Published in final edited form as:

Dev Psychobiol. 2014 September ; 56(6): 1406–1415. doi:10.1002/dev.21226.

HPA Stability for Children in Foster Care: Mental Health Implications and Moderation by Early Intervention

Heidemarie K. Laurent¹, Kathryn S. Gilliam¹, Jacqueline Bruce², and Philip A. Fisher^{1,2}

Heidemarie K. Laurent: hlaurent@uoregon.edu

¹Department of Psychology University of Oregon Eugene, OR

²Oregon Social Learning Center Eugene, OR

Abstract

Research on stress-sensitive biological systems has typically focused on activation at one time, yet recent theories emphasize dynamic, context-specific adaptation. This study tested hypothesized calibration of one such system by examining both mean levels and longitudinal stability of daily cortisol—reflecting hypothalamic-pituitary-adrenal axis activation—in children exposed to high-risk versus lower-risk caregiving contexts. Context-specific effects of longitudinal cortisol profiles were addressed via relations with child psychiatric symptoms. Children from regular foster care, foster children participating in a family-based intervention, and community comparison children (n=96 total) collected saliva samples for cortisol assay at 29 timepoints across 6+ years. High-risk (regular foster care) children showed lower and more variable cortisol levels than their lower-risk (treatment foster care, community comparison) counterparts. For the high-risk children only, higher and more stable cortisol related to elevated anxiety symptoms. Implications for contextual calibration of stress systems and family intervention mechanisms are discussed.

Keywords

cortisol; stress sensitivity; longitudinal; foster care; intervention

INTRODUCTION

There is substantial evidence that activation of biological systems involved in the stress response—particularly the hypothalamic-pituitary-adrenal (HPA) axis—helps to explain links between early adversity and developmental outcomes (e.g., Danese & McEwen, 2011; Fisher, Kim, Bruce, & Pears, 2011; Hunter, Minnis, & Wilson, 2011). Recent theories about the role of stress systems in psychological adjustment emphasize context-specific, dynamic calibration over time (Boyce & Ellis, 2005; Del Giudice, Ellis, & Shirtcliff, 2011); however, there is little empirical research on the conditions for and outcomes associated with HPA stability across development. To fully elucidate the ways in which stress systems are shaped by early environments and what this means for child adjustment, longitudinal research must

examine not only levels of HPA activity, but also stability or instability over time. The present study aims to address this gap by investigating stability of daily cortisol levels (sampled in the morning and evening) and the relation between cortisol stability and psychiatric symptoms in children exposed to varying levels of early adversity.

Development of the HPA axis in humans begins during the fetal period and continues throughout early childhood, with the typical daily pattern of cortisol release (i.e., peak approximately 30 min after waking followed by a decline over the course of the day) stabilizing between the ages of 4 and 6 (Gunnar & Donzella, 2002). During this time, caregiver support and buffering from stress play a critical role in developing HPA regulation. Importantly, a lack of adequate caregiving can result in alterations in HPA axis regulation (as indexed by high or low basal cortisol levels) associated with behavioral problems (Cutuli, Wiik, Herbers, Gunnar, & Masten, 2010; Engert, Efanov, Dedovic, Dagher, & Pruessner, 2011).

Foster care provides an ideal context for studying early caregiving effects on the development of HPA axis function because children in foster care have typically experienced both early caregiver disruptions and maltreatment and are at heightened risk for psychopathology. Below, we outline what is known about early adversity-HPA-child adjustment links, what theories of dynamic environment-physiology interaction may add to understanding these paths, and next steps to advance this research.

RELATIONSHIP BETWEEN EARLY ADVERSITY, HPA AXIS FUNCTIONING, AND CHILD ADJUSTMENT

A rich literature links early adversity with HPA axis functioning and concomitant behavioral and psychological outcomes (Juster et al., 2011). Notably, both elevated and blunted HPA basal and stress-induced activity have been associated with later adjustment problems. In the case of hypercortisolism, early adversity is hypothesized to sensitize the HPA axis, making it highly reactive. This hyperreactivity is thought to promote internalizing behaviors consistent with withdrawal from threat, as shown in school-aged maltreated children (Cicchetti & Rogosch, 2001). High basal cortisol has also been associated with increased risk for major depressive disorder in both adolescents and adults (Bhagwagar, Hafizi, & Cowen, 2005; Vrshek-Schallhorn et al., 2012). The mechanism by which early adversity contributes to hypocortisolism is less clear, but hypotheses include a higher threshold for HPA activation following repeated stress exposure, enhanced negative feedback sensitivity of the HPA axis, and downregulation of adrenocorticotrophic hormone (ACTH) response to corticotropin-releasing hormone (CRH) hypersecretion during chronic stress (Heim, Ehlert, & Hellhammer, 2000). Low basal cortisol levels have been found in young foster children who have experienced significant early adversity (Bruce, Fisher, Pears, & Levine, 2009; Gunnar & Vazquez, 2001); in contrast to the above, hypocortisolism has been more commonly related to externalizing behavior in high-risk populations (Laurent, Neiderhiser et al. 2014; Shirtcliff, Granger, Booth, & Johnson, 2005).

Recently, longitudinal research designs have allowed more nuanced assessment of dynamic changes in the HPA axis over time and their relationship to child adjustment (Bush,

Obradovi, Adler, & Boyce, 2011; Ruttle et al., 2011). Longitudinal designs afford the opportunity to examine not just basal cortisol levels at a given time, but also stability over time. Examining daily cortisol stability longitudinally may help to address inconsistencies in the literature and allow a deeper understanding of the dynamic effects of early adversity. Basal cortisol levels are typically conceptualized as a trait measure, and analytic approaches thus treat variation in cortisol responses across sampling points (i.e., days) as statistical noise. However, an alternative strategy exists: variation can be used as an additional source of information to explain effects of early adversity on future outcomes.

Very little research has examined cortisol stability within individuals over time, let alone variables related to greater or lesser stability. Whereas infant research conducted over 4 months indicated high intraindividual variability (De Weerth & van Geert, 2002), large studies of children and adolescents have demonstrated moderate to high cortisol stability (Rotenberg, McGrath, Roy-Gagnon, & Tu, 2012; Shirtcliff et al., 2012). Importantly, higher variability of cortisol over a 6-day sampling period has been associated with more severe depressive symptoms in unmedicated outpatients with major depressive disorder (Peeters, Nicolson, & Berkhof, 2004).

Only two studies exist to our knowledge addressing early adversity and cortisol stability. Laurent et al. showed effects of family adversity on adopted children's cortisol levels and stability—operationalized as a lagged effect of cortisol measured at age 4.5 on cortisol measured at age 6—which in turn related to both internalizing and externalizing problems (Laurent, Neiderhiser et al. 2014). Essex and colleagues (2011) demonstrated relations between early adversity and cortisol stability, operationalized as developmental change in morning and daily cortisol levels over 4 time points from age 9 to 15. Children exposed to more early adversity showed greater developmental change in cortisol over time and larger intraindividual changes in conjunction with increases in mental health symptoms. Though these studies only examined two and four longitudinal timepoints, respectively, they highlight examination of cortisol stability as a valuable method for investigating adversity-related dynamics of the HPA axis. The above research further suggests that stability of cortisol could be an informative predictor of outcomes in at-risk populations.

INTERVENTION EFFECTS ON STABILITY

Family-based psychosocial interventions for children exposed to early adversity have been shown to effect change in both behavioral adjustment and HPA axis activity (Dozier, Peloso, Lewis, Laurenceau, & Levine, 2008; Fisher, Gunnar, Dozier, Bruce, & Pears, 2006; Fisher & Stoolmiller, 2008). This work has focused predominantly on assessing pre- to post-intervention change in cortisol levels within children, as well as between-child comparisons of post-intervention cortisol levels in an intervention group with a services-as-usual group and a nonmaltreated community comparison group. Within these designs, a favorable effect of the intervention is often conceptualized as similarity between the post-intervention cortisol profile of the intervention group and the nonmaltreated community comparison group. However, the effect of these interventions on variability in cortisol levels over time has not been extensively examined. Fisher, Stoolmiller, Gunnar, and Burraston (2007) reported increases in stability of daily cortisol levels in young foster children participating in

an intensive, family-based intervention (Multidimensional Treatment Foster Care for Preschoolers; MTFC-P). This finding suggests that variability in HPA axis functioning over time can be a meaningful index of the ways in which interventions such as MTFC-P shift the developmental trajectory of the HPA axis.

THE CURRENT STUDY

The current study examines the long-term effects of a family-based intervention on HPA axis functioning over time. Morning and evening cortisol levels were measured every month for 2 years, with further 6-month follow-up assessments yielding child cortisol data over a span of 6+ years. At the end of this assessment period, when children were approximately 10 years old, parents reported on child psychiatric symptoms. The stability of child cortisol levels over time was conceptualized as a lagged effect between a given cortisol assessment and the previous assessment. Based on previous findings linking early adversity exposure to low cortisol and instability, we hypothesized (1) that children in the services-as-usual foster care group would exhibit lower, less stable cortisol levels compared to children in the treatment foster care group and the community comparison group, and (2) that children in the treatment foster care and community comparison groups would exhibit similar cortisol levels and stability, consistent with previous findings related to MTFC-P. Additionally, based on previous work linking child behavior problems with different cortisol profiles, we predicted (3) an association between higher cortisol levels and internalizing problems, and (4) an association between lower cortisol levels and externalizing problems.

METHOD

Participants

Preschool-aged (3–6-year-old) children ($n=177$) were recruited from a public child welfare agency and the community in a moderate-sized Pacific Northwest city. Foster children were randomly assigned to the Multidimensional Treatment Foster Care for Preschoolers (MTFC-P) intervention condition ($n=57$) or to a regular foster care (RFC) comparison condition ($n=60$). A group of same-aged, low-income community children (CC) who had not been involved in the child welfare system ($n=60$) was recruited to serve as an additional comparison. Children in the two foster care groups did not differ on placement type (i.e., first-time foster placement vs. change in foster home vs. re-entry into foster care following failed permanent placement) or number of days in foster care. They also did not differ on number of placements throughout the study or likelihood of permanent placement at the end of the study. All research staff involved in data collection were blind to the child's condition. There were no differences between the three groups on child age, gender, or ethnicity. Across groups, the sample was 89% European American, 1% African American, 5% Latino, and 5% Native American, representative of the community from which children were recruited.

Of the total sample, the subset ($n=96$) with child diagnostic data available at the final assessment was included in the current investigation. A comparison of cases included versus those not included showed that the former contained a greater proportion of CC children, $\chi^2(1)=11.29$, $p<.05$, and a lower proportion of RFC children, $\chi^2(1)=18.40$, $p<.05$ (no

difference in MTFC-P children). There were no demographic differences between groups, but those included in the current sample had higher mean cortisol values, $t(175) = 2.10$, $p < .05$. See Table 1 for further descriptive information about the sample.

Procedure

All children were assessed 29 times across 6+ years: the first 25 assessments were at 1-month intervals, followed by a gap in data collection ($M = 32$ months), and then four further assessments occurred at 6-month intervals. At each assessment, saliva samples were collected for cortisol assay in the morning and evening over two consecutive days. (The final four assessments involved morning, afternoon, and evening samples collected across three consecutive days; for the present study, only the matched morning/evening samples from the first 2 days were considered to remain consistent with earlier assessments.)

Intervention—Multidimensional Treatment Foster Care for Preschoolers (MTFC-P) is a family-based therapeutic intervention designed to address the developmental and social-emotional needs of foster preschoolers and delivered via a team approach to foster children, their foster parents, and their permanent placement caregivers (birth parents or adoptive parents). Foster parents completed 12 hr of intensive training prior to the children's placement, and they worked with trained consultants throughout the intervention period to maintain a warm, consistent environment encouraging positive child behavior and limiting problem child behavior. Support was provided via daily telephone contacts, weekly foster parent group meetings, and 24-hr crisis services. Children received individualized treatment designed to improve behavior in preschool/daycare and home settings, and they attended weekly therapeutic playgroup sessions to facilitate school readiness. Children typically received services for 6–9 months, including the transition period to a permanent placement. For children who remained in long-term foster care, services continued until their behavior stabilized. A more detailed description of the MTFC-P program and its theoretical foundation can be found in Fisher and Chamberlain (2000). RFC children received routine services in state foster care, typically weekly individual psychotherapy and (if developmental delays were detected) special education services.

Measures

Salivary Cortisol Collection and Assay—Saliva collections occurred 30 min after the child awoke and before eating or drinking (AM) and 30 min before bedtime (PM). Parents were trained by research staff to complete saliva collection at home following procedures described in Schwartz, Granger, Susman, Gunnar and Laird (1998). Saliva was collected in a plastic tube via a Salivette¹ absorbent roll for the first 25 assessments and via passive drool for the final four assessments. The parent wrote the date and time of collection on the tube label, and samples were frozen at the lab until assayed. Samples were assayed using the High Sensitivity Salivary Cortisol Enzyme Immunoassay Kit (Salimetrics, State College, PA), with samples from each child assayed in the same batch to minimize within-subject

¹Models including only 6-month interval data were also examined to determine whether denser sampling during early childhood played a role in these findings. The group $\times$ anxiety symptoms interaction was no longer significant (though several other group $\times$ symptom interactions in the same direction emerged), suggesting that anxiety-related effects found here relied on HPA function during early childhood (proximal to the intervention).

variability. All samples were assayed in duplicate and averaged, with duplicates varying more than 15% reassayed. Intraassay and interassay coefficients of variance were 2.7% and 11.0% for the first 25 assessments and 7.7% and 9.8% for the final four assessments.

To minimize extraneous sources of cortisol variability, children who routinely used steroid-based medications (e.g., asthma inhalers) were excluded from the study, and parents were instructed to avoid sampling when their children were using steroid-based medications or were ill. Parent responses to questionnaires regarding sampling times and child eating and sleeping behaviors on sampling days were also examined to ensure compliance with sampling guidelines. Of 20,532 possible samples for the total sample ($n = 177$), 1,190 (5.8%) were missing because the parent failed to collect and/or return the sample, 30 (.1%) were missing because the cortisol value was out-of-range ($>2.0 \mu\text{g/dl}$), 208 (1.0%) were missing because the sampling time was incorrect (inconsistent report of time or time did not correspond to the specified sampling window), and 4,400 (21.4%) were missing for other reasons (i.e., caseworker or family refusal, lost sample, child unable to do the collection). Of possible control variables considered—that is, child medication use, child illness, child wake time, sample collection time—only sample collection time related significantly to cortisol values, so this was included as a control in analyses.

Diagnostic Interview Schedule for Children (DISC)—At the final assessment time, parents were interviewed about their child's psychiatric symptoms using a standard diagnostic tool, the DISC (Shaffer, Fisher, Lucas, Dulcan & Schwab-Stone, 2000). This interview includes modules for (1) anxiety disorders (social phobia, separation anxiety, specific phobia, panic disorder, agoraphobia, generalized anxiety disorder, obsessive-compulsive disorder, and post-traumatic stress disorder), (2) eating disorders (anorexia, bulimia), (3) mood disorders (major depression, dysthymia, mania), (4) disruptive behavior disorders (attention deficit hyperactive disorder, oppositional defiant disorder, conduct disorder), and (5) alcohol and substance use disorders (alcohol, marijuana, nicotine, other drugs). Total symptom counts for each module were used to index child adjustment problems (see Table 1 for further description of the sample). One-way analyses of variance were used to test for group differences in symptom scores. The only difference detected was for disruptive behavior disorders, $F(2, 93) = 4.86, p = .01$; follow-up tests showed that community comparisons were lower than both foster care groups on this dimension. No children were reported to show alcohol/substance use disorder symptoms, so this scale was not considered further in analyses.

Analytic Strategy

Hierarchical linear modeling (HLM; Raudenbush & Bryk, 2002) was used to account for dependency in the data. This approach splits variability into within-person (Level 1) and between-person (Level 2) components; at Level 1, child cortisol data from all 29 AM and PM assessments (both days) were modeled with a variable intercept (there was no significant linear slope), which could in turn be explained by child group and psychiatric symptom variables at Level 2. An advantage of HLM is that it allows missing data at Level 1 while using full information maximum likelihood (FIML) methods to arrive at parameter estimates; thus, children with missing cortisol data could still be included in analyses.

To assess stability in HPA activity over time, a grand mean-centered time-varying covariate was added at Level 1 representing the lagged effect of cortisol values from the previous assessment (matched AM/PM sample on day 1 or 2, meaning cortisol sampled at the same time of day either one [for assessments 1–24] or six [for assessments 25–29] months ago). Child-level predictors were also added to explain variability in this cortisol stability term. For illustration, the full hypothesized model is given below:

Level 1 (within-child)

$$\text{Cortisol} = \beta_0 + \beta_1 (\text{sample time}) + \beta_2 (\text{lagged cortisol}) + \text{error}$$

Level 2 (between-child)

$$\beta_0 = \gamma_{00} + \gamma_{01} (\text{group}) + \gamma_{02} (\text{symptoms}) + \gamma_{03} (\text{group} \times \text{symptoms}) + \text{error}$$

$$\beta_1 = \gamma_{10}$$

$$\beta_2 = \gamma_{20} + \gamma_{21} (\text{group}) + \gamma_{22} (\text{symptoms}) + \gamma_{23} (\text{group} \times \text{symptoms}) + \text{error}$$

RESULTS

The baseline HLM model containing no predictors confirmed that there was significant between-child variability in both cortisol levels (intercepts) and cortisol stability, $\chi^2(95) = 477.37$ and 275.15 , p 's $< .001$, which meant that predictors could be added at Level 2. Of the control variables tested (i.e., child medication use, child illness, child wake time, and sample collection time), only sample collection time proved significant. As expected, cortisol values were lower for samples taken later in the day. This covariate was included in all further model testing. The lagged cortisol effect was significant, $b = .122$, $p < .001$, suggesting a sample-wide tendency for stability in HPA activity over time.

Tests of the main effects of group revealed that children in the RFC group had lower ($b = -.026$, $p = .02$) and less stable cortisol ($b = -.074$, $p = .03$), compared to both the MTFC-P and the CC group, which were not significantly different from one another. Figure 1 depicts predicted cortisol trajectories over time by group. Next, main effects of parent-reported symptom modules from the DISC were tested. Cortisol stability was strengthened by child symptoms from the anxiety disorders module ($b = .031$, $p = .02$). There were no significant effects of symptoms from the other DISC modules.

To determine whether the above patterns might be conditioned by an interaction, a model including child group $\times$ anxiety disorder symptoms was tested. The interaction term significantly predicted both child cortisol levels and stability (see Table 2). Examining predicted effects of anxiety in each group showed that anxiety symptoms related to higher, more stable cortisol in the RFC group only (see Figs. 2 and 3). This means that whereas lower, more variable HPA activation appeared beneficial for the high-risk (RFC) children, there was no such implication for lower-risk (MTFC-P, CC) children. Importantly, these results suggest the intervention moved foster care children toward the patterns of HPA function found in community children.¹ This final model yielded a significant improvement in fit compared to the baseline model containing only the sample collection time, $\chi^2(6)$

=21.12, $p < .01$, explaining 7.7% of the variance in cortisol intercepts and 21.8% of the variance in cortisol stability.

Follow-up analyses were conducted to identify the source of reported effects. First, AM and PM cortisol samples were examined in separate models. Both the main effect of child group and the group-moderated anxiety effect on cortisol levels were driven by AM cortisol (*ns* associations with PM cortisol). Main effects and interaction effects on cortisol stability were present for both AM and PM cortisol, though the former were stronger. This suggests that cortisol level effects were specific to morning HPA function, whereas stability effects applied more broadly to daily HPA activity. Second, given that gender is proposed to moderate certain cortisol-symptom associations (Del Giudice et al., 2011), child gender interactions with both group and symptoms were tested. These were all nonsignificant, as were main effects of gender on cortisol.

DISCUSSION

Results of this study indicate that the HPA axis functions as a dynamic system, with differing implications of stability based on developmental context. Specifically, the present findings highlight differences between children living in high- versus lower-risk caregiving contexts not only in their morning cortisol levels, but also in daily cortisol stability over a period of 6+ years. We further found differing associations between cortisol and anxiety symptoms in high- versus lower-risk children. Below, we consider how these findings inform models of dynamic, context-specific stress sensitivity, as well as potential routes of intervention effects for children in high-risk contexts such as foster care.

Children in regular foster care showed lower morning cortisol and more variable daily cortisol levels compared to both community comparison children and foster children in the intervention condition. These differences echo previous research relating lower, more variable cortisol levels to higher levels of family adversity exposure in adopted children (Laurent et al., 2013, Laurent, Neiderhiser et al., 2014), but on a much longer temporal scale (over 6 years vs. 1.5 years). A potentially relevant theoretical lens through which to understand these findings is provided by biological sensitivity to context (BSC) theory (Boyce & Ellis, 2005) and its extension, the Adaptive Calibration Model (ACM; Del Giudice et al., 2011). BSC postulates that individual differences in HPA axis activity constitute a biomarker of sensitivity to the environment, “for better and for worse.” The adaptive consequences of a sensitive phenotype characterized by high HPA axis activity are postulated to vary, conferring benefits in supportive environments and risk for disorder in adverse environments. ACM further posits that individual differences in HPA axis functioning are the result of adaptation to changing environmental conditions, yielding distinct activation profiles that map onto behavioral adjustment.

The regular foster care children in the current study are likely to have experienced adverse early caregiving environments (with their birth parents) and inconsistent subsequent experiences involving shifts between more and less sensitive caregivers. Although caution in relating to BSC and ACM is warranted, given that “sensitivity” in these models typically refers to reactivity rather than diurnal activation, patterns observed here fit broadly with

proposals that exposure to adverse conditions would induce downward regulation of HPA activity and unpredictable or changing conditions would drive ongoing modulation of stress systems. Conversely, children in relatively more stable, supportive caregiving conditions could remain more sensitive to the social environment, with less modulation needed because the environment remained fairly consistent. It is also possible to interpret these effects outside the ACM as evidence of normative downregulation in response to chronic stress (Miller, Chen, & Zhou, 2007). This would be consistent with the lower total cortisol output, and especially lower morning cortisol levels, observed here and in other samples following exposure to threat and trauma.

For regular foster care children, variations from the average profile for their group carried mental health consequences; in this group only, higher morning and more stable daily cortisol levels were associated with higher anxiety symptoms. Possible explanations for this include: (a) these children may have started with especially high dispositional HPA activity they could not modulate downward enough to protect themselves, or (b) they may have adjusted to adversity with increased stress sensitivity (the vigilant type of the ACM). Either way, becoming “stuck” at a stable level of elevated morning HPA activity may have made these children more vulnerable to a high-threat and/or changing caregiving environment, fostering anxiety problems. This adds to previous research relating hypercortisolism to child internalizing problems, while emphasizing the point that higher cortisol is not universally problematic (i.e., unrelated to symptoms for lower-risk children), but it is for those in unsupportive environmental contexts. Notably, we did not find the hypothesized association between hypocortisolism and child externalizing problems. This effect has not been as consistent in the literature. Research involving different age ranges (including adolescence) and adversity conditions might reveal further associations with externalizing psychopathology.

The long-term intervention effects in this study are a testament to the power of the MTFC-P approach to shift not only child HPA activation, but also the implications of such activation. Participation in the treatment produced an HPA profile similar to the community comparison children—that is, higher morning cortisol levels and daily stability, as shown previously in this sample (Fisher et al., 2007)—but without the symptom cost noted for their regular foster care counterparts. As laid out by the ACM, these children may have upregulated their stress sensitivity to benefit from a more consistent, supportive caregiving environment afforded by the treatment. Both the child-focused and caregiver-focused services could have played a role in this calibration. Consistent with previous research in normative samples, developing more competent social skills in a group setting may lead to child cortisol increases (Gunnar, Tout, de Haan, Pierce, & Stansbury, 1997; Turner-Cobb, Rixon, & Jessop, 2008).

On the caregiver side, the training and support offered by MTFC-P likely allowed foster parents and permanent placement caregivers to provide more sensitive scaffolding for children’s developing stress regulation, which could also foster a progression toward the HPA profiles found in lower-risk developmental contexts. A more fine-grained analysis of cortisol levels and stability from pre- through post-intervention might reveal when this shift typically occurs, and which aspects of the treatment are most important to bring it about.

The fact that observed findings were derived from the more frequent cortisol sampling early in the study period may speak to the importance of early childhood HPA function, proximity to the intervention, or both, and future research examining intervention effects at different developmental periods will be needed to disentangle these influences. Possible benefits of enhanced stress sensitivity should be further explored by testing effects not only on symptoms, but also on positive psychosocial and cognitive outcomes. For now, this study supports the effectiveness of MTFC-P for getting “under the skin” of high-risk children to enhance adjustment.

Limitations of the present study point to future steps in this research. The stress focus in this study was confined to daily levels of activation in the HPA system. As suggested by recent multisystem stress research (i.e., Laurent, Ablow, & Measelle, 2011, 2012; Laurent, Powers, & Granger, 2013), more could be learned about the nature of stress adaptation by examining coordination across multiple physiological and subjective measures over time. With only two daily cortisol assessments, more nuanced questions about stability of daily rhythms (i.e., slopes over the course of the day) and the cortisol awakening response could not be addressed; these represent directions for future research. Further, comparing the effects of daily cortisol levels and cortisol reactivity, as well as stability in each across development, would help to inform the sensitivity construct proposed by the BSC. Although the present sample offered a window into an important high-risk developmental context, it was not a clinically referred sample and measurement was confined to a relatively early stage of development before the expected onset of many psychiatric disorders. Also, the modest sample size available may have limited power, especially for detecting interaction effects, and null findings should be interpreted with caution. Studies with larger, clinically referred adolescent samples could reveal further associations with psychopathology than we were able to detect in the present study.

Limitations notwithstanding, this study offers several noteworthy contributions to the developmental stress literature. We demonstrated stability in children’s daily cortisol levels across a longer timeframe and more numerous longitudinal assessments than previous research, while highlighting differences in stability related to social–environmental risk. Patterns of differential cortisol levels and stability and associations with psychiatric symptoms across risk groups offered empirical support to theoretical proposals of adaptive calibration and context-specific effects of stress sensitivity. Finally, we add to knowledge of biological paths by which intervention with high-risk families can bring children closer to their lower-risk peers. These findings offer hope that all children could benefit from sensitivity to a supportive environment, whether they began life in such an environment or not.

Acknowledgments

The support for this research was provided by the grants MH59780 and MH65046 from the National Institute of Mental Health.

References

- Bhagwagar Z, Hafizi S, Cowen PJ. Increased salivary cortisol after waking in depression. *Psychopharmacology*. 2005; 182:54–57.10.1007/s00213-005-0062-z [PubMed: 15991000]
- Boyce WT, Ellis BJ. Biological sensitivity to context: I. An evolutionary-developmental theory of the origins and functions of stress reactivity. *Development and Psychopathology*. 2005; 17:271–301.10.1017/S0954579405050145 [PubMed: 16761546]
- Bruce J, Fisher PA, Pears KC, Levine S. Morning cortisol Levels in preschool-aged foster children: Differential effects of maltreatment type. *Developmental Psychobiology*. 2009; 51:14–23.10.1002/dev.20333 [PubMed: 18720365]
- Bush NR, Obradovi J, Adler N, Boyce WT. Kindergarten stressors and cumulative adrenocortical activation: The “first straws” of allostatic load? *Development and Psychopathology*. 2011; 23:1089–1106.10.1017/S0954579411000514 [PubMed: 22018083]
- Cicchetti D, Rogosch FA. The impact of child maltreatment and psychopathology on neuroendocrine functioning. *Development and Psychopathology*. 2001; 13:783–804. [PubMed: 11771908]
- Cutuli JJ, Wiik KL, Herbers JE, Gunnar MR, Masten AS. Cortisol function among early school-aged homeless children. *Psychoneuroendocrinology*. 2010; 35:833–845.10.1016/j.psyneuen.2009.11.008 [PubMed: 20022181]
- Danese A, McEwen BS. Adverse childhood experiences, allostasis, allostatic load, and age-related disease. *Physiological Behavior*. 2011; 106:29–39.10.1016/j.physbeh.2011.08.019
- De Weerth C, van Geert P. A longitudinal study of basal cortisol in infants: Intra-individual variability, circadian rhythm and developmental trends. *Infant Behavior and Development*. 2002; 25:375–398.10.1016/S0163-6383(02)00141-8
- Del Giudice M, Ellis BJ, Shirtcliff EA. The adaptive calibration model of stress responsivity. *Neuroscience and Biobehavioral Reviews*. 2011; 35:1562–1592.10.1016/j.neubiorev.2010.11.007 [PubMed: 21145350]
- Dozier M, Peloso E, Lewis E, Laurenceau JP, Levine S. Effects of an attachment-based intervention on the cortisol production of infants and toddlers in foster care. *Development and Psychopathology*. 2008; 20:845–859.10.1017/S0954579408000400 [PubMed: 18606034]
- Ellis BJ, Essex MJ, Boyce WT. Biological sensitivity to context: II. Empirical explorations of an evolutionary-developmental theory. *Development and Psychopathology*. 2005; 17:303–328.10.1017/S0954579405050157 [PubMed: 16761547]
- Engert V, Efanov SI, Dedovic K, Dagher A, Pruessner JC. Increased cortisol awakening response and afternoon/evening cortisol output in healthy young adults with low early life parental care. *Psychopharmacology*. 2011; 214:261–268.10.1007/s00213-010-1918-4 [PubMed: 20596856]
- Essex MJ, Shirtcliff EA, Burk LR, Ruttle PL, Klein MH, Slattery MJ, Armstrong JM. Influence of early life stress on later hypothalamic–pituitary–adrenal axis functioning and its covariation with mental health symptoms: A study of the allostatic process from childhood into adolescence. *Development and Psychopathology*. 2011; 23(4):1039–1058.10.1017/S0954579411000484 [PubMed: 22018080]
- Fisher PA, Chamberlain P. Multidimensional treatment foster care: A program for intensive parenting, family support, and skill building. *Journal of Emotional and Behavioral Disorders*. 2000; 8:155–164.10.1177/106342660000800303
- Fisher PA, Gunnar MR, Dozier M, Bruce J, Pears KC. Effects of therapeutic interventions for foster children on behavioral problems, caregiver attachment, and stress regulatory neural systems. *Annals of the New York Academy of Sciences*. 2006; 1094:215–225.10.1196/annals.1376.023 [PubMed: 17347353]
- Fisher PA, Kim HK, Bruce J, Pears KC. Cumulative effects of prenatal substance exposure and early adversity on foster children’s HPA-axis reactivity during a psychosocial stressor. *International Journal of Behavioral Development*. 2011; 36:29–35.10.1177/0165025411406863 [PubMed: 22962506]
- Fisher PA, Stoolmiller M. Intervention effects on foster parent stress: Associations with child cortisol levels. *Development and Psychopathology*. 2008; 20:1003–1021.10.1017/S0954579408000473 [PubMed: 18606041]

- Fisher PA, Stoolmiller M, Gunnar MR, Burraston BO. Effects of a therapeutic intervention for foster preschoolers on diurnal cortisol activity. *Psychoneuroendocrinology*. 2007; 32:892–905.10.1016/j.psyneuen.2007.06.008 [PubMed: 17656028]
- Gunnar MR, Donzella B. Social regulation of the cortisol levels in early human development. *Psychoneuroendocrinology*. 2002; 27:199–220.10.1016/S0306-4530(01)00045-2 [PubMed: 11750779]
- Gunnar MT, Tout K, de Haan M, Pierce S, Stansbury K. Temperament, social competence, and adrenocortical activity in preschoolers. *Developmental Psychobiology*. 1997; 31:65–85.10.1002/(SICI)1098-2302(199707)31:1<65::AID-DEV6>3.0.CO;2-S [PubMed: 9222117]
- Gunnar MR, Vazquez DM. Low cortisol and a flattening of expected daytime rhythm: Potential indices of risk in human development. *Development and Psychopathology*. 2001; 13:515–538.10.1017/S0954579401003066 [PubMed: 11523846]
- Heim C, Ehler U, Hellhammer DH. The potential role of hypocortisolism in the pathophysiology of stress-related bodily disorders. *Psychoneuroendocrinology*. 2000; 25(1):1–35.10.1016/S0306-4530(99)00035-9 [PubMed: 10633533]
- Hunter AL, Minnis H, Wilson P. Altered stress responses in children exposed to early adversity: A systematic review of salivary cortisol studies. *Stress*. 2011; 14:614–626.10.3109/10253890.2011.577848 [PubMed: 21675865]
- Juster RP, Bizik G, Picard M, Arsenault-Lapierre G, Sindi S, Trepanier L, Lupien SJ. A transdisciplinary perspective of chronic stress in relation to psychopathology throughout life span development. *Development and Psychopathology*. 2011; 23(3):725–726.10.1017/S0954579411000289 [PubMed: 21756430]
- Laurent HK, Ablow JC, Measelle J. Risky shifts: How the timing and course of mothers' depressive symptoms across the perinatal period shape their own and infant's stress response profiles. *Development and Psychopathology*. 2011; 23:521–538.10.1017/S0954579411000083 [PubMed: 23786693]
- Laurent HK, Ablow JC, Measelle J. Taking stress response out of the box: Stability, discontinuity, and temperament effects on HPA and SNS across social stressors in mother-infant dyads. *Developmental Psychology*. 2012; 48:35–45.10.1037/a0025518 [PubMed: 21928882]
- Laurent HK, Neiderhiser JM, Natsuaki MN, Shaw DS, Fisher PA, Reiss D, Leve LD. Stress system development from age 4.5 to 6: Family environment predictors and adjustment implications of HPA activity stability versus change. *Developmental Psychobiology*. 2014; 56:340–354.10.1002/dev.21103 [PubMed: 23400689]
- Laurent HK, Powers SI, Granger DA. Refining the multisystem view of the stress response: Coordination among cortisol, alpha-amylase, and subjective stress in response to relationship conflict. *Physiology and Behavior*. 2013; 119:52–60.10.1016/j.physbeh.2013.05.019 [PubMed: 23684904]
- Miller GE, Chen E, Zhou ES. If it goes up, must it come down? Chronic stress and the hypothalamic-pituitary-adrenocortical axis in humans. *Psychological Bulletin*. 2007; 133:25–45. [PubMed: 17201569]
- Peeters F, Nicolson NA, Berkhof J. Levels and variability of daily life cortisol secretion in major depression. *Psychiatry Research*. 2004; 126:1–13.10.1016/j.psychres.2003.12.010 [PubMed: 15081622]
- Raudenbush, SW.; Bryk, AS. Hierarchical linear models: Applications and data analysis methods. 2. Newbury Park, CA: Sage; 2002.
- Rotenberg S, McGrath JJ, Roy-Gagnon MH, Tu MT. Stability of the diurnal cortisol profile in children and adolescents. *Psychoneuroendocrinology*. 2012; 37:1981–1989.10.1016/j.psyneuen.2012.04.014 [PubMed: 22658393]
- Ruttle PL, Shirtcliff EA, Serbin LA, Ben-Dat Fisher D, Stack DM, Schwartzman AE. Disentangling psychobiological mechanisms underlying internalizing and externalizing behaviors in youth: Longitudinal and concurrent associations with cortisol. *Hormones and Behavior*. 2011; 59:123–132.10.1016/j.yhbeh.2010.10.015 [PubMed: 21056565]

- Schwartz EB, Granger DA, Susman EJ, Gunnar MR, Laird B. Assessing salivary cortisol in studies of child development. *Child Development*. 1998; 69:1503–1513.10.1111/j.1467-8624.1998.tb06173.x [PubMed: 9914636]
- Shaffer D, Fisher P, Lucas CP, Dulcan MK, Schwab-Stone ME. NIMH Diagnostic Interview Schedule for Children Version IV (NIMH DISC-IV): Description, differences from previous versions, and reliability of some common diagnoses. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2000; 39:28–38.10.1097/00004583-200001000-00014 [PubMed: 10638065]
- Shirtcliff EA, Allison AL, Armstrong JM, Slattery MJ, Kalin NH, Essex MJ. Longitudinal stability and developmental properties of salivary cortisol levels and circadian rhythms from childhood to adolescence. *Developmental Psychobiology*. 2012; 54:493–502.10.1002/dev.20607 [PubMed: 21953537]
- Shirtcliff EA, Granger DA, Booth A, Johnson D. Low salivary cortisol levels and externalizing behavior problems in youth. *Development and Psychopathology*. 2005; 17:167–184.10.1017/S0954579405050091 [PubMed: 15971765]
- Turner-Cobb JM, Rixon L, Jessop DS. A prospective study of diurnal cortisol responses to the social experience of school transition in four-year-old children: Anticipation, exposure, and adaptation. *Developmental Psychobiology*. 2008; 50:377–389.10.1002/dev.20298 [PubMed: 18393279]
- Vrshek-Schallhorn S, Doane LD, Mineka S, Zinbarg RE, Craske MG, Adam EK. The cortisol awakening response predicts major depression: Predictive stability over a 4-year follow-up and effect of depression history. *Psychological Medicine*. 2012; 43:483–493.10.1017/S0033291712001213 [PubMed: 22652338]

FIGURE 1.
Cortisol trajectories over time by group.

FIGURE 2.

Associations between child anxiety disorder symptoms and cortisol levels by group.

FIGURE 3.
Associations between child anxiety disorder symptoms and cortisol stability by group.

Table 1

Sample Descriptives

Categorical Variables	Frequency	Percent
Males	48	50%
Community Group	46	48%
Regular Foster Care Group	22	23%
Treatment Foster Care Group	28	29%
Foster Child in Permanent Placement ^a	48	96%

Continuous Variables	Range	M, SD
Age at First Assessment (years)	2.99–6.78	4.40, .77
Age at Final Assessment (years)	8.74–12.88	10.33, .78
Number of Foster Care Transitions	2–15	7.16, 3.38
Anxiety Disorder Symptoms	0–39	7.38, 6.87
Eating Disorder Symptoms	0–3	.24, .52
Mood Disorder Symptoms	0–25	6.48, 5.03
Disruptive Behavior Disorder Symptoms	0–40	14.98, 9.34
Alcohol/Substance Use Disorder Symptoms	0–0	0

Symptom scores represent total count from DISC modules.

^aChild adopted or reunified with birth parent at final assessment.

Table 2

Final Predictive Model for Child Cortisol Levels and Stability

Predictor	Coefficient	p-Value
Cortisol intercept (mean level)		
Regular Foster Care Group	-.025	.03
DISC Anxiety Symptoms	-.009	.10
Regular Foster Care Group×Anxiety Symptoms	.027	.04
Lagged cortisol effect (stability)		
Regular Foster Care Group	-.064	.02
DISC Anxiety Symptoms	.015	.33
Regular Foster Care Group×Anxiety Symptoms	.094	.002