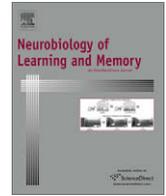




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## Post-learning psychosocial stress enhances consolidation of neutral stimuli

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### ABSTRACT

Post-learning stress has been reported to enhance memory consolidation in humans. This effect was observed in studies using physical stressors or an anticipatory speech task. In the present study 58 participants (28 females and 30 males) were exposed to a psychosocial stressor (Trier Social Stress Test) or a control condition following the presentation of neutral and emotionally arousing positive and negative pictures, which were accompanied by a brief narrative. The stressor induced a significant neuroendocrine stress response in men and women. In a 24 h delayed free recall test the stress group showed an enhanced memory for neutral but not for emotionally arousing positive and negative items. Additionally, a significant correlation between the cortisol stress response and memory for neutral items was evident. Thus, in contrast to previous studies, post-learning stress primarily enhanced consolidation of neutral material. Several theoretical and methodological explanations for the observed effects are discussed.

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### 1. Introduction

We know from everyday experiences that stressful events are well remembered and experimental laboratory research has shown that stress influences memory (Wolf, 2008). The modulatory effects of stress on memory are caused by the release of stress hormones. The activation of the sympathetic nervous system (SNS) in response to stress results in a release of catecholamines. Additionally, the hypothalamic-pituitary (HPA) axis is activated, which results in the release of glucocorticoids (GCs; de Kloet, Joels, & Holsboer, 2005).

The effects of stress on memory depend on the particular memory phase influenced by stress (Roozendaal, Okuda, de Quervain, & McGaugh, 2006; Wolf, 2008). Additionally, it became apparent that stress differs depending on whether it is related to the learning situation or is outside the learning context (Joels, Pu, Wiegert, Oitzl, & Krugers, 2006). Increasing the stressfulness of a learning episode was found to enhance memory in rodents (Akirav et al., 2004; Akirav, Sandi, & Richter-Levin, 2001; Sandi, Loscertales, & Guaza, 1997). Akirav et al. (2004) for example observed that rats performed better in a spatial task (Morris Water Maze) when the situation was so designed as to be more stressful (colder water temperature). The authors could demonstrate that this memory enhancement was due to the release of corticosterone. Similarly, glucocorticoids injected immediately after acquisition (post-learning)

and thereby influencing memory consolidation were found to enhance consolidation of newly learned material (Roozendaal, de Quervain, Ferry, Setlow, & McGaugh, 2001; Roozendaal, Nguyen, Power, & McGaugh, 1999).

The empirical picture becomes more complex when stressor and learning task are not directly associated and the stressor is detached from the learning episode. This is the case when the animal receives foot shocks or is exposed to a predator before or after learning a maze task (e.g. Park, Zoladz, Conrad, Fleshner, & Diamond, 2008).

Similarly, in human studies, the stressor (e.g. cold water immersion or a public speech) is typically unrelated to the memory tests conducted (e.g. Beckner, Tucker, Delville, & Mohr, 2006; Cahill, Gorski, & Le, 2003; Wolf, Schommer, Hellhammer, McEwen, & Kirschbaum, 2001). When reviewing previous human studies using this approach pre-learning and post-learning stress exposure need to be differentiated.

With respect to pre-learning stress, enhancing as well as impairing effects have been observed. The direction of the effects appears to depend on several variables. The delay between stress exposure and the learning episode (Diamond, Campbell, Park, Halonen, & Zoladz, 2007) and the delay between initial learning and recall (immediate vs. delayed recall; Elzinga, Bakker, & Bremner, 2005) have turned out to be important variables. Moreover the emotionality of the learning material has been reported to influence the outcome in that, although pre-learning stress impaired neutral memory, it often enhanced emotional memory (Jelici, Geraerts, Merckelbach, & Guerrieri, 2004; Payne, Jackson, Hoscheidt, Ryan, Jacobs, et al., 2007; Schwabe, Bohringer, Chatterjee, & Schachinger, 2008).

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For post-learning stress exposure, the empirical picture is more homogenous and reveals mostly enhancing effects. Several human studies observed that immediate post-learning stress either with the cold pressure test (CPT; Andreano & Cahill, 2006; Cahill et al., 2003; Smeets, Otgaar, Candel, Wolf, 2008) or with an anticipatory speech stressor (Beckner et al., 2006) led to enhanced memory consolidation. In those studies which used negative as well as neutral learning material, the effect was only found for the emotionally arousing negative items (Cahill et al., 2003; Smeets, Otgaar, Candel, & Wolf, 2008). In line with these stress studies we recently reported that basal cortisol levels were specifically associated with enhanced memory for emotional items (Preuss, Schoofs, Wolf, & emotional memory: influence of encoding instructions. *Stress*, in press). However, the beneficial effects of post-learning stress on memory consolidation have also been reported in studies where only neutral learning material was employed (Andreano & Cahill, 2006; Beckner et al., 2006).

An impact of sex on the relationship between stress and memory has been reported in previous research. One aspect is that the HPA stress response to performance based laboratory stressors is influenced by sex. Men often show a more salient response than women (Kirschbaum, Kudielka, Gaab, Schommer, & Hellhammer, 1999; Kirschbaum, Wust, & Hellhammer, 1992; Stroud, Salovey, & Epel, 2002) but contrary results have also been reported (Kelly, Tyrka, Anderson, Price, & Carpenter, 2008). Additionally there are not only sex differences in the HPA reactivity to psychosocial stress but also sex differences for the influence of stress on memory or emotional learning. The effects of GCs here were repeatedly found to be more pronounced for men than for women (Andreano & Cahill, 2006; Cahill, 2003; Jackson, Payne, Nadel, & Jacobs, 2006; Stark, Wolf, Tabbert, Kagerer, Zimmermann, et al., 2006; Wolf et al., 2001; Zorawski, Blanding, Kuhn, & LaBar, 2006). Possible sex differences should therefore be considered when exploring the influence of stress on memory (Cahill, 2006; Wolf, 2008).

Building up on recent findings in the field the present study was conducted to further clarify the influence of stress on consolidation. Existing studies evaluating the influence of stress on consolidation processes have either used a physical stressor (Andreano & Cahill, 2006; Cahill et al., 2003; Smeets et al., 2008) or an anticipatory speech stressor where the speech itself had not to be performed (Beckner et al., 2006). To date, no experiment has systematically assessed the influence of the Trier Social Stress Test (TSST, Kirschbaum, Pirke, & Hellhammer, 1993) on memory consolidation. This stressor typically leads to a more pronounced cortisol stress response compared to the CPS or anticipatory speech stressors used in previous consolidation studies (Beckner et al., 2006; Cahill et al., 2003; Kirschbaum et al., 1993; Kuhlmann, Piel, & Wolf, 2005; van Stegeren, Wolf, & Kindt, 2008). In addition it has a stronger 'cognitive load', since the subjects have to deliver a speech and work on a mathematical task. The aim of the present study was to evaluate the effects of post-learning stress on memory consolidation. Based on previous observations, as summarized above, the factors emotional arousal of the learning material as well as sex of the participants was taken into account.

## 2. Materials and methods

### 2.1. Participants

Participants were 30 healthy men and 30 healthy free cycling women. Women were tested during the whole menstrual cycle except menses. Two outliers with data above or below 2, 5 standard deviations in immediate memory recall scores had to be

excluded and the data of 58 participants (28 female, 30 male) was analyzed. Women were between the age of 19 and 28 (mean age  $23.68 \pm 0.45$ ). Men were between the age of 20 and 29 (mean age  $23.53 \pm 0.48$ ). Mean body mass index for the men was  $24.12 (\pm 0.45)$  and for the women  $21.56 (\pm 0.49)$ . Participants were excluded if they reported any use of medicaments that could have influenced the hormonal stress response (e.g. antibiotics, and antihistamines). Women were free of hormonal contraception. All participants were recruited at the university campus and written informed consent was collected from each subject. The study was approved by the national ethic committee of the German Psychological Association (Deutsche Gesellschaft für Psychologie).

### 2.2. Materials

#### 2.2.1. Stimuli

The stimuli and memory tests used in the present study were developed and validated by Buchanan, Karafin, and Adolphs (2003). The material, recently translated by our group, had been used in a first study testing the associations between basal cortisol levels and emotional memory (Preuss et al., in press). The stimuli consisted of five positive (e.g. two happy girls eating ice-cream), five negative (e.g. a diseased child from Africa with bandages and cannulae) and five neutral (e.g. people leaving or entering a building) pictures, each presented in a random order for a duration of 10 sec on a computer screen. Several of these pictures were chosen from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 1997) and the remaining drawn from print media sources. Each picture was accompanied by a single narrative sentence which consisted information that was not obvious in the picture. For example the picture with the little girls eating ice-cream was accompanied by a sentence in which the girls' names and the special kind of ice-cream they preferred being mentioned.

#### 2.2.2. Memory tasks

Participants solved several written memory tests.

#### 2.2.3. Immediate recall test

The immediate free recall test took place immediately after the presentation of the pictures. Participants were asked to write down everything they remembered from the pictures and narratives. Time was restricted to 5 min. Answers were evaluated by two independent judges. Differences in test scores were discussed and were solved by a third judge. A participant received three points, if the information noted could be clearly associated to one of the pictures and was correct in details. Two points were given for information that could be clearly associated to one of the pictures but consisted of some wrong details. If the information was completely wrong or could not be linked to one picture, participants got one point. A total of 45 points could be achieved.

#### 2.2.4. Delayed recall test

On the second day, 24 h after presentation of the pictures, the delayed free recall test was conducted. Again, participants were given 5 min to write down everything they remembered from the pictures and narratives. Answers were evaluated in the same manner as in the immediate recall test.

#### 2.2.5. Multiple choice test

This task consisted of six questions asking for information pertaining to pictures and narratives for each stimulus. In this task every correct answer scored a point, so that a total of 90 points was possible.

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