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# Hypothalamic–pituitary–adrenal axis reactivity to psychological stress and memory in middle-aged women: high responders exhibit enhanced declarative memory performance

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**Abstract**

According to recent studies, elevated cortisol levels are associated with impaired declarative memory performance. This specific effect of cortisol has been shown in several studies using pharmacological doses of cortisol. The present study was designed to determine the effects of endogenously stimulated cortisol secretion on memory performance in healthy middle-aged women. For psychological stress challenging, we employed the Trier Social Stress Test (TSST). Subjects were assigned to either the TSST or a non-stressful control condition. Declarative and non-declarative memory performance was measured by a combined priming–free-recall-task. No significant group differences were found for memory performance. Post hoc analyses of variance indicated that regardless of experimental condition the subjects with remarkably high cortisol increase in response to the experimental procedure (high responders) showed increased memory performance in the declarative task compared to subjects with low cortisol response (low responders). The results suggest that stress-induced cortisol failed to impair memory performance. The results are discussed with respect to gender-specific effects and modulatory effects of the sympathetic nervous system and psychological variables. 

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## 1. Introduction

Glucocorticoids are released from the adrenals as an effect of the activation of the pituitary by hypothalamic releasing hormones. The hypothalamic–pituitary–adrenal (HPA) axis is one of the major hormonal systems, which is activated under physiological as well as psychological stress. The hippocampus is a major target for glucocorticoids as it contains the highest concentrations of specific glucocorticoid receptors within the brain. It plays a crucial role in regulating basal and evoked HPA-axis activity (Jacobson and Sapolsky, 1991). Moreover, there is evidence that the hippocampus is involved in declarative memory function (Squire, 1992; Eichenbaum and Cohen, 1992). Glucocorticoids are known to influence neuronal metabolism, physiological function and genomic processes in the brain, including synaptic and dendritic changes and inhibition of glucose transport and metabolism, especially in the hippocampus (McEwen and Magarinos, 1997).

Today, there is increasing evidence from clinical and experimental studies that glucocorticoids have negative effects on human cognitive function, especially declarative memory (Lupien and McEwen, 1997). Patients with Cushing's disease show cognitive symptoms including decreased memory performance (Whelan et al., 1980; Starkman and Schteingart, 1981Starkman et al., 1986, 1992) which seem to refer to the high cortisol levels in this disease. Some investigators report that patients who develop a syndrome called "steroid psychosis" under high-dose glucocorticoid treatment show attention and concentration deficits and decreased mental speed (Ling et al., 1981; Varney et al., 1984; Wolkowitz et al., 1997). Case-control studies indicate decreased memory performance under prednisone treatment (Bender et al., 1991; Keenan et al., 1996). Finally, there are results that show an inverse relationship between plasma concentrations of cortisol and memory performance in dementia of Alzheimer type, depression, and schizophrenia (Newcomer et al., 1998; Rubinow et al., 1984; Jenike and Albert, 1984).

Studies on cognitive effects of synthetic glucocorticoid agonists in healthy humans indicate that pharmacological doses of prednisone and dexamethasone impair declarative memory performance (Wolkowitz et al., 1990; Newcomer et al., 1994). Some investigators found single high doses of cortisol given orally decreased declarative memory (Beckwith et al., 1986; Kirschbaum et al., 1996a), whereas others could not show such effects (Beckwith et al., 1986; Fehm-Wolfsdorf et al., 1993). Cortisol administration for four days resulting in plasma free cortisol concentrations similar to stress levels impairs declarative memory (Newcomer et al., 1999). De Quervain and colleagues showed cortisol to impair memory performance only when given before retrieval while there was no effect of cortisol on acquisition or consolidation (De Quervain et al., 2000). Other studies using a laboratory stressor to induce endogenous cortisol secretion indicate negative correlations between con-