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THE ENDURING EFFECTS OF EARLY INSTITUTIONALIZATION ON THE
DIURNAL CORTISOL REGULATION OF INTERNATIONALLY ADOPTED
CHILDREN

by

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ABSTRACT

Experiences during infancy and early childhood are believed to play a crucial and unique role in organizing children's neurobiological development. Specifically, experiences within early attachment relationships are expected to assist with regulating the diurnal functioning of the hypothalamic-adrenocortical (HPA) axis. International adoption offers a powerful test of the unique effects of early experiences on later HPA functioning because many internationally adopted children experience profound adversity prior to being adopted into highly resourced families. The purpose of the present study was to examine the potential longer-term consequences of early adversity on the HPA functioning of internationally adopted children at the age of 5 years. The results indicate that longer time in institutional care resulted in lower waking cortisol levels. The results also indicate that institution care is associated with more blunted diurnal patterns. These results indicate that the consequences of early institutionalization can endure up to four years after adoption. These results suggest that early adversity has lasting implications for neurobiological development.

TABLE OF CONTENTS

ABSTRACT	ii
INTRODUCTION	1
METHODS	5
RESULTS	8
DISCUSSION	10
REFERENCES	15

INTRODUCTION

Experiences during infancy and early childhood are believed to play a crucial and unique role in organizing children's neurobiological development. Specifically, experiences within early attachment relationships are expected to assist with regulating the diurnal functioning of the hypothalamic-adrenocortical (HPA) axis (Koss, Hostinar, Donzella & Gunnar, 2014). The HPA axis is an important component of the neuroendocrine system and involves communication between the hypothalamus, anterior pituitary and adrenal cortex. When a person experiences stress, the HPA axis becomes activated and begins to excrete hormones such as cortisol, in an effort to regulate important biological systems. Cortisol therefore, becomes an important neurobiological marker of the body's response to stress. Often, researchers struggle to identify specific predictors in dysregulated HPA functioning due to confounding variables such as genetic expression, sensitive caregiving and environmental stress. Recently, adoption models have been used to disentangle many of these confounding variables. The present study utilizes an international adoption model which offers a powerful test of the unique effects of early experiences of adversity on cortisol, which is one element of neurobiological development. As adopted children transition from institutional care into highly resourced families, predictor variables can be isolated and examined. In this way, this study has the potential to provide a deeper understanding into sensitive developmental periods and the neurobiological organization that occurs in infancy and early childhood and will examine whether the effects of early experiences of adversity during this time persist over time. With a deeper understanding of how early adversity impacts development, we can begin to intervene earlier in life and potentially influence and improve longer term mental health outcomes in vulnerable populations.

Function of the HPA Axis

There has been a recent surge of interest in the hypothalamic-pituitary-adrenocortical (HPA) axis among developmental researchers. The HPA axis is an important neuroendocrine system that controls reactions to stress and regulates several biological processes through the excretion of neurotransmitters and hormones such as cortisol. (Jacobson, 2014). Studies on early human development have suggested that early separations from caregivers are often associated with changes in the functioning of the HPA axis (Dozier, Peloso, Lewis, Laurenceau & Levine, 2008). HPA therefore becomes a powerful litmus test of stress and aversive experiences. The present study will use HPA changes to determine the impact of early experiences of adversity.

Early Adversity and Cortisol Regulation

Stress is a condition caused by aversive experiences in which an individual experiences threats to physical or emotional well-being that overwhelm the body's capacity to cope (Gunnar, Herrera, & Hostinar, 2009). When a body is overtaxed, the HPA axis becomes activated and cortisol is excreted. Cortisol regulation patterns are often discussed in terms of the change in cortisol levels between wake time and bed time. This change or natural decline in cortisol throughout the day is called diurnal cortisol. In low-risk samples, cortisol levels are typically high after waking in the morning and low prior to bed time, which creates a steep downward slope from wake to bed time. While some experience with manageable stress prove to be important for healthy development, prolonged, uninterrupted and overwhelming stress can have dire effects on biological systems (Gunnar, Morison, Chisholm, and Schuder, 2001). When the HPA axis is overstimulated, the body is forced to process excessive amounts of cortisol which, over time, cause undue wear-and-tear on the body. This type of chronic stress is often associated

with institutionalized care (Gunnar et al., 2001). Institutionalized care within orphanage settings in international countries has been shown to be particularly stressful to infants due to adverse conditions such as over population and limited adult-to-infant ratios (Gunnar et al., 2001). As a result, these children often experience poor quality caregiving, social neglect, which can thrust these children's bodies into overwhelming and prolonged stress responses.

Cortisol Outcomes among Children Adopted Internationally

One of the most valuable ways to study the effects of early adversity on development is through the use of internationally adopted children. Adoption models offer a powerful test of the unique influence of early experiences of adversity for HPA functioning because children experience profound shifts in care giving experiences post adoption by entering highly resourced homes (Koss, Hostinar, Donzella, & Gunnar, 2014).

In a study conducted by Gunnar and colleagues (2001), higher cortisol levels over the daytime hours were found in populations of children adopted from Romanian orphanages. These inflated cortisol levels persisted six and a half years post adoption demonstrating the long-term effects early experiences of adversity can have on HPA functioning.

In another study, HPA axis functioning was examined in internationally adopted children, biologically reared children, and children adopted during their first year from overseas foster care (Koss et al., 2014). HPA functioning was examined in all three samples during the transition to family care in the first two years post adoption. This study analyzed four time points of diurnal HPA samples taken from each child participant. Researchers discovered that post-institutionalized children with lower social care quality prior to adoption exhibited less steep cortisol slopes. In addition, blunted diurnal cortisol levels were found to be a mediator

between adoption status and increased behavioral problems two years post adoption. Taken together, research shows that children with early adverse experience demonstrate less strongly fluctuating levels of cortisol compared to low-risk samples of children with no early adverse experiences (Gunnar et al.2001).

Vegt, Ende, Kirschbaum, Verhulst, and Tiemeier(2009) conducted a longitudinal study of internationally adopted individuals who had experienced neglect and abuse early in life. The researchers found that these individuals had decreased waking cortisol levels, resulting in an altered diurnal cortisol slope . Thus, early experiences of adversity appear to have associations with cortisol levels and the diurnal slope, even when children are raised in another environment after their early maltreatment.

Enduring Effects Model Versus Revisionist Model

Amongst developmental researchers, it is commonly assumed that early experiences can have relatively long-term effects that do not fade with time (Raby, Roisman, Fraley, & Simpson, 2015). This “enduring effects model” could be used to describe the associations between early relational experiences and later outcomes. If the enduring effects model is applied to the present study, we could anticipate that the contributions of early adversity for internationally adopted children’s diurnal HPA outcomes should be relatively stable and persist across periods of development.

Conversely, the “revisionist model” predicts that the association between early experiences and later outcomes would become increasingly small over time, approaching zero as the temporal lag increases (Raby et al., 2015). If the “revisionist model” is applied to the present topic, the contributions of early adversity for internationally adopted children’s diurnal HPA

outcomes should decrease as time progresses and resemble HPA patterns more typical of individuals who have no early aversive experiences.

Present Study

There has been a plethora of research that has been conducted on young, internationally adopted children, yet there is a paucity of longitudinal research addressing longer-term consequences of early experiences of adversity. There appears to be limited evidence about whether post-adoptive caregiving experiences can facilitate recovery in internationally adopted children's diurnal cortisol outcomes or whether the effects of early adversity will persist despite substantial improvements in caregiving quality. The present study will seek to fill some of the gaps in prior research by examining the impact of early experiences of adversity on diurnal cortisol outcomes 4 years post adoption. This study is part of a larger longitudinal study conducted examining the significance of early experiences on development amongst samples of internationally adopted children. For the purposes of this study, the cortisol outcomes of 78 internationally adopted children were examined at the age of 5 years. Time spent in institutional care was used as a predictor of diurnal HPA functioning. Based on the Enduring Effects model of development (Raby et al., 2015), this study predicts HPA outcomes will remain blunted at the age of 5 years.

METHOD

Participants

This study examines 78 children adopted internationally (55% female, 45% male). The majority of children were adopted from China (42%), Russia or Eastern European countries (19%), South Korea (15%), or Ethiopia (10%). Families were recruited to participate shortly

after adoption. Adoptive parents' reports of the time children spent in institutional care prior to adoption was used as the indicator of early adversity. This sample of internationally adopted children spent between 0 and 35 months in institutional care prior to adoption ($M = 9.94$, $SD = 8.7$). Cortisol levels were checked at several time points post adoption but for the purpose of this study, we will be looking at diurnal cortisol patterns within the HPA system in the samples taken when children were approximately 5-years-old ($M = 5.44$, $SD = 0.56$). At the time of this assessment, the average time since adoption was 4.02 years (range = 1.78 to 6.38 years).

It is important to note that adoptive parents were randomized to receive one of two parent-training interventions. The first intervention was the Attachment and Biobehavioral Catch-up (ABC) intervention, and the control intervention was the Developmental Education for Families. Fifty percent of the adoptive parents received the ABC intervention while the remaining fifty percent received the control intervention. These interventions were not part of the present study and when controlled, we did not find a significant association between intervention condition and cortisol regulation.

Materials and Measures

Saliva Sampling

Identical salivary sampling methods used in prior studies were used in this study (Dozier, Peloso, Lewis, Laurenceau & Levine, 2008). Methods included training adoptive parents how to collect the saliva samples. Parents were instructed to collect saliva samples from children at wake-up and bedtime across three consecutive days. Specifically, the researcher instructed parents to collect a wake-up sample each day immediately when the child woke up, before even getting out of bed when possible. 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. For the bedtime collection, parents were told to collect the sample as close to bedtime as possible. Parents collected saliva samples by putting the end of a cotton swab in the child's mouth. After adequately soaking the cotton swab in saliva, the parents placed the cotton swab into a pre-labeled vial and recorded the date and time of sampling in a saliva sample journal and on the vial. Parents stored the vials in their freezers until the research staff retrieved the samples at a later home visit. Parents reported collecting wake-up samples between 6:10 a.m. and 10:02 a.m. with a mean wake up time of 7:45 am ($SD = 45.6$ minutes). Parents reported collecting bedtime samples between 7:11 p.m. and 11:07 p.m. with a mean bed time of 8:40 p.m. ($SD = 43.2$ minutes). To ensure families followed the guidelines, researchers gave each caregiver a binder with full sampling instructions (including directions and accompanying photographs of each step of the sampling protocol). Research staff instructed parents to delay the collection of saliva if children were sick and to not have the child eat or drink anything or brush their teeth within the 30 minutes prior to sampling.

After being collected by a research assistant, 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, Delaware). All samples from each child were assayed in duplicate on the same plate to minimize variability. Following procedures commonly used in previous studies (Dozier et al., 2008), cortisol values that were implausible (>2.0) and those that fell 3 SD s above the mean were considered outliers and excluded from analyses. Of 468 possible samples (i.e., 78 participants with up to 6 samples each), 18 outliers were removed and 53 samples were missing due to an inadequate volume of saliva or because no

sample was taken.

RESULTS

According to past research, cortisol levels may vary day-to-day (Gunnar et al., 2001). Composites were therefore created for all three cortisol measures across days within time periods (wake, bed, and the change between wake and bedtime levels (diurnal)). All available and valid samples per child were used to calculate composites. Cronbach alphas were computed to determine how closely the items cohered or reflected the composite values at each time point. The Cronbach alphas for the wakeup and evening composites were acceptable ($\alpha = 0.73$ for wakeup and $\alpha = 0.84$ bedtime). These results illustrated that both morning and evening cortisol measures were stable across days and the composites for both time periods were reliable. The measure of diurnal cortisol declines was created by developing a third composite by subtracting evening from morning cortisol levels.

To test the hypothesis that waking cortisol levels would remain low among children who experienced high levels of adversity prior to adversity, we ran a hierarchical linear regression with waking cortisol composites regressed onto institution time. Children's biological sex, age at the time of cortisol assessment, and cortisol sampling time were controlled for hierarchically. We found a significant negative relationship indicating that time spent in institutions predicts waking cortisol levels above and beyond the possible effects of sex, age, and sampling time ($\beta = -.27, p = .029$). This association indicates that more time spent in institutionalization results in reduced waking cortisol levels.

Bed time cortisol composites also were regressed onto institution time. Children's biological sex, age at the time of the cortisol assessment, and cortisol sampling time were

controlled for in this model. We observed no significant relationship between bed time cortisol and time spent in institutions ($\beta = -.21, p = .095$). This nonsignificant association indicates that more time spent in institutionalization did not impact bed time cortisol levels.

Finally, to test the hypothesis that predicted blunted (or less steep) changes (wake up to bed time) in cortisol levels throughout the day, we ran a hierarchical linear regression with diurnal cortisol regressed onto institution time. Children's biological sex, age at the time of the cortisol assessment, and cortisol sampling time were controlled for in this model. Significant, positive associations emerged for diurnal cortisol and time spent in institutions ($\beta = .24, p = .046$) even after controlling for sex, age and sampling time.

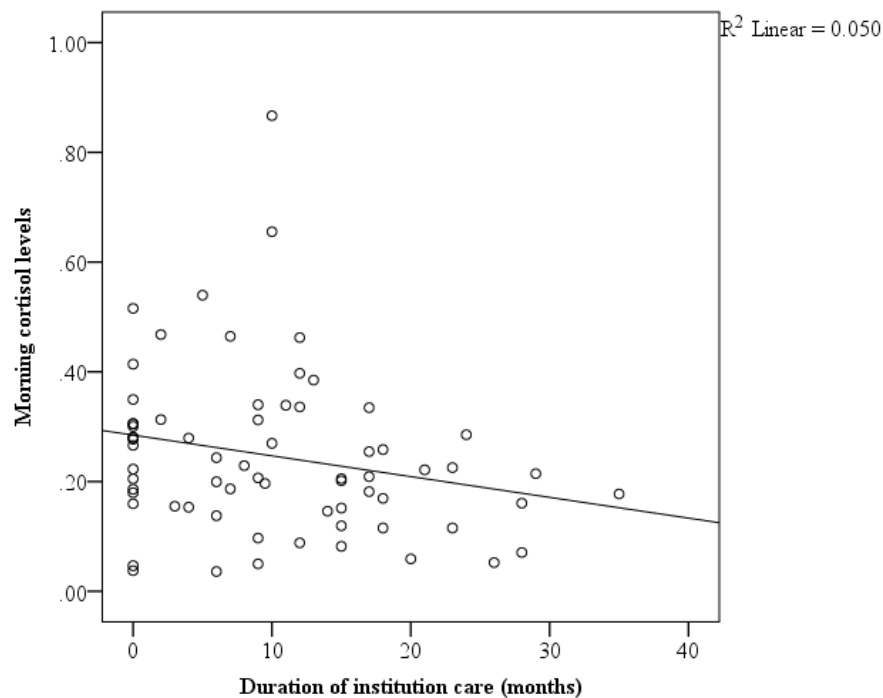


Figure 1. Children adopted internationally who experienced institutional care for long periods of time exhibited lower morning cortisol levels than children who experienced less institutional care prior to adoption.

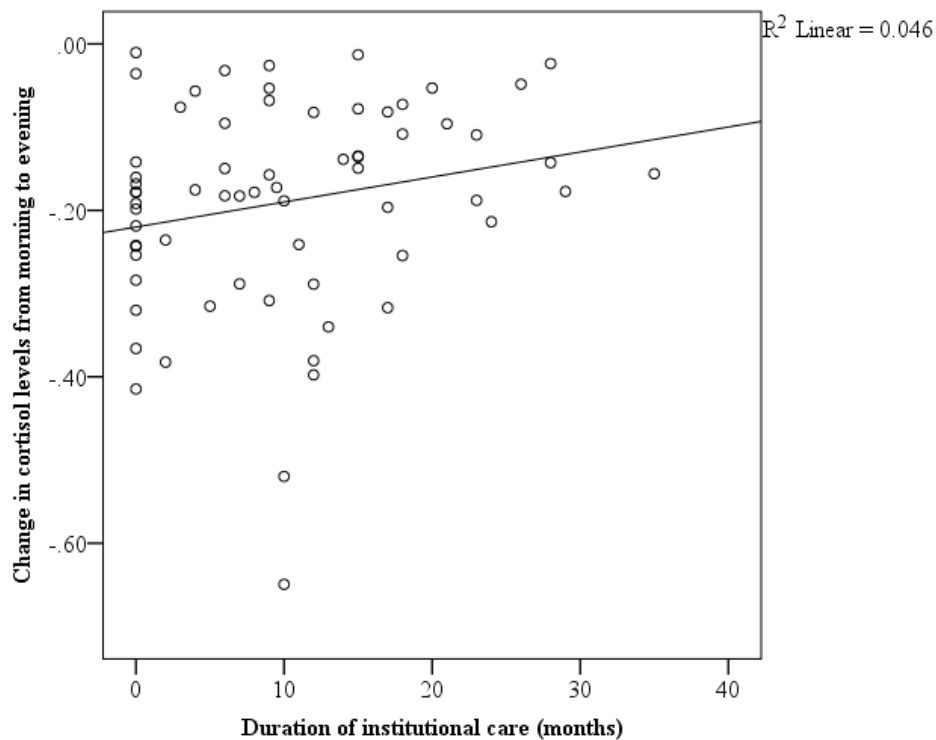


Figure 2. Children adopted internationally who experienced institutional care for long periods of time exhibited more blunted diurnal cortisol levels (i.e., exhibited less declines throughout the day) than children who experienced less institutional care prior to adoption.

DISCUSSION

The aim of the present study was to determine whether early experiences of adversity negatively impact internationally adopted children's neurobiological development, as measured by the regulation of diurnal cortisol patterns over time. This study predicted HPA outcomes would be blunted at the age of 5 years (approximately four years post adoption). Consistent with that prediction, the findings from this study indicate that longer time spent in institutional care prior to adoption is associated with lower cortisol levels in the morning and more blunted declines in cortisol levels throughout the

day. These low waking cortisol results indicate that early experiences of severe adversity can disrupt the regulation of children's cortisol regulation and the consequences can endure up to four years post adoption. These results thus support the Enduring Effects model of development and imply that early adversity may have lasting implications for neurobiological development (Raby et al., 2015). These findings therefore could inform the design of early interventions for both children and caregivers.

While many people may assume that less cortisol is good, lower waking cortisol levels are symptomatic of dysfunctional cortisol regulation pattern which can have detrimental impacts on physical health and cognitive functioning. Applying information gleaned from studies conducted by Shoal, Giancola and Kirillova (2003), blunted diurnal cortisol patterns appear to confer risk for later psychiatric disorders, most especially psychopathy and substance abuse. We can therefore infer that children experiencing extreme forms of early adversity, such as institutionalization, are at risk for developing psychopathology later in life. For example, blunted cortisol patterns are predictive of increases in aggressive behavior over time and characterize adolescent diagnoses such as conduct disorder and adults with antisocial personality disorder and substance use disorder, dependence, and addiction (van Goozen, Fairchild, Snoek, & Harold, 2007). Shirtcliff and colleagues (2009) have argued that HPA hypo-reactivity is central to the development of lack of empathy. The impaired neural circuitry of individuals with blunted or hyporeactive HPA systems leaves them under-aroused by the distress of others and thus vulnerable to behaving in indifferent ways (van Goozen, Fairchild, Snoek, & Harold, 2007). Although it is premature to suggest specific behavioral implications for the effects of children who experience early adversity, the findings are concerning.

One of the limitations of this study is the nature of the internationally adopted population. The extreme adverse environments these children faced prior to adoption makes it challenging to generalize these findings to other forms of less severe early experiences of adversity. Future research should use similar methodology with samples of domestic infant adoptions, which experiences far less adverse conditions prior to adoption, in order to get a clearer picture of how “typical” adversity in early childhood impacts HPA functioning longitudinally.

Another limitation for this study is the nature of saliva sampling. Saliva sampling is known to produce less accurate measures of physiological reactions to adversity when compared with more invasive measures such as the cosyntropin, tetracosactide, or Synacthen test (ACTH) or Corticotropin-releasing hormone (CRH). Unfortunately, these measurements are too invasive to be used with children (Gunnar, et al., 2009). Most researchers studying early adversity must rely on samples of cortisol obtained in saliva. Some of the issues that arise with the use of saliva samples include, time of day, child age, sleep/wake cycles, and social context. This study therefore, controlled for age, and time of day when samples were taken, and used diaries to assess external variables such as food, illness and medication in an effort to minimize measurement error. Even with the limitations of salivary samples, research on this neuroendocrine system has grown tremendously popular because of the ease of salivary cortisol measures.

Another critical challenge and possible limitation to the study is the complex and multifaceted nature of adversity in childhood. When researching stress and adversity, we must consider the type, severity, and duration of the adversity the child faces. Other factors such as the family and home environment, psychological mechanisms of coping and defense, individual

differences in reactivity and developmental status of the child must be account for when examining the effects of early adversity (Gunnar et al., 2009). When studying internationally adopted populations, it is often impossible to accurately discern the nature of the adversity these adopted children experienced in early childhood. This study relies on parent reports of observed conditions within the care institutions and many parents did not directly observe the actual institution from which their child came. We therefore relied heavily on the amount of time spent in institutional care in order to get a clear measurement early adversity. To further control for unknown environmental variables, recruitment efforts focused on institutionalized care within regions with well-reported adverse conditions such as eastern Europe and Asia.

One final limitation of this study remains the inability to parse out the interaction of the environment with an individual's unique genetic code to shape HPA functioning and brain development. Without biological samples from birth mothers, we have no way of accurately discerning what genetic factors influence HPA functioning and what is a product of the environment prior to adoption.

Future studies should look longitudinally beyond 4 years post adoption to see if diurnal cortisol outcomes remain dysregulated or if these outcomes fade over time. If these outcomes persist over time, future research can begin to look at different early interventions to regulate the HPA axis. Future research should also look at how HPA functioning may mediate effects of early adversity on executive function development. Executive function deficits often account for similar psychopathology found in HPA dysregulation and therefore may be an important predictor in psychopathology. If we can identify the specific neural networks and functioning

responsible for psychopathology, early interventions can be developed and implemented to curve the trajectory of mental health issues.

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