

Brain Development: The Connection Between Neurobiology and Experience

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Prepared December 1999, updated September 2003

Current research in brain development is revealing connections between early environmental experiences and neurobiological development. The formation of neural circuitry is driven by both genetic factors and experience. Genetic signals provide the neurological materials to create a mature brain. These are the biological preparations for the brain to incorporate sensory information. Environmental influences then take over to shape the subsequent circuitry and function.

GENETIC CONTRIBUTIONS

Research has firmly established that genes signal for the over-production of neurons from 3 weeks gestational age to 2 years, and that genes program for vastly accelerated formation of connections between neurons (synapses) in an infant's brain compared to an adult's (e.g. Bedi, 1989; Bertenthal and Campos, 1987; Chugani, 1998; Chugani, Phelps, and Mazziota, 1987; Fischer, 1987; Goldman-Rakic, 1987; Greenough, Black, and Wallace, 1987; Huttenlocher, 1994; Porter, Grunau, and Anand, 1999; Sengpiel, Stawinski, and Bonhoeffer, 1999). Genes also predispose neurons for certain functional responses to stimulation from the environment. For example, neurons in the visual cortex of kittens are already "wired" at birth to respond to specific horizontal/vertical orientations of visual input (Sengpiel et al., 1999), and the left-hemispheres of healthy newborn infants are more highly activated by complex speech sounds than their right hemispheres (Reilly, Bates, and Marchman, 1998). Furthermore, a study by Eimas

(1985) indicates infants may have a biologically determined ability to perceive phonemes. Indeed, the brain of a 3 month old infant can distinguish many more different spoken sounds than are present in a given language, and this sensitivity regresses over the first year (Dehaene-Lambertz and Dehaene, 1994; Eimas, 1985; Mayeux and Kandel 1991).

It thus appears that the neurons and initially abundant connections in these brain regions are genetically programmed to respond to "expected" stimuli in an animal's environment (Porter, et al., 1999). Then, environmental stimulation begins to shape neural functioning, and can even reverse genetic predisposition, as we will discuss below. In the 1970s and '80s, Chomsky proposed a biological predisposition for neurons to recognize the "universals" of language, such as syntax. Current researchers hypothesize that the "universals" apply to general cognition and not specifically to language; experiments are currently underway to test this idea (Mayeux and Kandel, 1991).

ENVIRONMENTAL CONTRIBUTIONS

Environmental stimulation during early periods of life is critical for normal development because neurons and their synapses require stimulation to persist. Abundant synapses created from genetic signals will not be retained unless they are stimulated. And, despite genetic encoding for over-production of neurons, if too many synapses are lost, the neurons will die, since they receive stimuli via their synapses. Even apoptosis, or genetically programmed neuronal cell death, which occurs before 2 years, is influenced by environmental stimulation because it is related to lack of activity

of the neuron (Bedi, 1989; Bertenthal and Campos, 1987; Chugani, 1998; Greenough, et al., 1987; Huttenlocher, 1994; Jessell, 1991; Nicholls, Martin, and Wallace, 1992; Porter, et al., 1999).

Greenough and colleagues (1987) reported on several studies on the visual cortex of rats in which rat pups reared in enriched environments (e.g. in cages with other pups with free access to a variety of objects, toys, and mazes) had 20 to 25% more synaptic connections as compared to rat pups reared in individual cages. Bedi (1989) demonstrated that rat pups reared in a dark environment have 30-35% fewer synapses per neuron, resulting in fewer connections to other neurons, than pups reared in typical light/dark cycles.

Ethical reasons obviate similar studies on synaptic density with human infants, but evidence from non-experimental studies suggests that environmental deprivation can have a similar affect on the functioning and/or number of neural cells. Neuroimages of the brains of Romanian orphans, who experienced severely deprived early environments and often exhibit persistent cognitive and behavioral deficits, show large regions of non-functioning neurons (Chugani, Behen, Muzik, Juhasz, Nagy, and Chugani, 2001).

In addition to influencing the number of neurons and connections between them, environment can also influence genetically programmed functional response of neurons. Research by Sengpiel and associates (1999) on kitten visual cortex indicated that if kittens did not see certain orientations in their environment (e.g. because they are raised in an artificial environment of striped lighting), neurons which were genetically predisposed to respond to those non-experienced orientations "switched" their

“preferred orientations” to those that were experienced. For example, a given neuron in the kitten’s visual cortex, which was genetically predisposed to respond to horizontal orientations in the environment, would instead respond to vertical orientations if the kitten was reared in an environment of only vertical orientations.

The importance of early sensory experience in human visual cortical development is demonstrated by the finding that surgery to correct strabismus (i.e. misalignment of the two eyes) after 6 months of age does not restore binocular vision for the child, as the development of binocularity requires simultaneous input from both eyes prior to 6 months of age (Julesz, 1991; Kirkwood, Lee, and Bear, 1995). Considering language development, Locke (1992) reviewed research on children born with severe hearing impairments that supports the contention that the experience of hearing is related to developing typical speech skills. These children were delayed in production of speech until after 2 years, and the range of sounds produced was restricted and qualitatively different in nature from children with normal hearing. In a review of current research in language development, Ruben (1997) also reported that hearing experience is critical in language development. For example, children who had hearing loss from otitis media during their first year of life exhibit detectable reductions in the ability to discriminate phonemes when they are 9 years old. On the other hand, children who acquired severe deafness after 2 years of age are better at syntax and semantics than children who were deaf before 2 years of age (Ruben, 1997).

Human children experiencing an environment characterized by undernutrition, especially during the first 4 years of life, exhibit under-myelination of neurons; lack of

this protective insulation can result in seizures and other abnormal neurological functioning (Nelson, 2000). Thus, experience can affect multiple aspects of neurological development. These examples of the influence of early experience on neural development create the basis for the concept of sensitive periods.

SENSITIVE PERIODS

Compared to an adult brain, the immature brain has a heightened ability to change itself (i.e. high plasticity), from birth through the first 4 years of life. After that, plasticity declines, but still remains higher than for adults, until age 10 to 12 years; however, even adult brains are plastic and can change, or we would not be able to learn anything past the age of 20! The heightened plasticity of the early years is mediated by the innate overproduction of neurons and synapses discussed above.

Specifically, connections in the brain are formed more quickly than they are broken for the first 4 years. By 1 year, certain areas of the brain have formed twice as many synapses as will be present in the adult brain. By age 4, synaptic density in all cortical regions is two-fold greater than adult densities (Greenough, et al., 1987; Huttenlocher, 1994). A converging line of evidence, Positron Emission Tomography (PET) studies by Chugani and colleagues (1987; Chugani,1998), revealed that glucose utilization of the brain (an indirect but highly associated measure of the number of synapses) at 1 year assumes adult-like distributions across the brain; by 2 years it is functioning at twice the adult metabolic rate. High synaptic density is maintained for several years (Chugani, et al., 1987; Huttenlocher, 1994; Greenough, et al., 1987). Around age 10 to 12 years, the number of synapses in the brain has declined to near adult levels, while

metabolic rate changes associated with synaptic connectivity continue until 16-18 years (Chugani, 1998; Chugani, et al., 1987; Fischer, 1987). This endogenous over-production of neurons and synapses is part of the neural mechanism underlying the developmental concept of sensitive periods.

Sensitive periods provide “windows of opportunity” for experience to maximally influence neurology and therefore subsequent behavior (Nelson, 2000; Porter, et al., 1999; Ruben, 1997; Yim, 1998). Under optimal conditions, experience-dependent fine-tuning of neural connections removes redundancies to create the more refined and efficient neural circuitry of an adult brain (Goldman-Rakic, 1987; Jessell, 1991; Nicholls, Martin, and Wallace, 1992). And, young children have a much better chance of recovery from adverse conditions than do adults, as demonstrated by the striking observation that young children with damage to language portions of their brains go on to develop nearly normal language, as compared to adult victims of similar injury. Although adolescents and adults who experienced brain damage as children still exhibit deficits in more complex aspects of language when compared to non-brain-injured, age-matched controls, they are nonetheless able to speak and write, despite the loss of their genetically predisposed language center (Huttenlocher, 1994; Reilly, et al., 1998).

Different areas of the brain, which mediate different skills and behaviors (Kandel, 1991), develop at different ages and have correspondingly different sensitive periods. Studies on synaptic density in different cortical and subcortical regions indicate a correspondence between reaching maximal synaptic density and emergence of behavior. Specifically, Fischer (1987) reported that several independent laboratories

confirmed periods of rapid change at 2-4 mo., 7-8 mo., 12-13 mo., and 18-21 mo. in humans. Developmentally, children are able to reliably control a single action to serve a simple goal at 2-4 mo. At 7-8 months they can consistently relate a few actions, such as coordinating vocalization and hearing to imitate words, and at 12-13 months children can relate a number of actions in a complex system, such as manipulating an object so it drops through small holes in a box. The ability to represent things that are not actually present and use symbols typically manifests around 18-21 months (Fischer, 1987).

Data on the frontal cortex indicate that the spurt in synaptic formation begins at 8 months and reaches a maximum at 2 years; behavioral evidence indicates that 8 month-old children do not perform well on spatial search, delayed response tasks, but by 12 months they are performing well even after 10 second delays. Repetition of simple words occurs around 8 months, and by 18-24 months children can typically speak in simple sentence and evidence a vocabulary spurt (Goldman-Rakic, 1987). These skills reflect attainment of object permanence and the ability to represent objects that are not physically present.

Additional evidence for the connection between explosive, genetically programmed synapse formation and emergence of behavior is found in developmental time course changes in glucose metabolism in the brain which parallel the emergence of behavioral skills throughout development (Chugani, 1998; Chugani, et al., 1987), and in head growth spurts which also coincide with the emergence of behavior (Fischer, 1987).

EXPERIENCE-DEPENDENT GROWTH

The fine-tuning of neural connections in response to stimuli from the environment, termed experience-dependent synaptogenesis by Greenough and colleagues (1987), is another part of the neural mechanism underlying sensitive periods. This process, which is much more localized to the area of the brain with functional control over what is being “learned,” allows novel stimuli unique to an individual’s experience to be encoded in the brain. These connections develop throughout life, and also require stimulation to persist (Chugani, 1998; Greenough et al., 1987; Huttenlocher, 1994; Jessell, 1991; Nicholls et al., 1992; Siegel, 1999). This process may underlie the plasticity of the brain into adulthood, making it possible for older children and adults to continue learning (Bertenthal and Campos, 1987).

Neurological evidence in cortical thickness patterns show a peak in the visual, parietal, temporal, and motor cortices at 10-20 months, which could be due to pre-programmed synaptic proliferation. But, a second peak occurs around 4 years in these areas, and prefrontal cortex reaches its peak thickness between 4 and 6 years (Greenough, et al., 1987), which may reflect the experience-dependent development of synaptic connections.

Supportive behavioral evidence is found in research on locomotion and infants’ performance on spatial search tasks. Kermorian and Campos (1988) demonstrated that 8.5 month old infants with locomotor experience (either on their own or in walkers) performed better than pre-locomotor infants on the visual cliff test (spatial cognition). Furthermore, the longer infants had been moving themselves, the better their performance. Becker and colleagues (1999) report that early motor delays of very low

birth-weight children can contribute to problems with later attention, language, learning disabilities, behavioral control, and social competence, suggesting early motor experience creates connections that will later subserve these behavior domains.

Although experience-dependent synaptogenesis occurs throughout life, intervention at an early age allows experience-dependent development to facilitate early neural reorganization, enhancing a child's potential for optimal development in a given area, with the concurrent potential of preventing secondary and tertiary delays.

SOCIAL INTERACTIONS

A child's relationships with his/her caregivers are an important aspect of his/her environment and are also related to behavioral and neurological development. The development of "attachment" to one or a few caregivers by 7 months leads to specific organizational changes in an infant's behavior and brain function (Siegel, 1999). The brain's emotional center is the limbic system, which has a neurological window of opportunity for experience-dependent effects on the brain from late infancy to around 4 years of age (Nelson, 2000; Yim, 1998). The limbic area connects to higher cortical regions, like the frontal cortex and particularly the right hemisphere. Healthy attachment is important in the formation of connections between these regions which allow the child to regulate him/herself emotionally through behavioral inhibition. Patterns in attachment relationships during infancy are also associated with social relatedness, access to autobiographical memory, and the development of self-reflection and narrative (Siegel, 1999).

Any type of attachment begins with experiencing a particular person and develops into a sort of preference for that person, regardless of the qualitative aspects of that preference. Considering neurobiological evidence, there is ample research indicating that faces activate the Fusiform Gyrus (FG) in the ventral temporal lobe more intensely than do objects, demonstrating a perceptual processing preference for faces. A growing body of evidence indicates that individuals with Autism Spectrum Disorders (ASD) process faces instead using the inferior temporal gyri (ITG), which in typical subjects are more intensely activated by objects. Typically developing infants are born with a perceptual preference for faces, but this must be practiced to develop into an “expertise” for faces (Schultz, et al., 2000). Limited social interaction, which is a diagnostic indicator of ASD and includes inadequate attention to, or “practice” with faces and limited eye contact, is certainly a factor in the etiology of this important perceptual processing difference.

More research must be done to determine the etiology and how this can inform therapies for young children with ASD and other social challenges. Progress has been made by Gauthier and colleagues (1999), who demonstrated that typically developing adults can be trained to be “experts” in visual recognition and classification of non-face items, and that this expertise is accompanied by an increased activation of the FG. The next step will be to determine if this is the case for individuals with social challenges and for young children. Nonetheless, evidence to date is encouraging about the possibility of therapies aimed at increasing “practice” with viewing faces to provide the

FG with the stimulation required to learn to recognize people's faces, a requisite for successful interpersonal relationships.

Research with children not known to have ASD indicates the neurophysiology of children's brains is affected by insecure attachments. The consequent chronic stress and pain activate the hypothalamic-pituitary adrenocortical system (HPA), which produces the steroid cortisol. Two functions of cortisol are to facilitate the processes that cause cell death and to reduce the number of dendrites available for synapses, causing shrinkage in certain areas of the brain, for example the hippocampus in the limbic system (Kupfermann, 1991). Chronic stress alters basic regulatory capacities and future response to stress, which carries important ramifications for several areas of later development and for physical health (Perry and Azad, 1999; Siegel, 1999; Yim, 1998).

Animal research shows that repeated or prolonged separation of infants from their mothers, or maternal stress, lead to elevated levels of cortisol (Nelson, 2000). And, chronically high levels of cortisol in the brain cause the amygdala to be overactive, which promotes anxious, hypervigilant behavior (Gunnar, 1996; Perry and Azad, 1999). The amygdala plays a role in establishing the emotional value of an experience, and working together with the hippocampus, processes memory. Excessive cortisol disrupts selective attention and impairs hippocampal and amygdala memory processing, which in turn can impair both the capacity to mediate stress response and academic achievement. Excessive cortisol can also damage circuits that link bodily response (brainstem) to brain function, contributing to increased risk of physical illness (Nelson 2000, Perry and Azad, 1999; Siegel, 1999). Together with emotional regulation

problems, a self-promoting negative cycle can ensue where hyperarousal and impaired attention lead to peer/adult relation difficulties and inability to perform well in school, which lead to poor self-esteem, which contributes to deficits in self regulation, and so on (Perry and Azad, 1999).

On the other hand, human infants with secure attachments do not show elevated cortisol levels in response to stressors, such as getting a shot or a brief separation from the attachment figure (Gunnar, 1996). Secure patterns of attachment can therefore offer “resiliency” for the child if the child should experience a stressful or traumatic event (Perry and Azad, 1999; Siegel, 1999).

EARLY INTERVENTION

The variety of evidence above provides a strong case for the link between neurophysiological development and behavior, and for the important role of the child’s environmental experiences in shaping neurophysiological development. Furthermore, although different skills have different sensitive periods, they are developmentally interdependent (Ruben, 1997). For example, infant visual and motor skills may be basic to mastering spatial and causal relations, and social and communication skills may establish the neurophysiological foundations for adult language skills (Greenough, et al., 1987). The potential for early intervention to help children is in large part due to the plasticity of the human brain, which is greatest during their early years. “Critical periods for intervention are most likely real phenomena based on actual neurobiological principles” (Nelson, 2000, p. 222). Consequently, intervention during these early

windows may be most effective in facilitating subsequent development (Bertenthal and Campos, 1987; Chugani, 1998; Locke, 1992; Perry and Azad, 1999; Ruben, 1997).

Children with or at risk for developmental delays are particularly vulnerable to experiences that may contribute to altered neurological development and insecure attachment patterns, which can lead to learning deficits. For instance, sensory deficits can prevent neural stimulation, which stabilizes synapses and determines which circuits will remain and which neurons will live. Motor delays can decrease sensory stimulation and experience required for later cognitive skills. Cognitive delays make the choice of stimulation critical in shaping the developing neural substrate. And, perceptual processing differences may mean that different types of parent-child interactions are necessary to promote the social skill development of children with ASD and other social challenges. Lack of an appreciation of these delays and what they entail can pose a threat to healthy development.

Furthermore, babies with special needs may experience higher levels of stress, both from the consequences of their delays (e.g. pain from sensory defensiveness, frustration from communication delays) and from their environment (e.g. children who live in high risk environments are exposed to poverty, substance abuse, caregiver incarceration, domestic violence, and have uneducated caregivers). Children with developmental delays are at risk for abuse, and attachment problems can follow from their special needs, and from parents' reactions to those needs. Parents may become emotionally unavailable to their child due to difficulty adjusting to their baby's special needs, feelings of hopelessness, depression, resentment, and fatigue from the burden

of extra care, like dealing with sensory defensiveness and feeding problems. A child who does not have a sensitive, available, warm, and steady attachment figure, is at increased risk for impairments in sense of self, ability to organize behavior and learning, ability to form social and intimate relationships, empathy, and self-esteem.

Early intervention timed to coincide with windows of opportunity during infancy and early childhood can adjust the kinds of sensory stimulation and the types of social interaction a child experiences to optimize neural development. It can also reduce the amount of stressors the child experiences through adaptations to accommodate his/her disability and through parental education and support. Early intervention can facilitate healthy attachment by helping to reduce parental stress, and by enhancing parents' ability to interact in optimal ways with their unique child. Further research is needed to refine the implications of brain research for specific therapies and interventions, but clear empirical evidence supports the wisdom in providing intervention as early as possible.

Suggested citation:

Derrington, T., Shapiro, B. & Smith, B. (1999). Brain development: The connection between neurobiology and experience. Unpublished manuscript.