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The persistent associations between early institutional care and diurnal cortisol outcomes among children adopted internationally

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Abstract

Young children in institutional care experience conditions that are incompatible with their needs for attachment relationships. As a result, early institutionalization is expected to have lasting effects on the regulation of the hypothalamic–pituitary–adrenocortical (HPA) axis. The current study tested whether early institutionalization has persistent consequences for diurnal HPA axis outcomes among 130 children who had been adopted internationally between the ages of 6 and 48 months. Daily cortisol samples were collected from children at two time points: shortly after adoption (average of 5.3 months after adoption) and approximately 3 years later (average of 39.2 months after adoption). Shortly after adoption, children who had experienced a long duration of institutional care had lower morning cortisol levels and more blunted declines in cortisol across the day than children who experienced minimal or no institutional care. Three years later, children who had experienced a long duration of institutionalization continued to exhibit low morning cortisol levels and also exhibited low bedtime cortisol levels. Altogether, these results support the idea that early adversity results in the downregulation of the HPA axis and suggest that the effects of institutionalization on HPA axis functioning may persist several years after children are adopted into highly enriched families.

KEYWORDS

cortisol, early adversity, institutional care, international adoption

1 | INTRODUCTION

Experiences during infancy and early childhood are theorized to play a crucial role in shaping children's early neurobiological development, including their stress response systems. Specifically, early interactions with parents and other caregivers are thought to assist with regulating the functioning of the hypothalamic–pituitary–adrenocortical (HPA) axis (Gunnar & Quevedo, 2007; Lupien, McEwen, Gunnar, & Heim, 2009; Shonkoff et al., 2012). One of the challenges for research in this area is evaluating whether early experiences uniquely contribute to later HPA axis functioning given that most children's caregiving environments are relatively stable over time. Studies that focus on children who were adopted internationally afford a unique opportunity for testing whether early experiences have unique effects on children's development because these children often experience stark changes in their caregiving experiences (Haugaard & Hazan, 2003). Prior to being adopted, many internationally adopted children experience group-based, institutional care, which is not well-suited to meeting young children's basic developmental need for stable, consistent attachment relationships (Dozier et al., 2012; Dobrova-Krol, van Ijzendoorn, Bakermans-Kranenburg, Cyr, & Juffer, 2008). After these children are adopted, they often experience highly enriched family environments. The current longitudinal study examined

whether early institutionalization is associated with children's diurnal HPA functioning shortly after adoption and whether these associations persist or weaken over a period of nearly 3 years as children adjust to their adoptive family environments.

1.1 | The hypothalamic–pituitary–adrenocortical axis

The HPA axis is a key component of the endocrine system. The paraventricular nuclei within the hypothalamus receive excitatory and inhibitory inputs from multiple neural regions, including the brainstem, the prefrontal cortex, and structures within the limbic system. These nuclei ultimately produce corticotrophin-releasing hormone, which binds with cells in the pituitary gland. This, in turn, prompts the release of adrenocorticotropic hormone (ACTH) into the bloodstream, where it is carried to the adrenal glands. This results in the production of the glucocorticoid cortisol in humans. The HPA axis includes a negative feedback loop. Specifically, circulating cortisol binds with receptors in the hypothalamus and the pituitary gland to inhibit the activity of the HPA axis (for in-depth reviews of the neurophysiology of the HPA axis, see Gunnar & Quevedo, 2007; Koss & Gunnar, 2018; Lupien et al., 2009).

The HPA axis has a diurnal pattern of activity that aids in maintaining homeostatic processes related to alertness and arousal that follow a circadian rhythm (Gunnar & Quevedo, 2007; Koss & Gunnar, 2018; Lupien et al., 2009). The typical pattern of diurnal HPA axis activity includes a cortisol awakening response, which involves a large increase in cortisol levels shortly after waking (Koss & Gunnar, 2018; Lupien et al., 2009). Cortisol levels tend to sharply decline following the cortisol awakening response and then continue to decline throughout the day, ultimately reaching their lowest levels in the evening while individuals are asleep.

This diurnal pattern of HPA axis activity emerges within the first few months of life and is apparent across the lifespan for most individuals (Ivars et al., 2017; Miller et al., 2016). Moreover, variations in diurnal cortisol levels are associated with physical and mental health outcomes among children, adolescents, and adults. Specifically, flat diurnal cortisol rhythms are associated with adverse health and mental health outcomes including depression, fatigue, poor immune system functioning, obesity, cancer, and risk for mortality (Adam et al., 2007).

1.2 | Early adversity and the HPA axis

The activity of the HPA axis is highly sensitive to features of the environment, especially experiences of stress and support. During early development, the HPA axis is regulated by the early caregiving environment, including children's experiences within attachment relationships (Gunnar & Quevedo, 2007). Because of the heightened plasticity in neurobiological systems during the first few years of life, children's early experiences with caregivers are thought to have unique and long-term effects on the functioning of the HPA axis (Gunnar & Quevedo, 2007; Lupien et al., 2009). For example, early adversity is expected to lead to dysregulation of the HPA axis, including low cortisol levels upon wake-up and a blunted slope throughout the day (Koss & Gunnar, 2018; Lupien et al., 2009). This profile of blunted HPA activity likely reflects a downregulation of the HPA axis in response to chronic exposure to stressful conditions early in life.

One especially potent form of early adversity is orphanage or institutional care. Institutional care environments often house relatively large numbers of children and have child-to-caregiver ratios of approximately 8:1 (Dobrova-Krol et al., 2008). Given the large number of children in their care, the professional caregivers tend to focus on caring for children's physical needs and perform their caregiving duties in a perfunctory way. In addition, children in institutions interact with large numbers of caregivers because caregivers work in shifts, are moved to new wards, or change jobs. For these reasons, these institutional environments are incompatible with young children's developmental needs to form attachment relationships with a small number of caregivers (Dozier et al., 2012; Dobrova-Krol et al., 2008).

Children who are adopted from institutional care experience extraordinary change in the quality of their caregiving environments. Internationally adoptive families tend to have low demographic risk, as most parents are married, have high levels of formal education, and high family incomes (Hellerstedt et al., 2008; Jones, 2009). Internationally adoptive parents also are more likely to have autonomous attachment states of minds—which are associated with the quality of care parents provide for their children (Verhage et al., 2016)—than non-adoptive parents (Raby et al., 2017). This dramatic shift from socially depriving to highly enriched environments represents a "natural experiment" for testing whether early adversity has unique effects on children's development, including HPA axis functioning (Haugaard & Hazan, 2003; Julian, 2013; Rutter, 2007).

1.3 | Institutional care and children's diurnal HPA outcomes

A handful of studies have examined the diurnal HPA axis outcomes among children residing in institutional environments. An initial study reported that children living in profoundly depriving Romanian institutions exhibited abnormally low morning cortisol levels as well as the absence of a decline in cortisol levels throughout the day (Carlson & Earls, 1997). Chernego et al. (2019) recently reported that children in Russian institutional care also exhibited blunted diurnal declines in cortisol. Importantly, this effect was due to high cortisol levels during the evening, rather than atypically low morning cortisol levels among institutionalized children. Other studies have reported that the diurnal cortisol levels of children living in institutional settings in Ukraine or Mongolia did not significantly differ from non-institutionalized children (Dobrova-Krol et al., 2008, 2010; Kohrt et al., 2015).

A growing literature has tested whether early institutional care is associated with diurnal HPA activity after children are removed from these adverse environments and adopted into stable, enriched family environments. Consistent with the research involving children living in institutions (e.g., Carlson & Earls, 1997; Chernego et al., 2019), the majority of the findings indicate that children adopted internationally exhibit unusually low cortisol levels upon wake-up and/or blunted diurnal declines (Flannery et al., 2017; Johnson et al., 2011; Koss et al., 2014; Leneman, Donzella, Desjardins, Miller, & Gunnar, 2018; Quevedo et al., 2012). That said, some studies have reported that a long duration of institutionalization prior to adoption is associated with *high* levels of cortisol throughout the day or *steep* diurnal declines in cortisol among children adopted internationally (Gunnar et al., 2001; Kroupina et al., 2012). Moreover, several studies have not observed an association between pre-adoptive adversity and diurnal cortisol levels among children adopted internationally (Kertes et al., 2008; Van den Dries et al., 2010). Although the exact reasons for the inconsistencies in the literature are not immediately apparent, possible explanations may include attenuated ranges in children's ages of adoption and durations of institutional care, creating dichotomous variables regarding children's duration of institutionalization, and modest sample sizes (for a review, see Gunnar & Reid, 2019). Regardless of the precise reasons, these inconsistent findings highlight the need for additional research examining the implications of early deprivation for internationally adopted children's diurnal cortisol levels. Thus, the first goal of the present study was to evaluate whether the duration of institutional care was associated with alterations in children's diurnal HPA axis activity shortly after being adopted internationally by families in the United States.

1.4 | Lasting consequences of early institutionalization

The second goal of this study was to evaluate whether early institutionalization had persistent associations with internationally adopted children's HPA axis activity by examining these children's diurnal cortisol outcomes several years after adoption. Specifically, we used a longitudinal design to evaluate whether the associations between early institutionalization and children's diurnal outcomes persist or weaken over time. Evidence for weakening effects of early institutionalization would suggest that the HPA axis of previously institutionalized children eventually recovers and functions in the typical manner after these children are placed with their adoptive families. In contrast, evidence for persistent associations between early institutionalization and children's diurnal cortisol levels would support the idea that early adversity has unique and long-term consequences for HPA axis functioning.

The few studies that have examined internationally adopted children's diurnal cortisol outcomes at more than one time point have not yielded consistent findings. For example, Koss et al. (2014) indicated that a group of approximately 100 internationally adopted children exhibited a blunted pattern of diurnal HPA activity that was sustained across the first 2 years after adoption. In contrast, Kroupina et al. (2012) reported that the age at which children ($n = 76$) were adopted from institutional care was associated with their diurnal cortisol activity at 1-month post-adoption but not 6 months later, and Van den Dries et al. (2010) reported that the diurnal cortisol levels of post-institutionalized children ($n = 50$) did not differ from adopted children who did not experience institutional care when cortisol was assessed 2 months post-adoption or 6 months post-adoption. The modest sample sizes of these latter two studies may have limited their ability to detect significant effects of early institutional care on internationally adopted children's diurnal cortisol outcomes. Moreover, nearly all of these studies focused on the initial transition from pre- to post-adoption environments, which prevent clear conclusions about whether early institutionalization results in sustained alterations to HPA axis activity. The present study addressed those limitations by assessing the diurnal cortisol levels of 130 children who were adopted internationally at two time-points: approximately 6 months post-adoption and approximately 3 years post adoption. The longitudinal nature of the present study provides a unique opportunity to examine whether the implications of early institutional care on children's HPA axis outcomes persist or weaken over time after children are placed with their adoptive families.

1.5 | Present study

The overarching purpose of this longitudinal study was to evaluate whether early institutional care had lasting consequences for the regulation of the HPA axis. The current study drew on data from a sample of 130 internationally adopted children whose families had participated in a randomized controlled trial evaluating the efficacy of a parenting-focused intervention. However, the current study focused on the potential significance of institutionalization prior to adoption. In particular, the current study sought to extend the current body of research on this topic by examining the associations between early institutionalization and the diurnal HPA outcomes of children adopted internationally at two time points: approximately 6 months post-adoption and nearly 3 years later. In this way, the current study directly tested whether the diurnal cortisol outcomes of previously institutionalized children show recovery after children are adopted or whether the harmful effects of early institutionalization on the functioning of children's HPA axes persist over time.

2 | METHODS

2.1 | Participants

This study included 130 children (52% female) who had been adopted internationally from orphanages and foster care systems in 13 countries, including China (39%), Russia (19%), South Korea (17%), Ethiopia (12%), Kazakhstan (4%), and Guatemala (2%) most commonly. The average age of children at the time of adoption was

17.2 months (*SD* = 8.9 months). Seventy-eight percent of children experienced institutional care prior to adoption, and the average duration of institutionalization was 10.0 months (*SD* = 8.4 months). Nearly all of the adoptive parents were married (93%), and 7% reported they were cohabitating, single, or widowed. In addition, 95% of the parents in the primary caregiver role were White, 3% were Asian-American, 1% were African-American, and 1% were Hispanic. The majority of parents in the primary caregiver role reported their educational attainment was either a college degree (39%) or a graduate degree (44%), whereas 15% reported attending some college and 2% reported a high school diploma. The majority of the adoptive families (62%) reported a household income of $100,000 or more, 32% reported a household income between $60,000 and $100,000, and 7% reported a household income between $40,000 and $60,000.

Families living in the Mid-Atlantic region of the United States were recruited to participate in this study shortly after adopting a young child internationally. Families were not enrolled in the study if the adoptive parents reported that the child had a congenital, endocrine, or severe cognitive disorder. Parents who expressed an interest in the study were contacted by research staff, and informed consent was obtained after parents were provided with a thorough explanation of the study. All components of this research study were approved by the Institutional Review Board at the University of Delaware's Department of Psychological and Brain Sciences.

2.2 | Data availability

The data used in these analyses are available upon request from the corresponding author but are not publicly available due to privacy restrictions.

2.3 | Procedures

After consenting to participate, families completed an initial research assessment. This assessment is hereafter referred to as Time 1. Children ranged in age from 6.3 months to 48.1 months (*M* = 21.7 months, *SD* = 8.9 months) at this assessment, and the average duration of time since adoption at Time 1 was 5.3 months (*SD* = 6.6 months). Over 80% of the families included in these analyses completed the Time 1 assessment within the first 6 months post-adoption.

After completing the Time 1 assessment, adoptive parents were randomly assigned to receive one of two parent-training interventions: Attachment and Biobehavioral Catch-up (ABC) or a control intervention (Developmental Education for Families). Dozier and Bernard (2019) provide a detailed description of these two intervention conditions. In this sample of 130 parents, 49% of the adoptive parents received the ABC intervention, and 51% received the control intervention. After completing the randomly assigned intervention, families were invited to participate in a series of follow-up research assessments. The intended schedule for these assessments was 1 month after the completion of the intervention and then annually at the time of the child's birthday between the ages 2 and 5 years. Samples of children's diurnal cortisol levels were collected at each of these visits. Because the goal of the current study was to test whether early institutionalization had a persistent influence on internationally adopted children's diurnal HPA axis outcomes, we selected the cortisol data from the last available post-intervention assessment. This assessment is hereafter referred to as Time 2. The average age of the children at the Time 2 assessment was 56.4 months (*SD* = 15.1 months), and the average duration since adoption was 39.2 months (*SD* = 15.7 months).

2.4 | Measures

2.4.1 | Diurnal cortisol levels

The methods for collecting salivary samples were identical to those reported in prior studies (e.g., Bernard et al., 2015). At Time 1 and Time 2, parents were instructed to collect saliva samples from children immediately upon wake-up and as close to bedtime as possible across three consecutive days. Although the researcher emphasized the importance of collecting a sample as close to wake-up as possible, parents were told that sampling within the first 30 min of wake-up was acceptable. Parents were shown how to collect saliva samples by placing a dental cotton role in the child's mouth. After adequately soaking the cotton swab in saliva, parents placed the cotton roll into a pre-labeled vial and recorded the date and time the saliva sample was collected on the vial and in a saliva sample journal. Parents also recorded the time of the child's wakening and bedtime for each day as well as information about children's medication use at the time the saliva samples were collected. Parents stored the vials containing the child's saliva samples in their freezers until the research staff retrieved the samples. To ensure families followed the guidelines, parents were given a binder with detailed instructions, including written directions and accompanying photographs of each step of the sampling protocol. Research staff instructed parents to delay the collection of the saliva samples if children were sick and to not have children eat or drink anything or brush their teeth in the 30 min prior to collecting the saliva sample.

After research staff collected the vials, the saliva samples were stored in a freezer at −20°C. The samples were then assayed using a high-sensitivity salivary cortisol enzyme immunoassay kit (Salimetrics, LLC, State College, Pennsylvania). All samples were assayed in duplicate on the same plate to minimize variability. Consistent with procedures used in other studies (Bernard et al., 2015), all cortisol values that were implausible (>2.0) and those that were more than three standard deviations above the mean were excluded. Wake-up cortisol samples that were collected more than 45 min after the time of wake-up were also excluded from analyses. Table 1 includes information about cortisol values, sampling time, and time since wakening for each of the six saliva samples collected at Time 1 and Time 2.

2.5 | Analytic strategy

The primary analyses were conducted using M*plus* 7.11 (Muthén & Muthén, 2007). At both Time 1 and Time 2, cortisol levels at wake-up and bedtime were defined as latent variables using the relevant measures from each of the 3 days as indicators. The time of day the cortisol samples were collected and the amount of time since wake-up were included as time-varying covariates for each of the six cortisol measures. The latent wake-up and bedtime cortisol variables were then used to estimate latent cortisol intercepts and latent cortisol slope variables. The latent intercept variable represented the average cortisol level at the time of wake-up, and the latent slope variable represented the change in cortisol levels from wake-up to bedtime. Because cortisol values were expected to decline from wake-up to bedtime, the factor loading for the latent slope variable was constrained to zero for the wake-up cortisol and one for bedtime cortisol values. The latent cortisol intercept and slope variables were regressed onto duration of institutional care in order to evaluate whether early institutionalization predicted diurnal cortisol outcomes. Separate models were conducted for cortisol outcomes collected at Time 1 and Time 2. This allowed us to examine whether the associations between early institutionalization and cortisol outcomes were persistent or changed at different points in time after adoption.

Children's medication use was coded for whether children were taking one or more medications that had the potential to influence salivary cortisol levels based on the information compiled by Granger et al. (2009), and a dichotomous measure of whether children were using a medication that could influence cortisol levels was included as a covariate in all statistical models. Children's biological sex was included as a covariate in both models because biological sex has been shown to be associated with cortisol levels in other studies (e.g., Miller et al., 2016). In addition, because families participated in one of two parenting-focused interventions in between the Time 1 and Time 2 assessments, intervention condition was included as a covariate in the model predicting cortisol outcomes at Time 2. Preliminary analyses indicated that children's ages at the time of the cortisol assessments were not associated with any of the cortisol outcomes at Time 1 or Time 2. Therefore, child age was not included as a covariate in the analyses presented below. However, time since adoption was associated with children's cortisol levels and therefore was included as a covariate in all models.

Cortisol data were available at either Time 1 or Time 2 for 130 internationally adopted children. Fifteen children were missing cortisol data at Time 1, and 19 children were missing cortisol data at Time 2. In order to include all relevant cortisol data and ensure that our analyses at Time 1 and Time 2 included the same sample of children, all parameters were estimated using full information maximum likelihood. Raw cortisol values were used in the analyses when estimating the latent cortisol variables, and parameters were estimated using robust standard errors given that this method is suitable for non-normal continuous data.

3 | RESULTS

3.1 | Predicting diurnal cortisol outcomes at time 1

The standardized regression coefficients for the model predicting cortisol outcomes at approximately 6 months after adoption (Time 1) are presented in Table 2. The three wake-up cortisol samples significantly loaded onto the latent variable representing wake-up cortisol levels, and the three bedtime samples significantly loaded onto the latent variable representing bedtime cortisol levels. In addition,

TABLE 1 Descriptive statistics of cortisol samples

	Raw cortisol values (μg/dl)		Time of sample (hours)	Time since wakening (hours)
	N	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)
Time 1				
Wake-up, Day 1	105	0.28 (0.19)	7.62 (0.81)	0.13 (0.19)
Wake-up, Day 2	95	0.27 (0.19)	7.61 (0.90)	0.14 (0.18)
Wake-up, Day 3	98	0.27 (0.22)	7.67 (0.87)	0.12 (0.19)
Bedtime, Day 1	103	0.06 (0.08)	20.17 (0.94)	12.72 (1.03)
Bedtime, Day 2	104	0.07 (0.08)	20.12 (0.87)	12.70 (1.06)
Bedtime, Day 3	100	0.08 (0.13)	20.09 (0.81)	12.65 (1.05)
Time 2				
Wake-up, Day 1	103	0.26 (0.16)	7.48 (0.80)	0.09 (0.18)
Wake-up, Day 2	102	0.25 (0.17)	7.51 (0.89)	0.10 (0.19)
Wake-up, Day 3	99	0.25 (0.19)	7.46 (0.76)	0.11 (0.18)
Bedtime, Day 1	101	0.07 (0.94)	20.48 (0.85)	13.02 (0.97)
Bedtime, Day 2	101	0.06 (0.08)	20.49 (0.85)	13.01 (1.02)
Bedtime, Day 3	99	0.07 (0.13)	20.50 (0.95)	13.09 (0.87)

TABLE 2 Predicting the diurnal cortisol levels of children adopted internationally at 6 months after adoption (time 1) and 3 years after adoption (time 2)

	Time 1			Time 2		
	B	*SE*	*P*	*β*	*SE*	*p*
Outcome: Cortisol intercept						
Time in institution	−0.27	0.10	0.01	−0.23	0.09	0.01
Child biological sex	−0.02	0.10	0.88	−0.10	0.10	0.31
Intervention condition	–	–	–	−0.10	0.10	0.33
Time since adoption	−0.22	0.09	0.02	−0.21	0.10	0.04
Medication use	−0.08	0.07	0.25	0.23	0.17	0.16
Outcome: Cortisol slope						
Time in institution	0.32	0.10	<0.01	0.14	0.12	0.25
Child biological sex	0.07	0.11	0.55	−0.05	0.12	0.68
Intervention condition	–	–	–	0.05	0.13	0.71
Time since adoption	0.22	0.09	0.01	0.29	0.15	0.06
Medication use	0.04	0.06	0.55	−0.32	0.23	0.15
Outcome: Cortisol intercept (re-centered on bedtime levels)						
Time in institution	0.08	0.14	0.58	−0.23	0.08	<0.01
Child biological sex	0.14	0.11	0.19	−0.22	0.09	0.02
Intervention condition	–	–	–	−0.12	0.13	0.38
Time since adoption	−0.05	0.10	0.63	−0.05	0.12	0.68
Medication use	−0.15	0.06	0.02	0.05	0.06	0.42
Measurement model loadings						
Wake-up cortisol						
Day 1	0.71	0.12	<0.01	0.90	0.05	<0.01
Day 2	0.87	0.12	<0.01	0.74	0.06	<0.01
Day 3	0.46	0.23	0.04	0.71	0.10	<0.01
Bedtime cortisol						
Day 1	0.52	0.12	<0.01	0.87	0.08	<0.01
Day 2	0.77	0.11	<0.01	0.76	0.11	<0.01
Day 3	0.56	0.1	<0.01	0.67	0.13	<0.01
Time-varying covariates						
Wake-up cortisol, Day 1						
Time of sample	−0.17	0.07	0.02	−0.17	0.08	0.03
Time since wakening	0.01	0.08	0.92	−0.11	0.07	0.11
Wake-up cortisol, Day 2						
Time of sample	−0.27	0.09	<0.01	−0.13	0.07	0.06
Time since wakening	0.04	0.08	0.56	−0.02	0.08	0.82
Wake-up cortisol, Day 3						
Time of sample	−0.10	0.11	0.37	−0.12	0.06	0.07
Time since wakening	0.17	0.17	0.32	−0.15	0.10	0.12
Bedtime cortisol, Day 1						
Time of sample	−0.03	0.07	0.65	−0.18	0.10	0.08
Time since wakening	0.08	0.09	0.33	−0.09	0.10	0.35
Bedtime cortisol, Day 2						
Time of sample	0.02	0.10	0.87	−0.18	0.10	0.07
Time since wakening	0.06	0.10	0.56	−0.05	0.10	0.58

Continued

TABLE 2 (Continued)

	Time 1			Time 2		
	B	*SE*	*P*	*β*	*SE*	*p*
Bedtime cortisol, Day 3						
Time of sample	−0.01	0.15	0.93	−0.08	0.07	0.20
Time since wakening	0.06	0.10	0.57	−0.09	0.08	0.27

Note: $N = 130$. For children's biological sex, 0 = male and 1 = female. For intervention condition, 0 = control intervention and 1 = Attachment and Biobehavioral Catch-up.

there was a negative association between the time of day the wake-up cortisol samples were collected and the wake-up cortisol values for day one and day two.

With regard to the focal research question, duration of time in an institution prior to adoption was negatively associated with children's cortisol intercepts. In other words, children who spent a longer amount of time in an institutional environment prior to adoption had lower cortisol levels at the time of wake-up than children who spent minimal or no time in an institution. In addition, duration of institutional care was positively associated with children's cortisol slopes. Children who spent a longer amount of time in institutional care exhibited less steep declines in cortisol levels from wake-up to bedtime than children who spent minimal or no time in an institution (see Figure 1). We reran the model after re-centering the cortisol intercept to represent children's cortisol levels at bedtime, and the results indicated that time in an institution was not significantly associated with children's bedtime cortisol levels. The results also revealed that time since adoption was associated with the cortisol intercept and diurnal slopes, indicating that children who had been living with their adoptive families for a longer period of time had lower morning cortisol levels upon wake-up and less sleep declines from wake-up to bedtime than children who had been adopted more recently. In addition, children who were taking a medication that had the potential to influence cortisol levels had lower bedtime cortisol levels than children who were not taking these medications.

3.2 | Predicting diurnal cortisol outcomes at time 2

The standardized regression coefficients for the model predicting cortisol outcomes at approximately 3 years after adoption (Time 2) are presented in Table 2. Similar to the Time 1 model, the three

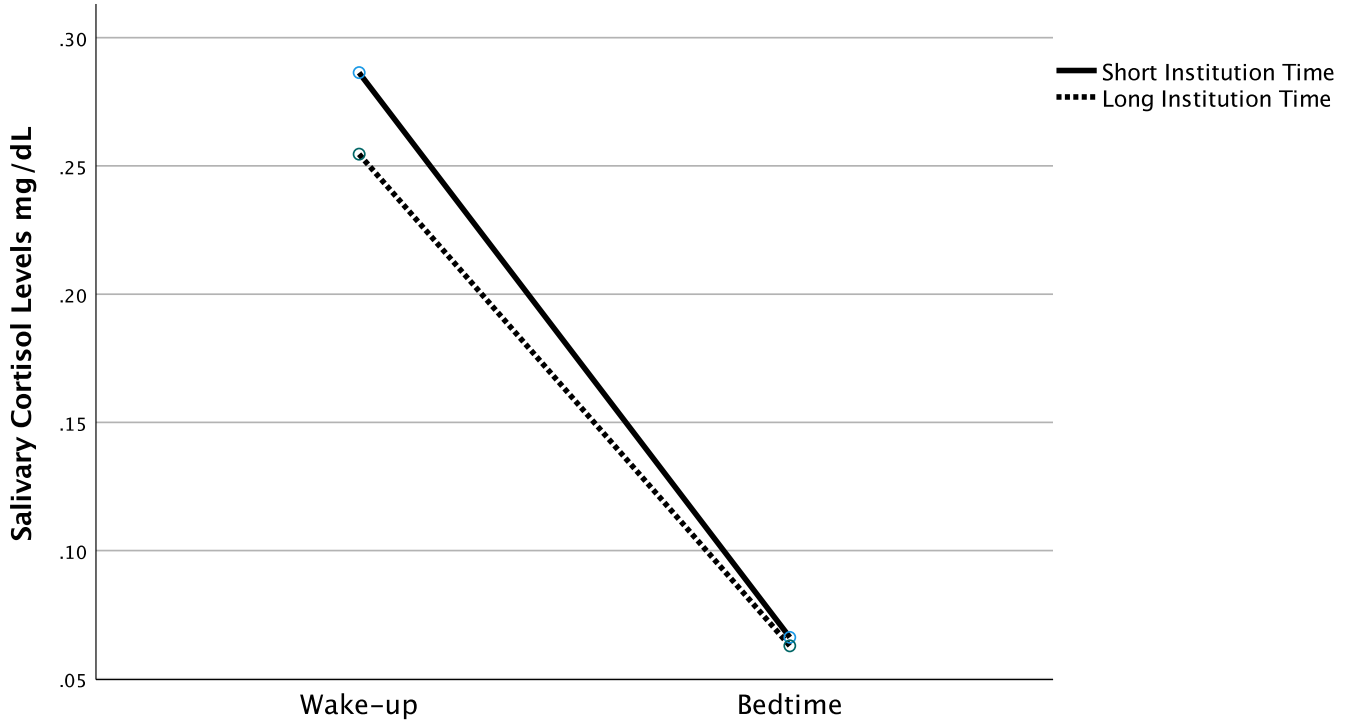

FIGURE 1 The association between duration of institutional care prior to adoption and internationally adopted children's diurnal cortisol levels approximately 6 months after adoption. Time in institutional care was dichotomized for illustrative purposes, with one standard deviation below the mean representing short institution time and one standard deviation above the mean representing long institution time

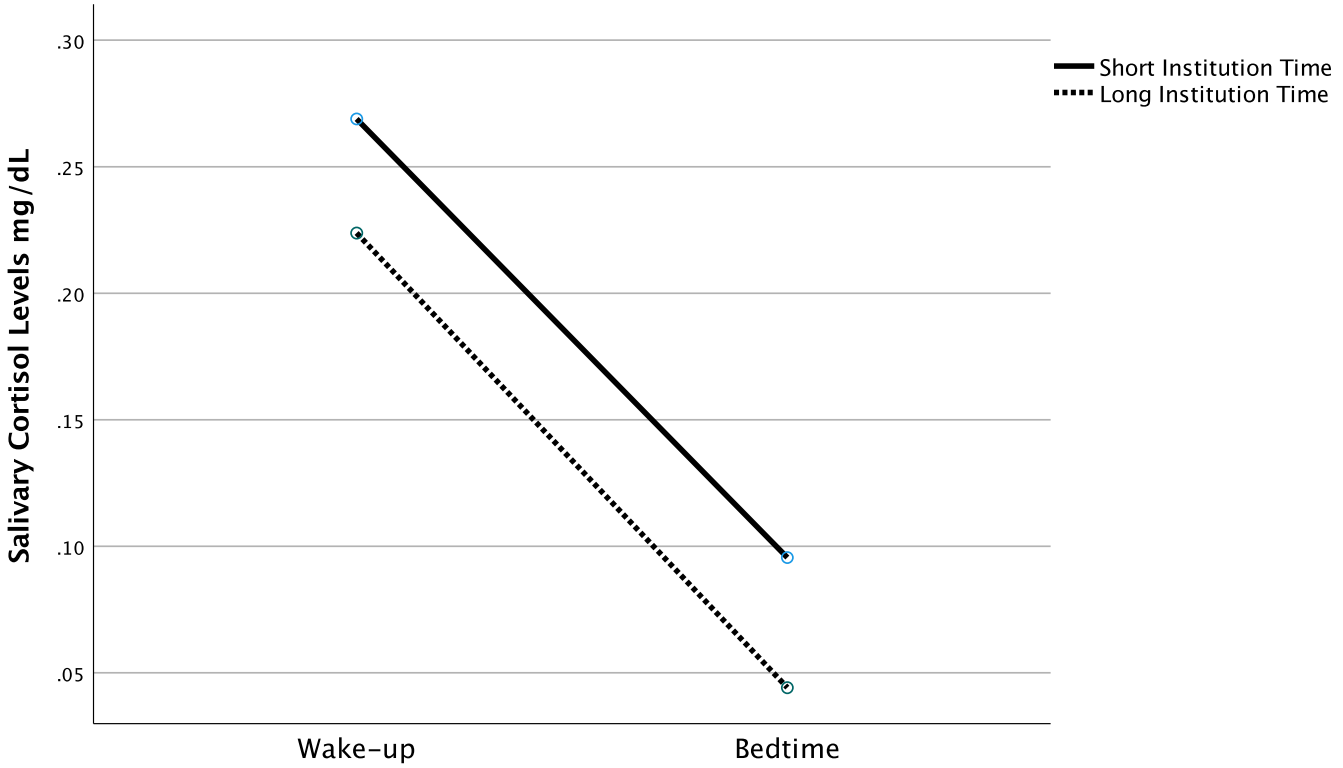

FIGURE 2 Predicting internationally adopted children's diurnal cortisol levels approximately 3 years after adoption from their duration of institutional care prior to adoption. Time in institutional care was dichotomized for illustrative purposes, with one standard deviation below the mean representing short institution time and one standard deviation above the mean representing long institution time

wake-up cortisol samples significantly loaded on the latent wake-up cortisol levels variable, and the three bedtime samples significantly loaded on the latent bedtime cortisol levels variable. In addition, there was a negative association between the time of day the wake-up cortisol samples were collected and the wake-up cortisol values for all 3 days.

Time in an institution continued to be associated with lower wake-up cortisol levels at Time 2. Unlike the Time 1 results, time in an institution was not significantly associated with children's cortisol slopes (i.e., changes in cortisol levels from wake to bedtime) at this later time-point. After re-centering the cortisol intercept to represent bedtime cortisol levels, time in an institution was negatively associated with bedtime cortisol levels (see Figure 2).

We also conducted a series of exploratory analyses testing whether the associations between duration of institutional care and children's cortisol outcomes at Time 2 were moderated by whether families received the Attachment and Biobehavioral Catch-up intervention or the control intervention. The results indicated that early institutionalization did not significantly interact with intervention condition when predicting children's wake-up cortisol levels, diurnal declines in cortisol levels, or bedtime cortisol levels at Time 2. Time since adoption was negatively associated with wake-up cortisol levels, and female children had lower bedtime cortisol levels than male children.

4 | DISCUSSION

The present study examined the consequences of early institutionalization for the diurnal regulation of the HPA axis among children adopted internationally. A unique feature of this study was that children's diurnal cortisol outcomes were collected at two time points: shortly after adoption and approximately 3 years later. This allowed us to test whether the diurnal HPA axis outcomes of previously institutionalized children show recovery after children are adopted or whether the associations between early institutionalization and HPA axis dysregulation persist over time. The results indicated that at approximately 6 months post-adoption, children who had experienced a long duration of institutional care had lower cortisol levels upon wake-up and a more blunted decline in cortisol across the day than internationally adopted children who experienced minimal or no institutional care. Children who had experienced long durations of institutional care continued to exhibit low wake-up cortisol levels nearly 3 years after adoption. Duration of institutional care also predicted bedtime cortisol levels, but not declines in children's cortisol levels between morning and evening, at this latter time point.

Altogether, these findings indicate that the consequences of early institutionalization for HPA axis regulation persist for several years after children are adopted. The evidence that children with histories of prolonged institutionalization exhibit low wake-up cortisol levels is

consistent with previous reports focused on children in institutional care (Carlson & Earls, 1997) as well children who have been adopted internationally (Flannery et al., 2017; Johnson et al., 2011; Koss et al., 2014; Leneman et al., 2018; Quevedo et al., 2012). The current set of findings extends this body of research by suggesting that the effects of early institutionalization on children's wake-up cortisol levels do not fade across the first few post-adoptive years. In fact, the magnitude of the effect of early institutional care on children's wake-up cortisol levels was nearly identical at the two time points.

The current study also provides novel evidence suggesting that early institutionalization is associated with low bedtime cortisol levels approximately 3 years after adoption. This finding, along with the finding that early institutionalization is also associated with low wake-up cortisol levels at this time point, may reflect a general profile of hypocortisolism (Fries et al., 2005). That said, it is not entirely clear why the association between early institutionalization and low bedtime cortisol levels was observed approximately 3 years after children were adopted but not at the earlier time point. Kroupina et al. (2012) reported that age of adoption was associated with lower bedtime cortisol levels 1-month post-adoption but not 6 months later, and other studies have reported that institutional care is associated with *higher* bedtime cortisol levels (Chernego et al., 2019; Gunnar et al., 2001). Thus, additional research is needed to clarify which components of the diurnal HPA axis pattern are altered by early institutional care as well as the time course of those alterations.

Overall, the findings from this study are consistent with the idea that early adverse experiences result in a downregulation of the HPA axis (Fries et al., 2005; Susman, 2006). Indeed, the findings from this study are consistent with other research indicating that children who experience maltreatment exhibit unusually low wake-up cortisol levels (e.g., Bernard et al., 2017). Because the current study focused on children adopted internationally and assessed children's diurnal cortisol outcomes at multiple time points, the current set of findings allows for a clearer understanding of the unique and potentially long-lasting consequences of early adversity for HPA axis downregulation.

Our analyses only considered potential linear relationships between early institutionalization and internationally adopted children's diurnal cortisol patterns. However, it is possible that there are specific thresholds of institutionalization that are especially influential, which would give to nonlinear associations between early institutionalization and later cortisol outcomes. For example, Leneman et al. (2018) reported that children adopted at 16 months exhibited a typical cortisol awakening response, whereas children adopted after age 16 months exhibited a blunted cortisol awakening response. A task for future research would be to utilize the statistical tools designed to test for threshold effects, such as piecewise regression analyses, LOESS models, or spline models, rather than dichotomizing children based on sample-specific characteristics (e.g., median age of adoption). Indeed, these types of analytic techniques have been profitably used in other areas of developmental science (e.g., Burchinal et al., 2016).

The time periods used in this study were determined by the research design. Specifically, data collection began approximately 6 months after children were adopted and ended when children were between 5 and 6 years of age. An important direction for future research is to examine whether the consequences of early institutionalization for internationally adopted children's diurnal HPA functioning continue to persist across childhood and into adolescence and adulthood. Cross-sectional studies have suggested that puberty may provide opportunities for recalibrating the HPA axis in ways that allow the dysregulated cortisol patterns of previously institutionalized children to recover within the context of stable and supportive family environments (Flannery et al., 2017; Quevedo et al., 2012; but see Leneman et al., 2018). In contrast, studies involving young adults who were adopted internationally as children have suggested that experiences of severe adversity prior to adoption may have long-term associations with blunted morning cortisol levels and flat diurnal patterns decades later (Kumsta et al., 2017; Van der Vegt et al., 2009). Thus, there is a critical need for longitudinal research that repeatedly assesses the diurnal cortisol patterns among individuals who were adopted internationally in order to assess whether the consequences of early institutionalization for the HPA axis change over time.

Low levels of cortisol upon wake-up and blunted diurnal cortisol patterns are associated with increased risk for the development of externalizing behavioral problems as well as poor executive functioning skills among children who have experienced early adversity (Frost et al., 2018; Gunnar & Quevedo, 2007; Lupien et al., 2009; Shonkoff et al., 2012). Early institutionalization has also been associated with these same behavioral problems (e.g., Juffer et al., 2011; Julian, 2013). These findings point to the possibility that alterations in diurnal HPA axis regulation may represent a mechanism by which early institutionalization shapes the behavioral outcomes of children adopted internationally (e.g., Koss et al., 2014). Additional research examining this mediational pathway will help advance our understanding of how early experiences of adversity become biologically embedded and exert a long-term influence on these maladaptive patterns of behavior.

International adoption designs represent a type of natural experiment for examining the unique role of early experiences for shaping individuals' development (Haugaard & Hazan, 2003; Rutter, 2007). However, early institutional care does represent an atypical and extreme form of early adversity. For this reason, findings based on these unique research designs may not generalize to non-institutionalized children's early experiences of stress. It will be important for researchers to continue to examine the influence of a wide variety of measures of early experiences—including normative variations in parenting behavior and other forms of early life stress, such as poor parental mental health, economic hardships, and environmental unpredictability (e.g., Hackman et al., 2018; Young et al., 2019)—to better understand how diverse forms of early experiences are associated with development of the HPA axis.

Interventions that aim to improve the quality of care parents provide for their young children may offer additional evidence of the

significance of early experiences for HPA axis regulation. Indeed, the Attachment and Biobehavioral Catch-Up (ABC) intervention has been shown to promote sensitive parenting and to enhance children's diurnal cortisol regulation among families referred to Child Protective Services due to risk for maltreatment (Bernard, Dozier, et al., 2015; Bernard et al., 2015; Garnett et al., 2020). In addition, the ABC intervention had effects on internationally adopted children's diurnal cortisol outcomes shortly after families completed the intervention (Raby et al., in press). Significant effects of the ABC intervention on children's diurnal cortisol regulation 3 years post adoption were not observed in this study, which may suggest that the effects of the intervention weaken with time and require booster sessions in order to have sustained effects on cortisol regulation outcomes for this group of families.

In summary, the current study indicates that experiences of institutional care early in life have consequences for internationally adopted children's diurnal HPA activity that persist up to 3 years after children are adopted. These results support the idea that early institutional care is incompatible with young children's needs for stable and consistent attachment relationships, resulting in potentially lasting harmful effects on children's neurobiological development.

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