts in Iraq and Afghanistan and it is unclear if the strength of these associations might differ in substantially older (or younger) populations. Third, we did not assess insulin, which would help to inform insulin resistance and would complement our assessment of blood sugar. Related to this, there was limited variability in the blood sugar indicators and this could contribute to attenuated associations with the MetS Severity factor, and indirectly, with PTSD and cortical thickness. Fourth, other structural models of MetS were not evaluated and could also be supported by the data, though the model we employed overlaps substantially with prior higher-order latent variable models of MetS (99). Replication and longitudinal research will be required to address these concerns. These limitations are offset by the strengths of the study which include the large sample size, the evaluation of MetS-related gray matter integrity throughout the cortex, with conservative corrections for multiple testing, and the use of multivariate data analyses to more accurately and parsimoniously reflect MetS in association with PTSD and cortical thickness.

The prevalence of PTSD is growing among our nation’s veterans (100) and the same is true for MetS, with some estimates suggesting that at least a quarter of VA health care users meet MetS criteria (101). Together, these two conditions reflect a tremendous cost to the individual and society (28–29;102). Results suggest that PTSD may serve as a catalyst for the association between MetS and widespread alterations to cortical integrity in temporal, parietal, and frontal regions. This speaks to the burden of PTSD and highlights the need to better understand the molecular mechanisms linking PTSD to MetS and for effective interventions to stem the tide of PTSD-related neurodegeneration and pre-mature medical comorbidities.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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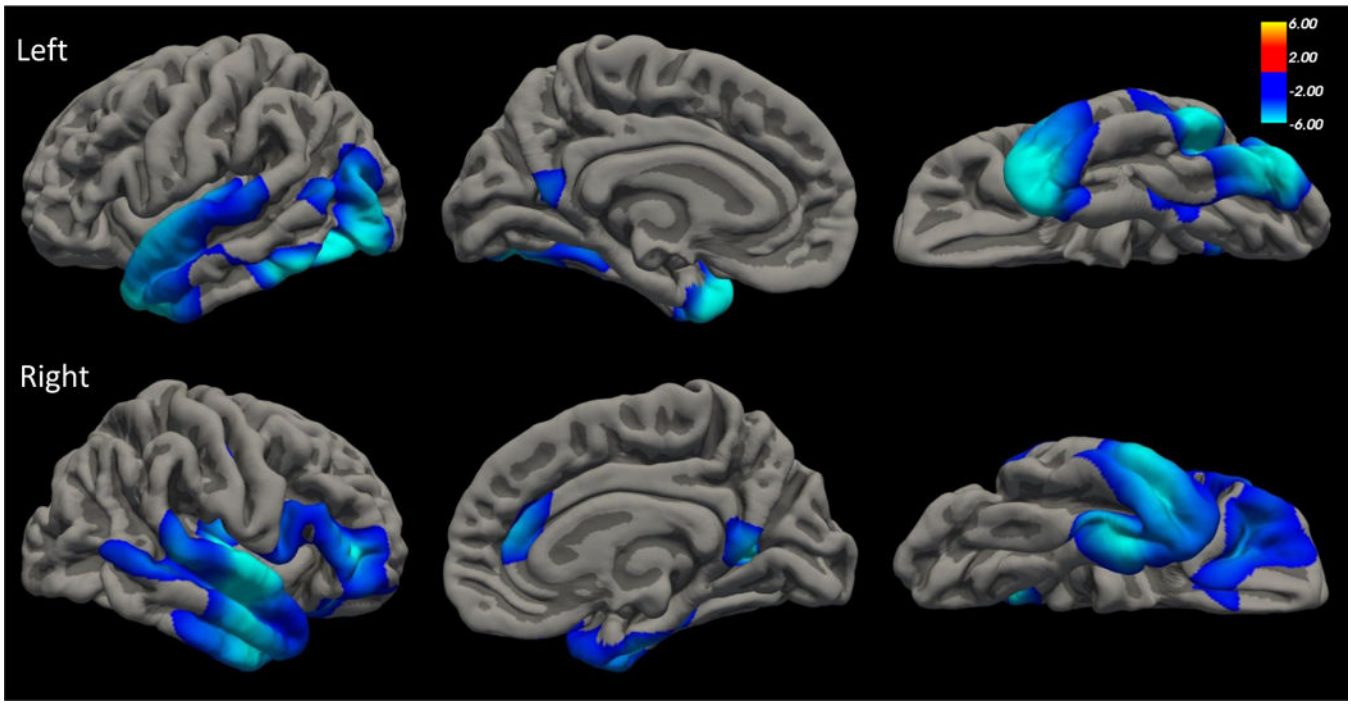

Figure 1.

The top and bottom panels show the regions of the left and right cortices, respectively, that were whole-brain associated with MetS factors scores, controlling for age and sex. The figures show lateral (left), medial (middle), and ventral (right) slices.

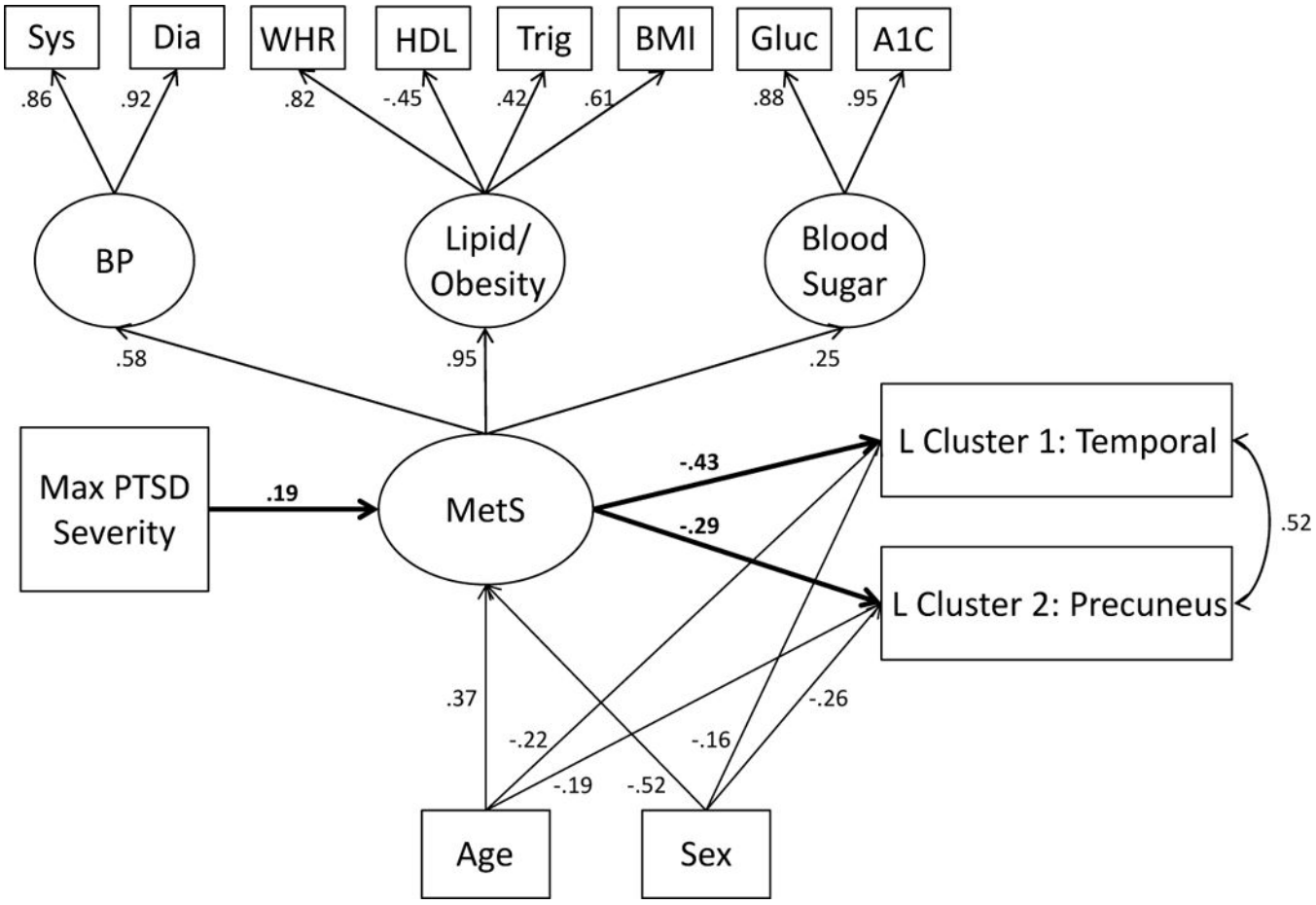

Figure 2.

The Figure shows the higher-order measurement model (confirmatory factor analysis) of MetS and the structural associations between maximum PTSD severity, MetS severity, and the left hemisphere cortical thickness clusters that emerged in the whole-brain analyses. Latent variables are denoted by circles and observed indicators by squares. The primary structural paths of interest are bolded for clarity. All lower- and higher-order factor loadings were significant at the $p < .001$ level. The primary paths of interest were significant at the $p < .001$ level except for MetS→ Cluster 2 where $p = .001$. For covariates, age and sex were significantly associated with MetS ($p < .001$) and with cluster 1 (ps =.004 and .02, respectively) and cluster 2 (ps = .004 and < .001, respectively). PTSD = posttraumatic stress disorder; MetS =metabolic syndrome; sys = systolic; dia = diastolic; WHR = waist-hip-ratio; HDL = high density lipoprotein; trig = triglyceride; BMI = body mass index; gluc = glucose; BP = blood pressure; L = left.

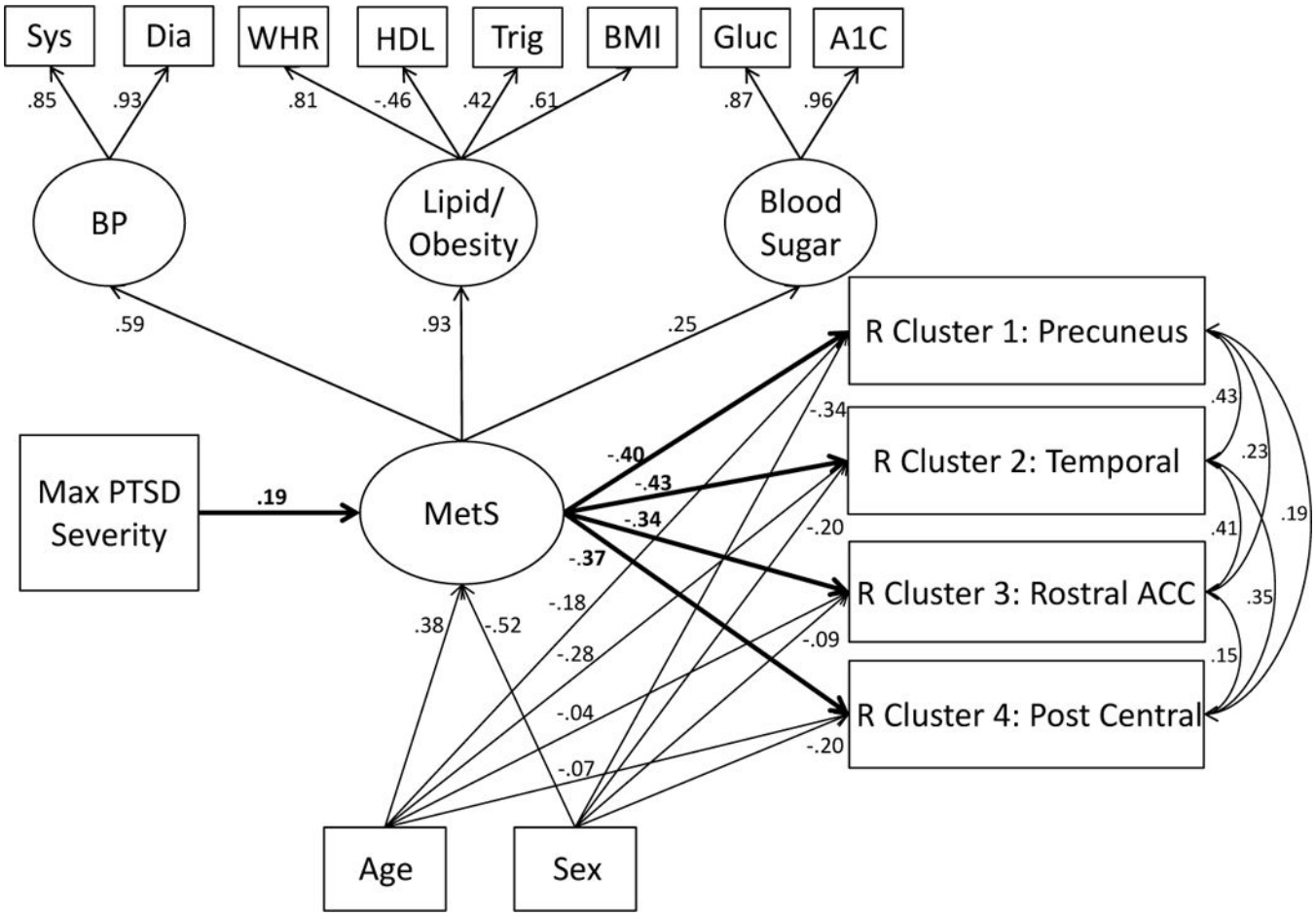

Figure 3.

The Figure is identical to Figure 2 except right hemisphere clusters are depicted. MetS predicted clusters 1 and 2 at the $p < .001$ level and predicted clusters 3 and 4 at the $p = .001$ level. Age and sex were significant covariates of cluster 1 (ps = .005 and < .001, respectively), and cluster 2 (ps < .001 and = .002, respectively), but not of cluster 3 (ps = .68 and .26, respectively) and only partially of cluster 4 (ps = .40 and .02, respectively). R = right; all other abbreviations as in Figure 2.

Table 1

Descriptive Statistics for MetS Criteria and Factor Indicators

		Mean (SD)			% Meeting MetS Criterion		
MetS Cluster	**NCEP MetS Criterion**	**All**	**PTSD+**	**PTSD−**	**All**	**PTSD +**	**PTSD−**
Obesity							
Waist-to-Hip Ratio	Men: >102cm/40in Women: >88cm/36in	0.88 (0.07)	0.88 (0.07)	0.88 (0.06)	30.1%	33.6%	23.4%
BMI		28.34 (4.69)	28.53 (4.89)	27.72 (3.91)			
Blood Pressure (mmHg)					14.7%	16.3%	10.3%
Diastolic	≥85	77.56 (9.55)	77.92 (9.72)	76.35 (8.91)			
Systolic	≥130	117.63 (12.79)	118.02 (13.02)	116.33 (11.96)			
HDL Cholesterol (mg/dL)	Men: < 40 Women: < 50	47.51 (12.64)	47.13 (12.81)	48.78 (12.06)	28.0%	30.9%	23.4%
Triglycerides (mg/dL)	≥ 150	144.12 (133.08)	147.81 (141.32)	131.82 (100.70)	28.0%	29.6%	25.6%
Glucose							
Fasting Glucose (mg/dL)	≥ 110	89.93 (29.19)	90.90 (32.57)	86.64 (11.58)	4.0%	4.6%	2.6%
A1C (% of hemoglobin)		5.43 (0.71)	5.45 (0.79)	5.35 (0.31)			

Note. There were no significant group differences as a function of lifetime PTSD diagnosis for any of the MetS-related variables listed above. However, individuals with lifetime PTSD met the threshold for a greater numbers of MetS criteria overall compared to those without PTSD (p = .027; see Supplementary Materials and Results). Criteria listed above are based on the NCEP Adult Treatment Panel III (9) definition of MetS. Criteria based on the International Diabetes Federation (103) are shown in the Supplementary Materials. BMI was defined as (weight [lbs])/height [in])^2*703. MetS = metabolic syndrome; PTSD = posttraumatic stress disorder; NCEP = National Cholesterol Education Program; SD = standard deviation; BMI = body mass index; HDL Cholesterol = high-density lipoprotein cholesterol; A1C = glycated hemoglobin. SI conversion factors: to convert cholesterol to mmol/L, multiply values by 0.0259; to convert triglycerides to mmol/L, multiply values by 0.0113; to convert fasting glucose to mmol/L, multiply values by 0.0555.

Table 2

Reductions in Cortical Thickness Associated with MetS

Cluster	Peak F-Value	Peak (x,y,z)	No. of Vertices	Cluster Size (mm^2)
L Temporal	−8.0	−30.6, 10.9, −32.5	18629	10864.37
L Precuneus	−4.7	−9.8, −56.2, 18.5	1234	566.98
R Precuneus	−9.3	17.1, −53.7, 12.5	2003	850.95
R Temporal	−7.0	55.1, −10.1, 1.6	24730	12887.62
R Rostral ACC	−5.3	8.1, 35.9, 12.1	1490	717.06
R Postcentral	−4.6	43.8, −15.7, 32.6	1329	569.07

Note. L = left; R = right. A description of the regions that comprise each cluster follows: (1) L Temporal: temporal superior/middle/inferior; temporal pole, fusiform, insula, occipital; (2) L Precuneus: precuneus, occipital-parietal, posterior cingulate, calcarine; (3) R Precuneus: precuneus, occipital-parietal, posterior cingulate, calcarine; (4) R Temporal: orbital medial, orbital middle/lateral, inferior frontal gyrus (pars triangularis, pars opercularis), insula, lateral fissure, temporal superior/middle/inferior; temporal pole, temporal medial/lingual; (5) R Rostral ACC: rostral anterior cingulate, pericallosal, mid-anterior cingulate; (6) R Postcentral: central sulcus, postcentral.