Stress and the Architecture of the Brain

By Dorian Friedman

Abstract: When faced with threats to physical or psychological well-being, our bodies and brains respond in a variety of self-protective ways, including the production of stress hormones adrenaline and cortisol. Our ability to turn this response on and off is critical to healthy functioning in society, and scientists now believe that significant adversity—and the lack of a supportive environment of relationships—in early childhood can trigger lifelong problems regulating this stress system. A nurturing, supportive environment may be the best protection a child can have against the harmful effects of stress in early life. Studies prove that it's easier and less expensive for society to provide what's needed in early childhood than to remediate for the aftereffects later in life. Scientists note four key areas in which policies and scientific knowledge are at greatest variance: starting before birth; confronting child abuse and neglect; ensuring the best possible child care; and addressing depression and other mental-health challenges.

Suggested citation: National Scientific Council on the Developing Child, Perspectives: Stress and the Architecture of the Brain. (2006). Retrieved [date of retrieval] from http://www.developingchild.net.

As the latest science reveals discoveries about human development, we are learning important lessons about what it takes to build sturdy architecture in the human brain, and about what can get in the way of its development. We know that the quality of a child's earliest experiences is critically important. Nurturing relationships are so fundamental, in fact, that the growing brain's architecture depends heavily on them. (For more on the relationship between caregiver-childhood interaction and the brain, see "Interaction and the Architecture of the Brain".)

At the same time, science is teaching us valuable lessons about how the brain's intricate architecture can be weakened or compromised when things go wrong. We now know empirically that exposure to frequent stress causes the release of harmful chemicals in a child's developing brain that can impair its physical growth and make it harder for neurons to form connections with each other. The weakening of the brain's architecture, in turn, impacts a child's ability to respond positively to future stresses, including normal life obstacles. In addition, it can have direct and long-lasting physiological consequences, such as increasing a child's vulnerability to later problems ranging from anxiety and depression to cardiovascular disease, diabetes and stroke.

What does "stress" mean in this context? Broadly defined by developmental scientists, stress refers to "the set of changes in the body and the brain that are set into motion when there are overwhelming threats to

physical or psychological well-being." (From *Neurons to Neighborhoods*, National Research Council and Institute of Medicine, 2000.) For our purposes, such stress can arise from a wide range of stimuli—from acute fear or mild anxiety, from physical ailments including sickness and hunger, or, most pointedly in children, from interaction with adults who are themselves under stress.

The Brain Responds

Well before birth, the human body choreographs its response to external events with a delicate interplay of hormones and neurochemicals. In the face of a stressful event such as fear or anxiety, receptors in the brain and the adrenal glands shift into high gear to produce two key hormones: adrenaline and cortisol.

"Childhood adversity shapes a stress system that has trouble flipping the 'off' switch."

Just as the immune system defends the human body, a well-regulated stress-response system is essential to preserve life. Without the so-called "flight/fight" instinct at the heart of our stress response, it seems unlikely that our prehistoric ancestors could have survived to evolve into modern humankind. However, like the immune system, our stress system can threaten our well-being if it is activated too often or without careful calibration. And that, in short, is what happens when a young child experiences stress for too long or too regularly. An excess of these chemicals floods the developing brain with a corroding effect on its architecture. Eventually, stress chemicals begin to damage vital regions—such as the hippocampus and amygdala—areas responsible for learning, memory, and emotional responses, among other critical functions.

It's useful to think of our stress system as a thermostat, suggests Pat Levitt, director of the Vanderbilt Kennedy Center for Research on Human Development at Vanderbilt University—and this thermostat can be damaged by unusual amounts of stress early in life. Under normal conditions, our bodies tell our brains when to raise the thermostat—producing needed hormones—and when to lower it as the source of stress subsides. "Our ability to turn this response on and off is very important," he says. Here's the rub: Early life experiences shape how readily the stress system is activated and how well it can be turned off. And childhood adversity, it turns out, "shapes a stress system that has trouble lowering the temperature, or flipping the 'off' switch."

Learning from Animal Research

Much of what science tells us today about stress and the brain comes from animal experiments. In various studies, researchers tested what would happen to baby rats if their mothers were subjected to stress. When they disrupted the mother's nest and interfered with her maternal instinct, for example, her "pups" grew into more fearful adults, poorly equipped to handle stress. In related studies, scientists also have shown how stress to rats during pregnancy causes a range of problems for their offspring later in life. Interestingly, though, these outcomes differ based on the care babies received from their mothers: Pups raised by nurturing rat mothers fared well, but those with inattentive mothers showed impaired memory and learning abilities, and were more

fearful and reactive to stress. But beyond these behavioral differences, the neglected pups showed physical problems in brain architecture—with fewer nerve connections in important parts of the brain.

Studies of rhesus monkeys have revealed similar patterns. Baby monkeys who are temporarily removed from their mothers develop brains that look different from "normal" monkey's brains, with structural differences in the amygdala and prefrontal cortex. These differences vary depending on how early the separation occurred. Further study of these differences may lead scientists to important conclusions about how the timing of stressful events may affect brain development. The research also may lead to cures.

And the Human Brain?

Can we apply these important findings about animals to our own children? A growing body of evidence suggests these are important lessons for human development, even though scientists can't yet say definitively what stress does to specific regions of the human brain.

Children who feel loved and secure seem to have a biological buffer against the threat.

At one end of the spectrum, the latest research demonstrates that young children exposed to stressful conditions in a setting as common as a child-care center often do respond physiologically. National Scientific Council member Megan Gunnar, a developmental psychologist at the University of Minnesota's Institute of Child Development, has shown that youngsters who must manage being with large groups of children for many hours each day experience rising levels of cortisol (the stress hormone) as the day progresses.

By afternoon, toddlers and preschoolers, especially those in large centers and those receiving poorer-quality child care, have stress hormone levels often double or triple what they show at home on non-child-care days. Researchers do not yet know how these rising stress-hormone levels in poorer-quality child-care arrangements affect brain development. However, because they are observed in the same settings that are associated with poorer behavioral outcomes for children, there is reason for concern, says Gunnar.

At the other end of the spectrum, we are slowly coming to understand the link between more severe forms of stress—which can be referred to as "toxic stress"—and the healthy growth of the brain's architecture. At least one study of youngsters who suffered serious child abuse drew conclusions that were most disturbing: Compared with their peers, these children had measurably smaller brain volume, with more ventricles (the fluid-filled, squiggly cavities) and weaker connections between the organ's left and right sides. Sadly, the longer they endured the abuse, the more severe were the effects on their developing brains.

Dance of Genes and Environment

Importantly, the relationship between stress and the brain is a function of both "nature" and "nurture." "All of this is a dance between genes and experience," says Gunnar, who offers the following analogy: The genes we are born with can be thought of

as our "genetic library." The experiences we have influence which books in that library we take out and read at different points in brain development. And this intertwining of genes and experience shapes our brain architecture. Scientists are just beginning to understand how particular genes in our library affect how we react to stress early in life and what effect this has on how our brains develop and respond to stress later.

We know that some children are much more adversely affected by stress than others, and we strongly suspect this is partly due to the genes they have in their genetic libraries, Gunnar says. For example, a study done in New Zealand (Caspi et al, 2003, *Science*, 301: 386-389.) demonstrated that abused children with a faulty version of the gene that regulates the brain chemical serotonin were more likely to develop depression, while those who had a more efficient serotonin gene were not likely to get depressed. What we don't yet know is how this particular gene influences brain development in abused children and whether the faulty version participates in producing the smaller brain volumes and weaker connections seen in many abused children. What we do know is that in the absence of abuse, even the children with the faulty serotonin gene were not likely to become depressed. So, it's not the genes in the child's library or that child's experiences that determine how the brain develops—it's very much both.

Being able to adapt and cope with stress is part of life, and you'd like to practice on small, manageable things.

What science also knows is that stress hormones connect with regions on many genes that open or shut the books' covers, allowing them to be read (turned on) or putting them back on the shelf (turned off). Increases in stress hormones mean that gene books are opened and shut all over the brain, allowing the experience of stress to affect the brain's development. We also know that nature has provided children with a powerful way of keeping stress from affecting brain development by blocking the rise in stress hormones, thus keeping the librarian sitting at her desk. Loving, supportive relationships are the "stress hormone blocker."

The power of this protective stress blocker can be seen in something as common as a visit to the pediatrician for immunizations. Gunnar's research shows that the way children react to this frightening situation varies greatly based on their relationships with their caregivers. Children who feel loved and secure seem to have a biological buffer against the threat. "That secure attachment literally blocks the baby's hormonal response to stress," she says, explaining that chemicals in the brain react differently in response to the perceived danger. Conversely, children who don't feel a sense of security from outside sources often overreact to fear of the shot; their bodies produce elevated levels of stress hormones when they are even mildly afraid.

Everything in Moderation

While toxic stress is clearly harmful to the developing brain, it turns out that exposure to mild stress is important, physiologically speaking. Animal studies illustrate this point. When rat pups are handled by researchers only occasionally or for short periods of time, they seem to acquire the ability to cope better with stressful situations as adults.

In fact, they mature into more skillful "stress responders" than rat babies exposed to extreme stress—and, interestingly, they handle stress better than those rat pups that endured no stress at all in the same lab tests. The simple hypothesis: Early exposure to manageable amounts of stress helps the body's chemical stress-response system evolve in an effective way.

Pat Levitt likens this finding to a familiar problem for any parent: How to introduce a child to candy without causing one of two undesirable outcomes: addiction to sugar because of too much early in life, or craving it because of deprivation. Experience and common sense—if not hard science—suggest the wisdom of moderate exposure to cultivate a healthy response in later years.

The body of animal research in the field seems to suggest that mild stress might be important for a human baby as well—conditioning her brain and hormone systems to respond appropriately to more serious threats that may arise. Betsy Lozoff, director of the Center for Human Growth and Development at the University of Michigan, explains, "We think it's important that children fall down sometimes, or get minor illnesses once in a while. Being able to adapt and cope with stress is part of life, and you'd like to practice on small, manageable things."

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Undoing the Damage, Repairing the Architecture

If harmful conditions can weaken the developing brain's sensitive architecture, can favorable ones strengthen it? Research suggests the answer is yes. Early in childhood, "the brain is plastic—or malleable—enough that if we provide different experiences we can change the developmental trajectory pretty dramatically," says Levitt. And the same holds true for the stress-response system "thermostat," which is most easily molded during the fetal and early childhood periods.

Hard evidence for this assertion comes, again, from animal studies. Remember those rat pups raised by different kinds of mothers? The ones reared by inattentive mothers were impaired in a number of ways, with intelligence, memory, and stress problems later in life. But when the same troubled pups were taken away from their inattentive mothers and placed in "enriched" settings in their first few weeks of life, their performance returned to normal. Brain researchers hypothesize that this quick reversal may result from an actual change in the brain's chemistry—a shift that helps the rat's brain find alternative pathways to reach the same level of performance and generate the right balance of neurochemicals. More to the point, findings like these suggest something else: That a nurturing, supportive environment may be the best protection a child can have against the harmful effects of stress in early life.

Research on this hypothesis is under way by several members of the National Scientific Council, and by many of their colleagues in the developmental sciences. Findings include compelling evidence relating to children reared in orphanages under terrible conditions, then later adopted into loving homes. The conclusion so far: Changing the

conditions that cause the problem and providing enriching experiences as early as possible can compensate for a great deal of early stress and neglect—but it cannot reverse all of the stress-related brain effects. On this point, the science suggests that early impairments to the brain are indeed amenable to change because the brain can, in effect, "rewire" itself. But doing so takes longer than did the original wiring, and we do not know what is lost in the process.

Jack Shonkoff, chairman of the National Scientific Council for the Developing Child, director of the Center on the Developing Child at Harvard University, and Julius B. Richmond FAMRI Professor of Child Health and Development at the Harvard School of Public Health and Graduate School of Education, agrees. "To be sure, significant and prolonged stress can permanently change the brain's circuitry," he says. "But that's different from saying these children are permanently doomed. Kids like these can still do well, but it's likely to take more—and harder—work to help them do well. We're either adding the burden of risk and vulnerability, or we're giving them the best shot from the start. Obviously, it's easier and less expensive to get things right the first time."

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Getting Things Right the First Time: Implications for Public Policy

Given what we now know and continue to learn about the costly consequences of stress on the brain architecture of the developing child, on families, and on society at large, the National Scientific Council's scientists are guided by this simple motto: "It's easier to get things right the first time." (Or, scientifically speaking, "prevention is better than remediation.") Toward that end, they point to a wide range of public policies and community investments—informed by developmental science—that are aimed at preventing or mitigating harmful sources of stress to developing children. In their ongoing conversations with policymakers, they highlight the following areas where current policy and the new scientific findings are at greatest variance:

• **Starting before birth.** Evidence demonstrates that developing fetuses and infants are especially vulnerable to many forms of environmental stress. Investments to ensure early, consistent prenatal care are among the most cost-effective ways to promote the healthy development of young children. While the nation has made great strides in expanding access to good prenatal care, too many poor and minority women and pregnant teenagers still fall through the health-care cracks. In 2003, 25 percent of expectant African American and Hispanic women received no prenatal care in their first trimester of pregnancy, and minority women were twice as likely as white women to delay prenatal care until their third trimester—a very risky practice. And despite big drops in teen pregnancy, fully one-third of teenagers who do become pregnant still receive inadequate prenatal care—sharply increasing the odds their babies will be born at low birth weight and with serious health problems. Intensive efforts must target these women at greatest risk and others lacking health insurance.

• **Confronting child abuse and neglect.** Any sound prevention strategy also must focus on the threat of child abuse and neglect. "From a developmental perspective, there's no such thing as a 'mild' case of child abuse or neglect," says Nathan Fox, professor of Human Development and Psychology at the University of Maryland. By definition, abuse and neglect are "harmful and may have long-term consequences on the developing brain and behavior." Science thus suggests the need for very new and different thinking about efforts to combat these problems.

One important way to start would be to address a troubling imbalance in the nation's current funding priorities: Many billions of dollars are spent on the consequences of childhood neglect—from foster care, child-welfare services, and special education, to juvenile delinquency, welfare dependency and adult criminality—while far less is spent on programs likely to prevent maltreatment in the first place. By one careful estimate from the organization Prevent Child Abuse America, we spend $258 million each day— some $94 billion a year—on these direct and indirect costs of child abuse. At the same time, a growing number of cost-benefit studies have concluded that prevention efforts (especially home-visitation programs for families at highest risk of child abuse) yield a significant return-on-investment for the financial costs of maltreatment—to say nothing of the emotional costs for the children and families affected.

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The nation's two main federal programs aimed at preventing abuse—the Child Abuse and Prevention Treatment Act and Promoting Safe and Stable Families, now part of the Social Security Act—are designed to promote effective investments in this critical policy area. But changing our priorities requires more than adequate funding. In the view of National Scientific Council members, those with influence over a developing child—including teachers, child-care providers, parents and even sports and recreation coaches—need a better grounding in the developmental stages of childhood. Society would reap the benefits of teaching adults how to deal with common behavioral challenges, including discipline and limit-setting. And by doing so, society should convey this clear message grounded in developmental science: that physical discipline, including spanking and hitting, is potentially harmful as well as ineffective Often, a young child who is punished is incapable of understanding what he or she has done wrong. By elevating adults' understanding of the ways young children are affected by these ill-informed actions, we could make a substantial contribution to child-abuse prevention in our culture. There are numerous ways to accomplish this, including the infusion of developmental teaching in health and life-studies curricula in high schools.

Moreover, in the public child-protection system, it is imperative that the agencies and officials responsible for investigating suspected child-abuse cases work more closely with child-welfare experts who are trained to diagnose and treat problems commonly associated with that abuse, including developmental delays and disabilities. Along

the same lines, all children who enter the protection system on suspicion of abuse or neglect should automatically receive careful screening and early intervention.

• **Ensuring the best possible child care.** This growing body of scientific knowledge has clear implications for child-care policies, too. "We know that humans, like animals, find excessive change to be really stressful," says Levitt. "If a child never gets to develop meaningful and consistent relationships, it can be a great source of stress," he adds. For young children especially, stable, loving relationships are critically important.

"Consistency builds an environment of relationships that provides the nurturing young children need," says Levitt. "And that's very important in helping them develop positive ways of responding to occasional stress."

Here, too, research should shape new public-policy priorities, ones that are crystal clear to developmental experts such as Nathan Fox. "Child care that's provided by experienced individuals with a good ratio of caregivers to kids greatly reduces stress," he says.

Among the many policy changes suggested: A major public investment that would fund more rigorous training for child-care providers; ensure top-quality programs for children of affluent families and needy ones; achieve higher ratios of teachers to children; and reduce the current epidemic of staff turnover and attrition. These improvements would result in more stable and healthy relationships for children in care. All of these conditions have been linked in careful research to better child-care experiences—with measurable outcomes for children. A footnote: The successful child-care experience of the U.S. Department of Defense could serve as a model.

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• **Addressing depression and mental-health challenges.** As outlined above, a youngster's ability to manage stress is a function of several variables, some more mysterious than others. But there is wide agreement on one significant risk factor for children: the mental health of their parents. Depressed mothers, in particular, have trouble responding to their children in ways that make them feel loved and secure. And that, in turn, has been shown to contribute to many adverse outcomes for children growing up with them—including problems in school, poor self-control, and an impaired ability to manage stress later in childhood.

It's a challenge of surprising magnitude, among women in particular. About one in every eight women suffers from clinical depression during their lifetime. The problem arises most often between ages 25 and 44, among women with young children, and with far higher prevalence among poor mothers. Most troubling, fewer than half of the women who experience clinical depression will ever seek care, which presents an urgent need for better public policies. According to the National Alliance for the Mentally Ill, the barriers to adequate care are threefold. Continuing stigmas associated with mental illnesses like depression dissuade many people from getting the treatment they need. Cost, too, remains a big barrier, as too few private insurance plans cover mental-health expenses. Finally, the nation's mental-health system is very fragmented—a

recent White House commission called it "a system in shambles"—and creates confusion for people who don't know where to turn for help. At minimum, programs should include a thorough screening for parents at greatest risk, and there should be access to resources for comprehensive mental-health counseling and treatment modeled on programs that have been shown to work.

Addressing a related need, Council members also endorse better public policies to improve the nation's seriously inadequate mental-health system as it pertains to children. Incentives to attract qualified experts to work with young children and professional training for those entering the childhood mental-health field are important steps toward more effective screening, early detection, treatment and prevention of serious childhood mental-health problems.

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• **Using science to inform interventions.** As they reflect on what science teaches about stress and the developing brain, members of the Council identify many other policies in need of rethinking. Everything we know about the protective qualities of nurturing relationships for children under stress, for instance, suggests the importance of investing in high-quality parenting and mentoring programs, and renewed efforts to protect children from family discord. Similarly, scientific evidence linking conditions of poverty to stress in children suggests an entire textbook of policy changes. These could include a rethinking of the nation's redistributive tax policies and subsequent increase in the existing but modest child tax credit; a boost in the Earned Income Tax Credit aimed at poor working families; a shift in current welfare-to-work requirements; and further expansion of the successful Head Start preschool model for disadvantaged children. Importantly, the current Head Start model that pays attention to health and economic stresses on the child's family would appear to be more congruent with the new brain science than a model that focused solely on the child's cognitive development.

Together, policy changes like these would represent wise economic investments in the future of our children, and avert problems sure to cost society far more in later years. But more than that, they represent a set of moral principles grounded in hard science. By helping to protect today's children from the most insidious sources of stress, we are literally building the brains of the future.

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