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NATIONAL SCIENTIFIC COUNCIL ON THE DEVELOPING CHILD

# Excessive Stress Disrupts the Architecture of the Developing Brain

WORKING PAPER 3



Center on the Developing Child  HARVARD UNIVERSITY

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# NATIONAL SCIENTIFIC COUNCIL ON THE DEVELOPING CHILD

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The National Scientific Council on the Developing Child, housed at the Center on the Developing Child at Harvard University, is a multi-disciplinary collaboration designed to bring the science of early childhood and early brain development to bear on public decision-making. Established in 2003, the Council is committed to an evidence-based approach to building broad-based public will that transcends political partisanship and recognizes the complementary responsibilities of family, community, workplace, and government to promote the well-being of all young children.

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# The Issue

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THE ABILITY TO COPE WITH NOVEL AND/OR POTENTIALLY THREATENING SITUATIONS, SUCH AS AN unfamiliar environment or physical danger, is essential to survival. This capacity is built into specific brain circuits whose development is influenced by multiple experiences beginning early in life. Environmental stimuli that activate these circuits are often referred to as stressors, and stress reactions are the body's chemical and neural responses that promote adaptation.

Stressful events can be harmful, tolerable, or beneficial, depending on how much of a bodily stress response they provoke and how long the response lasts. These, in turn, depend on whether the stressful experience is controllable, how often and for how long the body's stress system has been activated in the past, and whether the affected child has safe and dependable relationships to turn to for support. Thus, the extent to which stressful events have lasting adverse effects is determined more by the individual's response to the stress, based in part on past experiences and the availability of a supportive adult, than by the nature of the stressor itself. This matters because a child's ability to cope with stress in the early years has consequences for physical and mental health throughout life. Furthermore, categorizing the nature and severity of early stressful experiences helps us make better judgments about the need for interventions that reduce the risk for later negative impacts.

**Toxic stress** refers to strong, frequent or prolonged activation of the body's stress management system. Stressful events that are chronic, uncontrollable, and/or experienced without the child having access to support from caring adults tend to provoke these types of toxic stress responses. Studies indicate that such stress responses can have an adverse impact on brain architecture. In the extreme, such as in cases of severe, chronic abuse, toxic stress may result in the development of a smaller brain. Less extreme exposure to toxic stress can change the stress system so that it responds at lower thresholds to events that might not be stressful to others, thereby increasing the risk of stress-related physical and mental illness.

**Tolerable stress** refers to stress responses that could affect brain architecture but generally occur for briefer periods that allow time for the brain to recover and thereby reverse

potentially harmful effects. In addition to their relative brevity, one of the critical ingredients that make stressful events tolerable rather than toxic is the presence of supportive adults who create safe environments that help children learn to cope with and recover from major adverse experiences, such as the death or serious illness of a loved one, a frightening accident, or parental separation or divorce. In some circumstances, tolerable stress can even have positive effects.

## A child's ability to cope with stress in the early years has consequences for physical and mental health throughout life.

Nevertheless, it also can become toxic stress in the absence of supportive relationships.

**Positive stress** refers to moderate, short-lived stress responses, such as brief increases in heart rate or mild changes in the body's stress hormone levels. This kind of stress is a normal part of life, and learning to adjust to it is an essential feature of healthy development. Adverse events that provoke positive stress responses tend to be those that a child can learn to control and manage well with the support of caring adults, and which occur against the backdrop of generally safe, warm, and positive relationships. The challenge of meeting new people, dealing with frustration, entering a new child care setting, getting an immunization, and overcoming a fear of animals all can be positive stressors if a child has the support needed to develop a sense of mastery. This is an important part of the normal developmental process.

## What Science Tells Us

SCIENTIFIC KNOWLEDGE IN THIS AREA COMES from research on animals as well as humans. These extensive bodies of work have generated common principles of developmental biology that support valid generalizations across species and reasonable hypotheses about humans based on consistent findings from animal studies. The ability to control exposure to negative life experiences in animals makes it additionally possible to conduct studies of the impacts of more graded forms of stress on the brain than could be done in human research.

The capacity to deal with stress is controlled by a set of highly inter-related brain circuits and hormonal systems that are specifically designed

**The neural circuits for dealing with stress are particularly malleable (or “plastic”) during the fetal and early childhood periods.**

to deal adaptively with environmental challenges. When an individual feels threatened, stress hormones are produced that convert the physical or emotional stress into chemical signals that are sent throughout the body as well as to the brain.

**The neural circuits for dealing with stress are particularly malleable (or “plastic”) during the fetal and early childhood periods.** Early experiences shape how readily they are activated and how well they can be contained and turned off. Toxic stress during this early period can affect developing brain circuits and hormonal systems in a way that leads to poorly controlled stress-responsive systems that will be overly reactive or slow to shut down when faced with threats throughout the lifespan.<sup>1,2</sup>

**Well-functioning brain systems that respond to stress are essential to preserve life.** However, like the immune system, which defends the body against threatening infections but can cause autoimmune disease when it turns against the body’s own cells, a poorly controlled

response to stress can be damaging to health and well-being if activated too often or for too long.<sup>3</sup>

**Frequent or sustained activation of brain systems that respond to stress can lead to heightened vulnerability to a range of behavioral and physiological disorders over a lifetime.** These undesirable outcomes can include a number of stress-related disorders affecting both mental (e.g., depression, anxiety disorders, alcoholism, drug abuse) and physical (e.g., cardiovascular disease, diabetes, stroke) health.<sup>3</sup>

Stress responses include activation of a variety of hormone and neurochemical systems throughout the body. Two hormonal systems have received extensive attention in this regard: (1) the sympathetic-adrenomedullary (SAM) system, which produces adrenaline in the central part of the adrenal gland, and (2) the hypothalamic-pituitary-adrenocortical (HPA) system, which produces cortisol in the outer shell of the adrenal gland.<sup>4</sup> Both chemicals are produced under normal circumstances and help prepare the body for coping with stressors.

**Adrenaline production occurs in response to many forms of acute stress.** It mobilizes energy stores and alters blood flow, thereby allowing the body to effectively deal with a range of stresses. Its release is essential to survival.<sup>4</sup>

**Cortisol also is produced in response to many forms of stress, and likewise helps the body cope effectively with adverse situations.** It also mobilizes energy stores, as well as suppresses immune responses, when it is released acutely. Longer-term effects of cortisol include regulation of gene expression in neural circuits involved in modulating stress responsiveness, emotion, and memory.<sup>4</sup>

**Sustained or frequent activation of the hormonal systems that respond to stress can have serious developmental consequences, some of which may last well past the time of stress exposure.** For example, when children experience toxic stress, their cortisol levels remain elevated for prolonged periods of time. Both

animal and human studies show that long-term elevations in cortisol levels can alter the function of a number of neural systems, and even change the architecture of regions in the brain that are essential for learning and memory.<sup>5,6</sup>

MUCH OF WHAT WE KNOW ABOUT THE SPECIFIC effects of stress on the developing architecture of the brain comes from research on rodents, non-human primates, and other animal species. These studies indicate that:

**Increases in the level of cortisol in the brain actually can turn specific genes “on” or “off” at specific times and locations.**<sup>7</sup> Examples include regulation of the *glucocorticoid receptor* gene, which affects the long-term responsiveness of the brain to stress-induced cortisol release, and the *myelin basic protein* gene, which is involved in regulating the development of the “insulation” that increases the efficiency of nerve signal transmission.<sup>8,9</sup>

**High, sustained levels of cortisol or corticotropin-releasing hormone (CRH), which is the brain chemical that regulates the HPA system, result in damage to a part of the brain called the hippocampus.** This can lead to impairments in learning, memory, and the ability to regulate certain stress responses in both young and adult animals.<sup>10</sup>

**Significant maternal stress during pregnancy and poor maternal care during infancy both affect the developing stress system in young animals and alters genes that are involved in brain development.** Pregnant females who experience exceptionally high levels of stress have offspring that are more fearful and more reactive to stress themselves. Young animals that experience inattentive maternal care have similar problems and show impaired production of brain growth factors important for brain development and repair.<sup>11,12</sup> Both groups of animals also have impaired memory and learning abilities, and they experience more aging-related memory and cognitive deficits in adulthood.<sup>3,13</sup>

**Positive experiences after infancy in young animals, such as being exposed to an environment rich in opportunities for exploration and social play, have been shown to compensate to some degree for the negative behavioral consequences**

**of prenatal stress and postnatal neglect.** This compensation actually involves adaptive changes in both the architecture and the chemistry of the developing brain (such as reversal of the effects of mild adversity on stress hormone output), although deprivation-induced changes in some of the regulatory components of the stress system (e.g., reduced glucocorticoids receptors in the hippocampus) are more resistant to change.<sup>14</sup>

**Individual responses to early stressful experiences can vary dramatically.** This variability is thought to be related to differences among animals in the expression of so-called “vulnerability genes,” which make it more likely that early stressors will lead to subsequent problems in stress hormone

## The relationships children have with their caregivers play critical roles in regulating stress hormone production during the early years of life.

regulation and behavioral difficulties. In such cases, positive early caregiving can decrease the likelihood of these adverse outcomes, demonstrating that beneficial environmental influences can moderate the impact of genetic vulnerability.<sup>15</sup>

BUILDING ON THE EXTENSIVE KNOWLEDGE gained from animal research, studies of children are beginning to document a compelling story about the relation between early stress experiences and human development. The following findings appear to be particularly salient:

**The relationships children have with their caregivers play critical roles in regulating stress hormone production during the early years of life.**

Those who experience the benefits of secure relationships have a more controlled stress hormone reaction when they are upset or frightened. This means that they are able to explore the world, meet challenges, and be frightened at times without sustaining the adverse neurological impacts of chronically elevated levels of hormones such as cortisol that increase reactivity of selected brain systems to stress and threat. In contrast, children whose relationships are

insecure or disorganized demonstrate higher stress hormone levels when they are even mildly frightened. This results in an increased incidence of elevated cortisol levels which may alter the development of brain circuits in ways that make some children less capable of coping effectively with stress as they grow up.<sup>2</sup>

**Research has shown that the presence of a sensitive and responsive caregiver can prevent elevations in cortisol among toddlers, even in children who tend to be temperamentally fearful or anxious.**<sup>16</sup> Thus, sensitive and responsive caregiving from a parent or a child care provider

### Young children who experience debilitating anxiety and trauma as a result of personal abuse or neglect are amenable to early treatment.

can serve as a powerful buffer against stress hormone exposure, even in children who might otherwise be highly vulnerable to stress-system activation.

**The quality of the early care and education that many young children receive in programs**

**outside their homes also plays an important role in whether (and to what extent) their brains are exposed to elevated stress hormones early in life.**

For example, toddlers and young preschoolers show increases in cortisol as the child care day progresses, while older preschoolers and school-aged children can manage long hours in care without activating their stress system.<sup>17</sup> Young children in poorer quality child care show larger elevations, however, than those in better quality care.<sup>18</sup>

**Children who grow up in families facing economic hardship commonly exhibit elevated cortisol levels.** These elevations are often exacerbated when mothers experience symptoms of depression.<sup>19,20,21</sup> Recent research also has demonstrated that a mother's depression during her child's early years increases the child's cortisol reactions to adverse family conditions later in childhood.<sup>22,23,24</sup>

**Young children who are neglected or maltreated have abnormal patterns of cortisol production that can last even after the child has been moved to a safe and loving home.**<sup>25,26</sup> This is especially true for children who show symptoms of post-traumatic stress, even if their behavior is not sufficient to warrant a definitive diagnosis of post-traumatic stress disorder.<sup>27,28,29</sup>

## Popular Misrepresentations of Science

AS THE PUBLIC'S APPETITE FOR SCIENTIFIC INFORMATION about the development of young children is stimulated by exciting new findings, the risk of exposure to misleading or, frankly, irresponsible messages grows. Within this context, it is essential that we distinguish scientific fact from popularly accepted fiction.

**Science does not support the claim that infants and young children are too young to be affected by significant stresses that negatively affect their family and caregiving environments.** In fact, animal studies have shown that adverse early infant experiences (e.g., neglectful maternal care), as well as serious disruptions of the pre-natal environment (e.g., drug and alcohol exposure), can

lead to short-term neurobehavioral and neurohormonal changes in offspring that may have long-term adverse effects on memory, learning, and behavior throughout life. Human studies suggest that similar effects may be seen in infants and children.<sup>30</sup>

**Notwithstanding the preceding statement, there is no credible scientific evidence that supports the conclusion that young children who have been exposed to significant early stresses will always develop stress-related disorders.** In both animal and human studies, interventions that provide more appropriate and supportive care help to stimulate positive growth and prevent poor outcomes.<sup>14,25,31</sup>

# The Science-Policy Gap

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THE FACT THAT MANY YOUNG CHILDREN ARE exposed to significant stresses is old news. How different aspects of a child's environment can be a source of continuous stress, and the degree to which children's past developmental experiences influence their biological responsiveness to later stressful conditions are not appreciated by most adults. The realization that stresses experienced by parents and other caregivers can affect a child's developing brain architecture and chemistry in a way that makes some children more susceptible to stress-related disorders later in life is startling news to most people.

A rich and growing scientific knowledge base illuminates the multiple adverse effects of early life stresses, including their long-term impacts on how individuals cope with stress throughout the life cycle. Yet little attention has been paid to the development and implementation of strategies to reduce stressors that affect everyday life for families with young children. This gap between what we know about the potentially harmful developmental impacts of stresses experienced by both caregivers and children, and what we do to promote healthy coping and adaptation through informal supports, voluntary workplace practices, and formal public policies and programs, is illustrated by the following examples:

**Limited availability of family leave after the birth or adoption of a baby, and little financial support for parents who wish to stay at home with their newborns but do not have the economic resources to make ends meet in the absence of paid employment.** In some circumstances, this creates situations where the supportive relationships necessary to help very young children manage stress are intermittent or seriously compromised.<sup>32,33,34,35</sup>

**Limited supports for working parents at all income levels who are struggling to balance the demands and responsibilities of work and raising children.** These balancing challenges are particularly difficult for low-income, working families whose economic security depends on multiple low-wage jobs, often during non-

standard working hours, and for families whose children have chronic health problems or special developmental needs that require multiple medical appointments and skilled child care. In such circumstances, some young children are subjected to excessive stress that can have lasting effects on their health and well-being.<sup>31</sup>

**Limited efforts to reduce high job turnover in child care programs, which affects the quality of relationships between adults and the children under their care.** This is a particularly serious problem for those children whose family's socioeconomic circumstances limit their access to better-quality programs that have well trained, adequately compensated, and more stable staff.<sup>35,36,37,38</sup>

**Limited availability of expert help for parents and providers of early care and education who are struggling to manage behavioral difficulties in young children.** This is particularly problematic in the face of recent data on expulsion of children from preschool programs, which indicate the extent to which staff members are unable and/or unwilling to deal with challenging behavioral problems.<sup>39</sup> The growing "off-label" use of prescription drugs, particularly stimulant and anti-depressant medications, for increasingly younger children with emotional or behavioral difficulties is another sign of the extent to which parents are putting greater pressure on professionals to provide more help in managing behavior problems during the preschool years.<sup>40</sup>

**Limited access to clinical expertise in mental health for very young children and their families.** This is particularly problematic in child welfare agencies that are mandated to assess children who are coping with toxic stress that can have lasting adverse effects on their well-being. Most important, young children who experience debilitating anxiety and trauma as a result of personal abuse or neglect, or who witness violence in their family or neighborhood, are amenable to early treatment.<sup>41,42</sup>

## Implications for Policy and Programs

THE SCIENCE OF EARLY CHILDHOOD DEVELOPMENT, including knowledge about the impact of stress on the developing brain, is sufficiently mature to support a number of evidence-based implications for those who develop and implement policies that affect the health and well-being of young children. To this end, both public and private actions can prevent the kinds of adverse circumstances that are capable of derailing healthy development, as well as increase the likelihood that effective interventions

**Both public and private actions can prevent the kinds of adverse circumstances that are capable of derailing healthy development.**

will reduce potential damage to a young child's developing brain architecture and thereby promote greater resilience. Five points are particularly worthy of thoughtful consideration.

**The rich and growing scientific understanding of how individuals cope with stress should be used to strengthen a range of informal supports and formal services to bolster parents who are struggling to manage the challenges of raising their children.** These could be provided through varying combinations of extended family support, community-based volunteer efforts, flexible workplace policies, and publicly funded programs.<sup>43</sup>

**The availability of affordable expert assistance should be expanded for parents and providers of early care and education to provide them with sufficient knowledge and skills to help young children who have symptoms related to abnormal stress responses.** This is particularly important for children who exhibit excessive fears, aggressive behavior, or difficulties with attention and "hyperactivity."<sup>35,41</sup>

**Expertise in the identification, assessment, and clinical treatment of young children with serious, stress-related, mental health problems (as well as access to mental health services for mothers with**

**depression) should be incorporated into existing intervention programs to address these complex and widely unmet needs.** Research indicates that young children can experience a range of mental health impairments that used to be viewed solely as adult problems, such as depression, anxiety disorders, and anti-social behaviors.<sup>35</sup>

**Investigations of suspected child abuse or neglect should include a sophisticated assessment of the child's developmental status, including cognitive, linguistic, emotional, and social competence.** This could be accomplished through closer collaboration between child welfare services and early intervention programs for children with developmental delays or disabilities,<sup>44</sup> as mandated by the Keeping Children and Families Safe Act of 2003 and the recent reauthorization of the Individuals with Disabilities Education Act (IDEA).

**Children of mothers who are receiving welfare payments or related services under the Temporary Assistance to Needy Families (TANF) program represent another identified group whose experience with stress is likely to exceed that of the general population.** In this context, it is difficult to justify the extent to which public discussion about welfare reform focuses primarily on maternal employment and other adult behaviors, while the special needs of the young children in these families are afforded relatively little attention. Our knowledge of the importance of supportive relationships as buffers against the adverse effects of stress on the architecture of the developing brain indicates the need for serious reconsideration of mandated employment for mothers of very young children, particularly when access to high quality child care is not assured. Research also underscores the importance of timely assessments and intervention services (when indicated) for children living in stressful environments who show early signs of developmental difficulties.<sup>45,46</sup>



# References

1. Zhang, T., Parent, T., Weaver, I., & Meaney, M. J. (2004). Maternal programming of individual differences in defensive responses in the rat. *Annals of the New York Academy of Science*, 1032, 85-103.
2. Loman, M., & Gunnar, M.R. (in press). Early experience and the development of stress reactivity and regulation in children. *Neuroscience & Biobehavioral Reviews*.
3. McEwen, B. S. (2008). Central effects of stress hormones in health and disease: Understanding the protective and damaging effects of stress and stress mediators. *European Journal of Pharmacology*, 583, 174-185.
4. Sapolsky, R.M., Romero, L.M., & Munck, A. (2000). How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory and preparative actions. *Endocrine Reviews*, 21(1), 55-89.
5. Lupien, S.J., de Leon, M.J., Santi, S.D., Convit, A., Tarshish, C., Nair, N.P.V., Thakur, M., McEwen, B., Hauger, R.L., & Meaney, M.J. (1998). Cortisol levels during human aging predict hippocampal atrophy and memory deficits. *Nature Neuroscience*, 1(1), 69-73.
6. McEwen, B. S., & Sapolsky, R. M. (1995). Stress and cognitive function. *Current Opinion in Neurobiology*, 5(2), 205-216.
7. De Kloet, E.R., Rots, N.Y., & Cools, A.R. (1996). Brain-corticosteroid hormone dialogue: Slow and persistent. *Cellular and Molecular Neurobiology*, 16(3), 345-356.
8. Gunnar, M., & Vazquez, D. M. (2006). Stress neurobiology and developmental psychopathology. In D. Cicchetti & D. Cohen (Eds.), *Developmental Psychopathology, 2nd Edition, Volume 2: Developmental Neuroscience*. New York: Wiley.
9. Weaver, I.C., Diorio, J., Seckl, J.R., Szyf, M., & Meaney, M.J. (2004) Early environmental regulation of hippocampal glucocorticoid receptor gene expression: Characterization of intracellular mediators and potential genomic target sites. *Annals of the New York Academy of Sciences*, 1024, 182-212.
10. Brunson, Grigoriadis D.E., Lorang M.T., & Baram T.Z. (2002) Corticotropin-releasing hormone (CRH) down-regulates the function of its receptor (CRF1) and induces CRF1 expression in hippocampal and cortical regions of the immature rat brain. *Experimental Neurology*, 176(1), 75-86.
11. Roceri, M., Cirulli, F., Pessina, C., Peretto, P., Racagni, G., & Riva, M. A. (2004). Postnatal repeated maternal deprivation produces age-dependent changes in brain-derived neurotrophic factor expression in selected rat brain regions. *Biological Psychiatry*, 55, 708-714.
12. Roceri, M., Hendriks, W., Racagni, G., B.A., E., & Riva, M. A. (2002). Early maternal deprivation reduces the expression of BDNF and NMDA receptor subunits in rat hippocampus. *Molecular Psychiatry*, 7, 609-616.
13. Weinstock, M. (2001). Alterations induced by gestational stress in brain morphology and behaviour of the offspring. *Progress in Neurobiology*, 62(4), 427-451.
14. Francis, D., Diorio, J., Plotsky, P.M., & Meaney, M.J. (2002). Environmental enrichment reverses the effects of maternal separation on stress reactivity. *Journal of Neuroscience*, 22(18), 7840-7843.
15. Barr, C.S., Newman, T.K., Lindell, S., Shannon, C., Champoux, M., Lesch, K.P., Suomi, S., Goldman, D., Higley, J.D. (2004). Interaction between serotonin gene variation and rearing history in alcohol preference and consumption in female primates. *Archives of General Psychiatry*, 61(11), 1146-1152.
16. Nachmias, M., Gunnar, M. R., Mangelsdorf, S., Parritz, R., & Buss, K. A. (1996). Behavioral inhibition and stress reactivity: Moderating role of attachment security. *Child Development*, 67(2), 508-522.
17. Vermeer, H. J., & van IJzendoorn, M. H. (2006). Children's elevated cortisol levels at daycare: A review and meta-analysis. *Early Childhood Research Quarterly*, 21, 390-401.
18. Gunnar, M.R., Kryzer, E., VanRyzin, M.J., & Phillips, D. (in press). The rise in cortisol in family day care: Associations with aspects of care quality, child behavior, and child sex. *Child Development*.
19. Essex, M.J., Klein, M.H., Cho, E., & Kalin, N.H. (2002). Maternal stress beginning in infancy may sensitize children to later stress exposure: Effects on cortisol and behavior. *Biological Psychiatry*, 52(8), 776-784.
20. Lupien, S., King, S., Meaney, M.J., McEwen, B.S. (2000). Child's stress hormone levels correlate with mother's socioeconomic status and depressive state. *Biological Psychiatry*, 48(10), 976-980.
21. Lupien, S., King, S., Meaney, M.J., & McEwen, B.S. (2001). Can poverty get under your skin? Basal cortisol levels and cognitive function in children from low and high socioeconomic status. *Development and Psychopathology*, 13, 653-676.
22. Dawson, G. & Ashman, S.B. (2000). On the origins of a vulnerability to depression: The influence of the early social environment on the development of psychobiological systems related to risk for affective disorder. In C.A. Nelson (Ed.), *The Effects of Adversity on Neurobehavioral Development: Minnesota Symposia on Child Psychology*, (pp. 245-280). Mahwah, NJ: Lawrence Erlbaum & Assoc.
23. Ashman, S.B., Dawson, G., Panagiotides, H., Yamada, E., & Wilkins, C.W. (2002). Stress hormone levels of children of depressed mothers. *Development and Psychopathology*, 14(2), 333-349.
24. Jones, N.A., Field, T., & Fox, N.A. (1997). EEG activation in 1-month-old infants of depressed mothers. *Development and Psychopathology*, 9(3), 491-505.
25. Gunnar, M., Morison, S.J., Chisholm, K., & Schuder, M. (2001). Salivary cortisol levels in children adopted from Romanian orphanages. *Development and Psychopathology*, 13, 611-628.
26. Bruce, J., Fisher, P. A., Pears, K. C., & Levine, S. (2009). Morning cortisol levels in preschool-aged foster children: Differential effects of maltreatment type. *Developmental Psychobiology*, 51, 14-23.
27. Carrion, V.G., Weems, C.F., Ray, R.D., Glaser, B., Hessel, D., & Reiss, A.L. (2002). Diurnal salivary cortisol in pediatric posttraumatic stress disorder. *Biological Psychiatry*, 51(7), 575-582.
28. De Bellis, M.D., Baum, A.S., Birmaher, B., Keshavan, M.S., Eccard, C.H., Boring, A.M., Jenkins, F.J., & Ryan, N. (1999). Developmental traumatology, Part 1: Biological stress systems. *Biological Psychiatry*, 9, 1259-1270.
29. De Bellis, M.D., Keshavan, M.S., Clark, D.B., Casey, B.J., Giedd, J.B., Boring, A.M., Jenkins, F.J., & Ryan, N. (1999). Developmental traumatology, Part 2: Brain development. *Biological Psychiatry*, 45, 1271-1284.

30. Gunnar, M. (2003). Integrating neuroscience and psychosocial approaches in the study of early experiences. In J.A. King, C. F. Ferris & I. I. Lederhendler (Eds.), *Roots of Mental Illness in Children, 1008*, 238-247. New York: New York Academy of Sciences.
31. Bredy, T.W., Humpartzoomian, R.A., Cain, D.P., & Meaney, M.J.P. (2003). Partial reversal of the effect of maternal care on cognitive function through environmental enrichment. *Neuroscience, 118*(2), 571-576.
32. Kamerman, S., & Kahn, A. (1995). *Starting Right: How America neglects its young children and what we can do about it*. New York: Oxford University Press.
33. Waldfogel, J. (1999). The impact of the Family and Medical Leave Act. *Journal of Policy Analysis and Management, 18*(2), 281-302.
34. Waldfogel, J. (2001) International policies toward parental leave and child care. *The Future of Children, 11*(1), 99-111.
35. Shonkoff, J.P., & Phillips, D. (Eds.) (2000). *From Neurons to Neighborhoods: The science of early childhood development*. Committee on Integrating the Science of Early Childhood Development. Washington, D.C.: National Academy Press.
36. Phillips, D., Mekos, D., Carr, S., & Abbott-Shim, M. (2000). Within and beyond the classroom door: Assessing quality in child care centers. *Early Childhood Research Quarterly, 15*(4), 475-496.
37. NICHD Early Child Care Research Network (1996). Characteristics of infant child care: Factors contributing to positive caregiving. *Early Childhood Research Quarterly, 11*, 296-306.
38. NICHD Early Child Care Research Network (2000). Characteristics and quality of child care for toddlers and preschoolers. *Applied Developmental Science, 4*(3), 116-125.
39. Gilliam, W.S., & Shahar, G. (2006). Prekindergarten expulsion and suspension: Rates and predictors in one state. *Infants and Young Children*.
40. Zito, J.M., Safer, D.J., dosReis, S., Gardner, J.F., Boles, M., & Lynch, F. (2000). Trends in the prescribing of psychotropic medications to preschoolers. *Journal of the American Medical Association, 283*(8), 1025-1030.
41. Johnson, K., Knitzer, J., & Kaufmann, R. (2002). *Making Dollars Follow Sense: Financing early childhood mental health services to promote healthy social and emotional development in young children*. New York: National Center for Children in Poverty.
42. Melton, G.B., & Thompson, R.A. (2002). The conceptual foundation: Why child protection should be neighborhood-based and child-centered. In G.B. Melton, R.A. Thompson, & M.A. Small (Eds.), *Toward a Child-centered, Neighborhood-based Child Protection System: A report of the Consortium on Children, Families, and the Law*, (pp. 3-27). Westport, CT: Praeger.
43. Brooks-Gunn, J., Berlin, L.J., & Fuligni, A.S. (2000). Early childhood intervention programs: What about the family? In J.P. Shonkoff & S.J. Meisels (Eds.), *Handbook of Early Childhood Intervention* (2nd Ed.) (pp. 549-577). New York: Cambridge University Press.
44. Thompson, R.A., & Flood, M.F. (2002). Toward a child-oriented child protection system. In G.B. Melton, R.A. Thompson, & M.A. Small (Eds.) *Toward a Child-centered, Neighborhood-based Child Protection System: A report of the Consortium on Children, Families, and the Law*, (pp. 155-194). Westport, CT: Praeger.
45. Duncan, G., & Chase-Lansdale, L. (2002). *For Better and For Worse: Welfare reform and the well-being of children and families*. New York: Russell Sage.
46. Huston, A.C. (2002). Reforms and child development. *The Future of Children, 12*(1), 59-77.

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