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Enhancing effects of acute psychosocial stress on priming of non-declarative memory in healthy young adults

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Abstract
Social stress affects cognitive processes in general, and memory performance in particular. However, the direction of these effects has not been clearly established, as it depends on several factors. Our aim was to determine the impact of the hypothalamus–pituitary–adrenal (HPA) axis and sympathetic nervous system (SNS) reactivity to psychosocial stress on short-term non-declarative memory and declarative memory performance. Fifty-two young participants (18 men, 34 women) were subjected to the Trier Social Stress Task (TSST) and a control condition in a crossover design. Implicit memory was assessed by a priming test, and explicit memory was assessed by the Rey Auditory Verbal Learning Test (RAVLT). The TSST provoked greater salivary cortisol and salivary alpha-amylase (sAA) responses than the control task. Men had a higher cortisol response to stress than women, but no sex differences were found for sAA release. Stress was associated with an enhancement of priming but did not affect declarative memory. Additionally, the enhancement on the priming test was higher in those whose sAA levels increased more in response to stress ($r_{48} = 0.339$, $p = 0.018$). Our results confirm an effect of acute stress on priming, and that this effect is related to SNS activity. In addition, they suggest a different relationship between stress biomarkers and the different memory systems.

Keywords: *Alpha-amylase, cortisol, sex, oral contraceptives, psychosocial stress, TSST*

Introduction

Exposure to stress can have impairing or enhancing effects on memory, attention, and executive functions (Shors 2006, Lupien et al. 2007; Schwabe et al. 2010). The influence of stress on these cognitive processes has been related to the stress-induced activation of both the hypothalamus–pituitary–adrenal axis (HPA-axis) and the sympathetic nervous system (SNS). Indeed, it has been demonstrated that the release of cortisol, the end product of the HPA-axis activity and several SNS biomarkers (e.g. catecholamines) can influence cognitive processes (Roozeendaal 2002). Among the SNS biomarkers, salivary alpha-amylase (sAA), an oral cavity enzyme, has increasingly been used as an indicator of SNS activation because it is easier to measure than the circulating catecholamines (Nater and Rohleder 2009; Rohleder and Nater 2009). The current study investigated whether HPA-axis and SNS activation in response to acute psychosocial stress affects different memory systems (implicit and explicit systems).

The impact of stress on implicit memory has been understudied. Implicit memory represents the effect of unconscious prior experience on subsequent behavior (Graf et al. 1984). This type of memory includes priming effects, classical conditioning and non-associative learning, as well as motor, perceptual, and cognitive skill acquisition (Daum and Ackermann 1997). According to Henson, priming refers to a change in the speed, bias, or accuracy of the processing of a stimulus, following prior experience with the same, or a related, stimulus (Henson 2003). Only a few studies have investigated the impact of acute stress on priming, and results from these studies are inconclusive. No effects of acute stress on priming have been reported among people from middle to

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older ages (Lupien et al. 1997; Domes et al. 2002), but more recently Eich and Metcalfe (2009) found in a younger sample that a physical stressor (running a marathon) was associated with an enhancement of priming effects. However, Eich and Metcalfe did not include physiological measures in their study; therefore, we could not know whether this enhancing effect was related to HPA and/or SNS activation. To our knowledge, only one study, in young men, has directly investigated the impact of cortisol administration on priming and found that high cortisol concentrations did not have any effect on this kind of implicit memory (Kirschbaum et al. 1996). The current study further investigated whether the stress-induced change in the activity of the HPA-axis (i.e. cortisol) and SNS (i.e. sAA) affects implicit memory measured by priming.

Although the effects of stress on non-declarative memory have not been studied in detail, the relationship between stress and declarative memory has been investigated more thoroughly. It has been shown that cortisol exerts a modulatory effect on declarative memory performance through its action on brain areas that are also important for memory functioning. These brain areas are mainly the hippocampus and the prefrontal cortex, which have a large number of receptors for cortisol (de Kloet et al. 1999; Roozendaal 2000; Lupien et al. 2009). Cortisol can have either enhancing or impairing effects on declarative memory performance, depending on several factors such as the memory phase under investigation (i.e. acquisition, consolidation, or retrieval) or the emotional valence of the material to be remembered (i.e. emotional or neutral). Cortisol has been shown to enhance memory consolidation but to impair memory retrieval (Roozeendaal 2002); moreover, due to the moderating role of the amygdala, the impact of cortisol on memory performance is stronger for emotionally arousing material than for neutral material (McEwen 2002; Roozeendaal 2002; Lupien et al. 2005, 2007; Sandi and Pinelo-Nava 2007).

Our study investigated the impact of psychosocial stress on priming and declarative memory performance when stress is applied prior to learning, using neutral content. Previous studies with a similar design have found mixed results. Some studies show an impaired short-term declarative memory recall after exposure to stress (from 20 to 60 min after learning) compared to a control group (Jelicic et al. 2004; Payne et al. 2006, 2007; Smeets et al. 2006), while others found no effect (Wolf et al. 2001; Elzinga et al. 2005), or even an enhancing effect of stress on declarative memory performance (Schwabe et al. 2008). The majority of the studies showing that stress induction affected declarative memory performance failed to find that the release of cortisol during stress was proportionally related to declarative memory performance, either because these studies did not investigate this or because the results were non-significant (Jelicic et al. 2004; Payne et al. 2006, 2007; Smeets et al. 2006; Schwabe et al. 2008). Indeed, only two studies have shown that stress-induced cortisol increase was negatively related to declarative memory performance when stress was applied prior to learning (Kirschbaum et al. 1996; Wolf et al. 2001). In contrast, Nater et al. (2007) found the opposite result that the high cortisol responders to stress performed better on the declarative memory task than the low cortisol responders.

Only a few studies have investigated whether the stress-induced sAA release is related to declarative memory performance. These studies found enhancement of memory performance associated with sAA release (Segal and Cahill 2009; Smeets et al. 2009), or no effects (Preuβ and Wolf 2009).

The current study investigated, among young people, the hypothesis that cortisol and sAA responses to acute psychosocial stress would be associated with priming and declarative memory performance. It has been suggested that the relationship between acute stress and memory processes could be moderated by sex (Andreano et al. 2008). However, previous studies either only included one sex (Nater et al. 2007) or they included both sexes but without registering the menstrual cycle phase of the women, which should be taken into account when studying the impact of cortisol reactivity on acute stress (Kirschbaum et al. 1996; Jelicic et al. 2004; Elzinga et al. 2005; Payne et al. 2006; 2007; Smeets et al. 2006). Therefore, in this study we included women in their early follicular phase and women using hormonal contraception, both groups usually showing responses to stress that differ more than those of women in the luteal phase of the menstrual cycle when compared to responses of men. In a crossover design, the participants were exposed to both psychosocial stress (Trier Social Stress Test, TSST) and a control condition. Based on previous studies in young people, we expected a higher cortisol response to stress in men than in women (Kirschbaum et al. 1999) and no sex difference in the sAA response to stress (Rohleder and Nater 2009). Due to the mixed results of acute stress on priming and declarative memory, we explored whether acute stress affected these memory processes, taking into account the sex and hormonal state of the participants. Finally, we investigated whether the cortisol and sAA reactivity to stress had an effect on priming and declarative memory performance, and whether this effect was different for men and women.

Methods

Participants

The final sample was consisted of 52 subjects: 18 men, 17 women in the early follicular phase (2–5 days), and 17 women using monocyclic formulas for at least

6 months. The age of participants was between 18 and 35 years (total sample: $M = 21.56$, standard error mean, SEM = 0.55 years).

The subjective socioeconomic status scale (Adler et al. 2000) was medium to high, and there were no significant differences between groups (total sample: $M = 6.33$, SEM = 0.13). The groups did not differ with respect to age or body mass index. Most of them (94%) were college students from different areas. One hundred and fifty-nine volunteers were interviewed and they completed a standardized questionnaire to check whether they met the study prerequisites. The criteria for exclusion were as follows: smoking more than five cigarettes a day; alcohol or other drug abuse; visual or hearing problems; presence of a cardiovascular, endocrine, neurological, or psychiatric disease; having been under general anesthesia once or more than once in the past year; the presence of a stressful life event during the last year; using any medication directly related to cardiac, emotional, or cognitive function; one that was able to influence hormonal levels, such as glucocorticoids or β-blockers. One hundred and seven volunteers were excluded from the sample for two reasons: 34 of them did not meet the exclusion criteria mentioned above and the rest, 73, because their schedules were incompatible with the experiment's features (2 days, 4 h, and only in the afternoon).

The participants that met the criteria were contacted by telephone and asked to attend two sessions that took place in a laboratory at the Faculty of Psychology. No financial payment was made to the participation, although they received a pendrive (approximate value 15 €). Before each session, the participants were asked to maintain their general habits: sleep as long as usual, refrain from heavy activity the day before the session, and not consume alcohol since the night before the session. Additionally, they were instructed to drink only water and not to eat, smoke or take any stimulants, such as coffee, cola, caffeine, tea, or chocolate, 2 h prior to the session. The study was conducted in accordance with the Declaration of Helsinki, and the protocol and conduct were approved by the University of Valencia Ethics Research Committee. All the participants received verbal and written information about the study and signed an informed consent form.

Procedure

The procedure was similar to the one employed previously in a sample with old people (Almela et al. 2011a). It was a within-subject design with two completely randomized and counterbalanced conditions in two separate sessions: a stress condition and a control condition, with less than 2 weeks between sessions, except for the women in the follicular phase with 4 days between sessions. The test–retest interval was different in this group in order to ensure the same phase of the menstrual cycle in both conditions. The sessions consisted of several phases of equal duration for both conditions. The sessions took 1 h and 50 min to complete, and they were always held between 16:00 and 20:00 h. Each participant started his or her two sessions at the same hour (Figure 1). Upon arrival at the laboratory, the weight and height of the participants were measured, and the experimenter checked whether they had followed the instructions given previously.

Stress condition. To produce stress, we subjected the participants to the TSST (Kirschbaum et al. 1993). The stress task consisted of 5 min of free speech (job interview) and a 5-min arithmetic task, and it was performed in front of a committee composed of a man and a woman. The participants remained standing at a distance of 1.5 m from the committee. Additionally, a video camera and a microphone were clearly visible. Both the speech and arithmetic tasks were filmed.

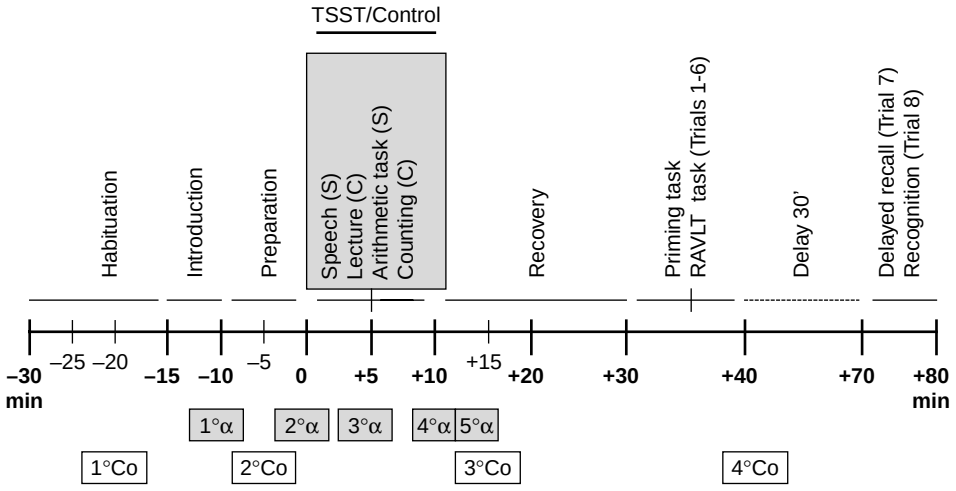

Figure 1. Timeline of the TSST (S) and control (C) conditions. Salivary cortisol samples = 1°Co, 2°Co, 3°Co, 4°Co. Salivary alpha-amylase samples = 1°α, 2°α, 3°α, 4°α, 5°α. RAVLT = Rey auditory verbal learning test.

The protocol started with a habituation phase of 15 min to allow the participants to adapt to the laboratory setting. During this phase, the participants remained seated. Five minutes after the start of this phase, the subjects provided the first cortisol saliva sample (−20 min pre-stress). After the habituation phase, the introduction phase started (duration: 5 min). In this phase, the participants were informed about the procedure for the stress task. They received the instructions in front of the committee in the same room where the task took place. After this, the subjects provided the first sAA sample (−10 min pre-stress). Next, the participants had 10 min to prepare for the task. At this point, they provided the second cortisol saliva sample (−5 min pre-stress), and the second sAA sample was provided when this phase ended (0 min).

Following the preparation phase, the stress task was carried out. During the stress task, the participants provided the third (after speech, +5 min) and fourth sAA samples (after the arithmetic task, +10 min). Then, subjects had 20 min to recover after the stress task, and they provided the fifth sAA sample (+14 min post-stress) and the third cortisol saliva sample (+15 min post-stress) during this recovery period. Each participant then performed two memory tests. The participants first did a priming task, specifically, a word-stem completion task, to assess non-declarative memory and then they performed a standardized memory test consisting of eight trials (Rey Auditory Verbal Learning Test, RAVLT) in order to measure declarative memory. The participants completed the first six trials between 30 and 40 min after the TSST. After trial 6, they waited 30 min (delay period) before they continued with the memory test. During the delay period, the participants provided the fourth saliva sample (+40 min post-stress). After the delay period, they completed the memory test with trials 7 and 8 and, finally, were debriefed.

Control condition. The control condition was similar to the experimental condition, except that the stressful task was replaced by a control task. This task was designed to be similar to the stress task in mental workload and global physical activity, but without the main components capable of provoking stress, such as evaluative threat and uncontrollability (Dickerson and Kemeny 2004). The control task was composed of 5 min of reading aloud and 5 min of counting. In the preparation phase, the participants did not prepare for their task, but instead they read a book with neutral content. The timing of the saliva samples and the phase durations were the same for the two conditions.

Memory

Priming. We used a word-stem completion task to assess priming. Two parallel word lists were used to avoid a learning effect (List A and List B). The order of the two versions was randomized and counterbalanced. First, the experimenter presented a list of 26 neutral words. The participants had to read each word aloud and rate its degree of familiarity on a Likert scale ranging from 1 (unfamiliar) to 7 (extremely familiar). After this step, the subjects performed a distracting task that lasted 2 min. The distracting task consisted of writing words beginning with the letters "b" and "l" (List A) or "d" and "p" (List B). Finally, the word-stem completion task was performed. The participants had to complete a list containing 78 stems of words (first three letters). Among these words were the 26 words read previously. No restriction was imposed as to the category of word that could be given for completion. The participants were instructed to complete the list of stems as fast as possible and with the first word that came to mind. This instruction, which provokes the priming effect through the implicit recall of the words presented previously, differs from the "word-stem cued-recall," which explicitly instructs participants to complete the stems using words that have been presented previously (Henson 2003).

We obtained three scores: (i) number of frequent words, (ii) number of non-frequent words, and (iii) number of total words (sum of frequent and non-frequent words) recalled from the target list. To control the effect of chance, another group of 31 young subjects did the word-stem completion task, but without the target lists being presented previously. This group was called the "priming baseline group." The number of words from the two lists that could be correctly completed by chance was subtracted from the scores of the experimental subjects (Lupien et al. 1994, 1997).

Declarative memory. To measure declarative memory, the Spanish version of RAVLT was used (Miranda and Valencia 1997). This test has several versions, and for each participant a different version of the RAVLT was used in the second session to avoid learning effects. The order of the two versions was randomized and counterbalanced. The RAVLT is composed of different trials. In the first five trials, the experimenter read aloud a target list of 15 neutral words, and each participant had to repeat as many words as possible in each of the five trials. The performance on these first five trials reflects the rate of learning (trials 1–5: *learning curve*). After trial 5, the experimenter read aloud an interference list of 15 words and tested the retention of these new words. Following this step, the participants were requested to recall the words from the target list (trial 6: *recall after interference*); after a delay of 30 min, they had to recall them a second time (trial 7: *delayed recall*). In trial 8 (*recognition*), the participants had to recognize the memorized words from a list presented verbally

containing 15 new and 15 previously learned words. Trial 8 was divided into two different scores: *Hits*, the number of words correctly recognized as being on the target list, and *False alarms*, the number of words incorrectly recognized as being on the target list.

Biochemical analyses

Salivary cortisol. The participants provided four saliva samples by depositing 5 ml of saliva in plastic vials. They took approximately 5 min to fill the vial. The samples were frozen at −80°C until the analyses were performed. The samples were analyzed by a competitive solid-phase radioimmunoassay (tube coated), using the commercial kit Coat-A-Count C (DPC, Siemens Medical Solutions Diagnostics). Assay sensitivity was 0.5 ng/ml. For each subject, all the samples were analyzed in the same trial. The within- and inter-assay variation coefficients were all below 8%.

Salivary alpha-amylase. Saliva was collected using salivettes (Sarstedt, Nümbrecht, Germany). The participants were instructed to keep the cotton swab in their mouth for exactly 1 min, not chew the cotton, and to move the swab around in a circular pattern to collect saliva from all the salivary glands (Rohleder and Nater 2009). The samples were frozen at −20°C after the completion of the session until the analyses took place. The samples were shipped to Dresden and analyzed at the Kirschbaum laboratory, Technical University of Dresden. The concentration of alpha-amylase in saliva was measured by an enzyme kinetic method according to the protocol specified by Rohleder et al. (2006). Inter- and intra-assay variation was below 10%. Analyses of sAA failed to detect sAA concentrations in the samples of one man and one OC user.

Statistical analyses

Data were checked for normal distribution and homogeneity of variance using Kolmogorov–Smirnov and Levene's tests before statistical procedures were applied. As neither the cortisol nor the sAA data had a normal distribution, they were square-root-transformed values.

One-way ANOVAs were used to investigate group demographic and anthropometric differences. Cortisol and sAA responses were assessed using ANOVAs for repeated measures with a between-subject factor (group: men, M; women in follicular phase, F; and women oral contraceptive users, OCs) and two within-subject factors, condition (stress vs. control), and time (cortisol: −20, −5, +15, +40 min; sAA −10, 0, +5, +10, +14 min).

Student's *t*-tests were used to investigate the priming effect between the groups, the experimental groups and the priming baseline group. We used an ANOVA for repeated measures to analyze non-declarative memory, employing condition as a within-subject factor and group (M, F, and OC) as a between-subject factor.

The declarative memory test that was used (RAVLT) provides one score for each trial performed, consisting of the number of correct words recalled in each trial. In trials 1–7, the words from the same target list have to be recalled; for this reason, we performed an ANOVA for repeated measures. We used condition (stress vs. control) and trials (trials 1–7) as within-subject factors and group as a between-subject factor. To analyze the effects on recognition (trial 8), we used d-prime (d′), which is the difference between the standardized proportion of correct hits and the standardized proportion of false alarms.

Due to the great variability among subjects in their cortisol reactivity to psychosocial stress, we divided the sample into responders and non-responders, according to Schommer et al. (2003). Responders were those individuals who had an increase of at least 2.5 nmol/l in salivary cortisol concentrations from the baseline levels (−20 min) to the third cortisol sample (+15 min), the sample immediately after the stress test. In addition, stress-induced sAA reactivity was calculated by subtracting sAA concentrations in the sample immediately after the TSST (+10 min) and baseline levels (−10 min). Pearson's correlations were calculated in order to assess whether cortisol reactivity and sAA reactivity to the stress task were related to priming and explicit memory performance.

We used Greenhouse–Geisser when the requirement of sphericity in the ANOVA for repeated measures was violated. *Post-hoc* planned comparisons were performed using Bonferroni adjustments for the *p* values. All *p* values reported are two-tailed, and the level of significance was taken as <0.05. When not otherwise specified, the results shown are means ± SEM. We used SPSS 15.0 to perform the statistical analyses. For ease of interpretation of the figures, the values in the figures represent raw values and not square-root-transformed values.

Results

Stress response

Salivary cortisol. The repeated measures ANOVA with salivary cortisol concentrations as the dependent variable showed the main effects for condition (F (1, 45) = 14.362, $p < 0.001$), time (F (1.64, 74.1) = 10.052, $p < 0.001$), and their interaction: condition × time (F (1.54, 69.49) = 50.132, $p < 0.001$). There were no baseline differences between the conditions ($p > 0.2$). In the stress condition, cortisol concentrations increased immediately after the stress task ($p < 0.001$), and

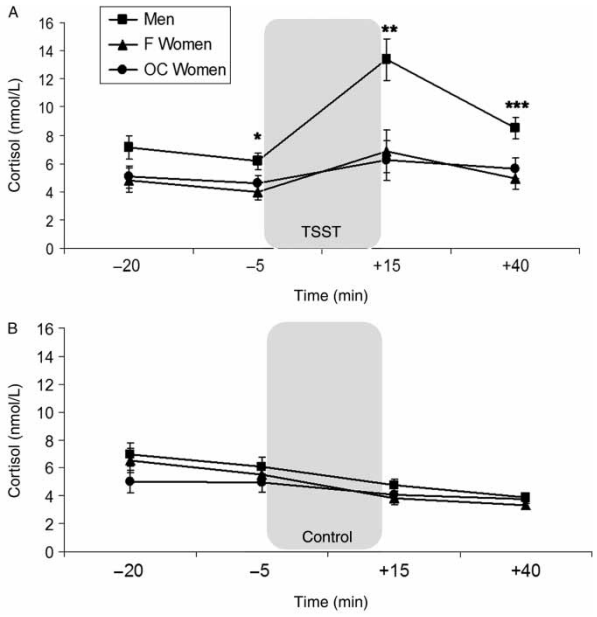

Figure 2. Salivary cortisol concentrations in the TSST (A) and control (B) conditions for men ($N = 16$), follicular stage women, F ($N = 15$), and women oral contraceptive, OC ($N = 17$). In the stress condition (A), the repeated measures ANOVA showed that men had higher cortisol concentrations than F women in the -5 min sample (*$p = 0.028$) and that men had higher cortisol concentrations than F and OC women in the $+15$ min sample (**both $p \leq 0.006$) and in the $+40$ min sample (***both $p \leq 0.024$). In the control condition (B), there were no significant group differences in cortisol concentrations (all $p > 0.3$). Depicted values are means and error bars represent the SEM.

they decreased, recovering baseline concentrations, in the last saliva sample ($p > 0.7$). In the control condition, cortisol concentrations decreased over time according to the normal cortisol circadian rhythm (all $p \leq 0.001$).

The group (M, F, and OC) factor was significant (F (2, 45) = 4.608, $p = 0.015$), as was the interaction between condition, time, and group (F (3.09, 69.49) = 3.699, $p = 0.015$). Baseline cortisol did not differ between groups (all $p > 0.1$). However, 5 min before the TSST, men had higher cortisol concentrations than the F group ($p = 0.028$), but not the OC users ($p = 0.2$). After exposure to the stressor, men had higher cortisol concentrations than both groups of women in the $+15$ min sample (all $p \leq 0.006$) and in the $+40$ min sample (all $p \leq 0.024$) (Figure 2A). Both groups of women had a lower cortisol response to stress than men, but their cortisol concentrations increased in response to stress, as they were higher in the stress condition than in the control condition in samples $+15$ min (for both $p \leq 0.045$) and $+40$ min (for both $p \leq 0.018$). In the two groups of women, the cortisol response to stress was not different ($p > 0.9$). In the control condition, there were no differences between groups for any cortisol sample ($p > 0.3$) (Figure 2B).

Salivary alpha-amylase. The repeated measures ANOVA with sAA concentrations as the dependent variable showed the main effects for condition (F (1, 45) = 27.764, $p < 0.001$), time (F (4, 18) = 25.795, $p < 0.001$), and their interaction: condition × time (F (3.19, 143.42) = 6.833, $p < 0.001$). The group factor and its interactions with the other factors were not significant (all $p > 0.3$).

Baseline sAA concentrations were similar between conditions ($p > 0.5$). In the stress condition, 1 min before the TSST there was an anticipatory increase in sAA concentrations ($p = 0.006$). The sAA concentrations continued increasing, reaching their peak at the end of the speech ($p = 0.002$), and remained increased at the end of the arithmetic task ($p > 0.99$). The participants had recovered to baseline in the last saliva sample ($p > 0.1$). In the control condition, the response profile was similar to that of the stress condition, except that there was no anticipatory response ($p > 0.5$). However, all the sAA concentrations, except baseline, were lower in the control condition than in the stress condition (all $p < 0.001$) (Figure 3).

Memory

Priming. The participants correctly completed a mean of 6 (±0.41, SEM) words from List A and 6.12 (±0.28) words from List B. The priming baseline group completed 2.94 (±0.36) words from List A and 3.86 (±0.60) words from List B. Therefore, there was a significant priming effect for the participants compared with the priming baseline group (List A: t (55.70) = 5.602, $p < 0.001$; List B: t (64) = 3.672, $p < 0.001$).

The repeated measures ANOVA with priming as a dependent variable revealed the main effect of

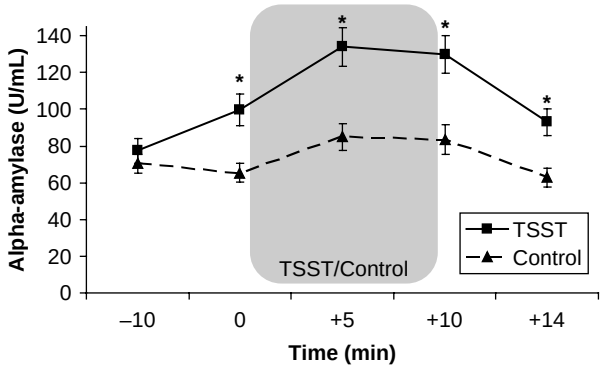

Figure 3. Salivary alpha-amylase (sAA) concentrations in the TSST and control conditions for total sample ($N = 48$). The repeated measures ANOVA showed significant differences in sAA concentrations between conditions. The participants had higher sAA concentrations in the stress condition than in the control condition in the -1, $+5$, $+10$, and $+15$ min saliva samples (*all $p < 0.001$). There was no difference in the baseline sAA levels between conditions ($p > 0.5$). Depicted values are means and error bars represent the SEM.

condition (F (1, 45) = 5.732, $p = 0.021$). The group factor and its interaction with condition were non-significant (for all $p > 0.7$) (Figure 4). The participants recalled more words from the target list in the stress condition than in the control condition. The frequency of the words did not affect their priming (all $p > 0.1$).

Declarative memory. The repeated measures ANOVA with declarative memory as the dependent variable only revealed a main effect of the trial (F (3.747, 161.113) = 196.223, $p < 0.001$), but not the condition, group, or the interactions between these factors (all $p > 0.4$). Across both the stress and control conditions, there was a positive learning curve from trial 1 to trial 4 (all $p < 0.001$). No more words were learned from trial 4 to trial 5 ($p > 0.2$). The participants recalled fewer words in the trial immediately after the interference list (trial 6) than in the trial before it (trial 5) ($p < 0.001$). Finally, they recalled a similar number of words after the 30-min delay (trial 7) and before this delay (trial 6) ($p > 0.9$). The repeated measures ANOVA with recognition as a dependent variable did not show any main effect for condition or group, nor was there an interaction between these factors (all $p > 0.4$) (Figure 5).

Stress reactivity and memory

Priming. Cortisol reactivity to stress induction was not correlated with the number of words correctly completed in the priming test ($p > 0.6$). There were no differences between the cortisol responders and non-responders to the stress induction in priming ($p > 0.2$). However, sAA reactivity was positively correlated with priming test performance ($r = 0.339$, $p = 0.018$). Thus, those who increased their sAA concentrations more in response to the stress induction completed more words from the target list on the priming test (Figure 6).

Declarative memory. Cortisol reactivity did not correlate with declarative memory performance (all $p > 0.3$). Declarative memory performance did not differ between cortisol responders and non-responders to the stress induction (all $p > 0.1$). The stress-induced sAA increase did not correlate with declarative memory performance (all $p > 0.5$).

Discussion

The aim of our study was to analyze the effects of acute psychosocial stress on non-declarative memory, measured by priming, and on declarative memory performance in young men and women. The main results of our study were that acute stress was associated with an enhancement of priming effects, and that this improvement in performance was positively related to the stress-induced sAA increase.

To provoke stress we employed the TSST, which is a standardized psychosocial stressor that has been shown to produce a consistent stress response (Dickerson and Kemeny 2004). The TSST was indeed able to induce stress, since it stimulated an increase in the participant's cortisol concentrations and a higher sAA release compared to the control condition. Sex had a modulating effect on the stress-induced cortisol response, as has been shown in other studies (Kirschbaum et al. 1992, 1999; Preuβ and Wolf 2009; Childs et al. 2010). Women in the follicular phase of their menstrual cycle or using OCs did not differ in their cortisol concentrations in any sample of the stress condition or the control condition. However, men increased their cortisol concentrations more in response to the TSST than both groups of women. Moreover, although with a blunted response, women did respond to the stress induction with an increase in their cortisol concentrations, because they had higher cortisol concentrations in the salivary samples taken after the TSST than in the salivary samples taken after the control task. Conversely, there were no sex differences in the stress-induced sAA

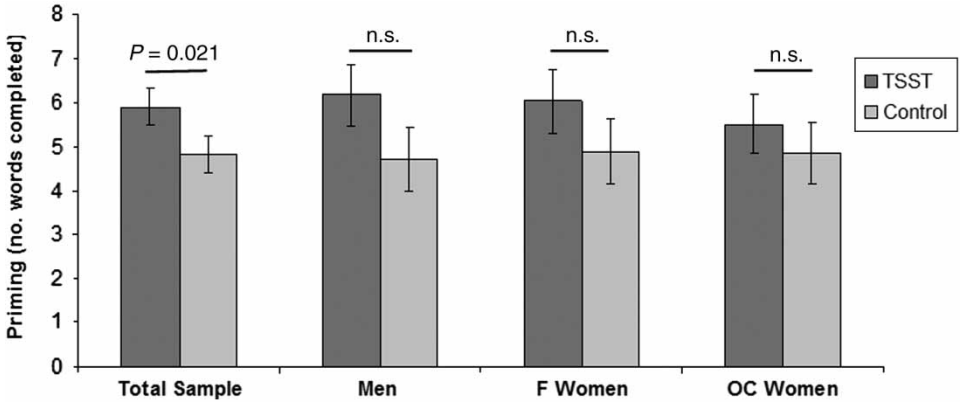

Figure 4. The effect of condition (TSST and control) on priming represented for the total sample ($N = 48$), for men ($N = 16$), follicular stage women, F ($N = 15$), and oral contraceptive women, OC ($N = 17$). The repeated measures ANOVA revealed significant differences in priming between conditions only for the total sample ($p = 0.021$). Depicted values are means and error bars represent the SEM.

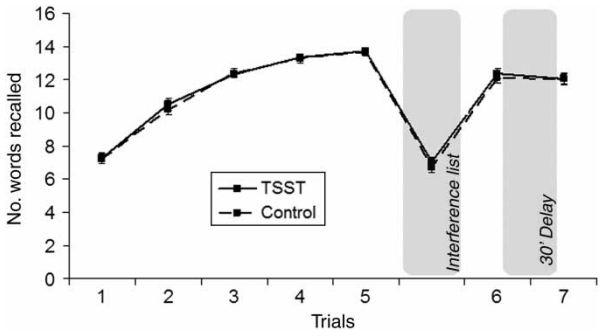

Figure 5. Number of words recalled in the TSST and control condition represented for the total sample ($N = 46$) in each trial of the RAVLT. Depicted values are means and error bars represent the SEM.

release, which is consistent with previous findings (Rohleder and Nater 2009; Almela et al. 2011b).

The stress response was associated with an enhancement of the number of words correctly completed on the priming test. Additionally, this improvement effect was not different between men and women, indicating that neither sex nor OC intake had an influence on this effect. Previously, Eich and Metcalfe (2009) found a similar result when measuring priming also with a word-stem completion task after exposure to a physical stressor (running a marathon). Others have reported enhancing effects of acute stress when measuring implicit memory through other kinds of strategies. For example, Luethi et al. (2009) found that the exposure to the TSST improved classical conditioning only for negative stimuli, and others have found that acute psychosocial stress enhances fear conditioning (Jackson et al. 2006; Zorawski et al. 2006). Furthermore, Schwabe et al. (2007) reported that the exposure to the TSST increased the classical-conditioning learning strategy for neutral material over spatial learning strategies, which require more conscious processing.

Taken together, these findings support the hypothesis that acute stress induces a shift between memory systems. Thus, learning strategies that require less conscious processing, and therefore are faster and less demanding, are favored under acute stress over strategies that require awareness and more complex processes (Schwabe et al. 2007). Additionally, in our study, the enhancing effect of stress on priming was greater among those who responded to stress with a larger sAA increase. Nevertheless, the cortisol response to stress apparently was not related to the outcome of the priming test. To our knowledge, this positive relationship between sAA reactivity to stress and an enhancement of priming has not been reported previously. This finding indicates that SNS activation is crucial for the enhancing effect of stress on implicit memory. Indeed, using a 3D spatial task, Schwabe et al. (2007) found that the participants used more implicit learning strategies to solve the task after being subjected to the TSST, which induces the activation of both the HPA-axis and SNS, but they employed more explicit learning strategies to solve the task after the infusion of glucocorticoids (Schwabe et al. 2009). Similarly, Kirschbaum et al. (1996) found that the administration of glucocorticoids did not have any effect on a short-term priming test. However, an involvement of HPA-axis activity on the modulation of implicit memory by stress cannot be completely

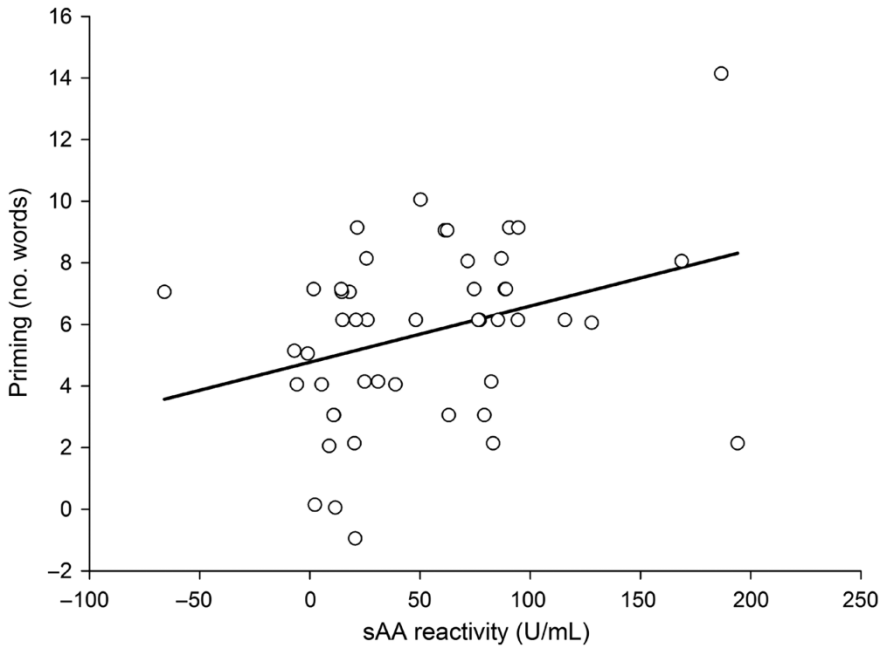

Figure 6. The relationship between sAA reactivity and priming in the stress (TSST), condition for the total sample ($N = 48$; $r = 0.339$, $p = 0.018$).

discarded because animal research has shown that cortiscosterone enhances long-term memory consolidation of implicit memory through its action on the dorsal striatum (Quirarte et al. 2009). In our study, we only measured short-term implicit memory; therefore, we could not know about long-lasting effects of HPA-axis activation on implicit memory. Further research is needed to disentangle these relationships.

In the current study, we did not find any effect of acute stress on declarative memory. Hence, throughout the five trials of the learning curve, the participants learned, recalled (immediate and delayed recall), and recognized a similar number of words in both the stress and control conditions. This result contrasts with the results of other studies that found an impairing effect of acute stress on declarative memory for neutral material when stress was applied prior to learning. We consider that the main reason for this divergent result could be related to the magnitude of the stress-induced cortisol reactivity, since cortisol reactivity to stress has been identified as a main factor involved in short-term declarative memory impairment (Kirschbaum et al. 1996; Wolf et al. 2001). The other studies were performed only in men (Nater et al. 2007), in men and women without controlling for their menstrual cycle or OCs intake (Kirschbaum et al. 1996; Jelicic et al. 2004; Payne et al. 2006, 2007; Smeets et al. 2006), or in men and women in their luteal phase (Wolf et al. 2001). It has been shown that men react to stress with larger cortisol increases than women in their follicular phase or women taking OCs. Moreover, women in their luteal phase have a cortisol reactivity to stress that is comparable to that of men (Kirschbaum et al. 1999). Therefore, it is likely that the null effects found in our study were due to the finding that the magnitude of the cortisol response in the majority of the sample (i.e. more women in their follicular phase or taking contraceptives than men) was low. Even when we divide the sample into responders and non-responders, we failed to find the effects of cortisol response to stress on declarative memory. This could be explained by our design, in which learning and retrieval processes occurred under the same stressful conditions, possibly leading to a compensatory process. Roozendaal's model, which indicates that cortisol enhances consolidation memory and impairs retrieval memory (Roozeendaal 2002), suggests that such a compensatory process would be explained by enhancing the effects of stress on consolidation being canceled by impairing the effects on retrieval.

Some limitations have to be considered in order to interpret our results. We aimed to test one group of women in their early follicular phase and this meant that this group of women had a different test–retest interval compared to the other two groups. Additionally, related to the null effects found for stress on declarative memory, it would be advisable in future studies to also include a group of women in the luteal phase, in order to ensure the comparability of the cortisol response between men and women. Finally, similar to other studies (Kirschbaum et al. 1996; Lupien et al. 1997), the order of the priming test and the declarative test were not counterbalanced, which made it impossible to know whether the effect found is specific to the priming task or whether it is specific to the point in time when the priming task took place.

In conclusion, we have confirmed that acute stress may not only affect declarative memory but also implicit memory, and that this enhancing effect is related mainly to the activity of the SNS.

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