PERGAMON

Psychoneuroendocrinology 25 (2000) 707–720

PNEC

www.elsevier.com/locate/psyneuen

Genetic factors, perceived chronic stress, and the free cortisol response to awakening

Stefan Wüst [a,*], Ilona Federenko [a], Dirk H. Hellhammer [a], C. Kirschbaum [b]

[a] *Center for Psychobiological and Psychosomatic Research, University of Trier, Dietrichstrasse 10-11, 54290 Trier, Germany*

[b] *Institute of Physiological Psychology II, University of Düsseldorf, Universitaetsstrasse 1, D-40225 Düsseldorf, Germany*

Received 24 February 2000; accepted 26 April 2000

Abstract

Recent studies have demonstrated that the free cortisol response to awakening can serve as a useful index of hypothalamus–pituitary–adrenal axis (HPA) activity. This endocrine marker is rather consistent, shows good intraindividual stability across time and appears to be able to uncover subtle changes in HPA regulation. The present twin study investigated genetic factors as sources of the interindividual variation of the cortisol awakening response. Furthermore, the relationship between psychological variables and morning cortisol levels was studied.

On two consecutive days saliva samples were collected 0, 30, 45 and 60 minutes after awakening in 52 monozygotic and 52 dizygotic twin pairs. Moreover, samples were obtained at 0800, 1100, 1500 and 2000 h. ('short day-time profile'). Additionally, the participants filled out questionnaires assessing chronic stress load, self-esteem and self-efficacy.

Heritability estimates of h^2=0.40 for the mean increase and of h^2=0.48 for the area under the response curve indicate a significant impact of genetic factors on cortisol levels after awakening. However, no genetic influence on the short day-time profile could be observed. Furthermore, several aspects of perceived chronic stress, namely 'worries', 'social stress' and 'lack of social recognition' were significantly associated with the awakening cortisol response.

The evidence for a medium-sized, yet distinct genetic influence on cortisol levels after awakening is discussed with regard to a potential clinical relevance of genetic determinants of HPA (re)activity. In line with several recent studies, the present findings further support the view

* Corresponding author. Tel.: +49-651-9758634; Fax: +49-651-9758640.
E-mail address: wuests@fpp.uni-trier.de (S. Wüst).

PII: S0306-4530(00)00021-4

that the cortisol awakening responses is consistently enhanced under chronic stress conditions.

Keywords: Cortisol awakening response; Twins; Behavioral genetics; Chronic stress

1. Introduction

The availability of appropriate markers of hypothalamus–pituitary–adrenal axis (HPA) activity can be regarded as a substantial prerequisite for clinical or basic science studies of this neuroendocrine system. Frequently, single blood or saliva samples for analysis of total or free cortisol are collected at a predefined time in the early morning hours and the resulting hormone value is interpreted as an index of unstimulated HPA activity (Gray et al., 1991; Vasankari et al., 1993; Walker et al., 1997). Although easy to assess, this index has a number of weaknesses. Single basal cortisol values measured during this time period are reported to have a rather low intraindividual stability (Coste et al., 1994; Schulz and Knabe, 1994). Moreover, they show large interindividual variation with a significant overlap between healthy individuals and patients with adrenal insufficiency or Cushing's disease (Laudat et al., 1988). Along with other factors these limitations may explain why significant and consistent correlations between single basal cortisol values and psychological variables, e.g. personality measures, cannot be expected.

Recently, it has been reported that cortisol levels rapidly increase after awakening (Späth-Schwalbe et al., 1992; Linkowski et al., 1993; Van Cauter et al., 1994). Studies from this and other laboratories suggest that repeated assessment of the awakening cortisol response can serve as a more useful index of adrenocortical activity which provides important information on the (re)activity of the HPA axis in addition to challenge tests like stimulation with hCRH or $ACTH_{1–24}$. Within the first 30 minutes after awakening, free cortisol levels rise by 50–60% and this response was found to be independent of the time of awakening, sleep duration, sleep quality, physical activity, or morning routines (Pruessner et al., 1997; Schulz et al., 1998; Schmidt-Reinwald et al., 1999; Wüst et al., 2000). Furthermore, although the cortisol awakening response was shown to be altered in subjects who were woken earlier than they expected (Born et al., 1999), in a large cohort the free cortisol response did not differ between subjects who either woke up spontaneously or used an alarm clock (Wüst et al., 2000).

However, a number of factors influence the response magnitude and time course including gender, use of oral contraceptives, persisting pain, burnout or chronic stress (Geiß et al., 1997; Pruessner et al. 1997, 1999; Schulz et al., 1998). Moreover, this HPA index is significantly correlated with the adrenocortical response to $ACTH_{1–24}$ (Schmidt-Reinwald et al., 1999) and with the decrease of secretory immunoglobulin A after awakening (Hucklebridge et al., 1998). The relatively high intraindividual stability of the free cortisol awakening response (mean correlation of r=0.55 across studies) justifies the hypothesis that it can, in part, be regarded as a person trait, which, in turn may be influenced by genetic factors.