INTRODUCTION
The landscape of the child public health literature in the twenty-first century has been strongly influenced by the Developmental Origins of Health and Disease (DOHaD) hypothesis (Van den Bergh 2011). This hypothesis proposes that human complex diseases and disorders, regardless of age of onset, have their roots in childhood and adolescence and are products of the dynamics of various forces that substantiate human development. Similar developmentally oriented views have been proposed by other theoretical frameworks (for example, Li 2003), but the DOHaD hypothesis has received the most traction in the literature and is a driving force behind studies that connect early development to lifespan health.

The human brain is arguably the most complex biological system, comprising a diversity of functionally distinct regions, structurally distinct neural circuits, and morphologically distinct cell types. Its lifespan is highly dynamic, encompassing continuity and changes at both structural and functional levels. The brain has a unique developmental trajectory compared with the rest of the body. Whereas at birth an infant is approximately 6 percent of its adult body weight, the brain is already 25 percent of its adult weight; by age two years, these proportions are 20 percent and 77 percent, respectively (Dekaban and Sadowsky 1978). This rapid rate of brain growth is accompanied by a slow rate of functional maturation that extends into early adulthood. One of the major premises of the DOHaD is that both structural and functional characteristics of brain development are highly informative predictors of the lifespan ratio of health and disease. As the brain substantiates behavioral change, understanding its development is key in constructing and disseminating interventions that maximize healthy development and minimize the impact of disabilities and disorders.

This chapter briefly outlines aspects of the brain literature that pertain to public health interventions, programs, and policy approaches to protecting, augmenting, and maximizing the healthy development of the brain. First, the essential characteristics of brain development are outlined. Second, a variety of research on brain development changes associated with public health is briefly discussed. The relevance of this research, conducted predominantly in high-income countries (HICs), is considered, with a view to its applicability in low- and middle-income countries (LMICs). Definitions of age groupings and age-specific terminology used in this volume can be found in chapter 1 (Bundy and others 2017).

DEVELOPMENT OF THE HUMAN BRAIN
Anatomical Maturation
The human brain’s maturation is remarkably prolonged and characterized by ongoing dynamic changes throughout the lifespan (Giedd and Rapoport 2010).
Postnatally, it follows (figure 10.1) an inverted U-shaped trajectory that peaks about age eight years and then declines monotonically (Ducharme and others 2016). The brain matures along its two dimensions, gray and white matter. Gray matter is composed chiefly of neuronal cell bodies, which determine the color, as well as dendrites, unmyelinated and relatively few myelinated axons, glial cells including astroglia and oligodendrocytes, synapses, and capillaries. White matter is composed chiefly of myelinated axons; the myelin, which determines the color; and relatively few neuronal cell bodies. In general and simplifying terms, the gray matter forms the structures of the brain, and the white matter ensures that these structures are connected; both are essential for all functions substantiated by the brain. The gray and white matter have different developmental trajectories; their relative proportions and rates of accumulation differ at different developmental stages and in healthy and disordered brains.

**Figure 10.1 Developmental Trajectories of Brain Morphometry**

Sources: Adapted from Giedd and Rapoport 2010, adapted from Lenroot and others 2007.  
Note: cc = cubic centimeters. The data were collected from a sample of males (N = 475 scans) and females (N = 354 scans) ages 6–20 years. The middle lines in each set of three lines represent mean values; the upper and lower lines represent upper and lower 95 percent confidence intervals. All curves differ significantly in height and shape.
By age six years, the brain reaches approximately 95 percent of its adult volume. Its size in boys is approximately 10 percent bigger than in girls; this gender difference persists throughout the lifespan, although the bodies of boys do not become larger than bodies of girls until adolescence, suggesting a decoupling of the maturation trajectories of brain and body size (Giedd and Rapoport 2010). The developmental trajectory of gray matter peaks in early childhood, preceding a peak in total brain volume, and then gradually decreases unevenly throughout the brain. The amount of gray matter peaks earliest in the primary sensorimotor areas and latest in the higher-order association areas. The volume of white matter increases gradually into early adulthood. Myelination not only enhances the parameters of signal transmission, it also boosts the connectivity and networking properties of the brain. Some evidence indicates that white matter increases are coupled with the emergence of specific psychological functions, such as language (Paus and others 1999). Recent technological advances resulted in the differentiation of cortical volume into two underlying components, cortical thickness and cortical surface area. Cortical thickness in the majority of brain regions demonstrates linear monotonic decline occurring mostly similarly for boys and girls between the ages of 4.9 and 22 years, with the peak of cortical thickness manifesting no later than age 8 years (Ducharme and others 2016).

Data on the developmental trajectories of the brain in HICs have accumulated rapidly within several initiatives, such as the BRAIN Initiative. Selected findings from these initiatives include the following:

- A remarkable amount of variability of individual brain size occurs, whether across or within groups, making individualized clinical predictions difficult.
- Subtle deviations from normal developmental trajectories of the brain anatomy appear to be at least associated with—if not causal factors of—a number of developmental disorders (Giedd and Rapoport 2010).
- There are different indicators of brain development, and some of them appear to be more clinically informative than others. For example, cortical thickness has a demonstrated association with the manifestation of developmental disorders (Thormodsen and others 2013).
- Cortical thickness appears to correlate with performance on complex cognitive tasks (Karama and others 2011).
- Different areas of the brain have differential maturational dynamics. In general, phylogenetically newer areas mature later than older ones, and higher-order association areas mature after lower-order somatosensory areas (Gogtay and others 2004). For example, the developmental imbalance between the earlier-maturing limbic system networks and later-maturing frontal systems might explain the psychological and behavioral texture of adolescence, which may occur as this imbalance is being resolved (Casey, Duhoux, and Cohen 2010).
- The maturing brain is characterized by the reshaping of its functional properties, particularly its connectivity, which peaks during adolescence and is defined by the physical links between codeveloping brain areas, the co-activational patterns between brain areas engaged in specific tasks, and the etiological connections between brain areas that are co-influenced by the same genetic and environmental factors.

**Functional Development**

The human brain is commonly represented as a system of tiered networks of highly organized neurons, where spatiotemporal biochemical and bioelectrical activity gives specialized functionality to structural anatomic components of the brain (Power and others 2010). The connection between structure and function is bidirectional, so that specific anatomical characteristics—such as lesions, synaptic development, and myelination—parameterize the functionality of a particular network. The functional dynamics of the network can change physical characteristics of the underlying brain structure. From conception through the lifespan and into senescence, this system’s developmental trajectory is shaped by the continuous co-influence of each individual’s genome and environome—the immediate system of environmental factors that influence human health and behavior. Understanding the stability and malleability of the system is a fundamental task of modern science and the focus of a number of large-scale projects, such as the Human Connectome Project.²

Because the system as a whole and each network emerge developmentally, studies have traditionally engaged research into where in the brain a network may be localized and how it operates. Such research historically used methods of anatomical localization, for example, through brain surgery or autopsy, but these methods are of limited value in living humans. More recent methods (electroencephalography, positron emission tomography, functional magnetic resonance imaging, and near infrared spectroscopy/optimal imaging) based on various technological advances study the brain in living humans, where the focus, along with anatomical structure, is on functional connectivity. These methods,
which at first were technology, skill, cost, and safety demanding, have been evolving to minimize these demands and maximize safety (such as applicability to pediatric populations), transportability (such as use in minimally equipped settings), and utilization (such as usability in low-resource settings).

The current view of the developmental trajectory of the brain’s functional networks and their systems converges on the following:

- From infancy into young adulthood, properties of the network change in such a way that initially strong correlations between brain activity in closely located anatomical regions tend to weaken, while initially weak correlations between more distant regions tend to increase (Power and others 2010), allowing, presumably, for the mental and behavioral functional repertoire of an adult to be substituted for that of a newborn.
- This change in the distribution of correlations may be related to anatomical developmental changes in the brain: synaptic pruning (Huttenlocher 1979), that is, the process of eliminating synapses connecting different neurons. Synaptic pruning may be the driving factor substantiating the decrease in proximal correlations, whereas myelination (Paus and others 2001)—the process of forming a myelin sheath around a nerve to allow nerve impulses to move more quickly—may be the driving factor for the increase in distal correlations.
- Developmental increases in functional connectivity appear to be, at least in part, due to spontaneous or orchestrated co-occurrences of activity (Lewis and others 2009), namely, the co-activation of different brain structures in the context of, for example, implicit or explicit learning, based on which functional connections within the brain might be established as new skills are acquired.
- Functionally different neural networks are thought to have differential maturational courses.
- Characteristics of functional networks have been associated in adulthood with indicators of intellectual performance (van den Heuvel and others 2009) and executive control (Seeley and others 2007). Although comparable data for children are limited, a careful investigation of the developmental trajectories of brain functional networks in conjunction with other maturing systems—for example, language, cognition, and self-regulation—might enhance the understanding of human development as a systemic transformation of a maturing individual guided by the brain.

GENOME-ENVIRONOME DYNAMICS OF BRAIN DEVELOPMENT

Blueprint of the Genome

The development of the brain is based on the apt expression of integral gene products (the transcriptome) coded by sequences of DNA (the genome), specifically, protein and RNA (Tebbenkamp and others 2014). Recent analyses of the human brain transcriptome have, for the first time, allowed a comprehensive picture of the trajectories of genes associated with specific neurodevelopmental processes to be constructed (figure 10.2). There are strong time-specific correlations between the characteristics of the transcriptome and the morphological and functional specialization of brain regions. Alterations to DNA sequences can result in modifications of gene expression, which can cause changes in the brain and the development of brain-based disorders.

Yet, the brain is a highly open and modifiable system—neuronal circuits, established early in life, undergo remodeling as they develop their adult functional properties in response to both genomic and environmental cues. This room for varying interpretations of a single genotype—that is, when the same genotype can exhibit different phenotypes in variable environments—is referred to as plasticity. The capacity of the human brain to respond to the environment and its fluctuations represents an adaptive system that allows individuals to better survive and reproduce. In other words, the brain, metaphorically, is the hub connecting the various information streams from the genome and the environome that allows for the organism’s interpretations of and adaptations to genetic and environmental forces.

Nutritional Requirements

As the most metabolically active organ, the brain’s adequate balanced nutrition prenatally and postnatally is essential for its development and for the proper maturation of the neural mechanisms substantiating child development (Gómez-Pinilla 2008). Overwhelming evidence demonstrates that malnutrition, especially when severe, has significant and lasting implications for development (Laus and others 2011). Malnutrition slows the brain’s development, thinning the cerebral cortex and reducing the numbers of neurons, synapses, dendritic arborization, and myelination—all of which decrease brain size, which, in turn, challenges the brain’s functional properties. Specifically, numerous cranial imaging studies of the brains of patients with protein energy malnutrition (for example, Atalabi and others 2010) have demonstrated cerebral atrophy and
ventricular dilation, which may lead to inadequate patterns of brain activity. Nutritional rehabilitation during childhood and adolescence can reverse these effects, at least partially.

Similarly, adequate specific microelements are essential for developing brains. For example, both severe lack of iodine and severe exposure to neurotoxins such as lead result in irreversible brain damage (Benton 2010). An adequate concentration of vitamin A is essential for the development of the visual system; levels that are too high or too low prenatally can be teratogenic (Reifen and Ghebremeskel 2001). Moreover, complex dynamics occur among different vitamins; a prenatal imbalance between folate and vitamin B₁₂ can increase the risk of postnatal insulin resistance, which is associated with poorer cognitive development (Yajnik and others 2008). The differential developmental trajectories of the brain’s features mean there are differential sensitive periods when the violation of nutritional requirements is most detrimental. Because the brain most rapidly develops prenatally and postnatally, these two periods are critical for subsequent outcomes. Yet, because brain development, although not as rapid as at the early stages of development, does not slow down substantially until individuals reach their early 20s, microelement deficiencies and malnutrition are also important in middle childhood and adolescence.

Specific strategies—such as salt iodization to prevent iodine deficiency, home fortification to prevent iron deficiency, and food and specific micronutrient supplementation in food-insecure populations—have been shown to be effective in preventing nutritional deficiencies. Yet, the research literature that qualifies and quantifies the impact of these strategies on brain development is limited (Prado and Dewey 2014).

**Environmental Experiences**

Substantial evidence indicates that both gray and white matter are susceptible to environmental perturbations (Lupien and others 2009). Although the direction of the causality—from brain to behavior or from behavior to brain—is often unclear, it is indisputable that environment is a critical ingredient of change in the brain’s structure and function. For example, children who experienced severe exposure to air pollution in South Mexico City were reported to have prefrontal white matter alterations and the precursors of Alzheimer’s disease (Calderon-Garciduenas and Torres-Jardon 2012).

Two environments that contextualize brain development are particularly prominent: socioeconomic status (SES), especially poverty (Hanson and others 2013), and early life experience in general and parenting quality in particular (Kundakovic and Champagne 2015). There is a growing field of studies on socioeconomic neurogradients, defined as neural differences associated with differences in SES (Schibli and D’Angiol 2013). For example, it has been demonstrated that low SES environments in general and poverty in particular influence the rate of human brain development (Hanson and others 2013). Specifically, children from lower SES environments differ in their gray matter accumulation in the frontal and parietal lobes, such that differences widen throughout development as the exposure to impoverished environments continues (figure 10.3). Of note is that volumetric brain differences are associated with the emergence of disruptive behavioral problems (Hanson and others 2013).

Anatomical brain differences have also been associated with characteristics of prenatal and postnatal environments. For example, prenatal maternal stress is associated with decreased dendritic spine density in multiple brain areas (such as the hippocampus and the anterior cingulate and orbitofrontal cortex) substantiating emotional regulation (Murmu and others 2006). Conversely, early maternal support postnatally is strongly
predictive at school age of healthy development of the hippocampus, a brain region key to memory and stress modulation (Luby and others 2012).

**Neuroplasticity**

The overriding principle of neuroplasticity is that behavioral change is associated with a specific gain or loss of synapses within neuronal networks (Caroni, Donato, and Muller 2012). Multiple factors differentiate the types of neuroplasticity in the typically developing brain (Kolb and Gibb 2014).

Neuroplasticity can be characterized as follows:

- **Experience-expectant.** When structural or functional changes in the brain require specific types of experience, for example, the maturation of binocular vision
- **Experience-independent.** When changes in the brain occur spontaneously and override its initial structure and function, for example, the development of the lateral geniculate nucleus in the maturation of the visual system
- **Experience-dependent.** When changes in the brain allow the acquisition of new behaviors, for example, all types of learning.

Neuroplasticity is related to the relevance, frequency, intensity, and sequences of experiences. It can be adaptive, as in the acquisition of a new skill, or maladaptive, as in the formation of a dependency or disorder. Of note is that changes in the brain that result from the same

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**Figure 10.3 Brain Growth Trajectories, by Age and Socioeconomic Status**

- **a. Total gray matter**
  - 5, 10, 15, 20, 25, 30, 35 months
  - SES = socioeconomic status; cm³ = cubic centimeters.

- **b. Frontal gray matter**

- **c. Parietal gray matter**

Source: Adapted from Hanson and others 2013.
Note: SES = socioeconomic status; cm³ = cubic centimeters.
environmental impact, such as injury, vary remarkably, depending on when in the developmental process the impact occurred. An experience can generate qualitatively different changes in different regions within the same brain. In addition, plastic changes themselves change over time; for example, the overproduction of synapses in the early stages of development is reversed by pruning in adolescence, which continues well into adulthood. One of the most rapidly developing areas of research pertains to the dynamics of infant and toddler neuroplasticity in response to severe negative environmental impacts, such as maltreatment (Graham and others 2015), and remediation, such as training of self-control (Berkman, Graham, and Fisher 2012).

SKILL ACQUISITION AND CHANGES IN THE BRAIN

This section focuses on different behavioral loci associated with brain changes that have been or can become targets for specific public health interventions. Only four selected loci are discussed here—early attachment, language development, acquisition of literacy and numeracy, and self-regulation (SR).

Early Environment and Attachment

Substantial evidence demonstrates that atypical early development in which the presence of the attachment bond between children and significant others—mothers, fathers, or primary caregivers—is disrupted is extremely detrimental for brain and behavior development. One source of such evidence comes from research into orphanhood, when children are raised in institutions, often characterized by nutritional, physical, stimulational (that is, cognitive, linguistic, and emotional), and care deficiencies. Institutionally reared children tend to be characterized by deviations from typical brain development, in particular, a distributed network of alterations in the white matter—limbic and paralimbic pathways, frontostriatal circuitry, and sensory processing pathways (for example, Bick and others 2015). No comparable studies have been completed in LMICs; yet, the frequency of orphaned children in LMICs—given conflict zones, child labor, deadly epidemics, and other maladies—is much higher than in HICs and, therefore, should be a priority for research.

Another source of such evidence comes from studies into the prevalence of childhood maltreatment in LMICs. For example, it has been reported that 25 percent to 50 percent of young South Africans are maltreated by family members (Pieterse 2015). In HICs, maltreatment has been consistently shown to be detrimental to brain development (Painter and Scannapieco 2013). Given the widespread opportunities for maltreatment in LMICs (Tomlinson, Cooper, and Murray 2005) due to early pregnancies, large numbers of children in the same home, high levels of poverty, and low levels of education, it is extremely important to identify programs demonstrated to be effective and efficacious in HICs and transportable, at least potentially, to LMICs. One such program is the Nurse-Family Partnership (Olds and others 1997), which is being introduced to South Africa (Pieterse 2015).

Language Development

Language acquisition occurs during a sensitive period of brain development (Knudsen 2004).

The neural signatures of language acquisition are detectable at very early stages of development (Rivera-Gaxiola, Silvia-Pereyra, and Kuhl 2005). These neural signatures, although themselves dynamically transforming, are highly predictive of numerous other indicators of child development, both linguistic and nonlinguistic.

However, children require several key elements to progress through the language acquisition process:

- First, children need to be immersed in environments in which they have high-frequency exposure to the language because the mechanism thought to be most used is statistical learning, which assumes an ongoing exposure to language data so that linguistic mental representations can be inferred and automatized (Saffran, Aslin, and Newport 1996). Yet, simple exposure to linguistic stimuli, no matter how intense, is not enough.
- Second, the motivation to learn language is social and requires the presence of a social context for language acquisition (Kuhl 2007). The acquisition of language engages and affects the computational and social areas of the brain. To master language, children both capitalize on and enhance systems of cognitive and social skills (Meltzoff and others 2009). Thus, the brain-behavior pathways that underlie and follow language acquisition are highly dynamic and future oriented as their properties predict subsequent steps in child development (Pascoe and Smouse 2012; Prathanee, Lorwatanapongsa, Makarabhirom, and Wattanawongsawang 2010).

These conditions—statistical exposure and social context—form appropriate targets for policies to enhance typical and to remediate atypical brain-behavior
development. Such policies, which have been developed in HICs and are being introduced to LMICs, include the following:

- Raising public awareness of atypical development (Mahmoud, Al jazi, and Alkhamra 2014)
- Promoting professional training of specialists able to diagnose, remediate, and support individuals with developmental difficulties (Cheng 2010)
- Facilitating early identification of developmental difficulties (Glumbic and Brojcin 2012; Hamadani and others 2010; Sidhu, Malhi, and Jerath 2010)
- Advocating inclusive preschool education
- Providing additional support to children with developmental language delays (Rakap 2015) and implementing specialized intervention programs (Amato and others 2015; De Cesaro and others 2013; Erasmus and others 2013; Fernandes, De La Higuera Amato, and Molini-Avejonas 2012; Fernandes and others 2014; Kotby, El-Sady, and Hegazi 2010; Pascoe and others 2010; Prathanee, Lorwatanapongsa, Makarabhirom, Suphawatjariyakul, and others 2010).

These systemic changes reflect the emerging emphasis on early child care and education in LMICs in general and language development in particular because all are extremely important for brain development. The relevant research accumulating in LMICs has replicated findings from HICs and reinforces the crucial significance of these systemic changes (Cheng 2010; Günhan 2011; Pascoe and Smouse 2012).

**Literacy and Numeracy**

Numerous studies have been conducted to isolate and map the specific brain pathways or functional systems that support literacy (Dehaene and Cohen 2007) and numeracy (Butterworth and Walsh 2011). Clearly, the acquisition of these skills is based on the use of existing areas of the brain, which are reorganized structurally and functionally while being recycled and recruited into systems of acquisition (Dehaene and Cohen 2007). Large and growing fields of research are investigating the impact of literacy and numeracy on brain functioning by (1) conducting longitudinal tracking of children as they move from preliteracy and prenumeracy stages into stages of mastery, (2) comparing groups of literate and numerate and illiterate and innumerate adults, and (3) comparing individuals with typical and atypical pathways of acquisition for literacy and numeracy. Each of these approaches is associated with its own methodological challenges, and limitations exist in the interpretations of the relevant data and findings. Yet, there is a remarkable convergence of multiple studies from different countries, including LMICs, specifying the impact of skill acquisition on brain structure and function.

**Literacy**

Literacy systems appear to involve brain areas substantiating early vision, script analysis, language analysis, and their mutual associations (Dehaene, Morais, and Kolinsky 2015). Literate individuals have been reported to demonstrate numerous advantages, compared with illiterate individuals, in the speed and accuracy of processing both letter-based and picture-based materials. The specificity of reading as a skill distinguishing literate and illiterate individuals is reflected by the fact that reading recruits a specific brain area located in the left ventral occipito-temporal cortex to become a visual word form area (VWFA)—an area that demonstrates specific, universal, and reproducible responses to script. The patterns of activation in the VWFA are correlated with the degree of mastery of reading.

It is important that adult plasticity in this area underlies the ability to acquire print—the graphic representation of a spoken language—either in a first or in subsequent languages. Also important is that the VWFA is strongly connected, both structurally and functionally, to the brain areas that support spoken language. Because reading assumes a conversion from vision to language, it requires activation of the language network, or at least its component. Indeed, literate, compared with illiterate, individuals demonstrate increased and modified activation of the language-related cortical and subcortical network (in particular, the planum temporale [PT]—an area of the brain that supports, along with surrounding areas, the neuronal representations of the consonants and vowels of spoken language) while engaged in specific language- and reading-related tasks. This means that literacy acquisition not only results in the creation of specific systems supporting reading, but also changes other systems supporting related functions, enhancing and automatizing them.

To illustrate (figure 10.4), literacy enhances the connectivity between the ventral temporal lobe (including VWFA) and the inferior parietal and posterior superior temporal regions (including PT) via enhanced myelination. This strengthening may enable the automatization of the grapheme-to-phoneme conversion, crystallization of reading skills, and subsequent development of related higher-order cognitive processes, such as reading comprehension. Moreover, reading mastery has been shown to increase gray-matter density in several regions of the brain that contribute to the establishment and functioning of the brain system that supports literacy.
Numeracy

Although this field is considerably smaller than that of literacy studies, systemic findings include the following (Butterworth, Varma, and Laurillard 2011):

- Groups of multiple-duty neurons that respond to object dimensions such as space, time, object size, and number appear to be located in the intraparietal cortex.
- These neurons are part of an extensive distributed network given that, similar to literacy, numeracy engages multiple processes such as early vision, motor, spatial, and mnemonic functions.
- Neuroimaging studies have converged on the intraparietal sulcus (novel numeric operations) and the angular gyrus (previously learned numeric operations) as the loci of numeric processing.
- The intraparietal sulcus is viewed as the foundational structure in the construction of numeric brain networks; it demonstrates structural abnormalities in individuals with the developmental disorder of mastering numeracy—dyscalculia—and changes in gray-matter density in expert mathematicians.

The evidence that education in general and the acquisition of literacy and numeracy alter the brain structure and function comes primarily from HICs. The relevant research in LMICs is focused predominantly on documenting the manifestation of difficulties in acquiring literacy and numeracy in different languages and societies (Pouretemad and others 2011), frequency of these difficulties (Ashraf and Najam 2014; Haïr Guidara and others 2013; Jovanovic and others 2013), and the development of relevant intervention approaches (Lee and Wheldall 2011; Obidoa, Eskay, and Onwubolu 2013).

Self-Regulation

One of the ultimate goals of development is to master the skill of SR—goal planning, inhibition, mental flexibility, sustained motivation, executive control, and self-agency. SR is a critical element in the dynamic system of health and disease and the key to productive adulthood and successful aging. SR is supported by a distributed brain system whose main task is to support the adequate appraisal of the system of demands of all relevant factors on individuals and the subsequent formulation of behavior to satisfy these demands. The executive load is developmentally uniquely intensified in adolescence, and corresponding changes occur in the brain (figure 10.5). These changes are related primarily to the maturation of the prefrontal cortex (PFC) and its connectivity with other brain areas as it recruits them to substantiate the system of SR.

Specifically, the following changes peak in the adolescent brain (Luciana 2013):
- A general thinning of the cortex and pruning in subcortical structures (gray matter) and an increase in the volume and enhanced organization of brain connections (white matter) crescendo. This results in...
increasingly efficient functioning within and across brain networks.
- Heightened distinctions occur in regional brain volumes, and functional brain responses to reward intensify.
- Maturation of the PFC and the SR network requires exposure to key environmental experiences, such as positive incentive and reward. Such exposures are particularly important in adolescence because they are coupled with age-dependent experience-expectant increases in dopaminergic tone (that is, the amount of distribution of the neurotransmitter dopamine) in the brain.

Dopaminergic signaling—the engagement of dopamine-based reward systems, exposure to uncertain and risky environments, behavioral explorations, and independence seeking—contributes to the maturation of the PFC and the related distributed system in general and the cross-talk between subcortical (limbic) and cortical (prefrontal) regions in particular. As consolidation through learning occurs, a brain system emerges whose role is to support decision making based on calculations of the probability and magnitude of risk and reward.

Our current knowledge of the development of the brain systems substantiating SR, although largely empirically based rather than explanatory, suggests several approaches for intervention. These interventions are connected to the nature of reward responsivity, its intersection with social strivings, and socioemotional context and content. Numerous relevant intervention approaches have been developed in HICs (Rothbart and Posner 2015), but their distribution has been limited in LMICs.

CONCLUSIONS

The DOHaD hypothesis assumes continuity between the adult profile of health and disease and the dynamics of child development in general and brain development in particular. The hypothesis also assumes another continuity—that between interventions and sensitive periods given that the presence of such periods is not limited to early childhood. Although the DOHaD hypothesis has been increasingly supported by empirical evidence in HICs, the corresponding evidence in LMICs is limited.

As this empirical evidence is being accumulated, it is becoming clear that the brain helps ensure both types of continuity. The brain is an ever-changing system whose structure and function reflect, at any given time, both the endowment of the genome and the investment opportunities available in various environmental contexts, including educational systems, public health policies, and specific intervention programs. As knowledge of the brain’s developmental trajectories accumulates, the extent of the brain’s modifiability, especially in response to targeted interventions, will become clearer. This understanding will help guide the development of intervention approaches suitable for and most effective at the sensitive periods of brain development that occur across the lifespan.

NOTES

Work on this essay was supported by NIH grants R01 HD085836 (Elena L. Grigorenko, PI) and P50 HD052120 (Richard Wagner, PI). Grantees undertaking such projects are encouraged to express freely their professional judgment. This chapter, therefore, does not necessarily reflect the position or policies of the abovementioned agency, and no official endorsement should be inferred. I am grateful to Eileen Luders and Tuong Viet Nguyen for providing helpful comments on the manuscript, to Mei Tan for her editorial assistance, and to Janet Croog for preparing the figures.

World Bank Income Classifications as of July 2014 are as follows, based on estimates of gross national income (GNI) per capita for 2013:
- Low-income countries (LICs) = US$1,045 or less
- Middle-income countries (MICs) are subdivided:
  a) lower-middle-income = US$1,046 to US$4,125
  b) upper-middle-income (UMICs) = US$4,126 to US$12,745
- High-income countries (HICs) = US$12,746 or more.

1. BRAIN Initiative, Washington, DC.

REFERENCES


