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ORIGINAL ARTICLE: SOCIAL RESEARCH, PLANNING AND PRACTICE

Relationship between cortisol reactivity to psychosocial stress and declarative memory decline during aging: Impact of age and sex

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Aim: To analyze the relationship between memory performance and the neuroendocrine and cardiovascular response to acute psychosocial stress in healthy older people, and the sex and age impact in this relationship.

Methods: We randomly selected 100 literate older adults, without cognitive or functional impairment. The neuroendocrine stress response was evaluated by measuring the concentration of salivary cortisol, whereas cardiovascular reactions were determined based on blood pressure and heart rate measures taken before, during and after participant exposure to an acute psychosocial stressor (the Trier social stress test [TSST]). Memory performance was evaluated by applying the word pairs test before and after the TSST.

Results: A significant reduction in the word pair test scores was observed after the TSST, and a negative correlation between cortisol concentration and immediate and delayed recall of the word pair. Cortisol concentration associated with age, sex and education explained memory performance variability before and after the TSST.

Conclusions: The results showed that the influence of acute stress on memory performance during aging might vary according to age and sex, highlighting potential differences in the vulnerability of older individuals to the neurotoxic effects of stress exposure on memory and consequently on the development of cognitive disorders. **Geriatr Gerontol Int 2018; 18: 169–176.**

Keywords: aging, cortisol, memory, metabolic stress response.

Introduction

For many years, the decline in cognitive function observed during the aging process was considered normal. However, this concept of normality was called into question after recognition that wide cognitive variability exists among older adults compared with younger adults.[1,2] This significant variability aroused the interest of many researchers, prompting them to identify factors that could explain the cognitive performance difference in these individuals.

A significant association between memory decline and glucocorticoids, a major class of peripheral stress hormones, in older adults has suggested that stress might be one of the factors responsible for interindividual variability in cognitive performance during the aging process.[3] This evidence is based on the fact that glucocorticoids (corticosterone, cortisol in animals and in humans) have a high affinity for specific receptors located in the hippocampus, amygdala, and prefrontal cortex intrinsically associated with learning and memory.[4] Declarative memory, that requires conscious and intentional recollection of information, and that is hippocampus-dependent, is a type of memory most affected by stress hormones.[2,3] During information processing, short and delayed recalls are affected by altered levels of cortisol, whereas consolidation of information seems to be improved by high levels of this glucocorticoid.[2–4] In particular, declarative memory performance could vary according to circulating levels of cortisol, and occupation of glucocorticoids receptors, the mineralocorticoid (MR) and the glucocorticoid (GR) receptors. Both, a high or low occupation rate of MR and GR by cortisol might lead to poor memory performance.[4]

Studies in animal models have shown brain glial changes (total and hypertrophy astrocytic cells), a measure of hippocampal pathology, associated with high plasma

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corticosterone concentrations in middle-aged and aged rats.[5] Similarly, adrenalectomized and chronically maintained middle-aged rats showed morphological evidence of reduced brain age (neuron loss and glial reactivity).[5] Meanwhile, in acute stress situations, it was noted that although older mice showed an adequate response to the stressor event, producing concentrations of glucocorticoids similar to that of young rats, inhibition of the hypothalamic–pituitary–adrenal axis, the main regulator of neuroendocrine stress reaction, was compromised. Thus, even after removal of the stress stimulus, older animals continued to produce corticosterone, taking 24 h to return to baseline concentration, thereby exposing the animal to elevated concentrations of glucocorticoids that was detrimental to hippocampal neurons, and therefore to declarative memory performance.[6]

Confirming this evidence, in humans, previous findings have shown a significant association between chronic exposure to elevated cortisol levels and declarative memory performance in older adults.[3,7] More specifically, these longitudinal findings show the existence of three subgroups of elderly patients with significantly different patterns of cortisol secretion classified as "progressively increased at high current levels," "progressively increased with moderate current levels" and "gradually moderately reduced current levels."[7] Furthermore, worse performance on declarative memory tests and reduced hippocampal size were observed among participants exposed to high levels of cortisol over the space of years compared with older people whose cortisol concentrations were low.[3] No association was observed between cortisol levels and non-declarative memory performance (type of memory that does not require conscious thought and is not dependent on the hippocampus).[3,7]

Altogether these studies sustain the "glucocorticoids cascade theory" that postulate that prolonged increases in the levels of glucocorticoids might be neurotoxic to the hippocampus, compromising the hypothalamic–pituitary–adrenal axis negative feedback and therefore contributing to keep elevated glucocorticoid concentration in a vicious circle. Given that declarative memory is dependent on the hippocampus, prolonged increases in the levels of glucocorticoids might be therefore detrimental to memory performance [4,6,7]

In relation to exposure to acute stress, the characterization of the neuroendocrine stress response and its association with cognitive performance has been little explored on older adults. Some authors have shown that, although the neuroendocrine reaction before a stressful event is similar in adults and older adults, the older group had higher total concentrations of cortisol than younger individuals.[8] Other authors showed that there is significant variability in the acute stress reaction among a single sample of older people. The association between elevated cortisol and low cognitive performance was observed only among older individuals who had a significant response to the stressful event compared with those showing no response.[9] Many factors can explain the disparate observations in studies investigating the stress response in older people. Possible factors include the methods used in assessments, sex differences and age, among others.[8]

In this sense, the relevance of the present study is in its contribution to the understanding of the factors influencing the aging process, allowing the identification of older groups more vulnerable to age-related cognitive decline. Briefly, the present study could contribute to understanding the role of stress in brain function and resultant impairment in cognitive performance during aging. The aim of the present study was to evaluate whether cortisol levels are associated with poor memory performance in healthy older people.

Methods

Study venue

The study was carried out at the Outpatient Unit of Internal Medicine (ACM), University Teaching Hospital, University of São Paulo (HU-USP), where older adults were undergoing regular monitoring for treatment and control of hypertension.

Participants

All the participants were randomly selected from the HU-USP elderly patients database (individuals aged ≥60 years according to the Brazilian Statute for elderly classification).[10] Only literate individuals registered at the ACM of HU-USP were considered. Those who met the following criteria were excluded: neurological or psychiatric disorder; cognitive and functional impairment; visual or auditory deficit; alcohol, smoking or drug abuse history in the past 5 years; use of antidepressant, benzodiazepines, steroids and beta-blocker drugs; and hospital admission in the past 6 months. All female participants were postmenopausal (>10 years from their last menstrual period) and were not receiving hormone replacement therapy. Cognitive and functional impairment was evaluated using the Mini-Mental State Examination and the Informant Questionnaire of Cognitive Decline.[11,12] Based on these, 404 elderly individuals were randomly selected as eligible participants and initially screened by a telephone interview. Of these, 115 were not contacted because they did not respond to telephone calls after two attempts or the number no longer belonged to the registered patient, 124 did not agree to participate, 46 did not meet the inclusion criteria, 10 showed cognitive and functional impairment, and nine did not attend the evaluation even after two attempts scheduling.

The sample was composed of 100 older adults (31 men and 69 women), aged between 60 and 88 years (total sample [mean ± SD]69.8 ± SD 6.0 years; men: 70.6 ± 6.0 years; women: 69.5 ± 5.9 years), with mean schooling of

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8.4 ± 4.4 years (men: 8.7 ± 4.4 years; women: 8.3 ± 4.3 years) and living in the metropolitan area of São Paulo, Brazil.

Psychological stress assessment

To evaluate the stress response, patients underwent the Trier social stress test (TSST). The TSST entails a standardized protocol of psychosocial stress evaluation in the laboratory, validated and internationally established in studies of reaction to stress, which can stimulate activation of the hypothalamic–pituitary–adrenal axis.[13] This test analyzes cortisol concentrations and cardiovascular outcomes in response to two stressful tasks: 5 min of public speech followed by a 5-min period of a mental arithmetic task, both in front of a panel of non-responsive examiners. Participants underwent the TSST individually at the ACM of the HU-USP, a familiar setting for the participant, in the afternoon period between 14.00 hours and 16.00 hours (Brasilia time zone). In this period, cortisol concentration undergoes less oscillation. A total of eight saliva samples to determine cortisol secretion throughout the experiment were obtained using a cotton swab (Salivette, Sarstedt, North Rhine-Westphalia, Nümbrecht, Germany) at baseline (−20 min), before the TSST (0 min), immediately after (10 min) and 25, 40, 55, 70 and 100 min after the beginning of TSST. All participants were instructed to not practice exercise on the day of assessment, and to not eat or drink anything or brush their teeth 1 h before the scheduled time to be in the experiment setting.

Salivary cortisol assays

Saliva samples were stored at –20°C until free cortisol levels were determined by an enzyme immunoassay kit (Salimetrics, State College, PA, USA). The limit of detection for cortisol was 0.01 μg/dL, the intra- and interassay variability was 5.0% and 7.4% (range 0.1–10 μg/dL dose). The enzyme immunoassay was carried out according to Salimetrics recommendations, and the assay technique were previously validated.

Cardiovascular reactivity

During the psychological stress protocol, at baseline, 0 min and 10 min, the heart rate and blood pressure (systolic and diastolic) were measured to analyze cardiovascular reactivity to the TSST. These measures were obtained using a wristwatch digital blood pressure monitor (Microlife, Corporation, Taipei, Taiwan).

Declarative memory assessment

The "word pair test" is a hippocampus-dependent declarative memory task, and was used to assess declarative memory performance at baseline and during the stress reactivity after the TSST. This test is a hippocampus-dependent declarative memory task with semantic links (related word pairs) and information requiring the formation of novel associations (unrelated word pairs).[9] This type of task involves a "paired associate memory" that is essential in everyday life; for example, to consolidate new information and recover it later.[9] In a previous study, the performance on this test was associated with cortisol levels.[9] The task consisting of a list of 12 word pairs, six pairs moderately related (metal–iron; baby–cry; north–south; rose–flower; lettuce–tomato; fruit–apple) and six unrelated (kale–pen; school–drugstore; obeying–centimeter; pilaster–rattle; gate–plush; nursery–cabin) that was presented in local language to the participants for immediate recall (−20 min), learning (−10 min) and delayed recall (25 min; Fig. 2). The pairs of words were presented in Arial font (size 44), black capital letters, with light gray background color on a computer screen using the presentation program PowerPoint (Microsoft, Redmond; WA, USA). Initially, the participant had to read each pair of words aloud. After this, the participant was shown one word and they were asked to recall the paired word. This task was carried out in two attempts, and the word pairs were presented in different orders. The number of hits in the first attempt corresponded to the "immediate recall," and the second attempt corresponded to the "learning." After 15 min at the end of the TSST (25 min) and without prior presentation, the participant had to recall the word according to its respective pair (delayed recall).[14]

Experimental protocol proceedings

On arriving at the ACM of HU-USP, the patient remained sitting at rest for 10 min before the beginning of the experimental protocol. The entire protocol was applied individually, and was composed of four stages as follows: baseline, stress anticipation, stress reactivity and recovery. In the baseline stage, the first saliva sample (−20 min) was collected followed by the word pairs test assessment (immediate and learning). In the stress anticipation stage, the participant was informed about the speech task of the TSST and oriented to elaborate in 10 min an oral presentation about "global warming" that would be presented to a panel of expert examiners in behavior analysis. After these 10 min, the second saliva sample was collected, and the heart rate and blood pressure measured (0 min). Subsequently, the participant was sent to another room for the TSST administration, which constituted the stress reactivity stage. In this room, a camcorder with a focus directed on the participant and a microphone on a pedestal for the participant's oral presentation were placed. Two "expert examiners" wearing white coats, sitting in front of and facing the participant guided the participant to start their oral presentation, which initiated the TSST. After 5 min of the speech task, the participant was requested to carry out the mental arithmetic task during an additional 5 min. The TSST lasted 10 min. After this, the third saliva samples were collected (10 min), and cardiovascular measures were obtained. A total of 15 min after the end of

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the TSST (25 min), the fifth saliva sample was collected and the participant was required to recall the list of 12 words pairs previously shown (delayed recall). After this, in the stress recovery stage, the participant remained in a private room, for more than 60 min, for the final saliva sampling (40, 55, 70 and 100 min). During this period, material for entertainment with reading and space for rest was offered. A schematic representation of the experimental protocol is shown in Figure 1.

Research ethics

The study was approved by the Research Ethics Committee of the Nursing School of Sao Paulo University (CEP-EEUSP 994/2010) and the University Hospital of the USP (CEP-HU / USP 1130/11). All participants signed an informed consent form.

Statistical analysis

All statistics were calculated using the Statistical Package for Social Sciences (SPSS), version 14.0 (SPSS, Chicago, IL, USA). The variables were normally distributed, except for cortisol concentration, which was therefore logarithm transformed. ANOVA for repeated measures was used for cortisol concentration and cardiovascular reactivity with age and sex as covariates, and for word pairs test score (immediate recall, learning and delayed recall) with age, sex and education as covariates. Pearson's correlation coefficient was carried out to investigate the association between cortisol and memory performance. Multiple linear regression models using the backward method (P entry = 0.05; P removal = 0.1) were used to analyze the predictor effect of cortisol levels and covariates analysis (age, sex and education), and the word pair test scores as the dependent variable. The significance level was set at 0.05.

Results

Stress reactivity

Cortisol and cardiovascular reactivity were observed before and after the TSST. The effect of time on cortisol concentration in response to an acute stressor, TSST ($F[2,202] = 27.7$, $P < 0.001$), was observed as well as a peak cortisol at 25 min ($P < 0.001$) after the initiation of the TSST was observed. A main effect of sex ($F[1.97] = 6.8$; $P = 0.010$) on the average of cortisol concentration across TSST was observed. Specifically, women showed lower cortisol concentration compared with men at baseline (−20 min; $P = 0.043$) and 10 min ($P = 0.020$), 25 min ($P = 0.005$), 40 min ($P = 0.005$), 70 min ($P = 0.011$) and 100 min ($P = 0.023$) after the beginning of TSST. No main effect of age was observed on the average of cortisol concentration ($P = 0.329$; Fig. 2). **F2**

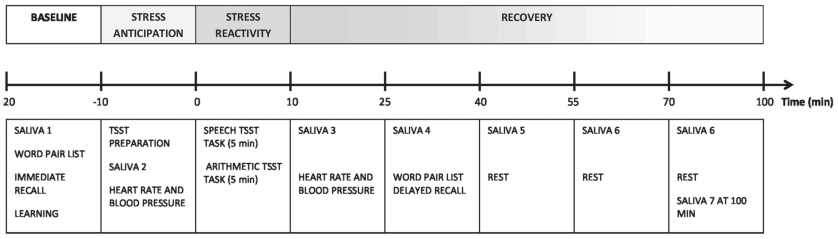

Figure 1 Schematic representation of the experimental protocol.

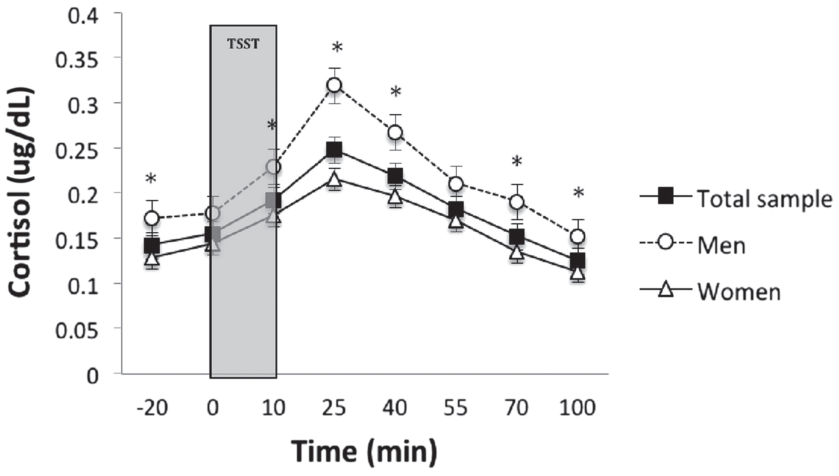

Figure 2 Mean cortisol concentration and sex differences. Participants showed higher cortisol levels at 10, 25, 40, 55, 70 and 100 min after the Trier social stress test (TSST; total sample). Men showed higher cortisol concentrations than women at baseline (−20 min), stress reactivity stage (10 and 25 min) and at recovery stage (40, 70 and 100 min). *$P < 0.05$. Bars represent standard error. ANOVA for repeated measures with Bonferroni's multiple comparison test for cortisol across time and Student's t-test for sex comparison.

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Regarding cardiovascular response, a significant increase in systolic blood pressure (SBP; $P < 0.001$) and diastolic blood pressure (DBP; $P = 0.002$) was observed after TSST (Fig. 3). There was no significant difference between heart rate before (76.4 ± 12.7) and after (76.1 ± 12.8; $P = 0.701$) the TSST. ANOVA for repeated measures showed a time × sex effect on SBP (F [1,97] = 6.7; $P = 0.011$). Men showed higher SBP before the TSST than women ($P = 0.046$). No effect of sex on DBP ($P = 0.112$) and heart rate ($P = 0.512$) was observed. No effect of age was observed in the comparisons of SBP, DBP and heart rate before and after TSST ($P \geq 0.382$).

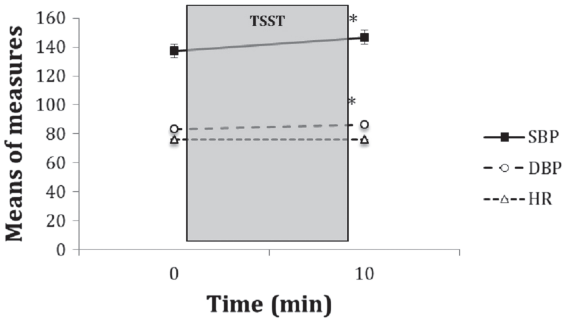

Figure 3 Mean systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) reactivity to psychological stress task. SBP and DBP increase was observed 10 min after the Trier social stress test (TSST). *$P < 0.05$. Bars represent standard error. Student's paired *t*-test.

Memory performance and acute stress task

A significant difference was observed between scores on the word pairs test for total words (F [2,299] = 25.2; $P < 0.001$), related words (F [2, 299] = 12.4; $P < 0.001$) and unrelated words (F [2,299] = 20.8, $P < 0.001$) 20 min before and 15 min after exposure to TSST. Scores were greater on the second try at word recall (learning) than on the first try (immediate recall) for total words, related words and unrelated words ($P < 0.001$). Regarding recall after the TSST (delayed recall), lower scores were observed for total words ($P = 0.011$), related words ($P = 0.002$) and unrelated words ($P = 0.004$) compared with immediate recall (Fig. 4A). ANOVA for repeated measures revealed a main effect of sex on the average of the word pairs test scores for total words (F [1.97] = 4.9; $P = 0.028$) and for related words (F [1.97] = 12.0; $P = 0.001$) and no effect for unrelated words ($P = 0.667$). Women showed better scores than men (Fig 4b–d). No effect of age was observed in the comparisons of total, related and unrelated words scores between immediate, learning and delayed recall ($P \geq 0.210$).

Association between cortisol concentration under acute stress and memory performance

There was a negative correlation between baseline cortisol concentrations (−20 min) and scores on pairs of related words in immediate recall ($r = -0.237$; $P = 0.017$). There

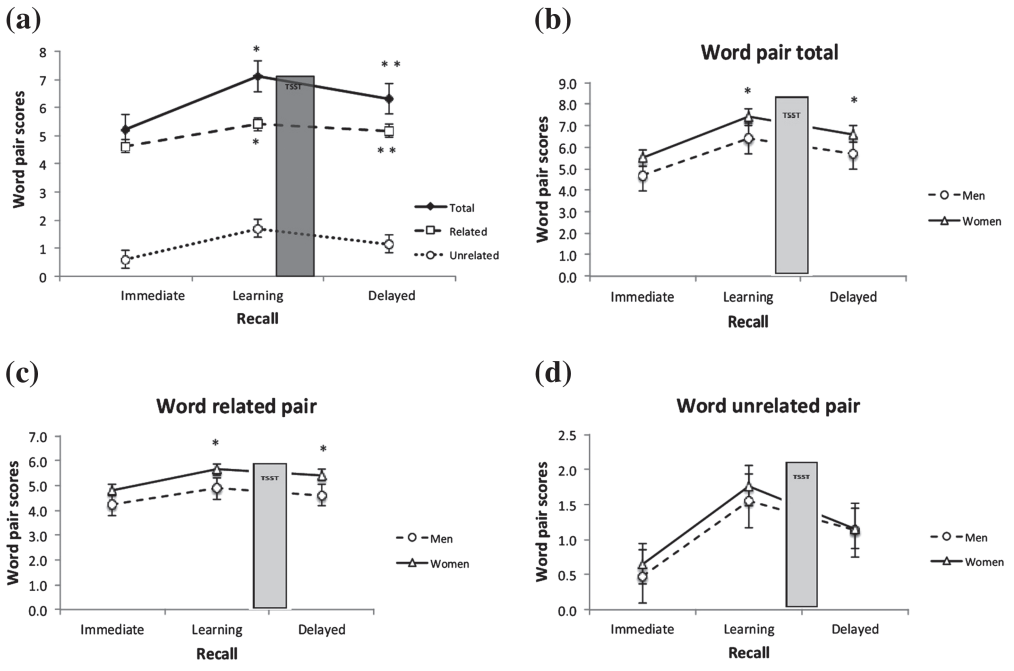

Figure 4 Memory performance before and after the acute psychological stress and sex effect. The word pair total and related pair scores were higher than immediate recall (*). Lower word pair total and related pair scores were observed after the Trier social stress test in the delayed recall compared with immediate recall scores (**). Men showed learning and delayed recall scores for (b) total and (c) related word pair. *,**$P < 0.05$. Bars represent standard error. ANOVA for repeated measures with Bonferroni's multiple comparison test for memory scores across time, and Student's *t*-test for sex comparison.

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was no association between cortisol and learning of word pairs. In addition, a negative correlation was observed between cortisol reactivity to TSST (10 min) and delayed recall of the pairs of related words ($r = -0.225$; $P = 0.024$). Multiple linear regression having cortisol levels, education, sex and age as the independent variable showed that age and baseline cortisol is associated with immediate recall of related word pair scores (F [2,99] = 6.2; $P = 0.003$), explaining 11.3% of the variability in the immediate recall (Table 1). The higher the age and the baseline cortisol, the poorer the immediate recall. Regarding delayed memory, cortisol reactivity to TSST associated with sex and education were associated to delayed recall of related word pair scores, with 20.5% of the variability in memory performance after TSST (F [3,99] = 8.2; $P < 0.001$; Table 1). In men, the lower the education and the higher the cortisol reactivity to TSST, the poorer the delayed recall.

Discussion

Corroborating the main hypothesis of the present study, a decline in declarative memory performance was observed after reaction of stress induced by the TSST in older people. In addition, we observed that both at baseline and after exposure to acute stress, the higher the concentration of cortisol the worse memory performance. Specifically, high cortisol levels at baseline were associated with low immediate memory regardless of sex, whereas being male, having a low education background and having high cortisol levels after acute stress exposure were associated with a low delayed memory performance. These data are consistent with the results of a previous study on healthy older people, in which worse declarative memory performance was observed after the induction of stress compared with the group not exposed to stressful conditions.[9] Another study also found that increased cortisol-induced stress was negatively correlated with memory performance after exposure to the stressor.[15] More specifically, individuals who responded with a greater increase of cortisol performed worse on the memory task compared with those individuals who had lower cortisol response to stress induction.[15]

The association between higher cortisol concentrations and worse memory performance can be explained by the modulatory role of glucocorticoids in memory. This modulation, exhibiting the profile of an inverted "U" function, has been explained by the occupation rate of glucocorticoid receptors, the MR found primarily in the hippocampus, and the GR presented in both prefrontal cortex and hippocampus.[2,16] Thus, when MR (greater glucocorticoid affinity) is saturated and GR (lower affinity) is partly occupied, there is better memory performance. However, when both MR and GR have low occupancy rates or are saturated, there is worse memory performance.[15] It can therefore be inferred that the increase in circulating cortisol concentration induced by the TSST mobilized saturation of MR and GR, leading to worse memory performance compared with baseline, when there would have been only total occupation of MR and partial occupation of GR.

Another interesting finding was that age, education and sex were associated with cortisol concentration effect on immediate and delayed memory performance, suggesting that the effect of stress on memory performance could vary depending on these variables. Corroborating this interpretation, a negative effect of psychosocial stress on memory was observed only in older individuals compared with young adults, suggesting that age might moderate stress-induced effects on declarative memory.[17] Similarly, several authors have also shown the effect of sex on

Table 1 Multivariate regression results between cortisol concentration and word pair scores adjusted for covariates

Model	Immediate recall related word pair					Delayed recall related word pair				
	β	P	R^2	F	P	β	P	R^2	F	P
Model 1			0.152	4.2	0.003*			0.212	6.4	< 0.001*
Baseline cortisol	−0. 252	0.012*				_	_			
Cortisol reactivity	_	_				−0.165	0.087			
Education	0.160	0.106				0.198	0.038*			
Sex	0.132	0.152				0.337	0.001*			
Age	−0.157	0.110				−0.090	0.338			
Model 2			0.113	6.2	0.003*			0.205	8.3	<0.001*
Baseline cortisol	– 0.254	0.009*								
Cortisol reactivity	_	_				−0.174	0.070†			
Education	_‡	_‡				0.218	0.020*			
Gender	_‡	_‡				0.344	<0.001*			
Age	−0.200	0.040*				_‡	_‡			

*$P \leq 0.05$; indicates trend level significance. †Trend level significance. ‡Not included in model 2 due to non-significant effect in the previous model.

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cortisol levels in adults[18–23] and older individuals, with men showing higher salivary cortisol responses.[8,18,19,23] However, previous findings regarding the effect of sex in the relationship between cortisol levels and memory are quite contradictory.[17–24] Although no difference related to sex was observed on memory performance after exposure to psychosocial stress in older individuals,[17] in young adults a significant enhancing effect of stress on declarative memory[24] and on working memory[25] was observed only in men compared with age-matched women. Interestingly, the present results showed an impaired effect of stress on declarative memory moderated by sex differences. Men showed higher cortisol reactivity to TSST and interestingly poorer delayed recall after TSST compared with women. Furthermore, cortisol reactivity to TSST associated with sex and education explained more than 20% of the delayed recall performance variability; the higher the cortisol-induced by TSST, the lower the education level, the poorer the delayed recall in men. In middle-aged individuals, an impaired effect of stress on memory was also observed, but only in women.[26] Women showed an acute impact of stress on memory, whereby the higher the cortisol reactivity to the stressor, the poorer the declarative memory performance. Although those findings seem to be quite opposite in terms of sex effect, it is noteworthy that our sample was older and with a lower education background compared with previous findings.[26] Current and previous findings sustain the hypothesis that the direction of the effect (improvement or impairment) of acute stress on memory depends on age (young, middle-aged or aged) and sex differences.

Altogether, these findings raise concerns regarding potential differences in the vulnerability of older individuals to the neurotoxic effects of stress exposure on memory and consequently on the development of cognitive disorders. Indeed, even adverse early-life experiences in combination with lifespan stress might produce negative effects on the brain and cognition though epigenetic mechanisms.[2] In this regard, some authors have found a significant association between high concentrations of cortisol and worse memory performance in older adults with mild cognitive impairment, considered an intermediate stage between the normal condition of cognitive functioning and the onset of a dementia.[27] In addition, stress resulting from the perceived feeling of being forgotten is associated with higher cortisol levels and less effective emotional coping in older adults with mild cognitive impairment[28]. Interestingly, the incidence of mild cognitive impairment is also dependent on sex, with higher rates being observed in men compared with women.[29]

It is important to emphasize that analysis of the harmful effects of prolonged exposure to cortisol should take into account individual protective factors, including biological, psychological and also socioeconomic backgrounds, as their interaction could contribute to interindividual variability in resilience to stress.[30]

In this regard, future studies should consider protective factors in the relationship between stress and memory impairment to determine why not all older individuals exposed to stressors show cognitive impairments.

Although in the present study interesting aspects regarding the acute stress response in healthy older adults as well as its relationship with worse memory performance were revealed, some limitations should be considered when interpreting the data. For instance, there was a predominance of female participants, and cortisol levels can vary according sex.[9,27] Even when sex was inserted as a covariate in the statistical analysis, studies with clusters of men and women investigating the moderator effect of sex in the relationship between cortisol and memory might produce additional findings. Additionally, even though the sample was obtained by the random sampling technique, a significant difference in relation to the age and education of the participants was evident. These factors, although controlled for it in the present study, might have influenced the acute stress response and its influence. Furthermore, a control group that did not carry out the TSST should have been included. If the scores of delayed recall of the word pairs test did not differ from immediate memory and learning scores in the participants of the control group, it would be possible to sustain more assertively that cortisol reactivity to acute psychosocial stressors might impair memory performance during aging. Finally, the investigation of other types of memory and cognitive domains, such as work memory, executive function and attention, should be considered in future studies among older adults, as the cortisol levels also interact with neuronal structures related to these cognitive abilities.[2]

Confirming the hypothesized influence of cortisol on declarative memory performance in healthy participants, a decline in memory performance was observed after induction of the stress response. Furthermore, cortisol concentrations before and after acute psychological stress predicted poor memory performance, and this relationship might be moderated by sex and age. Taken together, these results highlight the degree of vulnerability to pathological cognitive changes that the elderly population might be subjected to, given the everyday stressors often faced with inappropriate emotional and social support and adaptation.

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Disclosure statement

The authors declare no conflict of interest.

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