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# Lifetime stress exposure, cognition, and psychiatric wellbeing in women

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**ABSTRACT**

**Objectives:** Although life stress has been associated with worse cognitive and psychiatric functioning, few studies on this topic have examined these associations in older adults and no studies to date have assessed lifetime stress exposure in this context.

**Method:** To address this important issue, we investigated associations between lifetime stress exposure, cognition, and psychiatric wellbeing in 44 women aged 60 and older who completed a comprehensive lifetime stress exposure inventory, two memory tasks, and a complete psychiatric assessment.

**Results:** As hypothesized, greater acute and chronic lifetime stress exposure were both related to poorer psychiatric functioning and more somatic health complaints. Greater lifetime stress exposure was also associated with poorer subjective cognition as indicated by memory and thought problems but not objective indices of memory function.

**Conclusion:** Screening for high life stress exposure may therefore help identify older women at increased risk of experiencing negative psychiatric and cognitive outcomes.

## Introduction

Stress is known to negatively impact health in general, as well as brain functioning and psychiatric health especially in women (Gómez-Gallego & Gómez-García, 2019; Maestripieri & Hoffman, 2011; Slavich, 2016). In this context, the effects of lifetime stress exposure on psychiatric wellbeing in older adults has received relatively little attention. Specifically, very few studies have examined how acute and chronic stressors occurring over the entire lifetime are related to cognition and psychiatric wellbeing in women.

The mechanisms underlying stress and cognitive aging are closely related (Pardon, 2007). There is a high density of corticosteroid receptors in the hippocampus, which is believed to underpin the negative impact that chronic stress has on learning, memory, and psychiatric wellbeing (Gómez-Gallego & Gómez-García, 2019; Maestripieri & Hoffman, 2011; Magri et al., 2006; Miller & O'Callaghan, 2005). Several longitudinal studies have demonstrated that chronically high cortisol levels lead to deficits in hippocampally driven cognitive functions (Miller & O'Callaghan, 2005). Pardon (Pardon, 2007) argued that this negative association could be attributed to the aging process being regulated by factors that govern a person's ability to adjust to stress. Specifically, Pardon (Pardon, 2007) stated that aging is associated with stress as a consequence of high allostatic load and a long-lasting activation of the hypothalamic-pituitary-adrenal (HPA) axis, as seen in individuals with chronic stress (Maestripieri & Hoffman, 2011; Pardon, 2007). Additionally, Maestripieri and Hoffman (2011) found that chronic activation of allostatic load mediators, such as cortisol and cytokines, results in several negative outcomes including physiological dysregulation, neurological brain changes, accelerated aging, and disease.

Although individuals experience varying levels of stress exposure over the lifespan, women have a unique hormonal environment, as well as unique physiological stressors such as pregnancy, which influence how stress affects cognitive and mental health (Slavich & Sacher, 2019). In the present study, therefore, we investigated how acute and chronic stressors occurring over the entire lifetime relate to cognitive and psychiatric wellbeing in the context of the postmenopausal environment. We hypothesized that greater lifetime stress exposure, both acute and chronic, would exacerbate age-related changes in cognition and negatively impact psychiatric wellbeing in women aged 60 and above. Furthermore, to examine whether documented effects were similar across different types of life stress exposure, we examined how acute and chronic lifetime stress exposure were independently related to the outcomes assessed.

## Method

### Participants and procedure

This study protocol and informed consent documents were reviewed and approved by the Committees on Human Subjects Research – Behavioral and Social Sciences at the University of Vermont, number CHRBSS 18-0237. Participants were 44 women aged 60 years and older. They were recruited using advertisements posted around Chittenden County, VT and by emailing past research participants of the Clinical Neuroscience Research Unit in the Department of Psychiatry at the University of Vermont. Once an interested individual contacted the study staff, she was scheduled for her study visit on campus or in her home. Inclusion criteria were an age of 60 years or older and self-reported to be generally healthy. Exclusion criteria were an inability to complete the required tasks and questionnaires due to being non-English speaking or having a physical impairment or receiving a score less than 24 on the Mini Mental State

Exam (MMSE). After signing the informed consent form, participants completed a series of cognitive tests, answered questions about stress exposure, and performed cognitive tasks to examine working and episodic memory, and completed a psychiatric assessment (see below).

### Stress and Adversity Inventory for Adults (STRAIN)

The Stress and Adversity Inventory for Adults (STRAIN) was used to assess participants' lifetime exposure to acute and chronic stressors that are known to impact health (Slavich & Shields, 2018) (see https://www.strainsetup.com). Questions assess stressors occurring in several major life domains such as work, finances, and intimate relationships. For each stressor that is affirmed, a series of follow-up questions assesses each stressor's severity, frequency, timing, and duration. By design, the STRAIN differentiates between acute and chronic stressors. Some questions are designed to assess acute life events (e.g. accidents, getting bad news) and others are designed to assess chronic difficulties that generally last one month or longer, such as persistent housing or financial problems. Higher severity scores indicate more lifetime stress exposure, with possible scores ranging from 0-265. Similarly, higher stressor count scores are indicative of having experienced more stressors over the life course, with possible scores ranging from 0-166 (Slavich & Shields, 2018). The STRAIN has excellent test-retest reliability ($r = .904$-$.919$) over 2-4 weeks and has been validated against numerous different cognitive and health outcomes (Cazassa et al., 2019; Sturmbauer et al., 2019; Toussaint et al., 2016). Slavich and Shields (Slavich & Shields, 2018) assessed lifetime stress exposure in 205 adults drawn from the general community, and participants experienced an average of 25.77 stressors over their lifetime ($SD = 16.85$; range 1-83), with a mean lifetime stress severity of 63.26 ($SD = 37.73$; range, 0-167) (Slavich & Shields, 2018).

### Cognitive tasks

#### Letter-Number sequencing task (LNST)

The LNST is a subtest of the Wechsler Memory Scale, aimed at measuring working memory (Wechsler, 1955). The LNST is highly related to laboratory measures of working memory and has an internal consistency of .74 (Shelton et al., 2009). Each participant was read a series of letters and numbers. The task was to repeat the numbers first in order and then the letters in alphabetical order. The number of successful trials were counted.

#### Buschke selective reminding test (BSRT)

The BSRT is a measure of episodic memory that measures storage into and retrieval from memory in a multi-trial verbal list-learning task (Buschke & Fuld, 1974). Beatty and colleagues (Beatty et al., 1996) demonstrated excellent predictive validity of this short-term and long-term recall task. It consisted of eight immediate recall trials followed by one delayed recall trial that was administered 20 to 30 min after the eighth trial ended. The BSRT began by the experimenter reading the 16 words aloud to the participant who was then asked to recall the 16 words. If she was unable to recall a word (or words) she was reminded of the forgotten word/s by the experimenter and then asked to try and recall all 16 words again. The dependent variables were total recall and delayed recall. Total recall was the total number of words the participant recalled from the initial eight trials. Delayed recall was the number of words the participant recalled following the 20- to 30-minute retention interval during which time women continued completing other assessments in this study.

### Psychiatric assessment

The Older Adult Self Report (OASR) is a general psychiatric assessment that was completed by all participants (Achenbach et al., 2004). Participants were presented with statements such as "I make good use of my time", "I lack self-confidence", "There is very little that I enjoy", and "I seem to irritate people." They were then asked to indicate how much they agreed with each statement on a scale ranging from 0 (*not true*) to 1 (*somewhat or sometimes true*) to 2 (*very true or often true*). It yields seven syndromes, including anxious/depressed, worries, somatic complaints, functional impairment, memory/cognition problems, thought problems, and irritable/disinhibited. In addition to the seven syndromes, the OASR produces a total problems score, which is a summary score across the domains of strengths, worries, somatic complaints, anxious/depressed, thought problems, functional impairment, memory, and irritability. Another primary OASR score is the critical items score, which includes a variety of problem items such as self-harm, hallucinations, and feelings of sadness, and anger. The test-retest reliability of the OASR has been shown to be very good ($r = .86$-$.92$) when administered over a one-week period (Maruish, 2004).

### Analyses

First, we examined relationships between age and lifetime stress exposure, cognition, and psychiatric wellbeing. Then we examined associations between participants' lifetime stress exposure and cognition, as well as lifetime stress exposure and psychiatric well-being, using bivariate Pearson correlations. To correct for multiple comparisons, we used a Bonferroni correction and set the alpha level at $p < .001$. With a sample size of $N = 44$ and using an $\alpha$ of .001 and a $\beta$ of .80, we were able to detect a medium-sized correlation of .37. In addition, we report the Bayes factors ($BF_{10}$) for each correlation comparing the null hypothesis ($H_0$, there is no relation) to the alternative hypothesis ($H_1$, there is a relation). In general, the interpretation of the $BF_{10}$ is as follows: $BF_{10} < 1$ may indicate evidence for the $H_0$, $BF_{10} = 1$ indicates no evidence, $BF_{10} = 1$-3 indicates anecdotal evidence for $H_1$, and $BF_{10} > 3$ indicates strong evidence for $H_1$.

## Results

### Preliminary analyses

Participants ranged in age from 60 to 90 years old, with a mean age of 71.11 years ($SD = 8.85$). Their mean education level was 16.51 years ($SD = 2.31$) and ranged from 12 to 20 years. As shown in Table 1, participants had a mean lifetime stressor count of 37.7 ($SD = 19.31$) and a mean lifetime stressor severity of 79.98. ($SD = 43.53$).

We examined associations between age and the main variables of interest and found no associations between age and the lifetime stress measures ($ps > .13$, largest $BF_{10} = .542$) or the psychiatric wellbeing measures ($ps > .25$, largest $BF_{10} = .358$). There was evidence for the expected negative association

**Table 1.** Descriptive statistics for cumulative lifetime stressor count and severity.

| Stress Variable | N | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|---|
| Total Lifetime Stressor Count | 44 | 6 | 83 | 33.7 | 19.31 |
| Total Lifetime Stressor Severity | 44 | 16 | 172 | 79.98 | 43.53 |
| Lifetime Acute Stressor Count | 44 | 3 | 56 | 21.61 | 12.95 |
| Lifetime Acute Stressor Severity | 44 | 10 | 87 | 40.43 | 19.61 |
| Lifetime Chronic Stressor Count | 44 | 1 | 29 | 12.09 | 7.56 |
| Lifetime Chronic Stressor Severity | 44 | 4 | 101 | 39.55 | 25.9 |

between age and the objective cognitive measures on the delayed recall on the BSRT ($r = -.40$, $p = .007$, $BF_{10} = 6.313$), the total recall on the BSRT ($r = -.37$, $p = .01$, $BF_{10} = 3.751$), and the LNS score ($r = -.38$, $p = .01$, $BF_{10} = 3.956$). Descriptive statistics for the STRAIN, cognitive tasks, and psychiatric assessments are presented in Tables 1-3 respectively.

Since age was correlated with cognition, we also conducted partial correlation analyses of the life stress and cognitive measures while controlling for age. This analysis showed that when controlling for age, lifetime stress exposure was not related to these measures of cognition (largest $r = -.16$, $p = .31$).

### Stress, cognition, and psychiatric wellbeing

#### Lifetime stressor count and severity and cognition
Contrary to hypotheses, neither total lifetime stressor count (largest r = −.09, $p = .55$, $BF_{10} = .250$) nor total lifetime stress severity (largest r = −.12, $p = .44$, $BF_{10} = .233$) were associated with the BSRT immediate and delayed recall or the LNST. Since analyses revealed associations between age and objective cognitive measures, we examined regressions of age and each of the objective cognitive measures of lifetime stress exposure. None of the $BF_{10}$s were above 1 and none of the $r^2$ were greater than .05.

#### Lifetime stressor count and psychiatric wellbeing
As hypothesized, total lifetime stressor count was associated with exhibiting more symptoms of anxiety, depression ($r = .61$, $p < .001$, $BF_{10} = 2192$), subjective memory function ($r = .57$, $p < .001$, $BF_{10} = 448$), thought problems ($r = .63$, $p < .001$, $BF_{10} = 4820$), and irritability ($r = .43$, $p = .004$, $BF_{10} = 11$). Furthermore, total lifetime stressor count was associated with greater critical items ($r = .69$, $p < .001$, $BF_{10} = 70502$) and total problems ($r = .64$, $p < .001$, $BF_{10} = 7406$). In terms of acute vs. chronic stress exposure, lifetime acute stressor count was significantly associated with symptoms

of anxiety, depression ($r = .58$, $p < .001$, $BF_{10} = 705$), subjective memory function ($r = .56$, $p < .001$, $BF_{10} = 331$), thought problems ($r = .55$, $p < .001$, $BF_{10} = 290$), critical items ($r = .65$, $p < .001$, $BF_{10} = 12585$), and total problems ($r = .59$, $p < .001$, $BF_{10} = 883$). Similarly, lifetime chronic stressor count was significantly associated with anxiety, depression ($r = .57$, $p < .001$, $BF_{10} = 435$), subjective memory function ($r = .49$, $p = .001$, $BF_{10} = 49$), thought problems ($r = .66$, $p < .001$, $BF_{10} = 18989$), irritability ($r = .47$, $p = .001$, $BF_{10} = 30$), critical items ($r = .64$, $p < .001$, $BF_{10} = 6879$), and total problems ($r = .63$, $p < .001$, $BF_{10} = 4877$).

### Lifetime stressor severity and psychiatric wellbeing
Total lifetime stressor severity was significantly associated with symptoms of anxiety, depression ($r = .57$, $p < .001$, $BF_{10} = 448$), subjective memory function ($r = .53$, $p < .001$, $BF_{10} = 156$), thought problems ($r = .65$, $p < .001$, $BF_{10} = 11942$), critical items ($r = .65$, $p < .001$, $BF_{10} = 10753$), and total problems ($r = .64$, $p < .001$, $BF_{10} = 7448$). In terms of acute vs. chronic stress, acute stressor severity was significantly related to symptoms of anxiety and depression ($r = .55$, $p < .001$, $BF_{10} = 288$), subjective memory function ($r = .54$, $p < .001$, $BF_{10} = 204$), thought problems ($r = .57$, $p < .001$, $BF_{10} = 542$), critical items ($r = .62$, $p < .001$, $BF_{10} = 2791$), and total problems ($r = .60$, $p < .001$, $BF_{10} = 1598$). Similarly, chronic stressor severity was significantly associated with anxiety and depression ($r = .53$, $p < .001$, $BF_{10} = 157$), subjective memory function ($r = .49$, $p = .001$, $BF_{10} = 42$), thought problems ($r = .66$, $p < .001$, $BF_{10} = 18607$), irritability ($r = .45$, $p = .002$, $BF_{10} = 17$), critical items ($r = .62$, $p < .001$, $BF_{10} = 3602$), and total problems ($r = .62$, $p < .001$, $BF_{10} = 3175$).

### Associations between acute and chronic stress
In the present study, participants' acute and chronic lifetime stressor counts were associated at an expected level, $r = .76$, $BF_{10} = 4.303 \times 10^6$. Using partial correlations, we thus examined how

**Table 2.** Descriptive statistics of the cognitive assessments.

| Cognitive Assessment | N | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|---|
| MMSE | 44 | 24 | 30 | 28.41 | 1.39 |
| LNST | 44 | 5 | 16 | 9.84 | 2.87 |
| BSRT Total Recall | 44 | 34 | 106 | 71.18 | 20.65 |
| BSRT Delayed Recall | 44 | 0 | 16 | 8.57 | 3.98 |

*Note.* MMSE = Mini Mental State Exam; LNST = Letter-Number Sequencing Task; BSRT = Buschke Selective Reminding Test.

**Table 3.** Descriptive statistics of the older adult self-report.

| | N | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|---|
| Anxious/Depressed | 44 | 50 | 78 | 56.84 | 7.17 |
| Worries | 44 | 50 | 69 | 53.27 | 5.01 |
| Somatic Complaints | 44 | 50 | 65 | 51.57 | 3.02 |
| Functional Impairment | 44 | 50 | 76 | 54.2 | 5.88 |
| Memory Problems | 44 | 50 | 77 | 56.5 | 6.92 |
| Thought Problems | 44 | 50 | 69 | 55.52 | 5.9 |
| Irritability | 44 | 50 | 70 | 54.14 | 6.15 |
| Critical Items | 44 | 50 | 71 | 56.02 | 6.1 |
| Total Problems | 44 | 26 | 69 | 50.39 | 10.83 |

the relations between acute stress count and the measures from the OASR were related while controlling for chronic lifetime stressor count. For the most part, when controlling for chronic stressor count, all significant associations remained between acute life stressor count and memory ($r = .33$, $p = .03$), critical items ($r = .34$, $p = .03$), total problem items ($r = .35$, $p = .02$). In addition, we examined how chronic lifetime stressor count and the measures from the OASR were related while controlling for acute lifetime stressor count using partial correlations. When controlling for acute lifetime stressor count, associations remained significant between chronic lifetime stressor count and thought problems ($r = .35$, $p = .02$) and critical items ($r = .29$, $p = .06$).

## Discussion

Consistent with hypotheses, the present data demonstrated that lifetime stress exposure has a negative impact on psychiatric wellbeing. More specifically, we found that greater stress exposure in our sample of older women was associated with poorer psychiatric wellbeing, as indexed by the STRAIN and OASR, respectively. As lifetime stressor count and severity increased, OASR index scores also increased, indicating greater anxiety/depression, memory, thought problems, critical items, and total problems. Although the women in this study did not score in the clinical range indicating symptoms of mental illness, those who had higher levels of lifetime stress exposure scored closer to the clinical range on the OASR. Although the relation between lifetime stress exposure and psychiatric wellbeing was expected, very few studies have examined these associations in older adults in general and in older women specifically.

In contrast, we did not find support for the hypothesis that greater lifetime stress exposure was associated with decreased objective cognitive performance. However, lifetime stress exposure was related to participants' subjectively reported memory scores on the OASR. The lack of an association between lifetime stress exposure and objective measures of cognition in this study is likely not due to a lack of lifetime stress exposure. Indeed, the women sampled experienced a variety of life stressors, as measured by the STRAIN. We therefore discuss how these findings extend the current literature and raise questions for further studies.

A longitudinal study investigating the effects of perceived stress on dementia found empirical support for a positive association between perceived stress and risk of dementia in old age (Nabe-Nielsen et al., 2020). Furthermore, a study by Maestripieri and Hoffman (2011) demonstrated that subjective perceived stress was correlated with high allostatic load. Whereas Maestripieri and Hoffman (2011) emphasized the significance of perceived stress over objective stress, Finkenzeller and colleagues (2019) found that engaging in physical and psychological health promoting behaviors, such as having an active lifestyle, was beneficial in stabilizing stress regulation in response to both their perceived and objective stress. Our results showing that lifetime stress exposure negatively impacted subjective cognition are consistent with the findings of Maestripieri and Hoffman (2011) and Nabe-Nielsen and colleagues (2020). Specifically, the lack of an association between stress and objective cognitive assessments provides evidence for perceived stress and perceived cognitive performance having a greater impact on mental wellbeing than objective measures of cognitive performance, supporting the findings from both Maestripierei and Hoffman (2011) and Nabe-Nielsen and colleagues (2020).

Supporting this finding, Rabin and colleagues (2015) proposed that subjective cognitive decline in older adults may be indicative of non-normative cognitive aging. Additionally, subjective cognitive decline has been shown to precede the development of dementia (Rabin et al., 2015). Specifically, a study by Studart and Nitrini (2016) found that subjective cognitive impairments contribute to the formation of objective impairments, such as dementia. Research has repeatedly demonstrated that perceived changes in cognition is one of the first symptoms of dementia and precedes objective pathologies (Gatchel et al., 2020; Rabin et al., 2015; Studart & Nitrini, 2016). Subjective cognitive decline in older adults is known to be a marker for preclinical Alzheimer's Disease (Gatchel et al., 2020). Furthermore, epidemiological data have demonstrated that older adults with subjective cognitive decline are at an increased risk for the development of mild cognitive impairment (MCI) and dementia (Jessen et al., 2020). During normal aging there are both subjective and objective declines in memory, conceptual reasoning, and processing speed. Harada et al. (2013) emphasized that although some older women experience pathological aging, such as dementia or MCI, subtle subjective cognitive changes that affect day to day functioning still occur during normal aging that can impact everyday functioning.

However, changes in subjective cognition in older adults are often related to depressed mood and may be a proxy for depression (McDonough et al., 2020). In the present sample subjective memory was related to the anxiety-depression measure. In addition, we computed partial correlations of the stress measures and the memory factor from the OASR while controlling for the anxious/depressed factor. Overall, associations between subjective memory and total lifetime stressor count, total lifetime stressor severity, acute lifetime stressor count, and acute lifetime stressor severity remained significant. The associations between subject memory and chronic lifetime stressor count and severity were smaller and the $p$ values were not significant. Therefore, further studies are needed to disentangle the cognitive changes from mood in measures of subjective cognition and their relation to dementia risk and how increased levels of perceived stress may eventually lead to greater psychological health burdens.

Stress has been shown to have negative effects on human brain functioning at many stages of life. For example, childhood stress has been shown to result in permanent changes in learning, behavior, and physiology, leading to an unhealthy lifestyle resulting from the negative effects of stress on brain development, especially at young ages (Shonkoff & Garner, 2012). In adults, DeLongis and colleagues (1988) found that participants with high stress levels had increased psychological and somatic problems, especially if they had unsupportive social relationships and low self-esteem. The present study found that increased stress led to higher critical item and total problem scores on the OSAR indicating greater psychiatric distress. Therefore, these data provide further evidence of the detrimental effects of stress on mental health.

Although this study clearly demonstrated the negative effects of stress on psychiatric wellbeing, we did not find evidence for an association between stress and cognition in this sample of postmenopausal women. Cognitive functioning in later life has been shown to benefit from increased lifetime estrogen exposure, perhaps a result of the localization of estrogen receptors in the hippocampus and its influence on cognition (Asthana & Middleton, 2004; Bean et al., 2014; Hesson, 2012; Ryan et al., 2009;

Tulving & Markowitsch, 1998). We did not have any objective assessments of hormone values in this sample and prior literature suggests that estrogen may be protective against stress as well as cognitive changes in aging. Longitudinal studies have found that postmenopausal estrogen users have increased performance on cognitive tests and show less age-related deterioration over time as compared to women who did not use estrogen (Grodstein et al., 2000; Jacobs et al., 1998; Matthews et al., 1999; Resnick et al., 1997; Rice et al., 2000; Steffens et al., 1999; Yaffe, Haan, et al., 2000; Yaffe, Lui, et al., 2000). The existing literature suggests that estrogen may serve as a buffer to the effects of stress on cognition. This protective effect could provide an explanation for the lack of an association between stress and objective cognition in the present study. Further research is warranted to examine the relation between lifetime stress exposure, lifetime estrogen exposure, and cognitive performance. Additionally, how stress and estrogen interact to promote successful or pathological aging in relation to psychological wellbeing and cognition remains a gap in the literature (Finkenzeller et al., 2019).

## Limitations

One limitation of this study was that many of the measures were dependent on participants' memory and their ability to provide a self-report. However, while the OASR required reporting about current psychiatric health, it has excellent test-retest reliability ($r$s = .86-.92) when administered over a one-week period (Maruish, 2004). The test-retest validity of the STRAIN is also very good ($r$s = .904-.919) over a two-to-four week period, and the STRAIN also has high predictive validity and has been shown to be insensitive to negative mood and social desirability (Slavich & Shields, 2018). Nevertheless, the STRAIN and OASR are based on participants' self-report. A final limitation of this study was the limited sample size, which constrained power to detect effects. A larger sample size may allow associations that have smaller effect sizes to be observed, demonstrating additional associations between life stress, cognition, and wellbeing in older women.

## Conclusion

In conclusion, the results of the present study suggest that lifetime stress exposure plays a role in the functioning of the aging brain as it was related to measures of psychiatric wellbeing. Reducing acute and chronic life stress exposure may thus represent a helpful strategy for decreasing the prevalence of psychiatric disorders in older female populations. Looking forward, future research should examine the hypothesized mitigating role of estrogen on the association between life stress exposure and cognition. Specifically, research focusing on the relation between gonadal steroids and cortisol in the context of cognitive aging is warranted to elucidate the mechanisms through which these beneficial effects might occur.

## Acknowledgements

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