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# Early Deprivation Revisited: Contemporary Studies of the Impact on Young Children of Institutional Care

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## Keywords

institutional care, deprivation, early experience, previously institutionalized

## Abstract

There is clear evidence that early deprivation in the form of early institutional care affects children both immediately and long after they are removed from the institution. This article reviews the modern literature on the impact of institutional care from animal models to longitudinal studies in humans. Importantly, we examine the current understanding of neuroendocrine regulation in the context of early deprivation. We discuss the opportunities and limitations of studying the effects of deprivation in previously institutionalized children, review behavioral findings and related neurobiological studies, and address the physical health ramifications of institutional care. Finally, we touch on future directions for both science and intervention.

## Contents





# BRIEF HISTORY OF RESEARCH ON INSTITUTIONAL EFFECTS ON YOUNG CHILDREN

## Overview and Early Focus

Institutionalization in infancy is a well-studied adverse childhood experience. Research on children adopted early in life from institutional care provides evidence of deprivation's detrimental effects on development. Into the early twentieth century, placement into institutional care often ended in death (Lynch 2000, Ransel 2014). As higher standards of nutrition, nursing care, and disease prevention became the norm, mortality rates dropped. In the early era of scientific research on institutionalized children, researchers in the 1930s through the 1960s found that institutional

care resulted in serious developmental delays (Rutter 1972). This work resulted in the closure of most orphanages in industrialized countries in favor of foster care for children needing care.

### Modern Era

Research on the effects of institutional care was renewed with the fall of communism in the early 1990s, when the world learned of the many institutionalized children in Russia and Eastern Europe. Current studies of previously institutionalized (PI) children focus on the initial wave of Romanian children adopted into families and then the thousands of children arriving into high-income countries from institutions in Eastern Europe, Russia, East Asia, Central/South America, South Asia, and Africa. These PI adoptees typically experience institutional care as infants that ends with adoption into well-resourced families mostly before age 3. The modern era of research on institutionalization has addressed not only the impact of early deprivation but also the processes that underlie PI children's developmental trajectories. The heterogeneous, often co-occurring aspects of deprivation can be understood on three levels: (*a*) the failure to address basic needs such as adequate health care and nutrition; (*b*) the lack of developmentally appropriate stimulation that supports sensorimotor, cognitive, linguistic, and social development; and (*c*) the lack of stable, consistent relationships with adults in which attachment relationships can form (Gunnar 2001). Across all levels, deprivation acts as a lack of experience-expectant inputs for a young child.

In this article, we describe how modern studies of the institutional environment are conceptualized, how confounds are addressed, and how the work is aligned with animal models. We give a brief overview of behavioral findings and review research on the associations between behavioral and neurobiological impacts. We then address the role of neuroendocrine regulation, followed by an overview of physical health. Finally, we touch on the future directions for research.

## STUDIES OF THE INSTITUTIONAL ENVIRONMENT

### Description and Conceptualization

Though institutional care varies considerably across different countries and time periods, commonalities exist that reflect the demands of affordable care for a number of children with a limited number of adults. This often leads to a sort of assembly-line care, where adults move efficiently through a room of children as they engage in one caregiving task (e.g., diapering) followed by the next. The amount of individualized, face-to-face interaction with adults can be very limited (Smyke et al. 2007). While efficiency is enhanced by grouping children by age and caregiving needs, this further limits the opportunity to form stable attachments as children change rooms and caregivers as they grow. The overall effect has been described as benign neglect (van IJzendoorn et al. 2011). While children's basic physical needs are often met in those situations, children's needs for linguistic, sensory, and social stimulation often are not. Further, although the food provided may be adequate in calories and nutrients, it is not clear that children actually digest a sufficient diet. Group rearing increases the risk of disease, intestinal parasites, and stress, all of which can hamper the intestine's ability to absorb nutrients (Johnson & Gunnar 2011). This leads to many children suffering micronutrient deficiencies (Fuglestad et al. 2008). However, deprivation is not inevitable. Institutions can be reorganized to provide more family-like care (McCall et al. 2019). Generally, such care improvements are reflected in better physical and cognitive development (Woodhouse et al. 2018). However, even in model institutions with family-like groups, high staff-to-child ratios, and cognitive stimulation, children may still show psychosocial effects of institutional care, likely due to the lack of stable attachment figures (Tizard & Rees 1975).

## Confounds and Solutions

Children do not end up in orphanages by chance: The factors that led them into institutions may contribute to the outcomes observed. Many are born into poor families who cannot care for them. They are more likely to be the products of stressed pregnancies and may suffer from the impact of prenatal stress (Gunnar & Davis 2013). This is consistent with the evidence of low birth weight among children placed in institutional care (Dobrova-Krol et al. 2008). In some countries, disabled or HIV-infected children are institutionalized out of the belief that the institution has more resources for their care (Dobrova-Krol et al. 2010). These factors and others may help explain some of the variance in the cognitive, emotional, and physical outcomes observed among institutionalized children. The Bucharest Early Intervention Project (BEIP) attempted to control for many of these factors by assessing children early and then randomly assigning some to study-designed foster care while the others remained in care-as-usual (i.e., the institution and later a variety of care conditions) (Zeanah et al. 2003). However, this is the only random assignment study of institutional care. Because random assignment is not feasible in most instances, our understanding of the causal role of deprivation is supported by studies in animals, where causality can be better inferred.

## Animal Models

Beginning with studies of surrogate-reared monkeys (Harlow et al. 1971), animal studies have confirmed that psychosocial deprivation has major socioemotional consequences for infant primates. When reared only on a cloth surrogate, monkeys are profoundly disturbed. For this reason, after a week or so of nursery rearing, surrogate-reared infants are brought together with other infants daily to play and socialize. This does help to normalize their development, although considerable effects are still found (Champoux et al. 1991). On the surface, surrogate-peer rearing seems like institutional rearing. The difference, however, is that baby monkeys are motorically competent from birth and do play with one another. Infant humans cannot self-locomote for months and do not interact much with other infants. Thus, the surrogate-peer rearing paradigm is probably more enriched than most institutional rearing contexts. Regardless, many of the outcomes of surrogate-peer rearing mimic findings from PI children, including heightened anxiety, problems regulating emotional behavior, and decreased social competence (Suomi 1997).

One rodent paradigm approximates institutional rearing: the artificial rearing or "pup-in-the-cup" paradigm (Thomas et al. 1998). In this model, infant rats are placed in a cup that sits in a warm water bath. The pup is fed through a cannula into the gut or cheek, and its anogenital region is wiped several times a day to stimulate micturition (Lomanowska & Melo 2016). The consequences of this rearing are similar to what has been observed in PI children: specifically, problems in executive functions, heightened anxiety, impairments in reward processing, and blunted reactivity of the HPA axis (Lomanowska & Melo 2016). In sum, animal models that mimic elements of typical care of infants in institutions clearly demonstrate that early deprivation of psychosocial care has long-term impacts on cognitive and socioemotional functioning and that the unavoidable confounds in studies of human PI children are not likely to be the reason for many of the observed PI outcomes.

# BRIEF OVERVIEW OF BEHAVIORAL FINDINGS: RECAPITULATION AND EXTENSION OF EARLY WORK

There is tremendous heterogeneity in behavioral functioning following early institutional deprivation. In the English and Romanian Adoptees (ERA) study, which involved severe global

deprivation, one-fifth of the individuals adopted late (>6 months of age) did not exhibit problems in any of the domains studied from childhood to young adulthood (Sonuga-Barke et al. 2017). On the other hand, many PI children displayed problems in two or more areas: The likelihood of problems increased with the degree and duration of early deprivation (van IJzendoorn et al. 2011). The ERA researchers noted a suite of problems that they labeled deprivation-specific disorders, including quasi-autism, disinhibited social engagement disorder, impaired cognition, severe cognitive impairment, and attention-deficit/hyperactivity disorder (ADHD). Recent work suggests that these and other outcomes displayed may reflect a more general vulnerability to psychopathology imposed by early deprivation (Wade et al. 2018).

## Disinhibited Social Engagement Disorder

Much of the new research on the impact of institutional deprivation affirms the early work's interpretations, with one major exception. From the earlier work, it was strongly expected that children placed in families after age 2 would be unable to form attachments (Goldfarb 1945). In the initial work on Romanian PI children, many were classified with reactive attachment disorder of the disinhibited type (O'Connor et al. 2003). Interpreted as the result of not having formed an attachment to the adoptive parent, the behavioral criterion was indiscriminate friendliness or the tendency of children to approach and treat strangers as they would a familiar adult. In children raised with their parents since birth, this behavior likely indicates an attachment disorder. PI children, however, often met criteria for disinhibited attachment disorder and still acted securely attached with their foster or adoptive parents (Zeanah & Gleason 2015). Disinhibited attachment disorder is now termed disinhibited social engagement disorder (DSED) (Zeanah & Gleason 2015). PI children classified with quasi-autism or ADHD are also likely to be classified with DSED (Kreppner et al. 2010); thus, concerns about this behavioral problem make sense. Our research group divided social engagement behaviors into distal and physical contact categories. Increasing rates of physical contact with strangers over the first years after adoption better predicted developing DSED compared to distal engagement behaviors (Lawler et al. 2016). Duration of institutional care and placement instability were the best predictors of high levels of DSED behaviors (Guyon-Harris et al. 2018, Lawler et al. 2016). Though the neurobiological basis underlying DSED is unknown, DSED is correlated with executive function deficits, and this implicates prefrontal cortex circuitry (Bruce et al. 2009). Nonetheless, the adult follow-up in the ERA study found that high levels of DSED behaviors were not associated with problems in adjustment or other types of psychopathology after excluding participants who were comorbid for quasi-autism and ADHD. This led researchers to conclude that DSED is relatively benign (Kennedy et al. 2017).

## Attachment

It is now clear that children quickly form attachments even if adopted after age 2. Our data show that one to three months after entering their adoptive families, ~38% of children adopted between 1.5 and 3 years of age from institutions have fully formed an attachment to the parent, and 90% have done so seven to nine months after adoption (Carlson et al. 2014). While 23% of children exhibit a disordered/disorganized attachment pattern seven to nine months after entering the family, 69% appear securely attached. This is the same percentage of secure attachment seen in the BEIP study for children randomly assigned to foster care (Smyke et al. 2010). Forming a secure attachment appears to be an important pathway to recovery for PI children (Fox et al. 2017). Supporting the development of a secure attachment relationship is important for PI children (Yarger et al. 2019).

## Peer Relationships

Friendships and peer acceptance are critical facets of well-being (Hartup & Stevens 1997). Many PI children struggle with peer relations (Sonuga-Barke et al. 2010). Poor peer relations likely play a role in the increase in depressive symptoms in early adolescence seen in PI youth (Pitula et al. 2014). Most data on peer relations among PI children come from parent and teacher reports. To our knowledge, there is only one study that observed PI children interacting with familiar peers to examine peer functioning (Pitula et al. 2019). The study was conducted in kindergarten classrooms, and, consistent with parent and teacher reports, PI children had poorer relations with other children. Several studies investigated social behavior by observing PI children interact with an unfamiliar peer (Almas et al. 2015, DePasquale & Gunnar 2019). PI children in middle childhood do not behave differently than comparison children when meeting and playing games with a child they do not know. Nor is there much evidence that the unfamiliar peer responds differently to them as compared to never-institutionalized children. Thus, peer problems, including rejection, seem to require familiarity.

We do not yet understand what may lead to less peer acceptance as children get to know PI children. PI children tend to trust other children less and will withdraw trust more quickly if they experience an untrustworthy act by another child (Pitula et al. 2017). According to parent reports, aggression with peers does not seem to drive less peer acceptance: Parents report that PI youth are more likely to be victims of aggression (Pitula et al. 2014). Indiscriminate friendliness in PI children is associated with poorer peer relations in early adolescence (Sonuga-Barke et al. 2010): These behaviors involve failure to recognize or respond to social boundaries and social norms, which may be off-putting to other children. Impairments in social cognition may also contribute to peer problems (Colvert et al. 2008). Finally, ADHD symptoms predict peer problems in PI kindergarteners as they do in other children (Pitula et al. 2019). Therefore, peer problems may not be a direct outgrowth of early institutional care but may arise because of other neurocognitive deficits seen among PI children.

## Attention Regulation, Executive Functions, and Theory of Mind

Infants reared in institutions tend to lag behind in mental development and language. However, once removed from institutional care, IQ rebounds fairly rapidly to normal ranges (Nelson et al. 2007). Even those most impaired continue to improve in IQ into young adulthood (Sonuga-Barke et al. 2017). While IQ appears remarkably robust, more fluid aspects of intellectual functioning appear highly sensitive to the effects of early institutional deprivation. Some of the most consistent findings on the effects of early institutional deprivation are impairments in attention regulation or executive functioning (EF) more broadly (Pollak et al. 2010, Roy et al. 2004). EF deficits are apparent at adoption or soon thereafter (Hostinar et al. 2012) and persist for years postadoption (Merz et al. 2013, Wade et al. 2019). Though the deficits do increase with age at adoption, they do not seem to require prolonged institutional experiences, as children adopted as young as 7 months of age show them (Kumsta et al. 2010). EF depends on prefrontal-striatal and anterior cingulate circuitry (Burgess & Stuss 2017), which, as will be discussed, is consistent with imaging data showing significant structural and functional differences in PI youth.

Given deficits in EF, deficits in theory of mind (ToM) and perspective taking are unsurprising. These mental capacities depend, to some extent, on working memory and other EF skills (Devine & Hughes 2014). ToM impairment is consistent with increases in autism diagnoses among PI children (Rutter & Team 1999) but is not seen exclusively in PI children diagnosed with autism (Colvert et al. 2008). For example, among 6- and 7-year-olds adopted at 18 months of age, controlling for language ability, nearly half scored at chance on a standard false-belief task

(Tarullo et al. 2007). PI children scored lower than children reared in families and lower than children adopted internationally from foster care. That ToM deficits were not seen in the children adopted from foster care is consistent with the argument that one-on-one joint attention experiences are critical for ToM development (Charman et al. 2001).

### Psychopathology

The majority of studies of psychopathology in PI children were conducted before it became more common to use bifactor hierarchical modeling to examine a general psychopathology factor (P) along with internalizing and externalizing dimensions (Wade et al. 2018). The bifactor model is useful, as there is a real question about whether the problems common in PI children are fully captured by the standard diagnostic categories (Juffer & van Ijzendoorn 2005). Interestingly, thought problems are elevated in PI children, especially in those adopted after age 2 (Gunnar & van Dulmen 2007), and these problems contribute heavily to the P factor (Caspi et al. 2014).

Regardless of the statistical model, PI children adopted after 6 months of age exhibit elevated pathology symptoms. The most common problems are ADHD and DSED—not anxiety, depression, or conduct problems (Sonuga-Barke et al. 2017). When the bifactor model was used in the BEIP study, youth placed in BEIP foster care and those who remained in care-as-usual had elevated levels of P, while by 16 years, the foster care group did not differ on internalizing or externalizing from the never-institutionalized youth (Wade et al. 2018). PI children's trajectories of problems are also noteworthy. Internalizing and externalizing symptoms tend to increase with age (Gunnar & van Dulmen 2007, Sonuga-Barke et al. 2017), although this is not observed using the bifactor model (Wade et al. 2018). We have speculated that increases in affective pathology in adolescent PI youth may reflect the stress of poor peer relations at a time in life when peer acceptance is increasingly important (Koss & Gunnar 2018). In the new wave of research on the impact of early institutional deprivation, only the ERA study has adult participants. Their adult follow-up found that close to 50% of the individuals adopted after 6 months of age were above the threshold for emotional disorders (Sonuga-Barke et al. 2017). It is unclear why they observed such an increase from adolescence to young adulthood. It might reflect a general vulnerability to mental problems (i.e., P) combined with the fact that many PI young adults in the ERA study were unemployed, had low educational attainment, and were struggling to complete the developmental tasks of early adulthood.

## NEUROBIOLOGICAL EFFECTS

### Neuroimaging Studies

In recent decades, neuroimaging studies have uncovered both global and specific neurological impacts of institutional deprivation. Magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI) analyses find that PI children exhibit lower total brain volume, gray matter volume, and white matter volume in addition to smaller head circumferences (Eluvathingal et al. 2006, Hodel et al. 2015, Mehta et al. 2009, Sheridan et al. 2012). Some evidence suggests that removing children from institutional care has structural effects on brain development. Specifically, at 9 years of age, although foster care and care-as-usual groups in the BEIP had smaller total cortical gray matter volumes, those randomized to foster care had larger white matter volumes than care-as-usual children (Bick & Nelson 2016). These studies support the idea that early deprivation acts as a global insult to neural development and that interventions improve some outcomes.

Two brain areas are of interest due to their sensitivity to stress: the amygdala and hippocampus. Several studies have found that longer periods of early deprivation are associated with greater amygdala volumes (Mehta et al. 2009, Tottenham et al. 2010). However, in a large structural MRI

sample of 12–14-year-old PI children, larger amygdala volumes were not observed. The study did find that hippocampal volumes were negatively associated with duration of institutional care (Hodel et al. 2015; see also Mehta et al. 2009, Sheridan et al. 2012, Tottenham et al. 2010). Thus, the literature on early deprivation's impact on structural hippocampal and amygdala development is currently mixed. This could be due to a number of factors, including age differences at assessment and differing comparison group characteristics across studies.

Prefrontal cortex structure and connectivity are also altered following institutional rearing. PI children exhibit reduced cortical thickness in regions of the prefrontal cortex (McLaughlin et al. 2014). DTI studies found that PI children show disrupted organization of prefrontal white matter and more diffuse frontal-striatal projections between middle childhood and late adolescence (Behen et al. 2009, Eluvathingal et al. 2006, Govindan et al. 2010, Hanson et al. 2013). PI children exhibit reduced fractional anisotropy in the uncinate fasciculus, a white matter tract that acts as a major communication pathway between limbic and frontal lobe regions (Olson et al. 2015). As these regions are involved in higher cognitive and emotional functions, this altered connectivity may underlie deficits and/or delays in inhibitory control and emotion regulation.

Many imaging studies are cross-sectional and compare PI children with children who have never been exposed to deprivation. Due to the limitations and challenges of studying PI children, the studies of the neurobiological effects of institutionalization do not afford us the opportunity to examine neurobiological structure or functioning in the same children during their time in institutional care as compared to their time removed from institutional care. Additionally, studies have been mainly conducted in children and adolescents, leaving questions about these effects' persistence into adulthood. The neurobiological effects reviewed briefly here are particularly striking as many of the PI children studied were imaged many years after being removed from institutional care and placed in highly resourced, supportive families. Differences in brain structure and function suggest that early deprivation—even when limited to the first few years of life—appears to have lasting consequences for brain development.

## Attention and Externalizing

Neuroimaging studies on PI children have sought to understand the neurobiological connections between early deprivation and its effects on attention and externalizing. Much of this work has involved electroencephalogram (EEG) and event-related potentials (ERPs). With development, the EEG shifts to more high-frequency activity. Institutionalized children and those recently placed in families show an immature EEG pattern (Marshall et al. 2004, Tarullo et al. 2011), as do children with ADHD. Indeed, in the BEIP this immature pattern partially mediated the effects of institutionalization on ADHD symptoms (McLaughlin et al. 2010). In internationally adopted children, lower EEG power soon after adoption predicted indiscriminate friendliness several years later (Tarullo et al. 2011). In the BEIP study, foster placement before age 2, but not afterward, resulted in normalized EEG power by age 8 (Vanderwert et al. 2010). By 12 years of age, both early removal and stability in placement were required to predict EEG power, which likely reflects the development and maintenance of white matter (Vanderwert et al. 2016).

Structural MRI also reveals connections between institutionalization, attention, and externalizing. Children from the BEIP study were scanned at 8–10 years of age to compare structural changes with ADHD symptoms (McLaughlin et al. 2014). Relative to community controls, PI children exhibited widespread reductions in cortical thickness across prefrontal, parietal, and temporal regions, though no group differences were found in the volume of subcortical structures. Cortical thickness in the lateral orbitofrontal cortex, insula, inferior parietal cortex, precuneus, superior temporal cortex, and lingual gyrus mediated the association of institutionalization with

inattention and impulsivity. Furthermore, thickness in the supramarginal gyrus mediated the association with inattention, and thickness in the fusiform gyrus mediated the association with impulsivity (McLaughlin et al. 2014).

DTI in a small sample of 10-year-old PI children adopted into the United States showed more diffuse fronto-striatal connectivity compared to community controls, and externalizing behavior was a significant predictor of diffuse fronto-striatal connectivity (Behen et al. 2009). Resting-state fMRI data showed increased positive coupling between the ventral striatum and anterior regions of the medial prefrontal cortex (mPFC) in PI youth compared to youth raised in their families from birth. This increased positive coupling was associated with parent reports of social problems. Additional analyses revealed that the ventral striatal-mPFC connectivity mediated group differences in social problems, especially for older children, suggesting that this connectivity may play a role in social behaviors as PI children age (Fareri et al. 2017).



## Fearfulness and Internalizing

The idea that early life stress shifts neural processing towards threat sensitivity to support survival in hostile environments has informed a growing body of neurobiological research on PI youth. The amygdala and related limbic systems circuits are of particular interest. A study found that adopted PI children exhibited larger amygdala volumes, poorer emotion regulation in an emotional Go/No-Go task, and increased anxiety in comparison to US-raised comparison children (Tottenham et al. 2010). The group differences in amygdala volume were not driven by anxiety disorders (Tottenham et al. 2010). It has also been argued that deprived institutional care could accelerate the development of mPFC connections with the amygdala because children must prematurely regulate themselves as no one else is there to help. One study found that PI children did demonstrate relatively mature connections (negative amygdala-mPFC coupling) not typically seen until adolescence (Gee et al. 2013). Cortisol levels mediated this connectivity pattern, suggesting that stress plays a role in shaping the amygdala-mPFC circuity. Individually, the negative amygdala-mPFC coupling in PI children was associated with reduced anxiety, though as a group PI children still reported more anxiety symptoms than controls.

Functional MRI studies have found heightened reactivity to fear faces (Maheu et al. 2010). In one study, PI children generally exhibited greater amygdala activation to fear distractor faces in an emotional Go/No-Go task (Tottenham et al. 2011). A recent study used a visual search task to examine how rapidly fear faces could be located in a field of neutral faces (Silvers et al. 2017). Vigilant children in both PI and comparison groups were faster. However, only among the PI group did amygdala reactivity predict heightened anxiety symptoms (Silvers et al. 2016). There is also some evidence that neurological differences between PI and comparison youth may be protective. Thus, PI children showed an atypically mature pattern of hippocampal–prefrontal cortex connectivity relative to controls, but PI children exhibiting this pattern showed fewer anxiety symptoms two years later (Silvers et al. 2016). On the other hand, some prematurely advanced patterns of connectivity may create vulnerabilities. Children show larger amygdala responses to their mothers' faces than a stranger's face, while adolescents do not. Many PI children show the advanced pattern (no discrimination), but those who show the more immature pattern (larger amygdala response to mother than others) have better relations with their parents and less anxiety over time (Callaghan et al. 2019b). In all, these studies point to promising mechanisms and individual differences in the neurobiological correlates to symptoms of fearfulness and internalizing in PI children.

## Executive Functioning

Many studies of PI children show impairments in EF. Go/No-Go and Flanker paradigms have been used with ERPs to examine cognitive inhibitory control, one aspect of EF. Early

deprivation impairs performance on these tasks. In the BEIP assessment of 8-year-old children (McDermott et al. 2012), never-institutionalized children showed larger P300 amplitudes during No-Go trials compared to the foster care and institutionalized groups, suggesting that the never-institutionalized children had better inhibitory control. Shorter N2 latency was associated with faster reaction times in the foster care and the never-institutionalized groups, suggesting more efficient attention allocation. The foster care children showed lower processing speed compared to the never-institutionalized children. Foster care children showed differences in reactivity between correct and error trials compared to the institutionalized group. For foster care and institutionalized children, a larger P300 amplitude on Go trials was related to higher accuracy (McDermott et al. 2012). In a study of older 9–11-year-old PI children, PI youth had problems sustaining attention, making more errors in Go trials (Loman et al. 2013), similar to the finding by McDermott and colleagues (2012), and made more errors on both congruent and incongruent Flanker trials. Consistent with the behavioral data (Loman et al. 2013), PI youth exhibited a smaller N2 (attention recruitment) and error-related negativity (ERN) than comparison youth.

### Reward Sensitivity

In animal models, early deprivation increases the risk of substance abuse and anhedonia through impairing reward circuitry (Delavari et al. 2016). In the ERA studies, PI youth showed an absence of ventral striatal activity and no differences in activation between degrees of reward at age 16. The authors suggest that this is either a loss of reward anticipation or a lack of sensitivity to differences in reward value, which may lead to compensatory reward seeking (Mehta et al. 2010). Similarly, PI youth adopted into families in the United States showed nucleus accumbens hypoactivation in adolescence, which was associated with reports of depressive symptoms (Goff et al. 2013). Impairment in reward circuitry may be an important mechanism linking early adversity and later psychopathology (McLaughlin et al. 2019).

## NEUROENDOCRINE REGULATION

### Deprivation and the HPA Axis

The study of the HPA axis in institutional deprivation grew out of animal models showing that the quality of early care sets the tone and responsiveness of the axis and mediates some neurobehavioral outcomes (Sanchez et al. 2001). (For reviews of the HPA axis and its development, see Doom & Gunnar 2013, Xiong & Zhang 2013.)

Although a cursory reading of the animal literature might lead one to expect hyperreactivity of the axis, that is not actually what the animal literature says. As discussed earlier, the animal models most comparable to the care of infants and young children in institutions are deprivation paradigms that maintain adequate nutrition, such as nursery rearing of monkey infants and artificial rearing in rats. The impact of both paradigms is a hyporeactive HPA axis. Hundreds of rhesus infants reared under various conditions, including nursery rearing without maternal care, were examined for baseline levels of cortisol, responses to a psychosocial stressor, pharmacological stimulation, and pharmacological suppression (Capitanio et al. 2006). In all instances, those reared in the nursery had low levels of cortisol and failed to mount a vigorous cortisol response to stimulation or stressors. Similarly, blunted HPA axis activity has been observed across a number of studies of artificially reared rats (Lomanowska & Melo 2016).

The first examinations of HPA axis activity in institutionalized children focused on the diurnal rhythm, as it seemed unethical to conduct a stress test on this vulnerable population. In 46

institutionalized toddlers in Romania, not one showed a normal diurnal rhythm (Carlson & Earls 1997). This was not replicated in a smaller group of slightly older children examined in institutions in Ukraine (Dobrova-Krol et al. 2008), where chronically stunted children had lower cortisol by late afternoon than did family-reared children, while those who were temporarily growth stunted with later catch-up growth showed higher cortisol levels. Diurnal cortisol studies of PI children following adoption have yielded a mixed pattern. In one study, a flatter rhythm due to higher evening cortisol was noted (Gunnar et al. 2001). In a later study, children who were more stunted at adoption later exhibited elevated early morning levels (Kertes et al. 2008). In 1.5- to 3-year-old children transitioning into families from institutional care, a flatter slope for diurnal cortisol was observed two months postadoption and remained for at least the first two years postadoption (Koss et al. 2014). Individual differences in diurnal activity were associated with poorer-quality psychosocial care prior to adoption (Koss et al. 2014). Finally, in a study of PI children and adolescents, the PI children exhibited a flatter diurnal slope compared to family-reared children (Flannery et al. 2017).

There may be a sensitive period for altering the diurnal cortisol pattern. In a recent study, children and adolescents provided saliva samples on three days so that both the cortisol awakening response and the diurnal slope could be examined. Earlier-adopted children (adopted at <16 months of age) did not differ from family-reared children, while later-adopted children (adopted at 17–60 months of age) exhibited a blunted cortisol awakening response (Leneman et al. 2018). However, any early sensitive period may interact with the degree of deprivation, as individuals adopted as infants from Romania into the United Kingdom after experiencing intense deprivation still showed severely blunted morning awakening responses as young adults, even if adopted before 12 months of age (Kumsta et al. 2017).

While the diurnal data are somewhat uneven, studies examining cortisol responses to stressors are more consistent. Over a long testing session with many challenges, family-reared toddlers exhibited elevations in cortisol, and this increase was not noted among toddlers recently adopted from institutional care (Koss et al. 2016). Over repeated testing sessions spaced about six months apart, the family-reared children habituated to the testing sessions, while no change was noted for the PI children (Koss et al. 2016). In middle childhood, children in the BEIP study underwent a psychosocial stress test involving peer evaluation and a version of the Trier Social Stress Test for Children (TSST-C) (McLaughlin et al. 2015). Cortisol and various measures of the autonomic activity were blunted in the children placed in foster care and children who remained institutionalized relative to the family-reared children. Importantly, children placed in foster care before 2 years of age showed normative cortisol increases and parasympathetic responses. Our research group has also found that cortisol responses to the TSST-C are quite blunted for PI children relative to family-reared children in middle childhood (DePasquale et al. 2019).

## HPA Axis and Behavior

Do these altered patterns of HPA axis activity predict anything about behavioral functioning? We found that PI children who showed more hypoactivity of the axis in the first two years postadoption had kindergarten teachers who described them as more externalizing and with more problems of attention regulation (Koss et al. 2016). These findings were expected, because low HPA axis activity has been found in studies of family-reared children to be modestly associated with more externalizing behavior problems in children (Alink et al. 2008). To our knowledge, the only other mediational analysis was conducted by Gee and colleagues (2013), who found that children and adolescents with greater cortisol alterations associated with early institutional care showed less mature connectivity of the mPFC and amygdala, suggesting increased problems in regulating

emotionality. Thus, one of the major weaknesses in this area is the failure to go beyond measuring associations between institutional care and HPA axis activity to determining whether these associations statistically mediate any of the behavioral, psychological, or physical health sequelae of early institutional care.

## Social Buffering, Cortisol, and Oxytocin

The HPA axis is highly sensitive to social relationships. In secure attachment relationships, the presence of the attachment figure reduces or completely blocks elevations in cortisol (Gunnar 2017). The power of relationships to buffer the HPA axis is seen across many mammalian species (Hennessy et al. 2009). In humans, puberty appears to influence the extent to which parents are able to buffer the child's cortisol response to social evaluative stressors. Thus, children of 9–10 years of age show elevations in cortisol to the TSST-C unless they prepare for the task with their mothers, in which case they generally show little to no increase. However, 15- and 16-year-olds show an increase in cortisol to the TSST-C regardless of whether they prepared with their mothers or not (Hostinar et al. 2015b). When a restricted age range is used (i.e., 11–14 years) and children are selected to reduce the association between age and pubertal stage, the shift in the power of parents to buffer the HPA axis tracks pubertal stage more than age (Doom et al. 2015).

What is less clear is whether parents are capable of buffering the HPA axis for children adopted from institutional care. In a study of preschoolers, overnight urine samples were collected in the morning when the children woke up both after days in which researchers had come to the home and the child had played interactive games with either a stranger or their mother and after days in which researchers had not showed up (Wismer Fries et al. 2008). Overnight urinary cortisol was lower for family-reared children after they had played interactive games with their mothers, reflecting the regulatory power of parent-child interaction. For PI children, there was no difference in overnight urinary cortisol when they had played with their mother versus a stranger, even though they had been in the adoptive home for at least three years. Among 9- and 10-year-old PI children adopted after 18 months of age, preparing for the TSST-C with their mothers did not provide any buffering of the HPA axis. Children adopted before 18 months of age showed a buffering effect that was similar to that of the family-reared children (Hostinar et al. 2015a).

The mechanisms that allow for social buffering of the HPA axis are not well understood. In infant rats, the mother's presence modulates norepinephrine inputs to the hypothalamic neurons that regulate the axis (Hostinar et al. 2014). In adults, looking at a picture of a social support person reduces activity in brain regions that process pain and activates regions associated with safety for individuals anticipating shock (Eisenberger et al. 2011). Relationships also regulate the production of oxytocin, a neuropeptide that supports affiliation when acting in the brain and serves to increase relaxation and counteract HPA axis activity when acting in the body's periphery (Heinrichs et al. 2003). Thus, oxytocin may also play a role in stress buffering. Assessed in middle childhood, a child's physical proximity with their mother or just a phone call with her increases oxytocin production and speeds the recovery of baseline levels of cortisol following a stressor (Seltzer et al. 2010). Impairments in social buffering among PI children may reflect impairments in the social regulation of oxytocin. In the same study in which children played interactive games with mother or stranger, the researchers also examined overnight urinary oxytocin levels (Fries et al. 2005). Unlike children reared in their birth families, PI children did not exhibit increases in oxytocin when playing with their mothers. It is clear that we need to understand the mechanisms of social stress buffering to better understand how experiences like institutional rearing may impair the individual's ability to use relationships to regulate stress biology.

### Pubertal Stress Recalibration

There appears to be a sensitive period early in life when experiences shape the regulation of the HPA axis. At least for children reared in institutions, the consequence of remaining in institutional care throughout this sensitive period appears to be an axis that is hyporeactive. Does this early period set the HPA response for life? Two theories have guided much of the research on adversity and the HPA axis. The most dominant one is the allostatic load model. This model would predict that an individual with a history of adverse care in infancy and with cumulative adverse exposures over time would progress more rapidly towards elevated indices of allostatic load, which can include both hyper- and hypofunctioning of the HPA axis (Danese & McEwen 2012). A more recently proposed, alternative model argues that we adapt and calibrate our system to the challenges of our environment. Using life history theory, this alternative model expects individuals to recalibrate at different life history stages, including infancy, the juvenile period, and adolescence (Del Giudice et al. 2011). Because children adopted after infancy seem to retain altered HPA axis activity for many years, it is unclear how readily they recalibrate. Nonetheless, puberty does offer an interesting possibility for recalibration.

There is animal evidence that the peripubertal period may be one of heightened plasticity for the HPA axis, such that adverse experiences during that period will have longer-lasting consequences than the same experiences occurring in young adulthood (Romeo 2010). Importantly, plasticity cuts both ways: A system that in infancy was set to withstand harsh conditions might, with pubertal development, open to resample the environment and reset to match more benign current circumstances. The hypothesized trajectories of recalibration are outlined in **Figure 1**. The first paper to suggest this possibility was based on a cross-sectional study of children and adolescents in which the authors reported a blunted cortisol awakening response for the PI children relative to family-reared children but not for adolescents (Quevedo et al. 2012). Similarly, another study analyzed the diurnal slope from wake to bedtime in a larger sample of PI versus comparison children and adolescents. The slope did not vary as a function of age for the comparison children but increased from a flatter to a more marked slope with age in the PI group (Flannery et al. 2017). In follow-up analyses, the researchers found that both earlier age at adoption and pubertal stage predicted the improvement in diurnal slope. We have recently examined the cortisol response to the TSST-C as a function of pubertal stage and age. In a cross-sectional analysis of data obtained during the initial year of testing (DePasquale et al. 2019) and in a subsequent longitudinal analysis of three assessments over a two-year span (M.R. Gunnar, C.E. DePasquale, B.M. Reid & B. Donzella, manuscript in review), we found a normalization of the cortisol response to the TSST-C with increasing pubertal stage. It remains to be seen whether significant adversity during the period of pubertal recalibration will result in no recalibration for PI youth. It also remains to be determined whether this recalibration extends to other stress-mediating systems.

## PHYSICAL HEALTH AND GROWTH

### Growth Faltering, Recovery, and Pubertal Timing

Early life institutional care typically results in significant growth delays in height, weight, and head circumference (Johnson 2000, Johnson & Gunnar 2011). Many studies document catch-up growth in weight and height soon after children are placed in families. Most children are typically within normal anthropometric ranges within a year or two of adoption. Later age at arrival results in incomplete catch-up in growth. Head circumference catch-up growth is slower and tends to be less complete (Van Ijzendoorn et al. 2007). These findings appear to hold in later childhood and adolescence: At 7–14 years of age, PI youth remain shorter than comparison youth but are still within normal height ranges (Reid et al. 2017).

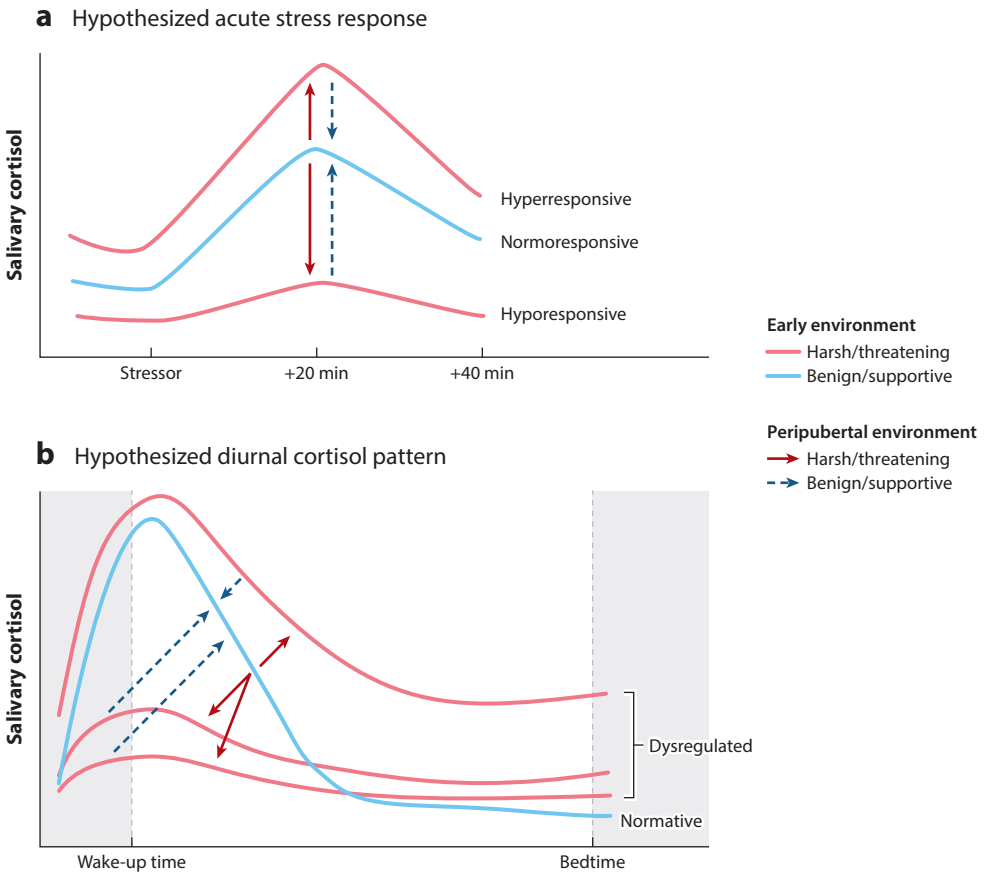


**Figure 1**

Hypothesized pubertal stress recalibration pattern in human youth. (*a*) In the hypothesized acute stress response recalibration, deprivation-exposed individuals move from a hyporesponsive stress response to a normative acute stress response as they move through puberty if the current conditions are supportive and nonthreatening. Note, however, that there remains a risk that the individual will recalibrate and become hyperresponsive or become or remain hyporesponsive to an acute stressor if the conditions during the peripubertal period are harsh/threatening. (*b*) Similarly, in the hypothesized diurnal cortisol recalibration pattern, individuals exposed to a harsh/threatening early environment move from a dysregulated diurnal cortisol pattern to a normative diurnal cortisol pattern if peripubertal conditions are benign/supportive. If an individual experiences a benign/supportive early environment, they may be at risk of moving to a dysregulated diurnal cortisol pattern if peripubertal conditions are harsh/threatening.

PI children with rapid catch-up growth may be at a higher risk for obesity, as the mechanisms of catch-up growth may promote body fat accumulation. In the BEIP study, children randomized to foster care showed greater rates of growth in height, weight, and body mass index (BMI) from 3 to 12 years of age compared to the care-as-usual group (Johnson et al. 2018). Disruptions in placement moderated this relationship: More disruptions were associated with decreased growth rates in height and weight (Johnson et al. 2018). The BEIP study found four different BMI trajectories through age 16: average-stable, low-stable, elevated, and accelerated (Tang et al. 2018). Children randomized to foster care were more likely to be in the accelerated BMI trajectory, especially children placed in foster care at younger ages. In contrast, a study of PI youth (aged

7–14 years) adopted into the United States found that PI youth had lower BMI-for-age than comparison youth years after adoption and had less body fat (measured by air displacement plethysmography), regardless of how height stunted they were at adoption (Reid et al. 2017). Differences between these two studies could be due to differences in the education, incomes, and attitudes towards diet and exercise of the foster parents in the BEIP study and the adoptive parents in the study by Reid et al. (2018). In a similar group of US-adopted PI youth, dual-energy X-ray absorptiometry scans showed that despite having normal to low BMIs, PI youth had lower total lean mass, lower gynoid lean mass, and a higher proportion of trunk tissue fat when compared to BMI-matched controls (Reid et al. 2018). Indeed, early institutional rearing may influence where fat is stored, and this may increase the risk of later cardiovascular problems even if the individual is not overweight or obese.

The evidence is mixed on pubertal timing. The rate of precocious puberty is 1 in 5,000 to 10,000 children, with an increased incidence (0.8–1.8%) in internationally adopted children, especially if they are growth stunted at adoption and experience rapid catch-up growth (Mul et al. 2002, Proos 2009). In children attending clinics for precocious puberty in Sweden, international adoption after age 2 was associated with an increased risk of precocious puberty (Teilmann et al. 2006). Recent studies question the ubiquity of an advance in pubertal timing for PI youth. A study of girls adopted from China into North America found no difference in the age of menarche relative to comparison girls (Hayes & Tan 2016). The BEIP used self-reported pubertal stage through age 14 and found no evidence of early puberty related to early institutional care. In the BEIP study, it was disruptions in placements that predicted Tanner stage, with more disruptions being associated with a more delayed pubertal timing for boys at age 12 and an advanced pubertal timing for girls at age 14 (Johnson et al. 2018). Notably, many of these studies relied on parent- and self-reports of pubertal status. In a study of PI youth adopted into US homes, nurse-assessed pubertal Tanner staging in 7–14-year-old youth demonstrated no difference in pubertal status between PI and comparison youth (Reid et al. 2017). When examining a subset of PI youth who were stunted at adoption, the previously stunted PI youth were less likely to be in central puberty compared to other PI youth. The age of menarche was not affected by PI status. Clearly, more objective assessments and examination in representative samples are needed to address issues of pubertal timing associated with early institutional deprivation.

## Cellular and Immune Functioning

Burgeoning research has begun to examine the effects of early adversity on cellular aging and immune functioning, driven by the interest in the mechanisms transducing early life adversity into poor health and early mortality (Brown et al. 2009, Shonkoff et al. 2009). Some research has focused on shorter telomere length as an index of cellular aging. In the BEIP project, those with longer time spent in institutional care exhibited shorter telomeres in buccal cells at 5, 6, and 15 years of age (Drury et al. 2012, Humphreys et al. 2016). Telomeres also shortened at a greater rate in ever-institutionalized children as they aged from 6 to 15 years, as randomization to foster care was not protective against telomere shortening (Humphreys et al. 2016). It is important to remember that as the BEIP children aged, many experienced multiple placement changes and thus ongoing significant adversity. Whether this ongoing adversity or the early institutional care influenced the rate of telomere shortening is not known, though perhaps it is instructive that in PI adults adopted as infants into families where placement was stable, no differences in telomere length were noted when compared to adults born and reared in their birth families (Elwenspoek et al. 2017b).

Recent research has focused on the immune cell profiles of children in early institutional care, especially T-cell profiles thought to be sensitive to early experience. An increase in CD8+ versus

CD4+ T cells, which when extreme is evidence of immune incompetence, has been noted in PI youth relative to comparison youth in two studies (Esposito et al. 2016, Reid et al. 2019). These findings are consistent with evidence that PI youth have difficulty containing the Epstein-Barr virus, herpes simplex, and cytomegalovirus (CMV) (Shirtcliff et al. 2009). Also consistent with the finding of less immune competence is evidence from two studies that PI adolescents and young adults show higher expression of immune senescence markers (CD57) on CD4+ and CD8+ T cells relative to comparison individuals (Elwenspoek et al. 2017b, Reid et al. 2019). In both studies, institutional care was associated with higher levels of CMV antibody titers, and CMV mediated the relationship between early institutional care and later T-cell profiles (Elwenspoek et al. 2017b, Reid et al. 2019). Taken together, these preliminary studies demonstrate that persistent immune differences are still evident even years after removal from institutional care.

Despite the intense interest in associations between childhood adversity and the development of a proinflammatory phenotype, there is so far relatively little evidence for these associations in relation to early institutional deprivation. The BEIP group did not find any increase in circulating inflammatory factors (e.g., CRP, IL-6) in their sample when assessed as adolescents. Similarly, Elwenspoek and colleagues (2017a) did not find either increases in circulating proinflammatory cytokines or larger increases in these cytokines following in vitro stimulation with several antigens. This group did report what they termed a proinflammatory T-cell distribution; specifically, PI individuals as young adults showed reduced numbers of CD69+CD8+ T cells and increased numbers of HLA-DR+ CD4, HLA-DR+ CD8, and CD25+CD8+ T cells. Clearly, more work is needed to determine whether early institutional deprivation has the same or different immune consequences compared to other forms of childhood adversity.

### Cardiometabolic Health

Finally, cardiometabolic health is another growing area of research in the PI population. In one study, PI youth adopted into US homes who were height stunted at adoption were compared with age- and BMI percentile–matched youths on arterial stiffness (augmentation index and pulse wave velocity), cardiac autonomic function (heart rate variability), blood pressure, and fasting lipid, glucose, and insulin levels (Reid et al. 2018). Relative to comparison children, the PI children had higher systolic blood pressure and higher levels of arterial stiffness as measured by the augmentation index. The PI youth had higher levels of the following: total cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides, insulin levels, and HOMA-IR (homeostatic model assessment of insulin resistance) values, suggesting increased insulin resistance risk. The PI children also had a lower low-frequency/high-frequency ratio in their electrocardiograms, indicating lower sympathetic tone. All of these results were controlled for parent education, age, trunk tissue fat, height for age, sex, and race, revealing concerning trends towards poorer cardiometabolic health at a mean age of 13.5 years (**Figure 2**) (Reid et al. 2018). The BEIP study also found signs of poorer cardiovascular health in adolescence, though these results were driven by youth in the accelerated BMI trajectory. Youth in this trajectory exhibited higher levels of glycosylated hemoglobin, indicative of a higher risk of insulin resistance, and of C-reactive protein, a risk factor for poorer cardiometabolic health (Tang et al. 2018).

## FUTURE DIRECTIONS

### For the Science of Early Institutional Deprivation

International adoption rates have plummeted in the United States and in many other countries. In 2004 approximately 23,000 children entered US homes, most of them from institutional care

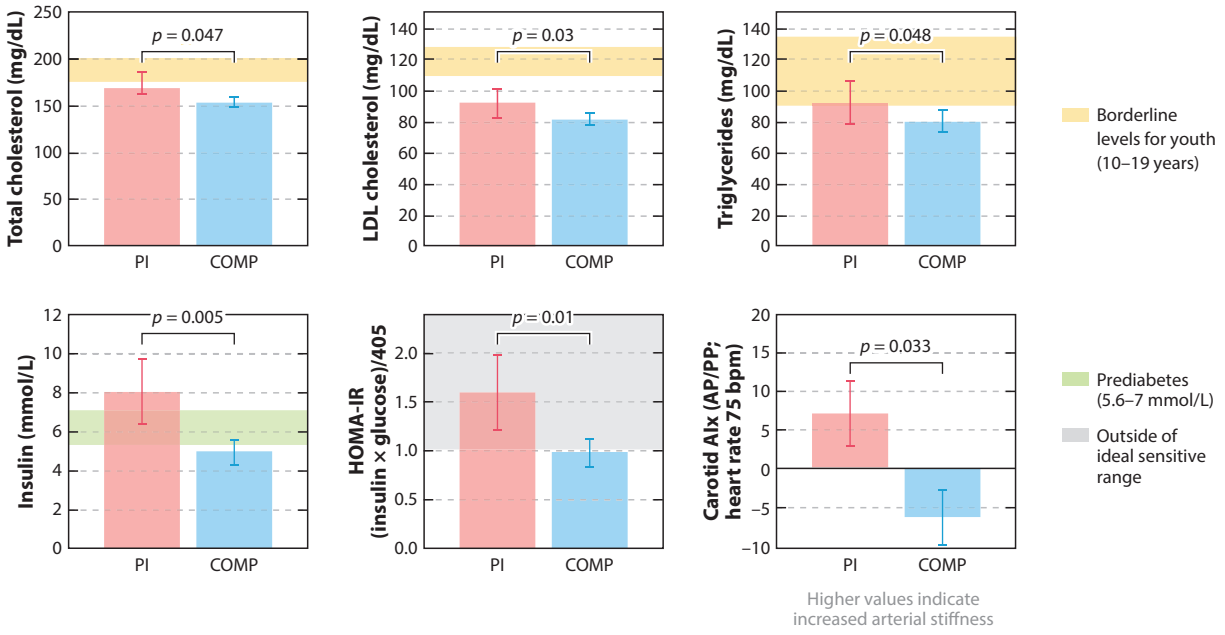


**Figure 2**

Cardiometabolic health profiles of postinstitutionalized youth (*pink bars*) and comparison youth who have never been institutionalized (*blue bars*), controlling for parent education, age, trunk tissue fat, height for age, sex, and race. The comparisons reveal concerning trends toward poorer cardiometabolic health at a mean age of 13.5 years. Error bars indicate a 95% confidence interval. Abbreviations: AIx, augmentation index; AP, aortic pressure; COMP, comparison youth; HOMA-IR, homeostatic model assessment of insulin resistance; LDL, low-density lipoprotein; *p*, p-value; PI, postinstitutionalized youth; PP, pulse pressure. Data are from Reid et al. (2018).

and nearly all under age 3; in 2017 the number was 4,714, and most were between 5 and 12 years of age (Budiman & Hugo Lopez 2017). Though international adoption is declining, children are still being adopted or fostered out of institutions into homes in their birth countries. Studies of the transition from deprivation to supportive families will need to be conducted in these countries in the future. Of course, there are many adolescents and young adults living in high-income countries who were adopted as infants and young children from institutional care. A number of important scientific questions regarding early institutional deprivation can be addressed working with these individuals as they age.

First, it is critical that we continue longitudinal follow-ups of individuals in the BEIP, ERA, and other longitudinal studies of PI individuals. Very little is known about the life-course impact of early deprivation when it is followed by adequate care, and studies of adopted individuals whose placements were supportive and stable are especially needed. Second, we need studies examining potential periods of plasticity when the impacts of early deprivation might be open for remediation. As we noted, puberty might be one such time, but there are other periods when our neurobiology is likely to be more plastic, such as pregnancy and the transition to parenthood. Periods of plasticity cut both ways; thus, there may be times when the consequences of early deprivation are more likely to create additional stress and thus further challenge healthy development. Alternatively, those might be periods in which supportive interventions could have the best long-term impact.

Third, we need more work addressing the physical health consequences of early institutional deprivation. We are beginning to observe the significant impacts of early institutional deprivation

on the immune and cardiovascular systems in adolescents and young adults. Increased risk of cardiometabolic disorder or early immune senescence need not necessarily increase morbidity and mortality if healthy lifestyle practices are implemented and/or maintained and if the medical personnel caring for adults with histories of early deprivation know how to attend to these health risks.

Fourth, with adolescents and adults, we can more readily address the neurobiological and other physiological mechanisms that may transduce early deprivation into the risk of poor mental and physical health. For example, there is increasing interest in gut-brain communication. One series of studies found that PI adolescents had an increased incidence of gastrointestinal symptoms, which were in turn associated with concurrent and future anxiety (Callaghan et al. 2019a). In a very small subsample of PI children, institutional care was associated with changes in diversity (both alpha and beta) of microbial communities. PI children exhibited less alpha diversity (i.e., lower counts of bacterial richness) and different bacterial species (i.e., beta diversity) than nonadopted children (Callaghan et al. 2019a). Bacteria levels were correlated with prefrontal cortex activation to emotional faces (Callaghan et al. 2019a). This is a tantalizing direction for further research.

Finally, and this is far from being an exhaustive list, we need more work relating early institutional deprivation to psychosocial and physical neglect in families. This work needs to be both conceptual and empirical, so that the evidence on deprivation contained to the infancy and early childhood period can inform efforts to support children growing up in families who are neglectful. This comparison work goes along with the need to unpack conditions of early care adversity to try to understand both unique and common effects of different elements that conspire to alter the course of development in different systems. Not only are the consequences of varying elements of deprivation/neglect likely to be different, but the interventions to address these deficits will also be different (Natl. Sci. Counc. Dev. Child 2012). Aligning the assessment of institutions and of neglect in families so that findings can inform one another should be a goal of future research in this area.

## Policy and Practice Implications

Recent estimates suggest that 2.7 million children are living in institutional care worldwide (Petrowski et al. 2017). Based on the research reviewed, family care advocates and UNICEF alike have appropriately called for an end to institutional care and the prioritization of family-based care for all children around the world (UNICEF 2017). The first obvious step is to keep children in their families of origin as much as possible. Children are often placed in institutional care due to situations of family breakdown, inadequate social services, disability, health issues, and poverty. Therefore, governments should first and foremost prioritize supporting families, investing in community-based family support, and preventing family separation. In situations in which a child is unable to stay in the family of origin, family-based care such as foster care or adoption is the next best alternative for most children (Julian & McCall 2011).

However, ending all forms of institutional care immediately, while a worthy goal, is perhaps impractical and might have iatrogenic effects. For one, there are both cultural and regional challenges: Rearing someone else's child might be culturally, politically, or historically unacceptable. Though it is the best option for children, recruiting and supporting families to adopt or foster children can be very difficult, and countries may be reluctant or unable to support families financially (Julian & McCall 2011). Throughout history and still in some places today, adoption was and is used as a means of acquiring servants (e.g., orphan trains in the United States), and this is not the family care condition that is being advocated. Governments need to develop a family care solution that is well suited to their populations. Each country also needs a child welfare system

to support the placement of children into family care and their continued well-being in family care placements. Deinstitutionalization takes time and an enormous commitment from many actors. The United States took several decades to deinstitutionalize and place children in families in the early twentieth century, and Ukraine's more recent effort to develop family care and deinstitutionalize was successful for ~7,000 children but still left 45,000 children in institutional care after five years of intensive efforts (Groark et al. 2009). Finally, as the deinstitutionalization is undertaken, children will inevitably remain in institutional care while systems are developed, and others will likely be left behind. While typically developing infants and young children are likely to find family care, the most vulnerable—older children and children with disabilities—are less likely to be placed into family care while family care systems are developed (McCall 2013). Some research on improving institutional care has found that creating more family-like care within institutions improves child outcomes both while the children are in institutional care and once they are placed in adoptive or foster homes (Groark et al. 2012, Julian & McCall 2012, McCall et al. 2010). Therefore, while family-based care systems are the first priority and deserve intensive resources and support, the best possible care needs to be provided for all children, whether they are institutionalized or not.

With that in mind, the research questions on the horizon are less about what outcomes are likely for children who enter family care after institutionalization and more about how to set standards of assessment to determine if children are in developmentally appropriate care settings. This includes assessments for family-based care and institutional care alike. Rigorous research is needed on both how and what we measure to assess the impact of interventions, whether those interventions are in an institution or in family-based foster or adoptive care. Many questions remain. Do we set standards of assessment based on the community that the child comes from? Or do we set them based on globally recognized standards? Much work is underway to assess child development on a global scale (Black et al. 2017, Young & Richardson 2007). This has a number of challenges. What assessments are culturally relevant for risk and resilience? Can we measure and are we measuring the same things across different groups of children? What are the best assessments to use for interventions to understand how children are being supported in their current care settings? Family separation and institutional care affect millions of children and will likely continue to affect millions. In the future, we must strive both to better understand early deprivation and to use this large body of research to improve outcomes for orphaned children on a global scale.



## DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health, the National Science Foundation, or The JPB Foundation.

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## LITERATURE CITED


Alink LRA, van IJzendoorn MH, Bakermans-Kranenburg MJ, Mesman J, Juffer F, Koot HM. 2008. Cortisol and externalizing behavior in children and adolescents: mixed meta-analytic evidence for the inverse relation of basal cortisol and cortisol reactivity with externalizing behavior. *Dev. Psychobiol.* 50:427–50

Almas AN, Degnan KA, Walker OL, Radulescu A, Nelson CA, et al. 2015. The effects of early institutionalization and foster care intervention on children's social behaviors at age 8. *Soc. Dev.* 24:225–39

Behen ME, Muzik O, Saporta AS, Wilson BJ, Pai D, et al. 2009. Abnormal fronto-striatal connectivity in children with histories of early deprivation: a diffusion tensor imaging study. *Brain Imaging Behav.* 3:292–97

Bick J, Nelson CA. 2016. Early adverse experiences and the developing brain. *Neuropsychopharmacology* 41:177–96

Black MM, Walker SP, Fernald LCH, Andersen CT, DiGirolamo AM, et al. 2017. Early childhood development coming of age: science through the life course. *Lancet* 389:77–90

Brown DW, Anda RF, Tiemeier H, Felitti VJ, Edwards VJ, et al. 2009. Adverse childhood experiences and the risk of premature mortality. *Am. J. Prev. Med.* 37:389–96

Bruce J, Tarullo AR, Gunnar MR. 2009. Disinhibited social behavior among internationally adopted children. *Dev. Psychopathol.* 21:151–71

Budiman A, Hugo Lopez M. 2017. Amid decline in international adoptions to U.S., boys outnumber girls for the first time. *Pew Research Center*, Oct. 17. **https://www.pewresearch.org/fact-tank/2017/10/17/amid-decline-in-international-adoptions-to-u-s-boys-outnumber-girls-for-the-first-time/**

Burgess PW, Stuss DT. 2017. Fifty years of prefrontal cortex research: impact on assessment. *J. Int. Neuropsychol. Soc.* 23:755–67

Callaghan BL, Fields A, Gee DG, Gabard-Durnam L, Caldera C, et al. 2019a. Mind and gut: associations between mood and gastrointestinal distress in children exposed to adversity. *Dev. Psychopathol.* In press. **https://doi.org/10.1017/s0954579419000087**

Callaghan BL, Gee DG, Gabard-Durnam L, Telzer EH, Humphreys KL, et al. 2019b. Decreased amygdala reactivity to parent cues protects against anxiety following early adversity: an examination across 3 years. *Biol. Psychiatry Cogn. Neurosci. Neuroimaging* 4:664–71

Capitanio JP, Mendoza SP, Mason WA, Maninger N. 2006. Rearing environment and hypothalamic-pituitary-adrenal regulation in young rhesus monkeys (*Macaca mulatta*). *Dev. Psychobiol.* 46:318–30

Carlson EA, Hostinar CE, Mliner SB, Gunnar MR. 2014. The emergence of attachment following early social deprivation. *Dev. Psychopathol.* 26:479–89

Carlson M, Earls F. 1997. Psychological and neuroendocrinological sequelae of early social deprivation in institutionalized children in Romania. *Ann. N. Y. Acad. Sci.* 807:419–28

Caspi A, Houts RM, Belsky DW, Goldman-Mellor SJ, Harrington H, et al. 2014. The p factor: one general psychopathology factor in the structure of psychiatric disorders? *Clin. Psychol. Sci.* 2:119–37

Champoux M, Metz B, Suomi SJ. 1991. Behavior of nursery/peer-reared and mother-reared rhesus monkeys from birth through 2 years of age. *Primates* 32:509–14

Charman T, Baron-Cohen S, Swettenham J, Baird G, Cox A, Drew A. 2001. Testing joint attention, imitation, and play as infancy precursors to language and theory of mind. *Cogn. Dev.* 15:481–98

Colvert E, Rutter M, Kreppner J, Beckett C, Castle J, et al. 2008. Do theory of mind and executive function deficits underlie the adverse outcomes associated with profound early deprivation? Findings from the English and Romanian Adoptees study. *J. Abnorm. Child Psychol.* 36:1057–68

Danese A, McEwen BS. 2012. Adverse childhood experiences, allostasis, allostatic load, and age-related disease. *Physiol. Behav.* 106:29–39

Del Giudice M, Ellis BJ, Shirtcliff EA. 2011. The Adaptive Calibration Model of stress responsivity. *Neurosci. Biobehav. Rev.* 35:1562–92

Delavari F, Sheibani V, Esmaeili-Mahani S, Nakhaee N. 2016. Maternal separation and the risk of drug abuse in later life. *Addict. Health* 8:107–14

DePasquale CE, Donzella B, Gunnar MR. 2019. Pubertal recalibration of cortisol reactivity following early life stress: a cross-sectional analysis. *J. Child Psychol. Psychiatry* 60:566–75

DePasquale CE, Gunnar MR. 2019. Affective attunement in peer dyads containing children adopted from institutions. *Dev. Psychobiol.* In press. **https://doi.org/10.1002/dev.21890**

Devine RT, Hughes C. 2014. Relations between false belief understanding and executive function in early childhood: a meta-analysis. *Child Dev.* 85:1777–94

Dobrova-Krol NA, van Ijzendoorn MH, Bakermans-Kranenburg MJ, Cyr C, Juffer F. 2008. Physical growth delays and stress dysregulation in stunted and non-stunted Ukrainian institution-reared children. *Infant Behav. Dev.* 31:539–53

Dobrova-Krol NA, van IJzendoorn MH, Bakermans-Kranenburg MJ, Juffer F. 2010. Effects of perinatal HIV infection and early institutional rearing on physical and cognitive development of children in Ukraine. *Child Dev.* 81:237–51

Doom JR, Gunnar MR. 2013. Stress physiology and developmental psychopathology: past, present, and future. *Dev. Psychopathol.* 25:1359–73

Doom JR, Hostinar CE, VanZomeren-Dohm AA, Gunnar MR. 2015. The roles of puberty and age in explaining the diminished effectiveness of parental buffering of HPA reactivity and recovery in adolescence. *Psychoneuroendocrinology* 59:102–11

Drury SS, Theall K, Gleason MM, Smyke AT, De Vivo I, et al. 2012. Telomere length and early severe social deprivation: linking early adversity and cellular aging. *Mol. Psychiatry* 17:719–27

Eisenberger NI, Master SL, Inagaki TK, Taylor SE, Shirinyan D, et al. 2011. Attachment figures activate a safety signal-related neural region and reduce pain experience. *PNAS* 108:11721–26

Eluvathingal TJ, Chugani HT, Behen ME, Juhasz C, Muzik O, et al. 2006. Abnormal brain connectivity in children after early severe socioemotional deprivation: a diffusion tensor imaging study. *Pediatrics* 117:2093–100

Elwenspoek MMC, Hengesch X, Leenen FAD, Schritz A, Sias K, et al. 2017a. Proinflammatory T cell status associated with early life adversity. *J. Immunol.* 199:4046–55

Elwenspoek MMC, Sias K, Hengesch X, Schaan VK, Leenen FAD, et al. 2017b. T cell immunosenescence after early life adversity: association with cytomegalovirus infection. *Front. Immunol.* 8:1263

Esposito EA, Jones MJ, Doom JR, MacIsaac JL, Gunnar MR, Kobor MS. 2016. Differential DNA methylation in peripheral blood mononuclear cells in adolescents exposed to significant early but not later childhood adversity. *Dev. Psychopathol.* 28:1385–99

Fareri DS, Gabard-Durnam L, Goff B, Flannery J, Gee DG, et al. 2017. Altered ventral striatal-medial prefrontal cortex resting-state connectivity mediates adolescent social problems after early institutional care. *Dev. Psychopathol.* 29:1865–76

Flannery JE, Gabard-Durnam LJ, Shapiro M, Goff B, Caldera C, et al. 2017. Diurnal cortisol after early institutional care—Age matters. *Dev. Cogn. Neurosci.* 25:160–66

Fox NA, Nelson CA III, Zeanah CH. 2017. The effects of psychosocial deprivation on attachment: lessons from the Bucharest Early Intervention Project. *Psychodyn. Psychiatry* 45:441–50

Fries AB, Ziegler TE, Kurian JR, Jacoris S, Pollak SD. 2005. Early experience in humans is associated with changes in neuropeptides critical for regulating social behavior. *PNAS* 102:17237–40

Fuglestad AJ, Lehmann AE, Kroupina MG, Petryk A, Miller BS, et al. 2008. Iron deficiency in international adoptees from Eastern Europe. *J. Pediatr.* 153:272–77

Gee DG, Gabard-Durnam LJ, Flannery J, Goff B, Humphreys KL, et al. 2013. Early developmental emergence of human amygdala-prefrontal connectivity after maternal deprivation. *PNAS* 110:15638–43

Goff B, Gee DG, Telzer EH, Humphreys KL, Gabard-Durnam L, et al. 2013. Reduced nucleus accumbens reactivity and adolescent depression following early-life stress. *Neuroscience* 249:129–38

Goldfarb W. 1945. Psychological privation in infancy and subsequent adjustment. *Am. J. Orthopsychiatry* 14:247–55

Govindan RM, Behen ME, Helder E, Makki MI, Chugani HT. 2010. Altered water diffusivity in cortical association tracts in children with early deprivation identified with Tract-Based Spatial Statistics (TBSS). *Cereb. Cortex* 20:561–69

Groark CJ, McCall RB, Li J. 2009. Characterizing the status and progress of a country's child welfare reform. *Int. J. Child Fam. Welf.* 12:145–60

Groark CJ, McCall RB, McCarthy SK, Eichner JC, Warner HA, Palmer K. 2012. *The Effects of a Social-Emotional Intervention on Caregivers and Children in Five Central American Institutions*. Pittsburgh, PA: Univ. Pittsburgh Off. Child Dev.

Gunnar MR. 2001. Effects of early deprivation: findings from orphanage-reared infants and children. In *Handbook of Developmental Cognitive Neuroscience*, ed. CH Nelson, M Luciana, pp. 617–30. Cambridge, MA: MIT Press

Gunnar MR. 2017. Social buffering of stress in development: a career perspective. *Perspect. Psychol. Sci.* 12:355–73

Gunnar MR, Davis EP. 2013. The effects of stress on early brain and behavioral development. In *Cognitive Development*, ed. HB Tager-Flusberg, pp. 447–66. New York: Elsevier

Gunnar MR, Morison SJ, Chisholm K, Schuder M. 2001. Salivary cortisol levels in children adopted from Romanian orphanages. *Dev. Psychopathol.* 13:611–28

Gunnar MR, van Dulmen M. 2007. Behavior problems in postinstitutionalized internationally adopted children. *Dev. Psychopathol.* 19:129–48

Guyon-Harris KL, Humphreys KL, Fox NA, Nelson CA, Zeanah CH. 2018. Course of disinhibited social engagement disorder from early childhood to early adolescence. *J. Am. Acad. Child Adolesc. Psychiatry* 57:329–35.e2

Hanson JL, Hair N, Shen DG, Shi F, Gilmore JH, et al. 2013. Family poverty affects the rate of human infant brain growth. *PLOS ONE* 8:e80954

Harlow HF, Harlow MK, Suomi SJ. 1971. From thought to therapy: lessons from a primate laboratory. *Am. Sci.* 59:538–49

Hartup W, Stevens N. 1997. Friendship and adaptation in the life course. *Psychol. Bull.* 121:355–70

Hayes P, Tan TX. 2016. Timing of menarche in girls adopted from China: a cohort study. *Child Care Health Dev.* 42:859–62

Heinrichs M, Baumgartner T, Kirschbaum C, Ehlert U. 2003. Social support and oxytocin interact to suppress cortisol and subjective responses to psychosocial stress. *Biol. Psychiatry* 54:1389–98

Hennessy MB, Kaiser S, Sachser N. 2009. Social buffering of the stress response: diversity, mechanisms, and functions. *Front. Neuroendocrinol.* 30:470–82

Hodel AS, Hunt RH, Cowell RA, Van Den Heuvel SE, Gunnar MR, Thomas KM. 2015. Duration of early adversity and structural brain development in post-institutionalized adolescents. *Neuroimage* 105:112–19

Hostinar CE, Johnson AE, Gunnar MR. 2015a. Early social deprivation and the social buffering of cortisol stress responses in late childhood: an experimental study. *Dev. Psychol.* 51:1597–608

Hostinar CE, Johnson AE, Gunnar MR. 2015b. Parent support is less effective in buffering cortisol stress reactivity for adolescents compared to children. *Dev. Sci.* 18:281–97

Hostinar CE, Stellern SA, Schaefer C, Carlson SM, Gunnar MR. 2012. Associations between early life adversity and executive function in children adopted internationally from orphanages. *PNAS* 109:17208–12

Hostinar CE, Sullivan RM, Gunnar MR. 2014. Psychobiological mechanisms underlying the social buffering of the hypothalamic-pituitary-adrenocortical axis: a review of animal models and human studies across development. *Psychol. Bull.* 140:256–82

Humphreys KL, Esteves K, Zeanah CH, Fox NA, Nelson CA III, Drury SS. 2016. Accelerated telomere shortening: tracking the lasting impact of early institutional care at the cellular level. *Psychiatry Res.* 246:95–100

Johnson DE. 2000. Long-term medical issues in international adoptees. *Pediatr. Ann.* 29:234–41

Johnson DE, Gunnar MR. 2011. IV. Growth failure in institutionalized children. *Monogr. Soc. Res. Child Dev.* 76:92–126

Johnson DE, Tang A, Almas AN, Degnan KA, McLaughlin KA, et al. 2018. Caregiving disruptions affect growth and pubertal development in early adolescence in institutionalized and fostered Romanian children: a randomized clinical trial. *J. Pediatr.* 203:345–53.e3

Juffer F, van Ijzendoorn MH. 2005. Behavior problems and mental health referrals of international adoptees: a meta-analysis. *JAMA* 293:2501–15

Julian MM, McCall RB. 2011. The development of children. *Int. J. Child Fam. Welf.* 3:119–47

Julian MM, McCall RB. 2012. *Attachment and indiscriminate friendliness among adopted children exposed to a social-emotional intervention in an institution*. Paper presented at the International Conference on Infant Studies, Minneapolis, MN, June 7

Kennedy M, Kreppner J, Knights N, Kumsta R, Maughan B, et al. 2017. Adult disinhibited social engagement in adoptees exposed to extreme institutional deprivation: examination of its clinical status and functional impact. *Br. J. Psychiatry* 211:289–95

Kertes DA, Gunnar MR, Madsen NJ, Long JD. 2008. Early deprivation and home basal cortisol levels: a study of internationally adopted children. *Dev. Psychopathol.* 20:473–91

Koss KJ, Gunnar MR. 2018. Annual research review: early adversity, the hypothalamic-pituitary-adrenocortical axis, and child psychopathology. *J. Child Psychol. Psychiatry* 59:327–46

Koss KJ, Hostinar CE, Donzella B, Gunnar MR. 2014. Social deprivation and the HPA axis in early development. *Psychoneuroendocrinology* 50:1–13

Koss KJ, Mliner SB, Donzella B, Gunnar MR. 2016. Early adversity, hypocortisolism, and behavior problems at school entry: a study of internationally adopted children. *Psychoneuroendocrinology* 66:31–38

Kreppner J, Kumsta R, Rutter M, Beckett C, Castle J, et al. 2010. IV. Developmental course of deprivation-specific psychological patterns: early manifestations, persistence to age 15, and clinical features. *Monogr. Soc. Res. Child Dev.* 75:79–101

Kumsta R, Kreppner J, Rutter M, Beckett C, Castle J, et al. 2010. III. Deprivation-specific psychological patterns. *Monogr. Soc. Res. Child Dev.* 75:48–78

Kumsta R, Schlotz W, Golm D, Moser D, Kennedy M, et al. 2017. HPA axis dysregulation in adult adoptees twenty years after severe institutional deprivation in childhood. *Psychoneuroendocrinology* 86:196–202

Lawler JM, Koss KJ, Doyle CM, Gunnar MR. 2016. The course of early disinhibited social engagement among post-institutionalized adopted children. *J. Child Psychol. Psychiatry* 57:1126–34

Leneman KB, Donzella B, Desjardins CD, Miller BS, Gunnar MR. 2018. The slope of cortisol from awakening to 30 min post-wake in post-institutionalized children and early adolescents. *Psychoneuroendocrinology* 96:93–99

Loman MM, Johnson AE, Westerlund A, Pollak SD, Nelson CA, Gunnar MR. 2013. The effect of early deprivation on executive attention in middle childhood. *J. Child Psychol. Psychiatry* 54:37–45

Lomanowska AM, Melo AI. 2016. Deconstructing the function of maternal stimulation in offspring development: insights from the artificial rearing model in rats. *Horm. Behav.* 77:224–36

Lynch KA. 2000. Infant mortality, child neglect, and child abandonment in European history: a comparative analysis. In *Population and Economy: From Hunger to Modern Economic Growth*, ed. T Bengtsson, O Saito, pp. 133–64. Oxford, UK: Oxford Univ. Press

Maheu FS, Dozier M, Guyer AE, Mandell D, Peloso E, et al. 2010. A preliminary study of medial temporal lobe function in youths with a history of caregiver deprivation and emotional neglect. *Cogn. Affect. Behav. Neurosci.* 10:34–49

Marshall PJ, Fox NA, Group BC. 2004. A comparison of the electroencephalogram between institutionalized and community children in Romania. *J. Cogn. Neurosci.* 16:1327–38

McCall RB. 2013. The consequences of early institutionalization: Can institutions be improved? Should they? *Child Adolesc. Ment. Health* 18:193–201

McCall RB, Groark CJ, Fish LA, Harkins D, Serrano G, Gordon K. 2010. A social-emotional intervention in a Latin American orphanage. *Infant Ment. Health J.* 31:521–42

McCall RB, Groark CJ, Hawk BN, Julian MM, Merz EC, et al. 2019. Early caregiver-child interaction and children's development: lessons from the St. Petersburg-USA Orphanage Intervention Research Project. *Clin. Child Fam. Psychol. Rev.* 22:208–24

McDermott JM, Westerlund A, Zeanah CH, Nelson CA, Fox NA. 2012. Early adversity and neural correlates of executive function: implications for academic adjustment. *Dev. Cogn. Neurosci.* 2(Suppl. 1):S59–66

McLaughlin KA, DeCross SN, Jovanovic T, Tottenham N. 2019. Mechanisms linking childhood adversity with psychopathology: learning as an intervention target. *Behav. Res. Ther.* 118:101–9

McLaughlin KA, Fox NA, Zeanah CH, Sheridan MA, Marshall P, Nelson CA. 2010. Delayed maturation in brain electrical activity partially explains the association between early environmental deprivation and symptoms of attention-deficit/hyperactivity disorder. *Biol. Psychiatry* 68:329–36

McLaughlin KA, Sheridan MA, Tibu F, Fox NA, Zeanah CH, Nelson CA III. 2015. Causal effects of the early caregiving environment on development of stress response systems in children. *PNAS* 112:5637–42

McLaughlin KA, Sheridan MA, Winter W, Fox NA, Zeanah CH, Nelson CA. 2014. Widespread reductions in cortical thickness following severe early-life deprivation: a neurodevelopmental pathway to attention-deficit/hyperactivity disorder. *Biol. Psychiatry* 76:629–38

Mehta MA, Golembo NI, Nosarti C, Colvert E, Mota A, et al. 2009. Amygdala, hippocampal and corpus callosum size following severe early institutional deprivation: the English and Romanian Adoptees study pilot. *J. Child Psychol. Psychiatry* 50:943–51

Mehta MA, Gore-Langton E, Golembo N, Colvert E, Williams SC, Sonuga-Barke E. 2010. Hyporesponsive reward anticipation in the basal ganglia following severe institutional deprivation early in life. *J. Cogn. Neurosci.* 22:2316–25

Merz EC, McCall RB, Groza V. 2013. Parent-reported executive functioning in postinstitutionalized children: a follow-up study. *J. Clin. Child Adolesc. Psychol.* 42:726–33

Mul D, Oostdijk W, Drop SL. 2002. Early puberty in adopted children. *Horm. Res.* 57:1–9

Natl. Sci. Counc. Dev. Child. 2012. *The science of neglect: the persistent absence of responsive care disrupts the developing brain*. Work. Pap. 12, Natl. Sci. Counc. Dev. Child, Cent. Dev. Child, Harvard Univ., Cambridge, MA

Nelson CA III, Zeanah CH, Fox NA, Marshall PJ, Smyke AT, Guthrie D. 2007. Cognitive recovery in socially deprived young children: the Bucharest Early Intervention Project. *Science* 318:1937–40

O'Connor TG, Marvin RS, Rutter M, Olrick JT, Britner PA, et al. 2003. Child-parent attachment following early institutional deprivation. *Dev. Psychopathol.* 15:19–38

Olson IR, Von Der Heide RJ, Alm KH, Vyas G. 2015. Development of the uncinate fasciculus: implications for theory and developmental disorders. *Dev. Cogn. Neurosci.* 14:50–61

Petrowski N, Cappa C, Gross P. 2017. Estimating the number of children in formal alternative care: challenges and results. *Child Abuse Negl.* 70:388–98

Pitula CE, DePasquale CE, Mliner SB, Gunnar MR. 2019. Peer problems among postinstitutionalized, internationally adopted children: relations to hypocortisolism, parenting quality, and ADHD symptoms. *Child Dev.* 90:e339–55

Pitula CE, Thomas KM, Armstrong JM, Essex MJ, Crick NR, Gunnar MR. 2014. Peer victimization and internalizing symptoms among post-institutionalized, internationally adopted youth. *J. Abnorm. Child Psychol.* 42:1069–76

Pitula CE, Wenner JA, Gunnar MR, Thomas KM. 2017. To trust or not to trust: social decision-making in post-institutionalized, internationally adopted youth. *Dev. Sci.* 20:e12375

Pollak SD, Nelson CA, Schlaak M, Roeber B, Wewerka S, et al. 2010. Neurodevelopmental effects of early deprivation in post-institutionalized children. *Child Dev.* 81:224–36

Proos LA. 2009. Growth & development of Indian children adopted in Sweden. *Indian J. Med. Res.* 130:646–50

Quevedo K, Johnson A, Loman M, Lafavor T, Gunnar MR. 2012. The confluence of early deprivation and puberty on the cortisol awakening response: a study of post-institutionalized children. *Int. J. Behav. Dev.* 36:19–28

Ransel DL. 2014. *Mothers of Misery: Child Abandonment in Russia*. Princeton, NJ: Princeton Univ. Press

Reid BM, Coe CL, Doyle CM, Sheerar D, Slukvina A, et al. 2019. Persistent skewing of the T-cell profile in adolescents adopted internationally from institutional care. *Brain Behav. Immun.* 77:168–77

Reid BM, Harbin MM, Arend JL, Kelly AS, Dengel DR, Gunnar MR. 2018. Early life adversity with height stunting is associated with cardiometabolic risk in adolescents independent of body mass index. *J. Pediatr.* 202:143–49

Reid BM, Miller BS, Dorn LD, Desjardins C, Donzella B, Gunnar M. 2017. Early growth faltering in post-institutionalized youth and later anthropometric and pubertal development. *Pediatr. Res.* 82:278–84

Romeo RD. 2010. Pubertal maturation and programming of hypothalamic-pituitary-adrenal reactivity. *Front. Neuroendocrinol.* 31:232–40

Roy P, Rutter M, Pickles A. 2004. Institutional care: associations between overactivity and lack of selectivity in social relationships. *J. Psychol. Psychiatry* 45:866–73

Rutter M. 1972. Maternal deprivation reconsidered. *J. Psychosom. Res.* 16:241–50

Rutter M, Team ES. 1999. Romanian adopted children: quasi-autism and isolated autistic features. *J. Child Psychol. Psychiatry* 40:537–49

Sanchez MM, Ladd CO, Plotsky PM. 2001. Early adverse experience as a developmental risk factor for later psychopathology: evidence from rodent and primate models. *Dev. Psychopathol.* 13:419–50

Seltzer LJ, Ziegler TE, Pollak SD. 2010. Social vocalizations can release oxytocin in humans. *Proc. R. Soc. B* 277:2661–66

Sheridan MA, Fox NA, Zeanah CH, McLaughlin KA, Nelson CA III. 2012. Variation in neural development as a result of exposure to institutionalization early in childhood. *PNAS* 109:12927–32

Shirtcliff EA, Coe CL, Pollak SD. 2009. Early childhood stress is associated with elevated antibody levels to herpes simplex virus type 1. *PNAS* 106:2963–67

Shonkoff JP, Boyce WT, McEwen BS. 2009. Neuroscience, molecular biology, and the childhood roots of health disparities: building a new framework for health promotion and disease prevention. *JAMA* 301:2252–59

Silvers JA, Goff B, Gabard-Durnam LJ, Gee DG, Fareri DS, et al. 2017. Vigilance, the amygdala, and anxiety in youths with a history of institutional care. *Biol. Psychiatry Cogn. Neurosci. Neuroimaging* 2:493–501

Silvers JA, Lumian DS, Gabard-Durnam L, Gee DG, Goff B, et al. 2016. Previous institutionalization is followed by broader amygdala-hippocampal-PFC network connectivity during aversive learning in human development. *J. Neurosci.* 36:6420–30

Smyke AT, Koga SF, Johnson DE, Fox NA, Marshall PJ, et al. 2007. The caregiving context in institution-reared and family-reared infants and toddlers in Romania. *J. Child Psychol. Psychiatry* 48:210–18

Smyke AT, Zeanah CH, Fox NA, Nelson CA, Guthrie D. 2010. Placement in foster care enhances quality of attachment among young institutionalized children. *Child Dev.* 81:212–23

Sonuga-Barke EJS, Kennedy M, Kumsta R, Knights N, Golm D, et al. 2017. Child-to-adult neurodevelopmental and mental health trajectories after early life deprivation: the young adult follow-up of the longitudinal English and Romanian Adoptees study. *Lancet* 389:1539–48

Sonuga-Barke EJS, Schlotz W, Kreppner J. 2010. V. Differentiating developmental trajectories for conduct, emotion, and peer problems following early deprivation. *Monogr. Soc. Res. Child Dev.* 75:102–24

Suomi SJ. 1997. Early determinants of behaviour: evidence from primate studies. *Br. Med. Bull.* 53:170–84

Tang A, Slopen N, Nelson CA, Zeanah CH, Georgieff MK, Fox NA. 2018. Catch-up growth, metabolic, and cardiovascular risk in post-institutionalized Romanian adolescents. *Pediatr. Res.* 84:842–48

Tarullo A, Bruce J, Gunnar MR. 2007. False belief and emotion understanding in post-institutionalized children. *Soc. Dev.* 16:57–78

Tarullo AR, Garvin MC, Gunnar MR. 2011. Atypical EEG power correlates with indiscriminately friendly behavior in internationally adopted children. *Dev. Psychol.* 47:417–31

Teilmann G, Pedersen CB, Skakkebaek NE, Jensen TK. 2006. Increased risk of precocious puberty in internationally adopted children in Denmark. *Pediatrics* 118:e391–99

Thomas JD, Melcer T, Weinert S, Riley EP. 1998. Neonatal alcohol exposure produces hyperactivity in high-alcohol-sensitive but not in low-alcohol-sensitive rats. *Alcohol* 16:237–42

Tizard B, Rees J. 1975. The effect of early institutional rearing on the behavioural problems and affectional relationships of four-year-old children. *J. Child Psychol. Psychiatry Allied Discipl.* 16:61–73

Tottenham N, Hare TA, Millner A, Gilhooly T, Zevin JD, Casey BJ. 2011. Elevated amygdala response to faces following early deprivation. *Dev. Sci.* 14:190–204

Tottenham N, Hare TA, Quinn BT, McCarry TW, Nurse M, et al. 2010. Prolonged institutional rearing is associated with atypically large amygdala volume and difficulties in emotion regulation. *Dev. Sci.* 13:46–61

UNICEF. 2017. *Data gaps on children in residential care leave the most vulnerable unaccounted for*. Press Release, June 1. **https://www.unicef.org/press-releases/data-gaps-children-residential-care-leave-most-vulnerable-unaccounted**

Van Ijzendoorn MH, Bakermans-Kranenburg MJ, Juffer F. 2007. Plasticity of growth in height, weight, and head circumference: meta-analytic evidence of massive catch-up after international adoption. *J. Dev. Behav. Pediatr.* 28:334–43

van IJzendoorn MH, Palacios J, Sonuga-Barke EJS, Gunnar MR, Vorria P, et al. 2011. Children in institutional care: delayed development and resilience. In *Children Without Permanent Parents: Research, Practice, and Policy*, ed. RB McCall, MH van IJzendoorn, F Juffer, CJ Groark, VK Groza, pp. 8–30. New York: Wiley

Vanderwert RE, Marshall PJ, Nelson CA III, Zeanah CH, Fox NA. 2010. Timing of intervention affects brain electrical activity in children exposed to severe psychosocial neglect. *PLOS ONE* 5:e11415

Vanderwert RE, Zeanah CH, Fox NA, Nelson CA. 2016. Normalization of EEG activity among previously institutionalized children placed into foster care: a 12-year follow-up of the Bucharest Early Intervention Project. *Dev. Cogn. Neurosci.* 17:68–75

Wade M, Fox NA, Zeanah CH, Nelson CA. 2018. Effect of foster care intervention on trajectories of general and specific psychopathology among children with histories of institutional rearing: a randomized clinical trial. *JAMA Psychiatry* 75:1137–45

Wade M, Fox NA, Zeanah CH, Nelson CA III. 2019. Long-term effects of institutional rearing, foster care, and brain activity on memory and executive functioning. *PNAS* 116:1808–13

Wismer Fries AB, Shirtcliff EA, Pollak SD. 2008. Neuroendocrine dysregulation following early social deprivation in children. *Dev. Psychobiol.* 50:588–99

Woodhouse S, Miah A, Rutter M. 2018. A new look at the supposed risks of early institutional rearing. *Psychol. Med.* 48:1–10

Xiong F, Zhang L. 2013. Role of the hypothalamic-pituitary-adrenal axis in developmental programming of health and disease. *Front. Neuroendocrinol.* 34:27–46

Yarger HA, Bernard K, Caron EB, Wallin A, Dozier M. 2019. Enhancing parenting quality for young children adopted internationally: results of a randomized controlled trial. *J. Clin. Child Adolesc. Psychol.* 16. In press. **https://doi.org/10.1080/15374416.2018.1547972**

Young ME, Richardson L. 2007. *Early child development from measurement to action: a priority for growth and equity*. Rep., The World Bank, Washington, DC

Zeanah CH, Gleason MM. 2015. Annual research review: attachment disorders in early childhood—clinical presentation, causes, correlates, and treatment. *J. Child Psychol. Psychiatry* 56:207–22

Zeanah CH, Nelson CA, Fox NA, Smyke AT, Marshall P, et al. 2003. Designing research to study the effects of institutionalization on brain and behavioral development: the Bucharest Early Intervention Project. *Dev. Psychopathol.* 15:885–907

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**Errata**

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