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The cortisol awakening response in infants: Ontogeny and associations with development-related variables

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Summary The cortisol awakening response (CAR) is a frequently used measure in psychoneuroendocrinological research, however, some of its more fundamental aspects still require attention. An important question in this respect concerns the ontogeny of the CAR. Data from two recent reports suggest that the CAR may only emerge relatively late during child development (≥16 months of age). However, as both enquiries did not use objective means of verifying participant adherence or infants' awakening times, it is unclear whether methodological factors may have contributed to these results. Here, we report data from a study on 33 infants aged 2—12 months with close care being taken to ensure the accuracy of sampling times by using wrist actigraphy and electronic monitoring containers. Salivary cortisol levels were assessed at 0 and 30 min post-awakening over three study days. Results revealed evidence for a significant CAR (≥2.5 nmol/L) in 32 (out of 33) infants and on a total 86.9% of study days, with a marked magnitude of the CAR across infants (mean estimated increase = 12.54 nmol/L). In addition, the cortisol level on awakening and the CAR were found to be associated with different aspects of infant's physical and sleep-related development as well as with their weight and body mass index (BMI) at birth. Contrary to previous reports, the current results thus indicate that the ontogeny of the CAR occurs at an early stage of development and that it is present from as early as two months of life. The data also suggest that post-awakening cortisol secretion may undergo considerable changes during the first year of life associated with different aspects of infant development.

1. Introduction

The cortisol awakening response (CAR), the marked increase of cortisol secretion following morning awakening, is frequently assessed in psychoneuroendocrinological research (see Fries et al., 2009; Clow et al., 2010). Despite a growing body of research examining the CAR in relation to different psychosocial and health-related variables, fundamental

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knowledge regarding the CAR is still fragmented (Clow et al., 2010). An area of investigation which has received little attention so far is the ontogeny of the CAR, i.e. its first occurrence during child development as well as the main correlates of this process. Enhancing current understanding of this issue may not only increase basic knowledge about the CAR but could also help to provide further insights into the functional role of this still poorly understood aspect of endocrine activity.

Information regarding the ontogeny of the CAR may be indirectly derived from research into the development of overall circadian cortisol rhythmicity. Here, most evidence suggests that the development of a stable circadian pattern of cortisol secretion tends to fall into the first half year of life (Price et al., 1983; Spangler, 1991; Antonini et al., 2000), even though with considerable individual differences (De Weerth et al., 2003). A factor which appears to be closely related to the appearance of a circadian cortisol rhythm is the development of a stable 24-h sleep—wake cycle (Price et al., 1983; Spangler, 1991; Antonini et al., 2000; De Weerth et al., 2003; but see Santiago et al., 1996). The relationship with sleep-related development may be particularly strong for cortisol secretion during the morning hours; e.g., the shifting of peak basal cortisol concentrations into the early morning period has been found to concur with the entrainment of a nighttime sleep rhythm between 12 and 16 weeks of age (Spangler, 1991; Larson et al., 1998). Infants who sleep through the night are also more likely to show an early morning peak (Larson et al., 1998). Similarly, more efficient and less fragmented sleep in toddlers aged 12—36 months has been found to be associated with lower awakening cortisol levels, perhaps due to a suppressive effect of unfragmented sleep on cortisol secretion (Scher et al., 2010).

The above evidence may suggest that, similar to the development of circadian cortisol rhythmicity, the ontogeny of the CAR could also take place during the first half year of life in concurrence with the establishment of a 24-h sleep—wake cycle. However, as the CAR is known to be a distinct aspect of basal cortisol secretion (Wüst et al., 2000a; Edwards et al., 2001; Wilhelm et al., 2007), it is unclear how well evidence on the development of general circadian rhythmicity translates to the CAR. To date only a small number of studies have directly examined the CAR in infants or preschool age children. A study on 366 infants aged 12—20 months revealed that on average infants below 16 months of age did not show a positive CAR (Saridjan et al., 2010). In line with this, a recently published study on 32 infants aged 7—17 months also failed to provide evidence for a positive CAR in this age group and, indeed, reported a declining pattern of cortisol levels from awakening to 30 min post-awakening (Bright et al., 2011). In a longitudinal study on somewhat older children, a positive CAR was only found in 68% of 60-month-old children and this increased to 93% at a second assessment eight months later (DeCaro and Worthman, 2008). While these results may suggest that in most children the CAR emerges only relatively late in development, it is important to note that the above studies did not employ means to objectively verify children' awakening times and/or times of saliva sampling. As participant non-adherence constitutes a major problem in CAR research (Kudielka et al., 2003; Broderick et al., 2004; Kupper et al., 2005), it is conceivable that the low responder rates in these studies may have also been influenced by methodological factors. This is also supported by recent evidence from a small but well-controlled study, using polysomnographic sleep recordings and wrist actigraphy, in which all of the seven examined children aged 30—48 months exhibited a robust CAR (Gribbin et al., 2011). To the best of our knowledge, no published research has examined the CAR in children below 12 months of age carefully controlling for the accuracy of saliva sampling in relation to awakening time.

Taken together, while evidence regarding the development of overall circadian cortisol rhythmicity suggests that the CAR might also develop early during the first year of life, this possibility is yet to be carefully examined. Here, we thus set out to provide first data on the ontogeny of the CAR in 2—12-month-old infants using repeated CAR assessments over three study days and rigorous control for participant adherence to the saliva collection protocol. In addition, as previous research had indicated potential influences of both infant-related and environmental factors on the ontogeny of the CAR (e.g., Saridjan et al., 2010), cortisol associations with different sleep-related, behavioural and anthropometric parameters of the infant as well as with relevant parent data were also examined.

2. Methods

2.1. Participants

The study sample comprised 33 healthy infants aged 2—12 months from the greater Dresden area (see Table 1 for sample characteristics). Only term-born infants (after 37 weeks gestational age) who were currently in good mental and physical health and not taking medication (based on parents' self-report) were included in the study. Families were recruited at local child care centres, paediatric practices, breastfeeding groups or parent—child courses. Of the participating infants, 30 were exclusively cared for by their primary caregiver (their mother in all instances) while 3 infants also received additional care by an extra-familial childminder. For all participating infants, at least one parent provided written informed consent. The study protocol was approved by the local ethics committee and carried out in accordance with the Declaration of Helsinki. Each parent—child pair received 20 Euro for participation in the study.

2.2. Design and procedure

Interested parents were first informed about the study via email or telephone. Those willing to participate were then invited to the Technical University of Dresden or visited at their homes by a researcher. Here, extensive oral and written information about the study was provided and informed consent was obtained. Parents were familiarised with the study package comprising saliva sampling materials, the study questionnaires (see below) and an instructional DVD on saliva sampling in infants. Careful on-site training on how to obtain saliva samples in young infants was then provided and the importance of strict adherence to the study protocol was emphasised to parents.

Following the initial visit, parents were asked to collect saliva samples from their infants on three non-consecutive