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HEARING ON "EXAMINING THE FAILURES OF THE TRUMP ADMINISTRATION'S INHUMANE FAMILY SEPARATION POLICY"

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SUMMARY

This testimony is based on strong scientific consensus supported by extensive research across multiple disciplines. A century of countless studies across the behavioral and social sciences provide extensive evidence of the consequences of separating children from their parents, especially if that separation is unexpected, abrupt, or in a frightening context. Recent advances in 21st-century biology are now providing a deeper understanding of the disruptions that occur in the developing brain and other biological systems, which explain *why* and *how* traumatic, parent-child separation can have such devastating effects.

The broad overview of peer-reviewed literature summarized in the section that follows this summary illustrates the depth of knowledge available to inform a credible, science-based analysis of the policies and actions that have separated thousands of children from their parents or other caregivers at the U.S.-Mexico border.

Sudden, forcible separation of children from their parents is deeply traumatic for both. Above and beyond the distress we see "on the outside," separating a child from his or her parents triggers a massive biological stress response "*inside*" the child, which remains activated until the parent returns and provides comfort. Continuing separation removes the most important resource a child can possibly have to prevent long-term damage—a responsive adult who's totally devoted to his or her well-being.

The results of thousands of studies converge on the following two core scientific concepts:

(1) A strong foundation for healthy development in young children *requires* a stable, responsive, and supportive relationship with at least one parent or primary caregiver.

(2) High and persistent levels of stress activation (known as "toxic stress") can disrupt the architecture of the developing brain and other biological systems with serious negative impacts on learning, behavior, and lifelong health.

Early experiences are literally built into our brains and bodies, and the experiences that are most important in driving positive development are the care and protection provided by parents and other primary caregivers. Stable and responsive relationships promote healthy brain architecture, establish well-functioning immune, cardiovascular, and metabolic systems, and strengthen the building blocks of resilience.

If these relationships are disrupted, young children are hit by the "double whammy" of a brain that is deprived of the positive stimulation it needs and assaulted by a stress response that disrupts its developing circuitry. When any of us feels threatened, our body's stress response systems are activated. Heart rate and blood pressure go up, stress hormone levels are elevated, blood sugar rises, and inflammatory responses are mobilized. This is the "fight or flight" response. We all know what that feels like physically when we're really stressed out! This response is automatic and essential for survival, but it is designed to go back to normal when the threat is over. If the sense of danger continues, ongoing activation of the stress response shifts from protection to disruption or outright damage. For example:

- Persistently elevated stress hormones can disrupt brain circuits that affect memory and the ability to focus attention and regulate behavior.
- Excessive inflammation and metabolic responses to stress in childhood increase the risk of heart disease, diabetes, depression, and many other chronic illnesses in the adult years.

Unlike "positive" or "tolerable" stress, which can build resilience, the excessive and prolonged nature of what we call "toxic stress" increases the risk of lifelong problems.

The scientific principles described above provide a powerful framework for assessing the damage caused by the current family separation policy. All children who were abruptly separated from their parents or primary caregivers experienced substantial stress and we must bear the responsibility for their well-being. Will some of these children survive without significant problems? The answer is yes. Will many be seriously impaired for the rest of their lives. The answer again is yes. The biology of adversity suggests three factors that are particularly important for understanding who is at greatest risk.

The first is age. Younger children are the most vulnerable to long-term impacts, both because their brain circuitry and other biological systems are relatively under-developed and because they are most dependent on adult caregivers.

The second is previous harm from adversity. The pile-up of stress on children who are already compromised shifts the odds against them even further. The intentional withholding of the most powerful healing intervention we could possibly offer—the care and protection that parents provide for their children when they're in danger— goes against everything science tells us.

The third reason for variation in outcomes is the duration of separation. Toxic stress is a ticking clock—and prolonged separation inflicts increasingly greater harm as each week goes by.

From a scientific perspective, both the initial separation and the lack of rapid unification are indefensible. Forcibly separating children from their parents is like setting a house on fire. Prolonging that separation is like preventing the first responders from doing their job.

PEER-REVIEWED LITERATURE ON THE SCIENCE OF CHILD HEALTH AND DEVELOPMENT AND THE BIOLOGY OF ADVERSITY

The remaining sections of this testimony provide a more detailed review of peer-reviewed evidence that reflects the cutting edge of 21st-century science. This content has been excerpted from almost two decades of working papers and related materials produced by the National Scientific Council on the Developing Child, which I have chaired since its founding in 2003. The following four documents (each of which has been subjected to intensive, scientific peer review) provide a wealth of complex scientific knowledge that has been synthesized and translated for non-scientists.

Excessive Stress Disrupts the Architecture of the Developing Brain: Working Paper 3 (2005, updated 2014)

Early Experiences Can Alter Gene Expression and Affect Long-Term Development: Working Paper 10 (2010)

The Science of Neglect: The Persistent Absence of Responsive Care Disrupts the Developing Brain: Working Paper 12 (2012)

Supportive Relationships and Active Skill-Building Strengthen the Foundations of Resilience: Working Paper 13

These and other relevant materials are available on the website of the Center on the Developing Child at Harvard University (www.developingchild.harvard.edu).

The Critical Importance of the Parent-Child Relationship

Nurturing and stable relationships with caring adults are essential to healthy development beginning from birth. These relationships affect virtually all aspects of development intellectual, social, emotional, physical, and behavioral—and their quality and stability in the early years lay the foundation that supports a wide range of later outcomes.¹⁻⁶ These outcomes include self-confidence and sound mental health, motivation to learn, achievement in school and later in the workplace, the ability to control aggressive impulses and resolve conflicts in nonviolent ways, behaviors that affect health risks, lifelong physical and mental health outcomes, and the capacity to develop and sustain friendships and close relationships and ultimately become a responsible citizen and successful parent of the next generation.⁷

"Serve and return" interactions (i.e., mutually responsive vocalizing, facial expressions, and gestures back and forth between young children and the adults who care for them) build sturdy brain architecture, beginning at birth, and create strong relationships in which the child's experiences are affirmed and new abilities are nurtured. Children who have healthy relationships with their parents and other important caregivers are more likely to develop insights into other people's feelings, needs, and thoughts, which form a foundation for cooperative interactions with others and an emerging conscience. Sensitive and responsive parent-child relationships also are associated with stronger cognitive skills in young children and enhanced social competence and work skills later in school, which illustrates the connection between social-emotional development and intellectual growth.⁸⁻¹⁷

The gradual acquisition of higher-level skills, including the ability to focus and sustain attention, set goals, follow rules, solve problems, and control impulses, is driven by the development of the prefrontal cortex (the large part of the brain behind the forehead) from infancy into early adulthood.¹⁸⁻²¹ A significant part of this formative development begins during early childhood and is refined and made more efficient during adolescence and the early adult years.^{22,23} Although these capabilities (known as executive function and self-regulation) do not emerge automatically, children are born with the potential to acquire them within the context of responsive relationships that model the skills and scaffold their development. Acquiring the

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building blocks of executive function and self-regulation is one of the most important and challenging tasks of early childhood, and the opportunity to build on these foundational capacities is critical to healthy development through middle childhood, adolescence, and into adulthood.²³

The stability and predictability of the caregiving environment affects the health and development of young children through its effect on the consistency, quality, and timing of daily routines which shape developing regulatory systems. Beginning in the earliest weeks of life, the predictability and nature of these experiences influence the most basic biological rhythms related to waking, eating, eliminating, and sleeping.^{24,25} When positive experiences are repeated regularly in a predictable fashion, the complex sequences of neural stimulations create pathways that become more efficient (i.e., "neurons that fire together wire together.") For example, infants who learn that being soothed and comforted occurs shortly after they experience distress are more likely to establish more effective physiological mechanisms for calming down when they are aroused and are better able to learn to self-soothe after being put down to sleep.^{24,26} In contrast, when eating and being put to bed occur at different times each day and when comforting occurs unpredictably, the organization and consolidation of sleep-wake patterns and self-soothing responses do not develop well, and biological systems do not "learn" healthy routines and self-regulation.²⁷

Just as early experiences affect the architecture of the developing brain, they also shape the development of other biological systems that are important for both physical and mental health. For example, responsive caregiving plays a key role in the normal maturation of the neuroendocrine system.²⁸⁻³⁰ A wealth of animal research that is now being replicated in humans demonstrates that caregiving behavior also shapes the development of circuits that regulate how individuals respond to stressful situations.^{31,32} Genes involved in regulating the body's stress response are particularly sensitive to caregiving, as early maternal care leaves a signature on the genes of her offspring that carry the instructions for the development of physiological and behavioral responses to adversity. That signature (known as an epigenetic marker) is a lasting imprint that affects whether the offspring will be more or less likely to be fearful and anxious

later in life.³³ Consequently, early overloading of the stress response system can have a range of adverse, lifelong effects on learning, behavior, health, and longevity.

Regulatory mechanisms that manage stress also influence the body's immune and

inflammatory responses, which are essential for defending against disease. Young children cared for by individuals who are available and responsive to their emotional and material needs develop well-functioning immune systems that are better equipped to deal with initial exposures to infections and to keep dormant infections in check over time.³⁴ Conversely, inadequate caregiving and limited nurturance very early in life can have long-term (and sometimes permanent) effects on immune and inflammatory responses, which increase the risk of chronic impairments such as asthma, respiratory infections, and cardiovascular disease.^{35,36}

The Biology of Adversity and Resilience

When faced with an acute challenge or threat, the body's stress response systems shift into immediate action mode. Heart rate and blood pressure go up, stress hormone levels are elevated, blood sugar rises, inflammation is increased, and blood flow is diverted preferentially to the brain and muscles. This is the classic "fight or flight" response and it is essential for survival.

Stressful experiences for children can be positive, tolerable, or toxic depending on their duration, intensity, and timing, and on whether protective relationships are available to help the child feel protected and thereby restore the biological activation to baseline levels. The National Scientific Council on the Developing Child created three categories of stress response that provide a framework for understanding the underlying biology of each.³⁷

• *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 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. Examples include meeting new people, dealing with frustration, or getting an immunization. This is an important part of the normal developmental process.

- *Tolerable stress* refers to stress responses that have the potential to negatively affect the architecture of the developing brain but generally occur over limited time periods that allow for the brain to recover and thereby reverse potentially harmful effects. Tolerable stress responses may occur as a result of the death or serious illness of a loved one, a frightening accident, an acrimonious parental separation or divorce, or persistent discrimination, but always in the context of ongoing, supportive relationships with adults. Indeed, the presence of supportive adults who create safe environments that help children learn to cope with and recover from adverse experiences is one of the critical ingredients that make serious stressful events such as these tolerable. In some circumstances, tolerable stress can even have positive effects, but in the absence of supportive relationships, it also can become toxic to the body's developing systems.
- *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 by children who do not have access to support from caring adults tend to provoke these types of toxic stress responses.* Studies indicate that toxic stress can have an adverse impact on brain architecture. In the extreme, such as in cases of severe, chronic abuse, especially during early, sensitive periods of brain development, 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 neural connections. 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, and, therefore, the stress response system activates more frequently and for longer periods than is necessary, like revving a car engine for hours every day. This wear and tear effect increases the risk of stress-related physical and mental illness later in life.³⁸

Protective relationships play a central role in building resilience by buffering children from sources of stress and providing the support needed to build their own capacities to cope with adversity. Decades of research have produced a rich knowledge base that explains why some people develop the adaptive capacities to overcome significant adversity and others do not. Whether the burdens come from the hardships of poverty, the challenges of parental substance abuse or serious mental illness, the stresses of war, the threats of recurrent abuse or chronic neglect, or a combination of factors, the single most common finding is that children who end up doing well have had at least one stable and committed relationship with a supportive parent, caregiver, or other adult. These relationships provide the personalized responsiveness, scaffolding, and protection that buffer children from the sources of disruption. They also build key capacities—such as the ability to plan, monitor and regulate behavior, and adapt to changing circumstances—that enable children to overcome adversity and thrive as they get older. This combination of supportive relationships, adaptive skill-building, and positive experiences constitutes the foundations of what is commonly called resilience. On a biological level, resilience protects the developing brain and other organs from the damage that can be produced by excessive activation of stress response systems. Stated simply, resilience transforms potentially toxic stress into tolerable stress.

Resilience requires relationships, not rugged individualism. There is no "resilience gene" that determines the life course of any individual irrespective of the experiences that shape genetic expression. The capacity to adapt and thrive despite adversity develops through the interaction of supportive relationships, gene expression, and adaptive biological systems.³⁹⁻⁴¹ *Despite the widespread belief that individual grit, extraordinary self-reliance, or some in-born, heroic strength of character can triumph over calamity, science now tells us that it is the reliable presence of at least one supportive relationship and multiple opportunities for developing effective coping skills that are essential building blocks for the capacity to do well in the face of significant adversity.*

Extensive evidence indicates that deprivation or neglect—defined broadly as the ongoing disruption or significant absence of caregiver responsiveness—can cause more harm to a young child's development than overt physical abuse.⁴²⁻⁴⁴ The clearest findings that support

this conclusion come from studies of children who have experienced severe neglect while being raised in institutions.⁴⁵ This research has provided an opportunity to investigate the distinctive consequences of extreme psychosocial deprivation apart from the impacts of other forms of maltreatment. Additional knowledge comes from studies involving institutionalized children whose life circumstances have been positively transformed through foster care placements or permanent adoption.⁴⁶⁻⁵⁰

There is extensive evidence that severe neglect in institutional settings is associated with abnormalities in the structure and functioning of the developing brain. Children who experience extreme levels of social neglect early in life show diminished electrical activity in the brain, as measured through electroencephalography (EEG).^{47,50} Institutionally reared children also show differences in the neural reactions that occur when looking at faces to identify different emotions.^{48,49} These findings are consistent with behavioral observations that neglected children struggle to correctly recognize different emotions in others.^{44,51} Children who experience severe neglect in institutional settings also exhibit decreased brain metabolism and poorer connections among different areas of the brain that are important for focusing attention and processing information, thereby increasing the risk for emotional, cognitive, and behavioral disorders later in life.^{46,52}

The impact of severe neglect can be manifested in different ways across different periods of development. At younger ages, maltreated children show impairments in their ability to discriminate different emotions, yet these difficulties are not observed at older ages.^{44,53,54} Conversely, antisocial behavior may be more salient among adults or older adolescents with early childhood histories of neglect.^{55,56} Given the fact that interpersonal relationships and life challenges (e.g., dealing with peers, becoming involved in romantic relationships, entering parenthood, achieving financial stability) change across the lifespan, it is essential that the adverse consequences of significant deprivation are addressed in a developmentally appropriate manner.

Early adversity can affect long-term health and development by chemically altering the expression of genes. Extensive research has demonstrated that the healthy development of all

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organs, including the brain, depends on how much and when certain genes are expressed. When scientists say that genes are "expressed," they are referring to whether they are turned on or off—essentially whether and when genes are activated to do certain tasks. Research has shown that there are many non-inherited environmental factors and experiences that have the power to chemically mark genes and control their functions. These influences create a new genetic landscape, which scientists call the epigenome. Some of these experiences lead to chemical modifications that change the expression of genes temporarily, while increasing numbers have been discovered that leave chemical signatures that result in an enduring change in gene expression. Research tells us that some genes can only be modified epigenetically during certain periods of development, defined as *critical periods* of modification.⁵⁷⁻⁶² In some cases, very early experiences and the environments in which they occur can shape developing brain architecture and strongly affect whether children grow up to be healthy, productive members of society.

Modification of the epigenome caused by stress during early childhood affects how well or poorly we respond to stress as adults and can result in increased risk of adult disease. Some of our genes provide instructions for how our bodies respond to stress, and research has shown that these genes are clearly subject to epigenetic modification. For example, research in animals has shown that stressful experiences soon after birth can produce epigenetic changes that chemically modify the receptor in the brain that controls the stress hormone cortisol and, therefore, determines the body's response to threat (the fight-or-flight response).⁶³⁻⁶⁵ Healthy stress responses are characterized by an elevation in blood cortisol followed by a return to baseline to avoid a highly activated state for a prolonged period of time. If young children experience toxic stress as a result of serious adversity in the absence of protective relationships, persistent epigenetic changes can result.⁶⁶ These modifications have been shown to cause prolonged stress responses, which can be likened to revving a car engine for long periods of time. Animal studies have shown correlations between excessive stress and changes in brain architecture and chemistry as well as behaviors that resemble anxiety and depression in humans.⁶⁷⁻⁷² Human studies have found connections between highly stressful experiences in childhood and increased risk for later mental illnesses, including generalized anxiety disorder and major depressive disorder.⁷³⁻⁷⁵ Atypical stress responses over a lifetime can also result in increased risk for physical ailments, such as asthma, hypertension, heart disease and diabetes.⁷³⁻⁸² Children who have experienced serious deprivation in infancy are at risk for abnormal physical development and impairment of the immune system. Severe neglect is associated with significantly delayed growth in head circumference (which is directly related to brain growth) during infancy and into the toddler years.⁸³ More extreme conditions of deprivation, such as those experienced in institutional settings that "warehouse" young children, are associated with even more pervasive growth problems, including smaller body size, as well as impairments in gross motor skills and coordination.⁸⁴⁻⁸⁶ Children who are raised in institutional settings also have more infections and are at greater risk of premature death than children who live in supportive homes.⁸⁷ One possible explanation for these findings is that chronically disrupted cortisol levels suppress immunologic reactivity and physical growth, thereby leading to a greater risk for infection and chronic, stress-related disease throughout life.⁸⁸

Chronic neglect over time can alter the development of biological stress response systems in a way that compromises children's later ability to cope with adversity. Extensive research indicates that the two primary stress response systems in humans—the sympathetic-adrenalmedullary (SAM) system, which produces adrenaline and affects heart and respiration rates, and the hypothalamic-pituitary-adrenal (HPA) axis, which elevates cortisol, a key stress hormone are both disrupted by significant deprivation. For example, years after adoption, children who experienced extreme neglect in institutional settings show abnormal patterns of adrenaline activity in their heart rhythms, which can indicate increased biological "wear and tear" that leads to greater risk for anxiety, depression, and cardiovascular problems later in life.⁸⁹

The consequences of severe neglect can be reduced or reversed through appropriate and timely interventions. The capacity for recovery in children who are removed from neglectful conditions and placed in nurturing environments in a timely fashion has been well-documented.⁹⁰⁻⁹⁴ However, improvement often requires more than simply the cessation of neglectful caregiving. Rather, systematic, empirically supported, and often long-term (six to nine months or longer) interventions are needed to promote effective healing. Successful treatments have been shown to reduce behavioral difficulties and attachment problems in previously neglected young children who have been placed in foster homes^{90,91,93} as well as to promote

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secure attachments in young children who continue to live with their families, while being monitored by child welfare agencies because of previous allegations of neglect.⁹⁴ On a biological level, systematic interventions targeting the social-emotional needs of young children living in foster care settings (the majority of whom were victims of neglect rather than physical abuse) have shown evidence of improved stress-regulatory capabilities with patterns of cortisol production that are indistinguishable from those of non-neglected, healthy children.^{17,91,92,94-96} With appropriate intervention, previously institutionalized children have also demonstrated improvements in brain activity as measured by EEG.^{97,98}

Children's recovery rates are influenced by the severity, duration, and timing of the deprivation as well as by the timing and type of the intervention that is provided. Children who experience more severe neglect, especially during the early childhood years, are more likely to withdraw when stressed and show more anxiety and difficulties regulating their mood than children whose experiences of deprivation are less severe.⁹⁹ Longer periods of deprivation have also been associated with greater deficits in attention and cognitive control,¹⁰⁰ academic achievement,^{101,102} brain activity,¹⁰³ and dysregulation of the HPA axis.¹⁰⁴ Previously institutionalized children who experienced the most extreme levels of deprivation often continue to struggle with problems in attention and behavioral regulation even after intervention has been provided.¹⁰⁵⁻¹⁰⁹

Concluding Thoughts

The scientific knowledge base available to inform policies that affect the health and development of children is extensive and accessible. Any policy that involves separating children from their families raises serious questions that require thoughtful reflection. When decisions are made that do not draw on authoritative knowledge for guidance, the well-being of children can be jeopardized and lead to serious, lifelong consequences. The evidence provided in this testimony is offered in the hope that it can be used to guide science-informed policies going forward. With respect to the children who remain separated from their families today, science is telling us that excessive stress activation will continue for as long as the separation persists—and the longer these children are deprived of the healing effect of supportive caregiving, the worse the consequences will be.

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References

1. Dawson, G., & Fischer, K. (Eds.) (1994). *Human behavior and the developing brain*. New York, NY: Guilford Press.

2. Berscheid, E., & Reis, H. T. (1998). Attraction and close relationships. In D. T. Gilbert, S. T. Fiske, & G. Lindzey (Eds.), *Handbook of social psychology, Vol. 1* (2nd Ed.).

3. Collins, W. A., & Laursen, B. (1999). Relationships as developmental contexts. *The Minnesota Symposia on Child Psychology, Vol. 30.*

4. Dunn, J. (1993). Sage series on individual differences and development, Vol. 4. Young children's close relationships: Beyond attachment. Thousand Oaks, CA: Sage Publications, Inc.

5. Reis, H. T., Collins, W. A., & Berscheid, E. (2000). Relationships in human behavior and development. *Psychological Bulletin, 126*(6), 844-872.

6. Panksepp, J. (1998). Series in affective science. Affective neuroscience: The foundations of human and animal emotions. New York, NY: Oxford University Press.

7. National Scientific Council on the Developing Child. (2004). *Young children develop in an environment of relationships. Working paper no. 1.* Retrieved from http://www.developingchild.net.

8. 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.

9. Bradley, R. H., Caldwell, B. M., Rock, S. L., & Ramey, C. T. (1989). Home environment and cognitive development in the first three years of life: A collaborative study involving six sites and three ethnic groups in North America. *Developmental Psychology*, *25*(18), 217-235.

10. Bradley, R. H., Caldwell, B. M., & Rock, S. L. (1988). Home environment and school performance: A ten-year follow-up and examination of three models of environmental action. *Child Development*, *59*(2), 852-867.

11. Estrada, P., Arsenio, W. F., Hess, R. D., & Holloway, S. D. (1987). Affective quality of the mother-child relationship: Longitudinal consequences for children's school-relevant cognitive functioning. *Developmental Psychology*, 23(2), 210-215.

12. Gottfried, A. W., & Gottfried, A. E. (1984). *Home environment and early cognitive development*. Cambridge, MA: Elsevier.

13. Peisner-Feinberg, E. S., Burchinal, M. R., Clifford, R. M., Culkin, M. I., Howes, C., Kagan, S. I., Yazejian, . . . Zelazo, J. (2000). *The children of the Cost, Quality, and Outcomes Study go to school: Technical report.*

14. Pianta, R. C., Nimetz, S. L., & Bennett, E. (1997). Mother-child relationships, teacher-child relationships, and school outcomes in preschool and kindergarten. *Early Childhood Research Quarterly*, *12*(3), 263-280.

15. Kochanska, G., & Thompson, R.A. (1997). The emergence and development of conscience in toddlerhood and early childhood. In J.E. Grusec & L. Kuczynski (Eds.), *Parenting and children's internalization of values* (pp. 53-77).

16. Thompson, R. A., Meyer, S., & McGinley, M. (2006). Understanding values in relationship: The development of conscience. In M. Killen & J. Smetana (Eds.), *Handbook of moral development*.

17. Kochanska, G. (2002). Mutually responsive orientation between mothers and their young children: A context for the early development of conscience. *Current Directions in Psychological Science*, 11(6), 191-195.

18. Diamond, A. (1988). Abilities and neural mechanism underlying AB performance. *Child Development*, 59(2), 523-527.

19. Goldman-Rakic, P. S. (1987). Circuitry of primate prefrontal cortex and regulation of behavior by representational memory. In F. Plum (Ed.), *Handbooks for physiology: A Spectrum of physiological knowledge and concepts: Section 1: Nervous system: Vol. V, 2 parts: Higher functions of the brain* (pp. 373-417).

20. Rothbard, M. K., & Posner, M. I. (2005). Genes and experience in the development of executive attention and effortful control. In L. A. Jensen & R. W. Larson (Eds.), *New horizons in developmental theory and research* (pp. 101-108).

21. LeDoux, J. (1996). Emotional networks and motor control: A fearful view. *Progress in Brain Research*, 107, 437-446.

22. National Scientific Council on the Developing Child. (2007). *The timing and quality of early experiences combine to shape brain architecture: Working paper no. 5.* Retrieved from http://www.developingchild.harvard.edu.

23. Center on the Developing Child at Harvard University. (2011). *Building the brain's "air traffic control" system: How early experiences shape the development of executive function: Working paper no. 11.* Retrieved from http://www.developingchild.harvard.edu.

24. Burnham, M. M., Goodlin-Jones, B. L., Gaylor, E. E., Anders, T. F. (2002). Nighttime sleepwake patterns and self-soothing from birth to one year of age: A longitudinal intervention study. *Journal of Child Psychology and Psychiatry*, 43, 713-725.

25. Heraghty, J. L., Hilliard, T. N., Henderson, A. J., & Fleming, P. J. (2008). The physiology of sleep in infants. *Archives of Disease in Childhood, 93*, 982-985.

26. Spruyt, K., Aitken, R. J., So, K., Charlton, M., Adamson, T. M., & Horne, R. S. (2008). Relationship between sleep/wake patterns, temperament and overall development in term infants over the first year of life. *Early Human Development*, *84*, 289-296.

27. Rosen, L. A. (2008). Infant sleep and feeding. *Journal of Obstetric Gynecologic, & Neonatal Nursing*, *37*, 706-714.

28. Coe, C. L., Lubach, G. R., Schneider, M. L., Dierschke, D. J., & Ershler, W. B. (1992). Early rearing conditions alter immune responses in the developing infant primate. *Pediatrics*, *90*, 505-509.

29. Hanson, L., Silfverdal, S. A., Stromback, L., et al. (2001). The immunological role of breast feeding. *Pediatric Allergy Immunology*, *12*(14), 15-19.

30. McGowan, P. O, Sasaki, A., D'Alessio, A. C., et al. (2009). Epigenetic regulation of the glucocorticoid receptor in human brain associates with childhood abuse. *Nature Neuroscience*, *12*, 342-348.

31. Gunnar, M. R., & Donzella, B. (2002). Social regulation of the cortisol levels in early human development. *Psychoneuroendocrinology*, 27, 199-220.

32. Tarullo, A. R., & Gunnar, M. R. (2006). Child maltreatment and the developing HPA axis. *Hormones and Behavior, 50*, 632-639.

33. Caldji, C., Tannenbaum, B., Sharma, S., Francis, D., Plotsky, P. M., & Meaney, M. J. (1998). Maternal care during infancy regulates the development of neural systems mediating the expression of fearfulness in the rat. *PNAS*, *95*, 5335-5340.

34. Shirtcliff, E. A., Coe, C. L., & Pollak S. D. (2009). Early childhood stress is associated with elevated antibody levels to herpes simplex virus type 1. *PNAS*, *106*, 2963-2967.

35. Danese, A., Pariante, C. M., Caspi, A., Taylor, A., & Poulton, R. (2007). Childhood maltreatment predicts adult inflammation in a life-course study. *Proceeding National Academy of Sciences of the United States of America*, *104*(4), 1319-1324.

36. Chen, E., Hanson, M. D., Paterson, L. Q., Griffin, M. J., Walker, H. A., & Miller, G. E. (2006). Socioeconomic status and inflammatory processes in childhood asthma: The role of psychological stress. *Journal of Allergy and Clinical Immunology*, *117*, 1014-1020.

37. National Scientific Council on the Developing Child. (2005). *Excessive stress disrupts the architecture of the developing brain* (Working Paper No. 3). Retrieved from http://www.developingchild.net

38. Shonkoff, J. P., Boyce, W. T., & McEwen, B. S. (2009). Neuroscience, molecular biology, and the childhood roots of health disparities: Building a new framework for health promotion and disease prevention. *Journal of the American Medical Association*, *301*(21), 2252-2259.

39. Masten, A. S. (2012). Risk and resilience in development. In P.D. Zelazo (Ed.), *The Oxford Handbook of Developmental Psychology, Vol. 2. Self and other*. New York: Oxford University Press, 579-607.

40. Russo, S. J., Murrough, J. W., Han, M.H., Charney, D. S., & Nestler, E. J. (2012). Neurobiology of resilience. *Nature Neuroscience*, *15*(11), 1475–1484.

41. Cicchetti, D. (2010). Resilience under conditions of extreme stress: A multilevel perspective. *World Psychiatry*, *9*(3), 145–154.

42. 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*(1), 14-23.

43. Egeland, B., Sroufe, A., & Erickson, M. (1983). The developmental consequence of different patterns of maltreatment. *Child Abuse & Neglect*, 7(4), 459-469.

44. Pollak, S. D., Cicchetti, D., Hornung, K., & Reed, A. (2000). Recognizing emotion in faces: Developmental effects of child abuse and neglect. *Developmental Psychology*, *36*(5), 679-688.

45. Provence, S & Lipton, R. (1962). *Infants in Institutions*. Oxford, England: International University Press.

46. Eluvathingal, T. J., Chugani, H. T., Behen, M. E., Juhasz, C., Muzik, O., Maqbool, M., ... & Makki, M. (2006). Abnormal brain connectivity in children after early severe socioemotional deprivation: A diffusion tensor imaging study. *Pediatrics*, *117*(6), 2093–2100.

47. Marshall, P. J., Fox, N. A. & the BEIP Core Group. (2004). A comparison of the electroencephalogram between institutionalized and community children in Romania. *Journal of Cognitive Neuroscience, 16*(8), 1327-1338.

48. Parker, S. W., Nelson, C. A., & the BEIP Core Group. (2005a). An event-related potential study of the impact of institutional rearing on face recognitions. *Development and Psychopathology*, *17*(3), 621-639.

49. Parker, S. W., Nelson, C. A. & the BEIP Core Group. (2005b). The impact of early institutional rearing on the ability to discriminate facial expressions of emotion: An event-related potential study. *Child Development*, *76*(1), 54-72.

50. Tarullo, A., Garvin, M. C., & Gunnar, M. (2011). Atypical EEG power correlates with indiscriminately friendly behavior in internationally adopted children. *Developmental Psychology*, *47*(2), 417-431.

51. Wismer-Fries, A. B., & Pollak, S. D. (2004). Emotion understanding in post institutionalized Eastern European children. *Developmental Psychopathology*, *16*(2), 355–369.

52. Sheridan, M. S., Fox, N. A., Zeanah, C. H., McLaughlin, K., and Nelson, C.A. (2012). Variation in neural development as a result of exposure to institutionalization early in childhood. *Proceedings of the National Academy of Sciences of the United States of America*, 109(32), 12927-12932.

53. Maheu, F. S., Dozier, M., Guyer, A. E., Mandell, D., Peloso, E., Poeth, K., ... & Ernst, M. (2010). A preliminary study of medial temporal lobe function in youths with a history of caregiver deprivation and emotional neglect. *Cognitive Affective and Behavioral Neuroscience*, *10*(1), 34-49.

54. Luntz, B. K., & Widom, C. (1994). Antisocial personality disorder in abused and neglected children grown up. *The American Journal of Psychiatry*, 151(5), 670-674.

55. Maxfield, M. G., & Widom, C. S. (1996). The cycle of violence: Revisited six years later. *Archives of Pediatrics Adolescent Medicine*, *150*(4), 390–395.

56. Pine, D. S., Mogg, K., Bradley, B. P., Montgomery, L., Monk, C. S., McClure, E., ... & Kaufman, J. (2005). Attention bias to threat in maltreated children: Implications for vulnerability to stress-related psychopathology. *The American Journal of Psychiatry*, *162*(2), 291-296.

57. Szyf, M. (2009a). Early life, the epigenome and human health. *Acta Paediatrica*, 98(7), 1082-1084.

58. Szyf, M. (2009b). The early life environment and the epigenome. *Biochimica Biophysica Acta (BBA), 1790*(9), 878-885.

59. Isles, A. R. & Wilkinson, L. S. (2008). Epigenetics: What is it and why is it important to mental disease? *British Medical Bulletin*, *85*(1), 35-45.

60. Jirtle, R. L. (2008). Randy L. Jirtle, PhD: Epigenetics a window on gene dysregulation, disease. Interview by Bridget M. Kuehn. *Journal of the American Medical Association (JAMA)*, 299(11): 1249-1250.

61. Nafee, T. M., Farrell, W. E., Carroll, W. D., Fryer, A. A., & Ismail, K. M. (2008). Epigenetic control of fetal gene expression. *BJOG: An International Journal of Obstetrics & Gynaecology*, *115*(2), 158-168.

62. Sinclair, D. A. & Oberdoerffer, P. (2009). The ageing epigenome: Damaged beyond repair? *Ageing Research Reviews*, 8(3), 189-198.

63. McGowan, P. O., Sasaki, A., D'Alessio, A. C., Dymov, S., Labonte, B., Szyf, M. ... & Meaney, M. J. (2009). Epigenetic regulation of the glucocorticoid receptor in human brain associates with childhood abuse. *Nature Neuroscience*, *12*(3), 342-348.

64. Meaney, M. J., Szyf, M., & Seckl, J. R. (2007). Epigenetic mechanisms of perinatal programming of hypothalamic-pituitary-adrenal function and health. *Trends in Molecular Medicine*, *13*(7), 269-277.

65. Weaver, I. C. G., Cervoni, N., Champagne, F. A., D'Alessio, A. C., Sharma, S., Seckl, J. R., & Meaney, M. J. (2004). Epigenetic programming by maternal behavior. *Nature Neuroscience*, 7(8), 847-854.

66. Shonkoff, J. P., Boyce, W. T., & McEwen, B S. (2009). Neuroscience, molecular biology, and the childhood roots of health disparities: Building a new framework for health promotion and disease prevention. *JAMA*, *301*(21), 2252-2259.

67. Champagne, F. A. & Curley, J. P. (2009). Epigenetic mechanisms mediating the long-term effects of maternal care on development. *Neuroscience and Biobehavioral Reviews*, 33(4), 593-600.

68. Champagne, F. A., Weaver, I. C., Diorio, J., Dymov, S., Szyf, M., & Meaney, M. J. (2006). Maternal care associated with methylation of the estrogen receptor-alpha1b promoter and estrogen receptor-alpha expression in the medial preoptic area of female offspring. *Endocrinology*, *14*7(6), 2909-2915.

69. Chen, Y., Dube, C. M., Rice, C. J., & Baram, T. Z. (2008). Rapid loss of dendritic spines after stress involves derangement of spine dynamics by corticotropin-releasing hormone. *The Journal of Neuroscience*, 28(11), 2903-2911.

70. Moriceau, S. & Sullivan, R. M. (2006). Maternal presence serves as a switch between learning fear and attraction in infancy. *Nature Neuroscience*, *9*, 1004-1006.

71. Rice, C. J., Sandman, C. A., Lenjavi, M. R., & Baram, T. Z. (2008). A novel mouse model for acute and long-lasting consequences of early life stress. *Endocrinology*, *149*(10), 4892-4900.

72. Thompson, J. V., Sullivan, R. M., & Wilson, D. A. (2008). Developmental emergence of fear learning corresponds with changes in amygdala synaptic plasticity. *Brain Research, 1200,* 58-65.

73. Bradley, R. G., Binder, E. B., Epstein, M. P., Tang, Y., Nair, H. P., Liu, W. ... & Ressler, K. J. (2008). Influence of child abuse on adult depression: Moderation by the corticotropin-releasing hormone receptor gene. *Archives of General Psychiatry*, *65*(2), 190-200.

74. Gillespie, C. F., Bradley, B., Mercer, K., Smith, A., Conneely, K., Gapen, M. ... & Ressler, K. (2009). Trauma exposure and stress-related disorders in inner city primary care patients. *General Hospital Psychiatry*, *31*(6), 505-514.

75. Hovens, J. G., Wiersma, J. E., Giltay, E. J., van Oppen, P., Spinhoven, P., Penninx, B. W. & Zitman, F. G. (2009). Childhood life events and childhood trauma in adult patients with depressive, anxiety and comorbid disorders vs. controls. *Acta Psychiatrica Scandinavica*. Oct 30 [epub]

76. Swanson, J. M., Entringer, S., Buss, C., & Wadhwa, P. D. (2009). Developmental origins of health and disease: Environmental exposures. *Seminars in Reproductive Medicine*, 27(5), 391-402.

77. Shonkoff, J. P., Boyce, W. T., & McEwen, B S. (2009). Neuroscience, molecular biology, and the childhood roots of health disparities: Building a new framework for health promotion and disease prevention. *JAMA*, *301*(21), 2252-2259.

78. Jovanovic, T., Blanding, N. Q., Norrholm, S. D., Duncan, E., Bradley, B., & Ressler, K. J. (2009). Childhood abuse is associated with increased startle reactivity in adulthood. *Depression and Anxiety*, *26*(11), 1018-1026.

79. Krupanidhi, S., Sedimbi, S. K., Vaishnav, G., Madhukar, S. S., & Sanjeevi, C. B. (2009). Diabetes-role of epigenetics, genetics, and physiological factors. *Zhong Nan Da Xue Xue Bao Yi Xue Ban, 34*(9), 837-845.

80. Quas, J. A., Carrick, N., Alkon, A., Goldstein, L., & Boyce, W. T. (2006). Children's memory for a mild stressor: The role of sympathetic activation and parasympathetic withdrawal. *Developmental Psychobiology*, *48*(8), 686-702.

81. Weidman, J. R., Dolinoy, D. C., Murphy, S. K., & Jirtle, R. L. (2007). Cancer susceptibility: Epigenetic manifestation of environmental exposures. *Cancer Journal*, *13*(1), 9-16.

82. Wilson, A. G. (2008). Epigenetic regulation of gene expression in the inflammatory response and relevance to common diseases. *Journal of Periodontology*, 79(8): 1514-1519.

83. Strathearn, L., Gray, P. H., O'Callaghan, F., & Wood, D. O. (2001). Childhood neglect and cognitive development in extremely low birth weight infants: A prospective study. *Pediatrics*, *108*(1), 142-151.

84. Johnson, D. E., & Gunnar, M. R. (2011), IV. Growth failure in institutionalized children. *Monographs of the Society for Research in Child Development*, *76*(4), 92–126.

85. Macovei, O. (1986). *The medical and social problems of the handicapped in children's institutions in Iasi Bucharest, Romania*. Bucharest, Romania: Institutl de Igiena si Sanatate Publica.

86. Miller, L. C., Kiernan, M. T., Mathers, M. I., & Klein-Gitelman, M. (1995). Developmental and nutritional status of internationally adopted children. *Archives of Pediatrics & Adolescent Medicine*, 149(1), 40-44.

87. De Bellis, M. D. (2005). The psychobiology of neglect. Child Maltreatment, 10(2), 150-172.

88. McEwen, B. S., Biron, C. A., Brunson, K. W., Bulloch, K., Chambers, W.H., Dhabhar, F. S., ...& Weiss, J. M. (1997). Neural-endocrine-immune interactions: the role of adrenocorticoids as modulators of immune function in health and disease. *Brain Research Review*, *23*(1-2), 79-133.

89. Gunnar, M. R., Frenn, K., Wewerka, S. S., & Van Ryzin, M. J. (2009). Moderate versus severe early life stress: Associations with stress reactivity and regulation in 10-12-year-old children. *Psychoneuroendocrinology*, *34*(1), 62-75.

90. Dozier, M., Lindhiem, O., Lewis, E., Bick, J., Bernard, K., & Peloso, E. (2009). Effects of a foster parent training program on young children's attachment behaviors: Preliminary evidence from a randomized clinical trial. *Child & Adolescent Social Work Journal, 26*(4), 321-332.

91. Dozier, M., Peloso, E., Lindhiem, O., Gordon, M., Manni, M., Sepulveda, S., ... & Levine, S. (2006). Developing evidence-based interventions for foster children: An example of a randomized clinical trial with infants and toddlers. *Journal of Social Issues*, *62*(4), 767-785.

92. Fisher, P. A., Gunnar, M. R., Chamberlain, P., & Reid, J. B. (2000). Preventive intervention for maltreated preschool children: Impact on children's behavior, neuroendocrine activity, and foster parent functioning. *Journal of the American Academy of Child & Adolescent Psychiatry*, *39*(11), 1356-1364.

93. Fisher, P. A., & Kim, H. K. (2007). Intervention effects on foster preschoolers' attachment-related behaviors from a randomized trial. *Prevention Science*, 8(2), 161-170.

94. Fisher, P. A., Stoolmiller, M., Gunnar, M. R., & Burraston, B. O. (2007). Effects of a therapeutic intervention for foster preschoolers on diurnal cortisol activity. *Psychoneuroendocrinology*, *32*(8-10), 892-905.

95. Dozier, M., Peloso, E., Lewis, E., Laurenceau, J., & Levine, S. (2008). Effects of an attachment-based intervention of the cortisol production of infants and toddlers in foster care. *Development and Psychopathology, 20*(3), 845-859.

96. Fisher, P. A., Gunnar, M., Dozier, M., Bruce, J., & Pears, K. C. (2006). Effects of a therapeutic intervention for foster children on behavior problems, caregiver attachment, and stress regulatory neural systems. *Annals of the New York Academy of Sciences, 1094*, 215-225.

97. Moulson, M. C., Fox, N. A., Zeanah, C. H., & Nelson, C. A. (2009). Early adverse experiences and the neurobiology of facial emotion processing. *Developmental Psychology*, *45*(1), 17-30.

98. Vanderwert, R. E., Marshall, P. J., Nelson, C., Zeanah, C. H., & Fox, N. A. (2010). Timing of intervention affects brain electrical activity in children exposed to severe psychosocial neglect. *PLoS ONE*, *5*(7), e11415.

99. Manly, J., Kim, J. E., Rogosch, F. A., & Cicchetti, D. (2001). Dimensions of child maltreatment and children's adjustment: Contributions of developmental timing and subtype. *Development and Psychopathology*, *13*(4), 759-782.

100. Colvert, E., Rutter, M., Kreppner, J., Beckett, C., Castle, J., Groothues, C., ... & Sonuga-Barke, E. S. (2008). Do theory of mind and executive function deficits underlie the adverse outcomes associated with profound early deprivation?: Findings from the English and Romanian adoptees study. *Journal of Abnormal Child Psychology*, *36*(7), 1057-1068.

101. Beckett, C., Maughan, B., Rutter, M., Castle, J., Colvert, E., Groothues, C., ... & Sonuga-Barke, E. (2007). Scholastic attainment following severe early institutional deprivation: A study of children adopted from Romania. *Journal of Abnormal Child Psychology*, *35*(6), 1063-1073.

102. Van IJzendoorn, M. H. & Juffer, F. (2006). The Emanuel Miller Memorial Lecture 2006: Adoption as intervention. Meta-analytic evidence for massive catch-up and plasticity in physical, socio-emotional, and cognitive development. *Journal of Child Psychology and Psychiatry*, 47(12), 1228-1245.

103. Marshall, P. J., Reeb, B. C., Fox, N. A., Nelson, C., & Zeanah, C. H. (2008). Effects of early intervention on EEG power and coherence in previously institutionalized children in Romania. *Development and Psychopathology*, *20*(3), 861-880.

104. Gunnar, M., Morison, S. J., Chisholm, K., & Schuder, M. (2001). Salivary cortisol levels in children adopted from Romanian orphanages. *Development and Psychopathology*, *13*(3), 611-628.

105. Hodges, J., & Tizard, B. (1989). IQ and behavioural adjustment of ex-institutional adolescents. *Journal of Child Psychology and Psychiatry*, 30, 53-75.

106. Kreppner, J., Kumsta, R., Rutter, M., Beckett, C., Castle, J., Stevens, S. & Sonuga-Barke, E. J. (2010). IV. Developmental course of deprivation-specific psychological patterns: Early manifestations, persistence to age 15, and clinical features. *Monographs of the Society for Research in Child Development*, 75, 79–101.

107. Rutter, M. and the English and Romanian Adoptees (ERA) study team. (1998). Developmental catch-up, and deficit, following adoption after severe global early privation. *Journal of Child Psychology and Psychiatry*, *39*(4), 465-476.

108. Verhulst, F. C., Althaus, M., & Versluis-den Bieman, H. J. (1990). Problem behavior in international adoptees: II. Age at placement. *Journal of the American Academy of Child and Adolescent Psychiatry*, 29(1), 104-111.

109. Verhulst, F. C., Althaus, M., & Versluis-den Bieman, H. J. (1992). Damaging backgrounds: Later adjustment of international adoptees. *Journal of the American Academy of Child and Adolescent Psychiatry*, *31*(3), 518-524.