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Stress and emotional memory retrieval: Effects of sex and cortisol response

Tony W. Buchanan *, Daniel Tranel

Department of Neurology, University of Iowa, USA

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Abstract

In some situations, memory is enhanced by stressful experience, while in others, it is impaired. The specific components of the stress–response that may result in these differing effects remain unclear, and the current study sought to address this knowledge gap. Forty healthy participants (20 women, 20 men) were exposed to emotionally arousing and neutral pictures. Twenty-four hours later, 20 participants underwent a social stressor (speech and math tests), and 20 underwent a control reading task, both followed by a delayed free recall task. Cortisol responders to the stress condition (5 men and 1 woman) showed reduced memory retrieval for both neutral and emotionally arousing pictures. Men and women in the stress condition who did not produce a cortisol response showed increased retrieval of unpleasant pictures compared to controls. The results provide further evidence that cortisol is a primary effector in the stress-induced memory retrieval deficit. At the same time, stress can enhance memory retrieval performance, especially for emotional stimuli, when the cortisol response is absent.

Keywords: Stress; Emotion; Memory retrieval; Cortisol

1. Introduction

Memory performance is affected by stress. The direction of this effect, however, depends on many factors: the nature of the stressor, the emotional arousal of the to-be-remembered material, sex of the stressed individuals, and interactions among these factors. Such factors have led to mixed findings with regard to the effects of stress on memory. Stress after learning can improve memory *consolidation* (see Roozendaal, 2000 for review). By contrast, stress before memory testing can impair memory *retrieval* performance (Buchanan, Tranel, & Adolphs, 2006; de Quervain, Roozendaal, & McGaugh, 1998; Kuhlmann, Piel, & Wolf, 2005). Roozendaal and colleagues have documented that these differences in the effects of stress on the different phases of memory are dependent on the amygdala. Specifically, the stress enhancement of consolidation as well as the impairing effects of stress on retrieval is dependent on the integrity of the basolateral amygdala (see Roozendaal, 2000 for review). This discrepancy in how stress affects memory—enhancing consolidation while impairing retrieval—may help explain some of the discrepant findings on stress and memory.

While a stress response is typically defined by an increase in corticosteroid release, there are considerable individual differences in this response, which have been well-documented in human studies (Pruessner et al., 1997). Some individuals show persistent, large cortisol increases in response to stress while others show little or no such response (Kirschbaum et al., 1995). In addition to individual differences in the cortisol stress response, situational factors inherent in stress tasks influence whether or not a cortisol response will be elicited. These situational factors are a perceived lack of control and experience of distress (Dickerson & Kemeny, 2004; Lundberg & Frankenhaeuser, 1980). Situations associated with challenge,

* Corresponding author. Present address: Department of Psychology, Saint Louis University, Shannon Hall, Saint Louis, MO 63103, USA.
E-mail address: Tbuchan7@slu.edu (T.W. Buchanan).

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such as moderate physical exercise, may result in autonomic nervous system (ANS) activity, but not a corticosteroid response (Lovallo et al., 1985). In situations associated with challenge, but without a cortisol response, mild stress may have a different effect on memory performance than a more severe stressful situation.

Studies have documented differential effects of moderate stress on memory. We recently showed that subjects who produced a cortisol response to a cold pressor task showed impaired memory retrieval performance for words learned one hour before the stressor (Buchanan et al., 2006). Subjects who produced a skin conductance response to the cold pressor (indicative of ANS activity), but not a cortisol response did not show reduced retrieval performance. These results suggest that cortisol, and not activation of the sympathetic nervous system, is the primary actor in the stress-induced retrieval deficit. There are important nuances to this effect, though. Some studies have shown that a mild stressor or a small dose of corticosterone can actually improve memory performance. Domes and colleagues (2005) showed that subjects who had lower salivary cortisol levels after a 25 mg dose of cortisol showed improved memory retrieval performance compared to both a placebo group and a high responder group, demonstrating the so-called inverted-U pattern of cortisol on performance (ala, Yerkes & Dodson, 1908).

Sex differences are often reported both in responses to stress (Kudielka & Kirschbaum, 2005) and in studies of learning and memory (Cahill, 2005; Wolf, 2006, among many other domains that are beyond the scope of our review). Men tend to show a greater cortisol stress response than women in laboratory studies (Kirschbaum, Kudielka, Gaab, Schommer, & Hellhammer, 1999). Studies examining sex differences have shown that men are more affected by stress than women on both declarative memory retrieval (Wolf, Schommer, Hellhammer, McEwen, & Kirschbaum, 2001) as well as in fear conditioning (Jackson, Payne, Nadel, & Jacobs, 2006; Zorawski, Blanding, Kuhn, & LaBar, 2006; Zorawski, Cook, Kuhn, & LaBar, 2005). The reason for this sex difference is unclear, although there has been speculation on the potential beneficial effects of female sex hormones (Wolf, 2006) and sex differences in cortisol response to stress (Kudielka & Kirschbaum, 2005).

The current study was designed to examine the effects of stress on memory retrieval in men and women. If corticosteroids are the main actor in producing a stress-induced retrieval deficit, then individuals who do not produce a cortisol response may show no effect (or even a beneficial effect, if the stress is not severe) of stress on memory retrieval. Additionally, if sex differences in cortisol response to stress are responsible for the sex differences in stress-induced memory effects, then it would be predicted that in the absence of a cortisol response, men and women may show similar memory performance. Finally, we investigated how this stress–effect interacted with the emotional arousal of the memory material, by using emotional and neutral pictures as to-be-remembered stimuli.

2. Methods

2.1. Participants

Forty healthy volunteers (20 women, 20 men) between the ages of 18 and 25 (mean age: 20 ± 2.0) participated in the study for class credit. Participants were excluded from the study if they were taking any psychiatric, neurological, or corticosteroid-based medications or if they reported working overnight shift work. One of the females in the control group and 4 females in the stress group (including the one female who showed a cortisol response) were taking oral contraceptives. The study was approved by the Institutional Review Board of the University of Iowa, and written informed consent was obtained from all participants.

2.2. Procedure

All participants were tested individually on 2 consecutive days. On both days, each participant reported to the laboratory between 1200 and 1600 h to control for the diurnal cycle of cortisol. Next, participants were connected to recording electrodes for measurement of heart rate. On the first day, participants were shown 20 color photographs, consisting of 10 unpleasant (e.g., mutilated bodies) and 10 neutral (e.g., a classroom setting) pictures chosen from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 2005). Each photograph was presented for 8 s on a computer monitor and was accompanied by a simple, single-sentence narrative description. An example of the narrative description for a photograph of a classroom setting read as follows: "The philosophy students listened to the guest speaker with much interest." Participants were told to watch the stimuli and listen to the narrative for the expressed purpose of monitoring their psychophysiological response to the visual and auditory stimuli. No mention of a memory test was made, and thus, encoding of the stimuli was incidental. Photographs were presented in a different, random order for each participant.

Immediately after stimulus presentation, participants completed a free recall test, during which they wrote down as much information as they could recall about the photographs and the narratives. Participants were allowed 10 min for the completion of the free recall task. After completion of the free recall task, participants were excused and asked to return at the same time the next day for completion of the "stress portion" of the experiment. Participants were not informed of their inclusion in the stress or control group until the following day.

Twenty-four hours later, participants returned to the laboratory. During a 10 min adaptation period, they filled out the Positive Affectivity/Negative Affectivity Schedule (PANAS; Watson, Clark, & Tellegen, 1988) for assessment of baseline affective state. Next, a baseline saliva sample was collected and participants were connected to recording electrodes for measurement of heart rate. At this point, half the participants were randomly assigned to the stress condition and the other half were assigned to perform the control reading task.

Participants in the stress condition were given instructions for a speech and math test, which is a modified version of the Trier Social Stress Test (TSST; Kirschbaum, Pirke, & Hellhammer, 1993). In this modified version, participants remained seated in the room in which they had prepared for their speech during the speech and math test, only 2 experimenters were in the room (as opposed to the 3 experimenters typically employed in the TSST), and were allowed to keep their notes prepared during the preparation period. The traditional TSST and other versions of this type of stress task (al'Absi et al., 1997; Buchanan, al'Absi, & Lovallo, 1999) typically require the participant to stand before a committee of experimenters, and the participants are not allowed to use their prepared notes. Additionally, no provocation of the participants was included in the current version of the speech and math test. Participants were given 10 min alone, to prepare for their speech, during which time heart rate data were

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collected. During the speech and math test, participants remained seated while two experimenters joined them in the testing room. At the end of the 5 min speech, the participant was instructed to complete the mental arithmetic task (serial subtraction of 13 from 1022).

Participants in the reading condition were given a general interest article on travel. During the preparation period, participants read the article for 10 min. At the end of this time, they were asked to write a summary of the article for 10 min to approximate the timing of the speech and math test. The participants were allowed to keep the article while writing the summary.

After the speech and math or reading tasks, participants again completed the PANAS, during a 10 min break. At the end of the break (30 min after the beginning of speech preparation/reading), a second saliva sample was taken and participants completed a free recall task for the pictures/narratives they had been presented with the previous day. Participants then completed a recognition memory test. In this test, participants viewed 40 photographs (20 they had seen previously, and 20 new ones) and were asked to respond 'yes' or 'no' as to whether they remembered seeing the photo before. After responding to the recognition question, the participant rated each photo on 5-point scales of pleasantness (1 = unpleasant; 5 = very pleasant) and arousal (1 = low arousal; 5 = high arousal). After the recognition task, participants contributed a third and final saliva sample.

2.3. Saliva assessment for cortisol measurement

Saliva was collected using Salivette collection tubes (Sarstedt, Rommelsdorf, Germany). As noted, three samples were collected: before, 30 min after, and 45 min after the speech and math or reading tasks. Samples were stored at −20 °C until assayed. Salivary cortisol was measured with a commercial immunoassay kit with chemiluminescence detection (CLIA; IBL Hamburg, Germany). Intraassay and interassay coefficients of variation were less than 10%.

2.4. Psychophysiological measures

Heart rate was measured using 2 electrocardiograph electrodes, one placed on the right side of the neck and the other on the left side of the torso 2 cm below the rib cage. Signals were recorded using a Biopac MP150 system (Biopac Systems, Santa Barbara, CA).

2.5. Data management and analysis

Free recall was scored by a trained technician who was blind to each participant's group membership. A recalled detail was counted as correct if it could be unambiguously linked to a particular picture or narrative. For example, a picture of children playing in a street was accompanied by the narrative, "These Cuban children were playing on a street in Havana." The response "Kids play on street in Havana" was given a score of 3:1 for kids (who), 1 for play (what), and 1 for street in Havana (where). Ambiguities in recalled details were resolved through discussion between the rater and the first author. The number of correct details included in each participant's description of each picture/narrative was counted, and the number of details recalled for the unpleasant and neutral picture/narratives served as the dependent measures. Retrieval performance was expressed as the percentage of details recalled at delayed free recall (on day 2, after speech and math or reading task) in relation to the number recalled at immediate free recall (on day 1).

Because we were interested in the effect of stress-induced cortisol on memory retrieval, participants in the stress group were split into responders (those who had higher cortisol values after the speech and math test compared to before the test; $N = 6$, 5 men and 1 woman) and nonresponders (those who had lower cortisol after the speech and math test compared to before the test; $N = 14$, 5 men and 9 women). The responders and nonresponders were compared to the control group ($N = 20$) using univariate ANOVAs.

In order to examine the interactive effects of stress and sex on memory retrieval, data were analyzed using a 2 Sex × 2 Group (nonresponders vs. control) × 2 Emotion (unpleasant vs. neutral pictures) multivariate analysis of variance (MANOVA) for the memory data and a 2 Sex × 2 Group (nonresponders vs. control) × 2 Time (pre- vs. during or after stress) MANOVA for affective and physiological responses (heart rate and cortisol) to the tasks. Data from the cortisol responders were excluded from analyses with sex as a factor because only one woman was represented in the responder group. Analyses include the η^2 measure of effect size where appropriate.

3. Results

3.1. Task responses

Cortisol data were analyzed using a 3 Group × 3 Time multivariate ANOVA. As expected, the responders showed higher cortisol levels after the task compared to the nonresponders and control participants (group by time interaction: $F(4,70) = 11.7$, $p < 0.0001$, $\eta^2 = 0.4$, see Fig. 1). Post hoc analysis shows that the groups were not significantly different at baseline ($ps > 0.7$); however, the responders had higher cortisol at both post-task time points compared to control and nonresponder groups ($ps < 0.01$). Both the responder and nonresponder groups showed greater negative affect response, $F(1,30) = 20$, $p < 0.0001$, $\eta^2 = 0.4$, and greater heart rate response, $F(1,30) = 4.4$, $p < 0.05$, $\eta^2 = 0.13$, than the control group. There were no significant differences in positive affect ($p > 0.3$) response to the tasks. The cortisol responders showed a trend toward greater

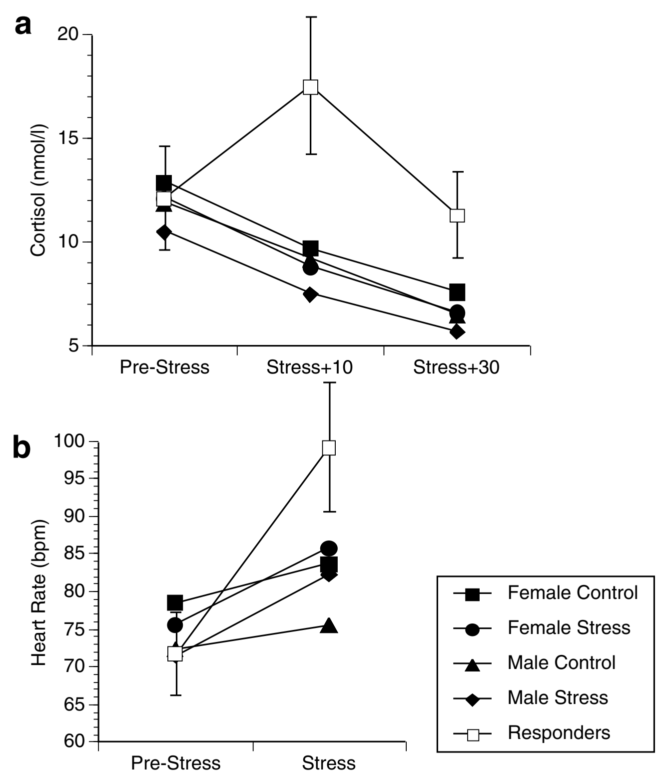

Fig. 1. (a) Cortisol levels throughout the experiment across groups. (b) Heart rate during the pre-stress period and during the stress or control period. Note that error bars indicate standard error of the mean. Error bars are shown only for the cortisol responder group for clarity of presentation.

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Table 1
Means and standard errors of the mean for affective responses and memory performance before and after task performance across sex and groups

Variable	Cortisol nonresponder group		Control group	
	Pre-stress	Post-stress	Pre-stress	Post-stress
Men				
Positive affect	33.0 ± 3.6	35.6 ± 1.4	31.0 ± 2.1	27.9 ± 1.6
Negative affect	18.6 ± 2.4	25.6 ± 3.4	13.9 ± 1.1	14.3 ± 1.5
Neutral free recall	14.4 ± 4.5	10.6 ± 2.5	14.9 ± 2.1	15.0 ± 2.1
Unpleasant free recall	24.2 ± 5.4	23.6 ± 5.5	28.3 ± 2.3	24.6 ± 2.3
Women				
Positive affect	32.4 ± 2.3	28.9 ± 2.5	35.5 ± 1.9	33.2 ± 2.7
Negative affect	14.3 ± 1.2	27.2 ± 3.4	13.6 ± 1.2	13.5 ± 1.6
Neutral free recall	20.2 ± 0.9	20.4 ± 1.1	17.8 ± 2.3	13.7 ± 1.8
Unpleasant free recall	33.7 ± 0.7	33.3 ± 0.9	29.5 ± 2.6	27.6 ± 3.3
	Cortisol responder group			
	Pre-stress	Post-stress		
Positive affect	27.8 ± 1.5	26.8 ± 4.2	—	—
Negative affect	13.3 ± 1.0	22.0 ± 2.8	—	—
Neutral free recall	12.0 ± 0.8	8.8 ± 1.4	—	—
Unpleasant free recall	28.5 ± 2.5	21.3 ± 2.0	—	—

Positive and negative affect indicates scores on the PANAS during the pre- and post-task periods. Neutral and unpleasant free recall are shown for immediate (pre-stress) and delayed (post-stress) time points.

heart rate response to the task compared to the nonresponders, $t(18) = 1.9$, $p = 0.08$, but no differences in positive or negative affect ratings (ps > 0.2; see Table 1).

3.2. Memory performance

For free recall, cortisol responders recalled fewer total pictures than the other groups, $F(2,37) = 3.98$, $p < 0.05$, $\eta^2 = 0.18$, showing lower retrieval than both the nonresponders ($p < 0.02$) and the control group ($p < 0.05$; see Fig. 2). Comparing the nonresponders and the control group, there was a significant interaction among sex, group, and emotion, $F(1,30) = 4.5$, $p < 0.05$, $\eta^2 = 0.13$. Further analysis of this interaction reveals that male nonresponders showed a trend toward recall of more unpleasant pictures than control men, ($t(13) = 1.8$, $p = 0.09$); in women the effect was not significant, $t(17) = 0.8$, $p > 0.4$ (see Fig. 2). To better address the pattern of results within each sex, a Group × Emotion analysis was conducted separately for men and women. Only men showed a differential recall of neutral versus unpleasant pictures based on their group membership (Group × Emotion interaction: $F(1,13) = 11.6$, $p < 0.01$, $\eta^2 = 0.47$). Women did not show this effect ($F(1,17) < 1$, $p > 0.9$, see Table 1).

Unpleasant pictures were recognized at a higher rate than neutral pictures across all groups, $F(1,30) = 13$, $p < 0.01$, $\eta^2 = 0.3$ (main effect of emotion). Additionally, women had higher recognition performance than men, $F(1,30) = 4.7$, $p < 0.05$, $\eta^2 = 0.14$. Finally, there was a trend toward an interaction between sex and group, $F(1,30) = 3.4$, $p = 0.08$, $\eta^2 = 0.1$, with women in the nonresponder group showing slightly better recognition than women in the control group. Men in the nonresponder group showed slightly worse recognition than men in the control group. There were no other significant interaction effects. Cortisol responders did not show a different pattern of recognition performance compared to the nonresponder or control group, ps > 0.3 (Table 2).

Correlation analyses were conducted between cortisol response to the task and memory retrieval to examine the potential effects that stress-induced changes in cortisol may exert on memory performance. Across the whole participant sample, there was a significant negative correlation between cortisol response and percentage recall ($r = -0.37$, $p < 0.05$). Analyses were next conducted within groups (control subjects and stress subjects).[1] The stress group showed a significant negative correlation between cortisol response and recall percentage ($r = -0.45$, $p < 0.05$), the control group showed the same direction of association, but this correlation was not significant ($r = -0.2$, $p > 0.3$). These correlations corroborate previous findings on the association of post-stress cortisol and retrieval performance.

3.3. Stimulus ratings

Ratings of the picture stimuli confirmed the *a priori* classifications, such that unpleasant pictures were rated lower on valence, $F(1,30) = 35$, $p < 0.0001$, $\eta^2 = 0.5$, and higher on arousal, $F(1,30) = 22$, $p < 0.0001$, $\eta^2 = 0.4$, than the neutral pictures. There were no significant effects of sex, group, or cortisol responder status, ps > 0.1.

[1] Cortisol responders and nonresponders were included together in the stress group for this analysis due to the small number of responders and to take advantage of the individual differences in response in order to examine the relationship between the range of responses and memory more fully.

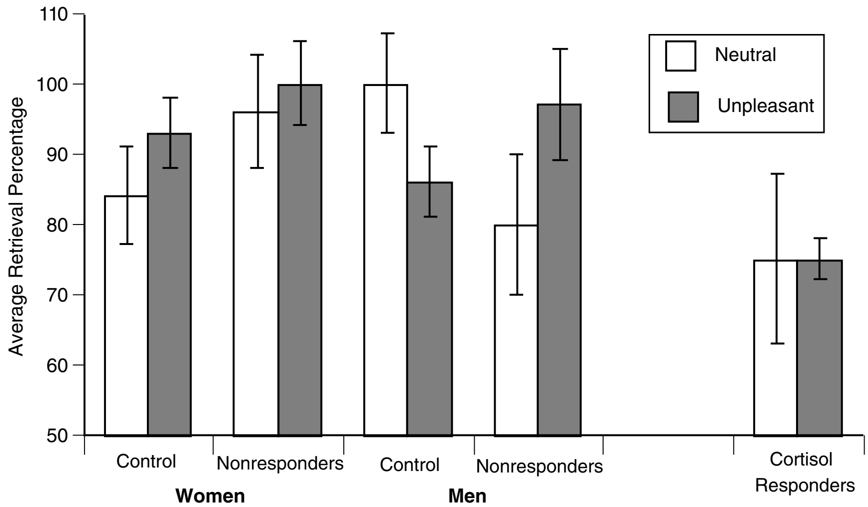

Fig. 2. Effects of stress on memory retrieval for neutral and unpleasant picture/narrative stimuli across sex and cortisol responder status. Results are expressed as percentage of immediate recall from day 1. Ns: women control: $N = 10$; women nonresponders: $N = 9$; men control: $N = 10$; men nonresponders: $N = 5$; cortisol responders: $N = 6$ (5 men, 1 woman).

Table 2
Means and standard errors of the mean for recognition performance (correct recognition–false alarms) across sex and groups

Variable	Cortisol nonresponder group		Control group	
	Mean	*SEM*	Mean	*SEM*
Men				
Neutral recognition	18.0	0.6	18.4	0.4
Unpleasant recognition	18.8	0.3	19.4	0.2
Women				
Neutral recognition	19.3	0.5	18.4	0.4
Unpleasant recognition	19.6	0.2	19.6	0.2
	Cortisol responder group			
	Mean	*SEM*		
Neutral recognition	19.2	0.5	—	—
Unpleasant recognition	20.0	0.3	—	—

3.4. Expectancy ratings

All participants were asked whether or not they expected a memory test. Responses were recorded on a scale of 1–10, with 1 indicating that the participant had no idea that there would be a memory test on the second day, and 10 indicating that the participant was sure there would be a memory test on the second day. Mean expectation ratings did not differ among the control ($M = 4.0$), nonresponders ($M = 4.1$), or cortisol responders ($M = 3.2$), $F(2, 37) < 1$.

4. Discussion

The results of this study corroborate previous work on the negative effects of stress-induced cortisol on memory retrieval. Consistent with our predictions, participants who produced a cortisol response to the stressor showed reduced memory retrieval performance. By contrast, stressed participants who did not produce a cortisol response showed an increase in memory retrieval after the stressor. Finally, results show that mild stress (without a cortisol response) may exert a beneficial effect on memory retrieval performance. In men, this effect was specific to memory for emotional stimuli, while women received a general boost for retrieval of both neutral and unpleasant pictures. The current results further advance the idea that cortisol is the primary actor in the stress-induced memory retrieval deficit.

Of the cortisol responders in the current study, only one was female. Men tend to show a greater cortisol response to laboratory stressors than do women (Kudielka & Kirschbaum, 2005). Men also tend to show more of a stress-induced memory effect, whether it be enhancement of fear conditioning (Jackson et al., 2006) or impairment of retrieval (Wolf et al., 2001). In addition to sex differences in behavior, several studies have shown a sex difference in the amygdala response to emotional stimuli and associations with subsequent memory for emotional stimuli (see Cahill, 2005). This sex-related difference in cortisol response is one potential reason for previously reported differences in memory performance. When cortisol is elevated through exogenous administration (resulting in an equally high level of cortisol in both sexes), women show the same retrieval deficit as men (Kuhlmann, Kirschbaum, & Wolf, 2005). Men and women in the nonresponder group showed comparable affect ratings, heart rate, and cortisol levels during and after the speech and math test. Additionally, both men and women nonresponders showed increased memory retrieval of unpleasant pictures. There was, however, a sex difference in the retrieval of emotionally neutral pictures. Male nonresponders showed poorer retrieval for neutral stimuli than men in the control group. These findings suggest that even when controlling for the physiological responses to a stressful situation, the effects

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of stress on memory differ between the sexes. The interaction between the emotion of the unpleasant stimuli and the emotion experienced during the stressor may have been necessary to enhance retrieval performance in men. The lack of arousal associated with the neutral pictures, then, may explain the men's poorer retrieval of these pictures. By contrast, women may receive a retrieval benefit by virtue of the enhanced arousal associated with the stressor, regardless of the emotional nature of the to-be-remembered stimuli.

Results from this study are similar to previous work demonstrating that the effects of stress on memory are dependent on a combination of the activity of the autonomic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis. One study recently demonstrated that participants showed impaired working memory while performing a stress task during which both cortisol and sympathetic activity (heart rate and blood pressure) were elevated (Elzinga & Roelofs, 2005). Increased sympathetic activity alone did not lead to impaired working memory; a combination of the two was required. We recently showed that only participants who showed both a skin conductance response and a cortisol response to a cold pressor task demonstrated reduced memory retrieval performance (Buchanan et al., 2006). Similarly in the current study, only participants who showed both a response in heart rate and cortisol demonstrated reduced memory retrieval performance. This replication demonstrates similar findings across different to-be-remembered stimuli (words versus pictures), different stressors (cold pressor versus social stressor), different encoding instructions (explicit versus implicit encoding), and different delay intervals between learning and retrieval testing (1 h versus 24 h). Two differences in the results of this study and the previous study are worth noting: (1) The increased retrieval performance in those who did not show a cortisol response in the current study is different from the pattern observed in our previous work. Perhaps the longer retention interval allowed for this enhanced retrieval performance to emerge. (2) In the previous study, retrieval of arousing stimuli was more affected by cortisol than was retrieval of neutral stimuli, but in the current study cortisol responders showed equivalent retrieval of both neutral and arousing stimuli. There is the possibility of differences inherent in the to-be-remembered stimuli (arousing words versus arousing pictures). Memory performance in the first study was determined solely by whether the subject was able to recall individual words seen prior to the stressor. By contrast, in the current study, the subject was asked to produce all the details they could recall about both a picture and a narrative. The richer stimuli in the current study may have proven more resistant to forgetting than arousing words. It is possible that although the cortisol responders recalled equivalent details about neutral and unpleasant stimuli, memories for the unpleasant stimuli were more affected by cortisol response. Comparison of the retrieval of neutral stimuli in the responders versus the other groups shows that responders retrieved 75% of their previously recalled details, compared with an average of 90% recall by the other groups, a difference of 15%. By contrast, the other groups recalled an average of 94% of the details of the unpleasant stimuli, while the cortisol responders recalled only 75%, a difference of 19%. Viewed in this light, the unpleasant stimuli may have been retrieved at a lower level compared to the neutral stimuli in the cortisol responders.

A recent study has demonstrated that under less formal testing conditions (perhaps similar to the conditions of our mild stressor) a single dose of cortisol (30 mg) did not reduce memory retrieval performance (Kuhlmann & Wolf, 2006). By contrast, these authors have shown that under formal testing conditions (which should elicit more arousal), a similar dose of cortisol exerts a significant impairing effect on memory retrieval (Kuhlmann et al., 2005). These authors speculated that the cortisol-induced impairment of memory retrieval requires the concomitant activation of arousal, such as during their formal testing, but not during the relaxed condition. These studies did not report measures of autonomic activity during testing, but we speculate that the autonomic response during the formal testing situation may be greater than in the less formal condition, thereby combining with the increased cortisol to impair memory retrieval performance.

Several studies have demonstrated a beneficial effect of stress on memory consolidation (Andreano & Cahill, 2006; Cahill, Gorski, & Le, 2003; Roozendaal, 2000), prospective memory (Nater et al., 2006), and source memory (Smeets et al., 2006). By contrast, memory retrieval tends to be impaired following a stressor (Buchanan et al., 2006; de Quervain et al., 1998; Kuhlmann et al., 2005). These effects are specific to stressors that result in increased corticosteroid release. The differential occupation of corticosteroid receptors in the brain is one possibility for these differences in cognitive performance (de Kloet, Oitzl, & Joels, 1999). High corticosteroid levels leads to the occupation of glucocorticoid (GR) and mineralocorticoid (MR) receptors in the brain whereas lower levels occupy GRs at a much lower level (Reul & de Kloet, 1985). These receptors are located throughout the forebrain, including areas necessary for memory such as the hippocampus and prefrontal cortex (Reul & de Kloet, 1985). Moderate occupation of MR and GR may result in an optimal level of mnemonic processing, perhaps facilitating memory performance. By contrast, higher levels of stress leading to greater occupation of GR may lead to maladaptive memory processing (de Kloet et al., 1999; Oitzl, van Haarst, & de Kloet, 1997). In the context of the current study and other studies of acute stress and human memory, increases in cortisol may negatively affect retrieval performance through greater occupation of GRs. By contrast, moderate cortisol response or mild stress without a cortisol response, may lead to an optimal level of memory performance at the peak of the inverted-U function (Yerkes & Dodson, 1908).

The current study had several limitations, including a relatively small sample size to address sex differences and a small number of cortisol responders. A greater number of men and women would help fully assess the role of sex on stress and memory. Issues such as menstrual cycle phase, oral contraceptive use, and levels of sex steroids may have affected the results of this study. As noted, one female in the control group and four in the stress group (including the one female responder) were taking oral contraceptives. As previous work has noted the effects of these variables on stress responding (Kirschbaum et al., 1999), these issues would also be important to address in future work on this topic. The small number of cortisol responders in this study was most likely due to the aforementioned modifications to the traditional format of the Trier Social Stress Test (see Kirschbaum et al., 1993). Thus, in a sense, the modification actually made available a unique scientific opportunity, albeit at the likely expense of reducing the number of cortisol responders. Our participants may not have experienced as much stress as those in the original task. While on one hand this is a limitation of the study, the variability in cortisol response to the current task has enabled the study of the effects of the cortisol stress–response while holding other variables constant.

Results from cortisol nonresponders support anecdotal reports of enhanced cognitive performance after stress. These findings lead to the intriguing possibility of the application of mild stressors (e.g., those that do not produce a cortisol response) to educational settings or to enhancing memory performance in cognitively impaired persons. Future research addressing the mechanisms of this mild stress-induced retrieval enhancement may help shift the negative effects of stress toward more positive outcomes.

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References

al'Absi, M., Bongard, S., Buchanan, T. W., Pincomb, G. A., Licinio, J., & Lovallo, W. R. (1997). Cardiovascular and neuroendocrine adjustment to public speaking and mental arithmetic stressors. *Psychophysiology, 34*(3), 266–275.

Andreano, J. M., & Cahill, L. (2006). Glucocorticoid release and memory consolidation in men and women. *Psychological Science, 17*(6), 466–470.

Buchanan, T. W., al'Absi, M., & Lovallo, W. R. (1999). Cortisol fluctuates with increases and decreases in negative affect. *Psychoneuroendocrinology, 24*(2), 227–241.

Buchanan, T. W., Tranel, D., & Adolphs, R. (2006). Impaired memory retrieval correlates with individual differences in cortisol response but not autonomic response. *Learning & Memory, 13*, 382–387.

Cahill, L. (2005). His Brain, Her Brain. *Scientific American*, 40–47.

Cahill, L., Gorski, L., & Le, K. (2003). Enhanced human memory consolidation with post-learning stress: Interaction with the degree of arousal at encoding. *Learning & Memory, 10*, 270–274.

de Kloet, E. R., Oitzl, M. S., & Joels, M. (1999). Stress and cognition: Are corticosteroids good or bad guys? *Trends in Neuroscience, 22*(10), 422–426.

de Quervain, D. J., Roozendaal, B., & McGaugh, J. L. (1998). Stress and glucocorticoids impair retrieval of long-term spatial memory. *Nature, 394*(6695), 787–790.

Dickerson, S. S., & Kemeny, M. E. (2004). Acute stressors and cortisol responses: A theoretical integration and synthesis of laboratory research. *Psychological Bulletin, 130*, 355–391.

Domes, G., Rothfischer, J., Reichwald, U., & Hautzinger, M. (2005). Inverted-U function between salivary cortisol and retrieval of verbal memory after hydrocortisone treatment. *Behavioral Neuroscience, 119*(2), 512–517.

Elzinga, B. M., & Roelofs, K. (2005). Cortisol-induced impairments of working memory require acute sympathetic activation. *Behavioral Neuroscience, 119*, 98–103.

Jackson, E. D., Payne, J. D., Nadel, L., & Jacobs, W. J. (2006). Stress differentially modulates fear conditioning in healthy men and women. *Biological Psychiatry, 59*(6), 516–522.

Kirschbaum, C., Kudielka, B. M., Gaab, J., Schommer, N. C., & Hellhammer, D. H. (1999). Impact of gender, menstrual cycle phase, and oral contraceptives on the activity of the hypothalamus-pituitary-adrenal axis. *Psychosomatic Medicine, 61*(2), 154–162.

Kirschbaum, C., Pirke, K.-M., & Hellhammer, D. H. (1993). The 'Trier Social Stress Test'—A tool for investigating psychobiological stress responses in a laboratory setting. *Neuropsychobiology, 28*, 76–81.

Kirschbaum, C., Prussner, J. C., Stone, A. A., Federenko, I., Gaab, J., Lintz, D., Schommer, N., & Hellhammer, D. H. (1995). Persistent high cortisol responses to repeated psychological stress in a subpopulation of healthy men. *Psychosomatic Medicine, 57*(5), 468–474.

Kudielka, B. M., & Kirschbaum, C. (2005). Sex differences in HPA axis responses to stress: A review. *Biological Psychology, 69*, 113–132.

Kuhlmann, S., Kirschbaum, C., & Wolf, O. T. (2005). Effects of oral cortisol treatment in healthy young women on memory retrieval of negative and neutral words. *Neurobiology of Learning and Memory, 83*, 158–162.

Kuhlmann, S., Piel, M., & Wolf, O. T. (2005). Impaired memory retrieval after psychosocial stress in healthy young men. *Journal of Neuroscience, 25*, 2977–2982.

Kuhlmann, S., & Wolf, O. T. (2006). A non-arousing test situation abolishes the impairing effects of cortisol on delayed memory retrieval in healthy women. *Neuroscience Letters*.

Lang, P., Bradley, M., & Cuthbert, B. (2005). *International affective picture system (IAPS): Digitized photographs, instruction manual and affective ratings*. Gainesville, FL: University of Florida.

Lovallo, W. R., Wilson, M. F., Pincomb, G. A., Edwards, G. L., Tompkins, P., & Brackett, D. (1985). Activation patterns to aversive stimulation in man: Passive exposure versus effort to control. *Psychophysiology, 22*, 283–291.

Lundberg, U., & Frankenhaeuser, M. (1980). Pituitary-adrenal and sympathetic-adrenal correlates of distress and effort. *Journal of Psychosomatic Research, 24*(3–4), 125–130.

Nater, U. M., Okere, U., Stallkamp, R., Moor, C., Ehlert, U., & Kliegel, M. (2006). Psychosocial stress enhances time-based prospective memory in healthy young men. *Neurobiology of Learning and Memory, 86*(3), 344–348.

Oitzl, M. S., van Haarst, A. D., & de Kloet, E. R. (1997). Behavioral and neuroendocrine responses controlled by the concerted action of central mineralocorticoid and glucocorticoid receptors. *Psychoneuroendocrinology, 22*, S87–S93.

Pruessner, J. C., Gaab, J., Hellhammer, D. H., Lintz, D., Schommer, N., & Kirschbaum, C. (1997). Increasing correlations between personality traits and cortisol stress responses obtained by data aggregation. *Psychoneuroendocrinology, 22*(8), 615–625.

Reul, J. M., & de Kloet, E. R. (1985). Two receptor systems for corticosterone in rat brain: Microdistribution and differential occupation. *Endocrinology, 117*(6), 2505–2511.

Roozendaal, B. (2000). Glucocorticoids and the regulation of memory consolidation. *Psychoneuroendocrinology, 25*(3), 213–238.

Smeets, T., Jelicic, M., Merckelbach, H., Peters, M., Fett, A., Taverniers, J., Henquet, C., & Dautzenberg, J. (2006). Enhanced memory performance on an internal-internal source monitoring test following acute psychosocial stress. *Behavioral Neuroscience, 120*(6), 1204–1210.

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology, 54*, 1063–1070.

Wolf, O. T. (2006). Effects of stress hormones on the structure and function of the human brain. *Expert Review of Endocrinology and Metabolism, 1*, 623–632.

Wolf, O. T., Schommer, N. C., Hellhammer, D. H., McEwen, B. S., & Kirschbaum, C. (2001). The relationship between stress induced cortisol levels and memory differs between men and women. *Psychoneuroendocrinology, 26*(7), 711–720.

Yerkes, R. M., & Dodson, J. D. (1908). The relation of strength of stimulus to rapidity of habit formation. *Journal of Comparative Neurology and Psychology, 18*, 31–39.

Zorawski, M., Blanding, N. Q., Kuhn, C. M., & LaBar, K. S. (2006). Effects of stress and sex on acquisition and consolidation of human fear conditioning. *Learning & Memory, 13*(4), 441–450.

Zorawski, M., Cook, C. A., Kuhn, C. M., & LaBar, K. S. (2005). Sex, stress, and fear: Individual differences in conditioned learning. *Cognitive, Affective & Behavioral Neuroscience, 5*(2), 191–201.

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