

Effects of Therapeutic Interventions for Foster Children on Behavioral Problems, Caregiver Attachment, and Stress Regulatory Neural Systems

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ABSTRACT: Young children in foster care are exposed to high levels of stress. These experiences place foster children at risk for poor social, academic, and mental health outcomes. The role of adverse events in stimulating neurobiological stress responses presumably plays a role in shaping neural systems that contribute to these problems. Systematic and developmentally well-timed interventions might have the potential to change developmental trajectories and promote resilience. Moreover, understanding how specific dimensions of early adversity affect underlying stress response systems and how alterations in these systems are related to later psychosocial outcomes might facilitate more precise and targeted interventions. Data are drawn from two ongoing randomized trials involving foster infants/toddlers and preschoolers. Consistent with prior animal models of early adversity, these studies have shown that early adversity—particularly neglect, younger age at first foster placement, and higher number of placements—is associated with altered hypothalamic-pituitary-adrenal (HPA) axis function. The interventions under investigation have produced evidence that it is possible to impact many areas that have been negatively affected by early stress, including HPA axis activity, behavior, and attachment to caregivers.

KEYWORDS: adrenocorticotrophic hormone (ACTH); cortisol; hypothalamic-pituitary-adrenal (HPA) axis; stress; stress hypo-responsive period (SHRP)

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INTRODUCTION

In a society in which approximately 900,000 children are reported to be maltreated every year,¹ foster care is a necessary societal institution. It is also a much-maligned institution in which shortcomings and failures often garner considerable negative public scrutiny and successes frequently go unnoticed. The tasks with which the U.S. foster care system and the larger national child welfare system are charged are monumental: to investigate alleged child maltreatment and protect children from further maltreatment; to ensure that physical and psychological needs of children in care are met; and to provide services to parents necessary to achieve permanent and stable living circumstances. Numerous studies comparing foster children to nonmaltreated children have found elevated rates of psychopathology, developmental delays, substance abuse, and mortality among individuals placed in foster care.²⁻⁴ There is also an apparent intergenerational transmission of risk for foster care involvement: individuals placed in care as children are more likely to have their own children placed in care.⁵

Although many foster children fare poorly, others appear to emerge relatively unscathed. Little scientific knowledge exists about which variables direct life course trajectories toward poor versus healthy adjustment in these children. In the context of two ongoing studies of foster children, involving infants and toddlers⁶ and preschoolers,⁷ we have worked to address these issues. This research, guided by a network of basic and applied scientists,⁸ has had two primary emphases. First, we have synthesized prior animal and human research on the neurobiology of early adversity into a model that specifies underlying neural mechanisms hypothesized to mediate the association between stress and later outcomes. Second, we have applied this model to research on caregiver-based interventions foster care. In this article we describe elements of the model and show how ongoing randomized trials to evaluate the efficacy of the interventions are being employed to test the validity of the model.

THE NEUROBIOLOGY OF STRESS AND EARLY ADVERSITY

More than half a century of research on rodents and nonhuman primates has demonstrated that disruption in early parental care exerts a profound and lasting impact on brain development, gene expression, and vulnerability to later stress, anxiety, and affective disorders.⁹ These studies have applicability to the foster care population and might indicate a window into basic mechanisms of risk in foster children. Although requiring cross-species translation and caution in drawing conclusions that are applicable to human experience, these studies have the potential to guide research toward far more precise linkages than have been established between specific dimensions of adverse early experience and later outcomes among foster children.

One neurobiological pathway that has been the focus of much of this preclinical research is the hypothalamic-pituitary-adrenal (HPA) axis. The HPA axis is activated in response to physical and psychological stressors. HPA axis activation involves a hormonal cascade in which corticotrophin-releasing hormone (CRH), secreted in the paraventricular nucleus (PVN) of the hypothalamus, stimulates the release of adrenocorticotrophic hormone (ACTH) in the anterior pituitary, which enters the bloodstream and ultimately stimulates the release of glucocorticoids (cortisol in humans and nonhuman primates; corticosterone in rodents) in the adrenal cortex. Glucocorticoids in turn exert negative feedback on the upstream structures, slowing the release of ACTH and CRH.¹⁰

Glucocorticoids have numerous additional effects throughout the body, including stimulation of the immune system and metabolism of stored energy. In the brain, glucocorticoids act through two types of receptors—mineralocorticoid (MR) and glucocorticoid (GR). MRs primarily maintain a homeostatic balance of neurotransmitters to neurons; in contrast, GRs are involved in stress responding, limiting the impact of other biological stress responses and facilitating return to prestress functioning following exposure to stress. Although GR actions are critical to stress regulation, this system operates optimally only in response to acute, short-term stressors. Exposure to chronic, long-term stress has been shown to have a negative impact on the HPA axis and other neural and bodily systems.¹¹

The HPA axis functions in concert with a number of other neural pathways in the regulation of stress responses. These include a second CRH pathway, emanating from the central nucleus of the amygdala (CeA), which is involved in threat detection and response. The CeA–CRH pathway has indirect connections to the HPA axis via the bed nucleus of the stria terminalis (BNST) and direct connections to the norepinephrine (NE) system via the locus coeruleus. NE is critical in supporting anxiety and fear responding. In addition, bidirectional linkages exist between the amygdala and areas of the medial prefrontal cortex (mPFC), which is involved in executive cognitive functioning, particularly the modulation of emotions and stress hormones (cortisol and adrenaline). Elsewhere,⁸ we describe the interrelationships among these stress regulatory neural pathways, and their implications for understanding early adversity effects in humans. For this article, we concentrate on the HPA axis.

Studies of rodents, using experimental paradigms in which pups are separated from their mothers at varying time points and for varying intervals postparturition, have documented long-term effects of disrupted caregiving on HPA axis function. Gunnar *et al.*⁸ have synopsised the results of these studies into three areas. First, the timing of the disruption to maternal care is likely to be of key importance. In particular, maternal separation during the first 1 to 2 weeks of life often appears to have the greatest impact on the development of the HPA axis. One explanation that has been offered for this is that there is extensive GR gene methylation during this developmental period in rodents that is clearly associated with maternal licking and grooming.¹² Methylation

of the GR gene results in it being inactivated and unavailable for stress modulation. In the absence of maternal care, or at lower levels of such care, there is more methylation and consequently less GR gene transcription (and fewer GRs). As is noted above, GRs play a central role in the regulation of neural stress responses; thus lowered potential for GRs would be expected to produce problematic outcomes. (It is interesting to note that the 1- to 2-week postparturition period in rodents corresponds roughly to the final trimester of pregnancy and early postnatal period in humans, suggesting that the effects of prenatal stress should be an emphasis in human studies of early adversity.)

Second, permanent alterations in HPA axis function are most likely to stem from events that occur during the stress hyporesponsive period (SHRP) of development. The SHRP in rodents occurs during the first 2 postnatal weeks and is believed to be critical in the development of neural circuitry involved in learning, memory, and stress responsivity. The presence of this period is marked by an absence of HPA axis activation in response to external stress.¹¹ Notably, studies of humans responding to laboratory and everyday stressors suggest that a much longer SHRP might exist, emerging in infancy and persisting until the onset of adolescence;⁸ however, this is an area of emerging knowledge in which cross-species translation of results is quite challenging. Additional research on normative and at-risk human populations will help to specify time points across this broad developmental span in which disruptions in care have more or less impact.

Third, the buffering from stress that occurs during the SHRP is caregiver mediated.¹³ Thus, disruptions in care during the SHRP appear to have the most pervasive effect on HPA axis function. A similar buffering role of supportive caregiving has been obtained in children. When children are in out-of-home care, cortisol levels tend to rise over the day, and this rise is sharper for younger children (toddlers) and children who receive less supportive care from their child care provider(s).¹⁴ Similarly, children in insecure attachment relationships are more likely than those in secure relationships to show elevations in cortisol when they encounter mildly threatening events (e.g., getting their childhood inoculations or being confronted by an intrusive stranger).^{14,15} In sum, the availability of a sensitive, responsive, and supportive caregiver during human infancy and childhood appears to be required to buffer the individual and the developing HPA axis from the negative effects of mild everyday threats and stressors.

IMPLICATIONS FOR CHILDREN IN FOSTER CARE

The implications of these studies for foster children run counter to some prevalent beliefs about this population. To summarize, in the rodent SHRP, the pup is unable to regulate competent physiological response to stressors independently and is therefore dependent on maternal care for stress modulation.

The absence of such a parental regulator during this time period renders the pup vulnerable to environmental adversity in ways that have the potential to permanently affect neurobiology and behavior. Although in the rat SHRP appears to extend from the postnatal into the late prenatal period in humans, the SHRP in humans appears to have a wider window, perhaps due to evolutionary influences that allow human children to use relationships with parents and other supportive adults to modulate stress for much longer in brain and behavioral development. Thus, in humans, the unavailability of a caregiver to serve as a stress regulator until a child is able to competently manage stressors more independently could have similar negative effects.

In the case of foster children, physical abuse and sexual abuse are often the focus of treatment efforts, as these events are deeply traumatic and can interfere with subsequent functioning in a number of ways. However, the above summary suggests that *the absence of a responsive, supportive caregiver to serve an external extension of the child's stress regulatory system* might have the most pervasive long-term effects on the child. There are a number of circumstances common in the lives of foster children in which a sufficient caregiving regulatory system might not be present. These include being severely neglected in the family of origin, being placed in foster care with a nonresponsive caregiver, and experiencing multiple brief foster placements with unexpected moves. Given this, we hypothesize that it is among children who have had these experiences that we will see the greatest impact on HPA axis functioning and the least resiliency in the face of subsequent stressful events.

If the absence of a caregiver to modulate responses to adversity has significant negative effects during infancy and childhood, perhaps introducing an external source of stress regulation during this same period has the potential to reverse any of these early adversity effects. There is some evidence from rodent studies that remediation of early adversity effects on neural development is possible.¹⁶ However, in the context of foster care, this is not a simple task. Simply placing children in foster care might not be a sufficient intervention, as not all foster parents can provide responsive, supportive care. This might not be due solely to foster parent limitations but also to the foster child's ability to communicate distress and more generally to accept the caregiver as a source of external regulation.¹⁷

Although placement in foster care might not prove a sufficient remedy to the effects of early adversity in the absence of an adequate caregiving regulatory system, it represents an opportunity. If foster parents are able to develop a relationship with the child that allows adequate stress regulation to occur, progress might be possible. Inasmuch as parenting is malleable, it might be possible to develop systematic interventions to help facilitate these processes. Our work has been based on the supposition that foster caregiver-based interventions might help to provide foster children with the necessary caregiver-child regulatory system to protect children from deleterious consequences of adversity and to support the development of the child's internal stress and emotion

regulatory capacity; as this capability develops, we hypothesize that changes in other domains will also be observable.

In the remainder of this article, we present relevant evidence from our ongoing research. First, we show that rates of atypical HPA axis activity are higher in foster children than in the general population. We then show that neglect and other experiences associated with lack of a caregiver who can serve as stress regulator are associated with alterations in HPA axis activity. Finally, we present evidence suggesting that foster children who show altered HPA axis activity show improvements in neurobehavioral functioning in the context of therapeutic caregiver-based interventions designed to address these underlying deficits.

One clarification is necessary: to date, we have focused on the daytime diurnal activity of the HPA axis, in particular on a blunting of the daily rhythm in cortisol levels in toddlers and preschoolers due to atypically low morning cortisol. Such blunting, which has been suggested to be a consequence of exposure to chronic as opposed to acute stress,¹⁸ is likely the result of downregulation of hypothalamic CRH in response to frequent HPA axis activation¹⁹ and downregulation of pituitary CRH receptors.²⁰ Such blunting has also been observed among young children living in institutional orphanages in Russia and Romania²¹ and in toddlers within a month following their adoption from Russian and Chinese orphanages.²² It is important to acknowledge that this sort of blunting in response to chronic stress does not presuppose that low levels of cortisol will also be observed in the same individuals in response to acute stressors. For example, Kaufman *et al.*²³ observed hyperresponding during a CRH challenge among depressed, abused children who were subject to ongoing emotional maltreatment. Given the ages of the children in our studies and the vulnerability of this population, examination of responses to laboratory stressors has not yet been possible.

CORTISOL LEVELS IN FOSTER INFANTS, TODDLERS, AND PRESCHOOLERS

As is noted above, the work described here occurred within the context of two ongoing longitudinal studies of children in foster care. Research by Fisher and colleagues⁷ included a sample of 117 foster children (FC) who were in the age range of 3 to 5 years and entering a new foster placement at entry into their study and a low-income, same-aged comparison sample of 60 community children (CC). Research by Dozier and colleagues⁶ included a sample of 60 foster infants and toddlers (less than 20 months old when first placed in care and 20–60 months old at entry into the study) and a comparison sample of 110 same-aged, nonmaltreated community children. Both investigators evaluated the impact of therapeutic caregiver-based interventions. The work by Fisher involved dividing the foster children roughly in half at entry into the study, assigning them to foster care intervention (FCI) or regular foster care

(RFC) conditions. Dozier's work involved a second foster care sample ($n = 60$) randomly assigned to one of two intervention groups at intake.

LOW MORNING CORTISOL LEVELS AMONG FOSTER CHILDREN

Analyses of baseline data from both studies have revealed atypical diurnal patterns of cortisol production in foster children. Most notable is the higher proportion of FC with low cortisol values. Bruce *et al.*²⁴ classified children into high (>0.60 $\mu\text{g/dL}$), average (0.30 – 0.60 $\mu\text{g/dL}$), or low (<0.30 $\mu\text{g/dL}$) morning cortisol groups based on upper and lower quartile values for the overall sample. In total, 32% of the FC were classified as having low morning cortisol, whereas 14% of the CC had low morning cortisol. In contrast, 61% of the CC had average morning cortisol, whereas 42% of the FC had average morning cortisol. There was a significant group difference in cortisol classification, Pearson $\chi^2(2, 176) = 8.00, P < 0.05$, with FC being more likely to have low morning cortisol than CC, Pearson $\chi^2(1, 176) = 6.73, P < 0.01$, and CC more likely to have average morning cortisol, Pearson $\chi^2(1, 176) = 5.75, P < 0.05$. The percentage of children classified as high did not differ across the two groups, Pearson $\chi^2(1, 176) = 0.02, ns$.

Very similar results were obtained by Dozier *et al.*,²⁵ who classified children into high, average, and low cortisol groups based on extreme values at morning, afternoon, or bedtime cortisol collections (>2 SD above the CC group M for high; <1 SD below the CC group M for low). Differences between groups were observed, Pearson $\chi^2(159) = 16.06, P < 0.001, \phi = 0.32, P < 0.001$. In total, 38% and 18% of FC showed low and high patterns of cortisol production, respectively, compared with only 14% and 11% of CC.

ASSOCIATIONS BETWEEN EARLY ADVERSITY AND LOW CORTISOL

As is discussed above, one component of the conceptual model is that alterations in HPA axis functioning occur in the context of disruptions in care. These can arise due to a caregiver who is unattentive to the child's needs or to frequent transitions in caregivers. Bruce *et al.*²⁴ used the maltreatment classification system (MCS)²⁶ and child welfare placement records to test these hypotheses. The MCS allows for categorization of incidents of maltreatment according to type and severity. Types of maltreatment defined in the MCS include physical abuse, sexual abuse, failure to provide, lack of supervision, and emotional maltreatment. Consistent with the conceptual model, one-way analyses of variance (ANOVAs) indicated that morning cortisol classification (low, average, or high) was significantly related to the severity of failure to provide, $F(2, 114) = 4.01, P < 0.05$. Children with low morning cortisol levels had significantly more severe failure to provide instances than children with

average or high cortisol levels, $t(84) = 2.15$, $P < 0.05$, and $t(66) = 2.68$, $P < 0.01$. In contrast, there were no main effects for morning cortisol classification on the number of maltreatment incidents, $F(2, 114) = 0.23$, *ns*, the number of different types of maltreatment experienced, $F(2, 114) = 0.03$, *ns*, the mean severity of physical abuse, $F(2, 114) = 0.29$, *ns*, the mean severity of sexual abuse, $F(2, 114) = 0.10$, *ns*, or lack of supervision, $F(2, 114) = 0.04$, *ns*. Also consistent with the conceptual model, separate analyses found that FC who had four or more prior foster placements, $F(2, 173) = 3.44$, $P < 0.05$, and FC first placed in care before the age of 2 years, $F(2, 173) = 3.23$, $P < 0.05$, had significantly lower morning cortisol than other FC or CC. It is notable that, when the maltreatment and placement variables were included in the analysis, failure to provide emerged as the significant predictor of low morning cortisol, whereas the placement variables did not.

EFFECTS OF FOSTER CARE INTERVENTIONS ON PROMOTING RESILIENCY

The interventions that have been the focus of the research described here focus on distinct age groups. Dozier's Attachment and Biobehavioral Catch-Up study is designed for infants and toddlers, whereas Fisher's Multidimensional Treatment Foster Care for Preschoolers (MTFC-P) study is designed for 3- to 5-year-olds. Although the treatment techniques and theoretical frameworks for these approaches differ, the interventions are strongly linked in targeting developmental issues that prevent foster caregivers from becoming a reliable resource for modulating stress and arousal. Dozier's study focuses on improving the caregivers' ability to detect signals of distress from the child—even when these signals are ambiguous or unclear—and to respond sensitively and to follow the child's lead. Fisher's study emphasizes supporting caregivers to respond consistently and contingently to positive and negative behavior. In both cases, an underlying assumption of the conceptual model is that, by supporting the foster parent-child relationship, adverse effects of early stress on the HPA axis and related neural systems will be reversed and that this will in turn increase the potential for improvements in psychosocial functioning.

Evidence from the randomized trials evaluating these interventions provides support for these assertions. Among FCI children with low morning cortisol, there was a significant Condition \times Time interaction for change in morning cortisol levels measured at entry into the study and at 8–9 months postentry, $F(2, 32) = 3.91$, $P < 0.05$. *Post hoc* analyses revealed that the cortisol levels of the FCI, RFC, and CC groups of children did not differ at entry, $F(2, 42) = 0.01$, *ns*. However, by 8–9 months postentry, the FCI and CC groups had significantly higher cortisol levels than the RFC group, $F(2, 32) = 3.92$, $P < 0.05$. Furthermore, among those with low morning cortisol, only FCI had a significant increase in cortisol from entry into the study to 8–9 months postentry.²⁴ In addition to these group differences, parallel effects were observed

in two related domains. Fisher and Kim²⁷ reported improvements in attachment security and decreases in avoidant attachment as (assessed by Dozier's Attachment Diary) for FCI children but not for RFC children. FCI children also had significantly fewer permanent placement failures than RFC following their time in foster care.⁷ Dozier *et al.*⁶ also noted intervention effects on cortisol. In her study, children in regular foster care showed diurnal cortisol patterns (as assessed by morning and bedtime salivary cortisol measures) that were significantly different from the intervention and community comparison groups postintervention. Fewer behavior problems were also observed on a caregiver-report measure for toddlers than for infants in the intervention group postintervention, but no age differences in behavior problems were observed for the regular foster care group.

SUMMARY AND CONCLUSIONS

Taken together, these studies provide evidence that caregiver-based interventions can help normalize HPA axis function, and that such changes co-occur with improved behavioral functioning. This is noteworthy, first, because it represents preliminary validation of a translational model derived largely from rodent studies of early stress. This model, as is discussed above, emphasizes the importance of the caregiver as an extension of the infant's regulatory system whose actions buffer or protect the infant from potentially deleterious effects of external stressors, thus promoting resiliency. In the absence of such caregiving, alterations in HPA axis activity appear likely to occur. Second, these studies show that, by supporting more responsive, competent caregiving in the context of foster care, some of these early adversity effects might be reversible.

In spite of the progress that this research represents, extensive work remains. First, the HPA axis is just one system known to be affected by early stress. Understanding whether similar results are possible in related structures, such as the amygdala and the medial prefrontal cortex, will be critical to the validation of a more comprehensive translational model of early adversity. Second, although changes in behavioral and biological systems have been documented in our studies, little is known about the temporal sequence of change in these domains. It will be important to develop a knowledge base about whether changes in stress regulatory neural systems occur prior to, simultaneously with, or after changes in behavior. Third, this research we have summarized here does not incorporate molecular genetics. Identifying genes that increase or decrease the stress vulnerability of neurobiological systems will increase the precision of our explanatory models. Finally, although we have emphasized children who show disturbances in HPA axis and/or behavioral functioning in foster care, many children do not show such disturbances. Our understanding of resiliency will be further enhanced by studying children who, despite early maltreatment and out-of-home placement, seem to function adequately without additional

support. In sum, this research represents only the initial iteration of a translational process. Additional iterations will be required to clarify associations between the effects of early stress on neurobiology, and subsequent outcomes.

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