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The Ingredients of Healthy Brain and Child Development

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Pat Levitt, PhD* and Kathie L. Eagleson, PhD**

INTRODUCTION

This review explains *why "early" matters* when it comes to brain and child development. Early is a critical concept that I and others have presented to policy makers and business leaders throughout the country. Early typically includes the prenatal and the first three years after birth. Here we focus on the early postnatal period. In addition, the adolescent period represents a distinct epoch of developmental changes. Positive development of children provides a strong foundation for healthy and competent adulthood, responsible citizenship, economic productivity, strong communities, and a just and fair society[1]. Below, we discuss the foundational principles of brain development that underlie why this is the case.

For much of the material presented here, it is important to acknowledge the contributions of the Center for the Developing Child at Harvard University and the National Scientific Council for the Developing Child.[2] The Center provides many resources, including material that will be covered in this review, on their website.[3] It is also important to recognize the FrameWorks Institute,[4] a non-profit organization comprised of social scientists, cultural anthropologists and linguists that has worked with the

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1. Jack P. Shonkoff, *Capitalizing on Advances in Science to Reduce the Health Consequences of Early Childhood Adversity*, 170 JAMA PEDIATRIC 1003, 1003-07 (2016).

2. CTR. ON THE DEVELOPING CHILD AT HARVARD UNIV., A DECADE OF SCIENCE INFORMING POLICY: THE STORY OF THE NATIONAL SCIENTIFIC COUNCIL ON THE DEVELOPING CHILD (2014), https://developingchild.harvard.edu/resources/decade-science-informing-policy-story-national-scientific-council-developing-child/.

3. CTR. ON THE DEVELOPING CHILD AT HARVARD UNIV., https://developingchild.harvard.edu/resources/ (last visited May 14, 2018).

4. FRAMEWORKS INST., http://www.frameworksinstitute.org (last visited May 16, 2018).

Council to inform future policy with early brain and child development research. For example, Nat Kendall-Taylor, the Chief Executive Officer of FrameWorks, and Pat Levitt co-authored a NeuroView article about how science advocacy is not just about asking policy makers for more money for research, which of course is important[5]: equally important is informing decision-makers, such as policy makers, business leaders, health service providers, educators and members of the public, who can make a difference in changing the approach towards investing in programs that improve healthy brain and child development.

I. MISCONCEPTIONS OF BRAIN AND CHILD DEVELOPMENT

There are some common misconceptions about development that often influence decisions about effect investment of resources:

A. Children are sponges who develop and learn simply by passively experiencing their environment.

Decades of research have demonstrated that learning is an active process[6]. Further, development of cognition and emotional regulation occurs in the context of social interactions for humans as well as all vertebrate species[7]. If there's one message to take from this review, it is that affiliative social interaction is a critical component of cognitive and emotional development, and both are impacted negatively in its absence—known as "neglect." Moreover, effective programs work because they facilitate interaction between the caregiver and the infant, and the caregiver and professionals, improving skills in the child and primary caregivers.[8]

5. Nathaniel Kendall-Taylor & Pat Levitt, *Beyond Hat and Hand: Science Advocacy is Foundational for Policy Decisions*, 94 NEURON 708 (2017).

6. Deborah Stipek, *Classroom Practices and Children's Motivation to Learn*, *in* THE PRE-K DEBATES: CURRENT CONTROVERSIES & ISSUES 98-103 *(*E.Zigler, S.W. Gilliam & S. Barnett eds., 2011).,

7. Nat'l Sci. Council on the Developing Child, *Young Children Develop in an Environment of Relationships* 1–8 (Ctr. on the Developing Child at Harvard Univ., Working Paper No. 1, 2004), https://developingchild.harvard.edu/resources/wp1/

8. CTR. ON THE DEVELOPING CHILD AT HARVARD UNIV., THREE PRINCIPLES TO IMPROVE THE OUTCOME FOR CHILDREN AND FAMILIES 3-4 (2017),

B. Eighty percent of brain development occurs by age two.

In the neuroimaging field, from the perspective of brain volume, this is accurate.[9] But, brain development and brain size are not equivalent concepts. The former includes the assembly and maturation of circuits that underlie higher cognitive, sensory, and motor functions. This process provides each infant and toddler with the ability to take in information from his or her environment, try to interpret and make sense out of the information, and subsequently generate a motor response. The brain, particularly the cerebral cortex[10], continues to grow through the juvenile period. It reaches its peak size just before the onset of puberty,[11] after which pruning of synapses and neuronal processes (i.e. normal reduction in gray matter) contribute to the reduction of brain volume observed in adulthood.[12] However, the brains of two-year-olds are not eighty percent of an adult in their functional capacities. Therefore, while brain size may be at eighty percent, an enormous amount of development continues over time, even into young adulthood for certain circuits; all this neurobiological activity simply occurs at a much more structurally subtle level.

C. Bad stuff happens—you just have to tough it out and you'll be fine.

This concept, which some erroneously define as resilience (resilience as defined by the National Science Council on the Developing Child[13]) is rooted deeply in our culture. It is probably one of the most challenging issues to address from a neuroscience perspective, because "rugged

https://developingchild.harvard.edu/resources/three-early-childhood-development-principles-improve-child-family-outcomes/.

9. Adolf Pfefferbaum et al., *A Quantitative Magnetic-Resonance-Imaging Study of Changes in Brain Morphology from Infancy to Late Adulthood*, 51 ARCHIVES NEUROLOGY 874-87 (1994).

10. The cerebral cortex is the largest structure of the human brain and provides our ability to perform higher social, emotional and cognitive functions.

11. Armin Raznahan et al., Brief Communications, *How Does Your Cortex Grow?*, 31 J. NEUROSCIENCE 7174, 7176 (2011).

12. Raznahan, *supra* note 11.

13. Nat'l Sci. Council on the Developing Child, *Supportive Relationships and Active Skill-Building Strengthen the Foundations of Resilience* 1–13 (Ctr. on the Developing Child at Harvard Univ., Working Paper No. 13, 2015), https://developingchild.harvard.edu/resources/supportive-relationships-and-active-skill-building-strengthen-the-foundations-of-resilience/.

individualism" is a powerful cultural frame in the United States[14]. Thus, we believe that this cultural frame may create a challenge for child welfare and juvenile justice programs and policies to recognize that "toughing it out" is not a path for making things better[15].

D. Ready to learn is all about cognitive development.

Intervention programs that focus solely on learning without addressing social-emotional development are counter to how the brain works. Children grow up in an environment of relationships, and integrating social, emotional and cognitive development is key.[16]

E. Teens are in more car accidents because they have a hole in their frontal lobe.

This popular concept appears to have influenced a graphic used in an insurance advertisement from Allstate Insurance.[17] But, are teens really missing part of their brain? To understand what is occurring in the teenage brain requires taking a step back to first understand the fundamentals of brain assembly and the nature-nurture factors that influence this process.

II. BUILDING CIRCUITS IN THE DEVELOPING BRAIN

For the purposes of this Article, we will summarize a primer of the biological events that contribute to human brain development.[18] Neurons are cells specialized to carry messages from one part of the brain to another. They have processes (axons) that serve to send information to the next neuron in line, with millions eventually coalescing to form tracts (white matter) that continue to grow in size throughout adolescence.[19]

14. Nat'l Sci. Council on the Developing Child, *supra* note 13, at 7.
15. Nat'l Sci. Council on the Developing Child, *supra* note 13.
16. Nat'l Sci. Council on the Developing Child, *supra* note 7.
17. *Why Do Most 16-year-olds Drive Like They're Missing Part of Their Brain?,* ALLSTATE INS. CO., https://www.allstate.com/resources/allstate/attachments/about/brain-ad.pdf.
18. Pat Levitt, *Structural and Functional Maturation of the Developing Primate Brain*, 143 J. PEDIATRICS 35 (2003).
19. Levitt, *supra* note 18, at S37-S38.

Neurons also have processes (dendrites and their spines) that receive input (synaptic connections) from other neurons. The cell bodies of the neuron, their dendrites, and their synapses form the gray matter, which grows in size through childhood.[20] This early gray matter growth occurs even though no new neurons are added.[21] In contrast, the growth of neuron processes that receive input is very robust. Indeed, from the third trimester through the age of two, there are approximately one million synapses added per second in the cerebral cortex.[22] Later in development, the gray matter becomes smaller over time due to the systematic elimination of connections that serve no purpose (determined by their limited use during development).

How do we explain that in the adult brain each neuron receives approximately two to three thousand synapses, while in a developing child's brain there actually may be twice as many synapses formed? There is a natural process, called pruning, which begins in late childhood, prior to the onset of puberty.[23] Because puberty timing varies across children, the timing of when synapses are lost is heterogeneous. Thus, for some children, this process may begin as early as seven years or as late as eleven years of age. The pruning process is influenced by the interaction of the child with his or her environments, through experiences that impact the activity of neural circuits.[24] Thus, the process stabilizes synapses that are used through having experiences—for example, using both eyes to fine tune binocular vision—and eliminates the synapses that are not activated sufficiently over time. The organization of the connections is highly dependent upon experience; neurons in the same circuit that activate together end up wiring together.[25] Further, a synaptic connection's use

20. Levitt, *supra* note 18, at S37-S38.
21. Levitt, *supra* note 18, at S38.
22. Levitt, *supra* note 18, at S37-S38.
23. JP Bourgeois, *Synaptogenesis, Heterochrony and Epigenesis in the Mammalian Neocortex*, 422 ACTA PAEDIATRICA 27, at 27–28 and Fig. 1 (1997).
24. Takao K. Hensch & Parizad M Bilimoria, *Re-opening Windows: Manipulating Critical Periods for Brain Development*, CEREBRUM, Aug. 2012, at 1; *see also* Nat'l Sci. Council on the Developing Child, *The Timing and Quality of Early Experiences Combine to Shape Brain Architecture,* 1–9 (Ctr. on the Developing Child at Harvard Univ., Working Paper No. 5, 2008), https://developingchild.harvard.edu/resources/the-timing-and-quality-of-early-experiences-combine-to-shape-brain-architecture/.
25. DONALD O. HEBB, THE ORGANIZATION OF BEHAVIOR (New York: Wiley and Sons 1949).

over time defines its stability (to remain) or instability (to be eliminated). If synapses are not used often, then they are more likely to be lost.[26] This means, by definition, that experience during development—beginning prenatally and extending well into postnatal life—is preeminent in driving development of the brain. Moreover, experience drives development in typically-developing children, in children with intellectual disabilities, and children with other special needs. That is, the brain of a child who has been diagnosed with an intellectual disability or a genetic disorder that affects brain circuits and functions still changes over time due to experiences. Because the circuits may be disrupted and thus not process information as in typically-developing children, the information is likely to be interpreted differently. This, in turn, will impact experience-dependent development of synapses and circuits.

If experience is so powerful as a driver of brain development, what is the role of genes inherited from parents? Two principles are essential here. First, early in development, prior to experience from the environment, genes establish the blueprint for the basic structure of the brain, including the production, during prenatal development, of nearly all the neurons that an individual will have for his or her life.[27] In other words, genes provide the fundamental basis for establishing brain architecture. Second, genes are designed to be controlled in ways that impact whether they will be expressed (or not), at what specific times, and at which locations in the brain.[28] In fact, there have been recent studies documenting that gene expression in the developing brain is highly dynamic and complex.[29] Moreover, the combination of genes expressed may differ between major neuron types, as different neuronal classes have distinct projections and functions in processing information. Research increasingly suggests that experiences, positive or negative, impact how

26. Carla J. Shatz, *The Developing Brain*, 267 SCIENTIFIC AMERICAN 60-67 (1992).

27. Sharon E. Fox et al., *How the Timing and Quality of Early Experiences Influence the Development of Brain Architecture*, 81 CHILD DEV. 28,,29-31.

28. Nat'l Sci. Council on the Developing Child, *Early Experiences Can Alter Gene Expression and Affect Long-Term Development,* 1–9 (Ctr. on the Developing Child at Harvard Univ., Working Paper No. 10, 2010), https://developingchild.harvard.edu/resources/early-experiences-can-alter-gene-expression-and-affect-long-term-development/.

29. Ed S. Lein et al., *Transcriptomic Perspectives on Neocortical Structure, Development, Evolution, and Disease*, 40 ANN. REV. NEUROSCIENCE 629 (2017).

the brain regulates genes through a process termed epigenetics ("above genetics"), in which the brain alters the chemical structure of DNA to impact whether genes are turned on or off.[30] For example, research in animal models and in humans shows that prenatal exposure to a toxin, such as lead or a pesticide, or maternal infection can change gene expression by altering the chemical structure of DNA that encodes genes.[31] In turn, these epigenetic changes may underlie in part altered brain development that occurs due to exposure.[32] Thus, nature and nurture are integrated processes, driving the finer details of building brain architecture as circuits mature over time. Epigenetic processes impact other organ systems as they mediate responses to experiences, such as early life stress.[33]

It is quite profound that the brain uses the natural experiences of the organism to facilitate its own development. However, it does not filter good experiences from bad. During development, experiences that deviate from the norm, such as early life stress, can challenge how the brain assembles circuits, creating adaptations to prepare the child to cope with what the brain thinks it will encounter later in life.[34] For example, in studies of rodent auditory development, for rats that were raised to hear only one frequency of sound during the experience-expectant period of development when auditory circuitry is being established, the neurons in those circuits were most adept at discerning the frequency to which it was exposed, and much poorer at discerning other frequencies.[35] This is a problem when the rat would need to survive in a world of diverse sound frequencies, such as detecting sounds made by their natural predators. If never exposed to those frequencies, their circuits would be poor at identifying the presence of the predator. Thus, the altered development is actually mal-adaptive.

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30. Sarah C. P. Williams, *Epigenetics*, 110 PROC. NAT'L ACAD. SCI. 3209 (2013).

31. Victoria K. Cortessis et al., Review Paper, *Environmental Epigenetics: Prospects for Studying Epigenetic Mediation of Exposure-Response Relationships*, 131 HUM. GENETICS 1565, 1568-70 (2012).

32. Nat'l Sci. Council on the Developing Child, supra note 28.

33. Bruce S. McEwen, Viewpoint, *Allostasis and the Epigenetics of Brain and Body Health Over the Life Course: The Brain on Stress*, 74 JAMA PSYCHIATRY 551, 551 (2017).

34. *Id.* at 552.

35. Etienne de Villers-Sidani et al., *Critical Period Window for Spectral Tuning Defined in the Primary Auditory Cortex (A1) in the Rat*, 27 J. NEUROSCIENCE 180,182-83 and Fig. 3 (2007).

It also bears noting that brain development is characterized by a simple-to-complex hierarchy of circuit formation.[36] Sensory information, such as auditory stimuli, can be processed in the third trimester,[37] and continues to mature postnatally. Thus, very early on one can measure a child's very basic sensory modalities and motor skills, as pediatricians do at well-baby visits. Later, more complex cognitive, social and emotional circuits assemble in the same experience-dependent fashion.[38] However, to process information from experiences, the brain heavily depends upon sensory circuits to be fine-tuned as early as possible.[39] At birth, the brain is ready to mediate social engagement with adults in their environment, particularly primary caregivers who provide the most substantive stimuli and security.

III. SOCIAL AND EMOTIONAL DEVELOPMENT ARE INTERTWINED

Infant-caregiver attachment and co-regulation are core to affiliative social behavior, which in turn contributes to tuning an infant's attention, reward, emotional and cognitive circuits.[40] Key experience in a social context, termed "serve and return," are interactions between infants and adults—the infant serves, through babbling and gestures, and adults return the serve, responding in a meaningful way.[41] Of course, the initiation and response can be reversed, but participants experience serve and return through dyadic interactions. Adults may believe that they have the

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36. Barbara L. Thompson & Pat Levitt, *The Clinical-basic Interface in Defining Pathogenesis in Disorders of Neurodevelopmental Origins*, 67 NEURON 702, 702-12 (2010).

37. Chartlotte T. Lee et al., *Fetal Development: Voice Processing in Normotensive and Hypertensive Pregnancies*, 8 BIOL. RES. NURS. 272, 272-82 (2007).

38. NATIONAL RESEARCH COUNCIL, FROM NEURONS TO NEIGHBORHOODS 184-90 (Jack P. Shonkoff & Deborah A. Phillips eds. 2000).

39. Elizabeth A.D. Hammock & Pat Levitt, *The Discipline of Neurobehavioral Development: the Emerging Interface of Processes that Build Circuits and Skills*, 49 HUMAN DEVELOPMENT 294, 294-309 (2006).

40. Ruth Feldman, *Mutual Influences Between Child Emotion Regulation and Parent-Child Reciprocity Support Development Across the First 10 Years of Life: Implications for Developmental Psychopathology*, 27 DEV. & PSYCHOPATHOLOGY 1007 (2015).

41. NAT'L SCI. COUNCIL ON THE DEVELOPING CHILD, THE SCIENCE OF EARLY CHILDHOOD DEVELOPMENT: CLOSING THE GAP BETWEEN WHAT WE KNOW AND WHAT WE DO 6 (2007), https://developingchild.harvard.edu/resources/the-science-of-early-childhood-development-closing-the-gap-between-what-we-know-and-what-we-do/.

responsibility to initiate every interaction with the infant. Yet, from a developmental perspective, it is very important to provide opportunities for the infant to initiate interactions as well—the game gets old quickly when the adult is doing all the serving. Moreover, social contexts are essential for cognitive development.[42] For language, research shows that the number of words an infant hears in a social setting directly correlates with the complexity of vocabulary (and use) that the child will develop.[43] Teaching language in the absence of a social context doesn't work, as it is a mechanism that is evolutionarily conserved.

IV. THE POWER OF EARLY EXPERIENCES – POSITIVE OR NEGATIVE

A study done by Seth Pollock and colleagues in 2002 speaks to the issue of early experience having a long-lasting and powerful impact on childhood development.[44] In this study, researchers asked young children with a history of physical abuse to distinguish between images of emotions in still face expressions. Across eleven images, facial expressions morphed from happy to fearful, or from happy to sad.[45] While the study divided participants into two groups—those who had experienced abuse and those who had not—all were able to distinguish the transition between those emotions[46]. What about when comparing angry to fearful, and angry to sad? Here, the two groups showed a disparity: children who had not experienced abuse could distinguish emotions while those who had experienced abuse over-represented anger.[47] This is a powerful study illustrating that because of the early life experience of abuse, in which there is an overabundance of anger "signals," children's ability to

42. *See supra* note 8.

43. Patricia K. Kuhl, *Brain Mechanisms in Early Language Acquisition*, 67 NEURON 713, 715 (2010). (Kuhl states: "In this review, I will explore a current working hypothesis and its implications for brain development – that to crack the speech code requires infants to combine a powerful set of domain-general computational and cognitive skills with their equally extraordinary social skills." The author interweaves this concept throughout the review, whether describing first or second language learning).

44. Seth D. Pollak & Doris J. Kistler, *Early Experience is Associated with the Development of Categorical Representations for Facial Expressions of Emotion*. 99 PROC. NATL. ACAD. SCI. U.S. 9072 (2002).

45. *See* Pollak & Kistler, *supra* note 44, Fig. 1.

46. *See* Pollak & Kistler, *supra* note 44, Fig. 3.

47. *See* Pollak & Kistler, *supra* note 44, Fig. 3.

discriminate anger from other emotions is disrupted. In a sense, their survival depends upon the child being in high threat detection mode, even if they exhibit biases in over-representing the specific anger emotion. In contrast, in other studies of children who experienced severe neglect, their capacity to distinguish between emotions appears to be blunted.[48]

Chronic activation of the stress response system, in the absence of supportive relationships, can produce a toxic stress response in the child[49]. Importantly, the absence of *serve and return*—that is, neglect—represents nearly eighty percent of child maltreatment.[50] Neglect is a major risk factor for both physical and mental health problems in childhood and later in life[51]. Yet, unless neglect generates physical risk for the child, physicians may not recognize it as a threat to healthy brain and child development.

V. EXECUTIVE FUNCTION DEVELOPS FROM HEALTHY AND POSITIVE RELATIONSHIPS

The ability to buffer and adapt positively to adverse childhood experiences that produce toxic stress is embedded in the circuits that mediate executive function.[52] This is a critical integrative skill, which

48. Victoria Doretto & Sandra Scivoletto, *Effects of Early Neglect Experience on Recognition and Processing of Facial Expressions: A Systematic Review*, BRAIN SCI., Jan. 6, 2018 at 1.

49. *Toxic stress*, as a term was developed by the National Scientific Council on the Developing Child in 2005, in the taxonomy of positive and tolerable stress that reflects the fact that not all challenges to our emotional regulatory circuits are bad. It is important to emphasize that in this taxonomy, the terms do not represent the stimulus. There are many sources of stress, including those that typically produce toxic stress (abuse, neglect, violence, limited resources), as well as those that may strengthen a child's stress response (meeting new people, talking in front of others in preschool, novel environments); *see also Excessive Stress Disrupts the Architecture of the Developing Brain* 1-16 (Nat'l Sci. Council on Dev. Child, Working Paper No. 3, 2005).

50. *The Science of Neglect: The Persistent Absence of Responsive Care Disrupts the Developing Brain* 1-20 (Nat'l Sci. Council on Dev. Child, Working Paper No. 12, 2012).

51. Judy L. Cameron et al., *Social Origins of Developmental Risk for Mental and Physical Illness*, 37 J. NEUROSCI. 10738, 10783-85 (2017); *see also* Nat'l Sci. Council on the Developing Child, *The Science of Neglect: The Persistent Absence of Responsive Care Disrupts the Developing Brain,* 1–17 (Ctr. on the Developing Child at Harvard Univ., Working Paper No. 12, 2012), https://developingchild.harvard.edu/resources/the-science-of-neglect-the-persistent-absence-of-responsive-care-disrupts-the-developing-brain/.

52. John D.E. Gabrieli & Silvia A. Bunge, *Does Poverty Shape the Brain*, SCIENTIFIC AMERICAN 54-61 (2017), https://www.scientificamerican.com/article/does-poverty-shape-the-brain/.

starts developing early in infancy and extends in the 20s and early 30s. This extended period of development provides opportunities for brain plasticity that interventions target. But, in the absence of interventions, early disruption of executive function development predicts poor life outcomes.[53] Risk thus is greater for physical and mental health problems, as well as higher incarceration rates, lower high school graduation rates, and reduced family wealth.[54]

What is executive function? The National Scientific Council on the Developing Child summarizes four features of executive function, using the metaphor of an air traffic controller as an example of someone who requires purposeful control over the following brain features to optimally perform their job[55]: 1) exhibiting selective attention to the most salient stimuli in the environment, while suppressing interfering stimuli; 2) working and long-term memory that allows one to remember facts, hold them *online*, and which serve to solve a current problem; 3) control of actions—selecting appropriate responses to a situation, and inhibiting those that may interfere; and 4) inhibitory control—suppressing emotions that may interfere with problem-solving and reappraisal of situations. These skills begin to emerge in late infancy and in early toddlers.[56]

A growing number of studies have looked at the impact of early executive function disruption on long-term outcomes. A Dunedin, New Zealand study has followed subjects born between 1972 and 1973,[57] Of the 1,037 children initially enrolled at age three, they have data on 972, a remarkable retention rate over this extended period of time. This study demonstrates that measurements showing low executive function skills in toddlers predicts increased risk for poor mental and physical health

53. Terrie E. Moffitt et al., *A Gradient of Childhood Self-control Predicts health, Wealth, and Public Safety,* 108 PROC. NATL, ACAD. SCI. 2683, 2693-98 (2011); *see also* Avshalom Caspi et al., *Childhood Forecasting of a Small Segment of the Population with Large Economic Burden*, 1 NAT. HUM. BEHAV. 5 (2016).

54. William G. Iacono, Stephen M. Malone & Matt McGue, *Behavioral Disinhibition and the Development of Early-Onset Addiction: Common and Specific Influences*, 4 ANNU. REV. CLINICAL PSYCHOL. 325 (2008).

55. *Building the Brain's "Air Traffic Control System": How Early Experience Shapes the Development of Executive Function* 1-20 (Nat'l Sci. Council on Dev. Child, Working Paper No. 11, 2011).

56. Adele Diamond, *Executive Functions*, 64 ANNU. REV. PSYCHOL. 135 (2013).

57. DUNEDIN MULTIDISCIPLINARY HEALTH AND DEVELOPMENT UNIT, THE DUNEDIN STUDY (2017), https://dunedinstudy.otago.ac.nz/.

outcomes, low socioeconomic status, and higher risk for criminal convictions when the children become adults.[58] In fact, a small fraction of the children (twenty-two percent) in the study accounted for forty percent of adult obesity, fifty-four percent of smoking, sixty-six percent of welfare benefits and seventy-eight percent of prescription drug fills, among other outcomes.[59] Jim Heckman, an economist from the University of Chicago, and colleagues analyzed data from the Abecedarian preschool project, which examined the long-term impact of high quality daycare coupled with adult skill-building in parenting. The economic analyses show that when you calculate physical health outcomes in middle age adults who were in that pre-school program, compared to the community sample without high quality preschool, there are lower rates of high blood pressure, pre-diabetes insulin resistance, obesity and cardiovascular disease.[60] These outcomes have developmental origins. Targeting both adult and child capacities are going to be most effective for any program.[61]

ADOLESCENCE—A TIME OF BRAIN AND BEHAVIORAL CHANGES

Development doesn't end in childhood but continues through adolescence, with three different patterns of skill acquisition: 1) skills that are not specific to adolescents, which improve steadily, in a linear fashion, over time from childhood, through adolescence and into adulthood; 2) adolescent emergent skills that plateau over adolescence and remain the same in adulthood; and 3) skills that are specific to adolescence or functions that are not apparent in childhood or adulthood. [62] A study by the Brain Development Cooperative Group has revealed that brain maturation is a complex process in which brain architecture changes during

58. Terry E. Moffitt et al., *A Gradient of Childhood Self-Control Predicts Health, Wealth, and Public Safety*, 108 PROCEEDINGS OF THE NAT'L ACAD. OF SCI. 2693 (2011).

59. Avshalom Caspi et al., *Childhood Forecasting of a Small Segment of the Population with Large Economic Burden*, NAT. HUM. BEHAV., Dec. 12, 2016, at 1.

60. Frances Campbell et. al, Early Childhood Investments Substantially Boost Adult Health (Mar. 28, 2014) (unpublished manuscript) (available in PMC 2014 September 28).

61. *See supra* note 8.

62. B.J. Casey, *Beyond Simple Models of Self-Control to Circuit-Based Accounts of Adolescent Behavior*, 66 ANNU. REV. PSYCHOL. 295, Fig. 1 (2015).

adolescence.[63] The research consortium examined gray (location of neurons and synapses) and white matter (location of fiber tracts) of developing brains from four to eighteen years of age. Gray matter is reduced in size during this period,[64] reflecting pruning of connections that are not stabilized by experience. In contrast, over the same period, white matter continues to develop, mostly because of additional myelination,[65] particularly in brain areas most vulnerable and sensitive to early adversity such as the prefrontal cortex and parts of the temporal lobe.[66] Keep in mind that there is a tremendous amount of variability in individuals across the population in terms of the timing of when the brains of juveniles and adolescents go through the changes in gray and white matter. Thus, while the fields of developmental psychology and neuroscience define average ages for the appearance of functional structural milestones, there is a lot of variation. This has implications for understanding the maturational state of the brain based on function and structure, rather than simply chronological age.

During adolescence, different circuits undergo maturational changes at different rates. B.J. Casey and others have developed a model in which there is an imbalance between the developmental trajectory of the connectivity between prefrontal cortex (control system) and 1) the amygdala, which is involved in threat detection and emotional regulation, and 2) other parts of the brain which are involved in motivation and reward.[67] Until these control and emotional regulatory regions reach similar maturation states in post adolescence, complex functions that are the ingredients of executive function, such as of decision-making, inhibitory control and response suppression may be challenging. The go/no-go task requires an individual to resist their initial impulse to perform a task when they see a stimulus on a video screen. Children, adolescents and adults can do the simple suppression similarly. But, when

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63. Brain Dev. Cooperative Group, *Total and Regional Brain Volumes in a Population-Based Normative Sample from 4 to 18 Years: The NIH MRI Study of Normal Brain Development*, 22 CEREBRAL CORTEX 1, 1-12 (2012).

64. *See* Brain Dev. Cooperative group, *supra* note 63.

65. Peter R. Huttenlocher & Arun S. Dabholkar, *Regional Differences in Synaptogenesis in Human Cerebral Cortex*, 387 J. COMP. NEUROL. 167, 167-78 (1997).

66. *See* Brain Dev. Cooperative group, *supra* note 63.

67. *See* Casey, *supra* note 62.

a visual distractor is introduced, children do just as well as adults in terms of the number of errors that they make, but teens tend to perform more poorly than both groups.[68] Thus, for specific functions, adolescence is not just a continuation of childhood, nor do they perform as young adults. The imbalances noted above may underlie the risk-taking and other decisions made by adolescents that put them at greater risk.

WHAT IS NEUROSCIENCE TELLING US?

More and more intervention programs recognize that healthy brain development is the foundational biological construct for positive child, adolescent and adult outcomes. Understanding that children grow up in an environment of relationships translates into targeting the natural serve and return relationships that are at the heart of cognitive and social-emotional skill-building and executive functioning. These skills are part of the recipe for building resilience—the adaptability to challenges that may otherwise negatively impact short- and long-term outcomes for children. Like physical illnesses such as cancer or cardiovascular disease, intervention programs in the world of promoting healthy brain and child development often produce heterogeneous responses to the intervention, working very well for some and poorly for others. Neuroscience tells us that variation in development is normal. When we become more precise, determining the factors that influenced an intervention that worked so well for some families and so poorly for other families, innovation in the form of targeted approaches will become the norm.

68. *See* Casey, *supra* note 62.