

Cortisol Production Patterns in Young Children Living With Birth Parents vs Children Placed in Foster Care Following Involvement of Child Protective Services

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Objective: To examine differences in waking to bedtime cortisol production between children who remained with birth parents vs children placed in foster care following involvement of Child Protective Services (CPS).

Design: Between-subject comparison of cortisol patterns among 2 groups of children.

Setting: Children referred from the child welfare system.

Participants: Three hundred thirty-nine children aged 2.9 to 31.4 months who were living with birth parents (n=155) or placed in foster care (n=184) following CPS involvement as well as 96 unmatched children from low-risk environments.

Main Exposures: Involvement by CPS and foster care.

Main Outcome Measure: Salivary cortisol samples obtained at waking and bedtime for children on 2 days.

Results: Child Protective Services-involved children who continued to live with birth parents and CPS-involved children placed in foster care differed in cortisol production, with children living with their birth parents showing flatter slopes in waking to bedtime values.

Conclusions: Continuing to live with birth parents following involvement of CPS is associated with greater perturbation to the diurnal pattern of cortisol production than living with foster parents. Foster care may have a regulating influence on children's cortisol among children who have experienced maltreatment.

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THE FUNCTIONING OF THE hypothalamus-pituitary-adrenal (HPA) axis is vulnerable to the effects of early adversity. Experimental studies with rodent and nonhuman primate young as well as correlational studies (or natural experiments) with young children have shown that neglect and separation from caregivers are associated with perturbations to the functioning of the HPA axis.¹⁻⁶ In particular, experiences of neglect and separation from caregivers affect the production of glucocorticoids (cortisol among humans), an end product of the HPA axis. Alterations to the diurnal pattern of cortisol production have been seen among children living with their birth parents following maltreatment and among neglected children placed in foster care.³⁻⁶ In previous studies, it has not been possible to discern whether children who continue to live with their birth parents or those placed in foster care have shown greater perturbations in HPA functioning following involvement of Child Protective Services (CPS). Our study addresses this question.

A typical daytime cortisol pattern is characterized by a high waking value (peaking about 30 minutes after waking), followed by a rapid decline and then a slow drop-off across the day, reaching a nadir at bedtime. This pattern begins to emerge in the first 2 months of life, with mature functioning emerging by 5 to 6 years of age.^{7,8} Young children who have experienced neglect often differ from children from low-risk environments in showing a more blunted pattern of cortisol production across the day.³⁻⁵ Morning levels of cortisol have been shown to be lower with a flatter waking to bedtime slope than for other children.

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These findings have emerged for neglected children living with their birth parents and for neglected children placed in foster care.³⁻⁵ In the studies conducted to date, high-risk children (neglected children living with birth parents or with

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Table 1. Child Demographic Characteristics

Group	Children, No. (%)						Age, Mean (SD), mo
	Sex		Race/Ethnicity				
	Male	Female	White	African American	Hispanic	Biracial	
CPS-involved, stayed with birth parents (n=155)	38 (54)	33 (46)	8 (11)	44 (62)	13 (18)	6 (9)	12.7 (6.6)
CPS-involved, placed in foster care (n=184)	69 (57)	52 (43)	32 (27)	77 (64)	7 (6)	4 (3)	11.2 (6.5)
Low-risk environment (n=96)	46 (54)	39 (46)	49 (58)	21 (25)	8 (9)	7 (8)	16.1 (6.6)

Abbreviation: CPS, Child Protective Services.

foster parents) have been compared with children with no known risk factors.³⁻⁵ To our knowledge, no study has contrasted HPA functioning of children living with birth parents vs HPA functioning of children living with foster parents following involvement of CPS.

The primary aim of this study was to examine daily cortisol production patterns among maltreated children following involvement of CPS. Specifically, we were interested in whether there were differences in daily cortisol production between CPS-involved children who continued to live with their birth parents and children who were placed into foster care. We included data from a third group of unmatched children from low-risk conditions to provide an estimate of typical levels of cortisol among children of this age. We hypothesized that, relative to children placed into foster care, CPS-involved children who continued to live with their birth parents would show a more perturbed pattern because they were likely experiencing ongoing neglect from caregivers.

METHODS

PARTICIPANTS

Primary participants included 339 children, ranging in age from 2.9 to 31.4 months (mean [SD], 12.9 [6.9] months). All children were involved with CPS and referred for participation in ongoing longitudinal studies assessing the effectiveness of an attachment-based parenting intervention; only children's pre-intervention data were included in this study. Following involvement of CPS, 155 of the children continued to live with their birth parents and 184 of the children were placed in foster care. For those placed in foster care, it was the first placement for 138 children (75%), the second placement for 42 (23%), the third placement for 2 (1%), and the fourth placement for 2 (1%). The duration with the current foster parent at the time of enrollment in our study ranged from 0.1 to 18.1 months (mean [SD], 3.6 [3.6] months). Secondarily, 96 children from low-risk environments were included. Participants in the low-risk group were recruited from a university-based child care center. **Table 1** shows demographic characteristics of each group.

PROCEDURES

The study had institutional review board approval and involved informed consent regarding research participation. Parents collected saliva samples from children at waking and bedtime for 2 consecutive days as part of the preintervention data collection for the larger study. Saliva samples were obtained by placing the end of a dental cotton roll in the child's mouth.

For children older than 12 months, flavored beverage crystals (cherry-flavored drink mix; Pathmark, Montvale, New Jersey) were provided to facilitate sampling. Parents were instructed to first wet the cotton in the child's mouth, then dip the cotton in a cup containing 0.8 g of the flavored crystals and place it back in the child's mouth until the cotton was soaking wet. Recent controlled studies have reported that flavored crystals only minimally affect cortisol levels when radioimmunoassay is used.^{9,10} The saturated cotton roll was returned to a prelabeled vial and stored in the freezer until it was picked up by a research assistant. Waking samples were collected between 5:00 AM and 12:00 PM (mean, 8:03 AM) and bedtime samples were collected between 6:30 PM and 12:47 AM (mean, 8:48 PM). **Table 2** shows descriptive statistics of sampling times. To ensure that sampling guidelines were followed, parents completed questionnaires about infant health status variables such as whether children were teething, were sick, or had eaten prior to sampling. If children were sick, parents were asked to delay sampling until the children were healthy again.

The saliva samples were stored in a freezer at -20°C prior to assay procedures. Samples were assayed using a high-sensitivity salivary cortisol enzyme immunoassay kit (Salimetrics, LLC, State College, Pennsylvania). All samples from a child were assayed in duplicate on the same plate to minimize variability. The intra-assay and interassay coefficients of variation fell below 7% and 14%, respectively.

CORTISOL DATA PREPARATION

Following procedures commonly used in previous studies,¹¹ cortisol values 3 SDs above the mean were considered outliers and excluded from analyses. Each child could have up to 4 cortisol values (ie, 2 waking and 2 bedtime samples). Of 1740 possible samples, 61 outliers were removed and 126 samples were missing due to an inadequate volume of saliva or because no sample was taken, representing approximately 11% of the data. Missing data patterns were comparable across groups, with children living with birth parents missing approximately 9%, children living with foster parents missing 13%, and children from low-risk environments missing 10% (Table 2). Log_{10} transformation was used to normalize the distribution of cortisol values owing to a positive skew.

PRELIMINARY ANALYSES

Demographic variables were examined to determine whether child characteristics were associated with log-transformed cortisol values. Child age, sex, and minority status were not associated with cortisol values at any of the time points ($P > .05$). Time of sample collection was also not associated with cortisol values at any of the time points ($P > .05$). Despite these findings, child age and sampling time were included in primary

Table 2. Descriptive Statistics

Group	Samples, No.	Time of Sample ^a			Cortisol Value, µg/dL			Log-Transformed Cortisol Value		
		Mean (SD)	Minimum	Maximum	Mean (SD)	Minimum	Maximum	Mean (SD)	Minimum	Maximum
CPS-involved, stayed with birth parents (n=155)										
Waking										
Day 1	145	8:32 (1:26)	5:00	11:55	0.26 (0.24)	0.006	1.15	-0.76 (0.43)	-2.22	0.06
Day 2	147	8:24 (1:44)	5:35	12:00 ^b	0.31 (0.29)	0.001	1.60	-0.72 (0.51)	-3.00	0.20
Bedtime										
Day 1	141	9:18 (1:20)	6:45	12:40 ^c	0.24 (0.27)	0.002	1.34	-0.91 (0.57)	-2.70	0.13
Day 2	133	9:11 (1:15)	6:30	12:35 ^c	0.26 (0.30)	0.004	1.66	-0.85 (0.52)	-2.40	0.22
CPS-involved, placed in foster care (n=184)										
Waking										
Day 1	161	7:47 (1:33)	5:00	11:55	0.35 (0.30)	0.001	1.65	-0.64 (0.49)	-3.00	0.22
Day 2	166	7:48 (1:12)	5:00	11:30	0.33 (0.32)	0.003	1.54	-0.68 (0.48)	-2.52	0.19
Bedtime										
Day 1	157	8:32 (1:33)	6:55	12:03 ^c	0.16 (0.22)	0.002	1.28	-1.08 (0.51)	-2.69	0.11
Day 2	157	8:23 (1:36)	6:33	11:30	0.16 (0.22)	0.001	1.18	-1.14 (0.57)	-3.00	0.07
Low-risk environment (n=96)										
Waking										
Day 1	88	7:49 (0:54)	5:50	10:25	0.40 (0.29)	0.002	1.22	-0.53 (0.40)	-2.70	0.09
Day 2	88	7:47 (0:54)	6:05	10:32	0.42 (0.31)	0.006	1.54	-0.52 (0.40)	-2.22	0.19
Bedtime										
Day 1	84	8:48 (1:03)	6:45	12:47 ^c	0.14 (0.23)	0.006	1.43	-1.12 (0.46)	-2.22	0.16
Day 2	86	8:44 (0:59)	6:45	12:15 ^c	0.10 (0.15)	0.011	1.10	-1.22 (0.39)	-1.96	0.04

Abbreviation: CPS, Child Protective Services.

SI conversion factor: To convert cortisol value to nanomoles per liter, multiply by 27.588.

^aMean waking times are shown as AM and mean bedtime times are shown as PM unless otherwise indicated.

^bTime is PM.

^cTime is AM.

analyses as both have been significantly related to cortisol levels in previous studies.^{7,8,11}

DATA ANALYTIC STRATEGY

Group differences in cortisol levels at waking and bedtime as well as change in cortisol levels across the day were analyzed using hierarchical linear modeling.¹² Hierarchical linear modeling treats repeated observations as nested within individuals, allowing for separate estimates of within-subject (level 1) and between-subject (level 2) variation. This nesting accounted for the nonindependence of multiple samples from the same child. Rather than aggregating across days to create an average waking cortisol level and an average bedtime cortisol level for each child (resulting in only 2 data points per child), all samples were used as level 1 data (resulting in up to 4 data points per child). This approach is more appropriate than averaging across samples because it accounts for measurement error associated with each sample.¹³ Data were analyzed in 2 steps. First, CPS-involved children living with birth parents were compared with CPS-involved children living in foster care. Then, children from low-risk environments were included as a reference group to provide an estimate of typical cortisol levels.

The dependent variable was the log-transformed cortisol value, measured in micrograms per deciliter. Cortisol sample collection time (in hours since the average waking sample time) was included as a time-varying covariate. The following level 1 within-individual model was specified:

$$\log \text{cortisol}_{it} = \pi_{0i} + \pi_{1i}(\text{sample}) + \pi_{2i}(\text{time}) + e_{it}$$

where $\log \text{cortisol}_{it}$ represents the log-transformed cortisol value for child i at time t ; π_{0i} represents child i 's estimated log cor-

tisol value at waking when controlling sampling time; π_{1i} is the estimated slope of cortisol change from waking to bedtime; π_{2i} is the regression coefficient representing the effect of the time-varying covariate (ie, sampling time); sample represents the time of day of the sample (with 0 representing waking and 1 representing bedtime); time represents the collection time of the sample in hours from the mean time for waking sample collection (ie, 8:03 AM); and e_{it} is the within-individual error in child i 's log cortisol value.

Level 2 variables were included to examine whether group status (ie, CPS-involved children living with birth parents or CPS-involved children living with foster parents) predicted individual differences in cortisol levels at waking or bedtime and in change across the day. Group status was dummy coded (0 for children living with foster parents, 1 for children living with birth parents) to allow for comparisons among individuals between the 2 groups. Child age was included as a control variable given that previous studies have found changes in cortisol production across development.⁸ The resulting level 2 model can be represented as follows:

$$\begin{aligned} \pi_{0i} &= \beta_{00} + \beta_{01}(\text{CPS-birth}) + \beta_{02}(\text{child's age}) + r_{0i} \\ \pi_{1i} &= \beta_{10} + \beta_{11}(\text{CPS-birth}) + \beta_{12}(\text{child's age}) + r_{1i} \\ \pi_{2i} &= \beta_{20} \end{aligned}$$

where π_{0i} represents the waking log cortisol value for an individual and π_{1i} represents the linear change (slope) in log cortisol across the day for an individual; the term β_{00} represents the average estimated log cortisol level at waking for CPS-involved children living with foster parents, controlling for child's age; β_{01} is the difference in the waking log cortisol value between the CPS-involved children living with foster parents and the CPS-involved children living with birth parents (ie, the group

Table 3. Multilevel Modeling Coefficients of Group Effects on Diurnal Cortisol Production

Effect ^a	Log-Transformed Cortisol Value			
	β Coefficient (SE)	<i>t</i> Statistic	<i>df</i>	<i>P</i> Value
Intercept, β_{00}	-.65 (.03)	-19.97	326	<.001
CPS-birth, β_{01}	-.09 (.05)	-1.94	326	.05
Child's age, β_{02}	-.00 (.00)	-0.71	326	.48
Sample slope, β_{10}	-.45 (.04)	-11.82	326	.002
CPS-birth, β_{11}	.30 (.06)	5.21	326	<.001
Child's age, β_{12}	-.00 (.00)	-0.77	326	.51
Time slope, β_{20}	-.00 (.01)	-0.21	1067	.84

Abbreviation: CPS, Child Protective Services.

^a β_{00} and β_{10} represent the waking level of cortisol and the slope of cortisol production across the day, respectively, for children living with foster parents. β_{01} and β_{11} represent the difference in the waking level of cortisol and the slope of cortisol production across the day, respectively, between CPS-involved children living with foster parents and CPS-involved children living with their birth parents.

dummy coded 1); β_{02} is the regression coefficient representing the effect of the child's age (grand centered at the mean); CPS-birth represents the dummy-coded group status (with 0 representing children living with foster parents and 1 representing children living with birth parents); child's age represents the child's age in months; and r_{0i} is the between-child individual differences left unexplained by the level 2 predictors. The equations for linear change (ie, π_{1i}) also included the group status variable to compare cortisol change across the day between the groups.

In the second analysis, the same level 1 was specified, this time including data from the children in low-risk environments. A similar model was identified at level 2, with group status dummy coded to allow for comparisons among individuals of any 2 groups against a selected reference group—the low-risk sample in this case. The resulting level 2 model can be represented as follows:

$$\pi_{0i} = \beta_{00} + \beta_{01}(\text{CPS-foster}) + \beta_{02}(\text{CPS-birth}) + \beta_{03}(\text{child's age}) + r_{0i}$$

$$\pi_{1i} = \beta_{10} + \beta_{11}(\text{CPS-foster}) + \beta_{12}(\text{CPS-birth}) + \beta_{13}(\text{child's age}) + r_{1i}$$

$$\pi_{2i} = \beta_{20}$$

where the term β_{00} represents the average estimated log cortisol waking level for the low-risk comparison group; β_{01} is the difference between the low-risk comparison group and the CPS-involved children living with foster parents (ie, the group dummy coded 1 in the first group dummy code) at waking; and β_{02} is the difference between the low-risk comparison group and the CPS-involved children living with birth parents (ie, the group dummy coded 1 in the second group dummy code). Other terms are similar to those described earlier for the first level 2 model.

RESULTS

To examine group-related differences in the diurnal pattern of cortisol production, we examined whether group status predicted the waking level of cortisol (intercept) and the change in cortisol level from waking to bedtime (slope). Results of the first model are summarized in **Table 3**. When controlling for sample collection time (at level 1) and child's age (at level 2), the log cortisol waking level differed significantly between CPS-involved children placed in foster care and CPS-involved children who continued to live with birth parents, with children living with birth parents showing a lower waking level of cortisol (Table 3).

The model was rerun with the bedtime sample as the intercept, indicating that CPS-involved children living with their birth parents had significantly higher cortisol levels at bedtime than children living with foster parents ($\beta_{01} = .20$; $P = .001$). Furthermore, the change in cortisol level across the day differed significantly between the groups, with CPS-involved children living with their birth parents showing a more blunted pattern (ie, flatter slope) than children living with foster parents (Table 3).

The secondary analysis including the low-risk children as the reference group indicated that both CPS-involved children living with their birth parents and those living with foster parents differed significantly from the low-risk children in terms of their waking cortisol levels and slope across the day (**Table 4**). Whereas CPS-involved children living with birth parents also differed from low-risk children in their bedtime cortisol levels ($\beta_{02} = .26$; $P < .001$), children placed in foster care did not ($\beta_{01} = .05$; $P = .46$). Comparison of the magnitude of differences between low-risk children and CPS-involved children indicates that CPS-involved children living with their birth parents showed the most blunted pattern of diurnal cortisol production. The **Figure** presents the estimates of the waking and bedtime values for each group.

COMMENT

Consistent with previous studies,³⁻⁵ our results indicate that CPS-involved children, who have typically experienced maltreatment, differ from low-risk children in showing lower waking cortisol values and flatter patterns of cortisol production from waking to bedtime. The findings go beyond prior studies to show that CPS-involved children who continue to live with their birth parents appear to have the greatest perturbation to their systems. Children living with their birth parents have lower waking cortisol values than both CPS-involved children living with foster parents and children from low-risk environments, and they have flatter slopes from waking to bedtime than other children.

Although foster care involves disruptions in children's relationships with parents, children are better able to regulate their neuroendocrine systems when living with foster parents than when they continue to live with ne-

Table 4. Multilevel Modeling Coefficients of Group Effects on Diurnal Cortisol Production With Low-Risk Children as Reference Group

Effect ^a	β Coefficient (SE)	t Statistic	df	P Value
Intercept, β_{00}	-.49 (.04)	-11.12	411	<.001
CPS-foster, β_{01}	-.18 (.05)	-3.27	411	.002
CPS-birth, β_{02}	-.26 (.06)	-4.71	411	<.001
Child's age, β_{03}	-.00 (.00)	-0.84	411	.40
Sample slope, β_{10}	-.67 (.14)	-4.72	411	<.001
CPS-foster, β_{11}	.22 (.07)	3.41	411	.001
CPS-birth, β_{12}	.52 (.07)	7.76	411	<.001
Child's age, β_{13}	-.00 (.00)	-0.60	411	.55
Time slope, β_{20}	-.00 (.01)	-0.18	1345	.86

Abbreviation: CPS, Child Protective Services.

^a β_{00} and β_{10} represent the waking level of cortisol and the slope of cortisol production across the day, respectively, for low-risk children. β_{01} and β_{11} represent the difference in the waking level of cortisol and the slope of cortisol production across the day, respectively, between low-risk children and CPS-involved children living with foster parents. β_{02} and β_{12} represent the difference in the waking level of cortisol and the slope of cortisol production across the day, respectively, between low-risk children and CPS-involved children living with their birth parents.

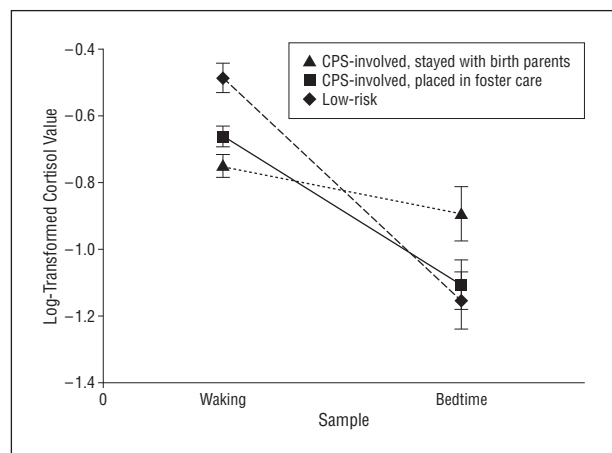


Figure. Cortisol patterns for Child Protective Services (CPS)-involved children who stayed with birth parents, CPS-involved children placed in foster care, and low-risk children. Cortisol levels were measured as micrograms per deciliter (to convert to nanomoles per liter, multiply by 27.588). Error bars indicate SE.

glecting birth parents. The advantages of being removed from a neglecting environment appear to outweigh the disadvantages associated with disruptions in care, at least in terms of HPA regulation. We interpret these results to suggest that foster care represents an effective intervention for children, at least with regard to enhancing children's ability to maintain a more typical diurnal pattern of cortisol production. Future research is needed, however, to examine what additional factors (eg, maltreatment history, ongoing neglect, conditions of poverty, parental insensitivity) contribute to these group differences. Clarifying possible explanatory factors may help target interventions for children at risk for biological dysregulation.

A blunted pattern of cortisol production appears to confer risk for later psychiatric disorders, most especially psychopathy and substance abuse problems. For example, blunted patterns of cortisol production are predictive of increases in aggressive behavior over time and characterize adolescents with conduct disorder and adults with antisocial personality disorder and substance use disorder.¹⁴⁻¹⁷ Shirtcliff and colleagues¹⁷ have argued that HPA hyporeactivity is central to the development of callous behavioral traits. The impaired neural circuitry of indi-

viduals with blunted or hyporeactive HPA systems leaves them underaroused by the distress of others and thus vulnerable to behaving in callous ways. Although it is premature to suggest specific implications for neglected children, the findings are concerning.

These and other findings suggest the plasticity of the HPA system in early development. On the one hand, conditions of neglect adversely affect children's HPA system functioning. On the other hand, interventions such as foster care and specialized services can remediate the system's functioning.¹⁸⁻²¹ For example, 2 randomized clinical trials have shown that specialized training for foster and birth parents results in children showing more normative cortisol patterns.¹⁸⁻²¹ These results emphasize the importance of prevention for young children exposed to early adversity given that neural circuitry and associated developmental trajectories become less plastic over time.

The greatest limitation of this study is that it did not use an experimental design. It is not possible to randomly assign children to conditions of neglect or foster care, and therefore a third variable (or variables) could account for the findings. Indeed, we expect that the 2 groups of children who experienced maltreatment differ from the comparison children perhaps in ways that are important to HPA regulation. Nonetheless, the 2 groups of CPS-involved children (those who continued to live with birth parents and those placed in foster care) provide reasonable comparisons for one another. Differences in prenatal histories would likely be expected to favor children living with birth parents, making it unlikely that obtained differences between these 2 groups are attributable to prenatal factors.

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