

Stress and Child Development

Ross A. Thompson

Summary

Children’s early social experiences shape their developing neurological and biological systems for good or for ill, writes Ross Thompson, and the kinds of stressful experiences that are endemic to families living in poverty can alter children’s neurobiology in ways that undermine their health, their social competence, and their ability to succeed in school and in life. For example, when children are born into a world where resources are scarce and violence is a constant possibility, neurobiological changes may make them wary and vigilant, and they are likely to have a hard time controlling their emotions, focusing on tasks, and forming healthy relationships. Unfortunately, these adaptive responses to chronic stress serve them poorly in situations, such as school and work, where they must concentrate and cooperate to do well.

But thanks to the plasticity of the developing brain and other biological systems, the neurobiological response to chronic stress can be buffered and even reversed, Thompson writes, especially when we intervene early in children’s lives. In particular, warm and nurturing relationships between children and adults can serve as a powerful bulwark against the neurobiological changes that accompany stress, and interventions that help build such relationships have shown particular promise. These programs have targeted biological parents, of course, but also foster parents, teachers and other caregivers, and more distant relatives, such as grandparents. For this reason, Thompson suggests that the concept of two-generation programs may need to be expanded, and that we should consider a “multigenerational” approach to helping children living in poverty cope and thrive in the face of chronic stress.

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Children depend on the care of adults in the environment of relationships in which they live. This provides a compelling justification for two-generation efforts to support healthy growth. In this issue, other scholars draw attention to the ways that family resources—such as assets (including income), parents' education and health, and family assistance programs—can have both direct and indirect benefits for children.

This contribution is different from the others in several ways. First, I focus not only on resources but also on how family stress, and especially sources of stress that are common to at-risk children, can threaten healthy development. The children in the studies I discuss live in poverty, witness domestic violence or persistent marital conflict, live in foster care, are abused or neglected, have a depressed mother, or experience other kinds of significant chronic stress. Second, I focus on developing biological systems, although the studies I review also have considerable implications for behavioral development, socioemotional adjustment, and cognitive growth. Third, I try to understand how parenting quality and parent-child relationships affect children's biological functioning in ways that can have enduring behavioral consequences. My argument is that children are biologically designed to rely on early social experiences to guide the organization of their developing biological systems in ways that can be healthy or maladaptive. Those social experiences, especially in the family, can assist or undermine positive coping and adjustment, or in some cases alleviate the effects of prior stressful experiences. This is where the research I discuss has implications for early, multigenerational interventions.

The next section outlines a general portrayal of a child's developing biology, drawing on research into fetal programming, the neurobiology of stress and development, and how immunological systems function.¹ The picture is incomplete because these research fields are rapidly advancing, but we know enough already to draw conclusions about how early experience affects the developing organization of these biological systems. In the third section, I expand on the concept of "stress," drawing on research into the interaction of genes and the environment, to provide a more refined analysis of the kinds of experiences and conditions that pose immediate and longer-term risks to young children. The fourth section introduces the concept of developmental plasticity as a way to understand why early intervention is important, and what characteristics distinguish promising interventions to ameliorate children's stress. This section also profiles several examples of interventions that improve the stress neurobiology of children who live in difficult circumstances. The final section offers several provisional conclusions and implications of this work for thinking about multigenerational approaches to strengthening healthy development.

Developing Brain, Biology, and the Environment

Children are born into a world of unknowns. Newborns have no idea whether the environment into which they are born is rich or deficient in food, dangerous or secure, or populated by nurturing or abusive adults. Yet the ability to quickly adapt to environmental conditions is crucial to the newborn's immediate survival and to long-term development, especially if these conditions are likely to persist. Depending on which environmental conditions are detected, for example, the

infant's developing metabolism might slow down to prepare for a world of deficient or inconsistent food resources, and its perceptual processes might become more or less vigilant for threats to its safety. Obviously, these adaptations are not made consciously. Rather, they reflect how young, developing biological systems organize themselves in response to environmental signals. The most important source of these signals is the quality of care that young children receive.

An illustration of how this occurs is early language learning.² Newborns cannot know whether they've been born in Paris, London, New York, Tokyo, or Kiev. Consequently, the young brain must develop the potential to learn any language, and studies show that six-month-olds can discriminate among a wide variety of human speech phonemes, many more than their parents can discern. Young infants are figuratively "citizens of the world."³ But this universal perceptual ability is lost by age one as the child overhears the language (or languages) spoken in the home. This signals the brain to reorient speech perception to language-specific phonemes, making the child a more efficient language learner, and soon afterward an explosion in language learning occurs. Early experience instructs the brain about the language environment into which the child has been born.

There is every reason to believe that this biological sensitivity to environmental signals is not unique to language learning, nor does it begin at birth. In the uterus, the fetus is exposed to a variety of signals from the mother's diet, her emotions, and extra-uterine influences that can have potent effects on development. This was dramatically illustrated by longitudinal research (that is, research that follows people over time) on the Dutch famine of 1944. During World

War II, the German military occupying the Netherlands blockaded food transports in reprisal for a strike by Dutch railway workers in support of the Allied invasion. As a result, official rations for the adult population fell abruptly to between 400 and 800 calories daily from December 1944 until April 1945, when the Allied liberation of the Netherlands began to succeed and adequate nutrition was quickly restored. The children born to the women who were pregnant during the Dutch famine have been followed into late adulthood. Although some of the immediate effects of maternal malnutrition (such as birth weight) did not significantly predict later outcomes, latent effects of malnutrition followed by food plenty had long-term consequences. In adulthood, these children were at significantly greater risk for a range of health and mental health problems, including obesity, heart disease, and schizophrenic disorders, compared with children, including same-sex siblings, whose gestation was not affected by the famine.⁴ Investigators have concluded that these adult health problems may have resulted from fetal "programming" for nutritional deprivation followed by a lifetime of plentiful food for which these individuals were biologically unprepared.

Another illustration of how developing biology adapts to environmental signals concerns the neurobiology of stress. At birth, newborns have no idea whether they are living in the West Bank or the East Side, but adapting quickly to environmental conditions of threat or security is crucial to their survival. Considerable evidence suggests that the fetus is sensitive to hormonal and other physiological indicators of maternal stress, and that heightened exposure to stress in the womb is associated with greater reactivity to stress after birth, as well as longer-term problems with emotional and cognitive functioning.⁵ In

one longitudinal study, for example, mothers' depression during pregnancy was associated with heightened cortisol levels when infants were observed three months after birth as they underwent a moderately stressful procedure (cortisol is an important stress-related hormone).⁶ In another longitudinal study, early exposure to maternal cortisol in the womb was associated with emotional difficulties and larger volume in the right amygdala (a brain structure that helps detect and respond to threat) in girls at age seven.⁷ These findings are consistent with substantial research on animals that documents similar effects in the offspring of pregnant females that were subjected to stress.⁸ In general, then, prenatal stress exposure makes children more reactive to challenge and threat.

After birth, a child's direct exposure to chronic stress alters developing stress neurobiology in comparable ways. A wealth of research with animals and humans has focused on the hypothalamic-pituitary-adrenocortical (HPA) axis, an important part of the neuroendocrine system (the body's regulatory system that integrates the nervous system with the endocrine system). The HPA axis matures significantly during the prenatal period and the early postnatal years.⁹ When the brain detects threatening events and activates the HPA system, the consequences include production of cortisol that mobilizes energy, suppression of immune functioning, enhanced cardiovascular tone, and other critical components of the stress response. These responses have important psychological consequences, including greater focus on threat vigilance, heightened motivation for self-defense, and emotional arousal. In addition, basal levels of HPA functioning, which follow a circadian clock, are important to cortisol output, which helps to maintain our capacity to regulate our emotions and cope with stress.

Chronic stress, however, changes HPA functioning over time by altering the neurological circuitry that underlies the body's regulation of responses to stress. This occurs as repeated exposure to stressful events alters the sensitivity of the HPA system, in part through its effects on the limbic and cortical processes that regulate HPA activity.¹⁰ The limbic system is central to motivation and memory; cortical processes influence thinking, reasoning, and emotional regulation. Owing to their effect on these systems that regulate HPA activity, stressful events can have far-reaching consequences for behavior and cognition.

The biological effects of stress undermine [children's] ability to concentrate, remember things, and control and focus their own thinking.

As the HPA system matures early in life, it is especially susceptible to the effects of chronic or severe stress. In a longitudinal study of children living in poverty, for example, environmental characteristics like poor housing quality, economic strain, and poor parenting were associated with disrupted HPA activity from seven months to age four.¹¹ Another study of poor children found that toddlers living in families characterized by violence between parents and mothers' "emotional unavailability" to the child also exhibited disruptions in normal HPA activity.¹² In older children, higher cortisol levels were associated with lower family socioeconomic status, and mothers of older children with higher cortisol levels were more likely to have symptoms of depression.¹³

The behaviors correlated with disrupted HPA activity are complex and depend in part on the nature of the stress that children experience. They include heightened vigilance and self-regulatory problems that may be manifested in poorer coping, cognitive and attention problems, poor emotional regulation, and difficulty in social functioning.¹⁴ This constellation of behavioral problems, which arise from chronic activation of the HPA axis and the influence of stress hormones like cortisol on other biological systems (described below), have important implications for children's academic functioning as well as their capacity to develop constructive relationships with peers and adults. Stated differently, one of the reasons that children in stressful circumstances fall behind academically is that, in addition to the other disadvantages they experience, the biological effects of stress undermine their ability to concentrate, remember things, and control and focus their own thinking. And one of the reasons they experience social difficulties—with peers, for example—is that, in addition to the other disadvantages they experience, the biological effects of stress heighten emotional reactivity and undermine emotional self-regulation.

Early, chronic stress is associated with other biological challenges that also contribute to these behavioral consequences. Stress is associated with sharp increases in the autonomic nervous system's activity, including elevated blood pressure. As we've seen, stress hormones influence the functioning of cortical systems (such as the prefrontal cortex, which regulates many other neurobiological and cognitive processes) and limbic structures, including the amygdala, the hypothalamus (which is involved in motivational processes, including emotion), and the hippocampus (which contributes to the creation

of memories from current experience).¹⁵ Chronic stress also suppresses the functioning of the immune system. Stress undermines the immune system's sensitivity to infectious challenges, increasing its response to cytokines (that is, inflammatory agents) and generally embedding "proinflammatory tendencies" into biological functioning.¹⁶ In short, chronic and severe stress influences multiple biological systems, with diverse behavioral consequences; when this occurs early in life, the organization and functioning of these systems may be permanently altered.

Viewed from the perspective of biological adaptation, these developments are consistent with the young child's preparation for a life of adversity. If early experiences of family conflict, limited resources, and poor parenting are biological signals of the environmental conditions into which the child has been born, then it makes sense that the child develops biological systems that allocate mental resources to threat vigilance, foster quick and strong reactions to perceptions of danger, enable rapid mobilization of energy, and alter immunological functioning, yielding a behavioral pattern well suited to this kind of environment.

But there are several trade-offs. First, mental resources devoted to vigilance cannot as readily be devoted to learning, problem-solving, and other constructive pursuits. Second, although this behavioral pattern is adapted to conditions of adversity associated with family experience, it may be poorly suited to other social settings, such as at school and with peers, that require a different and more constructive set of behavioral skills. A social orientation toward detecting threats makes it hard to develop constructive relationships. Furthermore, the trouble these children have controlling their impulses and emotions

limits their capacity to quickly adjust to the different requirements of other social settings. Because they respond to most situations in the way they have learned to respond at home, these children get into trouble.

A third trade-off of these biological adaptations to stress is that they are taxing. Chronic activation of the neuroendocrine, cardiovascular, and immunological systems extracts a cost. These systems are designed for short-term activation, and chronic arousal makes it more difficult to mobilize them and recover from their activation in the future. This principle is captured by the concept of “allostatic load,” which refers to the progressive “wear and tear” on biological systems from the long-term effects of chronic stress. Considerable research documents that people with high allostatic load—or overload—are more susceptible to physical and mental health problems.¹⁷

Here is another way to consider the effects of chronic stress on developing biological systems. Human young have evolved to depend on their caregivers for protection, nurturance, and emotionally responsive care. When they receive these things, their developing neurological, neuroendocrine, immunological, and other biological systems organize to function appropriately, which also helps their developing cortical systems facilitate the growth of learning, problem-solving, and self-regulation. Stated simply, healthy biological and behavioral development depends on a supportive, responsive human environment. When children instead experience poverty, parental depression, family violence, or other circumstances, these biological systems and their interactions are disrupted. Such disruption may help children adapt to these conditions, but it also has immediate and long-term costs for healthy development.¹⁸

Defining Stress

Throughout this discussion, I have used the term stress, with qualifiers such as *chronic* or *severe*. But what exactly is stress?

Stress is a complex psychobiological process with biological, emotional, mental, and behavioral consequences, all of which influence one another.¹⁹ It begins, of course, with the perception of threat or danger in the environment. Some threats are experienced in common by everyone (for example, the approach of a menacing stranger), and others are based more on individual experience (for example, the approach of a familiar person whom one fears). As I’ve noted, the biological processes associated with reactions to stress have psychological consequences for both children and adults.²⁰ Thus stress responses are accompanied by a mental orientation toward threat, mobilization of energy for self-defense, and emotional arousal. Stressful experiences vary significantly, however, in their severity, duration, and predictability. When children experience manageable stress, their developing biological systems are not disrupted. Indeed, children need such experiences to help these systems become adaptively self-regulating.²¹ “Good” stress yields positive developmental and behavioral outcomes throughout life by helping individuals acquire coping skills.

What are the characteristics of good stress? Generally speaking, stressful experiences that are mild or moderate, predictable, and of short duration can be characterized as manageable and are likely to enhance biological functioning and promote mastery and competence. When stressful experiences are severe, chronic, compounding, and unpredictable, they are generally more likely to exceed an individual’s self-regulatory capacities. For

children, of course, another important factor in making stress manageable is the supportive presence of a caregiver. Considerable research with human and animal young shows that a parent's support buffers stressful events and helps children cope.²² Although adults also rely on social support, for children the assistance of a caregiver is more fundamental in making stressful experiences manageable. When they experience a frightening injury or a routine immunization, the loss of a pet or a peer's rejection, children who have the support of caregivers manage more successfully than children who must rely on their own resources alone.

But this straightforward portrayal is complicated by individual differences in stress reactivity and coping. More resilient people may be able to manage amounts of stress that would undermine the coping of less resilient individuals. Research on how genes interact with the environment underscores how significantly individual characteristics moderate the effects of environmental events. In one widely publicized study, for example, a research team identified indicators of harsh or abusive parenting in the childhood histories of a large sample of men from Dunedin, New Zealand, who had been studied from birth through adulthood.²³ They also obtained information about the men's genetic characteristics—in particular, whether they were genetically prone to aggression and antisocial behavior. When the researchers sought to identify which adults would be most likely to exhibit antisocial behavior, they found that the combination of early harsh parenting and genetic vulnerability best foreshadowed behaviors like adolescent conduct disorder, criminal convictions for violent behavior, and antisocial personality disorder. Although genetic vulnerability and parenting history were each important, adults who had genetic

vulnerability together with a history of harsh parenting were most likely to exhibit antisocial behavior.

Other studies have shown similar results. In one study, researchers observed mothers' sensitivity to their children when their infants were 10 months old, and measured externalizing behaviors (that is, acting-out behaviors such as conduct difficulties and aggression) when the children were 39 months old. Maternal insensitivity was significantly associated with later externalizing problems, but only for children with a genetic vulnerability to novelty-seeking and conduct problems. For children without this genetic factor, earlier maternal insensitivity did not predict later problems.²⁴ Taken together, therefore, the effects of stressful experiences depend significantly on a person's individual characteristics.

But here is a complication. Stressful experiences may actually alter the expression of genetic characteristics. The discovery that environmental experiences can alter how genes function is one of the signal achievements of the field of epigenetics. Epigenetics is concerned with influences on gene expression—that is, the activation, or “turning on and turning off,” of genetic activity—that occur without changes in the DNA itself. These influences occur through changes in the biochemical regulatory systems surrounding the gene, which can be altered through the effects of environmental experiences.²⁵ As a result, a gene can remain the same but no longer be active. Epigenetic changes in gene expression can be short-term or enduring, and some can be transmitted across generations. Epigenetics has long been studied in plants and animals, but until recently we did not have the technology to study epigenetic influences in human behavior.

Epigenetic research on humans is still in its early stages, but it is already yielding important insights into how the environment influences gene expression. For example, early stress appears to produce changes in gene expression in children. One study examined children and adolescents born to mothers who said that they had experienced violence from their intimate partners while pregnant. The children exhibited epigenetic changes in the activation of the glucocorticoid receptor gene, which affects how the body reacts to stress. There was no evidence of epigenetic change in children whose mothers reported partner violence either before pregnancy or after the child's birth.²⁶ Looking at a more extreme situation, researchers found greater evidence for epigenetic changes in a group of children raised in orphanages than in a group raised by their biological parents, with changes evident in genes associated with brain development and functioning, stress reactivity, and immune function.²⁷ Indeed, there is some evidence that epigenetic changes in gene activation may help to account for some of the research findings discussed earlier in this article concerning the effects of early experience on developing stress reactivity. For example, the association between mothers' depression during pregnancy and greater cortisol reactivity in their children three months after birth was related to epigenetic changes in the activation of the glucocorticoid receptor gene.²⁸ Similarly, some of the adult health problems of people whose mothers were pregnant during the Dutch famine of 1944 may be related to a change in activation of the gene for insulin-like growth factor II (IGF2).²⁹ Thus epigenetics may be one reason that stress reactivity and other behaviors change in response to early adversity.

We don't know where the science of behavioral epigenetics will lead in understanding

behavioral development. It is clear, however, that gene activity is part of a surprisingly dynamic constellation of biological influences on behavioral development. Equally consequential, early experience is an important influence on gene activity, and an important feature of early experience is stress.

These considerations are relevant to the concept of *toxic stress*, which was recently adopted by the American Academy of Pediatrics (AAP).³⁰ In a policy statement, the AAP alerted the pediatric community to sources of toxic stress that may affect children and urged them to work to reduce these harmful influences. The value of reducing chronic, severe stress in children is self-evident, and the AAP's effort to enlist the pediatric community is admirable. To the extent that we understand toxic stress solely as a characteristic of the experiences that befall children, however, we overlook the child's own characteristics as factors that exacerbate or buffer the impact of stressful events. Harm from stress, in other words, is not only in the nature of the experience but also in the nature of the child. In addition, the concept of toxic stress misses one of the most important factors that can make these experiences toxic: their epigenetic effects, which can render some children less capable of adapting to cope with stress over time.

There is another way that the concept of toxic stress may simplify the effects of stress on children. It contributes to the expectation that the effects of stressful experiences can accumulate to eventually overwhelm children's coping capacities and thus contribute to the breakdown of their health, consistent with the concept of allostatic load.

Accumulation and overload is indeed one way that stressful events have their detrimental

impact. As we've seen, for example, infants and children in poverty, young children of chronically depressed mothers, and children who are abused show greater cortisol reactivity.³¹ In this manner, heightened cortisol activity—combined with its neurobiological, cardiovascular, and immunological correlates—contributes to long-term health and mental health problems.

But there is a second way that stress can harm children. Rather than fostering hyper-reactivity to stressful events, stress can make the body hyporesponsive; that is, it underreacts to stress. One way this occurs is in children's responses to acute stress: rather than reacting to stressful events with heightened cortisol activity, they instead show a lower cortisol response than other children do. Another way this occurs is in basal levels of cortisol throughout the day: rather than exhibiting the normal diurnal pattern of elevated morning cortisol followed by a gradual decline, they instead show a flat cortisol response from morning through night. Hyporesponsiveness has been found among children who live in homes characterized by domestic violence and mothers' emotional unavailability, and among preschoolers who live in foster care.³² This response pattern seems to reflect a stress system that shows signs of shutting down.

Hyperreactive and hyporesponsive stress responses are both disrupted patterns that arise from experiences of chronic stress with distinct risks to healthy development. Just as chronically high cortisol levels have many harmful consequences, including impaired immune function, chronically low cortisol levels can impair the body's ability to maintain appropriately high blood pressure and respond to stress with an increase in cardiovascular activity.³³ We don't know for certain

why some children manifest one disrupted pattern rather than the other. But one hypothesis is that the hyperreactive pattern is associated with recurrent threat and danger, and hyporesponsiveness is associated with the deprivation or withdrawal of caregiver support.³⁴ We also don't know the distinct behavioral characteristics that are associated with each pattern of stress response. Much more remains to be understood about how chronic stress affects children's development.

From what we do know, however, it is clear that the effects of chronic, severe stress on children's development are more complicated than simple concepts like toxic stress suggest. We must consider the nature of the event, children's individual vulnerability or resiliency, the availability of support from caregivers, and the effects of prior experiences on children's coping capacities. As the AAP policy statement recognizes, this web of interrelated factors makes it important to view at-risk children in the context of their experiential history and their social ecology. Children who experience chronic, severe stress may be biologically and psychologically less able to adapt and cope with new stresses when they occur, contrary to the idea that regular stress toughens people and increases their resiliency. The social ecology is also important because children's coping capacities are significantly affected by the availability of social support from adults who can act as caregivers. Research on the Louisiana child victims of Hurricane Katrina indicates, for example, that children who showed the best long-term recovery from this tragedy were in the care of adults who could provide support, while children fared much worse either when they lost contact with their parents or when their parents were so traumatized that they could no longer function as caregivers.³⁵

Studies like these, of course, are directly relevant to understanding multigenerational influences on child development. They illustrate how significantly children's ability to cope with stress relies on the support of caregivers. Unfortunately, they also illustrate how the stresses that affect children also have multigenerational impact, sometimes rendering the adults who could potentially provide support incapable of doing so. This is likely to be true not only when communities are beset by natural disasters, but also when they are economically impoverished, enmeshed in gang violence, or undermined in other ways. Indeed, when stressful events occur at the same time and compound one another—for example, when a family must cope with loss of income, parental depression, marital conflict, and moving to a different and more dangerous neighborhood in a short period of time—their impact is greater. These events affect not only children, but also the parents on whom children ordinarily rely for assistance, making the mobilization of two-generation efforts to support children much more challenging.

Plasticity

One reason that young organisms are more vulnerable to severe stress and other kinds of harm is the plasticity, or pliability, of their biological systems. Plasticity is the capacity of organisms to change with experience.³⁶ Biological and behavioral plasticity is greatest early in life, when the organism is developing most rapidly. It declines progressively with increasing age, as neural networks and behavioral patterns consolidate, although mature individuals retain some adaptive plasticity even at advanced ages. Early biological plasticity helps to explain why harmful experiences can have a more profound impact on the youngest children, whose immature systems are in their formative stages, than on

older children and adults, whose biological and behavioral systems have become consolidated. On the other hand, early plasticity also helps explain the remarkable pace of early-developing capacities, as the brain and other biological systems rapidly mature. Early biological plasticity, therefore, is a double-edged sword; it helps to explain why young children are affected so significantly by their experiences, for good or ill.

The early plasticity of the brain and other biological systems offers hope to those who aspire to help at-risk children. It suggests that even though early harm can undermine the organization of brain and behavioral systems, this disruption does not necessarily become immediately hard-wired to create dysfunction that cannot be changed. Because most of these systems remain relatively plastic (contrary to portrayals in the popular media of a fixed “brain architecture”), we may be able to intervene early in children's lives with experiences that help reorganize biological systems constructively. However, to capitalize on these opportunities, we must detect harm early. To be sure, we can intervene successfully at later ages. But later interventions are likely to require greater intensity (and cost) to overcome well-established neural networks or routinized behavior patterns that have consolidated over time. The fact that the plasticity of brain and behavioral functioning declines over time is one justification to focus on early experience, early screening, and early intervention when developmental problems are detected.

What kinds of rehabilitative interventions can have such effects? We can find clues in studies of interventions that have focused on at-risk children whose experiences of chronic adversity disrupted their biological stress systems. One such program, designed by

psychologist Philip Fisher of the University of Oregon and his colleagues, aimed to reduce the stress associated with foster care by easing young children's transitions to new foster homes and enhancing continuity of care.³⁷ After their earlier foster-care placements, these children showed the profile of cortisol hyporesponsiveness described earlier. The intervention was designed to promote warm, responsive, and consistent relationships between children and their new foster parents in which positive behavior was encouraged, problem behavior was reduced, and caregiver stress was lowered. The program included individualized sessions with child therapists, weekly playgroup sessions, and other child-focused services. Foster parents completed intensive training before the children's placement, and they continued to receive support and supervision in daily phone contacts and weekly group meetings, and through on-call assistance. The children's biological or adoptive parents also received special assistance to establish consistency with the care provided by foster parents and to ease transitional adjustments. The program was thus a two-generation intervention involving multiple adults who functioned as caregivers for the child. Over six to 12 months of treatment, children in the intervention group progressively showed patterns of HPA reactivity that resembled the normal patterns of a community comparison group of children who had not experienced abuse; a control group of children assigned to regular foster-care placements did not show such improvement.³⁸ The recovery of the children in the treatment group was directly linked to reductions in the foster parents' stress levels.³⁹

With a group of colleagues, Mary Dozier, a psychologist at the University of Delaware, designed another intervention to improve very young foster children's relationships

and behavioral competence by helping foster parents better interpret and respond to infants' signals, enhance affectionate behavior, and provide more reliable support for infants' self-regulation. After 10 weeks of the home-based program, infants and toddlers in foster care showed more typical daily patterns of HPA activity and more moderated cortisol reactivity to a stressor compared with a group of foster-care infants in a different treatment program.⁴⁰

Even though early harm can undermine the organization of brain and behavioral systems, this disruption does not necessarily become immediately hard-wired to create dysfunction that cannot be changed.

Nonexperimental studies of at-risk children paint a similar picture. In a study of families living in rural poverty, for example, another research group found that 24-month-old toddlers who had been exposed to chronic domestic violence were likely to have elevated cortisol reactions when presented with a challenging task. However, when mothers responded sensitively to their children—as recorded by the researchers when they observed the mothers and children together at seven, 15, and 24 months—this effect was buffered: children did not show such enhanced cortisol reactivity.⁴¹ This finding is consistent with other research on humans and animals that documents the social buffering

of children's responses to stress, primarily through support from parents.⁴²

The experimental studies with children in foster care show that time-delimited interventions can help to normalize the biological disruptions that occur when children are exposed to stress early in their lives. Of course, we need more research to confirm and expand on these findings. In particular, we need long-term studies that follow children in the intervention and comparison groups as they grow older; we need to see whether other researchers can replicate the findings with different groups of people; and we need studies that measure a wider range of biological and behavioral outcomes.

We also need to understand the limits of biological and behavioral plasticity, even early in life. For example, one study of children adopted from Romanian orphanages, where they were profoundly deprived of normal human relationships, found that after six and a half years of supportive adoptive care, children who had been adopted after less than four months in the institution had basal cortisol levels that resembled those of comparison children raised in families. However, children who had lived at the orphanage for eight or more months did not show such a recovery. In fact, the longer the children had been in the institution's care, the more likely they were to show evidence of enduring cortisol disruption.⁴³

These studies of children with adoptive and foster parents are promising, however, for at least two reasons. First, they expand the concept of two-generation interventions for at-risk children by targeting caregivers who are not biological parents. Such caregivers may also be important for other children in difficult circumstances whose parents are

either not available or not capable of providing the stress-buffering support their children need, even with outside assistance. Indeed, parents may themselves be the primary source of children's stress. In such circumstances, it may be especially important for two-generation programs to mobilize other adults in children's lives, such as grandparents, child-care providers, and teachers.

Second, these programs demonstrate that well-designed early interventions can produce parallel advances in behavior and biology. Research in developmental biology underscores that the connection between biology and behavior is complex, and biological changes often occur without the expected behavioral correlates, or vice versa. In both the Dozier study and the Fisher study, however, alongside their biological measurements, the researchers obtained measures of behavioral change that can be viewed as further indicators of the programs' efficacy. In the Dozier intervention, infants and toddlers showed greater evidence of attachment to their foster parents. The Fisher intervention saw a similar gain in secure attachment behavior, and foster-care placements were more likely to succeed.⁴⁴ Because insecure attachment is associated with disturbed biological stress responses, the increases in secure attachment and the improved HPA reactivity in each study together indicate that the intervention was effective. In the end, researchers and practitioners should measure both behavioral and biological outcomes when they evaluate promising interventions to ameliorate the effects of early stress.

Even if they do not measure both behavioral and biological outcomes, evaluation researchers can focus on behaviors that are theoretically tied to the biological consequences of early stressful experiences. For example,

one intervention for at-risk young children in poverty focused not on HPA reactivity (which, as we have seen, can contribute to self-regulatory problems for children experiencing stress), but on the difficulty in regulating their own behavior that at-risk young children in poverty commonly experience. At the beginning of the school year, the Chicago School Readiness Project gave Head Start teachers specialized training in classroom management strategies designed to help lower-income preschoolers better regulate their own behavior. When the school year ended, children in the treatment group showed fewer disruptive behaviors, less impulsiveness, and better preacademic performance than did children from classrooms where teachers underwent a different training regimen.⁴⁵ These findings are consistent with the results of other early intervention programs designed to help low-income preschool children with behavioral problems, especially the self-regulatory difficulties that can undermine academic success.⁴⁶ Significantly, these benefits for young children were obtained without parallel efforts to improve the quality of family functioning, which is sometimes the source of stress for at-risk young children. Once again, then, we see that two-generation programs can improve children's outcomes by targeting their relationships with adults who are not their biological parents.

Taken together, the studies I've discussed suggest ways to design two-generation interventions to ease the consequences of chronic stress for young children. In particular, they illustrate the value of an integrated biological-behavioral approach that considers children's needs from the standpoint of both stress neurobiology and behavioral competence. From a biological perspective, children exposed to chronic stress need rehabilitative experiences that minimize threat, maximize

consistency and support, and strengthen self-regulatory skills. From a behavioral perspective, these biological remediations are further supported by an environment of relational warmth and responsiveness in which children can begin experiencing self-directed mastery. Aside from their focus on early intervention, the programs I've discussed are also distinguished by their emphasis on relationships between children and adults in which these various elements of support can be integrated. Whether two-generation programs target parents, preschool teachers, foster parents, or biological parents, focusing on relationships is likely to enhance their success.

The research on biological and behavioral plasticity has another implication for two-generation interventions designed to improve developmental outcomes. Interventions that seek to change parents' conduct in an effort to improve their children's wellbeing must confront the fact that adults' behavioral and biological plasticity is more limited than children's. In "risky families," parents as well as children experience chronic stress, and parents are likely to exhibit the same neuroendocrine, immunological, and cardiovascular correlates of persistent stress that their children do.⁴⁷ The difference is that persistent stress over time has caused the adults' biological and behavioral systems to become more consolidated and less flexible. Parents are also likely to have developed a network of personal beliefs—attributions, self-referential beliefs, and social schemas—and behavioral routines that reinforce their biological patterns of threat vigilance, quick stress reactivity and poor self-regulation. In short, the early plasticity of biological and behavioral systems benefits young children, and the decline of plasticity as we grow older can impede interventions for their parents. Adults who have lived with chronic stress for a long

time are likely to have adapted to a life of challenge and adversity in ways that are not well-suited to sensitive, responsive parenting.

It is remarkable, therefore, that interventions to improve parenting behavior and thereby strengthen children's development can sometimes show such positive results. There is increasing evidence that carefully designed interventions, with goals suited to specific family needs, can promote changes in caregiver behavior that benefit young children.⁴⁸ Moreover, research is showing that preventive interventions to support the mental and emotional health of children in poverty are also yielding promising success.⁴⁹ By integrating our understanding of both the biological and behavioral consequences of chronic stress, we can carefully design interventions to better meet the needs of young children and their families. And we can conclude from these studies that young adult parents of at-risk children retain sufficient adaptive plasticity to promote beneficial change for the benefit of their offspring.

Conclusions

One theme of the articles in this issue of *Future of Children* is that adverse environments create stress that alters children's development. I have focused on the biological effects of stress on children to better understand how adversity "gets under the skin" to alter children's biological functioning and, partly as a consequence, their behavior. Of course, stress gets under the skin of parents and other caregivers, which is why two-generation interventions that strengthen child development are also important for adults. Because major sources of stress in young children's lives arise from family experience, and because the quality of parental care is children's major resource for buffering stress,

we must consider multigenerational interventions to address the multigenerational origins of children's stress. I use the term "multigenerational" deliberately. At times, three-generation interventions may be necessary, for example, to enlist a grandparent to help a parent provide the kind of sensitive care that young children need for healthy growth.

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What are the benefits of taking biology into account when we examine how stress affects early development? What does a biological approach contribute that an exclusive focus on behavioral development does not? Biological markers of disturbance from adverse early experiences are important because they provide a multilevel analysis of how stress affects children in which behavioral disruption and biological disruption mutually underlie young children's adaptive difficulties. Looking at biology and behavior together, we can better understand the causes and consequences of stress, the benefits and costs of behavioral plasticity, and, most of all,

the potential avenues for early intervention and remediation.

For this reason, one important avenue for future research is to look more deeply into the biological consequences of promising interventions to benefit at-risk young children. The intervention studies discussed in this article provide encouraging leads. But we need to expand the range of behavioral and biological markers that could tell us whether an intervention is achieving the desired developmental outcomes, so that we can use biological as well as behavioral indices in field studies of interventions for at-risk children and families. As one illustration, a pair of researchers showed that after three and a half years of participation in a conditional cash-transfer antipoverty program in Mexico, preschool children showed lower basal cortisol levels, and children of the most depressed mothers showed the greatest benefit.⁵⁰

In another instance, using data from the National Health and Nutrition Examination Survey to study mothers with two or more children, two economists showed that, over time, the 1993 expansion of the Earned Income Tax Credit significantly reduced the levels of multiple biological indicators that reflect allostatic stress and inflammation.⁵¹ In yet another example, a group of researchers reported that an intervention program for at-risk four-year-olds was effective in improving cortisol reactivity, and this led to reductions in aggression by the follow-up assessment.⁵² Studies like these are important not because biological outcomes are more important than behavioral ones (indeed, biological markers can be difficult to interpret without corresponding behavioral data), but because they give us added insight into the developmental processes that can make an intervention more or less effective.

The research discussed in this article also underscores that relationships are crucial to normalizing at-risk children's biological and behavioral systems. The Fisher and Dozier studies both emphasize strengthening young children's security in relationships by improving caregivers' responsiveness and reducing their stress. Nonexperimental studies also show the importance of secure relationships early in life. We've seen, for example, that sensitivity on the part of adults buffers the effects of young children's exposure to domestic violence, that negative relationship influences (such as mothers' "emotional unavailability" or fighting between parents) contributes to HPA hyperreactivity, and that harsh parenting produces epigenetic changes in gene expression that are related to conduct problems. Taken together, young children's early relationships seem to be the most important context for shaping individual differences in stress reactivity and coping. These early relationships can affect young children in many ways: solicitude and support may be reliable or unreliable; they may feel protected from or exposed to threats; adults may or may not respond to their specific needs; and they may or may not feel a generalized sense of security.⁵³ Unpacking these diverse relational influences can help us develop better theories, and strengthening the security and responsiveness of young children's early relationships seems to be a promising way to make interventions more effective.

If young children are born into a world of unknowns, they quickly begin to understand the characteristics of those who care for them. Those characteristics guide them biologically and behaviorally to prepare for a life of security or adversity. This is the foundation of two-generation interventions for young children.

ENDNOTES

1. For a more detailed overview of these topics, consult Ross A. Thompson, "Relationships, Regulation, and Early Development," in *Handbook of Child Psychology and Developmental Science*, 7th ed., ed. Richard M. Lerner, vol. 3, *Social and Emotional Development*, ed. Michael E. Lamb, and Cynthia Garcia-Coll (New York: Wiley, forthcoming).
2. Patricia K. Kuhl, "Is Speech Learning 'Gated' by the Social Brain?" *Developmental Science* 10 (2007): 110–20, doi: 10.1098/rstb.2007.2154; Patricia K. Kuhl et al., "Phonetic Learning as a Pathway to Language: New Data and Native Language Magnet Theory Expanded (NLM-e)," *Philosophical Transactions of the Royal Society London B: Biological Sciences* 363 (2008): 979–1000.
3. Janet F. Werker, "Baby Steps to Learning Language," *Journal of Pediatrics* 143 (2003): doi: 10.1067/S0022-3476(03)00403-7.
4. For an introduction to this extensive literature, consult L. H. Lumey et al., "Cohort Profile: The Dutch Hunger Winter Families Study," *International Journal of Epidemiology* 36 (2007): 1196–1204, doi: 10.1093/ije/dym126.
5. Curt A. Sandman et al., "Exposure to Prenatal Psychobiological Stress Exerts Programming Influences on the Mother and Her Fetus," *Neuroendocrinology* 95 (2012): 7–21, doi: 10.1159/000327017.
6. Tim F. Oberlander et al., "Prenatal Exposure to Maternal Depression, Neonatal Methylation of Human Glucocorticoid Receptor Gene (NR3C1), and Infant Cortisol Stress Responses," *Epigenetics* 3 (2008): 97–106, doi: 10.4161/epi.3.2.6034
7. Claudia Buss et al., "Maternal Cortisol over the Course of Pregnancy and Subsequent Child Amygdala and Hippocampus Volumes and Affective Problems," *Proceedings of the National Academy of Sciences* 109 (2012): E1312–19, doi: 10.1073/pnas.1201295109.
8. Marta Weinstock, "The Long-Term Behavioural Consequences of Prenatal Stress," *Neuroscience and Biobehavioral Reviews* 32 (2008): 1073–86, doi: 10.1016/j.neubiorev.2008.03.002.
9. Sonia J. Lupien et al., "Effects of Stress Throughout the Lifespan on the Brain, Behaviour, and Cognition," *Nature Reviews Neuroscience* 10 (2009): 434–45, doi: 10.1038/nrn2639.
10. Yvonne M. Ulrich-Lai and James P. Herman, "Neural Regulation of Endocrine and Autonomic Stress Responses," *Nature Reviews Neuroscience* 10 (2009): 397–409, doi: 10.1038/nrn2647.
11. Clancy Blair et al., "Allostasis and Allostatic Load in the Context of Poverty in Early Childhood," *Development and Psychopathology* 23 (2011): 845–57, doi: 10.1017/S0954579411000344.
12. Melissa Sturge-Apple et al., "Interparental Violence, Maternal Emotional Unavailability, and Children's Cortisol Functioning in Family Contexts," *Developmental Psychology* 48 (2012): 237–49, doi: 10.1037/a0025419.
13. Sonia J. Lupien et al., "Child's Stress Hormone Levels Correlate with Mother's Socioeconomic Status and Depressive State," *Biological Psychiatry* 48 (2000): 976–80, doi: 10.1016/S0006-3223(00)00965-3.
14. Clancy Blair and C. Cybele Raver, "Child Development in the Context of Adversity: Experiential Canalization of Brain and Behavior," *American Psychologist* 67 (2012): 309–18, doi: 10.1037/a0027493; Gary W. Evans and Pilyoung Kim, "Childhood Poverty, Chronic Stress, Self-Regulation, and Coping," *Child Development Perspectives* 7 (2013): 43–8, doi: 10.1111/cdep.12013.

15. Ulrich-Lai and Herman, "Neural Regulation."
16. Gregory E. Miller, Edith Chen, and Karen J. Parker, "Psychological Stress in Childhood and Susceptibility to the Chronic Diseases of Aging: Moving toward a Model of Behavioral and Biological Mechanisms," *Psychological Bulletin* 137 (2011): 959–97, doi: 10.1037/a0024768.
17. Andrea Danese and Bruce S. McEwen, "Adverse Childhood Experiences, Allostasis, Allostatic Load, and Age-Related Disease," *Physiology & Behavior* 106 (2012): 29–39, doi: 10.1016/j.physbeh.2011.08.019.
18. Camelia E. Hostinar and Megan Gunnar, "The Developmental Effects of Early Life Stress: An Overview of Current Theoretical Frameworks," *Current Directions in Psychological Science* 22 (2013): 400–6, doi: 10.1177/0963721413488889.
19. Megan Gunnar and Karina Quevedo, "The Neurobiology of Stress and Development," *Annual Review of Psychology* 58 (2007): 145–73, doi: 10.1146/annurev.psych.58.110405.085605.
20. Lupien et al., "Effects of Stress."
21. Richard A. Dienstbier, "Arousal and Physiological Toughness: Implications for Mental and Physical Health," *Psychological Review* 96 (1989): 84–100, doi: 10.1037/0033-295X.96.1.84.
22. Camelia E. Hostinar, Regina M. Sullivan, and Megan R. Gunnar, "Psychobiological Mechanisms Underlying the Social Buffering of the Hypothalamic-Pituitary-Adrenocortical Axis: A Review of Animal Models and Human Studies across Development," *Psychological Bulletin* 140 (2014): 256–282, doi: 10.1037/a0032671.
23. Avshalom Caspi et al., "Role of Genotype in the Cycle of Violence in Maltreated Children," *Science* 297 (2002): 851–4, doi: 10.1126/science.1072290.
24. Marian J. Bakermans-Kranenburg and Marinus H. van Ijzendoorn, "Gene-Environment Interaction of the Dopamine D4 Receptor (DRD4) and Observed Maternal Insensitivity Predicting Externalizing Behavior in Preschoolers," *Developmental Psychobiology* 48 (2006): 406–9, doi: 10.1002/dev.20152.
25. For a helpful introduction to this field, consult Michael J. Meaney, "Epigenetics and the Biological Definition of Gene x Environment Interactions," *Child Development* 81 (2010): 41–79, doi: 10.1111/j.1467-8624.2009.01381.x.
26. Karl M. Radtke et al., "Transgenerational Impact of Intimate Partner Violence on Methylation in the Promoter of the Glucocorticoid Receptor," *Translational Psychiatry* 1: e21, doi: 10.1038/tp.2011.21.
27. Oksana Yu. Naumova et al., "Differential Patterns of Whole-Genome DNA Methylation in Institutionalized Children and Children Raised by Their Biological Parents," *Development and Psychopathology* 24 (2012): 143–55, doi: 10.1017/S0954579411000605.
28. Oberlander et al., "Prenatal Exposure."
29. Lumey et al., "Cohort Profile."
30. Andrew S. Garner et al., "Early Childhood Adversity, Toxic Stress, and the Role of the Pediatrician: Translating Developmental Science into Lifelong Health," *Pediatrics* 129 (2012): e224–31, doi: 10.1542/peds.2011-2662.
31. Dante Cicchetti and Fred A. Rogosch, "The Impact of Child Maltreatment and Psychopathology on Neuroendocrine Functioning," *Development and Psychopathology* 13 (2001): 783–804.

32. Sturge-Apple et al., "Interparental Violence"; Philip A. Fisher, Mark J. Van Ryzin, and Megan R. Gunnar, "Mitigating HPA Axis Dysregulation Associated with Placement Changes in Foster Care," *Psychoneuroendocrinology* 36 (2011): 531–9, doi: 10.1016/j.psyneuen.2010.08.007; Mary Dozier et al., "Foster Children's Diurnal Production of Cortisol: An Exploratory Study," *Child Maltreatment* 11 (2006): 189–97, doi: 10.1177/1077559505285779.
33. Jacqueline Bruce et al., "Early Adverse Care, Stress Neurobiology, and Prevention Science: Lessons Learned," *Prevention Science* 14 (2013): 247–56, doi: 10.1007/s11121-012-0354-6.
34. Ibid.
35. Mindy E. Kronenberg et al., "Children of Katrina: Lessons Learned about Postdisaster Symptoms and Recovery Patterns," *Child Development* 81 (2010): 1241–59, doi: 10.1111/j.1467-8624.2010.01465.x.
36. Brian Kolb, Robbin Gibb, and Terry E. Robinson, "Brain Plasticity and Behavior," *Current Directions in Psychological Science* 12 (2003): 1–5, doi: 10.1111/1467-8721.01210.
37. Fisher et al., "Mitigating HPA Axis Dysregulation"; Philip A. Fisher et al., "Effects of a Therapeutic Intervention for Foster Preschoolers on Diurnal Cortisol Activity," *Psychoneuroendocrinology* 32 (2007): 892–905, doi: 10.1016/j.psyneuen.2007.06.008.
38. Ibid.
39. Philip A. Fisher and Mike Stoolmiller, "Intervention Effects on Foster Parent Stress: Associations with Child Cortisol Levels," *Development and Psychopathology* 20 (2008): 1003–21, doi: 10.1017/S0954579408000473.
40. Mary Dozier et al., "Effects of an Attachment-Based Intervention on the Cortisol Production of Infants and Toddlers in Foster Care," *Development and Psychopathology* 20 (2008): 845–59, doi: 10.1017/S0954579408000400; Mary Dozier et al., "Developing Evidence-Based Interventions for Foster Children: An Example of a Randomized Clinical Trial with Infants and Toddlers," *Journal of Social Issues* 62 (2006): 767–85, doi: 10.1111/j.1540-4560.2006.00486.x.
41. Leah C. Hibell et al., "Maternal Sensitivity Buffers the Adrenocortical Implications of Intimate Partner Violence Exposure During Early Childhood," *Development and Psychopathology* 23 (2011): 689–701, doi: 10.1017/S0954579411000010.
42. Megan R. Gunnar and Bonny Donzella, "Social Regulation of the Cortisol Levels in Early Human Development," *Psychoneuroendocrinology* 27 (2002): 199–200, doi: 10.1016/S0306-4530(01)00045-2.
43. Megan R. Gunnar et al., "Salivary Cortisol Levels in Children Adopted from Romanian Orphanages," *Development and Psychopathology* 13 (2001): 611–28, doi: 10.1017/S095457940100311X.
44. Mary Dozier et al., "Effects of a Foster Parent Training Program on Young Children's Attachment Behaviors: Preliminary Evidence from a Randomized Clinical Trial," *Child and Adolescent Social Work Journal* 26 (2009): 321–32, doi: 10.1007/s10560-009-0165-1; Philip A. Fisher and Hyoun K. Kim, "Intervention Effects on Foster Preschoolers' Attachment-Related Behaviors from a Randomized Trial," *Prevention Science* 8 (2007): 161–70, doi: 10.1007/s11121-007-0066-5; Philip A. Fisher, Bert Burraston, and Katherine Pears, "The Early Intervention Foster Care Program: Permanent Placement Outcomes from a Randomized Trial," *Child Maltreatment* 10 (2005): 61–71, doi: 10.1177/1077559504271561.

45. C. Cybele Raver et al., "Targeting Children's Behavior Problems in Preschool Classrooms: A Cluster-Randomized Controlled Trial," *Journal of Consulting and Clinical Psychology* 77 (2009): 302–16, doi: 10.1037/a0015302; C. Cybele Raver et al., "CSRPs Impact on Low-Income Preschoolers' Preacademic Skills: Self-Regulation as a Mediating Mechanism," *Child Development* 82 (2011): 362–78, doi: 10.1111/j.1467-8624.2010.01561.x.
46. Karen L. Bierman et al., "Executive Functions and School Readiness Intervention: Impact, Moderation, and Mediation in the Head Start REDI Program," *Development and Psychopathology* 20 (2008): 821–43, doi: 10.1017/S0954579408000394.
47. Rena L. Repetti, Shelley E. Taylor, and Teresa E. Seeman, "Risky Families: Family Social Environments and the Mental and Physical Health of Offspring," *Psychological Bulletin* 128 (2002): 330–66, doi: 10.1037//0033-2909.128.2.330.
48. See review in Blair and Raver, "Child Development in the Context of Adversity."
49. Hirokazu Yoshikawa, J. Lawrence Aber, and William R. Beardslee, "The Effects of Poverty on the Mental, Emotional, and Behavioral Health of Children and Youth," *American Psychologist* 67 (2012): 272–84, doi: 10.1037/a0028015.
50. Lia C. H. Fernald and Megan R. Gunnar, "Poverty-Alleviation Program Participation and Salivary Cortisol in Very Low-Income Children," *Social Science & Medicine* 68 (2009): 2180–9, doi: 10.1016/j.socscimed.2009.03.032.
51. William N. Evans and Craig L. Garthwaite, "Giving Mom a Break: The Impact of Higher EITC Payments on Maternal Health" (working paper, National Bureau of Economic Research, Cambridge, MA, 2010), <http://www.nber.org/papers/w16296.pdf>.
52. Colleen R. O'Neal et al., "Understanding Relations among Early Family Environment, Cortisol Response, and Child Aggression via a Prevention Experiment," *Child Development* 81 (2010): 290–305, doi: 10.1111/j.1467-8624.2009.01395.x.
53. Thompson, "Relationships, Regulation."