



Childhood Experience and the Expression of Genetic Potential: What Childhood Neglect Tells Us About Nature and Nurture

BRUCE D. PERRY

*The ChildTrauma Academy, 5161 San Felipe, Suite 320, Houston, TX 77056, USA
(E-mail: ChildTrauma1@aol.com)*

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Abstract. Studies of childhood abuse and neglect have important lessons for considerations of nature and nurture. While each child has unique genetic potentials, both human and animal studies point to important needs that every child has, and severe long-term consequences for brain function if those needs are not met. The effects of the childhood environment, favorable or unfavorable, interact with all the processes of neurodevelopment (neurogenesis, migration, differentiation, apoptosis, arborization, synaptogenesis, synaptic sculpting, and myelination). The time courses of all these neural processes are reviewed here along with statements of core principles for both genetic and environmental influences on all of these processes. Evidence is presented that development of synaptic pathways tends to be a “use it or lose it” proposition. Abuse studies from the author’s laboratory, studies of children in orphanages who lacked emotional contact, and a large number of animal deprivation and enrichment studies point to the need for children and young nonhuman mammals to have both stable emotional attachments with and touch from primary adult caregivers, and spontaneous interactions with peers. If these connections are lacking, brain development both of caring behavior and cognitive capacities is damaged in a lasting fashion. These effects of experience on the brain imply that effects of modern technology can be positive but need to be monitored. While technology has raised opportunities for children to become economically secure and literate, more recent inadvertent impacts of technology have spawned declines in extended families, family meals, and spontaneous peer interactions. The latter changes have deprived many children of experiences that promote positive growth of the cognitive and caring potentials of their developing brains.

Archeology first documents evidence of written language 5000 years ago in the Middle East. The genetic potential for humankind to learn and use written language had been present, but unexpressed, for 200,000 years prior to the first invention of written language.

One thousand years ago, less than 1% of the population of Western Europe could read. Essentially all of the population had the genetic potential to learn to read yet this potential remained untapped until the advent of universal public education.

In 1211, Frederick II, Emperor of Germany, in an attempt to discover the natural “language of God,” raised dozens of children in silence. God’s preferred language never emerged; the children never spoke any language and all ultimately died in childhood (van Cleve, 1972).

More than 200,000 years ago, the first homo sapiens sapiens, our genetic ancestors, began to spread across the planet. For 99 percent of the time our species has been on this planet, we lived in small hunter-gatherer clans. Humans lived with few material possessions, no written language, no complex world economy, advanced technologies or systems of governance. The major predator of humans was (and remains) other humans – usually from competing clans or bands. The lifespan was short, infant mortality high and the overall population of on the planet only slowly increased over tens of thousands of years. How different our Earth is today!

Only one of thousands of mammals on the planet, humankind – slow, naked and weak creatures, biologically suited to few of the Earth's many climates and ecosystems – ultimately came to dominate the planet. Humankind is now capable of living in all of the planet's climates and harsh environments. No longer bound by cold, absence of natural grains or migrating herds, the natural boundaries of sea and sky, we humans – unlike any other of the planet's species – have created our own world. We have learned to cultivate natural grains and fruits – and now alter their genome; to domesticate and now, create, other animal species; from our own genetic capacity to make complex associations, symbolic representations and 40 basic sounds we have created 10,000 languages, and invented writing; we have invented belief systems, styles of governance, housing, economies – we have invented ourselves. We have made our own world with its own rules. In good ways and in bad, we stand out from all other species. So much so that we often forget that we are ultimately accountable to the laws of nature.

Yet we *are* biological creatures, bound by the laws of nature to a time-limited existence. We are conceived and born, live our lives and then we die. From conception to death, our biological matrix organizes in remarkably complex ways to create multiple organ systems – bone and muscle, heart and liver, senses and brain. These biological systems allow each of us to move through space and time in a host of natural and, now, man-made, environments, interacting in complex ways with a diversity of biological creatures and environments. Within that single lifetime the range and variety in how we live is stunning. Genetically-comparable humans can live as Inuit in the tundra of Nunavut, a banker on Wall Street, a hunter-gatherer in the rainforest in Brazil. At times, a life is lived with grace and beauty, sharing with and caring for others, creating ideas, objects and concepts never before known on this planet. And at other times humans are cruel, ruthless and destructive – both random and systematic in the ways we destroy, hate and kill. How is this possible in the same species?

This question has been at the heart of centuries of debate on the “nature” of humankind. Are we born evil – natural born killers or the most creative and compassionate of all animals? Are we both? Does our best and our worst come from our genes or from our learning? Nature or nurture? These questions have tainted political, sociocultural and scientific processes for thousands of years. Its simplicity – suggesting that the essence of a person is the inevitable product of one or the other – genes or learning – is seductive. The human mind tends to prefer

simple linear explanations rather than complex ambiguity. Unfortunately, simple categorical explanations of humankind feed destructive belief systems and deflect from a healthy process of inquiry about our true complexity.

We now know more about our genes and more about the influence of experience on shaping biological systems than ever before. What do these advances tell us about the nature or nurture debate? Simply, they tell us that this is a foolish argument. Humans are the product of nature *and* nurture. Genes and experience are interdependent. Genes are merely chemicals and without “experience” – with no context, no microenvironmental signals to guide their activation or deactivation – create nothing. And “experiences” without a genomic matrix cannot create, regulate or replicate life of any form. The complex process of creating a human being – and humanity – requires both. The amazing malleability and adaptability of humankind is allowed by our genetically-mediated capacity to perceive and respond to myriad environmental cues including the complex social-emotional milieu created when humans live together; and the organ most sensitive and responsive to the environment is the human brain.

The Human Brain

Humankind’s transient but magnificent rebellion against nature is allowed by the brain. In ways not yet understood, activation of neural networks – chains of neurons – allow us to think, feel and act. It is our brain which allows us to laugh, cry, hope and act in humane ways. It is the brain that mediates our humanity – or not.

Yet the brain’s prime mandate is survival of the species. The human nervous system senses, processes, stores and acts on information from the inside and outside environments to promote survival of the species. Three key brain-mediated capabilities must be present for our species to survive: individual survival, procreation and the protection and nurturing of dependents. Failure in any of these three areas would lead to extinction of our species. The brain, therefore, has crucial neural systems dedicated to (1) the stress response and responding to threats – from internal and external sources; (2) the process of mate selection and reproduction and (3) protecting and nurturing dependents, primarily the young.

The primary strategy we use to meet these objectives is to create relationships. Relationships which allow us to attach, affiliate, communicate and interact to promote survival, procreation and the protection of dependents. It is the brain that allows humans to form the relationships which connect us – one to another – creating the myriad groups – that have been the key to our success on this planet. It is not as independent and solitary individuals that we succeed; it through our interdependent relationships – our families, clans, communities and societies – that we survive and thrive. We need each other. Therefore, some of the most powerful and complex neural systems in the human are dedicated to social affiliation and communication.

Yet even these essential neural systems do not develop without necessary experiences. The neural systems which allow us to create relationships – and think, feel and act – are the product of the interactive, dynamic processes taking place during the history of each individual. These neural systems, then, are created, organized and change in response to experience throughout the life-cycle. The time in life, however, when the brain is most sensitive to experience – and therefore most easy to influence in positive and negative ways is in infancy and childhood. It is during these times in life when social, emotional, cognitive and physical experiences will shape neural systems in ways that influence functioning for a lifetime. This is a time of great opportunity – and great vulnerability – for expressing the genetic potentials in a child.

Neurodevelopment

The mature human brain is comprised of 100 billion neurons and ten times as many glial cells – connected by trillions of synapses all. A complex dynamic of continuous activity, it is the product of neurodevelopment – a long process orchestrating billions upon billions of complex chemical transactions.

In a few short years, one single cell – the fertilized egg – becomes a walking, talking, learning, loving, and thinking being. In each of the billions of cells in the body, a single set of genes has been expressed in millions of different combinations with precise timing. Development is a breathtaking orchestration of precision micro-construction that results in a human being. The most complex of all the organs in the human body is the human brain. In order to create the brain, a small set of pre-cursor cells must divide, move, specialize, connect and create specialized neural networks that form functional units. This requires nature and nurture. The key role of genetics and environment are outlined for eight of the key neurodevelopmental processes involved in creating a mature, functional human brain.

MAJOR PROCESSES OF NEURODEVELOPMENT

1. Neurogenesis: The brain develops from cells present in the embryo in the first weeks following conception. From these few undifferentiated cells, come billions of nerve cells and trillions of glia. The vast majority of neurogenesis, the “birth” of neurons, takes place in utero during the second and third trimester. At birth, the vast majority of neurons used for the remainder of life are present. Few neurons are born after birth, although researchers have demonstrated recently that neurogenesis does take place in the mature brain (Gould *et al.*, 1999). Neurogenesis in the mature brain may be one of the important physiological mechanisms responsible for the brain’s plasticity (i.e., capacity to restore function) following injury.

Despite being present at birth, most neurons have yet to organize into completely functional systems. The billions of neurons present at birth need to

further specialize and connect with other neurons in order to create the functional neural networks of the mature brain.

2. Migration: As neurons are born and the brain grows, neurons move. Often guided by glial cells and a variety of chemical markers (e.g., cellular adhesion molecules, nerve growth factor: NGF), neurons cluster, sort, move and settle into a location in the brain that will be their final “resting” place. It is the fate of some neurons to settle in the brainstem, others in the cortex, for example. Cortical cell migration and fate mapping are some of the most studied processes in developmental neuroscience (Rakic, 1981, 1996). It is clear that both genetic and environmental factors play important roles in determining a neuron’s final location.

Migration takes place primarily during the intrauterine and immediate perinatal period but continues throughout childhood and, possibly, to some degree into adult life. A host of intrauterine and perinatal insults – experiences such as infection, lack of oxygen, exposure to alcohol and various psychotropic drugs can alter migration of neurons and have profound impact on the expression of genetic potentials for a host of functions (see Perry, 1988).

3. Differentiation: Neurons specialize during development. Each of the 100 billion neurons in the brain has the same set of genes, yet each neuron is expressing a unique combination of those genes to create a unique neurochemistry, neuroarchitecture and functional capability. Some neurons are large, with long axons; others short. Neurons can mature to use any of a hundred different neurotransmitters such as norepinephrine, dopamine, serotonin, CRF or substance P. Neurons can have dense dendritic fields receiving input from hundreds of other neurons, while other neurons can have a single linear input from one other neuron. Each of these thousands of differentiating “choices” are the product of the pattern, intensity and timing of various microenvironmental cues, i.e., experience, which tell the neuron to turn on some genes and turn off others. Each neuron undergoes a series of “decisions” to determine their final location and specialization. These decisions, again, are a combination of genetic and microenvironmental cues. Neurons are specialized to change in response to chemical signals. Therefore, any experience or event that alters neurochemical or micro-environmental signals during development can change the ways in which certain neurons differentiate, thereby altering the functional capacity of the neural networks in which these neurons reside (e.g., Rutledge *et al.*, 1974).

4. Apoptosis: During development, redundant or under-activated neurons die. In many areas of the brain, there are more neurons born than are required to make a functional system. Many of these neurons are redundant and when unable to adequately “connect” into an active neural network will die (Kuan *et al.*, 2000). Research in this area suggests that these neurons may play a role in the remarkable flexibility present in the human brain at birth. Depending upon the challenges of the

environment and the potential needs of the individual, some neurons will survive while others will not. Again, this process appears to have genetic *and* environmental determinants. Neurons that make synaptic connections with others and have an adequate level of activation will survive; neurons with little activity resorb. This is one example of a general principle of activity-dependence (“use it or lose it”) that appears to be important in many neural processes related to learning, memory and development (see below).

5. *Arborization*: As neurons differentiate, they send out one form of fiber-like processes called dendrites. Dendrites become the receptive area where other neurons connect. Dozens to hundreds of other neurons are able to connect to one neuron via this dendritic tree. The density of these dendritic branches is related to the frequency and intensity of incoming signals. When there is high activity, the dendritic network extends. This arborization allows the neuron to receive, process and integrate complex patterns of input that, in turn, influence its activity – including the activity and specificity of gene transcription. In turn, the neural signals coming into any give neuron are often dependent upon the complexity and activity of the sensory experiences of the animal (Diamond *et al.*, 1966; Greenough *et al.*, 1973). Dendritic density appears to be one of the most experience-sensitive physical features of a neuron.

6. *Synaptogenesis*: The most experience-sensitive feature of a neuron is, however, the synapse. Developing neurons also send out fiber-like processes which become axons and synapses. The major mechanism for neuron-to-neuron communication is ‘receptor-mediated’ neurotransmission that takes place at specialized connections between neurons called synapses. At the synapse, the distance between two neurons is very short. A chemical (classified as a neurotransmitter, neuromodulator or neurohormone) is released from the ‘presynaptic’ neuron into the extra-cellular space (called the synaptic cleft). The neurotransmitter crosses the synaptic cleft and binds to a specialized receptor protein in the membrane of the ‘postsynaptic’ neuron. By occupying the binding site, the neurotransmitter helps change the shape of this receptor which results in a cascade of catalyzed chemical reactions mediated by “second messengers” such as cyclic AMP, inositol phosphate and calcium. In turn, these chemicals shift the intracellular chemical milieu which will influence the activity of specific genes. This cascade of intracellular chemical responses allows communication from one neuron to another.

A continuous dynamic of synaptic neurotransmission regulates the activity and functional properties of the chains of neurons that allow the brain to do all of its remarkable activities. These neural connections are not random. They are guided by important genetic and environmental cues. In order for our brain to function properly, neurons, during development, need to find and connect with the “right” neurons. During the differentiation process, neurons send fiber-like projections (growth cones) out to make physical contact with other neurons. This process

appears to be regulated and guided by certain growth factors and cellular adhesion molecules that attract or repel a specific growth cone to appropriate target neurons. Depending upon a given neuron's specialization, these growth cones will grow (becoming axons) and connect to the dendrites of other cells and create a synapse. During the first eight months of life there is an eight-fold increase in synaptic density while the developing neurons in the brain are "seeking" their appropriate connections (Huttenlocher, 1979, 1994). This explosion of synaptogenesis allows the brain to have the flexibility to organize and function with a wide range of potential. It is over the next few years, in response to patterned repetitive experiences that these neural connections will be refined and sculpted.

7. Synaptic sculpting: The synapse is a dynamic structure. With continuous, but episodic release of neurotransmitter, occupation of receptors, release of growth factors, shifts of ions in and out of cells, laying down of new microtubules and other structural molecules, the synapse is continually changing. A key determinant in this synaptic sculpting process is the level of pre-synaptic activity. When there is a consistent active process of neurotransmitter release, synaptic connections will be strengthened with actual physical changes that make the pre- and post-synaptic neurons grow closer together, making neurotransmission between these two neurons more efficient.

When there is little activity, the synaptic connection will literally dissolve. The specific axonal branch to a given neuron will go away. While somewhat simplistic, it appears that synaptic sculpting is a "use it or lose it" process (see below). This powerful activity-dependent process appears to be the molecular basis of learning, memory and, therefore, at the core of neurodevelopment.

8. Myelination: Specialized glial cells wrap around axons and, thereby, create more efficient electrochemical transduction down the neuron. This allows a neural network to function more rapidly and efficiently, thereby allowing more complex functioning (e.g., walking depends upon the myelination of neurons in the spinal cord for efficient, smooth regulation of neuromotor functioning.) The process of myelination begins in the first year of life but continues in many key areas throughout childhood with a final burst of myelination in key cortical areas taking place in adolescence.

The eight key neurodevelopmental processes described above are dependent upon the genome and environmentally-determined microenvironmental cues (e.g., neurotransmitters, neuromodulators, neurohormones, ions, growth factors, cellular adhesion molecules and other morphogens). Disruption of the pattern, timing or intensity of these cues can lead to abnormal neurodevelopment and profound dysfunction. The *specific* dysfunction will depend upon the timing of the insult (e.g., was the insult *in utero* during the development of the brainstem or at age two during the active development of the cortex), the nature of the insult (e.g., is there a lack of sensory stimulation from neglect or an abnormal persisting activation of

the stress response from trauma?), the pattern of the insult (i.e., is this a discreet single event, a chronic experience with a chaotic pattern or an episodic event with a regular pattern?) (see Perry, 2001a).

Several key principles emerge from the research on these neurodevelopmental processes. These principles, as outlined below, further suggest that while the structural organization and functional capabilities of the mature brain can change throughout life, the majority of the key stages of neurodevelopment take place in childhood.

CORE PRINCIPLES OF NEURODEVELOPMENT

1. Genetic and environmental influences: Genes are designed to work in an environment. Genes are expressed by microenvironmental cues, which, in turn, are influenced by the experiences of the individual. How an individual functions within an environment, then, is dependent upon the expression of a unique combination of genes available to the human species. We don't have the genes to make wings. *And* what we become depends upon how experiences shape the expression – or not – of specific genes we *do* have. For thousands of years, the genetic potential to use “joysticks” was not expressed – nor that for written language or reading. Yet when experiences are provided in a structured, patterned and appropriately timed way, that potential can be expressed and neural systems which mediate all of those functions will develop.

The influence of gene-driven processes, however, shifts during development. In the just fertilized ovum, all of the chemical processes that are driving development are very dependent upon a genetically-determined sequence of molecular events. By birth, however, the brain has developed to the point where environmental cues mediated by the senses play a major role in determining how neurons will differentiate, sprout dendrites, form and maintain synaptic connections and create the final neural networks that convey functionality. By adolescence, the majority of the changes that are taking place in the brain of that child are determined by experience, not genetics. The languages, beliefs, cultural practices, and complex cognitive and emotional functioning (e.g., self esteem) by this age are primarily experience-based.

2. Sequential developmental: The brain develops in a sequential and hierarchical fashion; organizing itself from least (brainstem) to most complex (limbic, cortical areas). These different areas develop, organize and become fully functional at different times during childhood. At birth, for example, the brainstem areas responsible for regulating cardiovascular and respiratory function must be intact for the infant to survive, and any malfunction is immediately observable. In contrast, the cortical areas responsible for abstract cognition have years before they will be ‘needed’ or fully functional.

This means that each brain area will have its own timetable for development. The neurodevelopmental processes described above will be most active in different brain areas at different times and will, therefore, either require (critical periods) or be sensitive to (sensitive periods) organizing experiences (and the neurotrophic cues related to these experiences). The neurons for the brainstem have to migrate, differentiate and connect, for example, before the neurons for the cortex.

The implications of this are profound. In the development of socio-emotional functioning, early life nurturing appears to be critical. If this is absent for the first three years of life and then a child is adopted and begins to receive attention, love and nurturing, these positive experiences may not be sufficient to overcome the malorganization of the neural systems mediating socio-emotional functioning. Disruptions of experience-dependent neurochemical signals during early life may lead to major abnormalities or deficits in neurodevelopment. Disruption of critical neurodevelopmental cues can result from (1) lack of sensory experience during sensitive periods (e.g., neglect) or (2) atypical or abnormal patterns of necessary cues due to extremes of experience (e.g., traumatic stress, see Perry, 2001a).

3. Activity-dependent neurodevelopment: The brain organizes in a use-dependent fashion. As described above, many of the key processes in neurodevelopment are activity dependent. In the developing brain, undifferentiated neural systems are critically dependent upon sets of environmental and micro-environmental cues (e.g., neurotransmitters, cellular adhesion molecules, neurohormones, amino acids, ions) in order for them to appropriately organize from their undifferentiated, immature forms (Lauder, 1988; Perry, 1994b; Perry and Pollard, 1998). Lack, or disruption, of these critical cues can alter the neurodevelopmental processes of neurogenesis, migration, differentiation, synaptogenesis – all of which can contribute to malorganization and diminished functional capabilities in the specific neural system where development has been disrupted. This is the core of a neuroarcheological perspective on dysfunction related adverse childhood events (Perry, 2001b). These molecular cues that guide development are dependent upon the experiences of the developing child. The quantity, pattern of activity and nature of these neurochemical and neurotrophic factors depends upon the presence and the nature of the total sensory experience of the child. When the child has adverse experiences – loss, threat, neglect, and injury – there can be disruptions of neurodevelopment that will result in neural organization that can lead to compromised functioning throughout life (see below).

4. Windows of opportunity/windows of vulnerability: The sequential development of the brain and the activity-dependence of many key aspects of neurodevelopment suggest that there must be times during development when a given developing neural system is more sensitive to experience than others. In healthy development, that sensitivity allows the brain to rapidly and efficiently organize in response to the unique demands of a given environment to express from its broad genetic

potential those characteristics which best fit that child's world. If the child speaks Japanese as opposed to English, for example, or if this child will live in the plains of Africa or the tundra of the Yukon, different genes can be expressed, different neural networks can be organized from that child's potential to best fit that family, culture and environment. We all are aware of how rapidly young children can learn language, develop new behaviors and master new tasks. The very same neurodevelopmental sensitivity that allows amazing developmental advances in response to predictable, nurturing, repetitive and enriching experiences make the developing child vulnerable to adverse experiences.

Sensitive periods are different for each brain area and neural system, and therefore, for different functions. The sequential development of the brain and the sequential unfolding of the genetic map for development mean that the sensitive periods for neural system (and the functions they mediate) will be when that system is in the developmental 'hot zone' – when that area is most actively organizing. The brainstem must organize key systems by birth; therefore, the sensitive period for those brainstem-mediated functions is during the prenatal period. The neocortex, in contrast, has systems and functions organizing throughout childhood and into adult life. The sensitive periods for these cortically mediated functions are likely to be very long.

The simple and unavoidable conclusion of these neurodevelopmental principles is that the organizing, sensitive brain of an infant or young child is more malleable to experience than a mature brain. While experience may alter the behavior of an adult, experience literally provides the organizing framework for an infant and child. Because the brain is most plastic (receptive to environmental input) in early childhood, the child is most vulnerable to variance of experience during this time.

Two forms of "neglect" will be considered below: extreme multi-sensory neglect in childhood and a more subtle, insidious decrease in our opportunities to elaborate our socio-emotional potential caused by the sociocultural changes in how we choose to live. The sensory deprivation neglect results in obvious alterations in neurobiology and function while the second form has an almost invisible toxic impact on the developing child – and ultimately, society.

The Neurodevelopmental Impact of Neglect in Childhood

Neglect is the absence of critical organizing experiences at key times during development. Despite its obvious importance in understanding child maltreatment, neglect has been understudied. Indeed, deprivation of critical experiences during development may be the most destructive yet the least understood area of child maltreatment. There are several reasons for this. The most obvious is that neglect is difficult to "see." Unlike a broken bone, maldevelopment of neural systems mediating empathy, for example, resulting from emotional neglect during infancy is not readily observable.

Another important, yet poorly appreciated, aspect of neglect is the issue of timing. The needs of the child shift during development; therefore, what may be neglectful at one age is not at another. The very same experience that is essential for life at one stage of life may be of little significance or even inappropriate at another age. We would all question the mother who held, rocked and breastfed her pubescent child. Touch, for example, is essential during infancy. The untouched newborn may literally die; in Spitz' landmark studies, the mortality rates in the institutionalized infants was near thirty percent (Spitz, 1945, 1946). If one doesn't touch an adolescent for weeks, however, no significant adverse effects will result. Creating standardized protocols, procedures and "measures" of neglect, therefore, are significantly confounded by the shifting developmental needs and demands of childhood. Finally, neglect is understudied because it is very difficult to find large populations of humans where specific and controlled neglectful experiences have been well documented. In some cases, these cruel experiments of humanity have provided unique and promising insights (see below). In general, however, there will never be – and there never should be – the opportunity to study neglect in humans with the rigor that can be applied in animal models.

With these limitations, however, what we do know about neglect during early childhood supports a neuroarcheological view of adverse childhood experience. The earlier and more pervasive the neglect is, the more devastating the developmental problems for the child. Indeed, chaotic, inattentive and ignorant caregiving can produce pervasive developmental delay (PDD; DSM IV-R) in a young child (Rutter *et al.*, 1999). Yet the very same inattention for the same duration if the child is ten will have very different and less severe impact than inattention during the first years of life.

There are two main sources of insight to childhood neglect. The first is the indirect but more rigorous animal studies and the second is a growing number of descriptive reports with severely neglected children.

Environmental Manipulation and Neurodevelopment: Animal Studies

Some of the most important studies in developmental neurosciences in the last century have been focusing on various aspects of experience and extreme sensory experience models. Indeed, the Nobel Prize was awarded to Hubel and Wiesel for their landmark studies on development of the visual system using sensory deprivation techniques (Hubel and Wiesel, 1963). In hundreds of other studies, extremes of sensory deprivation (Hubel and Wiesel, 1970; Greenough *et al.*, 1973) or sensory enrichment (Greenough and Volkmar, 1973; Diamond *et al.*, 1964; Diamond *et al.*, 1966) have been studied. These include disruptions of visual stimuli (Coleman and Riesen, 1968), environmental enrichment (Altman and Das, 1964; Cummins and Livesey, 1979), touch (Ebinger, 1974; Rutledge *et al.*, 1974), and other factors that alter the typical experiences of development (Uno *et al.*, 1989; Plotsky and Meaney, 1993; Meaney *et al.*, 1988). These findings generally demonstrate that the brains of

animals reared in enriched environments are larger, more complex and functional more flexible than those raised under deprivation conditions. Diamond's work, for example, examining the relationships between experience and brain cytoarchitecture have demonstrated a relationship between density of dendritic branching and the complexity of an environment (for a good review of this and related data see (Diamond and Hopson, 1998)). Others have shown that rats raised in environmentally enriched environments have higher density of various neuronal and glial microstructures, including a 30% higher synaptic density in cortex compared to rats raised in an environmentally deprived setting (Altman and Das, 1964; Bennett *et al.*, 1964). Animals raised in the wild have from 15 to 30% larger brain mass than their offspring who are domestically reared (Darwin, 1868; Rehkamper *et al.*, 1988; Rohrs, 1955; Rohrs and Ebinger, 1978).

Animal studies suggest that critical periods exist during which specific sensory experience was required for optimal organization and development of the part of the brain mediating a specific function (e.g., visual input during the development of the visual cortex). While these phenomena have been examined in great detail for the primary sensory modalities in animals, few studies have examined the issues of critical or sensitive periods in humans. What evidence there is would suggest that humans tend to have longer periods of sensitivity and that the concept of critical period may not be useful in humans. It is plausible, however, that abnormal micro-environmental cues and atypical patterns of neural activity during sensitive periods in humans could result in malorganization and compromised function in a host of brain-mediated functions. Indeed, altered emotional, behavioral, cognitive, social and physical functioning has been demonstrated in humans following specific types of neglect. The majority of this information comes from the clinical rather than the experimental disciplines.

THE IMPACT OF NEGLECT IN EARLY CHILDHOOD: CLINICAL FINDINGS

Over the last sixty years, many case reports, case series and descriptive studies have been conducted with children neglected in early childhood. The majority of these studies have focused on institutionalized children. As early as 1833, with the famous Kaspar Hauser, feral children had been described (Heidenreich, 1834). Hauser was abandoned as a young child and raised from early childhood (likely around age two) until seventeen in a dungeon, experiencing relative sensory, emotional and cognitive neglect. His emotional, behavioral and cognitive functioning was, as one might expect, very primitive and delayed.

In the early forties, Spitz described the impact of neglectful caregiving on children in foundling homes (orphanages). Most significant, he was able to demonstrate that children raised in fostered placements with more attentive and nurturing caregiving had superior physical, emotional and cognitive outcomes (Spitz, 1945, 1946). Some of the most powerful clinical examples of this phenomenon are related to profound neglect experiences early in life.

In a landmark report of children raised in a Lebanese orphanage, the Creche, Dennis (1973) described a series of findings supporting a neuroarcheological model of maltreatment. These children were raised in an institutional environment devoid of individual attention, cognitive stimulation, emotional affection or other enrichment. Prior to 1956 all of these children remained at the orphanage until age six, at which time they were transferred to another institution. Evaluation of these children at age 16 demonstrated a mean IQ of approximately 50. When adoption became common, children adopted prior to age 2 had a mean IQ of 100 by adolescence while children adopted between ages 2 and 6 had IQ values of approximately 80 (Dennis, 1973). This graded recovery reflected the neuroarcheological impact of neglect. A number of similar studies of children adopted from neglectful settings demonstrate this general principle. The older a child was at time of adoption, (i.e., the longer the child spent in the neglectful environment) the more pervasive and resistant to recovery were the deficits.

Money and Annecillo (1976) reported the impact of change in placement on children with psychosocial dwarfism (failure to thrive). In this preliminary study, 12 of 16 children removed from neglectful homes recorded remarkable increases in IQ and other aspects of emotional and behavioral functioning. Furthermore, they reported that the longer the child was out of the abusive home the higher the increase in IQ. In some cases IQ increased by 55 points (Money and Annecillo, 1976).

A more recent report on a group of 111 Romanian orphans (Rutter *et al.*, 1998; Rutter *et al.*, 1999) adopted prior to age two from very emotionally and physically depriving institutional settings demonstrate similar findings. Approximately one half of the children were adopted prior to age six months and the other half between six months and 2 years old. At the time of adoption, these children had significant delays. Four years after being placed in stable and enriching environments, these children were re-evaluated. While both groups improved, the group adopted at a younger age had a significantly greater improvement in all domains. As a group, these children were at much greater risk for meeting diagnostic criterion for autism-spectrum disorder, a finding that sheds light on the evolving relationships between early life trauma, neglect and subsequent development of severe neuropsychiatric problems including psychotic disorders and schizophrenia (Read *et al.*, 2001).

These observations are consistent with the clinical experiences of the ChildTrauma Academy working with maltreated children for the last fifteen years. During this time we have worked with more than 1000 children neglected in some fashion. We have recorded increases in IQ of over 40 points in more than 60 children following removal from neglectful environments and placed in consistent, predictable, nurturing, safe and enriching placements (Perry *et al.*, in preparation). In addition, in a study of more than 200 children under the age of 6 removed from parental care following abuse and neglect we demonstrated significant developmental delays in more than 85% of the children. The severity of these developmental problems increased with age, suggesting, again, that the longer the

child was in the adverse environment – the earlier and more pervasive the neglect – the more indelible and pervasive the deficits.

NEGLECT IN EARLY CHILDHOOD: NEUROBIOLOGICAL FINDINGS

All of these reported developmental problems – language, fine and large motor delays, impulsivity, disorganized attachment, dysphoria, attention and hyperactivity, and a host of others described in these neglected children – are caused by abnormalities in the brain. Despite this obvious statement, very few studies have examined directly any aspect of neurobiology in neglected children. Yet clues exist. On autopsy, the brain of Kasper Hauser was notable for small cortical size and few, non-distinct cortical gyri – all consistent with cortical atrophy (Simon, 1978).

Our group has examined various aspects of neurodevelopment in neglected children (Perry and Pollard, 1997). Neglect was considered global neglect when a history of relative sensory deprivation in more than one domain was obtained (e.g., minimal exposure to language, touch and social interactions). Chaotic neglect is far more common and was considered present if history was obtained that was consistent with physical, emotional, social or cognitive neglect. History was obtained from multiple sources (e.g., investigating CPS workers, family, and police). The neglected children (n = 122) were divided into four groups: Global Neglect (GN; n = 40); Global Neglect with Prenatal Drug Exposure (GN+PND; n = 18); Chaotic Neglect (CN; n = 36); Chaotic Neglect with Prenatal Drug Exposure (CN+PND; n = 28). Measures of growth were compared across group and compared to standard norms developed and used in all major pediatric settings.

Dramatic differences from the norm were observed in FOC (the frontal-occipital circumference, a measure of head size and in young children a reasonable measure of brain size). In the globally neglected children the lower FOC values suggested abnormal brain growth. For these globally neglected children the group mean was below the 5th percentile. In contrast, the chaotically neglected children did not demonstrate this marked group difference in FOC. Furthermore in cases where MRI or CT scans were available, neuroradiologists interpreted 11 of 17 scans as abnormal from the children with global neglect (64.7%) and only 3 of 26 scans abnormal from the children with chaotic neglect (11.5%). The majority of the readings were “enlarged ventricles” or “cortical atrophy” (see Figure 1).

In following these globally-neglected children over time we observed some recovery of function and relative brain-size when these children were removed from the neglectful environment and placed in foster care (see Figure 2). The degree of recovery over a year period however was inversely proportional to age in which the child was removed from the neglecting caregivers. The earlier in life and the less time in the sensory-depriving environment, the more robust the recovery.

These findings strongly suggest that when early life neglect is characterized by decreased sensory input (e.g., relative poverty of words, touch and social interactions) there will be a similar effect on human brain growth as in other mammalian

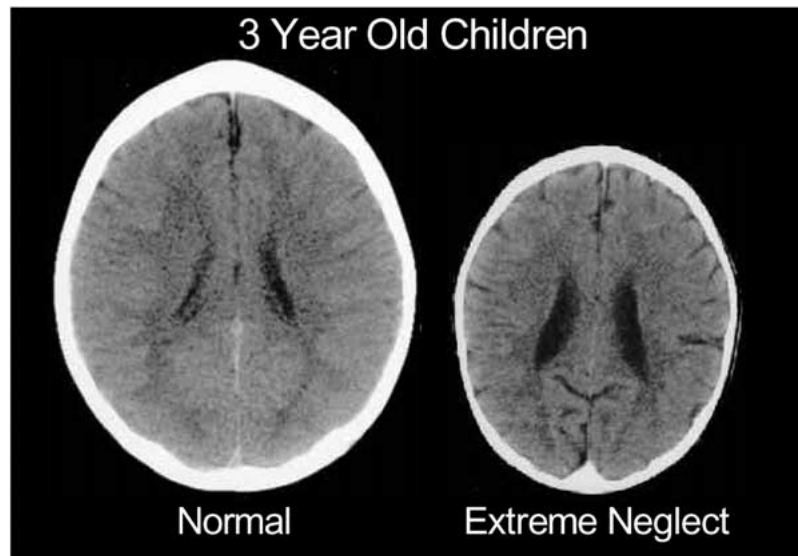


Figure 1. Abnormal brain development following sensory neglect in early childhood. These images illustrate the negative impact of neglect on the developing brain. In the CT scan on the left is an image from a healthy three year old with an average head size (50th percentile). The image on the right is from a three year old child suffering from severe sensory-deprivation neglect. This child's brain is significantly smaller than average (3rd percentile) and has enlarged ventricles and cortical atrophy.

species. The human cortex grows in size, develops complexity, makes synaptic connections and modifies as a function of the quality and quantity of sensory experience. Sensory-motor and cognitive deprivation leads to underdevelopment of the cortex in rats, non-human primates and humans.

Studies from other groups are beginning to report similar altered neurodevelopment in neglected children. In the study of Romanian orphans described above, the 38% had FOC values below the third percentile (greater than 2 SD from the norm) at the time of adoption. In the group adopted after six months, fewer than 3% and the group adopted after six months 13% had persistently low FOCs four years later (Rutter *et al.*, 1998; O'Connor *et al.*, 2000). Strathearn (submitted) has followed extremely low birth weight infants and shown that when these infants end up in neglectful homes they have a significantly smaller head circumference at 2 and 4 years, but not at birth. This is despite having no significant difference in other growth parameters.

More recently advanced neuroimaging techniques have demonstrated altered brain development in neglected children. Chugani and colleagues have been pioneers in neuroimaging studies in maltreated children. Their most recent study using functional MRI in Romanian orphans has demonstrated decreased metabolic activity in the orbital frontal gyrus, the infralimbic prefrontal cortex, the amygdala

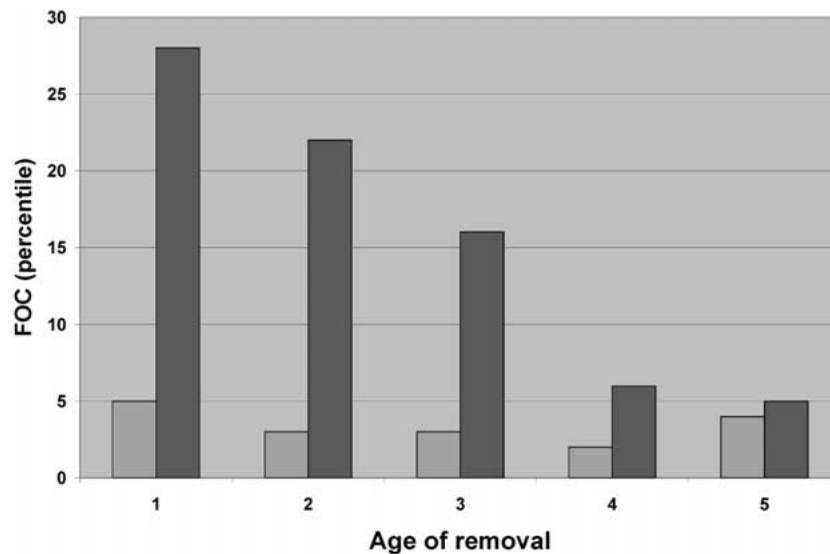


Figure 2. Sensory deprivation neglect: effects of early removal on recovery. Children were removed from neglectful environments at different ages (ages 8 months to 5.7 years). Their frontal-occipital circumference was measured and compared to same-aged norms (blue bars). Children were placed in foster care and one year later re-evaluated. FOC was measured (maroon bars) and in each group increased although with increasing age, the improvement after a year of foster placement started to decrease such that children removed after four years in the neglectful setting had no statistically-significant improvement one year later. Data are from 112 children with some form of severe neglect in the first five years of life (modified from Perry and Pollard, 1997).

and head of the hippocampus, the lateral temporal cortex and in the brainstem (Chugani *et al.*, 2001). Together these findings suggest a global set of abnormalities matched by the functional abnormalities in cognitive, emotional, behavioral and social functioning.

EMOTIONAL NEGLECT IN EARLY CHILDHOOD: THE UNDER-EXPRESSION OF SOCIO-EMOTIONAL POTENTIAL

Clinical attention has been focused on extremes of neglect. The obvious clinical syndromes which result from pervasive neglect have facilitated research in this area. More recently, however, many researchers have observed and studied abnormalities in the capacity of children – and adults – to form healthy relationships. An emerging area of study is focusing on “attachment” – a special form of emotional bond. While usually not framed in context of developmental neglect, attachment problems in children often are the result of mistimed, abnormal or absent care-giving interactions and, therefore, may represent a special case of neglect. As with other brain-mediated capabilities, the capacity to form relationships results from

the experience-based expression of an underlying genetic potential to create the neural systems mediating socio-emotional behaviors.

At birth an infant has yet to form a true relational bond with another person. In most instances, the infant will be cared for by an attentive, attuned and loving caregiver. When this happens, a caregiver will, again and again, come to the hungry or cold or scared infant. Warming, soothing, feeding, cleaning and calming the infant, the caregiver creates a set of specific sensory stimuli which are translated into specific neural activations in areas of the developing brain destined to become responsible for socio-emotional communication and bonding. The somatosensory bath – the smells, sights, sounds, tastes and touch – of the loving caregiver provides the repetitive sensory cues necessary to express the genetic potential in this infant to form and maintain healthy relationships. This first and most primary of all relationships is this attachment bond.

The attachment bond has several key elements: (1) an attachment bond is an enduring emotional relationship with a specific person; (2) the relationship brings safety, comfort, soothing and pleasure; (3) loss or threat of loss of the person evokes intense distress. This special form of relationship is best characterized by the maternal-child relationship. The maternal-child attachment provides the working framework for all subsequent relationships that the child will develop. A solid and healthy attachment with a primary caregiver appears to be associated with a high probability of healthy relationships with others while poor attachment with the mother or primary caregiver appears to be associated with a host of emotional and behavioral problems later in life. More than 85% of children removed from their parents for abuse or neglect have disturbed attachment capacity, for example (Carlson *et al.*, 1989). The relationships between disordered attachment and increased risk for violent and aggressive behaviors are well documented (see Perry, 2001a).

THE MODERN WORLD AND NEGLECT OF SOCIO-EMOTIONAL GROWTH

Healthy attachment capacity is not enough to create healthy socio-emotional functioning. Attachment is only one form of the many kinds of relationships we form to create a healthy productive life. Certainly a securely attached child will have an easier time forming friendships, relationships with teachers, coaches, siblings and, over time, in the work place and larger community. As the brain organizes and develops in response to patterned, repetitive experience, the nature, timing, intensity and quality of an array of other relationships in the developing child's life will make a difference in the development of complex socio-emotional development. Yet without the opportunities to have friends, teachers, coaches, grandparents, neighbors, team mates and the many other kinds of relationships of childhood, these capabilities remain unexpressed. And if a child starts with attachment problems and has few opportunities to develop other relationships, they will have very poor or even pathological socio-emotional functioning.

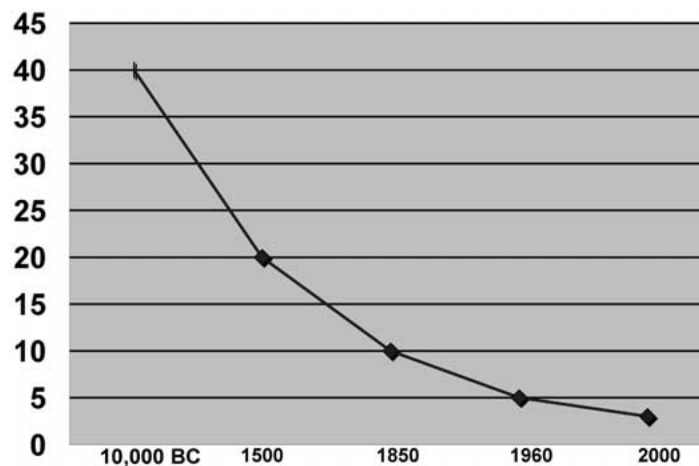


Figure 3. Decrease of number of persons living in a “household” in Western societies: From hunter-gatherer to the modern era. For more than 90 percent of human history we have lived in bands, clans or extended families of roughly 40 persons. In the West, by 1500 the average household had decreased to 20 persons; by 1850 to ten; in the United States to less than three persons in the average American household by 2000.

Our brain evolved over hundreds of thousands of generations in hominid and pre-hominid social groups. In these small hunter-gatherer bands a complex interactive dynamic socio-emotional environment provided the experiences for the developing child. At equilibrium in a group of fifty, there were three or more adult caregiving adults for every dependent child under age six. And there was little privacy. A dependent child grew up in the presence of the elderly, siblings, adults – related and not. There was a more continuous exposure and wider variety of socio-emotional interactions. The child in this situation had many opportunities to form relationships and, in a use-dependent way, develop the capacity to have a rich array of relationships. The genetic potential for healthy socio-emotional functioning – to be empathic, to share, to invest in the welfare of the community – is better expressed in children living in hunter-gatherer bands or extended families or close-knit communities in comparison with our compartmentalized modern world.

In this modern era, we separate from each other in many ways. The number of people we live with has shrunk (Figure 3); fewer than three people live in the average American household. And in our own homes, we have our own rooms. We rarely eat family meals. We spend thirty percent of our available time watching television – certainly not allowing for any use-dependent expression of an underlying genetic capacity for socio-emotional functioning. Our children are segregated with same age children for hours a day. In healthy homes the time a parent spends with older children is counted in minutes. We think a healthy ratio of adult caregiver to dependent child in our child care settings is one adult for five children – 1/16th the

ratio in a hunter-gatherer clan. We have over-scheduled our children and they have little time for spontaneous social play with peers.

The inadvertent effect of our modern advancements in lifestyle, communications, technology and economies is that we are now raising children in environments that are very different from the rich social context for which our brains are most suited. The effects of television and other electronic activities have significantly exacerbated this. Taking huge portions of the available day away from socio-emotional or other “human” activities, television ensures that new – and non-social – neural systems are being activated in comparison with humans raised one hundred years ago. The implications of this have yet to be fully understood although some indications suggest that we are losing “social capital.” One indicator of this is the percentage of individuals who volunteer and vote. From 1972 to 2000, the percentage of young adults (age 18–24) voting in the Presidential election fell from 47% in 1972 to 27% in 1996 to 23% in 2000!

Summary and Future Directions

The many functions of the human brain result from a complex interplay between genetic potential and appropriately timed experiences. The neural systems responsible for mediating our cognitive, emotional, social and physiological functioning develop in childhood and, therefore, childhood experiences play a major role in shaping the functional capacity of these systems. When the necessary experiences are not provided at the optimal times, these neural systems do not develop in optimal ways.

Healthy development of the neural systems which allow optimal social and emotional functioning depends upon attentive, nurturing caregiving in infancy *and* opportunities to form and maintain a diversity of relationships with other children and adults throughout childhood. In our modern world, we are more mobile, compartmentalized and socially-disconnected. The true costs of our lifestyle choices may be difficult to see; yet an understanding of neurodevelopment suggests that the modern world’s socio-emotional milieu is not sufficient for most children to express their true potential for forming and maintaining healthy relationships.

As a society, we value cognitive development and, therefore, provide consistent, repetitive and enriching cognitive experiences in the home and through our educational systems. In an age where more people must share increasingly limited resources, however, it is imperative that our children develop the capacity to share, be empathic and understanding of others. We must provide an investment in socio-emotional development comparable to our investment in cognitive development. The world, natural and manmade, now more than ever, needs the best of humankind.

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