

# **CHANGE AND CONTINUITY IN NEUROBEHAVIORAL DEVELOPMENT: LESSONS FROM THE STUDY OF NEUROBIOLOGY AND NEURAL PLASTICITY**

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The goal of this paper is to discuss our current understanding of change and continuity in neurobehavioral development. After describing the basic elements of neurobiological development, attention is focused on the myriad of ways experience influences the developing and developed brain. This literature is used to illustrate the complexity of both brain and behavioral development in the context of change and continuity. The implications of considering brain/behavior relations in the context of development comprise the final section of the paper.

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brain neural plasticity development cognition stress early experience

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## **INTRODUCTION**

My goal in writing this paper is to discuss change and continuity in neurobehavioral development. Although a great deal is known about neural development and behavioral development, the task of discussing change and continuity at the interface of these domains is challenging. For example, although few would dispute the claim that behavior represents the

ultimate instantiation of a neural process, it is also true that inferring neural processes solely from behavior is problematic, particularly early in life. That this is so is primarily due to the difficulty in mapping behavioral change onto underlying neurobiological change. For example, because the behavioral repertoire of the infant is limited, it is difficult to relate specific behaviors to the numerous changes occurring simultaneously in neurobiological

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systems. Moreover, a given neurobiological change (e.g., synapses per unit area in a given region of cortex) can presumably be related to countless different behaviors. As a result of this complexity, it will prove daunting to match the growth curves of neurobiological change to that of behavioral change, and to accurately identify continuities and discontinuities in development.

The approach I have elected to adopt in considering continuity and discontinuity in neurobehavioral development is to begin by examining the literature on basic neurobiological development. From this review, I hope to make clear that the events that transpire during the pre- and immediate postnatal periods represent a time of rapid change, and that vary in their dependence on experience for their growth and elaboration. This theme of experience-independent vs. dependent development—is continued in the next section, where I specifically consider the role of experience in influencing subsequent development. I conclude by drawing on the emerging literature in developmental cognitive neuroscience in order to demonstrate how one can couple changes at the neurobiological level with those at the behavioral level.

### ***Background to the Problem of Change and Continuity***

There is much in the field of developmental psychology that tells us that the first years of postnatal life represent a period of rapid change, and a critical period for subsequent development. With regard to the former, we know that vast aspects of perceptual development run their course in the first 1–2 years (see Slater, 1998), with key aspects of language development occurring on a similar albeit slightly elongated time frame (see Bloom, 1998). A similar developmental course (extending, perhaps, through the preschool years) appears to apply to emotional development (see Cicchetti, 1998; Hofer, 1998; Lewis, 1992). Paradoxically, there is work from the

neurosciences that suggests that the brain has the potential to be modified for much of the life span, not just the first few years (Nelson, 1999; Nelson & Bloom, 1997); further, in some instances, there are key aspects of brain development, such as the formation of synapses, that extend over at least the first 1–2 decades of life (Huttenlocher, 1994). How, then, can we reconcile these two views of development?

One way to do so is by carefully considering the literature on neural development, and examining those aspects of development that run their course relatively early in development vs. those that have an extended developmental trajectory. As we shall see below, much of the brain is assembled before birth, without benefit of experience; however, once the infant is born and the brain is exposed to experience, it becomes difficult to identify aspects of neural development that *do not* depend on experience. To further complicate matters, among those domains of behavior that depend on experience, some do so within a relatively narrow window (i.e., there is a sensitive or critical period) whereas others remain relatively open to experience throughout much of the lifespan. Examples from each domain will be discussed in turn.

### ***A PRIMER ON NEUROBIOLOGICAL DEVELOPMENT***

In general, the development of the brain has an enormously long trajectory, beginning within a few weeks after conception, and, at the cellular level, continuing through adolescence. As a rule, there are 4 stages of development:

- A. Induction of the neural tube
- B. Proliferation and generation of specific classes of neurons
- C. Migration of cells to characteristic positions
- D. Differentiation of cells and development of connections.

## Neural Induction (Neurulation)

As students of embryology are well aware, the initial blastocyst that is formed within days of conception undergoes an expansion that results in the formation of two layers. The outer layer will become the support structures for the embryo, such as the umbilical cord, placenta, and amniotic sac, whereas the inner layer becomes the embryo itself. Once the embryo itself has formed, a rapid process of differentiation occurs. Thus, three separate layers are formed, and it is the outermost layer, or *ectoderm*, that initially gives rise to the neural tube and eventually the nervous system. As the sheet of epithelial cells that lines the ectoderm begins to multiply, a neural plate forms. Shortly thereafter, a groove begins to form within the plate, following a longitudinal axis. This groove gradually begins to deepen and fold over onto itself, eventually forming a tube. The tube begins to close on the 18th day of gestation, and is completely closed by the 24th day. Assuming the tube closes normally (an error in neural tube closure is referred to as a *neural tube defect*), the rostral (top) end of the tube will go on to become the cortex, whereas the rest of the tube will become the spinal cord.

It is important to note that not all cells are trapped inside the neural tube. Thus, cells trapped between ectodermal wall and the neural tube are called *neural crest* cells, and give rise to the autonomic nervous system. This zone of cells will extend downwards along an axis *outside* of the neural tube. The cells on each side of this axis migrate to the dorsolateral side of the neural tube. These cells will eventually give rise to the *sensory ganglia* and several of the cranial nerves.

## Proliferation

Once the neural tube is completely formed, the layer of *epithelial* cells that line the tube continue to divide and multiply, and form a pseudostratified epithelium. These cells are

initially connected to each other. As mitosis continues, this layer thickens, gradually forming two zones: the *ventricular* zone of mitotic cells and a *marginal* zone of the cellular processes. As proliferation continues and migration (see below) begins, an *intermediate* zone of neurons forms. By 8 to 10 weeks, the intermediate zone has enlarged to form the region from which the cerebral cortex develops. This region is composed of two zones: the *cortical plate* and the *subventricular* zone. This subventricular zone is really a secondary zone that some think is responsible for the development of glia (the other major class of brain cell in addition to neurons).

## Migration

The initial formation of the cortical plate occurs by migration of cells to the deepest (layer VI) of the cortex, and subsequent migrations follow in what is called an inside-out pattern. In this manner young neurons leave their zone of origin and migrate past older cells to reach their final position. This results in a pattern whereby the earliest formed cells inhabit the deepest cortical layers (VI), whereas progressively later formed layers will occupy positions at more superficial layers. (The exception to this is the cerebellum—not discussed in this paper—where the process of laminar formation occurs in an outside-in formation.)

As a rule, the nervous system has many different types of cells. Each type of cell is typically generated during only one period of development, and each is likely to be determined by a sequence of molecular-genetic events. Where these cells originate will determine what specific cells will be produced, and ultimately, where they will wind up in the nervous system.

Migration times vary on the order of 20–30 hours. However, given the vast numbers of cells that must complete this journey, one can imagine that this general process is protracted. Cell proliferation and migration vary from

area to area but as a rule, proliferation is complete by the 6th prenatal month. There are two exceptions to this rule. The first is for the cerebellum, where migration continues for another month or more. The second is for glial cells, which continue to be produced by the subventricular zone into the postnatal period.

The mechanism whereby migrating neurons reach their final destination appears to depend on a special class of glial cell, the radial glial fiber (which by default precede neurons in development). Each immature neuron (neuroblast) is attached to the radial glial cell on the one hand, which in turn is attached to the epithelial layer. The neuroblast then simply "climbs" on this fiber as it is stretched between the two layers. Once the migrating cells have reached their final destination, the radial glial fiber undergoes a second mitosis, and becomes an astrocyte (another type of glia).

To summarize, the cortex consists of horizontal layers of particular types of neurons and vertical columns that extend across the layers and that are made up of many types of cells. Cell migration is completed fairly early in postnatal development, by approximately day 160 in the monkey and the 6th prenatal month in the human. An important point to consider is that clearly the outgrowth and invasion of target cells by particular neurons is an important step in neural development. However, because this process occurs so early in development, it cannot be a crucial step underlying the emergence of function.

### ***Differentiation***

Once cells have reached their target destination, they begin the process of differentiation. Some cells will die (apoptosis), others will mature but remain latent and not develop processes (axons, dendrites), still others will develop processes but will not form synapses, and still others will form processes and synapses. It is this last event that is most relevant to our discussion.

### ***Synaptogenesis***

Once a neuron has developed axons and dendrites (itself a complex process influenced by a variety of humoral and genetic factors), the potential for synapses to form is made possible. In the case of the most common type of synapse, axon-dendritic, a growing axon approaches the dendrites of a target cell, and forms a synapse. Once synaptogenesis begins, the absolute number of synapses increases sharply. For example, in mice there are 8,000 the first postnatal day, and 3,000,000 60 days later. Importantly, there is some evidence to suggest that synaptic activity itself can facilitate the formation of dendritic filopodia, a precursor to spine development and thus further synaptic development (Maletic-Savatic, Malinow, & Svoboda, 1999).

A great deal more is known about synaptogenesis in the monkey than in the human, although both literatures will be summarized. In the monkey, Pasko Rakic and his colleagues have reported that synaptogenesis in diverse regions of the brain (e.g., visual, somatosensory, motor, prefrontal, and hippocampal cortex) show virtually the same rate of increase. Thus, in each area, synaptic density increases rapidly during last third of gestation and this increase continues until the 4th postnatal month (approximately the 12th postnatal month in the human). The rate of increase is identical for each area examined. Furthermore, each area passes through a phase of excess synapses, much higher than adult levels, at roughly the same postnatal ages. This synapse overproduction is particularly high in the 2nd through 4th postnatal months. After 4 months synapse elimination increases, with the number of synapses eventually declining to adult numbers. This decline is steepest during the first postnatal year, followed by a more gradual rate of decline over the next several years.

This general pattern of synapse formation needs to be qualified in several respects. First, although synapses form concurrently in diverse regions of the brain, there is still a dif-

ferent time table *within* a particular region. For example, synapses in the entorhinal cortex are formed before those in the dentate gyrus (both structures are intimately connected to, or are part of, the hippocampal formation). Second, because development occurs on a much faster time frame in the monkey than in the human, this concurrent timetable may be an artifact of age compression. Third, it should be noted that the same process just described does not hold for subcortical sites; thus, for example, synapses form earlier in the caudate nucleus (part of the basal ganglia) than in the cerebral cortex.

The pattern described for monkeys is slightly different for humans. For example, Peter Huttenlocher has observed that in the visual cortex, there is a rapid burst of synapses at 3–4 postnatal months, with maximum density reached at 4 months. Synaptogenesis in primary auditory cortex follows a similar timetable, and is 80% complete by 3 months. In contrast there is a similar overshoot in the middle frontal gyrus but maximum density is not reached until 1 year of age. Importantly, the retraction of synapses differs in these 3 areas: in visual and auditory cortices, synapses reach their adult levels in early childhood (2–6 years), whereas in medial frontal gyrus it is not until adolescence.

Huttenlocher has also looked at synaptogenesis *within* a given brain area. For example, within the auditory cortex, synapses form earlier in Heschl's gyrus (for general auditory processing) than in the angular gyrus (for receptive language). By approximately the 4th postnatal year, synaptic density is the same in these two areas, and in Broca's area (a region in the frontal cortex involved in speech production), but is still twice as high as in the adult brain. Interestingly, Huttenlocher has not observed differences in synapse number in select areas of the left vs. right hemisphere.

In summary, synapse overproduction occurs early in development, within the first year of life, whereas synapse elimination occurs much later. As will be clear in the next section, this is a time when the nervous system is

critically governed by environmental determinants.

## Myelination

The final event to consider in our discussion of brain development is the process of myelination.

Myelin is a lipid/protein substance that is produced from *Schwann* cells (a type of glial cell, *oligodendroglia*). The principle purpose of myelin is to insulate the cell, thereby increasing conduction velocity. Thus, myelinated axons transmit information faster than unmyelinated axons. The process of myelination begins about 2 months after the differentiation of neurons and the growth of nerve fibers, and depending on the region of the brain, may continue through adolescence. Thus, the first part of the brain to myelinate is the peripheral nervous system, whose motor roots myelinate before sensory roots. This is followed by myelination of somesthetic cortex (where our tactile sense resides), and the primary visual and auditory cortices. In the first few postnatal months, the secondary association areas myelinate (i.e., areas that surround primary sensory or motor cortices). Finally, the last regions of the brain to myelinate include the association areas, notably those in the frontal lobe. (For recent overviews of brain development, from which I have drawn heavily, see Hatten & Heintz, 1999; Huttenlocher, 1994; Huttenlocher & Dabholkar, 1997; Kintner & Lumsden, 1999; Komuro & Rakic, 1998; McConnell, 1995; Nelson & Bloom, 1997; Nelson, 2000a, in press).

## Summary

It should be obvious from the cursory review provided that the macromorphological changes that occur in the brain—creation of neural tube, outgrowth of neurons, formation of the cortex, production of axons, dendrites, synapses—occurs on a very rapid time frame. Genetic scripts that occur independent of ex-

perience govern the vast majority of these anatomical events. This is not to say, however, that these events cannot be subverted by altering the environment. For example, we know that exposure to teratogens (e.g., alcohol) can compromise development (e.g., Jacobson, 1998). Similarly, McConnell has shown that one can alter the cellular makeup of cortical layers by transplanting "foreign" cells at a particular point in development (McConnell, 1988). Thus, as is the case in PKU (where the phenotype of this single-gene defect can be influenced by altering the environment; i.e., modifying the diet), even the genetic regularity of brain development can be influenced to some degree by experience. Fortunately, these tightly controlled events are *relatively* impervious to experience, for if they were not, one can imagine the casualties that would afflict our species, given the misfortunes to which we treat one another and ourselves (e.g., prenatal substance abuse, exposure to chronic stress). This is not the case, however, for the fine-tuning of the brain that goes on during the postnatal period. Thus, imagine a brain that is still forming and fine tuning its synapses, and in many cases, creating myelinated pathways *well beyond the first years of life*. Given the plethora of experiences that confront the developing child, one would think that such experiences would greatly impact the developing brain. Indeed, some have proposed that the *purpose* of the exuberance of synapses is to *capture* experience. The mechanism whereby the structure of experience is incorporated into the structure of the brain is described next.

### **THE ROLE OF EXPERIENCE IN BRAIN DEVELOPMENT**

It has been well documented from studies of deprivation, as well as studies of normal development, that many aspects of perceptual, linguistic, cognitive, and social-emotional development are heavily dependent on experience. For example, infants deprived of seeing or hearing the world normally (e.g., those born

with strabismus, those born deaf or otherwise deprived of speech and language input) develop vision and language problems. Similarly, infants deprived of what we have come to think of as "typical" caretaking experiences are at great risk for developing emotional disorders. We know that children reared in poverty with few cognitive challenges greatly benefit from early enrichment. Finally, we know that hearing the sounds of one's native language greatly influences one's ability to recognize and discriminate those sounds (for review of these literatures, see Nelson, 2000a). These and other examples have been used—and misused—to suggest that early experience *in general* is critical to brain and behavioral development (for discussion, see Bruer, 1999). As the next sections will make clear, early experience can be important, but so too can later experience.

### ***The Concept of Critical or Sensitive Periods***

There are some instances in which a particular experience must occur precisely at a particular point in time for some ability to develop normally. For example, the Zebra finch can only learn and remember a particular song if it is presented at a particular point in development (e.g., Doupe, 1997; Konishi, 1985). Similarly, in some mammals filial imprinting must occur early for "attachment" behavior to proceed normally (e.g., Hess, 1973). And as alluded to earlier, exposure to a normal visual world within the first 1–2 years is necessary to promote some aspects of visual development (e.g., Blake & Hirsch, 1975; Hubel, 1979). Lastly, we know that exposure to the sounds of one's own language must occur in the first year or two of life if the infant is to become successful in discriminating the sounds of that language, and eventually, in reproducing those sounds (e.g., Kuhl, 1993; Kuhl, Williams, Lacerda, Stevens, & Lindblom, 1992).

The extent to which there are strict critical



or sensitive periods for the acquisition of other, “higher-level” behaviors is less clear. For example, there is some debate over whether exposure to a particular caretaking style at a particular point in development truly has long term consequences (see Lewis, 1992; Thompson, in press). Similarly, there is ample evidence that some cognitive abilities, such as learning and memory, can occur throughout the lifespan, and it is unclear whether certain events must occur early in life to make this possible (see Nelson, 2000b, for discussion). Thus, it may well be the case that strict critical periods apply primarily to sensory systems (e.g., vision, speech) rather than “higher-level” systems like cognition and emotion. Nevertheless, experience clearly is known to exert powerful effects on these systems (e.g., the effects of maltreatment early versus later in life; the success of early versus later intervention on cognitive development). Thus, it is important to consider what the mechanism is behind these effects; that is, how *does* experience get into the brain?

The best answer to this question is that experience takes advantage of the brain’s ability to form new connections or alter existing ones. This can occur at a number of levels, including:

- a) sprouting of new axons and dendrites, and new synapses
- b) altering neurotransmitter synthesis and release
- c) altering metabolic activity, such as increasing blood flow to a given area.

These changes can most likely occur at any part of the life cycle, although some may be easier to accomplish earlier in life vs. later in life. In the sections that follow, examples of neural plasticity that occur early in development are contrasted with those that occur later in life.

## **Neural Plasticity in the Immature Organism**

Across a variety of species, there are now numerous demonstrations using a variety of species that positive or negative early life experiences can alter both the function and structure of the brain. Regarding the latter, it is known, for example, that prenatally stressed rats show increases in indices of emotionality in response to novelty. If you observe such rats engaged in “play” behavior with other rats, you find that such rats are much slower to initiate play. They get better if you repeatedly expose them to this same play environment, but if you even briefly reexpose them to mild stress, their behavior regresses. This suggests that prenatal stress induces long-term wariness in offspring in unfamiliar environments. Such an effect may greatly diminish an animal’s ability to benefit from experience by reducing active seeking of new information (see Black, Jones, Nelson, & Greenough, 1998 for review). However, on the other hand, if you take such rats and rear them in complex, enriched environments, and/or handle them at birth, they show fewer effects of this prenatal stress.

Moving closer to the human, Schneider and colleagues have demonstrated that pregnant monkeys exposed to unpredictable loud sounds give birth to infant monkeys who suffer from a range of neurobehavioral problems; for example, they are jittery, they startle more easily, and they do more poorly than control animals on orientation items of the Neonatal Behavioral Assessment Scale (NBAS; e.g., Schneider et al., 1998). Moreover, the effects of this prenatal exposure to stress has long-lasting effects on noradrenergic and dopaminergic activity and behavior as long as 1.5 years after birth. Finally, Schneider has also observed long-term effects on cognitive function; for example, prenatally stressed monkeys do more poorly than controls on object permanence and explicit memory tasks (Schneider, 1998).

The effects of prenatal exposure to stress are not limited to the monkey. For example,

using the NBAS Lou et al. (1994) compared the neonates who had been exposed to stress prenatally to those who had not. The authors reported smaller head circumference and head growth among the prenatally stressed infants; moreover, prenatal stress was related to neurological findings between 4 and 14 days after birth.

Lou et al. (1994) postulated that the effects of circulating maternal glucocorticoids on infant brain development mediated the reduced head size. It is well known that such hormones can have a profound effect on some domains of cognitive function, such as explicit memory, primarily because explicit memory is mediated by the hippocampus, a structure that is rich in glucocorticoid receptors (see Nelson & Carver, 1998 for a review of the relation between brain, memory, and stress). Thus, it is not surprising to learn that adults who survived physical or sexual abuse as children show reduced hippocampal volume and in some instances, impairments in memory (Bremner et al., 1995; Stein et al., 1997).

Overall, it is apparent that early deleterious experience can have significant negative effects that may be long-term. Unfortunately, little is known about the positive effects of early experience on subsequent development, as that is presumed to be the norm. And, when it is not the norm, as in the case of early socioeconomic disadvantage, the powerful effects of intervention have thus far only been examined at the behavioral level. Presumably, these effects are mediated by changes in the brain. This is not to say, however, that early deleterious experiences unalterably lead to poor outcomes. For example, Knudsen and colleagues have elegantly shown that the ability of the barn owl to develop a map of auditory space (for purposes of sound localization) is remarkably resilient to insult. For example, it is known that the auditory input the baby owl receives leads to the formation of a topographic map that is formed in portions of the inferior colliculus (IC). This map is then carried forward to the optic tectum (superior colliculus in the mammal), and then to the visual cortex. With additional flying experience, this

map continues to be refined. However, even if the animal's ears have been altered or the auditory canal has been plugged, the animal's brain adapts by recalibrating the neurons in the IC. Similar findings obtain if displacing prisms are placed over the owl's eyes (although the mechanism responsible for plasticity differs than with auditory deprivation). Thus, in some systems and in some species, early deleterious experiences does not always lead to poor (maladaptive) outcomes (see Knudsen, 1999 for discussion).

The work on exposure to stress early in life should not be taken to mean that beyond the infancy period our brain is spared such effects; indeed, the voluminous literature on adult stress (such as Posttraumatic Stress Disorder) illustrates the powerful effects of exposure to stress later in life (see Sapolsky, Krey, & McEwen, 1986). Thus, it would be wise not to think that there is a critical period for exposure to stress. Rather, it is simply that exposing the *developing* brain vs. the *developed* brain to stress leads to different outcomes. Such a distinction leads to our next topic, which is the effects of experience on the mature brain.

### ***Neural Plasticity in the Mature Organism***

It has been well known for decades that rats reared in complex environments<sup>1</sup> do better on a range of cognitive tests, and show demonstrable changes in their brains. For example, relative to control (cage-reared) rats, rats housed in complex environments, show increased dendritic spines, more synapses per neuron, and better performance on various maze tasks that require spatial memory. Similarly, rats trained to use one forelimb to reach through a tube to receive a cookie show increases in dendritic arborization (essentially a metric of the thickness and density of dendrites) within the cortex opposite that of the trained limb, relative to the control limb. Even more impressive is recent work by James



Black and William Greenough using so-called "acrobatic" rats. Here rats are required to master several new complex motor coordination tasks. These animals show increased numbers of synapses per neuron within the cerebellum in comparison to inactive controls. In contrast, animals exhibiting greater amounts of motor activity in running wheels or treadmills, where little information was learned, do *not* show significant alterations in synaptic connections in the cerebellum. Moreover, only those rats in the learning paradigm also show structural changes in the brain: that is, the density of capillaries in the involved region are significantly increased, corresponding to what would be seen if new blood vessels developed to support increased metabolic demand. Thus, it was learning and not simply the repetitive use of synapses that occurs during dull physical exercise that leads to synaptogenesis (for review and discussion of the literature on the effects of experience on brain-behavior relations in the mature animal, see Black et al., 1998).

There have been surprisingly few studies with the primate in which exposure to positive rearing conditions has been examined. More common are selective rearing studies in which monkeys have been exposed to some negative event and changes in brain and behavior are examined. In addition, the majority of this work has been limited to the motor domain, although some exceptions exist. In perhaps the best known of this genre of work, Pons and colleagues examined a group of monkeys who had experienced a limb deafferentation years earlier. In this procedure, the afferent fibers leading from the forelimb to the somatosensory cortex are severed, rendering the animal unable to sense stimulation of that limb (although the animal can move the limb should it choose). In an initial report on these animals, Pons et al. (1991) reported massive reorganization of the somatosensory cortex, along the lines of several millimeters. In addition, topographic mapping of this region of the brain revealed that the neighboring area (a region of the face) had encroached upon the area previ-

ously representing the missing limb. A more recent analysis of these animals revealed that some of the observed cortical alterations could be due to changes originating at the level of the thalamus (Jones & Pons, 1998), although other laboratories consistently point to such changes as originating in the cortex (e.g., Florence, Taub, & Kaas, 1998).

In the examples just cited, the somatosensory system was corrupted by injury or damage. Might such reorganization be observed in "healthy" individuals who suffered no brain injury? Two examples come to mind, both from the laboratory of Thomas Elbert.

First, Elbert and colleagues (Mühlnickel, Elbert, Taub, & Flor, 1998) have reported that adults suffering from the disabling condition *tinnitus* (ringing in the ears) show a dramatic reorganization of the auditory cortex. Second, this same laboratory has studied the reorganization that occurs in the cortex of musicians. For example, Elbert et al. (1995) used Magnetoencephalography (MEG) to map the somatosensory cortex of adults with and without experience playing a stringed instrument. The authors reported that the area of the somatosensory cortex representing the fingers of the left hand (the hand used on the finger board, which required greater fine motor skill) was larger than the area represented by the right hand (which was used, in the case of the violin, to bow, a gross motor skill), and larger than the left hand in non-musicians. Interestingly, there was a trend towards greater cortical representation to be larger in individuals who had begun musical training before the age of 10.

In a truly dramatic example of neural plasticity in the mature monkey, Gould, Tanapat, McEwen, Flugge, & Fuchs (1998) reported continued neurogenesis (birth of new cells) in the dentate region of the hippocampus in marmosets; further, if these animals were exposed to stress (such as putting adult males together in cages), there was a dramatic reduction in the birth of new neurons. Although this report was controversial at the time of publication (based on earlier reports by Rakic and col-

leagues that there is no new neurogenesis beyond the infancy period), recent evidence of continued neurogenesis in this same region of the brain *in the adult human* has crystallized support for this position (Eriksson et al., 1998; see Rakic, 1998 for discussion). The extent to which adult neurogenesis is responsible for other forms of behavioral plasticity remains to be determined.

Collectively, then, it appears that reorganization of cortical pathways in the adult human brain is possible beyond childhood, although the bulk of the evidence is that such reorganization may be limited to motor or sensory pathways.

### ***How Important are the First Years of Life?***

When viewed as a whole, the work on neural plasticity raises an intriguing question: *how important are the first years of life?*

Before proceeding to address this question, it is important to note that the evidence for neural plasticity in the "mature" organism was primarily limited to the motor domain. The fact that the motor system is capable of being modified throughout much of the lifespan should not be surprising, given that from the moment a child is born the motor system is being continually challenged, thereby keeping this system "open" to new experience.

In contrast, we know that the ability to acquire oral language may have a much shorter period of modifiability or may place different demands on the environment, such as the need for a specific form of input. For example, we know that English speaking adults who have not been exposed to languages such as Swedish or Thai (or Swedish speaking adults not exposed to English) are unable to discriminate speech contrasts from these languages, in contrast to the ceiling-level ability to discriminate speech contrasts from their own (English/Swedish) language. Kuhl et al., (1992) and others have demonstrated that between 6 and 12 months of life, the

infant's ability to discriminate phonemes from languages that they are not exposed to greatly declines. Thus, although a 6-month-old infant being raised in an English-speaking home may be able to discriminate contrasts from English, as well as those from Swedish, by 12 months, such infants become more like English speaking adults: that is, they lose the ability to discriminate contrasts from their non-native language. Kuhl and others have proposed that the speech system remains open to experience for a limited period of time, but if a particular experience in a particular domain (such as hearing speech contrasts in different languages) does not come along, the window begins to close early in life (e.g., Kuhl, 1993).

My argument, then, is that the motor system, in contrast to the speech system, may remain open for much of the life span. It is this openness that is likely responsible for everything from our ability to acquire new motor skills (e.g., dance, tennis, squash) and for our ability to recover from stroke.

Outside of the motor domain, there is a paucity of information on neural plasticity in the mature or normally developing organism. Of course, there is some suggestion in the social/affective domain that there may be sensitive periods; for example, recent work examining children reared in Romanian orphanages and adopted into homes in North America suggests that children adopted before the age of 1–2 years fare better psychologically than those adopted after this (e.g., Ames, 1997; Fisher, Ames, Chisholm, & Savoie, 1997).

Collectively, this evidence would suggest that the likelihood of a given behavioral system showing signs of recovery of function, or even sparing, would depend on whether the system being challenged is one that has had the right early experience to "set" the system (such as exposure to normal language) and is continually challenged thereafter. Conversely, one might argue that if the appropriate early experiences were lacking, then the efforts involved in changing the system may be more difficult. For example, if the expected social/emotional environment is not met (as might be

the case with neglected infants), then the deleterious effects these experiences have on the brain will create a situation whereby altering the course of development onto a normal trajectory must come early and intensively in order to be successful. Similarly, one might also argue that if the expected early environment *was* present, thereby setting the system correctly, but that the subsequent environment was lacking, then attempts to modify the system could come later and still be successful.

Finally, if there was some early injury to the brain that *prevented* it from taking full advantage of early experience or coded this experience inappropriately, then one would have to develop methods that would capitalize on the child's other capacities—that is, build on those functions that were spared. A recent series of case studies may illustrate this point. Vargha-Khadem and colleagues (Vargha-Khadem et al., 1997) reported on 3 children who all suffered discrete and significant bilateral damage to the hippocampus at or near the time of birth. Although all three demonstrated long-lasting impairments in explicit memory (indeed, they resembled the famous patient H.M., in that they suffered from significant anterograde amnesia), their semantic memory was surprisingly intact. It was believed that this was possible due to sparing of certain structures (e.g., surrounding cortex) coupled, perhaps, with school acting as form of intervention. Comparable damage to the adult brain typically shows no such sparing.

## CONCLUSIONS

From this review it should be clear that the events that transpire to mold and sculpt the brain are (a) not always limited to the first years of life and (b) are activity-dependent. As a result, we need to be careful in assuming blindly that the first few years of life are a critical period *in general*; rather, it is perhaps wisest to view these years as a critical period for some functions, a sensitive period for others, and broadly tuned and receptive to mod-

ification for the duration of the lifespan for still others. Finally, because so many aspects of development are activity-dependent, we should not be surprised to observe a broad range of individual differences; after all, given differences in prenatal histories, in genomes, in rearing environments, in caretaking, and in inculturation, to name just a few, each brain is left to incorporate experience differently. This, in turn, will result in differences in how infants embrace their environments, which in turn will lead to further differences in neural substrate . . . *ad infinitum*. Although this may at first represent a challenge to developing a *theory* of brain-behavior relations, in the long run any such theory will be the stronger because it incorporates this dimension.

What is the significance of this work for our understanding of change and continuity in neurobehavioral development? A few examples come to mind. First, given the intricate dance between experience and brain development, one would be hard pressed to argue that development proceeds linearly. Certainly this may appear to be the case given the methodological tools currently at our disposal, but as our armamentarium becomes more sophisticated we will undoubtedly gain sensitivity in picking up more subtle behavioral differences and more subtle developmental trajectories than is currently possible. It will be surprising if these trajectories take the form of discrete, uniform, and rigidly time-locked stages rather than abrupt, seemingly discordant shifts.

A second implication to this approach will be to revisit the age-old argument of nature vs. nurture, innate vs. learned, and so forth. The position argued for in this paper would be that these arguments are fallacious. Specifically, it would seem virtually impossible to tease apart that which is innate qua innate from that which is learned qua learned. Thus, to use one example, it is well known that infants recognize and discriminate faces at or shortly after birth (see Morton & Johnson, 1991). They may do so for a variety of reasons, but three that have been frequently discussed include:

- a) there is neural hardware dedicated to perceiving faces (presumably selected through evolutionary pressures),
- b) there is a powerful learning mechanism that facilitates the rapid development of a face "schema," and in a related fashion,
- c) even the briefest of exposure to faces triggers a bootstrapping mechanism whereby all subsequent faces are processed through some face "schema."

In contrast to these views, a more parsimonious perspective might be that there is neural tissue that has the *potential* to be hard-wired to perceive faces (tissue that in the adult likely exists in the fusiform gyrus or neighboring regions of the inferior temporal cortex). However, there will be no specification of this tissue without benefit of experience viewing faces (or face-like stimuli; see Morton & Johnson, 1991). Viewed in this light, we avoid the trappings of saying that face recognition is innate or learned; rather, the brain becomes specialized for perceiving faces *because* it is given experience viewing faces (see Nelson, in press b). Undoubtedly, this argument is not specific to face recognition, and may well extend to other domains of function, such as language.

A third and final implication of the approach explicated in this paper concerns the need for investigators to move beyond simply correlating brain with behavior. For example, given the plethora of tools that currently exist in the neurosciences for examining brain function in the developing child (e.g., electroencephalogram, event-related potentials, functional magnetic resonance imaging, behavioral marker tasks), we are in a position to be more precise than ever in describing the neural events that underlie behavior. Thus, rather than correlating data sets across time (e.g., changes in synaptic density with changes in memory performance), we need to examine changes in brain at the same time as we examine changes in behavior. In so doing, we will be in a far better position to relate changes

in underlying neurobiology to changes in behavior. This, in turn, will assist us in identifying change and continuity in development in general.

## NOTE

1. It is important to stress that Greenough's studies involve housing rats in complex environments, not "enriched" environments as so often has been reported. Thus, compared to normal laboratory rats housed in individual cages devoid of much stimulation, rats housed in complex environments live in larger cages filled with toys and other rats. Thus, relative to rats who live in the wild, the "normal" laboratory environment is actually quite deprived, whereas the "complex" environment most likely simulates the world of a rat living in some large metropolitan city.

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