Available online at www.sciencedirect.com
SCIENCE DIRECT®
Biological Psychology 69 (2005) 113–132
BIOLOGICAL PSYCHOLOGY
www.elsevier.com/locate/biopsycho

Review

Sex differences in HPA axis responses to stress: a review

Brigitte M. Kudielka[a,*], Clemens Kirschbaum[b]

[a]*Department of Clinical and Theoretical Psychobiology, University of Trier, Johanniterufer 15, D-54290 Trier, Germany*
[b]*Department of Psychology, Technical University of Dresden, Mommsenstr. 13, D-01069 Dresden, Germany*

Available online 25 December 2004

Keywords: HPA axis; Stress; Sex differences; Cortisol; Women's health; Trier Social Stress Test (TSST)

Contents

1. Overview

In this review article, we set out to update findings on sex differences in hypothalamus–pituitary–adrenal (HPA) axis responses to stress with a main focus on human responses to

* Corresponding author. Tel.: +49 651 201 2981; fax: +49 651 201 3690.
E-mail address: kudielka@uni-trier.de (B.M. Kudielka).

0301-0511/$ – see front matter
doi:10.1016/j.biopsycho.2004.11.009

acute psychological stress. First, we briefly describe normal HPA axis regulation under stress exposure as well as HPA axis dysfunction, which manifests in hyper- or hypo-reactivity, and discuss some important methodological issues in the study of acute HPA axis stress responses. We then outline observations of sex-disease dimorphisms that might be related to HPA axis dysfunction. A summary of empirical findings on sex differences in HPA axis stress responses over the life span with respect to laboratory as well as field studies is then provided. Finally, we discuss possible underlying mechanisms explaining at least some of the reported sex differences in the regulation of HPA axis stress responses. These are sexual dimorphisms in brain functioning and the role of circulating sex steroids and corticosteroid binding globulin (CBG).

2. The hypothalamus–pituitary–adrenal axis

The hypothalamus–pituitary–adrenal axis is a central control and regulatory system of the organism that connects the central nervous system (CNS) with the hormonal system. This stress-responsive neuroendocrine system helps the organism adapt to increased demands and maintain homeostasis after challenge but is also vital for supporting normal physiological functioning. The end product, cortisol, has a wide range of physiological effects in the body; virtually all of the body's single nucleated cells are potential targets for cortisol. Cortisol plays a critical role in metabolism by mobilizing resources to provide energy. This helps to overcome the increased metabolic demand presented by a host of challenges. It also regulates or impacts on other important physiological systems, like the immune system, the sympathetic-adrenal-medullary (SAM) axis, the cardiovascular system, as well as affective and cognitive processes.

Under stress, the hypothalamus secretes corticotropin-releasing hormone (CRH), and this provokes the release of adrenocorticotropic hormone (ACTH) from the pituitary. ACTH triggers the secretion of glucocorticoids from the adrenal cortex. In humans, the main glucocorticoid is cortisol. Cortisol is predominantly (90–95%) bound to binding proteins in blood, only 5–10% of the total plasma cortisol circulates as biologically active, unbound, ''free'' cortisol. Overall functioning is controlled by several negative feedback loops (for an overview, see Dallman et al., 2000; Tsigos and Chrousos, 2002; Watts, 2000).

A dysfunctional HPA axis is associated with manifestations of psychosomatic and psychiatric disorders (for reviews, see Chrousos and Gold, 1992; Heim et al., 2000a,b; Holsboer, 1989; Raison and Miller, 2003; Stratakis and Chrousos, 1995; Tsigos and Chrousos, 1994; Tsigos and Chrousos, 2002; Young, 1998). For example, HPA *hyper*activity is often found in major depression (Björntorp, 1996; Carroll et al., 1976; Gold et al., 1984; Sachar et al., 1970) and also seems to be associated with susceptibility to infectious diseases (Mason, 1991) and cardiovascular problems (McEwen, 1998a). *Hypo*reactivity of the HPA axis system is associated with autoimmune processes such as lupus erythematosis (Weiner, 1991), multiple sclerosis (Adams and Victor, 1989), neurodermatitis (Buske-Kirschbaum et al., 1997; Schnyder, 1960) or fibromyalgia, chronic fatigue syndrome, and rheumatoid arthritis (see Tsigos and Chrousos, 2002). It is generally accepted that exposure to stress can cause and/or intensify numerous diseases. It has been suggested that HPA axis functioning might serve as an indicator of allostatic load, an index