

## Stress and Memory Retrieval in Women: No Strong Impairing Effect During the Luteal Phase

Daniela Schoofs and Oliver T. Wolf  
Ruhr-University Bochum

Stress has been shown to impair delayed memory retrieval, but so far no study has been conducted solely with naturally cycling women. In a crossover design, 36 women (all in the luteal phase) participated in two experimental conditions (stress vs. control). Delayed memory retrieval of a wordlist learned 24 hours earlier was tested after stress or control treatment. Although stressed subjects showed a strong cortisol increase following stress, no influence on memory retrieval occurred. In an additional data analysis, subjects were split up into a cortisol responder and a cortisol nonresponder group. However, again no evidence for a stress-induced retrieval impairment became apparent. Similarly, no correlation was observed between the stress-induced cortisol increase and memory. This study failed to find an influence of stress on memory retrieval in women tested in the luteal phase. The findings are in contrast to our previous results obtained with men. Evidence is discussed that the luteal phase, which is characterized by elevated gonadal steroids, is associated with reduced glucocorticoid sensitivity. This might underlie the missing impact of stress on memory.

*Keywords:* stress, cortisol, memory, retrieval, sex differences

There is evidence that women and men differ in how they respond to stress behaviorally as well as endocrinologically (Taylor et al., 2000). For the behavioral response, evidence from humans and animal studies suggests that men under stress show the typical fight-or-flight response. In contrast, women seem to affiliate with social groups, especially other women, to reduce risk and manage stressful conditions (tend and befriend behavior). Endocrinologically, both sexes show an activation of the hypothalamus-pituitary-adrenal (HPA) axis, but the magnitude of the response is modulated by gonadal steroids (Taylor et al., 2000).

However, it is less clear whether the effects of stress on learning and memory also differ between the sexes. One issue that has hindered research in this area is the fact that sex steroids are known to influence the response of the major stress system (HPA axis) in a complex fashion (Kajantie & Phillips, 2006; Kudielka & Kirschbaum, 2005). As a result, a substantial number of experimental human studies have been conducted exclusively with males. Moreover, in studies with women information about menstrual cycle phase and/or hormonal contraception were often not taken into account. Similarly, most rodent studies focusing on stress effects on memory have been conducted exclusively with males (Diamond, Campbell, Park, Halonen, & Zoladz, 2007; Joels, Pu, Wiegert, Oitzl, & Krugers, 2006; Sandi & Pinelo-Nava, 2007).

Animal studies that addressed the issue of sex differences have sometimes reported quite striking findings. For example, Shors

observed that stress enhances eyeblink conditioning in males, while impairing it in females (Shors, 2004). In contrast, Conrad observed that stress enhanced spatial memory in female rats while impairing it in males (Conrad et al., 2004). For spatial memory, similar sex differences have been shown after chronic stress (Luine, 2002). However, it is important to note that not all rodent studies observed sex differences. For example, one recent study employing predator stress found a similar impact of stress on spatial memory tested with the radial arm water maze in male and female rats (Park, Zoladz, Conrad, Fleshner, & Diamond, 2008). Thus, although there are examples for sex differences, the direction of the effect appears to differ depending on the memory domain tested (Wolf, 2008). One possible explanation could be that sex-dependent opposing effects of stress on memory might occur for those tasks only where sex differences are apparent under basal (stress free) conditions.

In human stress research, evidence for sex differences has been found in studies investigating the relationship between stress, cortisol, and fear conditioning (Jackson, Payne, Nadel, & Jacobs, 2006; Stark et al., 2006; Zorawski, Blanding, Kuhn, & LaBar, 2006; Zorawski, Cook, Kuhn, & LaBar, 2005). Thus, for this form of emotional learning, which depends on the amygdala (LaBar & Cabeza, 2006), stress or cortisol appears to exert sex dependent effects.

With respect to hippocampal based episodic memory (LaBar & Cabeza, 2006), empirical evidence for sex differences is less consistent. At least some correlational studies pinpoint toward sex differences. We previously reported that the stress-induced cortisol increase is correlated with immediate recall after stress in men but not women (Wolf, Schommer, Hellhammer, McEwen, & Kirschbaum, 2001b). Similarly, in a post learning stress study cortisol levels were correlated with memory consolidation in men but not women (Andreano & Cahill, 2006, but see Andreano, Arjomandi, & Cahill, 2008).

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Daniela Schoofs and Oliver T. Wolf, Department of Cognitive Psychology, Ruhr-University Bochum, Bochum, Germany.

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Correspondence concerning this article should be addressed to Oliver T. Wolf, Department of Cognitive Psychology, Ruhr-University Bochum, Universitätsstr. 150, D-44780 Bochum, Germany. E-mail: oliver.t.wolf@rub.de

One of the best-established effects of stress or cortisol treatment in animals and humans is its impairing effect on delayed retrieval (Roosendaal, Okuda, de Quervain, & McGaugh, 2006; Wolf, 2008). In humans, pharmacological studies have repeatedly reported that cortisol treatment impaired delayed memory retrieval in men (Buss, Wolf, Witt, & Hellhammer, 2004; de Quervain et al., 2003; Wolf et al., 2001a), women (Kuhlmann, Kirschbaum, & Wolf, 2005a; Kuhlmann & Wolf, 2005), or in mixed sex samples (de Quervain, Aerni, & Roosendaal, 2007; de Quervain, Roosendaal, Nitsch, McGaugh, & Hock, 2000).

Our group has shown that a retrieval impairment occurs after psychosocial stress in men (Kuhlmann, Kirschbaum, & Wolf, 2005b), but we had not conducted a similar study with women. Studies from other groups have reported similar findings in male samples (Domes, Campbell, Park, Halonen, & Zoladz, 2004; Tollenaar, Elzinga, Spinhoven, & Everaerd, 2008). Additional studies suggested that the effect was restricted to subjects showing a cortisol stress response (Buchanan & Tranel, 2008; Buchanan, Tranel, & Adolphs, 2006) or was only detectable with correlations (Oei, Everaerd, Elzinga, van Well, & Bermond, 2006). Four studies have tested the effects of stress on memory retrieval in mixed sex samples. As further addressed in the Discussion section, findings have been somewhat mixed (Beckner, Tucker, Delville, & Mohr, 2006; Buchanan & Tranel, 2008; Buchanan et al., 2006; Smeets, Otgaar, Candel, & Wolf, 2008). In addition, in those studies no effort was undertaken to control for hormonal contraceptive use and/or to obtain information about the menstrual cycle phase of the subjects.

The aim of our current study was to investigate the effects of stress on memory retrieval in a sample of women using the identical experimental design that we had used previously with men (Kuhlmann et al., 2005b). All women were naturally cycling and were tested in the luteal phase of their menstrual cycle. This phase is characterized by elevated estradiol and progesterone levels (Kirschbaum, Kudielka, Gaab, Schommer, & Hellhammer, 1999). In addition, during this phase the hypothalamic–pituitary–adrenal (HPA) stress response to laboratory stressors has been reported to be relatively comparable to those of men (Kirschbaum et al., 1999).

## Method

### Subjects

Forty-one healthy, young women initially participated. Two reported retrospectively using a mnemonic technique in the last testing condition, and three showed substantially enhanced basal cortisol levels (more than 2.5 *SDs* above mean). Thus, 36 women (mean  $\pm$  *SEM*; age:  $24.47 \pm 0.63$  years) were included in the final analysis. All subjects were naturally cycling with menstrual cycles between 24 and 36 days ( $28.88 \pm 0.36$  days). Only women reporting to have a regular menstrual cycle were included. Participants were tested in the luteal phase (4th to the 8th days before the onset of the new menstrual cycle). None of the women reported acute or chronic disease or regular medication intake. All subjects were normally weighted (body mass index [BMI]:  $21.81 \pm 0.40$  kg/m<sup>2</sup>) and provided written informed consent before their participation. The study was approved by the national ethic committee of the German Psychological Association (DGPs).

### Procedure

The design and material of this study is identical to those employed in our previous study conducted with healthy men (Kuhlmann et al., 2005b). In a crossover design, participants were tested in two experimental conditions (stress vs. control). The treatment sequence was randomized. For each condition the subjects had to appear at the laboratory on two consecutive days. The time interval between the two treatment conditions was one menstrual cycle length, except for 3 participants, for whom the interval consisted of two cycles. On the first day subjects arrived between 10:00 and 11:00 a.m. in the laboratory and had to learn one of two possible parallel versions of a word list (see below) containing 30 nouns (the parallel versions were also randomized between both conditions). On the second day the subjects started at the same time and filled out a mood questionnaire and rested for the first 30 min. Thereafter, the subjects took part either in a nonstressful control condition or in a psychosocial stress situation. Subsequently, subjects filled out the mood questionnaire again. Ten minutes after the treatment participants were tested for delayed memory retrieval (words learned on the previous day). This design allows testing of the specific effects of stress on memory retrieval, because encoding and consolidation take part one day prior to the experimental treatment (see de Quervain et al., 2000; Kuhlmann et al., 2005b).

### Stress Induction

Stress was induced using the Trier Social Stress Test (TSST), a well-established psychosocial stressor (Dickerson & Kemeny, 2004; Kirschbaum, Pirke, & Hellhammer, 1993). In the TSST subjects have an initial preparation period (5 min). Afterward they are asked to give a free speech (5 min) in front of a reserved acting committee. Next, subjects have to perform demanding mental arithmetic (5 minutes). Additionally, the subjects were videotaped. The nonstressful control condition was similar in physical and cognitive demand (speech and math task), but here the subjects were neither videotaped nor evaluated by a committee (lack of socio evaluative threat; (Dickerson & Kemeny, 2004; Kuhlmann et al., 2005b; Schoofs, Preuss, & Wolf, 2008).

### Endocrine Measurement

All testing sessions took place in the late morning similar to our previous study, which observed impairing effects of stress on memory retrieval in men (Kuhlmann et al., 2005b). Participants were requested to abstain from eating, drinking, or smoking during the hour preceding the beginning of the experiment. Saliva samples for the analysis of the HPA axis and sympathetic nervous system (SNS) stress response were taken immediately before (baseline), 1 (sample + 01), 10 (sample + 10), and 25 minutes (sample + 25) after the cessation of the treatment. Salivary Alpha Amylase (sAA) served as an indirect measure of SNS activation (Ehlert, Erni, Hebisch, & Nater, 2006; van Stegeren, Rohleder, Everaerd, & Wolf, 2006). Saliva was collected using Salivette devices (Sarstedt, Nuembrecht, Germany). Cortisol was measured using an immunoassay (IBL, Hamburg, Germany). For sAA, a quantitative enzyme kinetic method was used as described else-

where (van Stegeren et al., 2006). In two cases not enough saliva was available so that only cortisol but not sAA could be measured.

Furthermore, one additional saliva sample was taken on the first testing session only. This sample was taken before the treatment (after the saliva sample for the cortisol and sAA Analysis was provided). Originally, it was designated for another analysis, but was post hoc used to assess the sex hormones progesterone and estradiol in order to determine whether or not at the first test session the two gonadal hormones were within the expected range for the luteal phase. Saliva was collected using Salicap devices (IBL, Hamburg, Germany). Progesterone and estradiol were measured using commercially available immunoassays (IBL). One subject had not provided enough saliva for the analysis.

### Affect Measurement

The negative affect scale of the Positive and Negative Affect Schedule (PANAS; (Watson, Clark, & Tellegen, 1988) was used. On the treatment days participants filled out the scale twice, at baseline (pretreatment) and immediately after the stressor or the control condition (posttreatment). Subsequently, a delta score was created.

### Memory Test

Two parallel versions of a word list containing 10 positive, 10 negative, and 10 neutral nouns were used. The word lists were the same as used in the previous study (Kuhlmann et al., 2005b). The three valence categories as well as the two lists were matched for word length, word frequency, and semantic cohesion (Kuhlmann et al., 2005b).

Subjects had 2 min to learn the list and were subsequently tested for immediate recall. This procedure was repeated once resulting in two learning trials. On the following day, delayed free recall of the words was tested 10 min after cessation of the treatment (either TSST or non-stressful control condition). To reduce possible between- and within-subject variance in initial learning, the delayed recall performance was defined as the percentage of words remembered correctly in relation to the second learning trial on day one (Kuhlmann et al., 2005b).

## Results

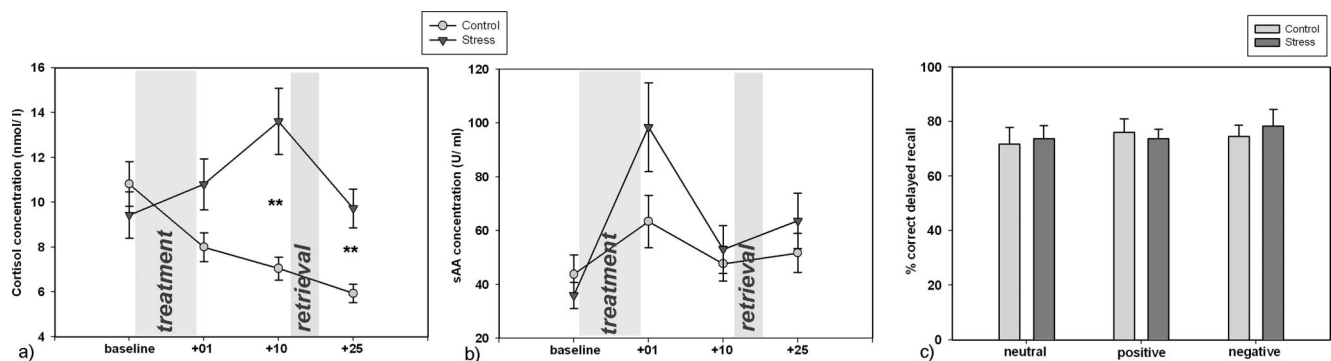
### Analysis for the Whole Group

**Sex hormones: Progesterone and estradiol.** For validation of self-reports regarding the menstrual cycle of the subjects, the sex hormones progesterone and estradiol were measured in the first testing session immediately before treatment. The luteal phase is characterized by high levels of progesterone and estradiol (Franz, 1988). Results revealed average progesterone levels of  $180.56 \pm 19.87$  pg/ml (mean  $\pm$  SEM) and average estradiol levels of  $3.39 \pm 0.31$  pg/ml. Those levels are in line with norm values reported for the luteal phase by the producer (progesterone = 127–446 pg/ml; estradiol = 0.8–10.8 pg/ml), as well as with values obtained in a previous menstrual cycle study of ours (Walpurger, Pietrowsky, Kirschbaum, & Wolf, 2004).

**Salivary and subjective stress markers.** Cortisol and sAA concentrations were analyzed with analyses of variance (ANOVA) for repeated-measurements with the within-subject factor Treatment (TSST vs. control situation) and a second within factor Time (the four sampling points). For both cortisol and sAA, the ANOVAs showed significant Treatment  $\times$  Time interactions ( $p < .001$ ). Post hoc Bonferroni-Holm corrected dependent  $t$  tests revealed significantly higher cortisol levels in the stress condition for the +10 and the +25 measurement (see Figure 1 a). For sAA, post hoc analyses showed no significant difference between both treatments for the 4 sampling points (uncorrected  $p = .023$  for the +01 sampling point; see Figure 1b).

The paired  $t$  test for the delta negative affect score was significant ( $p < .001$ ). Negative affect increased in response to stress but did not change in the control condition (data not shown).

**Delayed memory retrieval.** An ANOVA with the two within-subject factors Treatment and Valence (neutral, positive, and negative words) was calculated for the percentage of words retrieved correctly. ANOVA yielded neither a significant effect for Treatment,  $F(1, 35) = 0.06$ ;  $p = .81$ , or Valence,  $F(2, 70) = 0.41$ ;  $p = .66$ , nor a significant Treatment  $\times$  Valence interaction,  $F(2, 70) = 0.23$ ;  $p = .80$ . After stress subjects retrieved a similar percentage of words as after the control condition (stress  $74.14\% \pm 3.23$  vs. control  $73.06\% \pm 3.24$ , see Figure 1c).



**Figure 1.** Effects of psychosocial stress exposure on salivary cortisol levels (1a) and salivary Amylase levels (1b) in a group of women ( $n = 36$ ) tested with a crossover design in the luteal phase of their menstrual cycle. For both stress markers the conducted analyses of variance (ANOVAs) revealed a significant Treatment  $\times$  Time interaction. \*\*  $p < .01$  in adjusted post hoc tests. Stress had no effect on delayed memory retrieval of neutral, positive or negative words (1c).

**Analysis for responder and nonresponder.** We were interested in whether those subjects mounting a robust cortisol stress response would show an impairing effect on memory retrieval. Similar to previous studies (e.g., Schommer, Hellhammer, & Kirschbaum, 2003) subjects were defined as showing an HPA axis response if they had a cortisol increase of larger than 2.5 nmol/L between the baseline and the +10 sampling point, which is a rather conservative responder definition (Weitzman et al., 1971; Wust et al., 2000). Eighteen participants were defined as responders, while the remaining 18 were nonresponders. To investigate responder and nonresponder separately appears reasonable because previous studies suggested that impaired memory retrieval only occurs in cortisol responder (Buchanan & Tranel, 2008; Buchanan et al., 2006).

**Salivary and subjective stress markers.** In two ANOVAs, the cortisol and sAA concentrations were again analyzed with the within-subject factors Treatment and Time. In addition, the between-subject factor Stress Responder (responder vs. nonresponder) was introduced. For cortisol a significant triple interaction for Treatment  $\times$  Time by Stress Responder,  $F(3, 102) = 21.66$ ;  $p < .001$ , was obtained, verifying that the two responder groups differed significantly in their cortisol response (see Figure 2a). For sAA, the ANOVA failed to detect a significant effect of Stress Responder (main effect as well as all possible interactions). Results are displayed in Figure 2b.

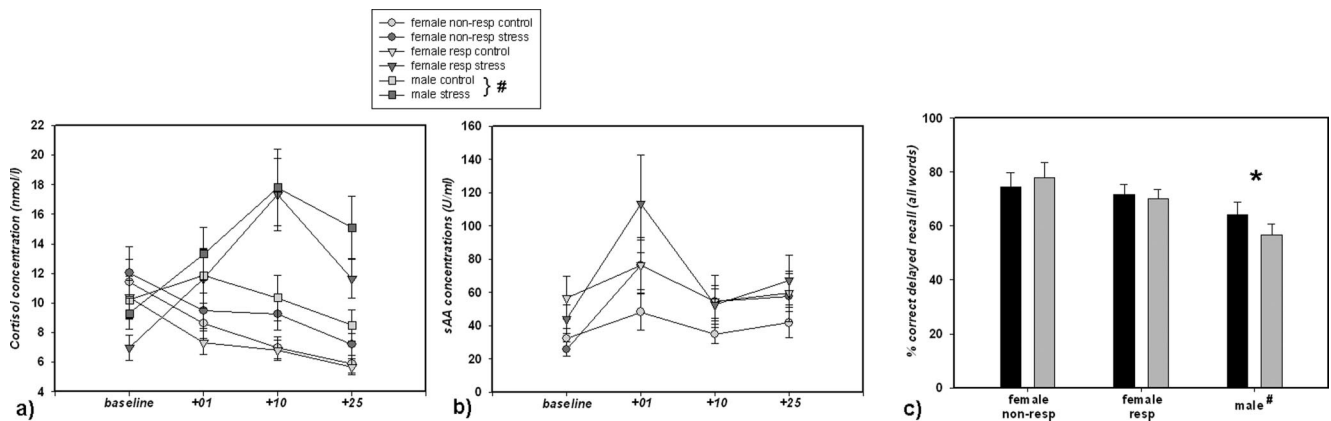
For affect, the repeated-measurement ANOVA resulted in a significant main effect for Treatment but neither a significant main effect for Stress Responder, nor a significant interaction was found (data not shown).

**Delayed memory retrieval.** For memory retrieval, an ANOVA was conducted for the percentage of words retrieved correctly with

the two within-subject factors Treatment and Valence and the between-subject factor Stress Responder. The analysis revealed neither a significant main effect for Stress Responder,  $F(1, 34) = 2.02$ ;  $p = .16$ , nor a significant Stress Responder  $\times$  Treatment interaction,  $F(1, 34) = 0.09$ ;  $p = .76$ , nor a significant triple interaction, Stress Responder  $\times$  Treatment  $\times$  Valence;  $F(2, 68) = 0.38$ ;  $p = .69$ ; see Figure 2c. In sum, neither in cortisol stress responders nor in cortisol stress nonresponders an impairing effect of stress on memory retrieval was observed.

**Correlational analysis.** Furthermore, it was investigated whether changes in delayed retrieval were correlated with the individual cortisol responses. For this, the difference in the percentage of retrieved words between both conditions (percentage of retrieved words after stress minus percentage of retrieved words after the control condition) was calculated. The same calculations were performed for each valence (neutral, positive, and negative) separately. Similarly for cortisol the change was calculated by subtracting the cortisol increase in response to stress (delta measure of the +10 value minus baseline) from the cortisol changes during the control condition (delta measure of the +10 value minus baseline). The correlations revealed no significant association between changes in retrieval and changes in cortisol (all  $ps > .05$ ).

In addition, another correlation was calculated between the change of cortisol and the change of negative affect (increase of negative affect in response to stress minus the negative affect changes during the control condition). For this analysis, a significant correlation was observed ( $r = .349$ ;  $p = .037$ ). Women showing a stronger cortisol response to the stressor also reported a more pronounced increase in negative affect. However, similar to the missing association between cortisol and memory retrieval we



**Figure 2.** Effects of psychosocial stress exposure on salivary cortisol levels (2a) and salivary Amylase levels (2b) for female responder (defined as subjects showing a robust cortisol stress response with an increase in cortisol of larger than 2.5 nmol/L,  $n = 18$ ), female nonresponder ( $n = 18$ ), and males ( $\# =$  subjects from Kuhlmann et al., 2005b; data available only for cortisol and retrieval, but not for Salivary Alpha Amylase [sAA];  $n = 19$ ). The cortisol levels in men (part of Figure 2a) are reprinted with permission from "Impaired memory retrieval after psychosocial stress in healthy young men," by S. Kuhlmann, M. Piel, and O. T. Wolf, 2005, *Journal of Neuroscience*, 25, pp. 2977–2982. Copyright 2005 by the Society for Neuroscience. For the cortisol stress response (2a), no significant differences were observed in the cortisol increase between males and female responder while female nonresponder even displayed a decrease of cortisol for the stress condition. For sAA (2b), female responder and nonresponder showed a similar sAA response to the stressor. Neither in the responder group nor in the nonresponders memory retrieval was influenced by stress, although in men a significant memory impairment following stress was observed (2c). \*  $p < .05$  in adjusted post hoc  $t$  tests comparing the percentage of correctly retrieved words between the control and the stress condition.

failed to find a significant association between changes in affect and memory retrieval (all  $p$ s > .10).

*Comparison Between Female Responder, Female Nonresponder, and the Male Subjects Tested by Kuhlmann et al. (2005b)*

So far, the conducted statistical analyses have failed to find an impairing effect of stress on memory retrieval in a large sample of women tested in the luteal phase. The results are therefore in contrast to our previous findings obtained in men. To characterize possible differences between the neuroendocrine and behavioral findings obtained in those two studies, we directly compared the results obtained with these two samples.

**Cortisol.** For cortisol concentrations, an ANOVA was calculated with the two within-subject factors Treatment (stress vs. control) and Time (the four sampling points) and the between-subject factor Group (males, female responder, and female nonresponder). The analysis revealed a significant Treatment  $\times$  Time  $\times$  Group interaction,  $F(6, 156) = 7.17$ ;  $p < .001$ . Post hoc Bonferroni-Holm corrected independent  $t$  tests calculated for the cortisol response (+10 measurement minus baseline) during the stress condition revealed a significant difference between the cortisol changes in female nonresponder compared with female responder,  $t(34) = 4.60$ ;  $p < .001$  and males,  $t(35) = -4.50$ ;  $p < .001$ . While men and female responder displayed a considerable increase of cortisol between the baseline and the +10 measurement, female nonresponder displayed a decrease of hormone concentrations (mean of change baseline = +10 measurement  $\pm$  SEM; female nonresponder =  $-2.77 \pm 0.97$ ; female responder =  $10.35 \pm 1.77$ ; males =  $8.53 \pm 2.24$ ). On the other hand, between female responder and men no significant differences were observed ( $p > .10$ ). Results are displayed in Figure 2a.

**Delayed memory retrieval.** For memory retrieval, an ANOVA was conducted for the percentage of all words (independent of valence) retrieved correctly with the within-subject factor Treatment (stress vs. control situation) and the between-subject factor Group (males, female responder, and female nonresponder). The ANOVA revealed no significant main effect for Treatment,  $F(1, 52) = 0.64$ ;  $p > .10$ , but a significant main effect for Group,  $F(2, 52) = 3.88$ ;  $p < .05$ . The Treatment  $\times$  Group interaction failed short of being significant,  $F(2, 52) = 2.12$ ;  $p = .13$ . While women in the control condition descriptively showed better retrieval performance than men, this effect fell short of significance ( $p > .10$ ). Only in the male sample a significant stress-induced retrieval performance occurred (see Figure 2c), whereas in both female groups no retrieval impairment could be detected.

## Discussion

The objective of this study was to examine the effect of stress on delayed memory retrieval in women in the luteal phase. Based on our previous pharmacological studies in women and men (e.g., Buss et al., 2004; Kuhlmann et al., 2005a; Kuhlmann & Wolf, 2005; Wolf et al., 2001a) and our previous stress study in men (Kuhlmann et al., 2005b), we expected to find a stress-induced retrieval impairment in the current study as well.

However, results revealed that memory retrieval of a word list containing neutral, negative, and positive nouns were not affected

by the stressor. This was true despite the fact that women showed substantial changes in the endocrine and subjective stress markers. Even when the statistical analyses were conducted separately for cortisol responder and cortisol nonresponder (divided according to their cortisol stress response) no influence of stress on memory retrieval became apparent.

When discussing nonsignificant findings the first issue which comes into ones mind is a potential lack of power. In the current study 36 women were tested in a cross over design. The sample size of this study was substantially larger than those of most previous studies on this topic and was twice as large as our previous study in men (Kuhlmann et al., 2005b). Effects of stress or cortisol treatment on memory retrieval have been found to be medium to large (corresponding to an effects size  $d$  of .5 to .8). With our current sample size, the power to detect a medium effect ( $d = .5$ ) was larger than 90% (analysis conducted with G-power 3; see Faul, Erdfelder, Lang, & Buchner, 2007). Thus, a potential lack of power appears not to be a major concern.

Two recent studies have observed effect of stress on memory retrieval only in subjects showing a cortisol stress response (Buchanan & Tranel, 2008; Buchanan et al., 2006). When we used a similar approach, we still failed to find an impairing effect of stress. In the two Buchanan studies women were included but the sample size was relatively small. Thus, the issue of sex differences could not be addressed adequately. Two additional experiments have tested the effects of stress on memory retrieval in a mixed sex sample (but containing a majority of women). In both studies, unfortunately, no information about oral contraceptive use or menstrual cycle phase was obtained or reported (Beckner et al., 2006; Smeets et al., 2008). Beckner and colleagues failed to find an effect of speech anticipation on memory retrieval (Beckner et al., 2006). Smeets, however, observed that the cold pressor stressor (a more physical and less social stressor) impaired memory retrieval in a sample consisting mostly of women who were however not further characterized regarding their hormonal status (Smeets et al., 2008). In contrast, results obtained in studies conducted solely with male subjects are more uniform. Here, repeatedly an impaired memory retrieval after stress exposure was observed (Domes et al., 2004; Kuhlmann et al., 2005b; Oei et al., 2006; Tollenaar et al., 2008).

Because our current findings were in contrast to our previous results obtained in males using the identical design, we conducted additional analyses in order to elucidate possible reasons for the observed sex differences. With respect to the cortisol stress response the analysis revealed that the females in our group showed a smaller cortisol increase compared with the male sample. This appears to be in contrast to findings published by Kirschbaum et al. (1999), who reported that women in the luteal phase show a comparable cortisol stress response to the TSST than men do. Reasons for these discrepancies might be secondary to several differences in the design of the two studies. For example, the present study was conducted at a different time of day and used a crossover design. However, it is important to note that, as illustrated in Figure 2a, female stress responder showed comparable cortisol concentrations to those obtained in our previous studies with males (Kuhlmann et al. (2005b)). Thus, at least in the cortisol responder group the missing effects of stress on retrieval cannot be attributed to a reduced HPA response to the stressor. In comparison to the women tested in this study the previously published

male sample was characterized by a somewhat poorer retrieval performance on the control day, which however was not significant. In sum, the comparison with the male group suggests that the missing effects of stress on memory retrieval observed in the current study can neither be explained by sex differences in the cortisol stress response nor by sex differences in memory retrieval abilities.

We suggest that the missing retrieval effects of stress observed in our current sample might reflect a decreased sensitivity of women in the luteal phase to the impairing effects of a stress-induced cortisol response. The luteal phase is characterized by elevated estradiol and progesterone levels (Franz, 1988). Because we initially intend to rely on self-reported data to validate the menstrual cycle phase, a post hoc analysis of the sex hormones progesterone and estradiol could be conducted for the first session only. Results revealed that participants displayed levels typical of women in the luteal phase. Since all women reported a regular cycle it could be assumed that they were also tested during their luteal phase on the second testing session. Having said this, a more detailed assessment of sex steroids before but also after stress exposure (Shors, Pickett, Wood, & Paczynski, 1999) would be desirable in future studies.

During the luteal phase HPA axis feedback is diminished (Altemus et al., 1997) and the HPA stress response is enhanced (Andreano et al., 2008; Kirschbaum et al., 1999). Most interesting, peripheral glucocorticoid sensitivity after stress is reduced during the luteal phase, which is in contrast to findings obtained in men (Rohleder, Schommer, Hellhammer, Engel, & Kirschbaum, 2001). We have data suggesting that peripheral and central glucocorticoid (GC) sensitivity are associated with each other (Rohleder et al., in press). Thus during the luteal phase stressed women might be less susceptible to the impairing effects of cortisol on memory retrieval. Effects of gonadal steroids on the glucocorticoid receptor might underlie these effects (Altemus et al., 1997).

Several problems with the above outlined hypothesis need to be addressed. First, cortisol treatment is associated with impaired memory retrieval in women tested during their luteal phase (Kuhlmann & Wolf, 2005). This indicates that high cortisol levels can influence memory retrieval in this cycle phase (at least in a stress free sample). Thus, sensitivity to cortisol might be reduced but is by no means absent.

Second, we observed in a previous study that stress-induced cortisol levels were not associated with immediate word recall in a group of women tested during their luteal phase (Wolf et al., 2001b). However, a recent study by Andreano and Cahill (2008) obtained contradictory results. They tested the effects of post learning stress on memory consolidation in women at three different phases of their menstrual cycle. Overall stress had no effect on memory (Andreano et al., 2008). However, cortisol levels were correlated with memory in women during their luteal phase (Andreano et al., 2008). This is in contrast to our findings. Andreano and Cahill (2008) used a different stressor (cold pressor stress), investigated a different memory phase (consolidation), used a different definition for the luteal phase and tested their subjects in a between group comparison. Any of those factors might explain the differences in the observed findings. Additional studies are needed to find out under which hormonal circumstances cortisol levels are correlated with memory in women.

A limitation of our current experiment is that we exclusively focused on one menstrual cycle phase to increase the power. We thus do not know whether or not stress would have impaired memory retrieval in women at a different stage of their menstrual cycle, or whether women in general show less retrieval impairments after psychosocial stress. The latter conclusion would be in line with the findings from Beckner et al. (2006). What we were able to do is to compare our present findings with our previous findings in men (Kuhlmann et al., 2005b). This comparison revealed that even those women (cortisol stress responder) showing a cortisol increase comparable to that observed in males, did not show any evidence for a stress reduced retrieval impairment.

A second limitation is that we did not measure sex steroid levels on the second testing session. Although analysis for the first testing session indicated that women displayed estradiol and progesterone levels typical for the luteal phase the assessment of sex steroids in both sessions could have provide valuable additional information (Andreano et al., 2008). Along these lines the pharmacological manipulation of gonadal hormones would allow drawing causal conclusions regarding their effects on glucocorticoid sensitivity in particular and stress sensitivity in general (Newhouse et al., 2008).

In sum, the current study failed to detect any evidence for a stress-induced retrieval impairment in a large sample of young women all tested during the luteal phase. We suggest that this might be reflective of reduced glucocorticoid sensitivity during this phase of the menstrual cycle. However, alternative explanations cannot be ruled out and the current finding is in clear need of a replication.

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