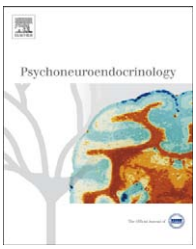
Psychoneuroendocrinology (2008) **33**, 643–653

Available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/psyneuen



Psychosocial stress induces working memory impairments in an *n*-back paradigm

Daniela Schoofs, Diana Preuß, Oliver T. Wolf*

Department of Cognitive Psychology, Ruhr-University Bochum, Universitätsstr. 150, D-44780 Bochum, Germany

Received 24 October 2007; received in revised form 11 February 2008; accepted 12 February 2008

KEYWORDS
Working memory;
n-Back paradigm;
Psychosocial stress;
HPA;
SNS;
Prefrontal cortex

Summary
In contrast to the substantial number of studies investigating the effects of stress on declarative memory, effects of stress on working memory have received less attention. We compared working memory (numerical *n*-back task with single digits) in 40 men exposed either to psychosocial stress (Trier Social Stress Test (TSST)) or a control condition. Task difficulty was varied using two conditions (2-back vs. 3-back). Salivary cortisol (as a marker of hypothalamus–pituitary–adrenal (HPA) activity) and salivary alpha-amylase (sAA as a marker of sympathetic nervous system (SNS) activity) were assessed immediately before and three times after the stress or control condition. As expected stress resulted in an increase in cortisol, sAA, and negative affect. Subjects exposed to stress showed significant working memory impairments in both workload conditions. The analysis of variance indicated a main effect of stress for reaction time as well as accuracy. In addition, for reaction time a stress × block interaction occurred. Follow up tests revealed that only during the first block at each level of difficulty performance was significantly impaired by stress. Thus, the effects of stress became smaller the longer the task was performed. Results provide further evidence for impaired working memory after acute stress and illustrate the time course of this phenomenon.

1. Introduction

Stress leads to activation of the sympathetic nervous system (SNS) and an increased activity of the hypothalamic–pituitary–adrenal axis (HPAA; de Kloet et al., 2005). The first rapid response of the SNS is mediated via the catecholamines adrenaline and noradrenaline. The second somewhat slower stress response consists of activation of the HPAA and leads to the release of glucocorticoids from the adrenal cortex (GCs; cortisol in humans; corticosterone in rodents).

Numerous studies have demonstrated that acute stress or elevated SNS and/or GC concentrations affect learning and memory in animals and humans (LaBar and Cabeza, 2006; Wolf, 2006; Roozendaal et al., 2006). Stress can result in enhancing as well as impairing effects on declarative long-term memory (Wolf, 2006; Roozendaal et al., 2006; Joels et al., 2006; Lupien et al., 2007). The direction of the effect appears to depend primarily on the phase of

*Corresponding author. Tel.: +49 234 32 22670; fax: +49 234 32 14308.
E-mail address: oliver.t.wolf@rub.de (O.T. Wolf).

0306-4530/$ - see front matter © 2008 Published by Elsevier Ltd.
doi:10.1016/j.psyneuen.2008.02.004

declarative memory affected. While the consolidation of emotional material is enhanced by stress, delayed retrieval of previously learned material is impaired (Wolf, 2006, 2008; Roozendaal et al., 2006; Lupien et al., 2007). Those effects appear to be caused by the action of glucocorticoids on GC sensitive receptors in the amygdala and hippocampus (Roozendaal, 2002; Joels et al., 2006; Diamond et al., 2007). However, findings suggested that the modulation of memory functions through GCs require concurrent SNS activity. Animal and human studies observed a dependence of the level of arousal and/or adrenergic activity during testing on the GC effects on declarative memory (Abercrombie et al., 2006; Kuhlmann and Wolf, 2006a, b; de Quervain et al., 2007).

While the effects of stress on declarative memory have received considerable attention fewer studies tested its influence on working memory (WM). The concept of WM refers to the structures and processes used for temporarily maintaining, updating, and manipulating information (Baddeley, 2003). Multiple studies indicate that these processes mainly rely on the integrity of the prefrontal cortex (PFC) (Fuster, 2000; Petrides, 2000; Muller and Knight, 2006) and parietal structures (Baldo and Dronkers, 2006), although this view is not without controversy (Andres, 2003).

Evidences from histopathological studies in rodents, monkeys, and humans indicate a large number of glucocorticoid receptors within the PFC and thus suggest that the PFC might be a target for GCs in the brain (Meaney and Aitken, 1985; Patel et al., 2000; Webster et al., 2002; Perlman et al., 2007). Moreover, the PFC is influenced by stress-sensitive noradrenergic projections from the locus coeruleus. Animal studies observed an enhancing effect of moderate noradrenaline concentrations on WM and an impairment under high concentrations (Arnsten, 1997, 2000; Arnsten and Li, 2005). It is suggested that within a normal range noradrenaline increases the prefrontal control of behaviour, whereas high levels induced a decreased behavioural PFC control (Chamberlain et al., 2006). For WM, comparable to declarative memory processes, human and animal studies revealed a tight interaction between the HPAA and the SNS. GCs did not unfold their modulating influence on WM in the absence of concurrent (nor)adrenergic activity (Arnsten, 2000; Elzinga and Roelofs, 2005; Roozendaal et al., 2006).

Even though a few previous studies in humans observed negative effects of cortisol- or stress-treatment on WM (Lupien et al., 1999; Wolf et al., 2001a; Elzinga and Roelofs, 2005; Oei et al., 2006) the empirical situation is rather heterogeneous. Several previous studies have used the digit span task to assess WM. Here participants are asked to repeat a series of digits either in the same order (forward condition) or in the reversed order (backwards condition). The length of the digit series typically increases up to a maximum of nine digits (eight for backwards). There are most often two trials for each series length and the task is stopped if a subject fails to correctly repeat both digit series of a particular length (Wechsler, 1987).

While some studies using the digit span test observed an impairing effect of cortisol administration (Wolf et al., 2001a) or psychosocial stress exposure (Elzinga and Roelofs, 2005) other studies failed to find effects using the same task (Hoffman and al'Absi, 2004; Kuhlmann and Wolf, 2005; Kuhlmann et al., 2005; Smeets et al., 2006). However, it is questionable whether the digit span task is a sensitive measure for small changes induced by experimental manipulations in young, healthy subjects (Reynolds, 1997; D'Esposito and Postle, 1999; Unsworth and Engle, 2007).

Besides the digit span task some previous studies used the immediate recall of wordlists to test the effects of stress on memory. These tasks rely at least in part on WM functions but also reflect declarative memory processes (Tops et al., 2004; Lezak et al., 2004). Again inconsistent results are reported. Some studies found an impaired immediate recall for neutral (Jelici et al., 2004) and pleasant words (Tops et al., 2004) after acute cortisol administration or psychosocial stress. Other studies in contrast only observed effects for the delayed, but not the immediate recall (de Quervain et al., 2000; Wolf et al., 2001a; Smeets et al., 2006). One contributing factor for the heterogeneous results might be related to the higher susceptibility of simple WM tasks for influencing experimental variables (e.g. phonological similarity or word length) compared to more complex tasks (Unsworth and Engle, 2007). In addition, immediate recall not only depends on WM but also on declarative memory processes and therefore a theoretical interpretation of the findings mentioned above remains difficult (but see Tops et al., 2004).

For more complex WM tasks results seem to be more consistent and impairments were repeatedly found after stress or GC administration (Lupien et al., 1999; Young et al., 1999; Oei et al., 2006). Two well-employed paradigms in WM research are the Sternberg- and the *n*-back-paradigm (Sternberg, 1966; Owen et al., 2005). In the Sternberg paradigm (Sternberg, 1966) a memory set containing one to four digits or letters is presented. Subsequently, a series of recognition sets are displayed and subjects have to decide as quickly and as accurately as possible whether or not one of the target stimuli is present. Target as well as recognition set size can vary in the number of letters/digits they contain (see Lupien et al., 1999; Oei et al., 2006). The WM load is manipulated by the number of required comparisons. This task thus focuses especially on the processes of maintenance and controlled search (Unsworth and Engle, 2007).

Using the Sternberg paradigm studies showed that both, the acute administration of high doses of hydrocortisone (Lupien et al., 1999) and the induction of psychosocial stress (Oei et al., 2006) impaired WM. These effects were in both studies restricted to trials with high task difficulty (a high comparison load; Lupien et al., 1999; Oei et al., 2006).

Another WM task is the *n*-back paradigm. Here subjects are asked to monitor series of briefly presented stimuli and have to decide in each trial if the currently presented stimuli is the same as the one presented two or three trials before (a more detailed description can be found in the method section). The main emphasis of this task is thus on monitoring and constant updating in WM (see Unsworth and Engle, 2007). Imaging studies demonstrated that frontal and parietal regions are continuously involved when subjects attend to various forms of the *n*-back paradigm (Fletcher and Henson, 2001). For the *n*-back task only the effect of pharmacological GC manipulation on WM was tested in healthy subjects or patients (Monk and Nelson, 2002;