NATIONAL SCIENTIFIC COUNCIL ON THE DEVELOPING CHILD

Finding the Balance:
Transforming How We Think About the Body's Response to Stress in Early Childhood

WORKING PAPER 18

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Protective Factors, Individual Variation, and Developmental Timing Make the Difference in How Stress Affects Young Children

When a neighborhood or community supports the health and development of its youngest children, it improves not only childhood experiences but also lifelong physical and mental well-being. All parents and other adults who care for young children can promote healthy development through stable, nurturing, and responsive relationships. But personal relationships alone are not enough. The early foundations of child development and a lifetime of good health also rely on the broader environment, which includes *both* infrastructure that addresses basic needs where families live *and* policies that promote the well-being of people at all ages.

The places where children live span a continuum from densely populated, urban neighborhoods to suburban, small-town, and rural communities. In this paper, the words "neighborhood" and "community" are used interchangeably to refer to "place." The protective factors that are available and accessible for children vary across this wide range of settings. Risk factors that threaten the well-being of children and their families also vary considerably but are especially concentrated in areas that bear the burdens of intergenerational poverty and systemic racism. These include differential access to economic opportunity and nutritious food, discriminatory housing policies, unequal school funding formulas, disparate enforcement of environmental protections, and variable confidence in public safety. These persistent inequalities are the result of policy decisions that have been made over time and continue to be reinforced, which means that providing more equitable opportunities for all children and families requires making different policy decisions.[1]

Stress is an unavoidable reality of life across all socioeconomic, racial, and ethnic groups. Honing the biological response to adversity is key to protecting health and development, from a relatively manageable challenge all the way to a life-threatening experience. The stress response system is our body's most important first responder—and the ability of this system to provide lifelong protection is shaped early in life.

While significant adversity like the ongoing stresses of community violence, racism, or extreme poverty poses a serious threat to healthy development, avoiding challenging situations altogether is not a viable strategy for developing an effective stress response system and building resilience. Making reliable supports and opportunities available across a community enables families to provide the stable, predictable, and supportive environment young children need to learn how to deal with challenges and develop a healthy response to stress. Both responsive caregiving and supportive communities play an important role in strengthening the internal stress-response system, which sets children up for robust development and short-term school success, better health across the lifespan, and full participation in thriving communities as adults.

The stress response system is our body's most important first responder—and the ability of this system to provide lifelong protection is shaped early in life.

Beginning in the prenatal and early childhood periods, the brain, immune system, metabolic regulation, and other biological systems are building their capacities to respond to challenges and threats. When this happens in a stable and nurturing environment that includes manageable adversity, it strengthens

the foundations of resilience. But when sources of adversity are numerous or overwhelming, and protective factors are relatively limited, the risk of problems increases in early development (including social, emotional, cognitive, and behavioral domains), as well as in adult physical and mental health (including hypertension, heart disease, diabetes, and depression).[2,3] Importantly, that risk can be reduced and harm mitigated if effective supports are provided as early as possible.

Early experiences and exposures influence the way all biological systems develop. Positive experiences lay the groundwork for the development of the brain, immune, and metabolic functions to adapt well to challenges faced now and in the future. Excessive negative experiences that occur early in life can prime these systems to remain on high alert, creating an overload condition in the body that increases the risk of disruptions in early development, later difficulties in school, and long-term problems in social and economic mobility, as well as both physical and mental health.

By strengthening protective factors and addressing individual variation in sensitivity, we can prevent stress-related consequences for large numbers of children now and generate greater impacts on well-being as a society in the future.

It's critically important to underscore that *increased risk means that later problems may be more likely, but not that they are inevitable*. Both extensive research and a wealth of experience support the fact that how people respond to stress varies. Understanding how this variation is influenced by protective factors, individual differences in sensitivity to adversity, and developmental timing can help redirect financial and human resources to those who need extra support.

Between a well-adapted, healthy stress response and an overloaded one lies a wide spectrum of physiological reactions to stress-inducing situations. Key factors that shape how stress affects a young child's development (some of which are addressed in more detail later) include:

- Individual variation in children's sensitivity to both hardships and supports;[4]
- The intensity, duration, frequency,[5] and predictability[6] of the stressor;
- When the experiences or exposures occur during development;[7]
- Burdens and threats experienced by parents or other caregivers that affect the provision of a stable, secure environment for children;[8]
- The availability and quality of social capital (i.e., mutual aid, a shared sense of belonging, and informal supports from neighbors) at a community level that prevent or mitigate adversity;[9] and
- The distinctive burdens and threats associated with intergenerational poverty, racism, and other structural inequities that perpetuate inequalities in opportunity.[1]

Understanding the wide range of children's responses to stress requires a clear picture of the biological systems that detect threat, mobilize responses, and restore balance. The sections that follow describe the core components of that stress response system and explain how early experiences calibrate its activity, laying the foundation for increased resilience or a higher chance of negative outcomes across the lifespan. These insights help us understand that, by strengthening protective factors and addressing individual variation in sensitivity, we can prevent stress-related consequences for large numbers of children now and generate greater impacts on well-being as a society in the future.

Re-Examining the Concept of Toxic Stress

In 2005, the National Scientific Council on the Developing Child produced its third Working Paper, titled *Excessive Stress Disrupts the Architecture of the Developing Brain.*[10] That document coined the term *toxic stress* and explained its distinction from "positive" and "tolerable" stress. These concepts helped build public understanding of the disruptive impacts of significant stress on the developing brain and helped increase urgency and support for policies and practices that protect young children from excessive activation of their stress response systems.[11]

Unfortunately, with that urgency came an overly simplified view that *all* stress is dangerous. Continuing advances in the biology of adversity over the past two decades are pushing us to move beyond an unproductive and simplistic dichotomy between "stress builds character" or "stress is bad." While scientific consensus is clear that persistent overactivation of the stress response system can have negative effects on early development and lifelong health, research also shows how successful adaptation to a range of experiences is important to the development of well-regulated biological responses that are essential for resilience.

Building on two science-informed revisions of Working Paper #3 (in 2009 and again in 2014), this new Working Paper #18 addresses two objectives. The first is to build understanding of *both* the protective benefits *and* the disruptive effects of activating the body's stress response system and to make this science *actionable* for policymakers, community leaders, and service providers. An equally important aim is to promote broader recognition of the importance of community-level protective factors *as well as* responsive caregiving for preventing, reducing, or mitigating the adverse effects of excessive stress activation on the early foundations of lifelong physical and mental health. This latter insight is particularly critical given the longstanding and still-dominant mindset in the early childhood field that places the burden of protection primarily on families, despite their limited capacity to overcome broader systemic issues.

The updated knowledge presented in this Working Paper is intended to inform fresh thinking and new approaches to family and community sources of stress and develop more effective policies and programs to protect children facing significant adversity.

React, Adapt, Restore: How the Stress Response Works

The ability to cope with unfamiliar or potentially threatening situations, such as new experiences or physical danger, is essential to survival. The body must be able to react quickly to a wide set of challenges, ranging from physical wounds, infections, and injuries to the *lack* of essentials like adequate nutrition, clean water, or (for infants and young children) reliable, responsive interactions with adults.[12] Unpredictable environments, in particular, are stress-provoking and can disrupt the maturation of specific brain networks early in life.[13,14] The capacity to *react* to both psychological and physical threats and *adapt* to the expectation of similar experiences in the future is driven by specific brain circuits, immune responses, and other biological systems.

As early as infancy, the stress response system is activated by unpredictable experiences that cause fear, discomfort, frustration, or pain. These experiences stimulate multiple physiological reactions designed to protect the body from physical harm caused by wounds, extreme temperatures, or infections, among other things. These same systems are also activated by *psychological* and *emotional* threats, including disruptions of predictable patterns in an infant's daily life. Faced with either physical or psychological threats, brain cells (neurons) respond with changes that increase vigilance and attention; blood flow is redirected to other organs that are critical for responding to danger (e.g., muscles to fight or run); energy production reorients to help cells and organs adapt to a threatening environment; and the immune system activates to promote wound healing and resistance to infection. Without these automatic, protective responses, our bodies would be much more vulnerable, even when facing adversities that are typically seen as minor, such as a scraped knee or a snarling dog.[3]

Threat-response systems also have built-in mechanisms to turn off after activation, which is essential for returning to a normal, resting state and *restoring* the delicate balance of healthy functioning that the body needs for long-term physical and mental well-being.[15] As this cycle repeats, these systems become better prepared for similar challenges in the future, as they adapt to both responding to threats and returning to baseline functioning.

In contrast, if the stress response is chronically activated at high levels, it can cause adaptations in the developing brain, immune function, and other biological systems that are beneficial in the short term but lead to increased risk for cardiovascular disease, diabetes, depression, cancer, and other chronic diseases in the long term, as well as a shorter lifespan. In such circumstances, the stress response system adapts to being continuously on high alert but pays a price for relatively rare returns to a normal baseline, which are essential for sound physical and mental health.

Among the physiological systems that protect us from harm, the following three have broad impacts across the brain and the rest of the body:

The fight/flight/freeze response (known by scientists as the sympathetic-adrenomedullary or SAM system) surges adrenaline into circulation from the adrenal glands and is key to a quick defense. That response begins with increases in heart rate and blood pressure and helps liberate energy from fat stores to support a rapid response.[16]

The stress hormone system (known as the hypothalamic-pituitary-adrenocortical axis, or HPA axis) is centered on cortisol,

a powerful steroid hormone that occurs naturally in the body. Cortisol activates many defensive processes, including releasing long-term energy stores from muscles to sustain prolonged battles for survival, regulating immune responses so they do not overreact, and shaping brain function so it "remembers" threats and reacts to them faster the next time.[17,18] As part of the process of adapting to the environment, this system also causes changes in gene expression that regulate how much or little cortisol will be produced in the future.[19,20] Although many people think of cortisol as synonymous with the stress response system, it is important to underscore that it is only one of its many components.

The immune response, when activated by stressors, helps the body respond quickly to immediate threats. It increases the number of immune cells in the bloodstream, which improves the body's ability to detect infections or other hazards. Stress also boosts levels of **cytokines** (molecules that stimulate inflammation), which play important roles in both fighting infection and promoting healing. Stress can also cause immune cells from outside the central nervous system to enter the brain.[21] This increase in inflammation can influence how certain brain regions function, especially those involved in regulating emotions, processing rewards, and making decisions. In many circumstances, these changes can help the brain handle stressful situations more effectively.[22] In contrast to its protective benefits in an *acute* situation, however, the potentially disruptive effect of *chronic* inflammation on the brain includes a higher risk for depression and Alzheimer's disease later in life. Long-term risks of excessive inflammation affecting other organ systems include many of the most highly prevalent (and most costly) chronic health impairments, including heart disease, hypertension, stroke, diabetes, arthritis, autoimmune disorders, and various forms of cancer.[23]

Although rapid activation of these mechanisms is essential for protecting against significant harm, all of these systems are designed to wind down and restore the body's balance after it has successfully adapted to an acute challenge or threat (or when the threat no longer exists). Increases in heart rate and muscle tone associated with the SAM system are typically countered by the "rest and digest" system (what scientists refer to as the **vagal system**), which conserves energy and maintains vital bodily functions.[24] Increases in cortisol stimulate other mechanisms that then *inhibit* its production, allowing the body time to clear it from circulation.[15] Increases in immune activity often initiate countervailing actions that prevent the system from overactivation. Adequate sleep with consistent duration and quality is also an important contributor to the effectiveness of the **"rest and digest" system**, which helps restore equilibrium to these biological functions.[25] These mechanisms return the body to normal, baseline functioning when stress systems are activated infrequently and/or to a modest degree.

A complex set of interrelated brain circuits controls these interactive systems.[26,27] Some potential stressors elicit a response even if the individual only *interprets* a situation as threatening and uncontrollable. For example, meeting new people can be unsettling for young children who are shy, while extroverted children find it fun. Unpredictable signals from the environment around a baby or young child that break the patterns the brain has come to expect also threaten the sense of safety and activate the stress response.[14] In each case, brain circuits that process information about what is about to happen send messages throughout the body, initiating all of these responses.

Understanding the Continuum from Protection to Disruption

Activation of the body's stress response system is designed to be protective and is essential for survival. However, when this activation exceeds reasonable limits, either in magnitude or duration, it can overload the body and prevent it from returning to baseline and promoting healthy functioning.[28] Between these two alternatives, there is a broad continuum of physiological reactions and effects on the body, ranging from short-term protection to long-term harm.

Much of this continuum can be described as a **Positive Stress Response.** Within this healthy range, activation of the stress response stimulates the developing brain and other biological systems to go on alert, deal with a challenge, and return to a resting state. Over time, this repeated pattern develops a healthy, protective stress response. In contrast, the persistent *absence* of experiences, as in cases of significant neglect, leads to a *diminished* stress response, which is detrimental to the development of coping skills that are essential for effective learning, emerging social-emotional capacities, and lifelong physical and mental health.[29,30,31]

Multiple developing systems (e.g., brain, immune, metabolic, and cardiac, among others) are continuously "reading" the environment and adjusting to promote internal stability through a process called **homeostasis**. When the body adapts to manage a threat (for example, by increasing blood pressure in response to a stressful experience), scientists call this *allostasis*, which refers to the body's attempt to protect itself by temporarily moving out of the normal range before returning to its resting state. Only if the response to threat or hardship is too intense or prolonged will this result in the potentially damaging condition known as **allostatic load** or **overload** (e.g., if blood pressure remains too high for too long, it can damage arteries, increasing the risk of a heart attack or stroke).[12]

Extreme cases of allostatic overload can be described as a **Toxic Stress Response.** This is the strong, frequent, and prolonged activation of the body's stress response systems resulting from experiences that are typically unpredictable and difficult to control. In these situations, especially during the first 2-3 years after birth, the regions of the brain involved in fear, anxiety, and impulsive responses may *overproduce* neural connections while those regions dedicated to reasoning, planning, and behavioral control may produce fewer connections.[32] High levels and long duration of a toxic stress response, especially during the early years of life, can also reset the stress system so it responds at a lower threshold to later events that might not prompt a comparable biological reaction in others.[19,20] In such cases, the stress response system activates more frequently and for longer periods than necessary, like revving a car engine in a driveway for hours every day rather than just when it's needed to pass a truck on a highway. This excessive activation has a wear-and-tear effect on the body that can lead to significant, harmful psychological and physical health conditions over time.[17] When the body reaches this kind of "stress overload" condition, it is making a trade-off—survival now but at a later cost.

Preventing the body's stress response from becoming overloaded in these circumstances typically depends on strategies that mobilize a range of protective factors. These include reducing the severity and duration of whatever is causing excessive stress system activation and making supportive relationships readily and reliably available. Many early childhood programs also support the development of individualized

capacities that strengthen resilience in each child, such as teaching skills to regulate emotions and connecting children and their families to counseling services. Above and beyond the benefits of services focused directly on children and their caregivers, improving community conditions and strengthening neighborhood support for families facing significant adversity create a healthier environment for children *and* help reduce caregivers' stress, which enables them to provide more consistent, nurturing, and predictable support for children. Either separately or (more often) together, these protective influences can make the difference between a stress response that becomes toxic and one that returns to baseline without causing lasting harm.[10]

A wide range of stressors, from brief, mild challenges to severe, long-lasting adversity, influence the intensity of the body's response. For example, the more moderate end of the spectrum might include brief separations while at childcare, getting frustrated and/or being upset when told "no," or falling down and experiencing a mild bump that scares more than it hurts physically. Some experiences warrant more concern (e.g., a serious injury or illness, unstable home environment, moving to another town or school, or experiencing bullying). Yet, they can still result in a stress response that cycles back down to baseline without long-lasting harm if supports and protective factors are available, and the body has built a strong foundation for resilience.

Under conditions of extreme adversity, potential triggers of a toxic stress response might include severe neglect or active maltreatment; the sudden loss of a parent or sibling; exposure to recurrent family or neighborhood violence; significant upheaval or unpredictability in daily routines, particularly when linked to a perceived lack of safety;[6] or prolonged deprivation related to economic, housing, and/or food insecurity. All of these situations can occur alone or alongside a range of structural inequities that amplify and compound their negative impacts through both the material and psychological threats associated with racism, ethnic or religious discrimination, immigration status, or other reasons for marginalization that affect daily life experiences in large and small ways.[33] These may include various combinations of persistent economic insecurity, unstable housing, exposure to family and community violence, limited access to health care, social isolation, and/or chronic caregiving burdens.[3]

Although these threats are serious, a range of protective factors can still reduce (or prevent) their negative impacts on young children's well-being and long-term outcomes.[34] Supportive caregiving from parents, other family members, and childcare providers ranks among the top protective factors. That said, placing responsibility *entirely* on individualized, adult-child relationships misses the critical need to also direct attention "upstream." Community-focused action plays an important role in preventing or reducing sources of significant adversity for families and in strengthening sources of protection and security.[35]

A truck that's overloaded can only bear so much weight, and for people, challenging life circumstances can weigh caregivers down and make it hard to do the things they need and want to do for their children. Just as a truck can break down if it carries too much for too long, people can be worn down from the weight of hardships and threats when sufficient relief or support is not available. And just as we can remove cargo from an overloaded truck, communities can provide support and services that reduce the pile-up of stressors bearing down on families and empower them to focus more energy on caring for themselves and their children. Like performing regular maintenance to keep a vehicle in good shape, regular access to these services can help families be prepared to manage excessive loads during challenging times.

The Costs of High-Effort Adaptations

Two overgeneralizations about stress tend to dominate discussions about the effects of adversity on young children. One claims that stress is good as it makes us stronger and builds character. The other asserts that stress results in lasting and inevitable damage. Yet real-life experiences provide frequent examples that contradict each perspective. A deeper understanding of how developing biological systems manage adversity helps explain why a more nuanced approach to early life stress is needed. Viewed together, both science and lived experience can inform more effective community responses and public policies to promote successful outcomes for *all* young children and families experiencing significant adversity.

Advances in the science of adversity and resilience underscore the need to revisit the criteria used to define long-term "success" for children exposed to stressful conditions early in their lives. For example, traditional reliance on school-based reports fails to identify an important subset of children who receive positive teacher ratings on psychosocial adjustment but are nevertheless at greater risk for chronic stress-related diseases in the adult years due to persistent stress system activation. This is referred to as **high-effort coping** and is an example of how persistent striving against deeply embedded hardships may help increase academic success and positive mental health, but at a cost to physical health.[36] High-effort coping shows the importance of a more nuanced picture of stress that understands variation in development and guides the most effective ways of supporting a broad range of positive outcomes.

This pattern of significant effort at a high cost has been called "John Henryism,"[37,38] based on the folklore story of a Black railroad worker named John Henry who took on a machine and won the race, but died of exertion immediately thereafter. This concept of **adaptation at a cost** has been studied extensively in adults, and there has been one study showing that high-striving, Black and Hispanic youth as young as eight years old who experienced significant economic hardship had better mental health but worse cardiometabolic health; the opposite was true (i.e., more depressed or anxious mood and less high blood pressure) for those who experienced significant economic hardship but did not engage in high-effort coping.[36]

Focusing on school performance and mental health as *primary* markers of resilience is particularly problematic because it can mask physiological disruptions inside the body that increase the risk of later chronic diseases and a shorter life span—both of which are more prevalent in minoritized populations. Reducing biological disruptions caused by intergenerational poverty, racism, or other deeply embedded sources of stress requires increased attention to the protective roles of economic opportunity, stable housing, safe neighborhoods, and other community factors. A mindset that places the burden of protection on families and relationships alone is insufficient.

High-effort coping points to the need for a more thoughtful approach to assessing variation in how the body adapts to significant adversity. Although nurturing relationships and protective factors in the community shift the odds to positive outcomes in child development and school readiness, the possibility of persistent stress activation inside the body may still increase the risk of later chronic disease. This continuing risk calls for closer attention to measures of physical growth and screening for both physical and mental health problems in the context of primary health care, where warning signs may be subtle and opportunities for preventive intervention might be missed.

Factors That Affect Variation in Sensitivity to Stress

Even among siblings with the same biological parents living in the same household, some thrive in supportive environments but do very poorly in harsh ones, while other children in the same family seem to do well regardless of the conditions.[39] And, of course, there is a whole range in between these extremes. The amount of stress that is tolerable can even vary for the same individual at different times or in different circumstances. Among the many factors that determine the impact of stress activation are the following:

Predictability and Controllability. When our experiences confirm that certain things happen at typical times (predictability) and that we have some power to affect what is happening (controllability), our brain adjusts in ways that safeguard our physical and mental well-being in line with those expectations.[40,14] For young children, that sense of predictability and controllability is dependent on the reliable presence of one or more caregivers who are attuned to their development through frequent engagement in responsive serve and return interactions.[41]

The ability of parents and other caregivers to provide a secure environment with predictable routines for children, starting at birth, is heavily influenced by how well their own basic needs are met. Those needs include economic security, adequate housing, affordable nutritious foods, personal safety, and living in a neighborhood that provides a sense of belonging and mutual support. When children experience stress in a context in which their basic needs are secure and a responsive caregiver can meet daily challenges, this facilitates their growing ability to cope with stressful events over time.[42] In contrast, the burdens of poverty, racism, ethnic or religious discrimination, and fear related to immigration status or neighborhood violence are among the many ways in which a sense of safety and agency can be threatened. These sources of adversity, which are beyond the power of nurturing relationships alone to overcome, must be addressed at a policy and systemic level to support family functioning and restore a sense of stability and security for both children and the adults who care for them.[40]

Timing. *When* stress occurs over the life course is another important factor influencing whether or not there will be long-term consequences. The prenatal period and first 2-3 years after birth are times of particularly heightened sensitivity to all kinds of experiences and exposures, whether adverse or protective. During these early years, external conditions affect how developing biological systems, including the brain, immune system, cardiovascular system, and metabolic regulation, mature in anticipation of a lifetime of similar circumstances. During these sensitive periods, excessive stress activation, or the *absence* of important protective factors such as responsive serve and return interactions, can affect the development of systems that influence how children will cope with future stressful events.[43,44] Because different circuits in the brain mature on different timelines, some very early and others well into the adolescent years, different kinds of experiences are particularly important at different ages, a concept called **age-appropriate experience**.[45]

For example, the brain circuitry related to fear develops very early in a region called the amygdala, while the response that *calms* fear develops later in the prefrontal cortex. Therefore, experiences that result in neural responses that promote calming after experiencing

fear (e.g., a parent soothing a distressed toddler) are especially important when those circuits are forming.[46] The same principles apply to other developing systems, including those that fight infection, turn food into energy, or establish the composition of bacteria and viruses that live in our gut (a.k.a. the microbiome) and influence brain, metabolic, and immune functions. Adolescence is another period of development that provides opportunities to modify relevant brain circuits that affect the body's response to stress. Changes can also occur in the early adult years, but they require significantly more resources than earlier, and the results are rarely as good as they would have been if proper support had been provided in the first place. *Whether* and *when* these systems have certain experiences or exposures affect how they are set up to perform necessary functions throughout life, in ways that either promote good health or undermine it.[45]

Genetic Variation. Part of the reason individuals respond differently to their surroundings comes from their genes.[2] This variation is written into the unique genetic code established in each fertilized egg at the time of conception. Genes encode proteins that perform essential functions in cells, but the expression of that individual code is strongly influenced by early experiences or exposures that happen at critical times during development. Disruptive exposures and experiences, especially very early in life, can alter gene expression levels as well as the timing patterns for genetic activity. For example, a toxic stress response at a time when genes are being expressed can literally change whether, when, and how much of their code is activated. Some genes typically low in expression can go high and vice versa. These effects may have short-term benefits, but over time, they can create problems with how genes should function later in life.[2] If children who are highly sensitive to their surroundings grow up in a stressful or harmful environment, significant adversity can make them more vulnerable. But if they grow up in a caring and supportive environment, their heightened sensitivity allows them to benefit even more than others from positive learning experiences.[31,47] In other words, children who seem more at risk in challenging situations are often the ones who can thrive the most when given sufficient support and opportunity. Finally, genetic differences don't simply affect risk; they also influence how flexible and responsive (i.e., resilient) individuals are in different environments across the lifespan.[48] Even later in the life course, some especially powerful factors, such as chronic pain,[49] cancer, [50] or nutritional influences,[51] can activate gene networks that make an individual more or less responsive to stress, as well as more or less likely to recover from episodes of mental illness. Early experiences, however, remain critically important as they lead to structural and chemical adaptations in the developing brain that are more difficult to change later. In short, the interaction between genes and environment is influenced by age. Even though changes can happen later in life, what happens early matters a lot.

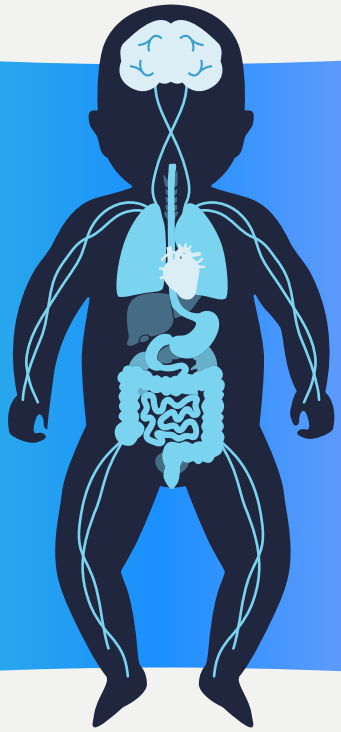
The Nature of the Stressor. The duration, frequency, and intensity of stressful experiences are also important factors that affect their impact on a young child.[45] If a stressor is particularly severe and/or prolonged, like extreme neglect, physical or emotional abuse, forced migration, or war, it is more likely to overload the body's developing systems than a less powerful experience.[52] If the body adapts to extreme situations like these, its biological systems become attuned to surviving at the extreme margins of human experiences in the short term, but at a cost to later well-being. These costs can include vigilance that is protective in a threatening environment but maladaptive at school (i.e., aggressive behavior) as well

as stress-related impairments in long-term health (e.g., cardiovascular disease). If the stress-inducing experience is repeated frequently or feels unchangeable, it can have a more serious, long-term impact on the body's systems than a transient or more controllable event. For example, when ongoing threats or daily indignities of racism and discrimination trigger the stress response constantly, it exacerbates the wear-and-tear effect of stress on all of the affected regions of the body.[33]

Individual Capacities for Resilience. All children adapt to the environment in which they live, but the strength and scope of that ability vary from person to person.[53,54] Resilience, the ability to thrive in the face of adversity, can shift over time and varies among children based on their age, nutritional status, and whether supportive caregivers and extended social support networks are available. Throughout life, individuals build unique sets of capacities and skills that help them adjust and thrive in challenging situations if they are well-developed. These include skills such as focusing attention, remembering tasks, and adjusting when conditions change, to name just a few.[52] Resilience is not a generalized capacity that applies equally to all types of stressors or outcomes. For example, a child who experienced trauma early in life may benefit from supportive peers or mentors and do very well academically in school, but later develop cardiovascular disease or diabetes related to chronic inflammation.[55,56] The brain plays a central role in maintaining stability during times of change or stressful situations, and early adversity leads to structural and neurochemical differences in parts of the brain that influence how children will respond to stress later in their life course.[20] These individual differences in the stress response also affect how much and for how long inflammatory pathways are activated.[57,58] Such physiological differences in response to stress create a distinctive pattern for each child, with specific consequences for long-term health.[59]

> **Children who seem more at risk in challenging situations are often the ones who can thrive the most when given sufficient support and opportunity.**

Understanding The Broad Range of Responses to Adversity



Positive Stress Response

Brain and other developing systems respond to stress activation and then return to baseline

Successful adaptation

Building blocks of resilience

Toxic Stress Response

Excessive activation of stress response system

Adaptation at a cost

Increased risk for problems in early development and lifelong health

FACTORS THAT INFLUENCE IMPACT

- Individual variation in sensitivity to adversity
- Availability of responsive caregiving in multiple settings
- Stable, community level, protective factors
- Developmental timing beginning prenatally
- Severity, duration, predictability & controllability of stressors

The figure above illustrates how multiple interacting factors—including the nature and timing of stressors, individual variation in sensitivity, and the availability of protective relationships and community supports—shape where a child's stress response falls along a continuum from adaptive to potentially harmful. As these influences combine, they can either support a positive stress response that builds resilience or push biological systems toward excessive activation and increased risk for problems in development and health. Most importantly, strengthening protective factors can shift this balance toward healthy adaptation, even in the presence of significant adversity.

Impacts of Stress Responses on Early Childhood Development

While the stress response is active throughout life, and its activation continues to have both short- and long-term effects on behavior and health, it affects young children in distinctive ways. Because all of the body's organ systems are developing rapidly during the prenatal and early childhood periods, both positive and negative influences have particularly long-lasting effects on how they function across the lifespan—from later school achievement and economic productivity to lifelong physical and mental well-being.

Influencing organ systems that affect lifelong physical and mental health. Neural circuits in the brain that deal with adversity are particularly malleable (or "plastic") during the fetal and early childhood periods. Early experiences shape how readily these circuits are activated and how well they can be regulated and turned off if not needed. As these circuits develop, positive stress responses activate and deactivate systems in a regulated and healthy way.

In contrast, toxic stress responses during this early period can alter developing circuits in many brain regions, including those critical for processing threat and both activating and regulating the body's stress response.[60] As they get older, some children who experienced earlier toxic stress responses may feel threatened by or respond impulsively to situations in which no real threat exists, such as seeing anger or hostility in a facial expression that is actually ambiguous.[61] Some children remain excessively anxious long after a threat has passed, while others develop an unemotional response to their own feelings and the emotions of others. Either way, frequent or sustained activation of brain systems that respond to stress can increase the likelihood of a range of behavioral and mental health challenges over a lifetime, including depression, anxiety disorders, and excessive use of alcohol or illicit drugs.[17] Severe mental illnesses that typically have their onset in adolescence and adulthood, including schizophrenia, are also more likely to develop in individuals who experienced significant trauma in early childhood.[62] This risk is likely an example of gene-environment interactions, or **epigenetics**, in which an inherited genetic risk for mental illness is activated by early adversity.

Because all systems in the body are connected, the consequences of toxic stress responses reach beyond the brain. For example, when cortisol is elevated for prolonged periods of time, this can not only change the architecture of regions in the brain that are essential for learning and memory, but also disrupt the immune system.[63,64] Frequent activation of the **sympathetic nervous system** (the broader system in which the SAM system is a component) not only increases inflammation but also elevates blood pressure.[65] Chronic low-grade inflammation and altered metabolic systems can also lead to the development of obesity, type 2 diabetes, and cardiovascular disease.[66] These conditions are often thought of as "disorders of aging," but increasing diagnoses in adolescents and young adults are being reported in youth who have experienced significant adversity earlier in childhood.[67]

Shaping how the body manages energy. Every cell in the body needs energy in the form of glucose to function. Often, the body must make choices about where to direct whatever glucose is available and which organs to prioritize. An adult brain makes up 2% of body mass and typically uses 20% of daily energy intake. That percentage is much higher during

early childhood; it peaks at about 40% of daily energy intake by the brain at age 5.[68] When we are threatened and need to react quickly, the SAM system and the HPA axis ensure the brain has sufficient energy by promoting changes in the liver, muscles, and fat cells. When the body responds and adapts in this way, beginning in early childhood, it develops the capacity to cope with challenges or threats immediately as well as in the future. If the stress response continues for a long time, these protective effects can be disruptive. For example, consistently high levels of glucose in the blood, called hyperglycemia, can harm the brain (as well as other organs, such as the kidneys and retina). This might slow down thinking and even damage the brain's **white matter** (insulation around nerves that facilitates efficient communication among its different regions). In some cases, this can lead to fewer glucose transporters at the blood-brain barrier, making it harder for the brain to get the energy it needs.[69]

Affecting cellular function throughout the body. In the process of producing energy to support various biological functions, human cells naturally produce molecules called **reactive oxygen species (ROS)** during normal activities. ROS help regulate important cell processes like cell growth, immune function, and cell death. When greater energy demands are put on the cell (e.g., during a stress reaction) more ROS are produced to manage that energy load. When the stress reaction subsides, so do the ROS, which, over time, creates a healthy energy-management system that has adapted to respond to changing conditions. However, if the stress response is excessive or chronic, the system can falter. In this condition of allostatic overload, high ROS can severely limit the ability of cells to generate energy. This phenomenon of cellular wear-and-tear caused by overactivation of the stress response, known as **oxidative stress**, has been measured as early as infancy[70] and is linked to the development or worsening of many diseases later in life, including diabetes, heart disease, cancers, mental illnesses, and other metabolic or inflammatory conditions.[71,72]

Regulating gene expression. Very early in development, genes are like recipes that tell the body how to make the proteins that influence how our biological systems operate. But just like a recipe in a cookbook, nothing happens unless the recipe is read and followed. Every cell in the body has the same genes, but the recipes (i.e., instructions) they carry are specialized. For example, brain cells and muscle cells use different instructions because they serve different purposes. Moreover, experiences and exposures (such as toxic substances in the air and water, important nutrients in our food, and threats that activate stress responses) cause the body to send signals to the cell nucleus, where genes are located. If a gene gets the signal, the recipe is copied and sent to the "kitchen" in the cell that makes proteins. This is part of the process known as epigenetics, which enables infants and older children to adapt to their environment at a genetic level. Whether it is safe and supportive or stressful and harsh, the signals from the environment reach the cells, and the DNA instructions are adjusted accordingly.

A good example of adaptation that has benefits as well as costs is the effect of trauma on the gene that regulates a protein designed to stop cortisol from being transported to the cell nucleus. When cortisol is elevated in the body, the gene's instructions call for adding more of this "shut-down" protein—a protective mechanism to prevent highly elevated cortisol levels from having immediate damaging effects. Traumatic experiences, especially early in life, cause that gene to call for even more of the "shut-down" protein at times of stress, which mutes activation of the stress response system. This muting is beneficial *during* the acute trauma, but if it continues, it can blunt the body's ability to respond to both challenges and interventions in the future.[45]

How Protective Factors Affect the Impact of Stress and How We Can Strengthen Them

Many external factors affect whether, how much, and for how long the stress response system is activated. Protective factors can help calm the stress response in young children directly through nurturing, responsive relationships, or indirectly, by promoting a stable, supportive environment that meets the basic needs of the adults who care for them. The wide range of influences that enhance positive life outcomes include nutritional, social, and medical support during pregnancy; a nurturing and predictable home environment after birth; clean air and water; safe and opportunity-rich neighborhoods; accessible health care; and high-quality childcare and schools. Yet, these basic needs are not being met for many families and children.[73] The material and psychological stresses of intergenerational poverty, racism, and other structural inequities impose a cumulative burden of hardships and threats that often include substandard housing, overcrowding, limited economic mobility, exposure to neighborhood violence, chronically elevated family stress, low-quality services, loud noise levels, malnutrition, polluted air and water, and excessive heat.[33] In rural communities, adverse conditions may include geographic isolation, limited access to health care and early childhood services, transportation barriers, environmental exposures related to agricultural chemicals (e.g., insecticides) or extractive industries (oil, coal, natural gas), and fewer employment options that provide economic stability.[74]

A pile-up of risk factors within a family and/or community increases the odds that young children will struggle and that both early development and lifelong health will be disrupted. *But poor outcomes are not inevitable*. Policies and programs that incorporate robust protective factors to prevent, reduce, or mitigate the adverse effects of excessive stress activation are a promising place to begin. Many communities already have effective strategies in place; others have fewer as a result of a long history of disinvestment. No community leader, service provider, policymaker, or researcher has all the answers, and effective solutions will vary from one place to another.

> **The following protective factors provide a framework to reinforce well-established best practices, catalyze fresh thinking, and test new ideas across a wide variety of contexts.**

Supportive Relationships. The most important protective factor for promoting healthy development, beginning immediately after birth, is a stable, nurturing, and responsive relationship with at least one adult caregiver. Children who experience the benefits of secure relationships develop a better-regulated stress hormone reaction when they are upset or frightened.[75] This means that they are able to explore the world, meet challenges, and be frightened at times, without sustaining the adverse consequences of excessive stress system activation. On the other hand, one recent study of families with low income found that during routine health checkups that included immunizations, toddlers with insecure relationships with their caregivers exhibited a stronger stress response (measured by higher cortisol levels) than children with secure relationships.[76]

Supportive relationships beyond those provided by family members can protect young children from adverse conditions when significant structural barriers and psychological distress limit the capacity of their parents *alone* to provide consistent protection. Moreover, the mutually responsive, "serve and return' interactions that infants and young children have with all the adults who care for them, including parents, extended family, neighbors, and/or childcare providers, can play important roles in calming stress responses that are activated by unpredictable or threatening conditions. Researchers have found that even when a child's primary caregivers are not consistently supportive, a positive relationship with a caring neighbor or teacher can serve as an important source of protection.[77]

Community-based systems and supports (e.g., doulas[78]) that proactively aim to reduce the burdens of stress on adults during pregnancy and on those caring for young children, as well as local efforts to create public spaces and opportunities that strengthen social connections among parents, are likely to reduce stress activation in young children.[79] Reducing stress for caregivers enables them to have the bandwidth to engage in more responsive serve and return interactions with young children, to bring less distraction and more emotional availability to those interactions, to model effective emotion regulation and problem-solving, to develop and maintain health-promoting daily routines, and to provide opportunities for all children to experience manageable challenges in a secure and predictable environment.[80] Especially when reinforced by other protective factors, supportive relationships help infants and young children develop healthy stress response systems.[81]

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Early Care and Education Programs. Two of the most extensively studied early education programs, the Perry Preschool Program and Abecedarian Project, have documented significant long-term impacts on improved educational attainment, reduced incarceration rates, and better health outcomes into adulthood.[82,83,84] Although the capacity to measure biological indicators of the stress response in young children was not available at that time, it is notable that follow-up studies of Abecedarian children past age 30 found lower rates of hypertension and metabolic syndrome than their peers who did not participate in the program,[83] which could be related to the program's prevention of excessive stress activation in early childhood.

A study of childcare programs in 2010 documented that young children who spent significant amounts of time in low-quality settings (i.e., programs with high ratios of children to adults, less-personalized relationships, inconsistent caregivers, and harsher adult-child interactions) had higher elevations of stress hormones across the day than those in better quality care.[85] Because lower-quality out-of-home care is most likely to be experienced by families facing economic insecurity, increasing access to high-quality care across the economic spectrum is an important goal.[86,87] The fact that all young children in the U.S. military's childcare system benefit from high-quality early learning experiences provided by well-compensated staff demonstrates what can be accomplished if quality standards are established, enforced, and financed.[88]

Whether it is home-based or center-based, the structural and interpersonal features of non-parental care received

by young children can help promote healthy development. Developmental science and program evaluation research both point to a set of key effectiveness factors for high-quality childcare. These include the following:[89,90]

- A language-rich environment, with warm and responsive serve-and-return interactions, which builds both receptive and expressive language and interpersonal skills;
- Structural factors, such as a safe physical setting, small group sizes, and high ratios of adults to children, which support more responsive interactions and more effective instruction; and
- Clearly defined goals and a curriculum or intervention plan with developmentally appropriate, engaging activities that are designed to achieve those goals.

Finally, actions to address implicit bias and improve cultural competence in early childhood programs are important protective factors for reducing stressful experiences for young children. One well-studied challenge is documented in a systematic review of 20 studies of infant, toddler, and preschool disciplinary actions that found disproportionate suspensions by race (Black more than White) and gender (boys more than girls) despite no differences in independent observations of disruptive behavior based on either race, gender, or socioeconomic status.[91] In the absence of appropriate staff training to raise awareness about implicit bias, differential management of challenging behavior imposes an additional source of adversity on the daily experiences of young Black boys while also undermining the potential protective role that early care and education programs could play for children facing racial, ethnic, or gender stereotyping.

Sound Nutrition. A healthy diet contributes to a more balanced stress response that can appropriately activate and calm itself. For example, the availability of nutritious foods promotes mental well-being,[92] reduces systemic inflammation, and is associated with a better balance in ROS production.[93,94] In contrast, both under-nutrition and overeating can have negative impacts on brain development as well as future metabolism, the process by which the body converts food into energy, which in turn affects weight, insulin resistance, fatigue, and blood pressure.[95,96]

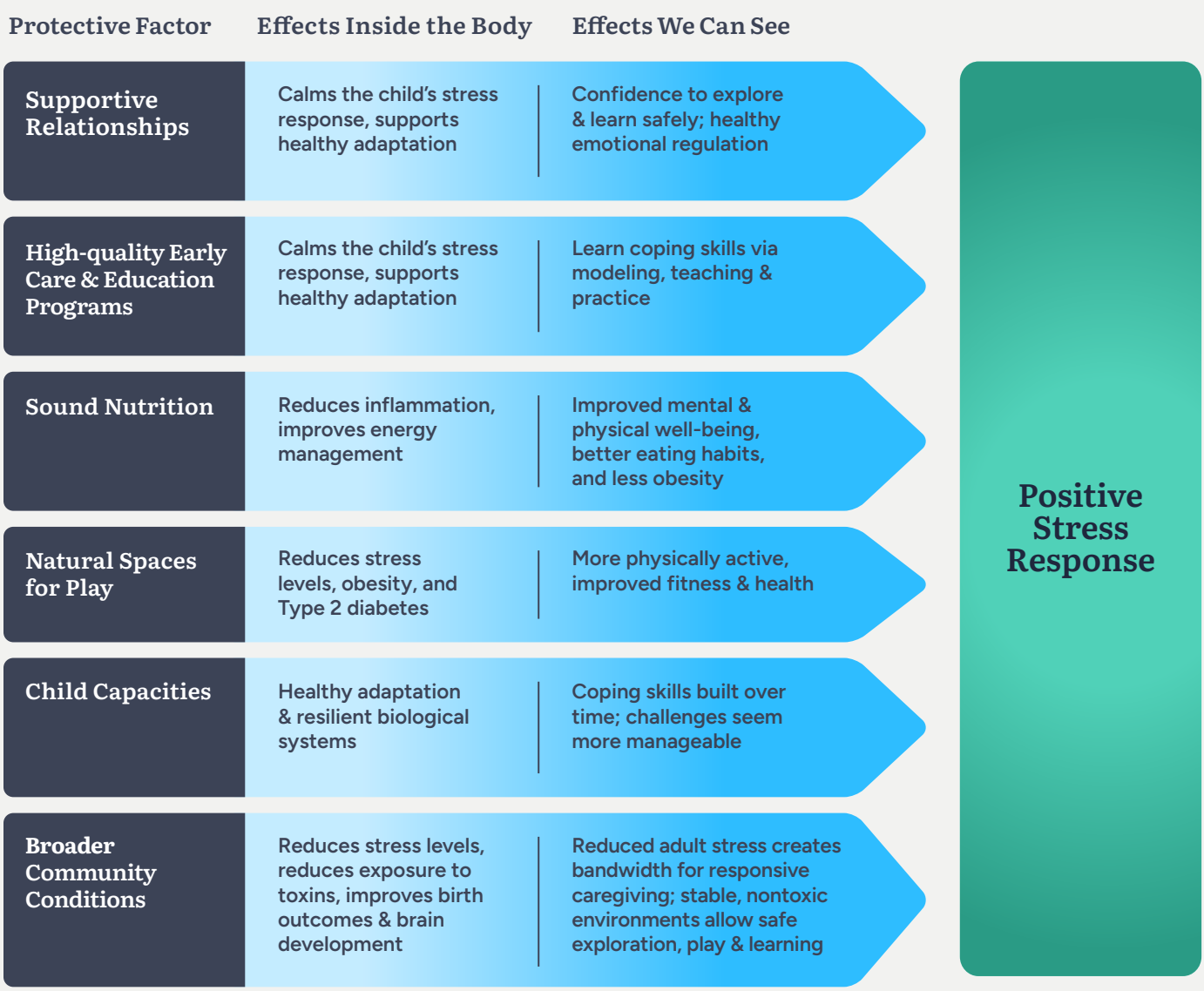
Persistent periods of prolonged stress during early phases of development also may influence a child's food preferences and eating behaviors. These problematic influences can lead to a higher intake of foods high in sugar and fats,[97,98] as well as inappropriate and inefficient use of these foods to "calm down."[99,100] This kind of behavior increases the risk for metabolic syndrome, obesity, type 2 diabetes, and cardiovascular disease later in life.

Ensuring that appropriate nutrition is affordable and readily accessible during pregnancy, infancy, and all stages of childhood is an important protective factor for reducing the impact of stress and maximizing lifelong metabolic, physical, and mental health.[101] Communities can support this basic need by addressing the problem of consuming highly processed foods as a result of "food deserts," where it is difficult to find affordable, fresh vegetables, fruits, and other healthy foods.[12] When needed, food assistance programs can ensure that the nutritional needs of young children and their caregivers are met, thereby promoting healthy brain development as well as overall physical and mental well-being for both the child and adult. For example, participation in the U.S. Supplemental Nutrition Program for Women, Infants, and Children (WIC) can reduce low birth weight, prevent iron-deficiency anemia among infants

in low-income households, and improve children's intake of iron, folate, and vitamin B-6.[102,103,104,105] And finally, support for breastfeeding remains a central part of assuring that the nutritional needs of infants are met.[106]

Natural Spaces for Play. When children can play in safe, natural environments, like parks and other spaces with trees and plants, they experience reduced stress that can have important protective effects on both physical and mental health in the present and later in life, including lower rates of obesity and type 2 diabetes.[107,108] High amounts of play are associated with low levels of cortisol in children, and play that is accompanied by nurturing caregiving is believed to reduce stress to levels that enhance

How Protective Factors Support Healthy Child Development



effective coping and resilience.[109] Research also shows that when children feel safe and have places to be active outdoors (particularly if the air quality is good and temperatures are moderate), they are more likely to engage in physical activity, which supports healthy growth and lowers the risk of obesity.[35]

Notwithstanding their benefits for all children, public green spaces are not distributed equitably across communities in the United States and around the world. Neighborhoods with the least green space and the highest average temperatures are predominantly comprised of residents of color and those with lower levels of education and income, compared to greener, cooler neighborhoods, where higher percentages of White and higher-income residents live.[110] Equalizing environmental protections so that all children can grow up in neighborhoods free of exposure to toxic substances (in the air and water) and rich in access to safe green spaces requires directing more resources to areas that have historically received less investment.[35] For example, policies that have replaced vacant land in disinvested U.S. cities with parks, trees, and other foliage have resulted in lower crime and improved health.[111] Although rural areas may offer greater proximity to natural environments, safety concerns, environmental hazards, lack of maintained public spaces, or extreme heat and weather events can still limit young children's access to stress-buffering outdoor play.

Child Capacities. Children whose stress response rarely becomes toxic, despite facing significant disadvantages, typically benefit from both a lower internal sensitivity to adversity (often manifested as temperament) and a strong set of protective factors in their family and community. This interaction between biology and environment builds strong capacities to cope with adversity. When adults model solutions, offer comfort and praise, and help children learn from past experiences, multiple systems (e.g., brain, immune, metabolic) develop the adaptive capacities needed to activate and then restore their response systems to baseline. Over time, these biological systems respond to comparable threats as increasingly manageable. Everyone in a society benefits when all children are better able to cope with life's obstacles and hardships, both physically and mentally.[52] One promising approach, particularly in a culture that rewards the ability to plan for and achieve goals, adapt to changing situations, and resist impulsive behaviors, is to intentionally strengthen these skills over time through practice and feedback.[52] The development of effective coping skills, however, must be viewed in context, as some children who grow up in harsh environments develop problem-solving skills that are appropriate for threatening circumstances but potentially problematic in safe contexts. For example, faster cognitive processing and the ability to respond rapidly to threatening challenges often play a critical role when threats are frequent and extreme, in contrast to relatively safe situations where a slower and more reflective response time often leads to better outcomes.[112]

In the final analysis, effective adaptation in a variety of contexts builds on existing strengths while providing opportunities to develop (or enhance) core skills essential for later school achievement, workplace effectiveness, future caregiving, and reducing the negative effects of excessive stress activation at any age.[81] Two-generation programs can strengthen adaptive capacities in young children (e.g., focusing attention and regulating behavior) through active coaching for the adults who care for them.[113]

Broader Community Conditions. Beyond policies focused on health care, childcare, and early education, the well-being of young children could be

enhanced by improvements in policies that are rarely viewed through an early childhood lens but govern a range of potential sources of excessive stress activation. These include housing, zoning, both urban and rural planning, economic development, criminal legal reforms, environmental protection, climate change policies and mitigations, and anti-discrimination policies.

Beyond policies focused on health care, childcare, and early education, the well-being of young children could be enhanced by improvements in policies that are rarely viewed through an early childhood lens.

Although research focused explicitly on the impact of these policy areas on early childhood development is limited, improving a wide range of community conditions for families presents a relatively untapped opportunity to reduce stress activation in young children.[35]

For example, fair access to good, affordable housing, readily available healthcare and other basic services, supportive social networks, and stable, well-paying employment opportunities are among the community assets captured by the Child Opportunity Index (COI). The COI contains data for every neighborhood in the United States and comprises 44 indicators in three domains (education, health/environment, and social/economic).[114] One study of families, all of whom were categorized as having low socioeconomic status (SES), found that children living in low-opportunity neighborhoods (as defined by the COI) had elevated cortisol levels at the beginning of the kindergarten school year and more health problems reported by their parents and teachers at the end of the year. In contrast, children in low-SES families living in neighborhoods defined as high opportunity by the COI had normal cortisol levels and no increase in health problems.[115] This study generated evidence that more advantageous community-level assets and opportunities can reduce child stress levels and improve child health in families with low SES.

Ensuring that the physical environment during pregnancy, infancy, and early childhood is safe and free of exposures that are known to be particularly dangerous for fetuses and infants is another critical investment in the future health and learning capacity of all children. During the prenatal and early childhood periods, exposure to toxic substances (e.g., certain farming insecticides; lead, mercury, or arsenic in drinking water; [116,117] nitrogen dioxide or ultrafine particle matter in auto exhaust; [118,119] or "forever chemicals" in food and plastics[120]) can have adverse effects on the developing brain directly, as well as indirect effects by activating immune and metabolic responses that can have long-term impacts on other organ systems. Growing concerns about rising temperatures associated with climate change also have particular relevance for infants, for whom excessive heat is a threat to health (and even survival). This increased vulnerability is attributed in part to a smaller body surface area and less capacity for sweating, which is necessary for lowering high body temperature.[121]

In summary, both the physical and social features of a neighborhood affect the well-being of its children, where the youngest are the most sensitive. Positive conditions facilitate healthy development by protecting young children from toxic chemical exposures, excessive heat, and other adverse experiences, and by strengthening the stress-buffering effects of the protective influences described in this report.[122] Communities differ in their balance between opportunities and adversity, and these differences are not randomly distributed; they are the result of policy decisions that have been made over time. Residential

segregation is the most prominent example of policies that explicitly restricted access to homeownership based on race when they were first enacted, and many consequences of those inequities continue to this day.[110] Persistent inequalities that have resulted from previous government action (whether intentional or inadvertent) could be reduced by new legislation. Moreover, policy changes focused on reducing inequities could provide more effective support for the healthy development of *all* children by mobilizing resources to address adverse conditions that expose *some* children to physical harm and/or the consequences of excessive stress activation.

Measuring Stress Activation in Young Children

Traditional approaches to measuring the effects of adversity on child health and development focus on two categories of risk. The first is named **social determinants of health**, which include family income, parent education, housing quality, neighborhood safety, and availability of basic supports such as health care, childcare, education, and social services. Although race and/or minority ethnic status are often included in this category, increased risk is related to the consequences of racism and other structural inequities, not anything intrinsic to race or ethnicity. The second category is **adverse childhood experiences (ACEs)**, which include abuse, neglect, and household dysfunction such as domestic violence, addiction, contentious divorce, and incarceration of a parent.

These categories reflect what's happening around children, but they don't tell us what's going on inside their developing bodies. Even more important, simply tracking demographic risk factors or adverse experiences is not enough to assess current well-being or predict future outcomes because children exposed to the same source or level of adversity will not all experience the same degree of stress system activation or its consequences. To direct attention where it is needed most, it's important to identify signs of greater sensitivity to adversity as well as signs of relative resilience.

A checklist or questionnaire asking parents to report on their child's development or behavior provides important insights into what the parent is thinking (or willing to share), but such reports are subjective in nature and sometimes difficult to interpret. While some measures of behavior based on independent observation might conclude that a child is experiencing significant stress, the interpretation can vary by the observer. For example, some children who are frightened rush to their parents to seek protection, while others retreat and hide. Some children eat more when they are stressed; others lose their appetite. Observable child behavior can provide valuable information, but it is not a measure of stress system activation that can tell us, at a biological level, whether there is reason for concern.

> **Opportunities to combine biological indicators of stress activation "inside the body" with observational assessments and parent reports would generate a deeper understanding of a child's response to adversity than any single data source by itself.**

All that said, opportunities to combine biological indicators of stress activation "inside the body" with observational assessments and parent reports would generate a deeper understanding of a child's response to adversity than any single data source by itself and thus promote a more comprehensive approach to identify relative risk and resilience.

One way to assess how the brain and other developing systems are responding to adversity is to measure biological indicators of stress activation that can be quantified in samples of saliva, cheek swabs, and hair, without the need for drawing blood. For example, inflammation can be measured by assessing cytokine levels in saliva. The accumulation of cortisol, along with molecules that regulate its production, can be quantified in a snip of hair, which provides a measure of how much the stress hormone system has been activated during the preceding few months. Signs of mitochondrial damage (e.g., ROS levels), individual genetic differences in stress activation, and biological "wear and tear" can be measured in cells obtained from a cheek swab inside the mouth.[123] These validated indicators of stress system activation could then be used to document variation among children in their reactivity to adverse experiences or exposures.[124,125]

Biological indicators of stress activation offer a rigorous, science-based approach to measuring the effects of neighborhood investments on building resilience in young children, preventing the risk of toxic stress, and constructing a strong foundation for later educational achievement and lifelong physical and mental health.

Measures of stress activation have been studied over many years to document effects of adversity on children,[3] as well as assess the biological impacts of interventions focused on caregiver-child interactions.[126] Building on these findings, growing interest among leaders of place-based initiatives has raised questions about measuring stress activation as a neighborhood health indicator to: (1) assess how young children, as a group, are doing within or across neighborhoods; (2) document the extent of within-group variation in sensitivity to adversity; (3) serve as an early warning system (i.e., the body's internal "first responders") before the effects of adverse community conditions are visible and when preventive interventions are likely to be most successful, and (4) measure the impact of place-based strategies on early childhood well-being, which can include effects on cognitive, social, and emotional development as well as physical and mental health.

Recent sampling and preliminary data analyses have focused on developing algorithms to combine multiple biomarkers into a composite measure. This has included analyzing variation for each component in isolation, as well as for all components in aggregate. As the collection and analysis of sufficient numbers to establish normative values continues, researchers are developing statistical models to determine relative biological risk by combining environmental data, biomarkers of stress activation, and concurrent child health status when available.[124,125]

By building on what is visible in statistics and surveys—and including data on what is happening inside children's bodies—biological indicators of stress activation offer a rigorous, science-based approach to measuring the effects of neighborhood investments on building resilience in young children, preventing the risk of toxic stress, and constructing a strong foundation for later educational achievement and lifelong physical and mental health.

With time and continued testing,

these measures also have the potential to be used at an individual level in pediatric practice, but only after sufficient data have been collected to establish the boundaries of normal stress system activation and differentiate positive adaptation from a worrisome or toxic response. Like screening for anemia, lead exposure, or blood sugar levels, measures of stress system activation do not identify a permanent state or lasting damage, but rather where a child fits within a range of responses at the time of testing. Given this information, pediatricians, parents, and other caregivers could address findings that fall outside the normal range in a variety of ways, from identifying and reducing external sources of stress to employing stress-reduction interventions and measuring their effectiveness. Such information could also help reassure parents whose child has experienced significant adversity but is demonstrating a well-regulated stress response.[123]

Finally, notwithstanding the potential benefits of enhanced measurement capacity, the sensitive nature of collecting biological data on stress activation in young children and the critical need for both accurate interpretation and an appropriate response all demand vigilant attention. This caution is particularly important for Black children and other minoritized populations, given centuries of egregious misuse of biology to promote racist ideologies and stigmatizing stereotypes based on ethnicity or national origin, as well as persistent inequities in medical research and delivery of health care and related services.[123] The importance of sustained collaboration among multiple stakeholders (e.g., clinicians, parents, community leaders, and researchers) within a governance framework that integrates different kinds of expertise is therefore essential for the ethical and equitable implementation of these measures.[127,128]

Toward a More Balanced Approach to Stress and Resilience

At the far end of the broad spectrum of adversity experienced by children around the world, extremely threatening conditions (e.g., personal experiences of war or famine) can rarely be weathered without harm, and intensive interventions tailored to specific contexts are always needed.[52] Although the majority of children in the United States do not experience unpredictable, uncontrollable, or chronic stressors that can lead to lifelong negative consequences, nearly one in four are estimated to have been exposed to multiple sources of significant adversity during the early childhood period.[129] This presents serious concerns for children who experience these types of adversities, their families, their communities, and society as a whole.

That said, not all young children who have been exposed to significant adversity will develop stress-related disorders, despite being at higher risk. Some are clearly more sensitive to different kinds of hardships or threats than others, as well as more or less responsive to an array of intervention strategies.[45] In the final analysis, when questions are asked about the short- and long-term effects of significant stress in the early childhood years, the answer is: *diversity rules*.

One popular framework for both public health and primary health care approaches to this persistent challenge

focuses on the identification of "children at risk" based on common indicators of socioeconomic disadvantage (e.g., social determinants of health or SDOH). This approach typically pays less attention to the fact that children vary in their sensitivity to those risk factors. In a related area of study focused on adversity within the family, high levels of childhood abuse, neglect, and household challenges (i.e., Adverse Childhood Experiences, known as ACEs) correlate with higher *population-level risk* for chronic impairments of physical and mental health. However, at an *individual level*, having a high ACE score as a child does not predict adult stress-related physical or mental illness any better than the flip of a coin.[130]

Neither SDOH nor ACE scores address the importance of developmental timing or the full breadth of intensity and diversity of early stressors that children face. Although sensitivity to environmental influences is highest during the prenatal and early childhood periods, significant adversity can have consequences at any age. That said, predictions of long-term outcomes must always be understood as probabilities, not foregone conclusions. A more complete picture, therefore, requires consideration of individual variation in the sensitivity of the stress response system, as well as individual differences in the effectiveness of an intervention.[45]

Neighborhood-focused investments… present a powerful framework to ensure that the wide range of stress responses exhibited by children and their families remain positive rather than toxic.

Neighborhood-focused investments that strengthen shared assets, address basic needs, break down structural barriers that perpetuate inequities, and increase opportunities for economic and social mobility present a powerful framework to ensure that the wide range of stress responses exhibited by children and their families remain positive rather than toxic. Building greater capacity to measure stress activation and resilience in the youngest children will help a broad range of stakeholders (from pediatricians, parents, service providers, and community leaders to policymakers, business leaders, and investors in community revitalization) to better assess, monitor, prevent, and reduce the disruptive effects of excessive adversity on healthy development.

Understanding that the developing body's response to adversity varies considerably can help reduce automatic thinking about early life stress as pathological. It does, however, underscore the importance of attention to *excessive* stress activation *as early as possible* and explain the limitations of one-size-fits-all approaches to reducing later disparities in educational achievement, economic mobility, and lifelong health. An activated stress response system can be both beneficial in the short term and harmful in the long term. That said, aligning science-informed knowledge with on-the-ground experience provides a promising opportunity to design, evaluate, and continuously refine more effective strategies to enhance the well-being of young children facing adversity today as well as increase the impacts of creative new investments in their future.

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