

Cortisol and Memory Retrieval in Humans

Influence of Emotional Valence

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ABSTRACT: Glucocorticoids secreted in response to stress modulate memory in animals and humans. Studies in rodents suggest that glucocorticoids enhance memory consolidation but impair delayed retrieval. Similar negative effects on memory retrieval have been reported in humans. The human studies so far have not addressed the issue of emotional valence, which conceivably could modulate the effects of cortisol on retrieval. The present mini-review discusses two recent studies from our laboratories that investigate the influence of emotional valence on the retrieval-impairing effects of cortisol. Both studies observed that cortisol impaired retrieval and that emotional valence influenced these effects. For autobiographical memory the impairing effects were stronger for neutral than for emotional items, whereas for word retrieval the opposite pattern was observed (stronger effects on emotional words). Possible reasons for these results are the different memory domains tested as well as the different sex of the subjects. Future studies will address these issues, which are of relevance for psychiatric disorders such as posttraumatic stress disorder or major depression.

KEYWORDS: cortisol; memory; retrieval; emotional valence

Studies in rodents have established that glucocorticoids (GCs) acutely modulate memory, the effects being influenced, among others, by the timing of GC administration and the used memory paradigms.¹⁻⁴ Roozendaal and McGaugh demonstrated in their elegant studies that GCs interact with beta-adrenergic activation in the basal lateral nucleus of the amygdala (BLA) to modulate memory stored in other parts of the brain (e.g., hippocampus).³ Their studies indicated that GCs enhance memory consolidation for a wide range of paradigms.³ However, GCs administered before memory retrieval had an impairing effect, a process again relying on the BLA.⁵ Studies in humans by de Quervain and colleagues and by our group^{6,7} could replicate the negative effects of GCs on memory retrieval for neutral words. However,

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negative effects of GC administration in humans have also been observed when GCs were given before the initial learning of declarative memory tasks and/or before working memory tasks.^{2,4}

Experimental studies in healthy human subjects as well as in patients with brain damage have repeatedly shown that emotional material (words, slides, or stories) is better remembered than neutral material. Again, beta-adrenergic activation in the amygdala is an important mediating factor in this process (see Ref. 8 for a recent review). Based on the empirical evidence just outlined, it is conceivable that the emotional valence of the learning material might also modulate the effects of GCs on memory in humans.

Buchanan and Lovallo⁹ tested the effects of cortisol administration before an incidental learning task (recall 1 week later) of positive, neutral, and negative slides. One week later, they observed in the cued recall condition that cortisol enhanced memory for those slides rated as "arousing" by the subjects.⁹ A second study, however, failed to find an effect of stimulus valence tested with negative and neutral words as well as with negative and neutral slides.¹⁰ Differences in the memory task as well as the testing time might account for those discrepancies. A third study investigated the effects of cortisol administration on immediate recall of positive, neutral, and negative words. The authors observed that cortisol impaired immediate recall of neutral and positive words, but not of negative words.¹¹

Two independent studies from our laboratories tested whether the impairing effects of cortisol on memory retrieval might also be modulated by emotional valence. In the first study, effects of oral cortisol administration on the autobiographical cuing test were studied in a sample of 22 young men using a placebo-controlled double-blind crossover design. One hour after cortisol ingestion, subjects retrieved significantly ($P < .05$) fewer specific episodes from their autobiographical memory. Exploratory followup analysis revealed that cortisol significantly impaired retrieval of neutral episodes, whereas only a trend was observed for an impaired retrieval of positive or negative episodes.¹²

The second study investigated the effects of cortisol administration on retrieval of a word list learned 5 hours earlier. The word list contained neutral as well as negative words. Again, a double-blind placebo-controlled design was chosen, but this time young women ($n = 16$) were studied. Cortisol significantly impaired delayed free recall of the word list ($P < .05$). Exploratory followup analysis detected that recall of emotional (negative) words was significantly impaired, whereas recall of neutral words only tended to be impaired.¹³

Taken together, both studies observed an impairing effect of cortisol on memory retrieval, which is in line with recent animal as well as human studies.⁵⁻⁷ In addition, both experiments indicated that the emotional and neutral material was differentially affected by cortisol, even though the direction of the effect differed between the two studies. Reasons for this might be differences in the tasks (autobiographical memory retrieval versus retrieval of a previously learned word list [episodic memory]) as well as differences in the subjects (men versus women). Ongoing studies will systematically investigate these issues.

The effects of stress hormones on emotional memory might play an important role in the development of several psychiatric disorders such as posttraumatic stress disorder (PTSD) and depression. Additional studies in animals and humans are needed to further characterize the neurobiological mechanisms involved. In humans,

neuroimaging studies as well as clinical studies in psychiatric patients appear to be especially promising.

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