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BRIEF REPORT

Foster parent responsiveness and young children's diurnal cortisol production

Aline K. Szenczy[1] | Kristin Bernard[1] | K. Lee Raby[2] | Mallory Garnett[3] | Mary Dozier[3]

[1]Department of Psychology, Stony Brook University, Stony Brook, NY, USA

[2]Department of Psychology, University of Utah, Salt Lake City, UT, USA

[3]Department of Psychological and Brain Sciences, University of Delaware, Newark, DE, USA

Correspondence
Aline K. Szenczy, Department of Psychology, Stony Brook University, 100 Nicolls Rd, Stony Brook, NY 11794, USA.
Email: aline.szenczy@stonybrook.edu

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Abstract

Foster children are at risk for dysregulated hypothalamic pituitary adrenal (HPA) axis functioning, conferring risk for negative health outcomes. Responsive parenting may support young children's HPA axis regulation; however, few studies have examined the association between responsive parenting and cortisol production among children in foster care. In a sample of 97 foster parent–child dyads, we examined whether variation in foster parent responsiveness was linked to children's waking and bedtime levels of cortisol. Children's saliva samples were collected at wake-up and bedtime for three consecutive days. Foster parent responsiveness, as indicated by parent sensitivity, intrusiveness, and positive regard, was assessed during video-recorded semistructured play interactions between foster parents and children. Foster parent responsiveness significantly predicted children's waking cortisol levels ($\beta = 0.26$, $p = .023$). Follow-up analyses revealed that foster parent sensitivity uniquely predicted waking cortisol ($\beta = 0.46$, $p = .006$), over and above other dimensions of parenting, such that children with more sensitive foster parents had higher waking cortisol than children with less sensitive foster parents. The association between foster parent sensitivity and the waking-to-bedtime slope of cortisol across the day was nonsignificant. Findings suggest that sensitive caregiving may support foster children's healthy HPA axis functioning.

KEYWORDS
diurnal cortisol, foster care, parental responsiveness

1 | INTRODUCTION

Children in foster care experience many forms of early adversity, such as maltreatment and disruptions in care, which place them at risk for mental and physical health problems (Chernoff et al., 1994; Jackson et al., 2014; Turney & Wildeman, 2016). Dysregulation of the hypothalamic pituitary adrenal (HPA) axis is one mechanism by which early adversity, including placement in foster care, may confer risk for health problems, as shown through human and nonhuman studies (Bernard et al., 2017; Ladd et al., 2004). Understanding predictors of variability in HPA functioning among foster children may offer insights into modifiable factors that can be leveraged for intervention. Given that parents serve a regulatory role early in development (Gunnar & Donzella, 2002; Hofer, 1994; Raver, 1996), caregiver responsiveness may be a key factor in predicting foster children's HPA axis functioning. However, few studies to date have examined whether the quality of interactions in foster parent-child dyads is linked to young children's cortisol regulation. Thus, for the present study, we aimed to examine whether foster parent responsiveness was associated with diurnal HPA functioning among children in foster care.

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1.1 | Early adversity and HPA axis functioning

The HPA axis connects the central nervous system and the endocrine system and plays an essential role in stress regulation and homeostasis. In addition to its role in activating the body in response to a stressor, the HPA axis supports the maintenance of the body's diurnal rhythm. A typical diurnal cortisol pattern is characterized by high levels of cortisol production in the morning, a peak approximately 30–45 min after waking, a gradual decline throughout the day, and reaching lowest levels shortly after bedtime. This waking-to-bedtime decline in cortisol typically emerges a few months after birth and persists throughout the lifetime (Gunnar & Cheatham, 2003; White et al., 2000).

Early childhood is a critical time period during which children rely on their caregivers as co-regulators for optimal physiological functioning. Thus, adverse caregiving experiences can affect the functioning of the HPA axis. For example, children exposed to maltreatment, including infants and toddlers in foster care, have been found to exhibit lower levels of morning cortisol and a flatter waking-to-bedtime slope of cortisol across the day than comparison children (Bernard et al., 2010; Bruce et al., 2009; Fisher et al., 2000, 2006). Notably, other studies have found that particular maltreatment experiences (e.g., emotional maltreatment) are associated with elevated, rather than reduced, morning cortisol levels (e.g., Bruce et al., 2009; Cicchetti et al., 2001), suggesting that the direction of effects may be mixed. Both hypocortisolism and hypercortisolism have been associated with mental and physical health problems (Gunnar & Vazquez, 2001; Heim et al., 1997, 2000).

1.2 | Responsive caregiving and diurnal HPA axis functioning

Although adverse early caregiving environments may result in atypical diurnal cortisol production, responsive caregiving that reflects prompt and contingent responding to children's cues may promote healthy regulatory processes in children (Dozier et al., 2008; Hofer, 1994). Indeed, Zalewski et al. (2012) reported that low parental warmth and high negative affect, important dimensions of responsive caregiving, were associated with blunted cortisol patterns among preschool-age children. In randomized clinical trials, children receiving interventions aimed at enhancing sensitive parenting had healthier HPA functioning, characterized by higher morning cortisol, than comparison children (e.g., Cicchetti et al., 2011). In a meta-analysis, Hackman et al. (2018) found that there was a small, positive association between parental warmth and morning cortisol levels among maltreated children ($r = .21$), but not nonmaltreated children. Thus, parental warmth may promote regulation (or prevent dysregulation) of morning cortisol production, especially among high-risk samples.

Taken together, these studies suggest that responsive parenting may support young children's HPA axis regulation; however, the association between responsive parenting and children's diurnal cortisol levels in foster care dyads has not received much attention empirically. One notable exception is an intervention study that compared a family-based therapeutic intervention to foster care as usual (Fisher et al., 2007). In this study, foster children who received the intervention exhibited more normalized patterns of diurnal cortisol than foster children who received care as usual, such that children in the intervention group had comparable waking cortisol levels and cortisol production across the day to a nonfoster care community comparison group. In contrast, children in standard foster care showed an atypical, blunted pattern of diurnal cortisol production from morning to evening, characterized by lower waking levels of cortisol. This intervention study did not specifically examine whether changes in foster parent responsiveness mediated changes in cortisol regulation. Thus, there is a gap in the literature necessitating more research that examines the link between responsive parenting and cortisol regulation among young children in foster care.

1.3 | The present study

We aimed to examine whether foster parent responsiveness is associated with young children's diurnal cortisol production. We hypothesized that children in foster care who experienced more responsive parenting, as indicated by sensitive, nonintrusive, and warm caregiving behaviors, would show more typical patterns of HPA axis regulation, as indicated by increased levels of morning cortisol and a steeper decline across the day, than children who experienced less responsive care from their foster parents.

2 | METHOD

2.1 | Participants

Participants included 97 foster children (mean age = 29.1 months, $SD = 7.5$, range = 18.0–54.2 months) and 78 foster parents (mean age = 45.1 years, $SD = 11.6$, range = 21.0–80.0 years) referred from foster care agencies for a randomized clinical trial of an attachment-based intervention. Only baseline (i.e., pre-intervention) data were included for the current study. Of the 78 foster parents, 60 had one child enrolled in the study, 17 had two children enrolled, and one had three children enrolled. In order to address the issue of nonindependence, follow-up analyses accounted for sibling pairs, including biological siblings living in separate homes, biological siblings living in the same home, and nonrelated children living in the same home.

Forty-nine (50.5%) children were male. Fifty-seven (58.8%) were African American, 31 (32.0%) were White, six (6.2%) were Biracial, and three (3.1%) identified as "Other." Additionally, seven (7.2%) were Hispanic. Seventy-five (77.3%) foster children were placed with nonrelatives, 21 (21.6%) were placed with relatives, and one (1%) was unknown. Reasons for removal were not mutually exclusive and included: physical or sexual abuse (20.6%), neglect (47.4%), parent incarceration (12.4%), parent substance abuse (38.1%),

dependency (i.e., inability to care for child; 56.7%), parent mental health issues (6.2%), domestic violence (12.4%), and "other" (7.2%). Thirteen children (13.4%) were missing information regarding their reason(s) for removal.

All foster parents were female, except for two males. Forty-three (55.1%) were African American, 31 (39.7%) were White, three (3.8%) were Biracial, and one (1.3%) was identified as "Other." Additionally, three (3.8%) were Hispanic. Eight (10.3%) foster parents completed some high school, 18 (23.1%) completed high school, 17 (21.8%) completed some college, 12 (15.4%) earned a college degree, 10 (12.8%) earned a higher degree, and 13 (16.7%) did not report on their education level. Family income ranged from "less than $10,000" (3.8%) to "more than $100,000" (10.3%), with a median family income between "$30,000 and $39,999" (16.7%).

2.2 | Procedure

2.2.1 | Home visit

Participants were referred by child welfare agencies in Delaware. If the foster parent expressed interest during an initial phone call, a research staff member conducted a home visit, during which they obtained written consent, administered demographic questionnaires, and provided parents with the supplies to collect chidlren's saliva samples. During a subsequent home visit, the researcher picked up the saliva samples and video-recorded a semi-structured play interaction between the foster parent and child; the foster parent was provided with developmentally appropriate toys and instructed to play with their child as they normally would for 7 min. Play interactions with children younger than 20 months included an additional 2-min distance interaction, during which foster parents were asked to interact with their child at a distance before the free play.

2.2.2 | Saliva sample collection

Parents collected saliva samples from children twice per day (within 30 min of waking and right before bedtime) across a three-day period. Given challenges with collecting saliva samples from young children, samples were collected for three days to allow for the likelihood of noncompliance and/or insufficient volumes of saliva. Additionally, previous research indicates that taking multiple saliva samples per day across several days allows for a trait-like, reliable measurement of diurnal cortisol (Adam & Kumari, 2009; Fernandes et al., 2013). The research staff provided parents with instructions and photos illustrating how to properly collect and store their child's saliva. Foster parents recorded the time that each saliva sample was collected, and answered questions about whether the child was crying during sampling, had food or medication prior to sampling, and was sick or teething on the day of sampling. Foster parents were instructed to delay saliva sample collection if the child was sick.

After being transported to the lab, samples were stored in a −20°C freezer until they were ready to be assayed. Samples were assayed using a high-sensitivity salivary cortisol enzyme immunoassay kit (Salimetrics, LLC). All samples from a child were assayed on the same plate in order to minimize variability and standards were included in every assay to ensure that assaying conditions remained constant. The intra- and interassay coefficients of variation were 3.99% and 7.39% respectively.

2.3 | Measures

2.3.1 | Foster parent responsiveness

Video-recorded foster parent–child interactions were coded by undergraduate- and graduate-level coders for parent sensitivity, intrusiveness, and positive regard, using three 5-point scales adapted from the Observational Record of the Caregiving Environment (NICHD Early Child Care Research Network, 1999). Sensitivity scores reflected foster parents' ability to follow the child's lead and respond contingently to child cues. Intrusiveness scores reflected foster parents' invasive behaviors, such as physically touching or moving the child without regard for their cues, repetitive question asking, or forcibly introducing toys. Positive regard scores reflected positive expressions, enjoyment, and warm tone of voice. All videos were double coded. The intraclass correlation coefficients (ICCs) for inter-rater reliability were 0.80, 0.84, and 0.80 for sensitivity, intrusiveness, and positive regard respectively. For each indicator of parent responsiveness, scores were averaged across the two coders. Then, to create a composite of parent responsiveness, sensitivity, reverse-scored intrusiveness, and positive regard scores were averaged ($\alpha = 0.60$).

2.3.2 | Cortisol

Established procedures were followed when preparing the cortisol data for analyses (Bernard, Hostinar, et al., 2015; Fisher et al., 2007). Specifically, samples were considered unreliable and removed from analyses if they had an intraassay coefficient of variation greater than 15%. Cortisol values greater than 2.0 μg/dl were considered to be biologically implausible, and values three *SD*s above the mean were deemed as outliers and were excluded from the analyses. When cortisol values were below detectable limit of the assay, values were replaced with 0.004 μg/dl. Log10 transformation was used to normalize the distribution of cortisol values due to high positive skew.

Of the 582 possible samples (three waking and three bedtime for 97 children), 37 were not collected or did not have enough saliva for assay, 12 were biologically implausible, and eight were outliers, leaving a total of 525 saliva samples that were included in the analyses ($n = 67$; 69.1%), with others having five ($n = 14$; 14.4%), four ($n = 9$; 9.3%), three ($n = 4$; 4.1%), two ($n = 2$; 2.1%), or one ($n = 1$; 1.0%).

2.3.3 | Placement variables and foster parent sociodemographic burden

Placement characteristics were considered as covariates, including child age at initial removal from the birth parent, duration of current placement, and total number of placements. To account for sociodemographic variables that may have been correlated with foster parents' sensitivity, we computed a foster parent sociodemographic burden score by adding together dichotomized indicators including: (a) single parent status (divorced, separated, widowed, or single; 50.0%), (b) low household income (less than $30,000; 25.6%), and (c) low education status (high school or less; 32.1%).

2.4 | Data analytic approach

Primary analyses were conducted in Mplus 8 (Muthén & Muthén, 1998) using structural equation modeling to allow for latent factors, nonindependent sampling, and missing data. Model fit was assessed using the χ^2/df ratio, root mean square error of approximation (RMSEA), the comparative fit index (CFI), and the Tucker-Lewis index (TLI).

We first constructed a measurement model of diurnal change in cortisol. Specifically, latent factors for waking and bedtime cortisol were each modeled with three indicators (i.e., log-transformed cortisol values from each day). The diurnal change in cortisol was specified as a latent change score, such that more negative values reflected a steeper waking-to-bedtime decline in cortisol across the day (Bernard, Zwerling, et al., 2015; McArdle & Hamagami, 2001). Sample collection times and lag time between parent-reported child wake time and sample collection time were included as time-varying covariates.

Second, using structural equation modeling, the intercept (i.e., waking cortisol) and slope (i.e., latent change score reflecting waking to bedtime change in cortisol) were regressed on the foster parent responsiveness composite and covariates. In order to explore the effect of foster parent responsiveness on bedtime cortisol, the same model was tested with the intercept re-centered to represent the latent factor for bedtime cortisol. Finally, we explored the effects of individual indicators of parent responsiveness on children's cortisol by including sensitivity, intrusiveness, and positive regard as simultaneous predictors in the model.

3 | RESULTS

3.1 | Preliminary analysis

In bivariate analyses, child and parent age, child and parent gender, and child non-White racial/ethnic status were not associated with averaged waking cortisol levels, averaged bedtime cortisol levels, or averaged waking-to-bedtime differences in cortisol levels (all $p > .05$). Additionally, parent-reported child crying, eating/drinking, medication, teething, and sickness at the time of sampling were not associated with cortisol values. Thus, we did not include these demographic variables or collection-related variables as covariates in primary analyses. Descriptive statistics and bivariates correlations among variables are presented in Table 1.

3.2 | Primary analysis

The measurement model of waking to bedtime change in cortisol fit the data well, $\chi^2/df = 0.77$, RMSEA = 0.00, CFI = 1.00, TLI = 1.08. There were no significant associations between sample collection time or wake-to-collection lag time and cortisol values (all $p > .05$); thus, these time-varying covariates were excluded from the structural equation model for simplicity.

Table 2 shows results of the full model with standardized coefficients and significance levels. The model fit statistics were adequate to good, $\chi^2/df = 1.64$, RMSEA = 0.08, CFI = 0.92, TLI = 0.86. Accounting for covariates, foster parent responsiveness was positively associated with children's waking cortisol levels ($\beta = 0.26$, $p = .023$), such that higher foster parent responsiveness was associated with higher waking cortisol levels. The association between foster parent responsiveness and children's cortisol slope was not statistically significant. When the intercept was re-centered to reflect bedtime cortisol, the association between foster parent sensitivity and the bedtime cortisol intercept was nonsignificant, $\beta = 0.18$, $p = .155$. The association between foster parent responsiveness and children's waking cortisol levels continued to be statistically significant when randomly excluding one sibling from each pair (or two for the foster parent with three children enrolled; $\beta = 0.27$, $p = .025$), and when excluding the other sibling from each pair ($\beta = 0.30$, $p = .009$).

Finally, we explored the effects of individual indicators of parent responsiveness on children's cortisol by including sensitivity, intrusiveness (reverse-coded), and positive regard as simultaneous predictors in the model (see Figure 1). While controlling for other indicators of responsiveness, sensitivity significantly predicted waking cortisol ($\beta = 0.46$, $p = .006$), whereas intrusiveness and positive regard did not. Sensitivity and intrusiveness were not significantly associated with cortisol slope, whereas positive regard was positively associated with cortisol slope ($\beta = 0.26$, $p = .044$). Given the moderate correlation between sensitivity and positive regard, we were concerned about issues of multicollinearity when including them as simultaneous predictors; thus, we explored each indicator of responsiveness in separate models. Sensitivity alone continued to predict waking cortisol ($\beta = 0.34$, $p = .003$). However, positive regard alone was not associated with waking cortisol ($\beta = 0.14$, $p = .200$) nor the cortisol slope ($\beta = 0.15$, $p = .215$), suggesting that the unexpected positive association between positive regard and cortisol slope while controlling for sensitivity should not be interpreted. In a model by itself, intrusiveness was not a significant predictor of waking cortisol nor slope.

TABLE 1 Descriptives and bivariate correlations for study variables

Variable	Mean	*SD*	Min.	Max.	1	2	3	4	5	6	7	8	9	10	11
1. Child age at cortisol collection (months)	29.1	7.5	18.0	54.2	—										
2. Child age at removal (months)	14.7	12.9	0.0	47.9	0.504**	—									
3. Placement duration (months)	10.9	10.2	0.1	36.8	−0.072	−0.712**	—								
4. Number of placements	2.2	0.7	1.0	4.0	0.152	0.026	−0.043	—							
5. Sociodemographic burden	1.2	1.1	0.0	3.0	−0.037	0.027	0.056	−0.233*	—						
6. Foster parent age (years)	45.3	11.4	21.0	80.0	−0.093	0.097	−0.038	−0.030	0.265*	—					
7. Foster parent sensitivity	2.8	1.0	1.0	5.0	0.060	0.106	−0.076	0.315**	−0.305**	−0.218*	—				
8. Foster parent (reverse- coded) intrusiveness	3.7	1.1	1.0	5.0	0.200*	0.059	0.039	0.227*	−0.057	−0.225*	0.654**	—			
9. Foster parent positive regard	3.6	1.0	1.0	5.0	−0.031	−0.043	0.145	0.116	−0.224*	−0.194	0.445**	0.078	—		
10. Average log morning cortisol (μg/dl)	−0.7	0.4	−2.7	−0.1	−0.093	0.210	−0.072	0.002	−0.192	0.085	0.287**	0.064	0.143	—	
11. Average log bedtime cortisol (μg/dl)	−1.3	0.4	−2.4	−0.2	0.022	−0.054	0.005	0.031	−0.244*	−0.152	0.169	0.073	0.247*	0.277**	—
12. Average log cortisol slope (μg/dl)	−0.5	0.5	−1.8	1.6	0.092	−0.223	0.164	0.027	−0.056	−0.190	−0.119	−0.043	0.123	−0.550**	0.650**

*$p < .05$,
**$p < .01$.

TABLE 2 Model estimated parameters for the full structural model

Effect	Standardized estimate	*SE*	Est/*SE*	*p*	95% CI	
					Lower	Upper
Measurement Model						
Wake-up cortisol						
Day 1	0.76	0.07	11.06	.000	0.63	0.90
Day 2	0.84	0.06	14.40	.000	0.72	0.95
Day 3	0.75	0.07	11.22	.000	0.62	0.88
Bedtime cortisol						
Day 1	0.91	0.04	25.46	.000	0.84	0.98
Day 2	0.86	0.05	18.92	.000	0.77	0.95
Day 3	0.73	0.07	11.18	.000	0.60	0.86
Structural Model						
Wake-up cortisol regressed ON						
Foster parent responsiveness	0.26	0.11	2.27	.023	0.04	0.48
Sociodemographic burden	−0.24	0.14	−1.78	.075	−0.51	0.03
Placement duration	−0.29	0.18	−1.59	.113	−0.64	0.07
Age at removal	−0.14	0.20	−0.66	.508	−0.53	0.26
Number of placements	−0.20	0.12	−1.68	.094	−0.43	0.03
Cortisol slope regressed ON						
Foster parent responsiveness	−0.00	0.13	−0.03	.975	−0.26	0.25
Sociodemographic burden	−0.02	0.15	−0.12	.908	−0.32	0.28
Placement duration	0.35	0.19	1.85	.064	−0.02	0.71
Age at removal	0.18	0.21	0.84	.403	−0.23	0.58
Number of placements	0.13	0.13	0.96	.340	−0.13	0.38

4 | DISCUSSION

Results showed that children placed with foster parents who provide highly responsive care, particularly sensitive care that follows the child's lead, showed higher levels of cortisol when waking in the morning than children placed with foster parents who provide less sensitive care. This study extends previous literature by demonstrating an association between parental sensitivity and children's HPA axis functioning among nonbiologically related dyads. Our findings support the potential role of sensitive caregiving, above and beyond other responsive parenting domains—even in the context of new and potentially temporary foster caregiver–child relationships—for promoting the regulation of children's HPA axes following early adversity.

These findings are consistent with other studies suggesting that early caregiving experiences may have especially pronounced implications for children's cortisol levels upon waking, a time when cortisol levels are typically at their peak (Bernard et al., 2017; Gunnar & Vazquez, 2001). Cortisol levels in the morning play an essential regulatory role in the circadian pattern by mobilizing stored energy and stimulating appetite (De Kloet, 1991). Moreover, waking cortisol levels are associated with a variety of health-related outcomes (Adam et al., 2017; Alink et al., 2008; Gunnar & Vazquez, 2001), suggesting that waking cortisol may be an important indicator of overall physiological functioning (Stalder et al., 2016).

We did not find support for the hypothesis that foster parent responsiveness would be associated with children's waking-to-bedtime cortisol slopes. Some studies have suggested that cortisol measured immediately upon waking is thought to index basal cortisol levels, whereas diurnal slope is thought to measure variation in the circadian rhythm (Girshkin et al., 2014). Alternatively, because cortisol collection was taken "within 30 min of waking," our measure of waking cortisol may in part be capturing the cortisol waking response (CAR), which is purported to be distinct from the diurnal pattern (Fries et al., 2009). It is also possible that we lacked the power to detect a significant association between foster parent responsiveness and diurnal slope. Indeed, the association was in the expected direction, such that higher sensitivity was associated with a steeper waking-to-bedtime decline.

There are many questions left unanswered by this study, which warrant further consideration. First, an important direction for future

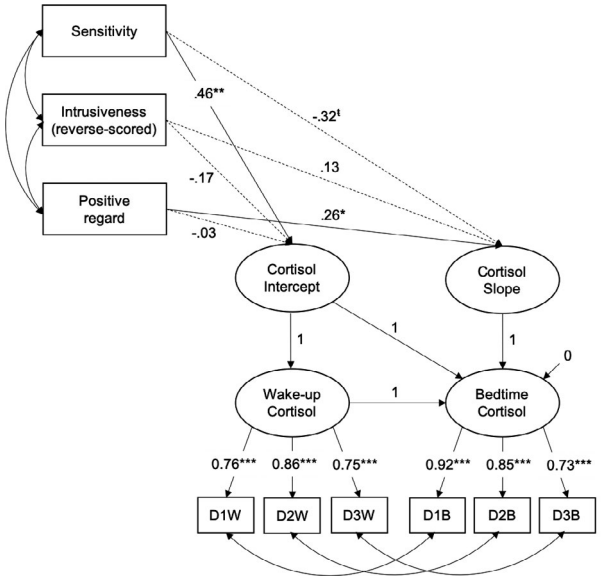

FIGURE 1 Structural equation model of the associations between indicators of foster parent responsiveness and children's cortisol. Standardized model coefficients are presented. This model controls for foster parent sociodemographic burden and child placement characteristics (i.e., duration of the current placement, age at initial removal, number of foster care placements). Model fit statistics indicated adequate to good fit: RMSEA = 0.07, CFI = 0.93, TLI = 0.88. Solid lines represent significant pathways and dashed lined represent non-significant pathways ($^{t}p < .10$, $^{*}p < .05$ and $^{**}p < .01$)

research will be to examine whether the effect of foster parent sensitivity on cortisol regulation varies depending on the type, timing, or severity of children's early adverse experiences. Second, we might expect that placement duration would moderate the association between foster parent sensitivity and children's cortisol, with stronger associations for children who spent more time with the foster parent. Although we explored this possibility, we did not find evidence of such an effect, perhaps because children were with caregivers for a relatively prolonged period of time on average in our sample ($M = 10.9$ months, $SD = 10.2$). Third, future research should incorporate child behavioral measures to test the extent to which HPA axis functioning explains the link between early caregiving experiences and behavioral outcomes. Related to this point, the correlational and cross-sectional nature of this study precludes us from drawing conclusions about the direction of causality; although it is possible that sensitive caregiving influences children's diurnal cortisol production, it is also possible that foster children who are biologically and/or behaviorally dysregulated may elicit less sensitive caregiving from their foster parents, or that these associations are bidirectional. Future longitudinal studies with repeated measurements of parent–child interaction, child behavior, and foster children's cortisol levels are needed to disentangle the extent to which children and their parents influence one another both physiologically and behaviorally. Fourth, our study examined parent sensitivity during a play observation; future research that examines parenting in other contexts (e.g., in response to distress, during bedtime routines) or day-to-day variability in sensitivity may find different associations with waking cortisol, bedtime cortisol, or the diurnal rhythm (e.g., Philbrook et al., 2014). Finally, our study lacked a comparison group of typically developing children raised in biologically intact dyads, which limited our ability to establish "normative" comparisons for children's cortisol levels.

Findings from this study suggest that foster parent sensitivity may be a viable target for interventions aimed at enhancing children's HPA axis functioning. Several interventions, including Attachment and Biobehavioral Catch-up and Multidimensional Treatment Foster Care Program for Preschoolers, have been shown to promote HPA axis regulation among children who have been maltreated (Bernard, Dozier, et al., 2015; Fisher et al., 2007). In order to strengthen causal claims regarding associations between foster parent sensitivity and children's cortisol production, future randomized clinical trials should examine to what extent intervention-induced changes in foster parent sensitivity promote foster children's healthy HPA regulation.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

AUTHOR CONTRIBUTION

M.D. developed the study concept and obtained funding for the longitudinal study. A.K.S. and K.B. developed the study concept for the present study. A.K.S. and K.B. performed data analysis and interpretation. A.K.S. drafted the manuscript under K.B.'s supervision. K.B., K.L.R., M.G, and M.D. provided critical revisions. All authors approved the final version of the paper for submission.

DATA AVAILABILITY STATEMENT

Research data are not shared.

ORCID

Aline K. Szenczy https://orcid.org/0000-0002-2576-7879
Kristin Bernard https://orcid.org/0000-0003-2421-8453
K. Lee Raby https://orcid.org/0000-0002-1041-080X
Mallory Garnett https://orcid.org/0000-0002-6516-4407
Mary Dozier https://orcid.org/0000-0002-3618-4361

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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