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AGE DIFFERENCES IN THE ACUTE STRESS EFFECTS ON DECLARATIVE MEMORY PERFORMANCE

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Abstract

In the last decades, there has been a growing interest in knowing the effects of acute stress on memory performance, particularly declarative memory. Research on this topic suggests that age is a crucial individual factor to consider in the stress-memory link. However, most of the evidence has been obtained from studies conducted in young people and, surprisingly, studies in older people are scarce. Thus, our aim was to investigate the age differences in the acute stress effects on declarative memory performance. To do this, we directly compared the effects of a psychosocial acute stressor (i.e. Trier Social Stress Test) on learning, consolidation and memory retrieval performance in two age groups (young: 18-35 years vs. 54- 78 years). As expected, worse memory performance was associated with age. Overall, stress did not affect learning, consolidation and memory retrieval performance in older people. However, stress caused greater interference in the older people's memory performance than a control task, but this result was not found in young people. In addition, stress impaired retrieval performance in young men but not in older people. Our results suggest that age moderates the stress-induced effects on declarative memory. In addition, they support the idea that older people could be less sensitive to acute stress effects on memory probably due to an age-related reduction of the sensitivity and density of the glucocorticoid receptors and a decrease in the functional amygdala and hippocampus interconnectivity.

Keywords: *Memory, stress, age, sex.*

1. Introduction

The effect of stress on memory performance is a research topic that has been getting growing attention in the last years. Stress is a common phenomenon in our daily lives that can clearly affect declarative memory. Given that declarative memory is a key cognitive process in people's functionality and independence, it is crucial to understand the mechanisms underlying the stress effects on this memory process.

The stress response is characterized by the activation of the sympathetic nervous system (SNS) and the hypothalamus-pituitary-adrenal axis (HPA-axis), leading to a large amount of catecholamines and cortisol secreted to the bloodstream. These hormones affect the activity of the hippocampus, prefrontal cortex, and amygdala, crucial brain areas for several cognitive functions, and especially memory. Thus, the neurobiological mechanisms that regulate the stress response are also involved in memory processes. Although there is evidence supporting the idea that stress-related changes in these brain areas affect memory performance, the direction of these effects is inconclusive. In this sense, several factors, some related to the task (i.e., the type and nature of the material to be learned and the phase of memory assessed) and others related to the individuals (i.e., age and sex) are critical to understanding the stress-memory link (Shields et al., 2017). It is important to note that, although stress may explain part of the large interindividual heterogeneity in the age-related cognitive decline, only a few studies have investigated the role of age in the acute stress effects on declarative memory performance (Hidalgo et al., 2019).

2. Objectives and hypothesis

The main objective of this study was to investigate the age differences in the acute stress effects on declarative memory performance. To do this, we directly compared the effects of a laboratory-based

psychosocial stressor on different phases (i.e., learning, consolidation, and retrieval) of declarative memory tasks. Based on previous studies, we expected enhancing stress effects on learning and consolidation and, in turn, impairing stress effects on retrieval, at least in young people.

3. Methods

To investigate the role of age in the acute stress effects on declarative memory performance, we directly compared the effects of the stressor on declarative memory performance in young and older adults in three independent studies. Each study investigated the stress effects on a different memory phase (i.e., learning, consolidation, and retrieval). In all of the three studies, we used the Trier Social Stress Test (TSST; Kirschbaum et al., 1993) to stress the participants.

The TSST is a standardized laboratory-based acute psychosocial stressor widely used in stress´ research. It consists of three parts: (i) a preparation phase, in which the participants are informed that they have to give a 5-min speech to convince a committee that he/she is the best candidate for a job position (a mock job interview), and they have 5 min to prepare the speech; (ii) the free speech task, and (iii) an arithmetic task, in which the participants have to perform as accurately and quickly as possible different subtractions in front of the committee. Each part o task lasted 5 minutes, and the participants remained standing in front of a committee composed of a man and a woman. In addition, both the speech and arithmetic tasks were recorded with a camera and microphone.

The exclusion criteria for the three studies were: smoking more than 10 cigarettes/day; alcohol or other drug abuse; dental, visual or hearing problems; a stressful life event during the past year; the presence of cardiovascular, endocrine, neurological or psychiatric disease; and using any medication related to emotional or cognitive function, or that may affect the activity of the HPA-axis and the SNS.

In addition, before assisting to each experimental session, the participants had to follow a series of recommendations: They were asked to maintain their general habits, sleep as long as usual, refrain from heavy physical activity the day before the session, not consume alcohol since the night before the session, and drink only water and not eating, smoking or taking any stimulants two hours before the session.

To control the sex hormones levels, all older women were postmenopausal, and none of them were receiving estrogen replacement therapy. Regarding young women, the phase of the menstrual cycle was controlled.

Finally, all studies were performed in accordance with the Declaration of Helsinki and the protocols were approved by the Ethics Research Committee of the University of Valencia, and the University of Zaragoza.

3.1. Study 1: Stress before learning

In this study, we investigated the psychobiological stress response in two age groups (young: 18-35 years vs. older: 54-78 years) of men and women and its effects on declarative memory when the stressor was applied before the learning phase. To do this, sixty-seven participants were divided into two age groups (young: 18 men and 17 women; older: 16 men and 16 women), and were asked to participate in two sessions (i.e., stress and control sessions) in a within-subject design. In the stress session, participants were exposed to the TSST, and in the control session, they performed a control task. The control task was very similar to the stress task in metal workload and global physical activity but without the evaluative threat and uncontrollability. The stress and control sessions were counterbalanced.

Briefly, the procedure consisted of a habituation phase of 15 min, then the participants performed the TSST or control task (15min), and afterward, a recovery phase of 20 min. The participants performed a declarative memory task, the Spanish version of Rey's Auditory-Verbal Learning Test (RAVLT) (Miranda and Valencia, 1997), during the recovery phase. This test is composed of eight trials. In the first five trials, participants listened to a list of 15 neutral words (list A) and after each trial, they had to repeat as many as words as possible. These first five trials are used to compute the learning curve. Then, a new word list (interference list) was read aloud by the experimenter, and the participants were asked to recall the words from list A immediately after the interference list and after a delay of 30 min. These trails reflect the recall after the interference and the delayed recall, respectively. After that, participants performed a recognition task in which they had to recognize words from a list containing 15 new and the 15 words from list A.

In this study, we assessed the activation of the SNS and HPA-axis measuring salivary alpha-amylase (sAA) and cortisol levels, respectively, during both sessions (for more details, see Hidalgo et al., 2014).

3.2. Study 2: Stress during consolidation

In the second experiment, we aimed to explore age differences in the stress effects on memory consolidation in a sample composed by one hundred and twenty-five participants divided into two age groups (young (18-29 years): 29 men and 31 women; older (56-75 years): 30 men and 35 women). All participants were asked to attend two sessions: the acquisition session and the memory testing session. In the acquisition session, after a habituation phase, participants viewed 60 color pictures (20 negative, 20 positive, and 20 neutral) from the International Affective Picture System (IAPS; Lang et al., 2005). After each picture, participants had to rate the emotional (negative, positive, or neutral) and the arousal (high, middle, or low) of the pictures presented. After that, participants were asked to recall as many pictures as possible (immediate free recall), and then, they were exposed to the TSST or a control task (see description in Study 1). Twenty hours later, in the memory testing session, participants were asked to recall as many pictures as possible from the set of images they had to see the previous day (delayed free recall). In this second experiment, we measured changes in cortisol, mood, and anxiety during the two sessions.

3.3. Study 3: Stress before retrieval

In the third study, we studied in two age groups (young (18-27 years): 26 men and 24 women; older (56-76 years): 27 men and 25 women), the psychobiological response (mood, cortisol, and sAA) to a stress or control task and its effect on memory retrieval performance of emotional and neutral pictures. As in the second study, participants had to attend two sessions: the acquisition and the memory testing session. In the first session, participants were asked to look at 30 pictures (10 negative, 10 positive, and 10 neutral) pictures extracted from the IAPS. As in Study 2, participants rated the valence and arousal of each picture. Twenty-four hours later, participants had to return to the lab. Half of them performed the TSST, and the other half the control task (see description in Study 1). After that, participants were asked to recall as many pictures as possible from the pictures seen the day before (free recall task). In addition, they were asked to perform a recognition task from a set of 60 pictures (30 new and 30 previously viewed pictures) (for more details see: Hidalgo et al., 2015).

4. Results and discussion

The stressor used in our experiments, the TSST, provoked a significant psychobiological response. At the psychological level, the TSST increased negative mood and decreased positive mood similarly in both age groups (Studies 2 and 3). In addition, the anxiety levels increased after the stressor compared to the control task (Study 2). At the physiological level, the TSST provoked a significant response of cortisol (Studies 1, 2 and 3) and sAA (Studies 1 and 3). Regarding the cortisol response, a clear effect of sex was observed across the three studies, with men showing higher cortisol response than women. This result is in line with most previous studies (for a review of this topic, see: Pulopulos et al., 2018). In contrast, although no age differences were found in the cortisol response in Studies 1 and 2, as in previous studies (Pulopulos et al., 2018), in Study 3, we found that young men showed higher cortisol response to the TSST than older men. This age modulating effect on the stress-induced cortisol response is in line with previous studies (Almela et al., 2011; Kudielka et al., 2004). In contrast to these studies, we did not observe a higher cortisol response in older than in young people. No age and sex differences were found in the sAA response to the TSST. However, in Study 1, we found that older people had higher sAA levels than young people in the control but not in the stress session. This result supports the idea of an increased basal sympathoneural activity in older people (Seal and Dinenno, 2004).

Regarding memory performance, as expected in the three studies, older people's memory performance was lower than young people. Overall, no stress effects on acquisition, consolidation, and retrieval performance were observed. However, we found that when the stressor was applied before the acquisition of a list of neutral words (Study 1), the stressor impaired immediate recall (retroactive interference) only in older people. In addition, when the stressor was applied before memory retrieval (Study 2), the stressor impaired free recall performance only in young men. No age and sex differences were found in the stress effects on memory consolidation (Study 2) (for a review of this topic, see: Hidalgo et al., 2019).

Together, our results suggest that older people could be less sensitive to acute stress effects on memory. These age differences found in the stress effects on declarative memory could be explained by an age-related reduction sensitivity and density of the glucocorticoid receptors (Mizoguchi et al., 2009) and a decrease in the functional amygdala and hippocampus interconnectivity (Mather, 2006; Murthy et al., 2010; St. Jaques et al., 2009).

5. Conclusions

In sum, our results suggest that age moderates the stress-induced effects on declarative memory performance in healthy people. In addition, other factors as the phase of memory assessed, or the sex of participants seem to be important factors to be considered when investigating the stress-memory link.

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