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Individual differences in the activity of the hypothalamic pituitary adrenal axis: Relations to age and cumulative risk in early childhood

Steven J. Holochwost[a,*], Jean-Louis Gariépy[b,e], W. Roger Mills-Koonce[c], Cathi B. Propper[b], Jacek Kolacz[b], Douglas A. Granger[d,e,f]

[a] Science of Learning Institute, Johns Hopkins University, United States
[b] Center for Developmental Science, University of North Carolina at Chapel Hill, United States
[c] Department of Human Development and Family Studies, University of North Carolina at Greensboro, United States
[d] Institute for Interdisciplinary Salivary Bioscience Research, University of California Irvine, United States
[e] School of Nursing, Bloomberg School of Public Health, School of Medicine, Johns Hopkins University, United States
[f] Salivary Bioscience Laboratory and Department of Psychology, University of Nebraska, Lincoln, United States

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ABSTRACT

This study examined individual differences in the function of the hypothalamic-pituitary-adrenal (HPA) axis with regard to age and cumulative risk during challenging laboratory tasks administered at 6, 12, 24, and 36 months. Saliva samples were collected from a majority-minority sample of $N = 185$ children (57% African American, 50% female) prior to and following these tasks and later assayed for cortisol. Cumulative distal risk was indexed via a composite of maternal marital status, maternal education, income-to-needs ratio, the number of children in the household, and maternal age at childbirth. Probing of hierarchical models in which cortisol levels and age were nested within child revealed significant differences in cortisol as a function of both age and cumulative risk, such that children exposed to high levels of risk exhibited higher levels of cortisol both within and across age. These results highlight the sensitivity of the HPA axis to environmental context at the level of the individual, even as that sensitivity is manifest against the background of species-typical biological development.

1. Introduction

Decades of research link altered hypothalamic-pituitary-adrenal (HPA)-axis activity to adverse caregiving environments, but less is known about whether more distal forms of adversity are reliably associated with individual differences in HPA-axis activity. Studies that have addressed this question have typically examined HPA-axis activity at a single age (or a single cross-age composite), and thus few studies have followed the association between adversity and individual differences in HPA-axis activity through early childhood. Moreover, distal adversity has most commonly been indexed by poverty and measured in majority-Caucasian samples, and thus the operationalization of environmental adversity has been a narrow one that often excludes the effects of cumulative risk and minority status. This study seeks to address these gaps in the literature by examining the relation between exposure to cumulative distal risk and the activity of the HPA axis in a diverse sample across early childhood.

1.1. The activity of the HPA axis in early childhood: relations to age

The HPA axis is one of the principal systems that mediate the physiological response to challenge. When activated in response to novel events, unfamiliar circumstances, or distressing conditions, the HPA axis initiates a signaling cascade resulting in the release of cortisol into the bloodstream (Chrousos and Gold, 1992). Levels of cortisol in blood and saliva are highly correlated (Kirschbaum and Hellhammer, 1989), and therefore assaying saliva offers a minimally-invasive method for studying the HPA axis in young children.

Studies indicate that although HPA-axis activity is responsive to challenge in infancy (e.g., Gunnar, 1992; Lewis and Thomas, 1990), over the course of early childhood the threshold for response changes, such that by preschool most children do not exhibit reactivity to laboratory-based challenge tasks (Gunnar et al., 2009; Lupien et al., 2009). There is evidence that this reduction in HPA reactivity across early childhood is coupled with decreases in HPA-axis activity under various conditions at rest: Watamura et al. (2004) reported significantly lower cortisol levels at 30 months than at 12 months, while Ursache and

* Corresponding author at: Science of Learning Institute, Johns Hopkins University, Krieger Hall, Room 167, Baltimore, MD 21218-2685, United States.
E-mail addresses: steven.holochwost@gmail.com (S.J. Holochwost), lgariepy@email.unc.edu (J.-L. Gariépy), r_millsk@uncg.edu (W.R. Mills-Koonce), propper@email.unc.edu (C.B. Propper), jkolacz@live.unc.edu (J. Kolacz), dagrange3@uci.edu (D.A. Granger).

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colleagues reported a similar finding for baseline (i.e., pre-challenge) levels of cortisol from 7 to 24 months (Ursache et al., 2014; note that here and throughout "baseline" refers to cortisol levels prior to the onset of a challenging task). Though there is considerable debate regarding the meaning of this apparent shift (e.g., Hostinar et al., 2014), some have speculated (Gunnar and Quevedo, 2007) that it could be analogous to the stress hyporesponsive period (SHRP) described in rodents (see Nelson, 2015 for a review). Animal models suggest that the SHRP serves to protect the anabolic process of brain development in early life from the catabolic effects of glucocorticoids (Levine, 1999).

1.2. The HPA axis and environmental adversity

Although Hostinar et al. (2014) proposed that in humans the developmental transition towards lower levels of HPA-axis activity is instantiated by social support, there is evidence that this shift may be undermined by exposure to environmental adversity. Poverty has been associated with increased diurnal levels of cortisol among infants (Saridjan et al., 2010), elevated levels of baseline cortisol among toddlers (Blair et al., 2011), higher levels of cortisol throughout laboratory procedures among preschoolers (Blair et al., 2005), and higher overnight levels of cortisol among school-aged children (Evans and English, 2002). In the largest prospective study to date, longer exposure to poverty was associated with higher levels of cortisol at 48 months of age (Blair et al., 2013).

Defining environmental adversity exclusively in terms of poverty (e.g., household income below a certain threshold) overlooks other risk factors that, though correlated with poverty, co-occur with poverty at varying frequencies at the individual level of analysis (Sameroff et al., 1993). Studies demonstrate that it is the accumulation of risk factors, rather than the presence of any specific factor, that is most strongly associated with individual differences in development (cf., Appleyard et al., 2005; Masten and Wright, 1998; Trentacosta et al., 2008). It is therefore surprising that few studies have examined HPA-axis activity in early childhood as a function of cumulative risk. Blair and colleagues linked exposure to high levels of cumulative risk with higher aggregate levels of cortisol during a laboratory procedure at 15 months (Blair et al., 2008), whereas Zalewski et al. (Zalewski et al., 2016) found that exposure to higher levels of cumulative risk were associated with 'blunted' or 'flattened' diurnal patterns of HPA axis activity at 36 months of age.

1.3. Current study

The current study employs a prospective longitudinal design to examine the function of the HPA axis prior to and following a series of developmentally-appropriate, challenging laboratory tasks adapted from a commonly-used protocol (Lab-TAB; Goldsmith and Rothbart, 1999). Environmental adversity was operationalized as cumulative distal risk, rather than poverty, and the study sample was majority minority. This allowed us to examine whether the accretion of distal risk factors might reliably be associated with HPA-axis function, and whether the effects of risk were significant after controlling for the effects of race to the extent permitted by our analyses. Based on prior research, we hypothesized that levels of cortisol prior to and following challenging tasks would decrease as a function of age (with the caveat that even at younger ages we may not observe a significant increase in cortisol in response to challenge, given that our tasks do not involve nociceptive stimuli). However, we also hypothesized that children exposed to higher levels of cumulative risk would exhibit higher cortisol levels at each age.

The latter hypothesis was based on both diathesis-stress (and in particular, the concept of allostatic load; McEwen, 1998) and biological sensitivity to context theories (BSC; Boyce and Ellis, 2005). As Hostinar and Gunnar (2013) note, both of these theoretical perspectives would predict that exposure to greater adversity would be associated with higher levels of activity in the physiological systems that mediate the stress response, including the HPA axis. These theories differ, however, in two important ways: first, according to diathesis-stress theory and the concept of allostatic load, higher levels of cortisol are an unfortunate consequence of exposure to adversity that impose a drag (or load) on optimal physiological function, whereas according to BSC, elevated cortisol levels are an adaptive response that prepares the individual for the challenges likely to be encountered in an adverse environment. Second, BSC asserts that elevated levels of physiological activity would also be observed in the context of highly-supportive environments, a prediction that is not tested here given that low levels of risk do not indicate high support. In short, the current study was not designed to evaluate competing accounts for the etiology of altered HPA-axis activity, but rather to test a broader hypothesis about that activity informed by both of these theoretical perspectives.

2. Methods

2.1. Participants

Participants were full-term, healthy infants recruited at 3 months of age by the Durham Child Health and Development Study (DCHDS) via fliers and postings at birth and parenting classes or through phone contact via birth records. The DCHDS included $N = 206$ children (48.5% female), 85 of whom were European American (41.3%) and 121 of whom were African American (58.7%). The final sample for analysis ($N = 185$, 50.3% female) consisted of 80 European-American children (43.2%) and 105 African American children (56.8%). There were 21 children without cortisol data who were excluded from the analysis. These children did not differ from the analysis sample by race ($p = 0.259$), gender ($p = 0.338$), or cumulative distal risk ($p = 0.105$). Note that these participants did not necessarily leave the study, but rather did not provide cortisol data at any age. For further information about attrition from the study between 6 and 36 months, see Holochwost et al. (2016).

2.2. Procedures

At 6, 12, 24, and 36 months children participated in one or more challenging tasks designed to elicit a physiological stress response. The nature of these tasks changed across assessments to be developmentally appropriate. At 6 months, children and their parents participated in the still-face procedure (SFP; Tronick et al., 1978), during which mothers look at their child for 90 s without facial movement or vocalization, and then in the arms restraint task (Goldsmith and Rothbart, 1999), wherein mothers gently hold their child's arms down for 2 min while maintaining a neutral expression. Children participated in the strange situation procedure at 12 months (SSP; Ainsworth et al., 1978), which features two episodes of maternal separation. At 24 months children participated in the barrier task (Goldsmith and Rothbart, 1999), in which an attractive toy is taken from the child and placed behind a transparent barrier for 2 min. Finally, at 36 months children participated in the gift-wrap task (Kochanska et al., 2000), wherein the child attempts to refrain from opening a wrapped present while left alone for 2 min. At each of the four laboratory visits, three saliva samples were obtained from the child. The first sample was obtained a few minutes after the child's arrival at the lab. The mean time of initial sample was 12:34 p.m. ($SD = 2.74$ h) at 6 months, 12:44 p.m. at 12 months ($SD = 2.96$), 12:26 p.m. at 24 months ($SD = 2.96$) and 12:17 p.m. at 36 months ($SD = 2.76$). The other two samples were taken 15 min and 30 min after the conclusion of the challenge tasks following a strict protocol in which researchers used a timer to cue the collection of the post-challenge samples.