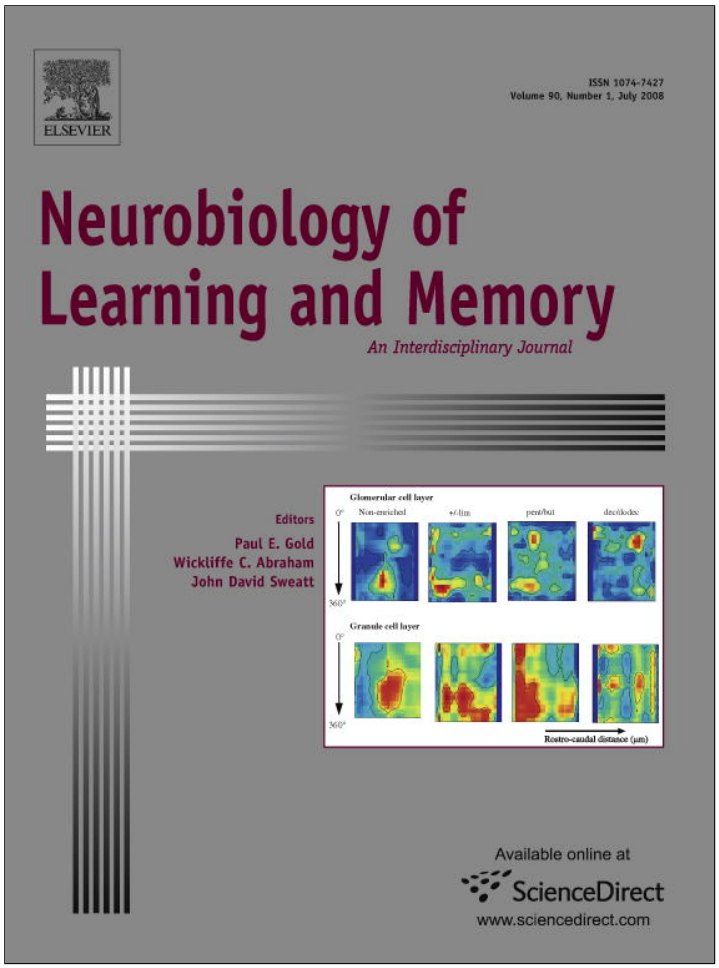

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# Effects of pre-learning stress on memory for neutral, positive and negative words: Different roles of cortisol and autonomic arousal

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**Abstract**

Stress can have enhancing or impairing effects on memory. Here, we addressed the effect of pre-learning stress on subsequent memory and asked whether neutral and emotionally valent information are differentially affected by specific stress components, autonomic arousal and stress-induced cortisol. Ninety-six healthy men and women underwent either a stressor (modified cold pressor test) or a control warm water exposure. During stress, participants showed comparable autonomic arousal (heart rate, blood pressure), while 60 percent showed an increase of cortisol (responders vs. 40 percent non-responders). Ten minutes after the cold pressor test neutral, positive and negative words were presented. Free recall was tested 1 and 24 h later. Overall, positive and negative words were better recalled than neutral words. Stress enhanced the recall of neutral words independently of cortisol response. In contrast, the free recall of negative words was enhanced in cortisol responders in the 1-h but not 24-h test which might suggest different effects of cortisol on consolidation and reconsolidation processes. Recall for positive words was unaffected by stress-induced cortisol. To summarize, (i) pre-learning stress can enhance memory for neutral words independently of cortisol and (ii) stress effects on memory for negative words appear to rely on stress-induced cortisol elevations, the absence of this effect for positive words might be at least partly due to differences in arousal evoked by positive vs. negative words.


*Keywords:* Declarative memory; Pre-learning stress; Cortisol; Cold pressor test

## 1. Introduction

Stress affects memory in many ways. Stress within a short period after learning facilitates memory (Roozendaal, 2000), but stress shortly before testing impairs memory (de Quervain, Roozendaal, & McGaugh, 1998; Kuhlmann, Piel, & Wolf, 2005). The influence of stress prior to learning is less clear. Several studies indicated that declarative memory can be impaired when people are exposed to stress before learning (Elzinga, Bakker, & Bremner, 2005; Kirschbaum, Wolf, May, Wippich, & Hellhammer, 1996; Lupien et al., 1997; Payne et al., 2006); but other studies found enhanced memory performance in individuals stressed before learning (Domes, Heinrichs, Reichwald, & Hautzinger, 2002; Nater et al., 2007; Smeets, Giesbrecht, Jelicic, & Merckelbach, 2007). This discrepancy might be explained by such diverse factors as the different memory functions tested (long-term vs. working memory), the sample size of the study (Kirschbaum et al. (1996) tested only 13 subjects) and the time of testing (morning vs. afternoon), which is a factor crucial for the direction of the stress (hormone) effect on memory (see the review by Het, Ramlow, & Wolf, 2005).

There is a body of the literature suggesting that cortisol, the adrenocortical hormone that is released during stress in humans, is a primary effector in the effects of stress on memory functions (de Kloet, Oitzl, & Joels, 1999; Het et al., 2005; Lupien & McEwen, 1997). A recent model proposes that cortisol released around the time of learning facilitates ongoing learning processes and thus would predict memory enhancing effects of stress experienced shortly

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before learning (Joels, Pu, Wiegert, Oitzl, & Krugers, 2006). Furthermore, it has been suggested that the effects of stress (hormones) are mediated via the basolateral amygdala (Roozendaal, 2000; Roozendaal, Okuda, Van der Zee, & McGaugh, 2006). According to Roozendaal (2000), stress affects memory only if the actions of cortisol and autonomic arousal converge in the basolateral amygdala, which then modulates memory processes in other brain structures. Importantly, several studies show that relative to neutral items, positively and negatively valenced stimuli elicit significantly greater activity in the amygdala, which suggests that emotional but not neutral words are processed by the amygdala (Garavan, Pendergrass, Ross, Stein, & Risinger, 2001; Hamann & Mao, 2002). This raises the question whether the assumptions of Roozendaal (2000) hold for both emotional and non-emotional information. Is a co-occurence of autonomic arousal and cortisol required for stress effects on memory for both emotional and non-emotional stimuli? Indeed, there is some evidence that the effects of pre-learning stress on memory depend on the emotionality of the material to be learned. Both Elzinga et al. (2005) and Payne et al. (2006) showed that stress prior to learning affected the recall of non-emotional information, but did not affect memory for emotional information. However, none of these studies separated the contributions of stress-induced cortisol and autonomic arousal.

Although stress is typically defined as an elevation in cortisol levels, individuals differ considerably in their cortisol responses. While some individuals show persistently high cortisol responses to stress, others show little or no such responses (Kirschbaum et al., 1995). Comparing individuals who show autonomic and cortisol responses to a task (cortisol responders) with others who respond with autonomic changes but without increases in cortisol (cortisol non-responders), provides the opportunity to assess the influences of stress-induced cortisol elevations and to separate these from effects of autonomic arousal. For instance, Buchanan, Tranel, and Adolphs (2006) exposed participants to a cold pressor stress or control condition before testing them for previously learned words. The authors split the stressed subjects into cortisol responders and cortisol non-responders to dissect the effects of cortisol and autonomic activity on memory retrieval and found cortisol responders impaired relative to non-responders. Thus, Buchanan et al. (2006) concluded that stress-induced cortisol affects memory retrieval independently of autonomic activity. A very recent study used the same strategy to disentangle the contribution of autonomic arousal and stress-induced cortisol on the effect of pre-learning stress on subsequent memory (Nater et al., 2007). In line with the model of Joels et al. (2006), Nater and colleagues (2007) found that participants with high cortisol responses had better recall performance than participants that showed low cortisol responses to the stressor. These authors, however, did not differentiate between emotional and non-emotional stimuli.

The present study aimed to test the influence of pre-learning stress on the memory for neutral, positive and negative terms. Therefore, we exposed participants to a modified cold pressor test (videotaped hand immersion into ice water) shortly before they saw a list of neutral, positive and negative words. Earlier studies indicated that the cold pressor test reliably causes stress expressed for example as increases in skin conductance (Buchanan et al., 2006) and high levels of discomfort (Cahill, Gorski, & Le, 2003). Based on the theoretical framework of Joels and colleagues (2006), we hypothesized a memory enhancing effect of stress shortly before learning. In order to dissect the possible contributions of stress-induced cortisol and autonomic arousal on memory for neutral, positive and negative words, we subdivided the stressed participants into cortisol responders and cortisol non-responders. If cortisol is required for stress effects on amygdala-mediated emotional memory only, then cortisol responders should show better memory performance than cortisol non-responders for positive and negative words but not for neutral words.

## 2. Materials and methods

### 2.1. Participants

Ninety-six healthy volunteers (age: $M = 23.3$ yrs, $SD = 3.2$ yrs; 48 women: age range 19–36 yrs, BMI: $21.8 \pm 2.6$ kg/m$^2$; 48 men: age range 20–37 yrs, BMI: $23.3 \pm 2.7$ kg/m$^2$) recruited at the University of Trier participated in this study. Individuals who met any of the following criteria, which were assessed in a standardized interview by a physician, were excluded from participation: medical illness within the prior 3 weeks; current or lifetime psychopathology; cardiovascular disorders; skin diseases; left-handedness; current treatment with psychotropic medications, narcotics, β-blockers or steroids; current alcohol or tobacco use; or body-mass-index (BMI = weight (in kg)/height (in m)$^2$) lower than 19 or higher than 26. To avoid menstrual cycle effects in women only oral contraceptive using women were included. Moreover, subjects were asked to refrain from fatty meals, caffeine and excessive exercise within the 4 h prior to the experimental session on day 1 and the 4 h prior to retention testing on the following day.

Participants were paid 20 € for participation. All participants provided written informed consent. The study protocol was approved by the local ethics committee.

### 2.2. Procedure

The time line of the experiment is shown in Fig. 1. To control for the diurnal cycle of cortisol, all testing was carried out between 2 pm and 5.30 pm. Participants were randomly assigned to the control and stress group. Sexes were counterbalanced with $n = 24$ women and $n = 24$ men per group.

After subjects were informed about the study procedure, they sat in a chair and baseline measurements of cortisol, heart rate (ECG) and blood pressure (Finapres) were taken.

#### 2.2.1. Stress protocol

Participants were then informed that they will be exposed to a cold pressor test (CPT), videotaped and were requested to look into the camera during CPT. They were told that the video recordings would be analyzed for facial expression and asked to provide consent that the recordings can be used for scientific purposes later on. Participants were videotaped during the CPT in order to include characteristics of the Trier Social Stress Test (TSST; Kirschbaum, Pirke, & Hellhammer, 1993), i.e. to strengthen

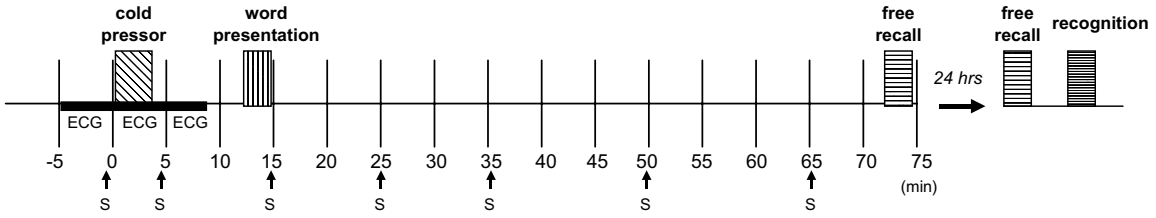


Fig. 1. Sequence of events during the experimental session. $t = 0$ denotes the beginning of the cold pressor test. While ECG was recorded also blood pressure was measured. S—saliva sample.

the social-evaluative character of the task which is known to boost cortisol responses (Dickerson & Kemeny, 2004). After signing the declaration of consent participants immersed their right hand up to and including the wrist into ice cold water (0–2 °C). Subjects were told that they should try to keep their hand as long as possible in the water, at maximum 3 min, but could remove their hand at their discretion. The experimenter asked them repeatedly to concentrate on their right hand. All participants kept their hand in the water for the 3 min and were instructed at this point to take their hand out of the water.

Participants in the control group submerged their right hand for 3 min in warm water (35–37 °C); there was no camera.

To verify the efficacy of the stress protocol, heart rate, blood pressure and saliva cortisol measurements were taken at several time points across the experiment.

#### 2.2.2. Subjective stress

Immediately after the hand immersion participants in both groups rated on a 11-point scale ranging from 0 (“not at all”) to 100 (“extremely”) how stressful, painful and unpleasant the cold pressor and control condition, respectively, had been.

#### 2.2.3. Word presentation

Ten minutes after cessation of the stress manipulation the learning phase started. This interval between stress and learning was suggested previously by other authors (Domes et al., 2002; Kirschbaum et al., 1996). Moreover, after a 10 min interval specific sensations associated with the cold pressor (in particular hyperaemia) are most likely gone. Participants were presented a list of 18 words (see Section 2.3). To make sure that words were really encoded, subjects were instructed to read each of the words aloud and rate its emotional valence on a scale from −3 (“very negative”) to 3 (“very positive”). They were not informed that memory for these words would be tested subsequently. During the 60 min break between word presentation and the free recall test, participants remained in a separate room. Subjects were allowed to bring an own book and read during the waiting period, except when saliva samples were taken.

#### 2.2.4. One hour-free recall

One hour after rating the words participants completed a free recall test in which they wrote as many words as they could remember on a sheet of paper. There was no time limit for the completion of the free recall test. All participants finished within 5 min. They were not told about the retention tests which followed 24 h later.

#### 2.2.5. Twenty four hour-free recall

The following day, subjects returned to the laboratory and completed a free recall test again. They were told that they have as much time as needed to recall and write down the words presented the day before. The recall test took no longer than 5 min.

#### 2.2.6. Recognition test

Immediately after the 24 h-free recall task participants completed a recognition memory test. Participants heard 36 words (18 words they had rated the day before and 18 new ones) and were asked to say “old” or “new” as to indicate whether or not they remembered rating the word on the previous day. New words were valence-matched to the learned words. The order of new and old words was random but constant for all subjects.

To assess the participants’ ability to discriminate between previously presented and new words we used signal detection theory parameters hit (i.e. identification of previously presented words as “old”), false alarm (i.e. misclassification of new words as “old”) and the sensitivity index $d'$ (computed as $z\,[p\,(\text{hit})] - z\,[p\,(\text{false alarm})]$; see Wickens, 2002). A perfect hit rate of 100 percent was corrected and set to 97.5 percent (18 “old” words; $\frac{17}{18} + \frac{1}{18} \times 0.5 = 0.975$) as suggested by Wickens (2002). Accordingly, if a participant made no error of commission, the false alarm rate was set to 2.5 percent.

### 2.3. Word material

A separate group of 67 subjects (38 women, 29 men; age: $M = 25.9$ yrs, $SD = 5.7$ yrs) was presented a list of 85 German two-syllable nouns and asked to rate the emotional valence of these words on a 7-point scale ranging from −3 (“very negative”) to 3 (“very positive”). Words were accepted as negative if their mean was smaller than −2.0 ($SD < 0.5$), as positive if the mean was higher than 2.0 ($SD < 0.5$), and as neutral if the mean valence score was between 0.5 and −0.5. Thirty-six words (16 neutral, 10 positive, 10 negative) were selected and divided into two valence-matched lists, each containing 8 neutral words (e.g. street, cup), 5 positive words (e.g. love, sun) and 5 negative words (e.g. torture, murderer).

### 2.4. Cardiovascular data and analysis

Heart rate and blood pressure measurements were taken 5 min before (baseline), during (test) and 5 min after hand immersion (post).

Heart rate was derived from a single standard lead II ECG configuration employing telemetric HP 78100A transmitter and HP 78101A receiver system (Hewlett Packard Corp.). ECG was sampled by 1 kHz with 12 bit resolution. Beat detection was performed offline by WinCPRS (Absolute Aliens Oy, Turku, Finland) as was artifact control.

Continuous blood pressure was recorded using the Finapres system (Ohmeda, Englewood, CO, USA); a cuff was placed on the middle finger of the left hand which was put on a box to keep the hand at heart-level. Beat-to-beat systolic and diastolic blood pressure were determined offline with the help of WinCPRS software. Owing to technical failure we lost the blood pressure data of 6 subjects of the control group and 7 subjects of the stress group.

### 2.5. Collection of saliva and biochemical analyses

Saliva was collected by the subjects using customary straw 1 min before (−1), immediately after (+5), 10 min after (+15), 20 min after (+25), 30 min after (+35), 45 min after (+50) and 60 min after (+65) the modified cold pressor or control condition.

The saliva was put directly into standard Eppendorf tubes (1.5 ml, Eppendorf, Hamburg; Germany), stored at room temperature until completion of the session and then kept at −20 °C until analysis. After thawing for biochemical analysis, the fraction of free cortisol in saliva (salivary cor-

tisol) was determined using a time-resolved immunoassay with fluorometric detection, as described in detail elsewhere (Dressendorfer & Kirschbaum, 1992).

### 2.6. Cortisol responders and non-responders

To dissect the possible contributions of autonomic arousal and the adrenocortical stress hormone cortisol on memory performance we split the participants who had completed the modified cold pressor test into cortisol "non-responders" and "responders". Cortisol non-responders are subjects who show a stress-induced increase in autonomic parameters such as heart rate and blood pressure but not in cortisol. Cortisol responders, on the other hand, show both an increase in autonomic activity and cortisol in response to a stressor (Buchanan & Tranel, 2008; Buchanan et al., 2006; Fehm-Wolfsdorf et al., 1993). Comparing unstressed control subjects and cortisol non-responders provides the opportunity to assess the contribution of autonomic arousal on memory whereas the comparison of cortisol non-responders and cortisol responders indicates the effect of stress-induced cortisol on memory performance.

Post hoc, we characterized subtypes of cortisol profiles; a cortisol increase of at least 1.5 nmol/l relative to the individual baseline (i.e. the cortisol concentration 1 min before the beginning of the CPT) was used to subdivide participants into cortisol responders and cortisol non-responders, respectively. Other authors used a median-split to assess the effect of stress-induced cortisol (Nater et al., 2007). While this is appropriate to distinguish cortisol high and low responders, an absolute cut-off is required when trying to separate cortisol responders and non-responders. The chosen cut-off criterion (cortisol increase of at least 1.5 nmol/l) has been suggested earlier by Fehm-Wolfsdorf and colleagues (1993; see also Lupien et al., 1997).

### 2.7. Statistical analyses

In order to examine the possible interactions between stress, sex and word valence, memory data were subjected to 3 (group: controls, cortisol non-responders and cortisol-responders) × 2 (sex) × 3 (valence: neutral, positive and negative) ANOVAs. Significant main effects were further analyzed using Bonferroni adjusted post hoc tests. In case of significant interactions, we first analyzed simple main effects by means of ANOVA. To pursue this analysis interaction contrasts were performed. All calculations were done with SPSS-statistical package (version 14.0; SPSS Inc.). Reported $p$-values are two-tailed. $p < .05$ was accepted as statistical significance. Analyses include the partial $\eta^2$ as measure of effect size where appropriate. Following the conventions by Cohen (1988) partial $\eta^2 = 0.01$ is considered a small effect, partial $\eta^2 = 0.06$ a medium sized and partial $\eta^2 = 0.14$ a large effect.

## 3. Results

### 3.1. Effectiveness of the stress-induction

Autonomic and cortisol measurements as well as participants' subjective stress ratings verified the stress-induction by the modified cold pressor test (CPT).

#### 3.1.1. Autonomic stress responses

Stressed participants showed an increase in autonomic stress indices while controls did not. As shown in Table 1 systolic and diastolic blood pressure were significantly increased in response to the modified cold pressor test (group × time interaction: both $F$s > 25, both $p$s < .001, both $\eta^2 > .24$; group: both $F$s > 32, both $p$s < .001, both $\eta^2 > .25$; time: both $F$s > 15, both $p$s < .001, both $\eta^2 > .17$). Similarly, we obtained a significant group × time interaction for heart rate ($F(2,176) = 7.36$, $p < .01$, $\eta^2 = .08$; group: $F(1,89) = 1.06$, $p = .31$, $\eta^2 < .01$; time: $F(2,176) = 12.41$, $p < .001$, $\eta^2 = .12$) indicating that heart rate changed in subjects in the stress group but not in controls.

Interestingly, heart rate was increased in stressed participants already before the stress manipulation. This is most likely due to the announcement of the cold pressor test and video recording and questions the value of the pre-stress measurement as a baseline. A measurement prior to the announcement of the stress procedure would have been useful.

Moreover, we found significantly higher systolic and diastolic blood pressure in men compared to women, whereas women had higher heart rates than men (all $F$s > 5, all $p$s < .03, all $\eta^2 > .05$). However, there were no significant interactions between sex and the other factors (all $F$s < 3, all $p$s > .10, all $\eta^2 < .02$) which suggest that the effects of the stress manipulation were equivalent for both sexes.

#### 3.1.2. Salivary cortisol responses

Cortisol was increased in participants of the stress group (group $F(1,91) = 4.17$, $p < .05$; $\eta^2 = 0.05$; Fig. 2a with a different time course from controls (time $F(6,546) = 8.12$, $p < .0001$, $\eta^2 = .08$; time × group $F(6,546) = 5.96$, $p < .0001$, $\eta^2 = .29$). There were no differences between men and women in cortisol response ($F(1,91) = 1.54$, $p = .22$, $\eta^2 < .01$), nor was there an interaction between sex and one of the other factors ($F$s < 1, $p$s > .40, $\eta^2 < .01$) meaning that cortisol was elevated comparably in both men and women.

Inspection of individual data revealed a subgroup of 19 "cortisol non-responders" in the stressed subjects (Fig. 2b). Participants were classified as "cortisol non-responder" if they showed an increase in salivary cortisol concentrations of less than 1.5 nmol/l relative to baseline, otherwise they were classified as "cortisol responder". While 60 percent (29 out of 48) of the stress group were classified as cortisol responders, only 4 percent (2 out of 48) of the control subjects were cortisol responders ($\chi^2(1) = 34.73$, $p < .0001$). The two cortisol responders to the control condition (both were female) were excluded from further analyses. Men and women were comparable with respect to the number of cortisol responders and cortisol non-responders ($\chi^2(2) = 3.15$, $p = .21$).

Importantly, cortisol responders and cortisol non-responders did not differ with respect to their increase in heart rate, systolic and diastolic blood pressure (all $F$s < 1.57, all $p$s > .22, all $\eta^2 < .01$), i.e. they were similar in their autonomic arousal.

Please note that we report saliva cortisol concentrations here. The rise in saliva cortisol is about 10 min delayed compared to plasma and serum cortisol concentrations (see Kirschbaum, Kudielka, Gaab, Schommer, & Hellhammer, 1999; Kudielka, Schommer, Hellhammer, & Kirschbaum, 2004). Thus, although this is not reflected in saliva cortisol, groups did most likely differ in their (plasma) cortisol concentrations during learning already.

Table 1
Heart rate, systolic and diastolic blood pressure before, during and after the experimental manipulation

| | Cold pressor | | | Control manipulation | | |
|---|---|---|---|---|---|---|
| | Heart rate | Systolic bp | Diastolic bp | Heart rate | Systolic bp | Diastolic bp |
| Before | 73.2 ± 1.5 | 126.0 ± 2.2* | 71.6 ± 1.9 | 70.1 ± 1.5 | 118.3 ± 2.4 | 68.0 ± 1.9 |
| During | 73.5 ± 1.5 | 151.6 ± 3.1# | 86.8 ± 2.3# | 70.0 ± 1.6 | 117.8 ± 2.3 | 65.4 ± 1.9 |
| After | 69.2 ± 1.4 | 127.7 ± 2.2# | 72.8 ± 1.9# | 69.5 ± 1.5 | 118.5 ± 2.0 | 66.6 ± 1.5 |

Increased heart rate, systolic and diastolic blood pressure (bp) indicate the success of the stress-induction. No change in these measures in the control group. Note the increased heart rate in subjects of the stress group before the experimental manipulation: These participants were informed that they have to immerse their hand in ice cold water and will be videotaped. Data represent means ± SEM.
Bold—$P < .01$ within group.
* $P < .05$ between groups.
\# $P < .01$ between groups.

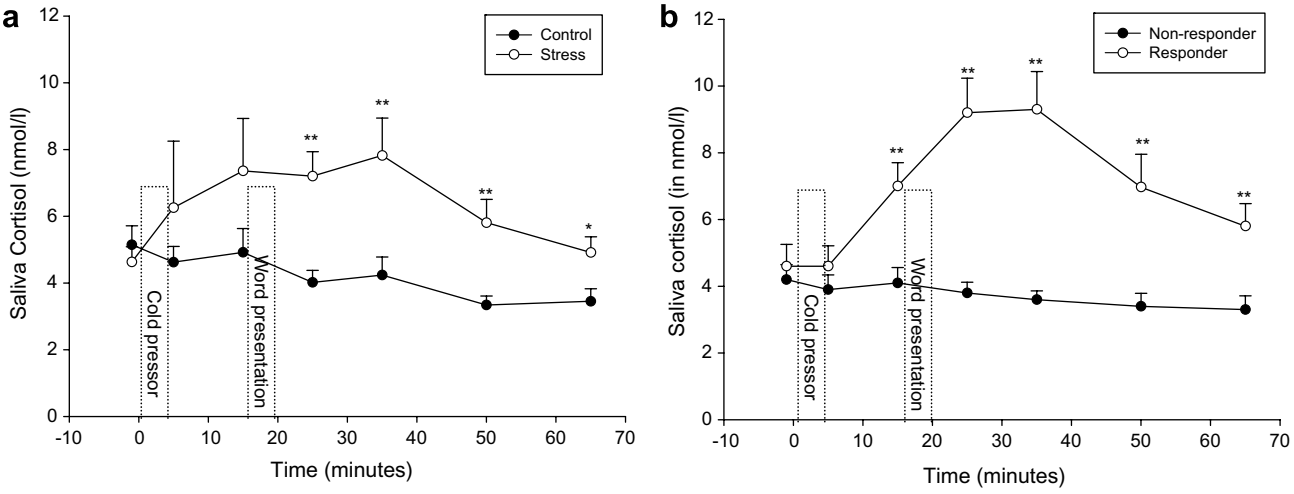


Fig. 2. Salivary cortisol in nanomoles per liter (mean ± SEM) was measured at several time points throughout the experiment. The boxes in the graph denote the time point and duration of the cold pressor stress or control manipulation as well as the time point of the word presentation. (a) Comparison of stress group and control group ($n = 48$ per group). Subjects in the stress group exhibited significantly higher cortisol concentrations than controls. (b) Comparison of stressed participants with an increase in cortisol of at least 1.5 nmol/l relative to baseline (responders; $n = 29$) and those who did not show such an increase (non-responders; $n = 19$). Note that words were presented during the cortisol rise. $^{*}p < .05$; $^{**}p < .01$.

### 3.1.3. Subjective stress ratings

As expected, participants in the stress group rated the experimental manipulation as significantly more stressful, painful and unpleasant than did controls (all $ts > 7$, all $ps < .0001$).

## 3.2. Effects of stress on memory

### 3.2.1. Free recall 1 h after learning

This study investigated the effect of stress prior to learning on memory for neutral and emotional information. As shown in Fig. 3a, stress and stress-induced cortisol elevations had differential effects on memory for neutral, positive and negative words (group × valence $F(4,174) = 2.53$, $p = .04$, $\eta^2 = .06$). Analyses of simple main effects indicated that controls, cortisol non-responders and cortisol responders differed in their recall performance for neutral ($F(2,91) = 5.30$, $p < .01$, $\eta^2 = 0.11$) and negative ($F(2,91) = 2.83$, $p = .06$, $\eta^2 = .06$) but not for positive words ($F(2,91) = 0.07$, $p = .93$, $\eta^2 < .01$). These differences were pursued by interaction contrasts comparing controls and cortisol non-responders as well as cortisol non-responders and cortisol responders. For neutral words, we obtained significantly better recall in cortisol non-responders than in controls ($p < .04$; cortisol responders vs. controls: $p < .01$) while there was no difference between cortisol non-responders and cortisol responders ($p = .33$). For negative words, however, controls and cortisol non-responders were similar in their memory performance ($p = .22$) whereas cortisol responders recalled more words than cortisol non-responders ($p = .02$; cortisol responders vs. controls: $p = .09$). Furthermore, we found a main effect of group ($F(2,87) = 3.07$, $p = .05$, $\eta^2 = .06$) indicating that cortisol responders tended to recall more words than controls (Bonferroni adjusted post hoc test; $p = .06$). Additionally, there was a significant main effect of word valence ($F(2,174) = 25.97$, $p < .001$, $\eta^2 = .23$). Bonferroni adjusted post hoc tests revealed that there was a better memory performance for both positive and negative words compared to neutral words (both $ps < .01$; positive vs. negative: $p > .50$). We found no significant effect of sex on 1-h recall ($F(1,87) = 2.11$, $p = .17$,

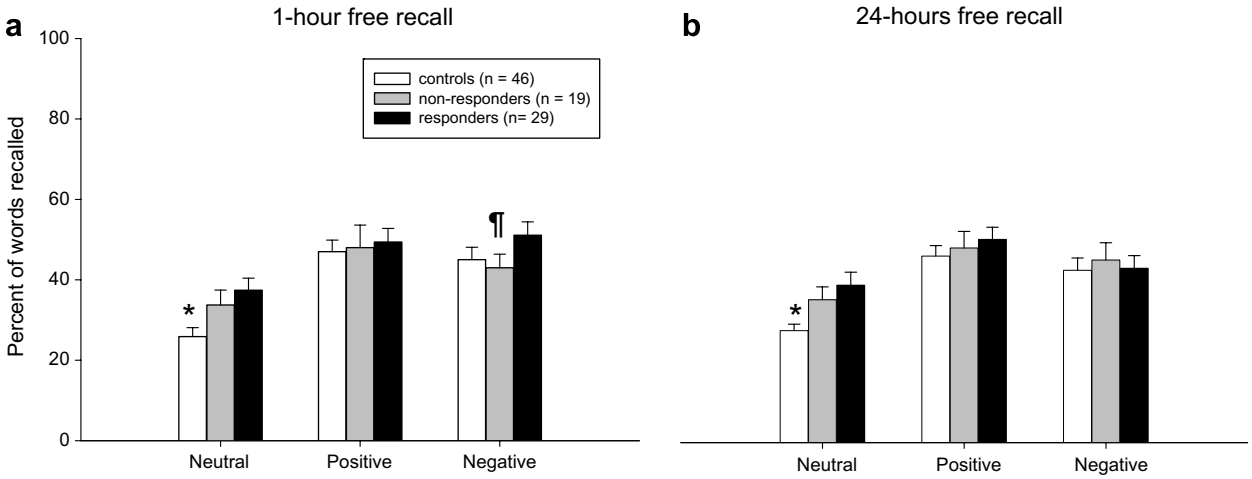


Fig. 3. Recall of neutral, positive and negative words in controls, cortisol non-responders and cortisol responders (a) 1 h after encoding and (b) 24 h after encoding. Results are expressed as percentage of 1 h delayed and 24 h delayed recall, respectively; bars represent mean ± SEM. *Significant difference from the other two groups; ¶Significant difference from cortisol responders.

Table 2
Recognition performance for neutral, positive and negative words expressed as sensitivity index $d'$ in men and women of the 3 groups

| $d'$ | Controls | | Cortisol non-responders | | Cortisol responders | |
|---|---|---|---|---|---|---|
| | Men | Women | Men | Women | Men | Women |
| Neutral words | 2.20 ± 0.19 | 2.25 ± 0.31 | 2.13 ± 0.29 | 2.35 ± 0.21 | 2.51 ± 0.19 | 1.96 ± 0.15 |
| Positive words | 2.76 ± 0.15 | 2.80 ± 0.33 | 2.39 ± 0.31 | 2.39 ± 0.20 | 2.60 ± 0.24 | 2.41 ± 0.22 |
| Negative words | 2.80 ± 0.14 | 3.07 ± 0.28 | 2.74 ± 0.18 | 2.60 ± 0.26 | 2.83 ± 0.22 | 2.71 ± 0.20 |

Recognition performance was very high in all participants. Perfect performance: $d' = 3.57$; hit rate of 90 percent and false alarm rate of 10 percent: $d' = 2.56$. Data represent means ± SEM.

$\eta^2 = .01$), nor was there an interaction between sex and one of the other factors (all $F$s < 1, all $p$s > .60, all $\eta^2$-values < .01).

### 3.2.2. Free recall 24 h after learning

Stress 10 min prior to learning affected recall performance on the following day (Fig. 3b). Again, we found different effects of stress and stress-induced cortisol on memory for neutral, positive and negative words (group - valence $F(4,174) = 2.42$, $p < .05$, $\eta^2 = .05$). Significant group differences were obtained for neutral ($F(2,91) = 6.62$, $p < .01$, $\eta^2 = .13$) but neither for positive ($F(2,91) = 0.97$, $p = .38$, $\eta^2 = .02$) nor for negative words ($F(2,91) = 0.14$, $p = .87$, $\eta^2 < .01$). Contrasts indicated that cortisol non-responders recalled more neutral words than controls ($p = .04$; cortisol responders vs. controls: $p < .01$) while cortisol non-responders and cortisol responders showed a comparable memory performance for neutral words ($p = .21$). There was a significant main effect of group on memory performance ($F(2,87) = 4.15$, $p = .02$, $\eta^2 = .09$) with cortisol responders recalling more words than controls (Bonferroni adjusted post hoc tests; $p < .05$). Moreover, participants showed significantly better recall performance for both positive and negative words compared to neutral words (valence $F(2,174) = 19.36$, $p < .001$, $\eta^2 = .18$; Bonferroni adjusted post hoc tests: negative/positive vs. neutral: both $p$s < .01; negative vs. positive: $p = .21$). There was no main effect of sex on 24 h-recall ($F(1,87) = 1.08$, $p = .30$, $\eta^2 < .01$), nor was there an interaction between sex and the other factors (all $F$s < 1.5, all $p$s > .22, all $\eta^2$-values < .01).

Correlations between percent of neutral ($r = .81$), positive ($r = .71$) and negative words ($r = .70$) recalled in the 1 h- and 24 h-free recall tests were high. Words recalled on day 2 were essentially the same as those recalled the day before.

### 3.2.3. Recognition memory

Recognition memory as assessed by signal detection indices of performance (discriminability $d'$) was remarkably good in all participants (Table 2). It was not affected by group ($F(2,89) = 0.46$, $p = .64$, $\eta^2 < .01$), nor was there an interaction of group and one of the other factors (all $F$s < 1, all $p$s > .35, all $\eta^2$-values < .02). Men and women were similar in their recognition memory ($F(1,89) = 0.05$, $p = .82$, $\eta^2 < .01$; sex × valence $F(2,178) = 0.14$, $p = .87$, $\eta^2 < .01$). However, recognition performance was significantly influenced by word valence ($F(2,178) = 19.13$, $p < .001$, $\eta^2 = .18$)[1]: Negative words were best recognized,

[1] We used the total error rate to correct.

neutral words worst (Bonferroni adjusted post hoc tests: all $ps < .01$).

*3.2.4. Ratings of word material*

Participants' ratings of the presented words confirmed the classification of words as positive, negative and neutral. Neutral words were rated significantly lower in valence than positive words ($t(94) = 41.86$, $p < .0001$) and significantly higher in valence than negative words ($t(94) = 47.82$, $p < .0001$). Valence ratings were independent of experimental group (group $F(2,91) = 0.01$, $p = .91$, $\eta^2 < .01$; group × valence $F(4,184) = 0.26$, $p = .88$, $\eta^2 < .01$).

## 4. Discussion

The main aim of this study was to assess the involvement of specific stress components, autonomic arousal and stress-induced cortisol, in the effect of pre-learning stress on the memory for neutral and emotional stimuli. Overall, our data indicate that autonomic arousal (measured by heart rate and blood pressure) and stress-induced cortisol are differentially involved in the effects of pre-learning stress on memory for neutral, negative and positive words.

For neutral words, we obtained enhanced recall in stressed compared to control subjects both in the 1-h and 24-h delayed recall tests while there was no difference between cortisol responders and cortisol non-responders suggesting that autonomic arousal but not cortisol facilitated memory recall for neutral words. Participants were stressed prior to learning, thus stress could have affected memory encoding as well as memory consolidation and (at least on day 1) retrieval. In our view, it is relatively unlikely that stress affected memory retrieval of neutral words because the interval between stress and retention testing was relatively long (about 70 min), i.e. the stress-induced autonomic arousal was most likely over at the time of the 1-h free recall. Rather, the observed influence of stress on recall of neutral words might be a consolidation effect. This would be in line with earlier findings showing consolidation enhancing effects of autonomic activity (Nielson, Radtke, & Jensen, 1996; for a review: McGaugh, 2006). It is noteworthy, that there was a very high correlation between memory for neutral words in the 1-h and 24-h delayed recall tests. This may be because the act of retrieval strengthens the memory for the information recalled (Sara, 2000).

A different picture emerged for emotional words. Let us consider the effect of pre-learning stress on memory for negative words first. At 1-h after learning, recall of negative words was enhanced in cortisol responders compared to cortisol non-responders while cortisol non-responders and controls performed similarly. Thus, different from neutral words 1-h delayed recall of negative words was affected by stress-induced cortisol elevations. We argue that this difference is due to a differential involvement of the amygdala in the processing of neutral and negative material. The amygdala complex has been identified as part of the neural circuitry critical for emotional reactivity and emotional memory (Gallagher & Chiba, 1996; LeDoux, 2000; McGaugh, Cahill, & Roozendaal, 1996). It is supposed to process emotionally valent but not neutral stimuli (Garavan et al., 2001; Hamann & Mao, 2002). Recent ideas regarding the amygdala's role in mediating stress effects on memory emphasize the interaction of sympathetic and adrenocortical systems. In other words, modulation of memory processes by the amygdala requires a co-occurrence of autonomic activity *and* glucocorticoids (Roozendaal, 2000).

At the 24-h recall test, however, the effect of cortisol on memory for negative words disappeared. Both cortisol responders and cortisol non-responders performed similarly to participants in the control group. Interestingly, except a slight overall reduction in performance from the 1 h- to the 24 h-test, the only significant change appeared in cortisol responders for negative words. In contrast to previous studies showing retrieval impairing effects of stress (hormones) (Buchanan & Tranel, 2008; Buchanan et al., 2006; de Quervain et al., 1998; Kuhlmann et al., 2005), this pattern of results suggests that cortisol, which was still elevated at the time of the 1-h recall, may have had an enhancing effect on retrieval. Alternatively, our findings for negative words could be due to differential effects of stress-induced cortisol on consolidation and reconsolidation processes. Increased glucocorticoid concentrations after learning facilitate memory consolidation (Buchanan & Lovallo, 2001; Cahill et al., 2003; Sandi, Loscertales, & Guaza, 1997). In particular, it has been reported that brief stress can enhance early, i.e. synaptic, consolidation processes via an activation of endogenous plasticity mechanisms (such as long-term potentiation) in the hippocampus and the amygdala (see Diamond, Campbell, Park, Halonen, & Zoladz, 2007). This might explain the enhanced memory for negative words 1-h after encoding. The retrieval of the words, however, activates a reconsolidation process. Reconsolidation refers to the process in which a memory item is rendered transiently malleable after its reactivation (Dudai, 2006; Nader, Schafe, & LeDoux, 2000). We argue that the still elevated cortisol concentrations during the 1-h delayed recall, i.e. during memory reactivation, impaired the fragile memory trace and thus nullified the memory benefit of cortisol responders for negative words 24 h later. Indeed, several studies show memory impairing effects of glucocorticoids administered around the time of the reactivation of emotional memories (Aerni et al., 2004; Cai, Blundell, Han, Greene, & Powell, 2006; Maroun & Akirav, 2008; Soravia et al., 2006). Cai and colleagues (2006), for example, demonstrated in rats that the administration of glucocorticoids immediately after reactivation of previously acquired contextual fear diminishes subsequent recall of the fear. Interestingly, recent clinical trials suggest that post-reactivation treatment with mild doses of cortisol has beneficial (i.e.

impairing) effects on established fear or trauma memories in patients suffering from specific phobia (Soravia et al., 2006) or post-traumatic stress disorder (Aerni et al., 2004).

If stress-induced cortisol facilitates the early consolidation of negative stimuli and impairs their memory trace during reactivation and if this is found in negative but not neutral words, presumably because these effects are mediated via the amygdala which processes emotional information: then why did we not find the same effects for positive items? Why was the recall performance for positive words unaffected by stress and cortisol both on day 1 and day 2? A possible answer lies in the arousal associated with the presented material. Stress effects on memory for emotional stimuli depend also on the emotional arousal produced by the material to be learned (e.g. De Quervain, Aerni, & Roozendaal, 2007; Roozendaal et al., 2006). Roozendaal and colleagues (2006) reported that corticosterone injections after training in an object recognition task enhanced memory in rats that were naïve to the training context, i.e. for which the training situation was arousing. In rats that were previously habituated to the training context, i.e. in which novelty-induced arousal was reduced, there was no effect of post-training corticosterone administration. In the same line, De Quervain et al. (2007) found that cortisol administration impairs memory retrieval for emotionally high-arousing words but not for medium- or low-arousing words.

Looking at the positive (e.g. sun, love, pleasure, vacation) and negative words (e.g. torture, murderer, violence, bomb) that were used in the present study, it appears reasonable to assume differences between both stimulus classes regarding the arousal level. Positive words were most likely less-arousing than negative words, which could explain the absence of a stress (hormone) effect on memory for positive words. As many other studies in the field (Elzinga et al., 2005; Kuhlmann et al., 2005; Tops et al., 2003), we did not measure the emotional arousal associated with the words. This is to be considered as a limitation of the present study and future research will have to corroborate our interpretation by systematically varying the valence *and* arousal associated with the test material.

Importantly, neutral words are usually less well recalled than emotional words (see also Abercrombie, Kalin, Thurow, Rosenkranz, & Davidson, 2003; Buchanan & Lovallo, 2001; Payne et al., 2006). Here, the induction of stress made the recall performance for neutral words more similar to that for emotional words. This could be interpreted in light of the frequently reported inverse u-shaped relationship between arousal and memory performance (for a review: Baldi & Bucherelli, 2005). Accordingly, the enhanced memory for emotional words would be attributable to the higher arousal level associated with these stimuli. The stress prior to word presentation might have substituted the lack of arousal associated with neutral words at least partly and thus increased their memorability.

Enhanced memory for emotional relative to neutral words was observed in the recognition test 24-h after encoding, too. Interestingly, recognition performance was also better for negative than for positive words. This might be due to the higher arousal associated with negative compared to positive words, as argued above. We did not find an effect of the modified cold pressor test on recognition memory. However, recognition performance was exceedingly good in all participants. Especially, recognition memory for emotional words was close to perfect. These "ceiling effects" limit the value of the stress-recognition analyses and are probably due to the rather small number of words presented.

In line with recent studies of Smeets et al. (2007) and Domes et al. (2002) we obtained memory enhancing effects of pre-learning stress. We also corroborate the findings of Nater and colleagues (2007) who reported better memory performance in participants with a high cortisol response to stress administered before learning than in those that showed a low cortisol response. However, our results extend these previous findings in a very important point. None of the aforementioned studies controlled the valence of the presented material. Here, we provide evidence that the effects of pre-learning stress and stress-induced cortisol depend on the valence of the presented material.

Recently, a model was presented to account for the effects of acute stress on memory (Joels et al., 2006). The core of that model is that stress enhances memory if it is experienced around the time of learning. We stressed subjects within 10 min prior to learning and obtained results in line with the model of Joels and colleagues (2006). It is noteworthy that according to the framework of Joels et al. (2006) one would expect different effects of pre-learning stress on memory performance, if the stress-learning interval is extended (e.g. 30 min). Glucocorticoids initiate a gene-mediated pathway which will bring the brain in a "consolidation mode" and suppress the processing of unrelated information. If encoding occurs some time after stressor exposure, this gene-mediated process will have developed and learning will be most likely impaired (Joels et al., 2006).

Finally, three study limitations have to be addressed. First, because women's cortisol responses to stress depend critically on menstrual cycle phase (Kirschbaum et al. 1999) we studied only oral contraceptives using women to increase homogeneity in our sample. However, women taking oral contraceptives show usually blunted cortisol responses compared to men which is most likely owing to an ethinyl-estradiol induced increase in corticosteroid-binding globulin (CBG) which in turn lowers salivary (i.e. free) cortisol levels (Kirschbaum et al., 1999; Kirschbaum, Platte, Pirke, & Hellhammer, 1996). Therefore, it is questionable whether the present findings for men and women can be compared. Second, the stress manipulation was announced to the cold pressor group at the beginning of the study. Thus, different expectations in the control and stress group might be potentially confounded with the results. Second, a more consistent control task during the waiting period might be valuable in future studies because

this could help to avoid possible differences in rumination about the presented material.

For decades, the effects of stress on memory function have been viewed as mainly disruptive (e.g. Sapolsky, 1996). Results from this experiment extend previous reports indicating that stress may also have enhancing effects on memory formation and suggest a differential involvement of specific stress components, autonomic activity and stress-induced cortisol, in these effects, depending on the emotional valence of the learned material.

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## References

Abercrombie, H. C., Kalin, N. H., Thurow, M. E., Rosenkranz, M. A., & Davidson, R. J. (2003). Cortisol variation in humans affects memory for emotionally laden and neutral information. *Behavioral Neuroscience, 117*, 505–516.

Aerni, A., Traber, R., Hock, C., Roozendaal, B., Schelling, G., Papassotiropoulos, A., et al. (2004). Low-dos cortisol for symptoms of posttraumatic stress disorder. *American Journal of Psychiatry, 161*, 1488–1490.

Baldi, E., & Bucherelli, C. (2005). The inverted "u-shaped" dose-effect relationships in learning and memory: Modulation of arousal and consolidation. *Nonlinearity in Biology, Toxicology, and Medicine, 3*, 9–21.

Buchanan, T. W., & Lovallo, W. R. (2001). Enhanced memory for emotional material following stress-level cortisol treatment in humans. *Psychoneuroendocrinology, 26*, 307–317.

Buchanan, T. W., & Tranel, D. (2008). Stress and emotional memory retrieval: Effects of sex and cortisol response. *Neurobiology of Learning and Memory, 89*, 134–141.

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

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

Cai, W. H., Blundell, J., Han, J., Greene, R. W., & Powell, C. M. (2006). Postreactivation glucocorticoids impair recall of established fear memory. *The Journal of Neuroscience, 26*, 9560–9566.

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd ed.). Hillsdale: Lawrence Erlbaum.

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

De Quervain, D. J., Aerni, A., & Roozendaal, B. (2007). Preventive effect of β-adrenoceptor blockade on glucocorticoid-induced memory retrieval deficits. *American Journal of Psychiatry, 164*, 967–969.

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

Diamond, D. M., Campbell, A. M., Park, C. R., Halonen, J., & Zoladz, P. R. (2007). The temporal dynamics model of emotional memory processing: A synthesis on the neurobiological basis of stress-induced amnesia, flashbulb and traumatic memories, and the Yerkes–Dodson law. *Neural Plasticity, 2007*, 1–33.

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., Heinrichs, M., Reichwald, U., & Hautzinger, M. (2002). Hypothalamic-pituitary-adrenal axis reactivity to psychosocial stress and memory in middle-aged women: High responders exhibit enhanced declarative memory performance. *Psychoneuroendocrinology, 27*, 843–853.

Dressendorfer, R. A., & Kirschbaum, C. (1992). Synthesis of a cortisol–biotin conjugate and evaluation as a tracer in an immunoassay for salivary cortisol measurement. *The Journal of Steroid Biochemistry and Molecular Biology, 43*, 683–692.

Dudai, Y. (2006). Reconsolidation: The advantage of being refocused. *Current Opinion in Neurobiology, 16*, 174–178.

Elzinga, B. M., Bakker, A., & Bremner, J. D. (2005). Stress-induced cortisol elevations are associated with impaired delayed, but not immediate recall. *Psychiatry Research, 134*, 211–223.

Fehm-Wolfsdorf, G., Soherr, U., Arndt, R., Kern, W., Fehm, H. L., & Nagel, D. (1993). Auditory reflex thresholds elevated by stress-induced cortisol secretion. *Psychoneuroendocrinology, 18*, 579–589.

Gallagher, M., & Chiba, A. A. (1996). The amygdala and emotion. *Current Opinion in Neurobiology, 6*, 221–227.

Garavan, H., Pendergrass, J. C., Ross, T. J., Stein, E. A., & Risinger, R. C. (2001). Amygdala response to both positively and negatively valenced stimuli. *NeuroReport, 12*, 2779–2783.

Hamann, S., & Mao, H. (2002). Positive and negative emotional verbal stimuli elicit activity in the left amygdala. *NeuroReport, 13*, 15–19.

Het, S., Ramlow, G., & Wolf, O. (2005). A meta-analytic review of the effects of acute cortisol administration on human memory. *Psychoneuroendocrinology, 30*, 771–784.

Joels, M., Pu, Z., Wiegert, O., Oitzl, M. S., & Krugers, H. J. (2006). Learning under stress: How does it work? *Trends in Cognitive Sciences, 10*, 152–158.

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*, 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., Platte, P., Pirke, K. M., & Hellhammer, D. H. (1996). Adrenocortical activation following stressful exercise: Further evidence for attenuated free cortisol responses in women using oral contraceptives. *Stress Medicine, 1996*, 137–143.

Kirschbaum, C., Pruessner, J. C., Stone, A. A., Federenko, I., Gaab, J., Lintz, D., et al. (1995). Persistent high cortisol responses to repeated psychological stress in a subpopulation of healthy men. *Psychosomatic Medicine, 57*, 468–474.

Kirschbaum, C., Wolf, O. T., May, M., Wippich, W., & Hellhammer, D. H. (1996). Stress- and treatment-induced elevations of cortisol levels associated with impaired declarative memory in healthy adults. *Life Science, 58*, 1475–1483.

Kudielka, B. M., Schommer, N. C., Hellhammer, D. H., & Kirschbaum, C. (2004). Acute HPA axis responses, heart rate, and mood changes to psychosocial stress (TSST) in humans at different times of day. *Psychoneuroendocrinology, 29*, 983–992.

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

LeDoux, J. E. (2000). Emotion circuits in the brain. *Annual Review of Neuroscience, 23*, 155–184.

Lupien, S., & McEwen, B. S. (1997). The acute effects of corticosteroids on cognition: Integration of animal and human model studies. *Brain Research Reviews, 24*, 1–27.

Lupien, S. J., Gaudreau, S., Tchiteya, B. M., Maheu, F., Sharma, S., Nair, N. P., et al. (1997). Stress-induced declarative memory impairment in healthy elderly subjects: Relationships to cortisol reactivity. *Journal of Clinical Endocrinology and Metabolism, 82*, 2070–2075.

Maroun, M., & Akirav, I. (2008). Arousal and stress effects on consolidation and reconsolidation of recognition memory. *Neuropsychopharmacology, 33*, 394–405.

McGaugh, J. L. (2006). Make mild moments memorable: Add a little arousal. *Trends in Cognitive Sciences, 10*, 345–347.

McGaugh, J. L., Cahill, L., & Roozendaal, B. (1996). Involvement of the amygdala in memory storage: Interaction with other brain systems. *Proceedings of the National Academy of Science USA, 93*, 13508–13514.

Nader, K., Schafe, G. E., & LeDoux, J. E. (2000). The labile nature of consolidation theory. *Nature Reviews Neuroscience, 1*, 216–219.

Nater, U. M., Moor, C., Okere, U., Stallkamp, R., Martin, M., Ehlert, U., et al. (2007). Performance on a declarative memory task is better in high than low cortisol responders to psychosocial stress. *Psychoneuroendocrinology, 32*, 758–763.

Nielson, K. A., Radtke, R. C., & Jensen, R. A. (1996). Arousal-induced modulation of memory storage processes in humans. *Neurobiology of Learning and Memory, 66*, 133–142.

Payne, J. D., Jackson, E. D., Ryan, L., Hoscheidt, S., Jacobs, W. J., & Nadel, L. (2006). The impact of stress on neutral and emotional aspects of episodic memory. *Memory, 14*, 1–16.

Roozendaal, B. (2000). 1999 Curt P. Richter award. Glucocorticoids and the regulation of memory consolidation. *Psychoneuroendocrinology, 25*, 213–238.

Roozendaal, B., Okuda, S., Van der Zee, E. A., & McGaugh, J. L. (2006). Glucocorticoid enhancement of memory requires arousal-induced noradrenergic activation in the basolateral amygdala. *Proceedings of the National Academy of Science USA, 103*, 6741–6746.

Sandi, C., Loscertales, M., & Guaza, C. (1997). Experience-dependent facilitating effect of corticosterone on spatial memory formation in the water maze. *European Journal of Neuroscience, 9*, 637–642.

Sapolsky, R. M. (1996). Why stress is bad for your brain. *Science, 273*, 749–750.

Sara, S. J. (2000). Strengthening the shaky trace through retrieval. *Nature Reviews Neuroscience, 1*, 212–213.

Smeets, T., Giesbrecht, T., Jelicic, M., & Merckelbach, H. (2007). Context-dependent enhancement of declarative memory performance following acute psychosocial stress. *Biological Psychology, 76*, 116–123.

Soravia, L. M., Heinrichs, M., Aerni, A., Maroni, C., Schelling, G., Ehlert, U., et al. (2006). Glucocorticoids reduce phobic fear in humans. *Proceedings of the National Academy of Science USA, 103*, 5585–5590.

Tops, M., van der Pompe, G., Baas, D., Mulder, L. J., den Boer, J. A., Meijman, T. F., et al. (2003). Acute cortisol effects on immediate free recall and recognition of nouns depend on stimulus-valence. *Psychophysiology, 40*, 167–173.

Wickens, T. D. (2002). *Elementary signal detection theory*. Oxford: University Press.