

The effects of cortisol increase on long-term memory retrieval during and after acute psychosocial stress

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Abstract

In this study the effects of stress-induced cortisol increases on long-term memory retrieval during and after acute psychosocial stress were examined. Seventy male students were exposed to either a psychosocial stress task or to a non-stressful control task. During and after this task, retrieval was tested for idiosyncratic emotionally negative and neutral word pair associations that were learned 1 day or 5 weeks earlier. Within the stress condition, retrieval of negative words, 5 weeks after learning, was impaired both during and after the stress task compared to the control group. Further, during the stress task, when sympathetic activity was enhanced, impaired retrieval of both neutral and emotional words was significantly related to enhanced cortisol response. In contrast, after the stress task, when cortisol levels were still increased but sympathetic activity was low again, no association was found between cortisol increase and retrieval of either neutral or emotional material. These results are in line with the previous animal research showing that when arousal is high, cortisol increase can impair memory retrieval.

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1. Introduction

Glucocorticoid (GC) hormones and catecholamines are secreted by adrenal glands during stressful or emotional experiences. Besides regulating the bodily response to a challenging environment (Sapolsky, Romero, & Munck, 2000), these hormones also influence cognitive functions (de Kloet, Oitzl, & Joels, 1999; Roozendaal, 2002). One of the cognitive functions that is sensitive to stress hormones is memory, due to a high number of mineralocorticoid (MR) and glucocorticoid (GR) receptors in brain structures that play an important role in memory functioning, including the hippocampus, amygdala and prefrontal

cortex (see Wolf, 2008; de Kloet et al., 1999; Kirschbaum, Wolf, May, Wippich, & Hellhammer, 1996; Lupien & Lepage, 2001; Roozendaal, 2002).

While learning seems to be facilitated by increased levels of stress hormones (Andreano & Cahill, 2006; Buchanan & Lovallo, 2001; Cahill, Gorski, & Le, 2003; Kuhlmann & Wolf, 2006a), retrieval of previously learned material has repeatedly been found to deteriorate with increased levels of GCs. That is, placebo controlled studies administering exogenous doses of cortisol to humans have consistently found impaired memory retrieval (Buss, Wolf, Witt, & Hellhammer, 2004; de Quervain, Roozendaal, Nitsch, McGaugh, & Hock, 2000; Domes, Rothfischer, Reichwald, & Hautzinger, 2005; Het, Ramlow, & Wolf, 2005; Kuhlmann, Kirschbaum, & Wolf, 2005; Wolf et al., 2001). Other studies have used a psychosocial stress task like the Trier Social Stress Task (TSST: Kirschbaum, Pirke, &

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Hellhammer, 1993) to study the effects of endogenous cortisol increases on memory retrieval. Results are similar to, but less consistent than the pharmacological studies (Domes, Heinrichs, Rimmele, Reichwald, & Hautzinger, 2004; Kuhlmann, Piel, & Wolf, 2005; Oei, Everaerd, Elzinga, van Well, & Bermond, 2006; Wolf, Schommer, Hellhammer, Reischies, & Kirschbaum, 2002). While Kuhlmann et al. (2005) found impairing effects of stress on memory retrieval of both negatively and positively valenced (or arousing) material, Domes et al. (2004) found this effect only on the recognition of positive material. Oei et al. (2006) found a relation between increasing cortisol levels and impaired retrieval of only moderately and not highly arousing material, while Wolf et al. (2002) did not find any effect of stress or cortisol increase on the retrieval of neutral material.

The discrepancy between findings of pharmacological and psychosocial stress studies may be related to the level of cortisol, as cortisol levels obtained in stress studies are generally much lower than after exogenous administration of cortisol. However, the effects of endogenous cortisol levels on memory retrieval may also depend on several other modulating variables, e.g. the arousing properties of the material, concurrent activation of the noradrenergic system, and the time interval between learning and retrieval. Each of these variables will be discussed briefly.

First of all, stress-induced cortisol increases are found to affect retrieval of emotionally arousing material more than neutral material (Domes et al., 2004; Kuhlmann et al., 2005), possibly explaining the non-results of Wolf et al. (2002) using only neutral material. Recent animal studies have pointed to the role of the noradrenergic system in mediating the cortisol effects on retrieval. A number of such studies have shown that noradrenergic activation of the basolateral amygdala is necessary for effects of cortisol to occur on memory functioning in general, including memory retrieval (Roozendaal, de Quervain, Schelling, & McGaugh, 2004; Roozendaal, Griffith, Buranday, de Quervain, & McGaugh, 2003; Roozendaal, Hahn, Nathan, de Quervain, & McGaugh, 2004). This adrenergic activity could be elicited either by intrinsic arousing properties of the learned material (explaining the effects on emotional versus neutral material), or by the level of arousal induced by the environment, such as novelty stress (Okuda, Roozendaal, & McGaugh, 2004). In fact, a study by Elzinga and Roelofs (2005) has shown that in humans, cortisol-induced working memory impairments are only found under acute stress conditions, when sympathetic activation (as a measure of adrenergic activity) is elevated. They differentiated between a situation of acute psychosocial stress, during which participants had to perform in front of an audience (when both sympathetic activation and cortisol levels were high), and a situation where cortisol levels were high, while sympathetic activation was back to basal levels, that is, after the stress task. High cortisol responders showed impaired working memory compared to low cortisol responders only during, but not after the stress task.

Testing after the stress task, when the audience has left and participants have been able to recover, is the usual approach in studies investigating the effects of psychosocial stress (and related cortisol increase) on memory functioning. Conflicting reports regarding the role of endogenous cortisol increases on memory retrieval might thus be due to the level of arousal that participants experience at the time of memory testing.

Two human studies have looked into the effects of arousal elicited by the testing situation in combination with cortisol increases during memory retrieval. Buchanan, Tranel, and Adolphs (2006) measured skin conductance (as a measure of sympathetic activity) and cortisol levels in response to a cold pressure test, after which memory retrieval was tested. They found that increased cortisol levels, but not the skin conductance levels, were related to impaired memory retrieval. From this study, however, we cannot conclude whether sympathetic arousal is necessary for the impairing effects of cortisol increases on memory retrieval to occur. Recently however, Kuhlmann and Wolf (2006b) reported a comparison of studies in which arousal related to the testing environment was manipulated while testing the effect of exogenous cortisol on retrieval. They compared two of their previous studies (Kuhlmann et al., 2005; Kuhlmann & Wolf, 2005) that were conducted in a standard formal testing situation, with a highly similar study in which they had changed the testing situation into a more relaxing, non-arousing, environment. The impairing effect of administered cortisol on retrieval that was found earlier in the standard formal testing situations did not occur in the more relaxed setting. While these results may suggest that in humans, adrenergic activation is also necessary for the effect of cortisol to occur on memory retrieval, they did not assess sympathetic activity (or a more direct measure of adrenergic activity) in their participants, and hence it remains undecided whether the different findings are indeed related to differences in sympathetic arousal levels.

Another factor that could influence the effect of cortisol on memory retrieval is the time frame between learning and recall. The usual paradigm in retrieval studies is to test recall of material that has been learned a few hours to a day before, not always allowing a clear separation between consolidation and retrieval processes. Whether memory retrieval remains sensitive to the effects of stress long time after learning is a topic that has not been well studied. To date, only the study of Wolf et al. (2002) examined the effects of a social stress task on the retrieval of material learned 4 weeks earlier. They did not find any effects of stress or cortisol increase on long-term memory retrieval, but this could also have been due to the nature of material that was learned (e.g., not emotionally arousing) and the testing situation (e.g. the arousing stressor was no longer present at the time of retrieval testing). Another issue might have been a floor effect, with only few words remembered after 4 weeks.

In summary, further work is clearly required taking into account the factors described above. The study we describe

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