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Posttraumatic stress disorder symptoms and cognitive function in a large cohort of middle-aged women

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Abstract

Background—Posttraumatic stress disorder (PTSD) has been linked to cognitive decline, but research in women is generally lacking. We examined whether trauma and elevated PTSD symptoms were associated with worse cognitive function in middle-aged civilian women. A secondary objective was to investigate the possible role of depression in the relation of PTSD symptoms to cognitive function.

Methods—The sample comprised 14,029 middle-aged women in the Nurses' Health Study II. Lifetime trauma exposure, lifetime PTSD symptoms, and past-week depressive symptoms were measured in 2008. Cognitive function was measured in 2014–2016 using the Cogstate Brief Battery, a self-administered online cognitive battery that assesses psychomotor speed, attention, learning, and working memory. We used linear regression models to estimate mean differences in cognition across PTSD symptom levels.

Results—Compared to no trauma, elevated PTSD symptoms consistent with probable PTSD (i.e., 4+ symptoms on a screening questionnaire) were associated with worse performance on psychomotor speed/attention (b=−0.08 standard units, p=.001) and learning/working memory (b=−0.09, p<.001) composites, after adjusting for socio-demographics. Although attenuated, associations remained significant when adjusted for depressive symptoms and other cognitive risk

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factors. We found the strongest associations among women with comorbid probable PTSD and depression.

Conclusions—PTSD symptoms were negatively related to measures of psychomotor speed/attention and learning/working memory in middle-aged women. Our study adds to a growing literature that suggests that mental disorders are associated with worse cognitive function over the life course.

Keywords

posttraumatic stress disorder; depression; cognitive function; women

Introduction

Posttraumatic stress disorder (PTSD) is associated with increased risk for cardiometabolic and other diseases of aging.[1] With a growing aging population in the United States (U.S.), cognitive decline is a significant public health issue.[2] Furthermore, mounting evidence suggests that brain aging and cognitive decline begin in midlife, long before clinical signs of cognitive decline typically manifest.[3–5] Therefore, identifying potentially modifiable early risk factors for cognitive decline is critical.

PTSD has been linked to decrements in multiple cognitive systems, including processing speed, learning, memory, and executive function.[6–9] Most of this research has been cross-sectional, with many samples comprising male veterans and/or patients with PTSD recruited from healthcare clinics.[9] Neural structural differences that may contribute to poor cognitive function have also been observed in individuals with PTSD compared to those without the disorder, including smaller hippocampal, frontal lobe, and total brain volumes.[10–13] Evidence suggests that the association between PTSD and impaired cognitive function is bidirectional. For example, research indicates that low intelligence and poor pre-trauma cognitive function increase risk of developing PTSD.[14–16] Indeed, prospective analyses indicated that poor pre-deployment visual immediate memory was associated with greater post-deployment PTSD symptom severity in a predominantly male sample of war-deployed soldiers.[17] In addition, research suggests that PTSD is associated with acquired cognitive deficits. In a male Vietnam veteran sample, PTSD severity was negatively correlated with cognitive performance, even when cognitive measures were adjusted for estimated premilitary intelligence.[18] Additionally, among young adults exposed to a natural disaster, higher PTSD symptom levels (particularly re-experiencing symptoms) were associated with lower levels of verbal memory improvement from pre- to post-trauma, although those who developed PTSD had worse pre-trauma cognitive function than those without post-disaster PTSD.[16] These findings highlight the bidirectional nature of the PTSD-cognitive function relation. In another longitudinal sample of predominantly male, war-deployed soldiers, higher PTSD symptom levels were associated with worse attention one year after returning from deployment, over and above pre-deployment attention.[19] Furthermore, initial research in predominantly male samples of treatment-seeking older veterans has found that PTSD is associated with an approximately two-fold increased risk of incident dementia.[20–22] Notably, associations of PTSD with cognitive function have been largely independent of

depression. Depression is frequently comorbid with PTSD,[23] and has been linked to cognitive decline.[24–26]

Although studies suggest an association between PTSD and poor cognitive function, further research is needed to examine the generalizability of these findings. In particular, work in civilians, non-treatment-seeking individuals, and women will address key limitations of prior research. Studying non-treatment-seeking samples is especially important because ascertainment bias might inflate associations between PTSD and cognitive decline in treatment-seeking samples (i.e., if greater PTSD severity and cognitive difficulties both independently motivate greater engagement with healthcare providers). Furthermore, it is important to examine the relation between PTSD and cognitive function in women in particular. PTSD is twice as common in women than in men,[23] and cognitive decline is more common in women because they live longer. Additionally, women are less likely than men to experience certain traumas, such as combat and accidents,[27] that may result in severe head injury—a risk factor for dementia.[28] However, studies of PTSD and cognitive function in civilian women exposed to a wide range of traumatic experiences are generally lacking.

We investigated associations among trauma exposure, PTSD symptoms, and cognitive function in a large cohort of middle-aged women participating in the Nurses' Health Study II (NHS II). We hypothesized that, compared to no trauma, elevated PTSD symptoms would be associated with worse performance on measures of psychomotor speed/attention and learning/working memory. Consistent with previous research, we predicted that the PTSD symptom-cognitive function relation would be independent of depression, although we hypothesized that comorbid elevated PTSD and depressive symptoms would have the strongest associations with cognition.

Materials and Methods

Participants

The NHS II cohort comprises 116,429 female nurses in the U.S., aged 25–42 years at enrollment in 1989. Women complete questionnaires biennially; follow-up is ongoing. In 2008, a supplemental questionnaire on trauma exposure and PTSD[29] was mailed to 60,804 women selected according to their prior NHS II participation; 54,224 women returned this questionnaire (89% response rate). From 2014–2016, 40,082 women with information on trauma/PTSD, and with known email addresses, were invited to complete the Cogstate Brief Battery, a self-administered online cognitive battery; 14,151 women completed this assessment (35% response rate). This study was approved by the Partners Healthcare Human Research Committee and conducted in compliance with the Code of Ethics of the World Medical Association (Declaration of Helsinki). Return of questionnaires and Cogstate completion constituted consent.

Trauma and PTSD Symptom Assessment

Trauma exposure was measured with a 16-item modified version of the Brief Trauma Questionnaire,[29,30] a reliable and valid trauma exposure measure that parallels interview

measures.[30] Lifetime exposure to 15 traumatic events (e.g., physical assault, natural disaster exposure), in addition to "a seriously traumatic event not already covered," was assessed. Respondents reported whether events occurred, and identified the first event and the worst/most distressing event. The Short Screening Scale for *DSM-IV* PTSD[31] was used to assess whether women ever experienced any of seven PTSD symptoms subsequent to their worst trauma. Women provided information on the following symptoms of PTSD only if they reported a history of trauma exposure: 1) avoided places/people/activities associated with the trauma; 2) lost interest in important/enjoyable activities; 3) felt isolated/distant from others; 4) found it hard to have love/affection for others; 5) had a sense of foreshortened future; 6) had sleep difficulties; 7) became jumpy/easily startled. Reliability of self-reported age-of-onset of trauma and PTSD has been excellent in this sample (intraclass correlation coefficient=.95).

Women were classified into four groups indicating lifetime trauma/PTSD symptom status: 1) no trauma exposure, 2) trauma-exposed with no PTSD symptoms, 3) trauma-exposed with 1–3 symptoms, and 4) trauma-exposed with 4–7 symptoms. This classification was based on previous research with this screening questionnaire recommending a score of 4+ as a clinical cutoff for PTSD.[31] This cutoff defined positive PTSD cases in other community-based samples with a sensitivity of 85% and specificity of 93%.[31]

Depression Assessment

The 10-item Center for Epidemiologic Studies Depression (CES-D) scale was administered in the 2008 trauma/PTSD supplemental questionnaire. This CES-D short form has excellent psychometric properties and performs similarly to the 20-item version.[32] Responses were summed to indicate past-week depressive symptom severity (possible range=0–30). The 10-item CES-D was also administered with the 2013 NHS II biennial questionnaire and examined in a sensitivity analysis. Reported history of depression diagnosis at trauma/PTSD assessment (i.e., reporting physician-diagnosed depression on any of the 2003–2009 NHS II biennial questionnaires) was considered in secondary analyses.

Cognitive Assessment

Cognitive function was measured using the Cogstate Brief Battery,[33] a self-administered online battery. The Cogstate Brief Battery has four tasks: Detection, Identification, One Card Learning, and One Back (see Supplemental Methods for details).[33,34] The validity of Cogstate has been well-established,[33,35,36] with evidence of good criterion[37,38] and construct validity.[35,37] Moreover, Cogstate has been shown to be a sensitive indicator of early cognitive deficits.[35] Cogstate performance has been found to be similar in supervised and unsupervised settings,[39] and the feasibility and utility of an unsupervised, online administration of the brief battery has been demonstrated in a large population-based sample.[34] Internet speed does not affect Cogstate performance data because the Cogstate tasks are first loaded via the Internet and then run locally on a participant's computer.

As in previous research,[34] scores on the Detection, Identification, and One Back tasks were calculated by $\log_{10}$ transforming mean response times for correct trials; scores on the One Card Learning task were calculated by arcsine transforming the square root of the proportion

of correct responses. Some research suggests that composites formed from scores on the Cogstate tasks may be more sensitive measures of cognitive function than individual task scores;[40,41] this approach is consistent with neuropsychological models that highlight the benefit of using composite scores in clinical research.[42,43] We created two composite scores based on within-sample z-scores for the individual tasks (task scores were standardized before being combined in composites). A psychomotor speed/attention composite averaged the Detection and Identification task z-scores, and a learning/working memory composite averaged the One Card Learning and One Back task z-scores (see Supplemental Methods for details).[34] These two composites have had high test-retest reliability and clinical utility in identifying cognitive impairment.[40]

Covariates

Potential confounders included age at cognitive assessment, race/ethnicity (African American, Latina, Asian, Caucasian, other), parental education at participant's birth (high school or less, some college, 4+ years of college), husband's education (high school or less, 2- or 4-year college, graduate school), subjective social standing in the U.S., and subjective social standing in the community. Subjective social standing was rated on a 1–10 scale; lower scores indicated higher social standing. Adult body mass index (BMI, kg/m^2) was computed from height and weight self-reported in 2009.[44] Physical activity (<3,3–<9,9–<18,18–<27,27+ metabolic equivalent hours/week), cigarette smoking (nonsmoker, former smoker, current smoker of 1–14, 15–24, or 25+ cigarettes/day), parity (nulliparous, 1, 2–3, 4+ children), oral contraceptive use (never used, current user, former user), and menopausal status (pre-menopausal, post-menopausal) were also measured in 2009. Diet quality based on the Alternative Healthy Eating Index[45] (divided into quintiles) and alcohol consumption (0,1–<5,5–<10,10–<20,20+ grams/day) were assessed in 2011. Variables indicating lifetime history of physician-diagnosed hypertension, myocardial infarction, and type 2 diabetes were computed from women's reports on the 1989–2009 questionnaires.

Statistical Analysis

Using established thresholds,[33,34] we excluded the small number of participants (n=122, 0.9% of Cogstate completers) who failed integrity checks on all four tasks, which suggests that participants did not understand Cogstate instructions. We examined whether lifetime trauma and PTSD symptoms were associated with cognitive function using multivariable linear regression. Separate models were conducted for each cognitive composite; mean differences and 95% confidence intervals (CIs) were estimated. In one model, we adjusted for age at cognitive assessment. In a second model, we further adjusted for race/ethnicity; parental education, husband's education, and subjective social standing were also included as proxies for participants' socioeconomic status. In a third model, we additionally adjusted for depression. In a fourth model, we further adjusted for health behaviors and medical conditions.

To investigate how comorbidity of PTSD and depression might be associated with cognitive function, we categorized women into six groups: 1) no trauma/no depression, 2) no trauma/depression, 3) trauma only (reporting no PTSD symptoms)/no depression, 4) trauma only/depression, 5) PTSD (reporting 4+ symptoms)[31]/no depression, and 6) PTSD/depression.

We classified women as having depression if they had a CES-D score≥10[32] in 2008. In a secondary analysis, we classified women with a history of physician-diagnosed depression as having depression. In these analyses, we focused on differences associated with trauma alone and probable psychiatric conditions (PTSD and depression) for clarity of presentation.

In supplemental analyses, we repeated the primary analyses for the individual Cogstate tasks. Additionally, since we were concerned about depressive symptoms near the cognitive assessment, we conducted a sensitivity analysis adjusting for depressive symptom severity from the 2013 questionnaire, along with Model 3 covariates. Analyses were conducted with SAS 9.4; a 2-tailed *p*-value of .05 was considered statistically significant.

Results

Participant Characteristics

Responders to the invitation to complete the Cogstate battery were highly similar to non-responders (Table 1). Women in these two groups were comparable on socio-demographics, trauma/PTSD symptom status, depression, health behaviors, and medical conditions relevant to cognitive function.

Characteristics for women in the analytic sample (n=14,029) by trauma/PTSD symptom status are presented in Table 2. The vast majority of women (81.6%) reported lifetime trauma exposure. Compared to women without trauma or with trauma and fewer than 4 PTSD symptoms, women with elevated PTSD symptoms (i.e., 4+ symptoms) had slightly worse subjective social standing and their husbands had lower educational attainment. Additionally, these women were more likely to be current or former cigarette smokers, and had higher BMI, lower physical activity, and higher prevalence of medical comorbidities. Women with elevated PTSD symptoms also had higher depressive symptom severity at trauma/PTSD assessment and higher prevalence of history of physician-diagnosed depression.

Trauma, PTSD Symptoms, and Cognitive Function

Distributions of the Cogstate composites are shown in Figure 1. The composites were relatively normally distributed, with a slight negative skew for psychomotor speed/attention. As expected, each increasing year of age was associated with significantly worse cognitive performance: mean difference (b)=−0.037 (95% CI, −0.040, −0.033) for psychomotor speed/attention; b=−0.027 (95% CI, −0.030, −0.024) for learning/working memory, ps<.001.

Compared to no trauma, elevated PTSD symptoms were associated with significantly worse cognitive performance on both composites (Table 3). In age-adjusted models, we found a mean difference of −0.08 (95% CI, −0.13, −0.03) for psychomotor speed/attention for women with 4–7 PTSD symptoms vs. women without trauma. Additionally, among women with 4–7 PTSD symptoms, we found a mean difference of −0.10 (95% CI, −0.14, −0.06) for learning/working memory, compared to women without trauma. The larger mean difference —that for learning/working memory—was equivalent to the mean difference associated with nearly 4 years of aging. Results of models adjusted for age and also socio-demographics (Models 1 and 2, Table 3) were nearly identical. Tests for linear trends of trauma/PTSD

symptoms in these models were significant, *p*s<.01. Although attenuated, associations remained significant when adjusting for depressive symptoms and other cognitive risk factors (Models 3 and 4, Table 3). Trauma exposure alone and subclinical PTSD symptoms were associated with significantly worse cognitive function on the learning/working memory composite compared with no trauma in models adjusting for socio-demographics (Models 1 and 2, Table 3). However, effect sizes were smaller than for elevated PTSD symptoms (mean differences ranged from −0.04 to −0.05, compared to women without trauma). Furthermore, only the association between trauma exposure alone (vs. no trauma) and learning/working memory remained significant when adjusting for depressive symptoms and other potential confounders. Results were similar when we operationalized depression as a history of physician-diagnosed depression (Supplemental Table 1). Results of the models for the primary analyses for the individual Cogstate tasks are presented in Supplemental Table 2.

Findings on comorbidity of probable PTSD and depression and cognitive function are shown in Table 4. In analyses of women with both elevated PTSD and depressive symptoms (consistent with probable PTSD and depression), we found strongest associations with cognitive function, compared to women with neither trauma nor depression (mean differences ranged from −0.12 to −0.15 in age-adjusted models). Additionally, among women with trauma (but not PTSD) and with depression, we found a mean difference of −0.17 (95% CI, −0.23, −0.11) for learning/working memory in age-adjusted models, compared to women without trauma or depression. Women with probable PTSD and without depression also performed worse on all outcomes vs. women without trauma or depression (mean difference of −0.06 for both composites). Results were highly similar when we considered comorbidity of probable PTSD and depression based on a history of physician-diagnosed depression (Supplemental Table 3). Results of the models for the primary analyses for the individual Cogstate tasks are presented in Supplemental Table 4.

In analyses adjusting for depressive symptom severity assessed in 2013 in addition to Model 3 covariates, elevated PTSD symptoms remained significantly associated with worse performance on the learning/working memory composite [*b*=−0.05 (95% CI, −0.09, −0.01), *p*=.02], and with nominally worse performance on the psychomotor speed/attention composite [*b*=−0.05 (95% CI, −0.10, 0.002), *p*=.06].

Discussion

To our knowledge, this is the first study to demonstrate that elevated lifetime PTSD symptoms are associated with worse cognitive function in a large civilian sample of middle-aged women. Traditionally, cognitive function research has focused on older persons; however, it is increasingly clear that cognitive decline starts in mid-life.[3–5] In these middle-aged women, we found that elevated PTSD symptoms falling above the recommended clinical cutoff were associated with worse performance on measures of psychomotor speed/attention and learning/working memory. Even after adjustment for depression, health behaviors, and medical conditions associated with cognitive risk, the association between elevated PTSD symptoms and cognitive function remained significant.

Moreover, strongest associations were observed among women with both elevated PTSD and depressive symptoms. PTSD and depression frequently co-occur,[23] and women with comorbid PTSD and depression may be particularly likely to exhibit impaired cognitive function. However, it is worth noting that women with elevated PTSD and depressive symptoms in our study might have had more severe PTSD manifestations, as co-occurring depression is often observed in individuals with higher PTSD symptom levels.[46,47] Thus, findings from this group could reflect worse cognitive performance in women with particularly severe PTSD rather than comorbidity per se. Future research with diagnostic interview assessments of PTSD and depression is needed to better understand this issue. Women with trauma and probable depression, as well as those with probable PTSD without depression, also had worse cognitive performance on the different composites compared to women without trauma or probable depression. This latter finding indicates that PTSD alone may be related to poor cognition. These results add to growing evidence that mental health is not just associated with psychological experience but also long-term brain health.[4849]

Our findings build on prior studies of treatment-seeking, predominantly older, male veterans linking PTSD to worse cognitive function.[20–22] We examined a large sample of middle-aged community-dwelling women who were exposed to a wide range of traumas. By demonstrating an association between PTSD symptoms and cognitive function in women from the general population, our results suggest that the findings of these previous studies were not solely due to ascertainment bias related to use of treatment-seeking samples. We also accounted for a wide range of potential confounders, including socio-demographics, depression, health behaviors, and medical conditions relevant to cognitive function. Notably, associations between elevated PTSD symptoms with cognitive function were almost identical in models adjusted for age and socio-demographics. Although this may reflect the relatively homogeneous sample (participants were predominantly white professionals), it also suggests that confounding by socio-demographics was unlikely.

Several behavioral and biological mechanisms may underlie relations between elevated PTSD symptoms and cognitive function. For example, PTSD is associated with numerous behavior-related disturbances and conditions (e.g., physical inactivity,[50] obesity,[51] sleep disturbances[52]) that may contribute to poor cognition.[53] PTSD is also characterized by increased oxidative stress[54] and dysregulation of the hypothalamic-pituitary-adrenal axis, neuroendocrine system, and inflammatory response,[55,56] which could lead to cognitive decline (e.g., via increased neuronal death).[54,57] Animal research indicates that glucocorticoid exposure (like that resulting from chronic stress) can result in hippocampal damage,[58] and it is possible that these psychiatric disorders may inflict damage on the brain,[59] although we note that our study does not address these causal relations directly. However, neural structural deficits may also be risk factors for PTSD that predate trauma.[60] Research that distinguishes between pre-existing and acquired brain deficits is critical to establishing mechanisms and, eventually, interventions.

Several limitations of the current study merit consideration. First, lifetime PTSD symptoms were measured with a *DSM-IV* PTSD screening questionnaire, and research using gold-standard diagnostic interviews updated for *DSM-5* is needed. However, our less rigorous measures would likely lead to misclassification and bias results toward the null rather than

create spurious associations. Additionally, further research examining how PTSD duration and remission influence associations with cognition is needed in order to develop a more nuanced understanding of the PTSD-cognitive function relation. Second, similar to many studies of PTSD and cognitive function,[6,9,21] we lacked measures of pre-trauma cognitive function. It is possible that lower cognition preceded, rather than resulted from, trauma/PTSD symptoms. Our findings require confirmation in research with pre-trauma measures of cognitive function. Third, the Cogstate battery was administered several years after the PTSD and depression measures. Accordingly, we were able to include a slight lag between our hypothesized risk factors and cognition to reduce the possibility of reverse causation,[34] but were unable to capture current PTSD or depression status at cognitive assessment. This aspect of our study would likely bias results toward the null. Fourth, although likely minimal, variability in hardware and situational factors could have contributed to increased noise in the Cogstate data, which would also be expected to bias results toward the null. Fifth, although we assessed several domains of cognition using the Cogstate battery, further research with more comprehensive neuropsychological batteries is needed to understand the full extent of associations between elevated PTSD symptoms and cognitive function. Sixth, women needed to remain in the NHS II until 2008 to provide trauma/PTSD data. Survivor bias is thus a potential concern, although only 1.6% of the cohort (n=1,826) was deceased by trauma/PTSD assessment. Selection bias is also a potential concern. Only a subset of the NHS II cohort was eligible to complete Cogstate, and 35% of those invited to participate did so. Nevertheless, Cogstate responders and non-responders were highly similar on numerous characteristics.

Conclusions

Risk factors in mid-life play a role in later cognition.[3] Thus, it is essential to identify determinants of early cognitive decline in middle-aged individuals. Our findings suggest that elevated PTSD symptoms (with and without comorbid depression) are associated with worse cognitive function in middle-aged women. Future research is needed to examine how PTSD symptoms in civilian women relate to trajectories of cognitive decline over time and if they predict faster onset of disorders like dementia. Ultimately, results that elevated symptoms of PTSD (and depression) are negatively associated with cognitive function in middle-aged women from the general population emphasize that mental health has significant implications for other major health outcomes as women age.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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References

1. Levine AB, Levine LM, Levine TB. Posttraumatic stress disorder and cardiometabolic disease. Cardiology. 2014; 127:1–19. [PubMed: 24157651]
2. Anderson LA, Day KL, Beard RL, et al. The public's perceptions about cognitive health and Alzheimer's disease among the US population: a national review. Gerontologist. 2009; 49:S3–S11. [PubMed: 19525214]
3. Launer L. The epidemiologic study of dementia: a life-long quest? Neurobiol Aging. 2005; 26:335–340. [PubMed: 15639311]
4. Singh-Manoux A, Kivimaki M, Glymour MM, et al. Timing of onset of cognitive decline: results from Whitehall II prospective cohort study. BMJ. 2012; 344:d7622. [PubMed: 22223828]
5. Salthouse TA. When does age-related cognitive decline begin? Neurobiol Aging. 2009; 30:507–514. [PubMed: 19231028]
6. Schuitevoerder S, Rosen JW, Twamley EW, et al. A meta-analysis of cognitive functioning in older adults with PTSD. J Anxiety Disord. 2013; 27:550–558. [PubMed: 23422492]
7. Qureshi SU, Long ME, Bradshaw MR, et al. Does PTSD impair cognition beyond the effect of trauma? J Neuropsychiatry Clin Neurosci. 2011; 23:16–28. [PubMed: 21304135]
8. Aupperle RL, Melrose AJ, Stein MB, Paulus MP. Executive function and PTSD: disengaging from trauma. Neuropharmacology. 2012; 62:686–694. [PubMed: 21349277]
9. Scott JC, Matt GE, Wrocklage KM, et al. A quantitative meta-analysis of neurocognitive functioning in posttraumatic stress disorder. Psychol Bull. 2015; 141:105–140. [PubMed: 25365762]
10. Woon FL, Sood S, Hedges DW. Hippocampal volume deficits associated with exposure to psychological trauma and posttraumatic stress disorder in adults: a meta-analysis. Prog Neuropsychopharmacol Biol Psychiatry. 2010; 34:1181–1188. [PubMed: 20600466]
11. Hedges DW, Woon FL. Premorbid brain volume estimates and reduced total brain volume in adults exposed to trauma with or without posttraumatic stress disorder: a meta-analysis. Cogn Behav Neurol. 2010; 23:124–129. [PubMed: 20535062]
12. Childress JE, McDowell EJ, Dalai VV, et al. Hippocampal volumes in patients with chronic combat-related posttraumatic stress disorder: a systematic review. J Neuropsychiatry Clin Neurosci. 2013; 25:12–25. [PubMed: 23487189]
13. Karl A, Schaefer M, Malta LS, et al. A meta-analysis of structural brain abnormalities in PTSD. Neurosci Biobehav Rev. 2006; 30:1004–1031. [PubMed: 16730374]
14. Brewin CR, Andrews B, Valentine JD. Meta-analysis of risk factors for posttraumatic stress disorder in trauma-exposed adults. J Consult Clin Psychol. 2000; 68:748–766. [PubMed: 11068961]
15. Macklin ML, Metzger LJ, Litz BT, et al. Lower precombat intelligence is a risk factor for posttraumatic stress disorder. J Consult Clin Psychol. 1998; 66:323–326. [PubMed: 9583335]
16. Parslow RA, Jorm AF. Pretrauma and posttrauma neurocognitive functioning and PTSD symptoms in a community sample of young adults. Am J Psychiatry. 2007; 164:509–515. [PubMed: 17329477]
17. Marx BP, Doron-Lamarca S, Proctor SP, Vasterling JJ. The influence of pre-deployment neurocognitive functioning on post-deployment PTSD symptom outcomes among Iraq-deployed Army soldiers. J Int Neuropsychol Soc. 2009; 15:840–852. [PubMed: 19891817]
18. Vasterling JJ, Duke LM, Brailey K, et al. Attention, learning, and memory performances and intellectual resources in Vietnam veterans: PTSD and no disorder comparisons. Neuropsychology. 2002; 16:5–14. [PubMed: 11853357]
19. Marx BP, Brailey K, Proctor SP, et al. Association of time since deployment, combat intensity, and posttraumatic stress symptoms with neuropsychological outcomes following Iraq war deployment. Arch Gen Psychiatry. 2009; 66:996–1004. [PubMed: 19736356]
20. Meziab O, Kirby KA, Williams B, et al. Prisoner of war status, posttraumatic stress disorder, and dementia in older veterans. Alzheimers Dement. 2014; 10:S236–S241. [PubMed: 24924674]
21. Yaffe K, Vittinghoff E, Lindquist K, et al. Posttraumatic stress disorder and risk of dementia among US veterans. Arch Gen Psychiatry. 2010; 67:608–613. [PubMed: 20530010]

22. Qureshi SU, Kimbrell T, Pyne JM, et al. Greater prevalence and incidence of dementia in older veterans with PTSD. J Am Geriatr Soc. 2010; 58:1627–1633. [PubMed: 20863321]
23. Kessler RC, Sonnega A, Bromet E, et al. Posttraumatic stress disorder in the National Comorbidity Survey. Arch Gen Psychiatry. 1995; 52:1048–1060. [PubMed: 7492257]
24. Byers AL, Covinsky KE, Barnes DE, Yaffe K. Dysthymia and depression increase risk of dementia and mortality among older veterans. Am J Geriatr Psychiatry. 2012; 20:664–672. [PubMed: 21597358]
25. Rock PL, Roiser JP, Riedel WJ, Blackwell AD. Cognitive impairment in depression: a systematic review and meta-analysis. Psychol Med. 2014; 44:2029–2040. [PubMed: 24168753]
26. Chodosh J, Kado DM, Seeman TE, Karlamangla AS. Depressive symptoms as a predictor of cognitive decline: MacArthur Studies of Successful Aging. Am J Geriatr Psychiatry. 2007; 15:406–415. [PubMed: 17353297]
27. Tolin DF, Foa EB. Sex differences in trauma and posttraumatic stress disorder: a quantitative review of 25 years of research. Psychol Bull. 2006; 132:959–992. [PubMed: 17073529]
28. Guo Z, Cupples LA, Kurz A, et al. Head injury and the risk of AD in the MIRAGE study. Neurology. 2000; 28(54):1316–1323.
29. Morgan CA III, Hazlett G, Wang S, et al. Symptoms of dissociation in humans experiencing acute, uncontrollable stress: a prospective investigation. Am J Psychiatry. 2001; 158:1239–1247. [PubMed: 11481157]
30. Schnurr PP, Vieilhauer MJ, Weathers F, Findler M. The brief trauma questionnaire. White River Junction: National Center for PTSD. 1999
31. Breslau N, Peterson EL, Kessler RC, Schultz LR. Short screening scale for DSM-IV posttraumatic stress disorder. Am J Psychiatry. 1999; 156:908–911. [PubMed: 10360131]
32. Andresen EM, Malmgren JA, Carter WB, Patrick DL. Screening for depression in well older adults: evaluation of a short form of the CES-D. Am J Prev Med. 1994; 10:77–84. [PubMed: 8037935]
33. Fredrickson J, Maruff P, Woodward M, et al. Evaluation of the usability of a brief computerized cognitive screening test in older people for epidemiological studies. Neuroepidemiology. 2010; 34:65–75. [PubMed: 20016215]
34. Koyama AK, Hagan K, Okereke O, et al. Evaluation of a self-administered computerized cognitive battery in an older population. Neuroepidemiology. 2015; 45:264–272. [PubMed: 26501919]
35. Maruff P, Thomas E, Cysique L, et al. Validity of the CogState brief battery: relationship to standardized tests and sensitivity to cognitive impairment in mild traumatic brain injury, schizophrenia, and AIDS dementia complex. Arch Clin Neuropsychol. 2009; 24:165–178. [PubMed: 19395350]
36. Maruff P, Collie A, Darby D, et al. Subtle memory decline over 12 months in mild cognitive impairment. Dement Geriatr Cogn Disord. 2004; 18:342–348. [PubMed: 15316183]
37. Hammers D, Spurgeon E, Ryan K, et al. Validity of a brief computerized cognitive screening test in dementia. J Geriatr Psychiatry Neurol. 2012; 25:89–99. [PubMed: 22689701]
38. Collie A, Myers C, Schnirman G, et al. Selectively impaired associative learning in older people with cognitive decline. J Cogn Neurosci. 2002; 14:484–492. [PubMed: 11970807]
39. Cromer JA, Harel BT, Yu K, et al. Comparison of cognitive performance on the Cogstate brief battery when taken in-clinic, in-group, and unsupervised. Clin Neuropsychol. 2015; 29:542–558. [PubMed: 26165425]
40. Maruff P, Lim YY, Darby D, et al. Clinical utility of the cogstate brief battery in identifying cognitive impairment in mild cognitive impairment and Alzheimer's disease. BMC Psychol. 2013; 1:30. [PubMed: 25566378]
41. Lim YY, Pietrzak RH, Ellis KA, et al. Rapid decline in episodic memory in healthy older adults with high amyloid-β. J Alzheimers Dis. 2013; 33:675–679. [PubMed: 23001710]
42. Nuechterlein KH, Green MF, Kern RS, et al. The MATRICS Consensus Cognitive Battery, part 1: test selection, reliability, and validity. Am J Psychiatry. 2008; 165:203–213. [PubMed: 18172019]
43. Crane PK, Narasimhalu K, Gibbons LE, et al. Composite scores for executive function items: demographic heterogeneity and relationships with quantitative magnetic resonance imaging. J Int Neuropsychol Soc. 2008; 14:746–759. [PubMed: 18764970]

44. Rimm EB, Stampfer MJ, Colditz GA, et al. Validity of self-reported waist and hip circumferences in men and women. Epidemiology. 1990; 1:466–473. [PubMed: 2090285]
45. Chiuve SE, Fung TT, Rimm EB, et al. Alternative dietary indices both strongly predict risk of chronic disease. J Nutr. 2012; 142:1009–1018. [PubMed: 22513989]
46. Momartin S, Silove D, Manicavasagar V, Steel Z. Comorbidity of PTSD and depression: associations with trauma exposure, symptom severity and functional impairment in Bosnian refugees resettled in Australia. J Affect Disord. 2004; 80:231–238. [PubMed: 15207936]
47. Shalev AY, Freedman S, Peri T, et al. Prospective study of posttraumatic stress disorder and depression following trauma. Am J Psychiatry. 1998; 155:630–637. [PubMed: 9585714]
48. Frodl TS, Koutsouleris N, Bottlender R, et al. Depression-related variation in brain morphology over 3 years: effects of stress? Arch Gen Psychiatry. 2008; 65:1156–1165. [PubMed: 18838632]
49. Frodl T, O'Keane V. How does the brain deal with cumulative stress? A review with focus on developmental stress, HPA axis function and hippocampal structure in humans. Neurobiol Dis. 2013; 52:24–37. [PubMed: 22426398]
50. Chwastiak LA, Rosenheck RA, Kazis LE. Association of psychiatric illness and obesity, physical inactivity, and smoking among a national sample of veterans. Psychosomatics. 2011; 52:230–236. [PubMed: 21565594]
51. Kubzansky LD, Bordelois P, Jun HJ, et al. The weight of traumatic stress: a prospective study of posttraumatic stress disorder symptoms and weight status in women. JAMA Psychiatry. 2014; 71:44–51. [PubMed: 24258147]
52. Germain A. Sleep disturbances as the hallmark of PTSD: where are we now? Am J Psychiatry. 2013; 170:372–382. [PubMed: 23223954]
53. Barnes DE, Yaffe K. The projected effect of risk factor reduction on Alzheimer's disease prevalence. Lancet Neurol. 2011; 10:819–828. [PubMed: 21775213]
54. Miller MW, Sadeh N. Traumatic stress, oxidative stress and post-traumatic stress disorder: neurodegeneration and the accelerated-aging hypothesis. Mol Psychiatry. 2014; 19:1156–1162. [PubMed: 25245500]
55. Pitman RK, Rasmusson AM, Koenen KC, et al. Biological studies of post-traumatic stress disorder. Nat Rev Neurosci. 2012; 13:769–787. [PubMed: 23047775]
56. Brouwers, C., Wolf, J., von Känel, R. Inflammatory markers in PTSD. In: Martin, CR.Preedy, VR., Patel, VB., editors. Comprehensive guide to post-traumatic stress disorders. Cham, Switzerland: Springer International Publishing; 2016. p. 979-993.
57. Gorelick PB. Role of inflammation in cognitive impairment: results of observational epidemiological studies and clinical trials. Ann NY Acad Sci. 2010; 1207:155–162. [PubMed: 20955439]
58. Sapolsky RM, Uno H, Rebert CS, Finch CE. Hippocampal damage associated with prolonged glucocorticoid exposure in primates. J Neurosci. 1990; 10:2897–2902. [PubMed: 2398367]
59. Kasai K, Yamasue H, Gilbertson MW, et al. Evidence for acquired pregenual anterior cingulate gray matter loss from a twin study of combat-related posttraumatic stress disorder. Biol Psychiatry. 2008; 63:550–556. [PubMed: 17825801]
60. Gilbertson MW, Shenton ME, Ciszewski A, et al. Smaller hippocampal volume predicts pathologic vulnerability to psychological trauma. Nat Neurosci. 2002; 5:1242–1247. [PubMed: 12379862]

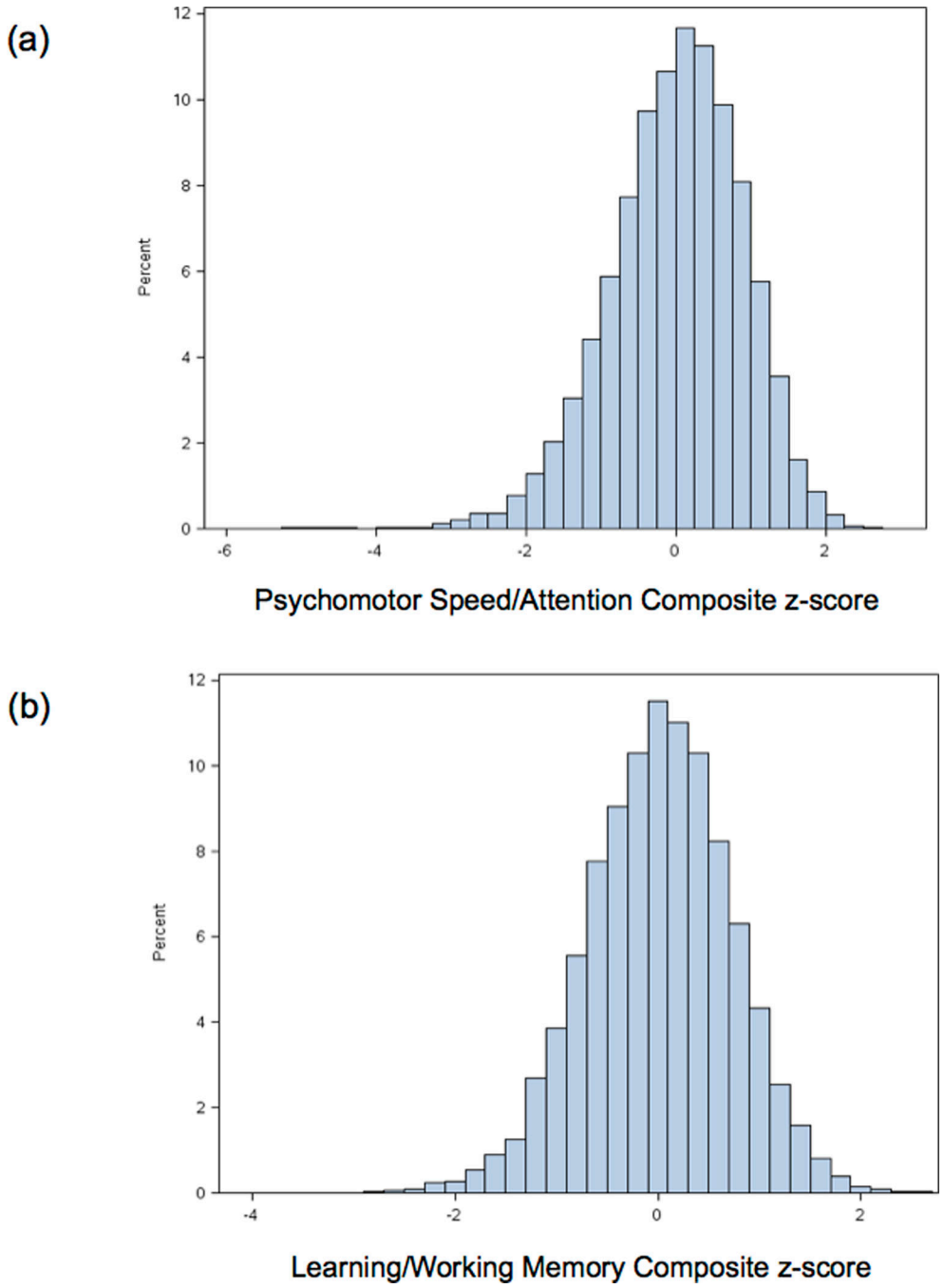

Figure 1.
Distributions of Cogstate composite scores: (a) psychomotor speed/attention and (b) learning/working memory.

Table 1

Characteristics of non-responders and responders to Cogstate invitation.

	Non-responders (*n*=25,931)	Responders (*n*=14,151)
	Mean (SD) or % (n)	**Mean (SD) or % (n)**
Age at Cogstate invitation, years	60.3 (4.6)	61.2 (4.6)
Parents' education at birth, ≥college, %	23.4 (6,072)	24.5 (3,473)
Husband's education, ≥college, %	72.3 (18,744)	72.4 (10,242)
Subjective social standing in the US[a]	3.9 (1.3)	3.8 (1.3)
Subjective social standing in the community[a]	4.0 (1.6)	4.0 (1.6)
Caucasian race, %	93.8 (24,311)	94.9 (13,435)
Body mass index, kg/m^2	27.2 (6.2)	27.3 (6.3)
Cigarette smoking, %		
Never	65.9 (17,093)	65.8 (9,317)
Former smoker	29.1 (7,557)	30.3 (4,280)
Current smoker	4.7 (1,223)	3.8 (530)
Alcohol intake, grams/day	6.9 (10.9)	7.0 (11.0)
Physical activity, MET hrs/wk	24.7 (29.6)	25.0 (29.0)
Mean diet quality on the Alternate Healthy Eating Index[b]	61.2 (12.7)	61.7 (12.8)
Oral contraceptive use, %		
Never	11.3 (2,927)	10.6 (1,502)
Former user	85.6 (22,208)	86.9 (12,301)
Current user	2.3 (605)	2.1 (298)
Menopausal status, %		
Pre-menopausal	22.7 (5,883)	22.3 (3,154)
Post-menopausal	68.9 (17,865)	70.0 (9,907)
Unknown menopausal status	5.6 (1,444)	5.7 (806)
Parity, %		
Nulliparous	17.7 (4,576)	20.3 (2,877)
1 child	13.8 (3,569)	13.4 (1,894)
2–3 children	61.2 (15,873)	59.8 (8,458)
4+ children	7.4 (1,913)	6.5 (922)
Lifetime trauma/PTSD symptom status, %[c]		
No trauma	19.9 (5,168)	18.4 (2,601)
Trauma/no symptoms	47.2 (12,243)	47.5 (6,727)
Trauma/1–3 symptoms	16.3 (4,225)	17.4 (2,459)
Trauma/4–7 symptoms	16.6 (4,295)	16.7 (2,364)
Depressive symptom severity[d]	5.9 (4.9)	5.7 (4.8)
History of physician-diagnosed depression, %[e]	26.1 (6,761)	27.2 (3,855)
History of hypertension, %	36.2 (9,392)	35.1 (4,971)

	Non-responders (*n*=25,931)	Responders (*n*=14,151)
	Mean (SD) or % (n)	**Mean (SD) or % (n)**
History of myocardial infarction, %	1.3 (333)	1.1 (161)
History of type 2 diabetes, %	6.9 (1,787)	6.0 (848)

Note. All health behaviors and medical conditions in the table were collected in the 2009 or 2011 Nurses' Health Study II questionnaires, except depressive symptoms, which were assessed in 2008. History of hypertension, myocardial infarction, or type 2 diabetes was based on data from study baseline through the 2009 questionnaire. MET=metabolic equivalent.

[a] Subjective social standing was rated on a scale from 1–10, with lower scores indicating higher social standing.

[b] Higher scores on the Alternate Healthy Eating Index reflect better diet quality (possible range=0–110).

[c] Lifetime history of trauma exposure and PTSD symptoms based on the Short Screening Scale for *DSM-IV* PTSD administered in 2008.

[d] Total score on the Center for Epidemiologic Studies Depression (CES-D) scale, short form (possible range=0–30).

[e] History of physician-diagnosed depression reported at the 2003–2009 questionnaires.

Table 2

Participant characteristics according to trauma exposure and PTSD symptoms (*N*=14,029).

		Trauma-exposed (*n*=11,450)		
	No trauma (*n*=2,579)	**No symptoms (*n*=6,662)**	**1–3 symptoms (*n*=2,442)**	**4–7 symptoms (*n*=2,346)**
	Mean (SD) or % (n)	**Mean (SD) or % (n)**	**Mean (SD) or % (n)**	**Mean (SD) or % (n)**
Age at Cogstate assessment, years	61.1 (4.7)	61.2 (4.6)	61.3 (4.5)	61.2 (4.5)
Parents' education at birth, ≥college, %	25.3 (652)	24.1 (1,604)	24.4 (596)	25.4 (595)
Husband's education, ≥college, %	72.4 (1,868)	73.5 (4,895)	72.6 (1,773)	69.0 (1,619)
Subjective social standing in the US[a]	3.8 (1.2)	3.8 (1.3)	3.8 (1.3)	4.0 (1.4)
Subjective social standing in the community[a]	4.0 (1.5)	3.9 (1.5)	4.0 (1.5)	4.2 (1.7)
Caucasian race, %	94.8 (2,446)	94.8 (6,317)	95.3 (2,328)	95.0 (2,229)
Body mass index, kg/m^2	27.0 (6.2)	27.3 (6.2)	27.2 (6.0)	28.0 (6.8)
Cigarette smoking, %				
Never	69.3 (1,786)	66.9 (4,455)	64.2 (1,567)	61.4 (1,441)
Former smoker	26.5 (683)	29.0 (1,933)	31.5 (770)	33.1 (777)
Current smoker	4.1 (106)	4.0 (267)	4.3 (105)	5.3 (124)
Alcohol intake, grams/day	7.3 (10.7)	7.0 (11.0)	7.4 (11.4)	6.5 (11.0)
Physical activity, MET hrs/wk	24.4 (28.1)	25.9 (30.1)	25.3 (29.7)	22.6 (24.8)
Mean diet quality on the Alternate Healthy Eating Index[b] %	65.2 (13.2)	65.2 (13.0)	65.8 (12.9)	65.9 (13.5)
Oral contraceptive use, %				
Never	12.7 (327)	10.6 (709)	9.6 (235)	9.3 (218)
Former user	84.4 (2,176)	87.0 (5,794)	88.0 (2,149)	88.5 (2,077)
Current user	2.5 (65)	2.0 (134)	2.1 (50)	1.9 (45)
Menopausal status, %				
Pre-menopausal	25.4 (654)	23.0 (1,530)	19.5 (477)	20.2 (473)
Post-menopausal	67.9 (1,752)	69.2 (4,609)	72.2 (1,762)	72.0 (1,690)
Unknown menopausal status	4.9 (125)	5.7 (382)	6.3 (153)	6.0 (141)
Parity, %				
Nulliparous	22.9 (591)	19.0 (1,268)	20.0 (488)	21.6 (507)
1 child	11.1 (286)	13.5 (900)	12.7 (310)	15.7 (368)
2–3 children	61.2 (1,579)	60.6 (4,035)	60.2 (1,470)	56.0 (1,313)
4+ children	4.8 (123)	6.9 (459)	7.1 (174)	6.7 (158)
Depressive symptom severity[c]	4.5 (3.9)	4.9 (4.1)	6.2 (4.6)	9.0 (6.0)
History of physician-diagnosed depression, %[d]	16.8 (433)	18.2 (1,214)	29.1 (711)	50.3 (1,181)
History of hypertension, %	29.9 (771)	31.2 (2,081)	32.8 (802)	35.2 (825)
History of myocardial infarction, %	0.3 (8)	0.8 (56)	1.4 (35)	1.8 (43)
History of type 2 diabetes, %	3.8 (97)	5.1 (340)	5.3 (129)	5.6 (132)

Note. All health behaviors and medical conditions in the table were collected in the 2009 or 2011 Nurses' Health Study II questionnaires, except depressive symptoms, which were assessed in 2008. History of hypertension, myocardial infarction, or type 2 diabetes was based on data from study baseline through the 2009 questionnaire. MET=metabolic equivalent.

[a] Subjective social standing was rated on a scale from 1–10, with lower scores indicating higher social standing.

[b] Higher scores on the Alternate Healthy Eating Index reflect better diet quality (possible range=0–110).

[c] Total score on the Center for Epidemiologic Studies Depression (CES-D) scale, short form (possible range=0–30).

[d] History of physician-diagnosed depression reported at the 2003–2009 questionnaires.

Table 3

Associations between trauma, PTSD symptoms, and Cogstate composite scores.

	No trauma	Trauma/no symptoms		Trauma/1–3 PTSD symptoms		Trauma/4–7 PTSD symptoms		
Psychomotor Speed/Attention (*n*=13,766)								
		b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*p*-linear trend
Model 1[a]	Ref	−0.02 (−0.06, 0.02)	.32	−0.03 (−0.07, 0.02)	.31	−0.08 (−0.13, −0.03)	.001	.001
Model 2[b]	Ref	−0.02 (−0.06, 0.02)	.35	−0.03 (−0.07, 0.02)	.32	−0.08 (−0.13, −0.03)	.001	.001
Model 3[c]	Ref	−0.02 (−0.06, 0.02)	.41	−0.01 (−0.06, 0.04)	.58	−0.05 (−0.10, −0.001)	.04	.07
Model 4[d]	Ref	−0.02 (−0.06, 0.02)	.38	−0.02 (−0.07, 0.03)	.49	−0.05 (−0.11, −0.002)	.04	.06
Learning/Working Memory (*n*=13,786)								
		b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*p*-linear trend
Model 1[a]	Ref	−0.04 (−0.08, −0.01)	.01	−0.05 (−0.09, −0.01)	.01	−0.10 (−0.14, −0.06)	<.001	<.001
Model 2[b]	Ref	−0.04 (−0.07, −0.01)	.01	−0.05 (−0.09, −0.01)	.01	−0.09 (−0.13, −0.05)	<.001	<.001
Model 3[c]	Ref	−0.04 (−0.07, −0.01)	.02	−0.04 (−0.07, 0.004)	.08	−0.05 (−0.09, −0.01)	.02	.03
Model 4[d]	Ref	−0.04 (−0.07, −0.005)	.02	−0.04 (−0.08, 0.003)	.07	−0.05 (−0.09, −0.01)	.02	.04

Note. Higher scores indicate better cognitive performance.

[a]Adjusted for age at cognitive assessment.

[b]Adjusted for Model 1 covariates plus race/ethnicity, parental education, husband's education, subjective social standing in the U.S., subjective social standing in the community.

[c]Adjusted for Model 2 covariates plus depressive symptom severity in 2008.

[d]Adjusted for Model 3 covariates plus body mass index, physical activity, diet quality, smoking, alcohol use, parity, menopausal status, oral contraceptive use, history of hypertension, history of myocardial infarction, history of type 2 diabetes.

Table 4

Comorbidity of PTSD and depression in relation to performance on Cogstate composite scores.

	No trauma/No depression (*n*=2,276)	No trauma/Depression (*n*=281)		Trauma/No depression (*n*=5,799)		Trauma/Depression (*n*=839)		PTSD/No depression (*n*=1,381)		PTSD/Depression (*n*=960)	
Psychomotor Speed/Attention (*n*=11,364)											
		b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI))	*p*
Model 1[a]	Ref	−0.01 (−0.12, 0.10)	.80	−0.01 (−0.06, 0.03)	.53	−0.08 (−0.15, −0.01)	.03	−0.06 (−0.12, −0.002)	.04	−0.12 (−0.18, −0.05)	.001
Model 2[b]	Ref	−0.02 (−0.13, 0.09)	.78	−0.01 (−0.05, 0.03)	.60	−0.08 (−0.15, −0.01)	.03	−0.06 (−0.12, −0.002)	.04	−0.12 (−0.18, −0.05)	.001
Model 3[c]	Ref	−0.01 (−0.12, 0.10)	.85	−0.01 (−0.06, 0.03)	.58	−0.07 (−0.14, −0.003)	.04	−0.06 (−0.12, −0.001)	.05	−0.11 (−0.18, −0.04)	.001
Learning/Working Memory (*n*=11,383)											
		b (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*	*b* (95% CI)	*p*
Model 1[a]	Ref	−0.03 (−0.12, 0.06)	.53	−0.03 (−0.06, 0.004)	.09	−0.17 (−0.23, −0.11)	<.001	−0.06 (−0.11, −0.02)	.01	−0.15 (−0.21, −0.10)	<.001
Model 2[b]	Ref	−0.03 (−0.12, 0.06)	.50	−0.03 (−0.06, 0.01)	.14	−0.17 (−0.22, −0.11)	<.001	−0.06 (−0.11, −0.01)	.01	−0.15 (−0.20, −0.09)	<.001
Model 3[c]	Ref	−0.02 (−0.11, 0.07)	.65	−0.02 (−0.06, 0.01)	.16	−0.16 (−0.21, −0.10)	<.001	−0.06 (−0.11, −0.01)	.02	−0.14 (−0.19, −0.08)	<.001

Note. Higher scores indicate better cognitive performance. Probable PTSD=4+ symptoms on the Short Screening Scale for *DSM-IV* PTSD. Probable depression=10+ symptoms on the Center for Epidemiologic Studies Depression (CES-D) scale, short form.

[a]Adjusted for age at cognitive assessment.

[b]Adjusted for Model 1 covariates plus race/ethnicity, parental education, husband's education, subjective social standing in the U.S., subjective social standing in the community.

[c]Adjusted for Model 2 covariates plus body mass index, physical activity, diet quality, smoking, alcohol use, parity, menopausal status, oral contraceptive use, history of hypertension, history of myocardial infarction, history of type 2 diabetes.