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Stressful Life Events and Cognitive Decline: Sex Differences in the Baltimore Epidemiologic Catchment Area Follow-Up Study

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Abstract

Introduction: The reasons why women are at higher risk than men for developing dementia are unclear. Although studies implicate sex differences in the effect of stress on cognitive functioning, whether stressful life events are associated with subsequent cognitive decline has received scant research attention.

Methods: In Wave 3 (1993–1996) of the Baltimore Epidemiologic Catchment Area study, 337 men and 572 women (mean age = 47 years) reported recent (within the last year) and remote (from 1981 until 1 year ago) traumatic events (e.g., combat) and stressful-life events (e.g., divorce/separation). At Wave 3 and Wave 4 (2004–2005), they completed the Mini Mental State Examination (MMSE) and a word-list memory test. Multivariable models were used to examine the association between traumatic and stressful-life events at Wave 3 and cognitive change by Wave 4.

Results: A greater number of recent stressful life events at Wave 3, but not of more remote stressful events, was associated with greater verbal memory decline by Wave 4 in women but not in men. Stressful events were not associated with change in MMSE, and there were no associations between traumatic events occurring at any time and subsequent memory or MMSE decline in either sex.

Conclusions: Unlike men, middle-aged women with a greater number of recent stressful life events demonstrate memory decline over a decade later. Sex differences in cognitive vulnerability to stressful life events may underlie women's increased risk of memory impairment in late life, suggesting that stress reduction interventions may help prevent cognitive decline in women.

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Keywords

stress; trauma; cognition; epidemiology; memory; cognitive decline; gender differences

Introduction

Compared to men, women are at increased risk of dementia^{1–3}. Although the reasons for this disparity are unclear, sex differences in the physiological stress response have recently been suggested as potential contributing factors⁴. In response to stressful experiences, a cascade of physiological responses ensues, including the release of glucocorticoids (principally cortisol) via activation of the hypothalamic-pituitary-adrenal (HPA) axis. In numerous animal and human studies, the adverse effects of prolonged stress-induced release of glucocorticoids on hippocampal structure and hippocampal-mediated learning and memory have been demonstrated^{5–8}.

As the effect of increasing age on the cortisol response to pharmacological (i.e., drug or hormone administration) or psychological stress is almost three times higher in women than in men⁹, women may be increasingly vulnerable to the cognitive effects of stress as they age. Indeed, acute stress impairs memory in older women but not in older men^{10,11}.

An association between stress and dementia has also been shown. In a retrospective study, patients who developed dementia experienced a greater number of stressful life events prior to the onset of dementia than did individuals who did not develop dementia¹². In prospective studies, traumatic events in early life are associated with an increased risk of dementia^{13,14}. The importance of considering an individual's *response* to stressful events, rather than simply the *occurrence* of such events, is supported by studies showing that individuals who develop post-traumatic stress disorder (PTSD) are at increased risk of dementia compared to those who experience trauma but do not develop PTSD^{15,16}. Similarly, distress proneness (as measured by high scores on measures of the personality trait neuroticism) is associated with a threefold higher risk of Alzheimer's disease¹⁷. Furthermore, although the presence of stressful life events was not associated with risk for dementia in a study that controlled for sex¹⁸, in a study of women only, Johansson and colleagues¹⁹ found that mid-life stress was linked to an increased risk of dementia 35 years later.

Taken together, prior studies suggest that there are sex differences in the stress response, and that these differences may render women particularly vulnerable to the negative cognitive consequences of stressful events. Sex differences in the association between stress exposure and subsequent cognitive decline have, however, received insufficient research attention. This underdeveloped area in the field of cognitive health and aging is worthy of further exploration because sex differences in the cognitive effects of stress may underlie the sex disparity in preclinical states of cognitive decline with potential consequences to dementia prevalence.

In this prospective study, we analyzed data from the Baltimore site of the Epidemiologic Catchment Area Follow-Up Study to examine sex differences in the association of stressful and traumatic events with subsequent cognitive decline. We hypothesized that exposure to a

greater number of stressful or traumatic events would be associated with subsequent cognitive decline among women but not in men.

Methods

Data for this study were obtained from the Baltimore site of the Epidemiologic Catchment Area (ECA) Study. The ECA Study was commissioned by the NIMH to estimate prevalence, incidence, and treatment seeking for psychopathology over the course of adulthood²⁰. One of five sites (along with New Haven, St. Louis, Raleigh/Durham, and Los Angeles), the Baltimore ECA Study enrolled 3,481 residents of East Baltimore at its initial wave in 1981 (Wave 1). Follow-up assessments were conducted in 1982 (Wave 2), 1993–1996 (Wave 3), and 2003–2004 (Wave 4).

At Wave 3, participants were asked in a structured interview to endorse or deny having experienced specific traumatic and stressful life events within the last year (“recent” events) or between 1981 and one year ago (“remote” events). Specific traumatic events queried were: combat, accident, physical attack, rape, mugging/theft, witness to another being hurt or killed, receiving threats, natural disasters. For trauma over the last year, participants were asked to respond “yes” or “no” if they had experienced any of the events. Thus, each participant was assigned either 0 (“no”) or 1 (“yes”), depending on the response to this question. Regarding traumas from 1981 until 1 year ago, participants were asked to indicate which of the traumatic events they experienced.

Specific stressful life events queried were: marriage, divorce/separation, death of spouse, death of other loved one, birth of child, child moving out, retirement, loss of job, and life-threatening injury/illness. Specific questions were phrased, for example: “In the last year, did you have an injury or illness that threatened your life?”...“Since 1981, did you have an injury or illness that threatened your life?” Positive responses were further queried to determine when they occurred.

At Waves 3 and 4, participants underwent brief cognitive assessment with a global cognitive screening measure (Mini Mental State Examination (MMSE), and an auditory verbal learning and memory task.

The MMSE is a brief global measure of cognition that is commonly used in clinical and research settings²¹. It measures orientation to place and time, simple attention and working memory, memory, language, recall, and visuospatial ability. Scores range from 0 to 30, with higher scores indicating better cognitive function.

Auditory verbal learning and memory was assessed with a word-list learning and recall task that was developed for the Iowa Established Populations for Epidemiologic Studies of the Elderly project²². For this task, examiners read aloud a list of 20 common words, after which participants were asked to state as many of these words as they could remember, in any order (immediate word recall trial). Twenty minutes later, participants were again asked to state as many words from the list as they could remember, in any order (delayed recall trial). Immediately following the delayed recall trial, a recognition trial was administered, wherein a list of 40 words—including the 20 words originally listed—were presented on a sheet of

paper. Participants were asked to identify the original 20 words by placing a mark next to each correct word. Scores for each trial reflected the number of words correctly recalled or recognized, and ranged from 0 – 20 for each of the immediate word recall, delayed word recall, and word recognition trials.

Also in Wave 3, the General Health Questionnaire (GHQ)²³, a screening measure assessing symptoms of anxiety, depression, somatic concerns, and social dysfunction, was administered via interview. Following the questions used in the original questionnaire, participants were asked to rate the degree to which they experienced each item “over the past few weeks,” with response choices for each item ranging from “better than usual” to “much less than usual.” The 20-item version of the GHQ²⁴, with scores ranging from 0 (least amount of distress) to 60 (greatest distress), was analyzed for this study.

In a complete-case analysis, only participants with data for stressful life and traumatic events and for cognitive tests at both Waves 3 and 4 were included, resulting in a sample of 909 individuals (337 men and 572 women).

Statistical analysis

Four separate indices of traumatic events and stressful life events were created. For traumatic events reported over the last year (“recent” traumatic events), the number of events experienced were summed to create the score. For traumatic events that were experienced between 1981 and 1 year ago (“remote” traumatic events), subjects were assigned a “0” if they did not experience any traumas or a “1” if they experienced any traumatic events. For the stressful life events, index scores were created by summing the number of events reported for each of the two time periods (“recent” events occurring within the last year, or “remote” events occurring between 1981 and one year ago). The four indices were: Recent traumatic events, remote traumatic events, recent stressful life events, remote stressful life events.

Cognitive change scores were calculated by subtracting individual test scores (i.e., MMSE total score; word-list memory test immediate word recall score, delayed word recall score, and word recognition score) at Wave 3 from those obtained at Wave 4. Upon inspection of the distribution of test scores, MMSE scores were not normally distributed, so we natural log-transformed those data to create a more normal distribution.

We used Student’s t-tests and Chi square tests to compare men and women on baseline demographic variables, cognitive test performance, and indices of traumatic and stressful life events. We estimated linear regression models, adjusted for age, education, and race to determine the cross-sectional association between sex and cognitive test score at Waves 3 and 4. Similarly, to examine the association between stressful life and traumatic events and change in performance on each cognitive test score between Waves 3 and 4 (i.e., over approximately 11 years), we fit separate linear regression models in women and in men, each adjusted for age, education, race, GHQ, and baseline (Wave 3) performance on the cognitive test score in question. In sensitivity analyses adjusted for other potential covariates (e.g., income, loss of consciousness due to traumatic brain injury), there were no meaningful differences in results (data not shown); thus, these variables were not included in models. All

analyses were performed with Stata versions 12.0 and 13.0 (StataCorp, College Station, TX).

Results

At Wave 4, 294 men and 496 women were lost to follow-up²⁵. There was no difference in attrition by sex ($p = 0.54$), reports of recent traumatic or stressful events ($p = 0.53$ for trauma; $p = 0.88$ for stress), or reports of trauma between 1981 and one year ago ($p = 0.22$). In contrast, participants who were lost to follow-up endorsed fewer remote stressful events (between 1981 and one year ago; $M = 2.13$, $SD = 1.26$) than did those who remained in the study ($M = 2.60$, $SD = 1.35$; $p < 0.001$).

In Table 1 we present participant characteristics at Wave 3 (study baseline) by sex. Women had fewer years of education, were less likely to be White or married, had higher GHQ scores, and had lower incomes than men. Additionally, women had lower MMSE scores, but higher delayed word recognition scores than men, although the differences were quite small.

As shown in Table 2, the likelihood of having experienced a traumatic event or a stressful life event within the last year (recent) or between 1981 and 1 year ago (remote) was not significantly different between men and women.

We next examined the multivariable-adjusted cross-sectional association between sex and cognitive test performance at Waves 3 and 4 (Table 3). In models adjusted for age, education, and race, women performed significantly better than men on the word-list learning task, including the immediate recall ($B = 0.69$; 95% CI 0.36, 1.03), delayed recall ($B = 0.47$; 95% CI 0.13, 0.81), and delayed word recognition ($B = 0.94$; 95% CI 0.59, 1.29) trials at Wave 3. Women continued to perform better on the immediate word recall ($B = 0.53$; 95% CI 0.20, 0.86), delayed word recall ($B = 0.47$; 95% CI 0.14, 0.80), and delayed word recognition ($B = 0.77$; 95% CI 0.37, 1.17) trials at Wave 4.

In models examining whether traumatic and stressful life events predicted cognitive *decline* (Table 4), we found that neither recent nor remote traumatic experiences reported at Wave 3 were associated with subsequent cognitive decline in men or women. In contrast, having experienced a greater number of stressful life events over the last year at Wave 3 was associated with greater decline in delayed word recall ($B = -0.28$; 95% CI -0.56 , -0.005) and recognition ($B = -0.35$; 95% CI -0.68 , -0.02) among women, whereas no association between stressful life events reported at Wave 3 and cognitive change between Waves 3 and 4 was found in men (Table 5). Stressful life events experienced between 1981 and 1 year ago did not predict memory decline in either men or women. No association between recent or remote stress or trauma reported at Wave 3 and change in MMSE score between Waves 3 and 4 were found in men or women.

To address the possibility that the duration of stress might be an important predictor of cognitive decline, we conducted exploratory analyses on the association between the amount of time (number of weeks) participants reported that they required to adjust to the stressful or traumatic events and cognitive change between Waves 3 and 4. These analyses revealed very few sex differences in time to adjust to stressful or traumatic events, and no significant

associations between time to adjust and cognitive change between Waves 3 and 4 (data not shown).

Exploratory analyses omitting the GHQ from the models did not change the findings (data not shown), indicating that our sex-stratified findings were not attributable to sex differences in symptoms of psychological distress.

To assist in interpreting the results of the sex-stratified analyses with regard to the effect of recent stress on subsequent memory decline, we included an interaction term between the recent stress index and sex in the models for change in delayed word recall and word recognition scores that combined data from women and men. The interaction terms were not significant for change in delayed word recall ($B=-0.11$; CI $-0.53-0.31$; $p=0.61$) or delayed word recognition ($B=-0.18$; CI $-0.70, 0.33$; $p=0.48$) score.

Sex by remote stress and sex by recent and remote trauma index interaction terms, fitted into separate model for each cognitive outcome, also did not yield significant results. Details from these analyses, for both unadjusted models and models adjusted for relevant covariates, are shown in Supplemental Tables 1 and 2.

Discussion

In this study, we tested the hypothesis that the experience of stressful life events would be prospectively associated with cognitive decline in women but not in men. Analyzing data from the Baltimore ECA study, we found that a greater number of recently occurring (i.e., past-year) stressful life events reported at Wave 3 was associated with greater memory decline 11 years later in women but not in men. Our hypothesis was thus supported with regard to recent stressors and subsequent memory decline. In contrast, stressful life events reported at Wave 3 to have occurred in the more remote past (i.e., between 1981 and 1 year ago) were not associated with cognitive decline in either sex. The experience of traumatic events was also not associated with cognitive decline in men or women. Although prior studies have shown that increasing age is associated with a much greater increase in the cortisol response to stress in women compared to men⁹, and that acute stress has a negative impact on memory in older women but not older men^{10,11}, we know of no prior studies reporting an association of stress with subsequent memory decline in women but not in men.

We note that unlike memory test scores, change in MMSE score was not associated stressful or traumatic events in either sex. Although it is plausible that those who are more physiologically responsive to stress may demonstrate global cognitive decline with advanced age, the mean age of participants in this study at Wave 4 was 58.9 years ($SD = 12.9$), most likely too young to manifest cognitive decline that is widespread or severe enough to be detected on the MMSE. We recognize that subjects in this study are younger than the typical age of onset of global cognitive decline associated with neurodegenerative disorders such as AD. Nevertheless, by Wave 4, participants were almost 60 years of age, arguably when the earliest manifestations of AD, most often reflected in memory decline, might begin to emerge. In Wave 5 of the ECA, we are following this cohort with a comprehensive cognitive examination to more fully characterize cognitive change over a longer period.

In addition to highlighting sex differences in the impact of stress on memory, the present findings elucidate several other aspects pertaining to the relation between stress and cognitive decline, some of which suggest further study whereas others suggest that alternatives to current theories should be considered. One issue highlighted by our findings concerns the timing of stressful events in women's lives. Stressful events that were reported at Wave 3 to have occurred more recently (within the past year) when women were aged 47 to 48 years on average, were associated with memory decline at Wave 4 (when women were 57 years old on average), whereas stressful events that occurred in the more remote past were not associated with cognitive decline. In addition to a possible survivor effect, such that women with less resilience, died, were not located, or dropped out of the study before Wave 4, the absence of a link between more remote stressors and cognition might be related to the effects of age on the cortisol response to stress, which is much greater in women than in men⁹. Thus, stressors that occur later in life would be expected to have a greater impact on cognition in women compared to men. What remains to be determined, however, is that should sex differences in the cortisol response to stress underlie our finding, then we might also expect women to have had poorer cognition at baseline (i.e., Wave 3), closer to the time when the stressors occurred. This line of reasoning would logically follow from the known negative cognitive effects of heightened cortisol responses to *acute* stress^{10,11}. We suspect, however, that prolonged stressors such as those we queried lead to *enduring* dysregulation of the cortisol response that causes subsequent memory decline. Thus, it may be that only when stressful experiences occur in conjunction with an age-related cortisol sensitivity to stress as well as age-related cognitive vulnerability that this dysregulation leads to memory decline.

Another issue addressed by our findings concerns the differential effects of traumatic and stressful life events on cognitive decline. The experience of trauma, either remotely or recently, was not associated with cognitive decline in men or women in this study. Prior studies have shown that older individuals with PTSD induced by combat or holocaust experiences have poorer cognitive functioning than those who experienced the same traumatic experiences but did not develop PTSD (see Schuitevoerder et al.²⁶ for a meta-analytic review). Taken together, these studies provide further evidence that it is not the *exposure* to trauma, but an individual's *response* to it, that results in negative consequences to cognition; the mere experience of trauma was not itself sufficient to produce cognitive decline in the current study. It is noteworthy that the traumatic events we interrogated included acute events (e.g., mugging/theft, rape), whereas the stressful life events we studied more often led to prolonged life changes (e.g., divorce, death of a spouse). This distinction would suggest that protracted stressors may be more likely than acute but traumatic events to be associated with adverse cognitive outcomes in the long term in women, perhaps by leading to more enduring physiological responses to stressful events.

Another consideration pertains to our finding that men and women were equally likely to report having experienced both traumatic and stressful life events. Given that women score higher on standardized measures of the personality trait *neuroticism* than do men²⁷, indicating that at a population level, women are more likely than men to perceive events as negative, one might predict that women would endorse more stressful life events due to their negative salience. It might be argued, therefore, that stress has an equal effect on cognition in men and women, but because women experience more events as stressful, they are more

likely to suffer cognitive decline *as a consequence of* stressful events⁴. Our findings would suggest, however, that the negative health consequences of stressful experiences may not be inevitable, as men and women reported the same number of stressful events but had differential risk for memory decline in relation to these events. Interventions aimed at altering the stress response may therefore reduce the risk for cognitive decline in later life.

Consistent with our *a priori* hypothesis that the association between stress/trauma and cognition would vary by sex, we conducted sex-stratified analyses. It is important to note, however, that when we tested this hypothesis by including an interaction term between the stress/trauma indices and sex in the models, none of these analyses yielded significant results. Thus, whereas we observed an association between stress and subsequent decline in women but not in men, this effect did not significantly differ by sex. This lack of statistical significance is important, as it suggests a need for caution in interpreting results from the stratified analysis. Indeed, the effect size of the effect of recent stress on later decline in delayed word recall is only slightly larger in women than in men. The effect size for delayed word recognition, however, is almost twice as large in women as it is in men.

Despite the non-significant sex-by-stress-index interaction, confidence in the robustness of the stratified analyses is supported by several aspects of this study, following criteria outlined by Sun and colleagues²⁸ to assess the credibility of subgroup analyses, including an *a priori* hypothesis with a specified direction of effect, examination of a single subgroup (sex), and biological plausibility that stress could negatively affect memory in women but not in men.

Ultimately, the degree to which our findings are meaningful depends on the context within which they will be applied. We aimed to determine whether there was any support to the overall notion that stress affects cognition in women but not in men. The present findings suggest that this is the case, but studies addressing this question in other samples are needed to evaluate their reproducibility.

Several weaknesses of the current study should be noted. First, its observational design does not allow us to make causal inferences. We set forth our hypothesis based on the factors we believe underlie the association between stress and cognition, but we are not able to test directly whether our assumptions are valid absent a true experimental design.

Second, we cannot be sure that other variables for which we did not control might have influenced our findings. It is possible, for example, that women who experienced greater numbers of stressful events differed from men who experienced a similar number of events in ways that could explain our findings. One candidate would be the likelihood of developing distress that leads to depression, in that a greater number of stressful life events increases the risk of developing depression that may in turn lead to cognitive decline. In an exploration of the effects of psychological distress, including symptoms of depression, we omitted the GHQ from the models. The findings, however, did not change, providing additional evidence that the association between stress and subsequent memory functioning is not dependent on subjective distress, but perhaps the physiological response to it. Moreover, findings from a recent population study²⁹ would also argue against the idea that

women might be more likely than men to develop stress-related depression. In that study, a greater number of stressful life events within 3 years of baseline predicted depression 25 years later in men but not in women. This finding suggests that men would be *more likely* than women to suffer from depression-related cognitive decline as a result of stressful life events, but this does not appear to be the case.

As mentioned above, the personality dimension of neuroticism—which reflects distress proneness—may also be relevant to our findings. A study of the subset of Baltimore ECA Follow-Up study participants who completed a personality inventory showed, in models that included adjustment for sex, that higher neuroticism was associated with greater decline in MMSE scores between Waves 3 and 4³⁰. Another possibility is that sex differences in sleep quality and quantity may also have contributed to our findings. Women are more likely than men to experience insomnia, and are at even greater risk for insomnia with advancing age³¹. Coupled with findings that insomnia is associated with cognitive impairment³², sex differences in sleep difficulties may underlie our findings. For this reason, we have added self-report and objective measures (wrist actigraphy) of sleep to the next Wave of the ECA study.

A third weakness is that we did not examine stressful life events at Wave 4, so we cannot rule out the possibility that those with more stressful events at Wave 3 continued to have a greater number of stressful events at Wave 4, and that our findings are due to the recent effects of the stressors experienced between Waves 3 and 4 on women's memory. With regard to the effects of stress duration, we performed exploratory analyses on the amount of time participants reported that they required to adjust to the stressful or traumatic events. These analyses revealed very few sex differences, and no significant associations with cognitive change between Waves 3 and 4. We will be able to more fully address this weakness in subsequent analyses of data obtained from Wave 4 participants who are now being studied in ECA Wave 5.

A fourth weakness is the limited number of cognitive tests available for analysis. It is possible, for example, that men are also vulnerable to the cognitive effects of stressful events, but in domains other than memory (e.g., executive functioning). Alternatively, it is possible that some women are particularly vulnerable to the negative cognitive effects of stress and experience a decline in more than one domain of cognition. More detailed cognitive assessment in Wave 5 of the ECA should permit a more comprehensive characterization of cognitive change over time, such that the identification of subgroups of individuals who experience varying patterns of cognitive decline may be appreciated.

Fifth, this study may have been underpowered to show a small effect of stress on cognitive outcomes in men. Future studies directly comparing men and women on the effects of stress on subsequent cognitive decline will be valuable in testing the hypothesis that women are at increased risk of Alzheimer's disease due to the effects of stress on cognitive decline.

The aforementioned limitations notwithstanding, the current study provides important evidence supporting our hypothesis that women's increased risk of developing dementia is

related to their greater physiological vulnerability to stressful life experiences. Efforts aimed at modifying this risk factor could therefore have far-reaching benefits to public health.

Conclusions

In sex-stratified analyses, women with a greater number of recent stressful life events reported at mid-life demonstrate memory decline over a decade later; in men, no association between stressful events and cognitive change was found. Sex differences in cognitive vulnerability to stressful life events may underlie women's increased risk of memory impairment in late life, suggesting that stress reduction interventions may help prevent cognitive decline in women. Future studies to determine the reproducibility of the current findings are needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key points:

- In sex-stratified analyses, stressful life events occurring in mid-life are associated with memory decline over a decade later in women but not in men.
- Traumatic events in mid-life are not associated with cognitive decline in either sex.
- Women with a greater number of stressful life events during mid-life might be targets for efforts aimed at preventing cognitive decline in later life.
- Studies in other samples are needed to determine the replicability of the current findings.

Table 1.Baltimore ECA participant characteristics by sex at Wave 3^{*}

	All (N=909)	Men (N=337)	Women (N=572)	<i>p</i>
Age				0.09
Mean (SD)	47.2 (12.0)	46.4 (11.9)	47.8 (12.1)	
Median	44	44	45	
Q1, Q3	38, 54	37, 52	39, 54	
Range	30, 86	30, 86	31, 86	
Education, years				0.01
Mean (SD)	12.3 (2.6)	12.6 (2.7)	12.1 (2.5)	
Median	12	12	12	
Q1, Q3	11, 14	12, 14	11, 14	
Range	3, 17	3, 17	3, 17	
Race, White, N (%)	547 (60)	235 (70)	312 (55)	<0.001
BMI				0.36
Mean (SD)	27.8 (6.4)	27.6 (4.7)	28.0 (7.2)	
Median	26.6	26.7	26.6	
Q1, Q3	23.6, 30.8	24.2, 30.2	22.8, 31.2	
Range	15.8, 85.8	18.1, 50.0	15.8, 85.8	
Marital Status, N (%)				<0.001
Married	474 (52)	214 (64)	260 (45)	
Widowed	97 (11)	12 (4)	85 (15)	
Separated	63 (7)	16 (5)	47 (8)	
Divorced	132 (15)	37 (11)	95 (17)	
Never Married	142 (16)	58 (17)	84 (15)	
Personal Income, N (%)				<0.001
\$10,000	165 (18)	26 (8)	139 (24)	
\$10,000–19,999	157 (17)	45 (13)	112 (20)	
\$20,000–49,999	301 (33)	146 (43)	155 (27)	
\$50,000	192 (21)	99 (29)	93 (16)	
GHQ				<0.001
Mean (SD)	14.52 (6.39)	14.54 (5.92)	15.94 (6.61)	
Median	14	14	15	
Q1, Q3	11, 18	11, 17	12, 19	
Range	1–58	1–58	1–53	
MSE				0.02
Mean (SD)	28.6 (1.9)	28.8 (1.8)	28.5 (1.9)	
Median	29	29	29	
Q1, Q3	28, 30	29, 30	28, 30	

	All (N=909)	Men (N=337)	Women (N=572)	<i>p</i>
Range	15, 30	15, 30	17, 30	
Immediate Word Recall				0.07
Mean (SD)	7.9 (2.7)	7.7 (2.5)	8.0 (2.8)	
Median	8	8	8	
Q1, Q3	6, 9	6, 9	6, 10	
Range	0, 19	2, 18	0, 19	
Delayed Word Recall				0.61
Mean (SD)	6.2 (2.7)	6.1 (2.6)	6.2 (2.8)	
Median	6	6	6	
Q1, Q3	4, 8	4, 8	4, 8	
Range	0, 17	0, 17	0, 15	
Word Recognition				<0.001
Mean (SD)	15.1 (2.6)	14.7 (2.5)	15.4 (2.6)	
Median	15	15	16	
Q1, Q3	14, 17	13, 17	14, 17	
Range	2, 20	5, 20	2, 20	

* Data are from subjects who also participated in Wave 4.

Table 2.

Trauma and Stress Indices Calculated at Wave 3, Count (%) and Mean (SD) *

	All (n=909)	Men (n=337)	Women (n=572)	p
Number of recent traumatic events (within the last year)				
0	707 (78)	264 (78)	443 (77)	
1	180 (20)	60 (18)	120 (21)	
2	21 (2)	13 (4)	8 (1)	
3	1 (0.11)	0 (0)	1 (0.17)	
Mean (SD)	0.25 (0.49)	0.26 (0.52)	0.24 (0.47)	0.717
Experienced a remote trauma (between 1981 and 1 year ago)				
0 (no)	470 (66)	189 (67)	281 (65)	0.632
1 (yes)	245 (34)	94 (33)	151 (35)	
Number of recent stressful life events (within in the last year)				
0	466 (51)	180 (53)	286 (50)	
1	336 (37)	113 (34)	223 (39)	
2	92 (10)	36 (11)	56 (10)	
3	14 (2)	7 (2)	7 (1)	
4	1 (0.11)	1 (0.30)	0 (0)	
Mean (SD)	0.62 (0.74)	0.62 (0.78)	0.62 (0.71)	0.988
Number of remote stressful life events (between 1981 and 1 year ago)				
0	15 (4)	2 (1)	13 (5)	
1	75 (18)	25 (16)	50 (19)	
2	123 (29)	47 (30)	76 (29)	
3	108 (26)	45 (28)	63 (24)	
4	59 (14)	25 (16)	34 (13)	
5	31 (7)	13 (8)	18 (7)	
6	9 (2)	2 (1)	7 (3)	
7	1 (0.24)	0 (0)	1 (0.38)	
Mean (SD)	2.61 (1.36)	2.71 (1.25)	2.54 (1.41)	0.216

* Recent traumatic events, n = 909; remote traumatic events, n = 715; recent stressful life events, n = 909; remote stressful life events, n = 421

Table 3.

Association between female sex (reference = male) and cognitive test performance in the Baltimore ECA.^a

	Wave 3^b	
	B (95% CI)	p
Log MMSE	−0.0004 (−0.009, 0.009)	0.930
Immediate Word Recall	0.69 (0.36, 1.03)	<0.001
Delayed Word Recall	0.47 (0.13, 0.81)	0.008
Word Recognition	0.94 (0.59, 1.29)	<0.001
	Wave 4^c	
	B (95% CI)	p
Log MMSE	0.002 (−0.01, 0.01)	0.681
Immediate Word Recall	0.53 (0.20, 0.86)	0.002
Delayed Word Recall	0.47 (0.14, 0.80)	0.006
Word Recognition	0.77 (0.37, 1.17)	<0.001

^a Adjusted for age, education, and race.

^b Wave 3: MMSE, n=898; immediate word recall, n=897; delayed word recall, n=890; word recognition, n=886.

^c Wave 4: MMSE, n=908; immediate word recall, n=905; delayed word recall, n=905; word recognition, n=885.

Table 4.

Association between trauma index scores and change in cognitive test performance (Wave 4-Wave 3) in the Baltimore ECA, by sex.^a

	Number of Recent Traumatic Events (Experienced Within the Last Year) ^b			
	Men		Women	
	B (95 % CI)	<i>p</i>	B (95 % CI)	<i>p</i>
Log MMSE	0.01 (−0.043, 0.03)	0.134	0.003 (−0.01, 0.02)	0.737
Immediate Word Recall	−0.12 (−0.60, 0.36)	0.627	0.07 (−0.34, 0.46)	0.738
Delayed Word Recall	−0.16 (−0.65, 0.32)	0.506	−0.23 (−0.66, 0.17)	0.264
Word Recognition	−0.58 (−0.66, 0.54)	0.850	−0.19 (−0.68, 0.30)	0.447
	Number of Remote Traumatic Events (Experienced Between 1981 and 1 Year Ago) ^c			
	Men		Women	
	B (95 % CI)	<i>p</i>	B (95 % CI)	<i>p</i>
Log MMSE	0.01 (−0.004, 0.03)	0.128	0.002 (−0.02, 0.02)	0.827
Immediate Word Recall	−0.20 (−0.74, 0.32)	0.458	0.42 (−0.05, 0.90)	0.079
Delayed Word Recall	−0.34 (−0.90, 0.21)	0.226	0.16 (−0.32, 0.64)	0.522
Word Recognition	−0.50 (−1.24, 0.24)	0.183	0.22 (−0.37, 0.81)	0.464

^aAdjusted for age, education, race, General Health Questionnaire (GHQ), and baseline (Wave 3) cognitive test performance.

^bLast Year (range of observations = 0–1): Men: MMSE, n=332; immediate word recall, n=337; delayed word recall, n=336; word recognition, n=326; Women: MMSE, n=572; immediate word recall, n=567; delayed word recall, n=561; word recognition, n=551.

^cBetween 1981 and 1 year ago: (range of observations = 0–3): Men: MMSE, n=277; immediate word recall, n=283; delayed word recall, n=282; word recognition, n=276; Women: MMSE, n=432; immediate word recall, n=435; delayed word recall, n=431; word recognition, n=421.

Table 5.

Association between number of stressful life events and change in cognitive test performance (Wave 4-Wave 3) in the Baltimore ECA, by sex.^a

	Number of Recent Stressful Life Events (Experienced Within the Last Year) ^b			
	Men		Women	
	B (95 % CI)	p	B (95 % CI)	p
Log MMSE	−0.0005 (−0.01, 0.009)	0.917	−0.006 (−0.02, 0.004)	0.277
Immediate Word Recall	−0.22 (−0.53, 0.10)	0.179	−0.14 (−0.41, 0.13)	0.325
Delayed Word Recall	−0.23 (−0.56, 0.09)	0.155	−0.28 (−0.56, −0.005)	0.046
Word Recognition	−0.19 (−0.58, 0.23)	0.381	−0.35 (−0.68, −0.02)	0.036
	Number of Remote Stressful Life Events (Experienced Between 1981 and 1 Year Ago) ^c			
	Men		Women	
	B (95 % CI)	p	B (95 % CI)	p
Log MMSE	0.004 (−0.004, 0.01)	0.321	0.006 (−0.002, 0.01)	0.160
Immediate Word Recall	−0.11 (−0.40, 0.17)	0.438	−0.11 (−0.33, 0.11)	0.347
Delayed Word Recall	−0.24 (−0.53, 0.05)	0.100	−0.12 (−0.35, 0.11)	0.330
Word Recognition	0.01 (−0.37, 0.39)	0.957	−0.21 (−0.48, 0.04)	0.107

^aAdjusted for age, education, race, General Health Questionnaire (GHQ), and baseline (Wave 3) cognitive test performance.

^bLast year (range of observations = 0–4): Men: MMSE, n=332; immediate word recall, n=337; delayed word recall, n=336; word recognition, n=326; Women: MMSE, n=572; immediate word recall, n=567; delayed word recall, n=561; word recognition, n=551.

^cBetween 1981 and 1 year ago (range of observations = 0–7): Men: MMSE, n=154; immediate word recall, n=264; delayed word recall, n=159; word recognition, n=157; Women: MMSE, n=262; immediate word recall, n=264; delayed word recall, n=262; word recognition, n=253.