Neural Plasticity and Cognitive Development

Joan Stiles

Department of Cognitive Science
University of California, San Diego

It has been well documented that the effects of early occurring brain injury are often attenuated relative to later occurring injury. The traditional neuropsychological account of these observations is that, although the developing neural system normally proceeds along a well-specified maturational course, it has a transient capacity for plastic reorganization that can be recruited in the wake of injury. This characterization of early neural plasticity is limited and fails to capture the much more pervasive role of plasticity in development. This article examines the role of neural plasticity in development and learning. Data from both animal and human studies show that plasticity plays a central role in the normal development of neural systems allowing for adaptation and response to both exogenous and endogenous input. The capacity for reorganization and change is a critical feature of neural development, particularly in the postnatal period. Subtractive processes play a major role in the shaping and sculpting of neural organization. However, plasticity is neither transient nor unique to developing organisms. With development, neural systems stabilize and optimal patterns of functioning are achieved. Stabilization reduces, but does not eliminate, the capacity of the system to adapt. As the system stabilizes, plasticity becomes a less prominent feature of neural functioning, but it is not absent from the adult system. The implications of this broader view of plasticity for our understanding of development following early brain damage are discussed.

A common claim in the literature from developmental neuropsychology is that the developing brain is plastic. This means that during development the brain is capable of reorganizing patterns and systems of connections in ways that the mature brain cannot. One important consequence of this early and transient property is that the developing brain is much less vulnerable to the detrimental effects of injury

Requests for reprints should be sent to Joan Stiles, Department of Cognitive Science 0515, University of California, San Diego, La Jolla, CA 92093–0515. E-mail: stiles@ucsd.edu

than more mature neural systems. Data from studies of pediatric clinical populations generally support this claim. Adults who suffered focal brain injury early in life do not manifest the same extent and magnitude of cognitive and affective impairment as adults with comparable, but later occurring, injury.

The purpose of this article is to examine the construct of early brain plasticity in greater detail. The definition of plasticity as it has been used historically in the literature from developmental neuropsychology is explored and the implications of that definition weighed. Then, the use of the term *plasticity* within the context of more recent literature on brain development is considered. The purpose of comparing these views is to offer what is not so much an alternative account of the processes that underlie recovery of function following early brain injury, but rather to provide a more specific, updated, and as a consequence, somewhat modified view of what early brain plasticity is and what role it plays in development.

TRADITIONAL NEUROPSYCHOLOGICAL USAGE OF THE TERM PLASTICITY

The observation that the developing brain is resilient to the effects of early injury is not new. In this century, Kennard's (1936, 1938, 1942) seminal studies of motor development following neonatal ablation of motor cortex in monkeys were among the first to point to the striking difference in functional outcome associated with age at injury. Kennard (1938) reported only minimal effects on the development of motor functions following neonatal hemispherectomy and unilateral ablation of motor cortex. Although Kennard was not the first to point to the importance of the idea of resiliency following early brain injury (for discussion, see Finger, LeVere, Almli, & Stein, 1988), she was among the first to study the phenomena systematically.

Within the literature on human developmental neuropsychology, the most common usage of the term plasticity has been with reference to the well-documented resilience of young children to the effects of early occurring neural pathology. There is a large body of data documenting the fact that focal brain injury in childhood results in more limited patterns of behavioral and cognitive deficit than comparable injury in adulthood. These differential and less devastating outcomes following early injury are attributed to the developing brain's capacity for plastic reorganization. This capacity for reorganization declines with maturation.

Lenneberg (1967), for example, proposed that the neural systems that mediate language, and by extension other higher cognitive functions, develop according to a maturational blueprint. Different brain regions are genetically prespecified for particular cognitive functions, and under a typical maturational timetable, specific regions become committed to predesignated functions. This profile of maturation gives rise to the patterns of brain organization observed in most normally functioning adults. However, if the immature neural substrate is damaged, alternative pat-

terns of organization are possible. This plastic alteration of brain organization comes about because the maturing brain system has not yet committed its full complement of resources. Thus, if injury occurs to one region of the brain, there are sufficient uncommitted resources available to support developing functions. However, there is a decline in brain plasticity with development. As the neural system matures, there is a gradual commitment of neural resources to maturationally defined functions and a concomitant loss in flexibility and in the capacity of the system to reorganize.

This characterization of the developing brain as plastic has not gone unchallenged. There has been considerable debate over the extent to which plastic processes play a role in early development. Through the 1970s, there was considerable debate over how long a period the capacity for plastic reorganization was available to the developing child. The focus of that controversy was again language development. In his 1967 book, Lenneberg suggested that the prognosis for linguistic recovery declined throughout childhood and placed the upper limit on linguistic recovery following injury at about age 12. In 1973, Krashen published a study reexamining Lenneberg's corpus of data, as well as his own data. He concluded that the upper age estimate of 12 years was far too optimistic, and suggested that the ameliorative effects of early brain plasticity were not observed with injury occurring after age 5. Woods and Carey (1978) placed limits of recovery even earlier at about the end of the first year of life. Studies of children with early hemispherectomy also suggested limits on the extent of early brain plasticity. Dennis and her colleagues (Dennis, 1980; Dennis & Kohn, 1975; Dennis, Lovett, & Wiegel-Crump, 1981; Dennis & Whitaker, 1976, 1977) reported cases of selective deficits of language processing following left hemispherectomy and deficits of spatial processing with right hemispherectomy (Kohn & Dennis, 1974). St. James-Roberts (1979) argued that claims of functional recovery following early injury were largely misinterpretations of data, and argued strongly against the notion of early functional plasticity altogether.

Regardless of their specific findings, all of these reports have in common a similar definition of the nature and role of early brain plasticity in development. As applied, brain development and plasticity are complementary, but relatively independent systems. Normal brain development proceeds according to a maturational blueprint or plan, which includes both genetic factors and input from the environment. If the maturational process is perturbed by insult or injury, the system has the capacity to respond flexibly, thus circumventing functional deficit. In that sense, the developing brain is plastic. Although there is disagreement over the extent of plasticity, most of the studies share underlying assumptions about plasticity as an ancillary system or capacity, which is available (or not available) for a restricted period early in development. There is a sense in this literature that plasticity serves a means of shielding the developing organism from the potentially debilitating effects of neural insult. Plasticity can thus be construed as a *reac-*

tive rather than an *active* property of the immature system. Witelson (1985) summarized this view in her work, which reviews early functional specialization and plasticity: "Abnormal conditions, such as brain damage or extremely atypical stimulation, which in effect may serve as a physiological lesion, may be an impetus for neural plasticity to operate and change the preprogrammed original pattern of hemisphere specialization" (p. 75).

Closely associated with this view of plasticity are two additional constructs, which specify the functional priorities of plastic reorganization. The first is the idea of preferential preservation of language over other cognitive functions, which is embodied in the idea of right hemisphere crowding effects for language (e.g., Almli & Finger, 1984; Teuber 1974). According to this construct, language is an essential human function, and under conditions of early brain insult, it is preferentially supported at the expense of other (specifically visuospatial) functions. If there is injury to traditional left hemisphere (LH) language areas, homologous areas of the right hemisphere (RH) are recruited for language, thus "crowding" out spatial functions that normally would have been mediated by these areas. This idea was summarized by Teuber (1974):

> These findings suggest a definite hemisphere specialization at birth, with a curious vulnerability to early lesions for those capacities that depend, in the adult, on the right hemisphere—as if speech were relatively more resilient or simply earlier in getting established. Yet this resiliency is purchased at the expense of non-speech functions as if one had to admit a factor of competition in the developing brain for terminal space with consequent crowding when one hemisphere tries to do more than it had originally been meant to do. (p. 73)

A closely related alternative to the construct of crowding is the notion of functional redundancy, which suggests that early in development there may be multiple language-specific neural systems. By this account, if the primary language system is injured or lost, these secondary systems are available to mediate language.

There is ample data to support the claim that language is better preserved than other cognitive systems following early insult. Patients with early injury to traditional LH language areas do have substantial preservation of language, and linguistic functioning appears to be mediated by the RH in a significant proportion of cases (e.g., Rasmussen & Milner, 1977). However, these findings do not require the introduction of constructs like crowding and redundancy (see also Finger et al., 1988, for similar arguments). Indeed, the concept of language-specific crowding is difficult to reconcile with basic principles of brain development. Why does language merit special treatment at the level of the neural system? By what account is language necessarily more critical for the individual's survival than visuospatial processing? Why would there be multiple systems targeted for language and not for visuospatial processing? Why this elaborate fail-safe system for language? This perspective pres-

ents unlikely developmental scenarios and implausible biological solutions. Nonetheless, there is indisputably a large body of empirical data documenting the attenuated effects of early injury on linguistic (and cognitive) functioning.

If this definition of plasticity and its associated constructs of crowding and redundancy do not provide an adequate description of the role and function of early brain plasticity, is there an alternative? I would argue that the basic ideas about how plasticity operates in the wake of early neurological insult are fundamentally correct within the traditional neuropsychological account. Developing neural systems have uncommitted resources, and there is competition for these resources among developing functional systems. The implausibility of the constructs associated with the traditional view arises out of too narrow a definition of plasticity and too limited a consideration of its operational context.

The traditional definition of plasticity is somewhat circular. It begins with the observation that in the wake of localized brain injury, children are more resilient than adults. The interpretation of these observations is that the developing system must be plastic because it can respond to injury in ways that the adult system cannot. Thus, plasticity is the explanatory construct for observed resilience. The circularity of the definition arises because the construct of plasticity is confirmed by the fact that the child with injury shows resilience. I argue that this circularity derives from a definition of plasticity that is too limited, and that a broader definition can circumvent the circularity. More important, a broader definition of plasticity can provide a clearer perspective on the nature of neural and behavioral development following early brain injury. I base these arguments on several lines of data, each of which are briefly summarized in the following sections of this article. First, I consider data from more recent animal studies of brain development. Second, I consider data that provided evidence for reorganization in adult brains. Finally, I consider the convergence of data from a prospective view of developmental neuropsychology.

Data from each of these areas contribute to a broader definition of plasticity and serve to redefine our understanding of the role of plasticity following early neurological insult. Based on these data, I argue that plasticity is a fundamental property of functioning neural and cognitive systems. It is a central feature of normal brain development. It is not primarily a system response to pathological insult. It is not a property unique to development. Rather, plasticity is a basic process that underlies neural and cognitive functioning. The same process operates in both normal development and in development following early injury. Although plasticity may be most apparent under the catastrophic conditions of neural insult, the basic process is not fundamentally different from that which serves the normally developing system.

Applications of the Term Plasticity

Before examining the data on plasticity, it is worthwhile to consider how the term has been used in different areas of neuroscience and what is consistent in the use of

the term across different fields. The term plasticity has been applied to processes operative at many levels of the neural and cognitive system. Figure 1 illustrates the range of events to which the term has been applied. It could be argued these events represent such widely varying functions that the use of a common term is inappropriate and even misleading. However, there are commonalities in the definition of the term plasticity as it is applied at all of these levels. These include

- *Reference to process*: In each case, the term plasticity refers to some dynamic feature of the neural system, which brings about change at a structural or functional level.
- *Adaptation*: The observed change is generally adaptive in that plastic systems marshal or recruit new or different resources in response to some external demand.
- *Organization*: The process is systematic and not haphazard. It reflects the systematic interaction of structural features and input from the environment.

Each of these features is consistent with the traditional definition of plasticity. However, for each of the events indicated in Figure 1, plasticity serves a primary organizational role in the normal development and functioning of the organism. It is important to note that these same principles of system organization may obtain under the nonoptimal or pathological conditions and may underlie system reorganization as well.

ANIMAL STUDIES OF BRAIN DEVELOPMENT

The animal literature on brain development is vast and covers a wide array of topics ranging from neurochemistry to behavior. The intent of this section is not to pro-

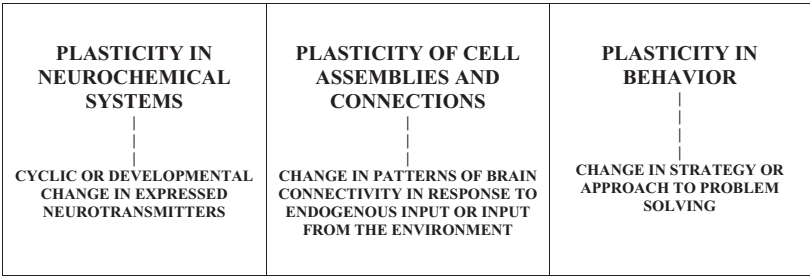| PLASTICITY IN NEUROCHEMICAL SYSTEMS	PLASTICITY OF CELL ASSEMBLIES AND CONNECTIONS	PLASTICITY IN BEHAVIOR
CYCLIC OR DEVELOPMENTAL CHANGE IN EXPRESSED NEUROTRANSMITTERS	CHANGE IN PATTERNS OF BRAIN CONNECTIVITY IN RESPONSE TO ENDOGENOUS INPUT OR INPUT FROM THE ENVIRONMENT	CHANGE IN STRATEGY OR APPROACH TO PROBLEM SOLVING

FIGURE 1   Examples of the use of the term plasticity at different levels of the cognitive and neural system.

vide anything approaching a summary of the field. Rather, it is a somewhat idiosyncratic selection of findings that illustrate the point that plasticity plays a critical role in brain development. In the first part of this section, a series of examples covering a range of topics central to defining early brain plasticity is presented. The second section offers examples of work focused specifically on the role of plasticity in cognitive development.

PLASTICITY AND BRAIN DEVELOPMENT

Input and the Development of the Visual System

The seminal work by Hubel and Wiesel (1967; Hubel, Wiesel, & LeVay, 1977; Wiesel, 1982; Wiesel & Hubel, 1963a, 1963b, 1965a, 1965b) provides an appropriate starting point for a discussion of brain development and plasticity. Their work on the development of ocular dominance columns highlighted the importance of both specific input and timing of experience on the development of conventional patterns of cortical organization. In the normal development of the primary visual cortex, a fairly even balance is observed between cells preferentially driven by one eye or the other. Input from each eye to the lateral geniculate nucleus (LGN) of the thalamus is distributed into a series of bands approximately .5 mm wide, which alternate with similar bands serving the other eye. This segregation is maintained in projections from LGN to Layer 4 of the primary visual cortex. This pattern of interleaved input gives rise to the characteristic striated appearance of the visual cortex and forms the anatomical basis for ocular dominance columns.

Hubel and Wiesel (1967; Wiesel & Hubel, 1963a, 1963b, 1965a, 1965b) experimentally manipulated the early visual experience of newborn kittens to examine the effects of varied input on subsequent brain organization. Across the series of experiments, they examined the effects of binocular and monocular deprivation at various points in development for different periods of time. In general, they found that monocular deprivation had a much greater effect on the organization of the striate cortex than binocular deprivation. Kittens binocularly deprived early in development showed only limited effects of deprivation. Recordings from cells in the visual cortex indicated that although the cells did respond somewhat sluggishly, the receptive field characteristics and organization of cells into orientation selective columns were similar to those observed in adult animals. By contrast, kittens monocularly deprived early in development showed profoundly defective vision in the deprived eye. The great majority of cortical cells were driven exclusively by input from the nondeprived eye. It is interesting to note that cells in LGN receiving input from retinal cells in the deprived eye were typical in size and functioned normally. However, in striate, the LGN terminals with input from the nondeprived eye took over much of the space that would normally have subserved the deprived eye, thus distorting the characteristic banded patterns of the striate

cortex (see also LeVay, Wiesel, & Hubel, 1980). In other experiments, Hubel and Wiesel (1970; Wiesel & Hubel, 1965b) determined that timing of deprivation was also a critical determiner of outcome. The disruption of cortical organization was most severe when deprivation began prior to 10 weeks of age. Some change was detectable with onset at 1 year, and no changes were observed in adult animals. The effects of duration of deprivation covaried with time of onset; with earlier onset, less time was required to induce substantial change. Recovery from early deprivation depended on both time of onset and duration.

   Recent studies suggest that it is also important to distinguish between the effects of neural activity and visual experience. For example, Stryker and colleagues (Crair, Gillespie, & Stryker, 1998) showed that visual experience appears to play little role in the initial establishment of ocular dominance (OD) and orientation columns but has dramatic effects later. Specifically, during the first 3 postnatal weeks, no differences in the cortical OD and orientation maps were observed for binocularly deprived cats and nondeprived littermate controls. However, during Week 4, significant deterioration was observed in the deprived group. A similar pattern of development was observed on measures of neuronal orientation selectivity. These data suggest that the basic patterns of connectivity in the visual system are established early in development, but normal development of the visual cortex requires normal visual input. Thus, the deprivation experiments showed that neural connections can be modulated by environmental input at least for a period early in development.

   Effects of enriched environment.   A more general case for the impact of the environment on brain development comes from studies in which the rearing conditions of younger and older animals are systematically altered. These types of studies show quite dramatically that rearing conditions can affect behavioral outcome. A classic early observation by Hebb (1947) suggested superior maze learning in "home-reared" versus "laboratory-reared" rats. In the 1960s, studies by Rosenzweig and the Berkeley Group (e.g., Bennett, Rosenzweig, & Diamond, 1969; Rosenzweig & Bennett, 1972; Rosenzweig, Krech, Bennett, & Diamond, 1962; Rosenzweig, Krech; Bennett, & Zolman, 1962; Rosenzweig, Love, & Bennett, 1968) were among the first to demonstrate explicit effects of environmental enrichment on brain anatomy and chemistry. More recently, Greenough (Greenough & Chang, 1989), in an extensive series of studies with rats, demonstrated that variation in environmental conditions can impact patterns of synaptic connectivity in the developing brain. Greenough looked specifically at changes in brain morphology associated with the rearing condition. Identical strains of rats were reared under three conditions: individual cage (IC), social cage (SC), and environmental complexity (EC). The IC and SC were standard laboratory cages containing only food and water. In the IC condition, rats were

reared in isolation, whereas in the SC condition, they were reared in small groups. In the EC condition, animals were housed in groups of 12 or more in large cages filled with a variety of objects. Animals were free to explore, and the objects in the cage were changed frequently. Different groups of rats were reared from birth to adolescence in the three conditions. Examination of the brains of animals in the three groups revealed significant differences in the numbers of dendrites per neuron, that is, in the amount of synaptic space available for each neuron. Animals reared in the EC condition had 20% to 25% more dendrites than animals reared in the other two conditions (for a discussion of selective increases in multiple vs. single synapse contacts, see also Jones, Klintsova, Kilman, Sirevaag, & Greenough, 1997). These effects were not associated with any specific feature of the enriched environment condition, and they were not accounted for by general metabolic differences in animals reared in the enriched condition. Animals fitted with a monocular occluder and reared in the EC environment showed evidence of unilateral exuberance of dendrites.

Greenough (Jones, Kleim, & Greenough, 1996) also used cortical lesion techniques to examine the effects of experience on brain organization. The forelimb region of the somatosensory cortex was lesioned in a group of adult rats. Different subgroups of lesioned animals were then sacrificed at 10, 18, or 30 days postsurgery. Systematic changes were observed in Layer 5 of the remaining contralateral somatosensory cortex. Specifically compared to sham-operated rats, the lesioned rats showed increases both in the number of synapses per neuron and in the surface area of the dentritic membrane, which were statistically significant by 30 days postsurgery. These changes coincided with observed increased use of the surgically unaffected limb during the postoperative period. Jones et al. suggested that these increases in neural elements are, at least in part, the product of lesion induced increases in the use of the unaffected limb. Thus, once again, these data provide an example of experience-based (in this case, activity-based) changes in the neural substrate.

The effects of environmental enrichment has also been shown to affect the survival of postnatally produced neurons. Traditional accounts of brain development have held that neuron production is restricted primarily to the prenatal period. However, a growing body of evidence suggests that new neurons are produced continuously across the life span, at least within the dentate gyrus of the hippocampus. However, little is known about the function or fate of these new neurons. Gage and colleagues (Kempermann, Kuhn, & Gage, 1997) used an experimental design similar to the one used by Greenough and Chang (1989) to examine the effects of rearing in an enriched environment on the production and survival of these neurons. Two groups of 21-day-old mice were randomly assigned to standard laboratory or enriched environmental conditions, where they were reared for a period of 40 days. During the last 12 days of this period, they were administered injections of BrdU, a thymidine analogue that is incorporated into the DNA of dividing

cells and can be detected in postmortum immunohistochemical studies. Following the 12-day BrdU treatment period, five animals from each group were sacrificed, and the number of BrdU labeled neurons in the dentate gyrus was counted. The remaining mice were reared in their respective environments for an additional 28 days. For the mice sacrificed immediately after the BrdU treatment, no difference in the number of labeled cells was observed between the groups. This suggests that enrichment had little effect on the production of new neurons. However, significant differences in the numbers of labeled cells were observed for the animals examined 4 weeks after the end of the BrdU treatment. Rats in the enriched rearing condition had 57% more labeled cells in the dentate gyrus than controls. These findings suggest that experience has an effect on the survival of new neurons in this region of the brain. Subsequent studies have demonstrated similar effects in macaque monkeys (Gould et al., 1999). A very recent study suggested that there is continued production of neurons in the dentate gyrus of humans as well (Kempermann & Gage, 1998).

Subtractive events in postnatal brain development.   The term *development* usually implies the growth and elaboration of systems. It is, therefore, counterintuitive that subtractive events play a central role in brain development. The principal subtractive events include naturally occurring neuronal cell death and the large-scale loss of synapses.

The phases of cell death and synapse loss follow periods of neuronal overproduction and synaptic profusion. The average regional rate of neuronal overproduction in mammalian species is estimated to be approximately 50% (Janowsky, 1993). During development, 20% to 80% of neurons in different cortical regions are lost (Oppenheim, 1985). Similar estimates have been obtained for synapse loss in humans (Huttenlocher, 1990; Huttenlocher & Dabholkar, 1997; Huttenlocher, de Courten, Garey, & Van der Loos, 1982). Both cell death and synapse retraction appear to be related to competition for resources, which is in turn regulated by input to the system (Changeux & Danchin, 1976). Factors that influence the retention or loss of synapses include the availability of neurotrophic factors, stimulation of afferents projecting to target sites, and stimulation emanating from the target zone (Purves, 1988). Some of this activity is endogenous, but much comes from remote sources. Although some cell and synapse loss may be pathological or serve to correct errors in connectivity, the major functions of these subtractive events appears to be population matching (Cowan, Fawcett, O'Leary, & Stanfield, 1984). The subtractive processes modulate local patterns of connectivity and thus help to establish stable patterns of brain connectivity. Thus, they serve to sculpt and shape the brain organization. Subtractive events in brain development demonstrate the dynamic nature of change in the neural substrate.

"Rewiring" the cortex.   Data from animal studies also demonstrate that optimal patterns of brain organization are not necessarily fixed. Rather, they depend on specific patterns of connectivity in local regions of the brain that can be altered by remote changes in brain structure or input. For example, Sur and his colleagues (Pallas, Roe, & Sur, 1990; Sur, Garraghty, & Roe, 1988) ablated the visual cortex and superior colliculus in 1-day-old ferrets, thus eliminating two major visual system target areas. They also deafferented the major input pathways to the medial geniculate nucleus (MGN) of the thalamus, thus greatly reducing input to the primary auditory cortex. They found that the retinal projections (whose normal target had been ablated) now projected to the MGN (whose projections had been eliminated). A visual input pathway to the primary auditory cortex was thus established. Furthermore, electrophysiological recordings from these animals showed that the auditory cortex was responsive to visual input. Thus, selective elimination of projections and target sites resulted in the reorganization of primary sensory systems. Neville (Neville, Schmidt, & Kutas, 1983) reported related findings in a group of congenitally deaf adult humans. Specifically, she recorded electrophysiological responses to visual input over traditional auditory cortical areas in congenitally deaf adults.

In subsequent studies, Sur (Angelucci, Clasca, Bricolo, Cramer, & Sur, 1997) used a somewhat different surgical procedure that allowed for closer examination of the role of both afferent input and target-specific factors in the development of these anomolously induced pathways. The modified procedure involved deafferentation of normal auditory input to MGN but sparing of normal visual targets (Angelucci et al., 1997). This procedure resulted in both the establishment of the normal visual projection pathway and in the induction of retinal projections into the MGN. Closer examination of the actual patterns of retinal connectivity revealed that, like the normal retinal projections to LGN, the retinal projections to MGN organized into distinct, eye-specific clusters. Further, the time course over which this segregation occurred was similar to that observed in the normal visual pathway. This finding suggests that the clustering phenomenon in both normal and rewired regions may be driven by retinal input. However, more fine-grained analysis showed that the actual organization of the connections within the retinal MGN clusters differed from that observed in the LGN and instead resembled patterns of cellular organization typical of MGN. This finding suggests that the organization within the eye-segregated clusters is driven by factors specific to the MGN target region.

Together, these studies showed that selective elimination of projections and target sites can induce reorganization of primary sensory systems. However, the final patterns of connectivity reflect the interaction of input and intrinsic regional specification.

Lineage and commitment.   Finally, there is evidence from fetal tissue transplantation studies that neurons from different regions of the neocortex can survive and adapt to conditions in cortical regions other than the one to which they ini-

tially migrated. For example, O'Leary and Stanfield (1989) transplanted sections of the sensorimotor and visual cortex from the brain of a late fetal rat into the opposite sites in the brain of a newborn rat. They found that cells survived the transplant and began to take on characteristics of cells in the host environment. Specifically, they found that projections from Layer 5 of the transplanted visual cortex extended permanent axons to the spinal cord, a subcortical target for sensorimotor neurons. Sensorimotor tissue transplanted into the visual cortex initially extended axons to the spinal cord, but these connections were subsequently lost. However, these cells also extended axons to the superior colliculus, a subcortical visual target, which were retained. Finally, transplanted tissue in both areas established callosal and thalamic projections typical of their host environment. These data argue against a fixed model of brain development and provide a strong case for adaptive, plastic change in the developing brain.

Brain Plasticity and Cognitive Development

A number of investigators have used animal models to examine the relations between brain and cognitive development. These studies typically use experimental lesion techniques to look at the effects of injury on the development of particular cognitive functions. A variety of factors have been shown to affect development of cognitive functions including age, site, and extent of lesion. The remainder of this section presents a few studies that illustrate these effects.

Effects of early frontal lobe lesions.   In an elegant series of studies, Goldman-Rakic (Goldman, 1971; Goldman, Rosvold, & Mishkin, 1970) examined performance of infant and juvenile monkeys on delayed response and alternating delayed response tasks. In these tasks, monkeys were trained to retrieve bait hidden at one of two locations after a period of delay. In the standard delay task, the monkey learned to retrieve the bait at the original hiding location. In the delayed alternation task, the monkey learned over a series of trials to retrieve the bait from the location opposite where it was found on the preceding trial. In adult monkeys, lesions to the dorsolateral prefrontal cortex profoundly affects performance on both of these tasks. Goldman (1971) demonstrated that timing of cortical lesions has a marked effect on performance. She compared the performance of monkeys lesioned during infancy with that of monkeys lesioned at 1 year. After comparable periods of recovery, she found that monkeys with early lesions performed significantly better than monkeys with later lesions on the delayed response task; performance on the delayed alternation was somewhat impaired in the early lesion group, but to a lesser degree than among the animals with later lesions. Longitudinal examination of these same monkeys 1 year later revealed that the monkeys with early lesions had

"lost ground" relative to normally developing monkeys on the delayed alternation task. Rather than showing the normal profile of developmental improvement with age, no change in performance was observed.

In another series of studies, Goldman (1974) examined the effects of lesions to subcortical structures that would normally have extensive connections to the dorsolateral prefrontal cortex. It has been well documented that, in adult monkeys, lesions to the caudate nucleus produce deficits on the delayed response tasks. Goldman-Rakic (Goldman, 1974) reported that, in contrast to the effects of cortical lesions, comparable impairment is observed among monkeys with early lesions.

Across this series of studies, the developmental effects associated with early versus late occurring lesions were somewhat mixed. The performance of monkeys with early cortical lesions was better than that of monkeys with later lesions both initially and with development. Nonetheless, some evidence of deficit following early lesion was apparent on a subset of the spatial tasks when performance was compared with normally developing animals. Initially, the early lesion monkeys were only mildly impaired on the delayed alternation task compared to normal controls, but with development, the disparity between the groups became more pronounced. Furthermore, early subcortical lesions produced deficits comparable to those observed among animals lesioned in adulthood.

These data suggest that the neural systems responsible for processing information at different points in development may not be identical. One account of the data reported here is that early in development, the subcortical system may play a larger role in performance on the delayed response tasks than it does later in development, thus producing the initial sparing of function with early cortical lesions on the delayed alternation task. However, the subcortical system is not optimal for this task, and in the normal course of development, the prefrontal cortical system takes over the function. The early lesioned animal continues to rely on the subcortical system and thus appears to lose ground with development relative to its normally developing, cortically intact peer. Early subcortical lesions deprive the animal of the early primary processing system, thus resulting in initial deficit and poor developmental outcome.

Site and timing of lesion.   Kolb (1995) conducted an extensive series of ablation studies on young rats to examine the effects of early lesions on cognitive outcome. Across this series, they reported differential effects of lesions depending on the age at lesion, lesion location, and environmental input following early injury. The primary cognitive task used in these experiments was a spatial problem-solving measure using the Morris water maze task (Morris, 1980). In this task, rats were placed in a tank filled with opaque liquid and trained to find a submerged platform. Normal rats solve this task in a few trials. Decrements in measures of latency to target, distance swum, and accuracy of path to target are indexes of impaired perfor-

mance on this task. Kolb found significant differences in performance related to the site and timing of the lesion. First, the effects of bilateral frontal lobe lesions (Kolb, 1987; Kolb & Elliot, 1987) differed from those of hemidecortication (Kolb, Mackintosh, Sutherland, & Whishaw, 1984; Kolb, Sutherland, & Whishaw, 1983; Kolb & Tomie, 1988). In separate studies, animals were lesioned on the first day (D1) after birth, on Day 5 (D5), or Day 10 (D10). The effects of bilateral frontal lobe lesions on D1 and D5 were devastating; when tested as adults, performance was worse than that of rats lesioned as adults (DA). The performance of the D10 rats, however, was significantly better than that of the DA rats. The effects of hemidecortication differed dramatically from that of frontal lobe lesioning. Animals with lesions administered throughout the first 2 weeks of life performed significantly better than DA rats.

Kolb suggested that the dramatic differences in the performance of the frontal lesion and hemidecorticate animals may be related to the extent of cortical disruption. Lesioning of the frontal lobes disrupts both hemispheres, whereas hemidecortication leaves one hemisphere intact (Kolb, 1995). However, Kolb also showed that even the detrimental effects of frontal lesions can be mitigated with input from the environment. In a separate study, Kolb (Kolb & Whishaw, 1989) combined the lesion methodology with the enriched environment technique. Animals with frontal lobe lesions administered at D1, D5, and D10 were raised either in an enriched environment or in isolated laboratory cages. After 3 months, the performance of the D1 and D5 rats raised in the enriched environment was indistinguishable from that of the D10 rats, indicating a dramatic enhancement in the performance of the D1 and D5 rats (Kolb & Elliot, 1987). These studies suggested that early brain development is dynamic and subject to both endogenous and external effects. Early brain damage had detrimental effects that are specific to the timing and location of the lesion. However, the effects of early injury can, at least in some cases, be mitigated by the organism's interaction with the environment.

Spatial memory and early temporal lobe lesions.   Early temporal lobe lesion studies have been used to examine the development of the brain systems mediating spatial memory in monkeys. Visual recognition memory relies in part on the visual system pathway responsible for processing information about objects. This pathway begins in the primary visual cortex, projects to multiple prestriate areas in the occipital cortex, to area TEO in the posterior inferior temporal lobe, to area TE in the anterior inferior temporal lobe, and then to limbic structures in the medial temporal lobe (amygdala, hippocampus, rhinal cortex). The interaction of area TE with the limbic system structures is critical for visual recognition memory (Mishkin, 1982; Webster, Bachevalier, & Ungerleider, 1995; Webster, Ungerleider, & Bachevalier, 1991).

The delayed nonmatch to sample (DNMS) task has been widely used to test spatial memory performance in monkeys. In the standard DNMS task, monkeys first watch as a sample object is placed over a baited well, and then they are allowed to retrieve the bait. Then after a 10-sec delay, the sample object and a novel object are placed over separate, adjacent wells. Only the well near the novel object contains a food reward. Thus, the monkey's task is to select the novel object. Monkeys are typically trained over several days to criterion of 90 correct trials out of 100. Two weeks later, they are retrained to criterion, and then a series of trials with increasing delays (10, 30, 60, or 120 sec) is presented, followed by a series of trials with increasing numbers of sample objects.

In adult monkeys, lesions to temporal area TE impair performance on the DNMS task. Bachevalier and Mishkin (1994) tested normal infant and adult monkeys and monkeys with early or late lesions to area TE. Over all of the delay and multiobject conditions, performance was 96% for normal adult monkeys and 91% for normal infant monkeys. For monkeys lesioned in adulthood, performance dropped to 71%, whereas the performance of monkeys lesioned within the first 2 weeks of life and tested at 10 months of age was near normal at 84%. Furthermore, on these tasks the enhanced performance observed in the monkeys with early lesions was retained. When these same monkeys were tested at age 4, their performance remained high at 85% (Malkova, Mishkin, & Bachevalier, 1995). These data suggest that early in development the neural substrate may be capable of compensatory reorganization. Indeed, other work by this group of investigators has suggested a possible profile of reorganization. Webster et al. (1991) showed that early in development, both area TE and area TEO establish direct connections with structures in the limbic system. In the normal course of development, the connections between TE and the limbic system stabilize and become part of the primary pathway for visual recognition memory, whereas the connections between TEO and the limbic system are lost. However, when area TE is lesioned early in development, the normally transient connections between TEO and limbic structures are retained, thus providing a possible alternative pathway for visual memory processing. In addition, these investigators demonstrated that a number of visual association areas including the superior temporal polysensory (STP) area, area PG in the inferior parietal cortex, and TF in the posterior parahippocampal gyrus, which are not typically involved in visual recognition memory, become important links following early TE lesions. In separate studies, monkeys with infant lesions of area TE were given second lesions as adults. In one group, the second lesion involved area TEO only. In a second group, only areas STP, PS, and TF were involved; and in a third group, area TEO plus STP, PG, and TF were lesioned. Only the third group of monkeys showed evidence of impairment on the DNMS task. Ablation of TEO or the visual association area alone was not sufficient to impair performance on this task. In these monkeys with early TE lesions, it was only when both TEO and the visual association areas were ablated that performance was affected (Web-

ster et al. 1995), suggesting considerable reorganization and plasticity within this temporal lobe system.

Finally, it should be noted that not all structures associated with the visual recognition memory pathway display the impressive profile of plasticity evident in areas TE and TEO. Bachevalier (Bachevalier & Mishkin, 1994; Malkova et al., 1995) showed that infant lesions to medial temporal regions result in pronounced and permanent deficits on the DNMS tasks. In addition, Webster (Webster, Bachevalier, & Ungerleider, 1994) reported that the more anterior projections of areas TE and TEO to parietal and prefrontal cortex appear to be adult-like as early as the first week of life.

Summary.   These studies of brain development suggest that the organization and state of developing neural system is the product of dynamic processes involving interactions that extend from the genes to the environment. Neural pathways develop to serve specific functions both because these pathways have evolved to process specific classes of information and because in the course of ontogenetic development they received appropriate input. Thus, the course of normal neural development is not fixed. Rather, in the normal course of development, specification and stabilization of neural systems relies on dynamic processes that are the product of the multidirectional interaction of genetic processes, neural systems, and input (for discussion of the closely related idea of probabilistic epigenesis, see Gottlieb, 1992, and Gottlieb, Wahlsten, & Lickliter, 1997). One important component of this interaction appears to be an interactive sculpting process involving initial overproduction of neural resources, competition for resources, and the elimination of nonessential connections. These sculpting processes occur within the context of ongoing additive events, creating a complex dynamic in which the biological system progressively adapts to contingencies of input and the demands of the learning environment (see Quartz & Sejnowski, 1997). The construct of plasticity is best defined by these complex dynamic processes, which are a central feature of normal brain development. They are not, as suggested by the earlier discussions in the developmental literature, ancillary, optional, or reactive. Rather, plasticity is a fundamental and essential property of brain development, normal or abnormal. Furthermore, recent data from studies of adult animals and humans suggest that these dynamic plastic processes are not unique to development. The basic processes that are pervasive in childhood appear to persist into adulthood. The next section reviews data demonstrating the operation of plastic processes in adults.

NEURAL PLASTICITY IN ADULTS

Recent studies of adult animals have provided evidence that flexibility in the organization of neural systems is not limited to the early phases of development. Studies

from a number of laboratories examining the reorganization of cortical maps in somatosensory, primary visual, primary auditory cortices, and in thalamus have demonstrated that the capacity of the neural system for plastic adaptation is not lost (for a review, see Buonomano & Merzenich, 1998).

Reorganization in the Somatosensory Cortex

In an important early series of studies, Merzenich and his colleagues (Merzenich & Jenkins 1995; Merzenich, Kaas, Wall, Nelson, et al., 1983; see also Kaas, 1991, for a review) documented systematic change in the somatosensory cortex following surgical ligation and cutting of the median nerve, which serves portions of the hand in owl and squirrel monkeys. Merzenich (Merzenich & Jenkins 1995; Merzenich, Kaas, Wall, Nelson, et al., 1983) first used microelectric mapping procedures to document patterns of neuronal activity in the region of the sensorimotor cortex associated with different parts of the hand. The distribution of nerves serving different regions of the hand is well documented. The median nerves serve the radial side of the glabrous surface of the hand including the thumb (Digit 1), index (Digit 2), and most of the middle (Digit 3) fingers and adjacent regions of the palm. The radial nerve serves the dorsal surface of the same region. The ulnar nerve serves the dorsal and ventral surfaces of the parts of the hand including the remaining parts of Digits 3, 4, and 5. The somatosensory region of the parietal cortex contains a complete topographical mapping of the hand surface.

    After mapping the normal, prelesion organization of the regions of the parietal cortex subserving the hand, Merzenich (Merzenich, Kaas, Wall, Nelson, et al., 1983) then severed the median nerve, thus eliminating input from the radial, ventral portion of the hand to the somatosensory cortex. After a period of 2 to 9 months, Merzenich recorded patterns of activity over the region of the cortex formerly activated by the median nerve. He found that the representation of the dorsal surface of Digits 1, 2, and 3 was greatly enlarged within the region formerly representing the glabrous surface of those digits. Within the reorganized region, somatotopic organization was retained. In a later study, Merzenich, Kaas, Wall, Sur, et al. (1983) examined the timecourse for the observed reorganization. Initially, the deafferented region of the cortex was silent. Then, new profiles of activity began to emerge, but they were initially incomplete and poorly organized. Over time, the somatotopic organization emerged, beginning at the border of the deafferented cortical region and gradually extending inward. Reorganization was complete after 22 days.

Reorganization in the Primary Auditory Cortex and the Visual Cortex

Similar patterns of cortical reorganization have been reported for primary auditory and visual cortex. The primary auditory cortex is typically organized tonotopically,

with high tones represented in the most caudal regions and low tones in the most rostral regions. Schwaber (Schwaber, Garraghty, & Kaas, 1993) used ototoxic chemicals to selectively destroy cochlear fibers responsive to high frequencies and, thus, eliminate input to the most caudal regions of the primary auditory cortex. Microelectrical recordings taken 2 to 3 months later in the primary auditory cortex showed reorganization. Neurons that were formerly responsive to high frequencies now responded to midrange tones. The reorganized cortex retained the tonotopic mapping, but the range now extended from low to midrange tones across the full extent of the cortex, including that region that formerly responded to high frequencies. Similar findings have been reported for the visual cortex (Gilbert, 1996; Gilbert & Wiesel, 1992; Kaas et al., 1990). Small bilateral retinal lesions initially produce a zone of unresponsive neurons in the primary visual cortex. Over a period of several months, that region of cortex gradually acquires new receptive fields from retinal areas adjacent to the lesion.

Evidence from Human Studies

Studies of human patients also suggest patterns of cortical reorganization. Mogilner et al. (1993) used magnetoencephalographic techniques to measure the distribution of activity in the hand region of the somatosensory cortex in an adult with congenital fusion of the fingers (syndactyly). Presurgical mapping of the somatosensory cortex in the region of the hand revealed poor somatotopic definition and a lack of clear boundaries between digits. Recordings taken several weeks after surgery showed dramatic change in the somatosensory map, including clearly defined representation of individual digits.

Recent work by Ramachandran (1993; Ramachandran, Rogers-Ramachandran, & Stewart, 1992; Ramachandran, Stewart, & Rogers-Ramachandran, 1992) examined sensory reorganization following limb amputation. Patients examined weeks to months after loss of an arm reported referred sensations from their phantom limb to regions of the face and spared arm segments. In three patients, Ramachandran (1993) was able to define clearly articulated reference fields across regions of the face that maintained the somatotopic organization of digits of the hand. For example, in one patient, when the cheek was touched, sensations were reported in both the cheek and the phantom thumb; when the chin was touched, sensation in both the chin and fifth digit were reported. A similar somatotopically organized representation of the hand was found in seven patients in the spared region of the arm above the amputation line. The distribution of the referred sensation is consistent with the organization of somatosensory cortex. Ramachandran (1993) noted that in normal maps of the somatosensory cortex, regions innervating the face are adjacent to the hand and arm regions. As was the case in the animal studies, it appears that regions of the adjacent cortex invade the deafferented region of the somatosensory cortex, thus giving rise to the highly organized patterns of referred sensation reported by the patients.

These data from both animal and human adults extend the range of operation for functional plasticity. They show quite clearly that plasticity is not exclusively a developmental phenomenon, and that reorganization and plastic change are properties of the mature as well as the immature organism. The greater complexity of the mature neural system may limit the range over which plastic processes may operate. It is, nonetheless, evident that the capacity for dynamic change is retained in the adult neural system.

LINGUISTIC, COGNITIVE, AND AFFECTIVE DEVELOPMENT FOLLOWING EARLY BRAIN INJURY

The data presented in the last two sections on animal models of brain development and reorganization in adult neural systems suggest a very different view of development following early injury than that offered by traditional neuropsychological accounts. Plasticity is a central process in both brain development and in the processes that underlie neural reorganization in older organisms. The data suggest that the alternative patterns of brain organization observed following early injury do not require special, transient plastic mechanisms. These data indicate that what is observed following early injury is a perturbation of a normally operating system. One property of a normally operating system is its flexibility and capacity for adaptation.

However, it is also clear that an injured system should not be an optimal system, even under conditions where the injury occurs very early. The work of investigators like Goldman-Rakic (Goldman, 1974; Goldman et al., 1970) and Kolb (1995) provide evidence of this. Data from the animal studies such as theirs demonstrate that whether a function will be preserved depends on the site and timing of the injury. How do these kinds of findings apply to humans? The following section summarizes data from a large prospective study of cognitive, linguistic, and affective development in a group of children who suffered unilateral, focal brain injury in the prenatal or perinatal period (Stiles, Bates, Thal, Trauner, & Reilly, 1998). Data from this large study include a range of behavioral domains. One important finding from this study has been that the profiles of development emerging from individual behavioral domains are somewhat different with regard to the extent of initial deficit and developmental trajectory. There is evidence of initial deficit, in at least some subset of the focal lesion (FL) population, for all of the domains thus far examined, and the data examining the profiles of developmental "recovery" are mixed. These findings suggest that the optimistic reports from the neuropsychological literature may need qualification; even these very early injuries have notable consequences. An early injury that destroys a significant part of the neural substrate creates a nonoptimal system. A normal developmental trajectory should not be expected. Yet, there is ample documentation for attenuated deficit following early, as compared to late, occurring injury. The purpose of this work has been to specify the content and course of development following early injury. Central to our understanding of these developmental

processes is the explication of nature and role of neural plasticity in determining brain organization and development.

The work with the FL population has been guided by the following set of questions:

1. Are specific behavioral deficits evident early in development?
2. Is the association between pattern of behavioral deficit and site of brain injury among children comparable to the patterns of association observed among adults?
3. Is there evidence of a persistent behavioral deficit over time, or is there significant recovery of function?
4. Do patterns of behavioral deficit change over time?

I have attempted to address each of these questions within three behavioral domains: language, spatial cognitive processing, and affect. The major findings of this work are summarized later.

Population Description

All of the children in this study suffered localized cortical brain injury either prenatally or within the first 6 months of life. Within the population of this study, the most common cause of injury is stroke. Children with focal brain injury are typically identified in one of three ways: (a) neonatal seizures; (b) hemiplegia; or (c) routine ultrasound for other medical reasons such as meconium staining, premature birth, and so forth. The identification of lesion site is based on results of neuroimaging using either CT scan or MRI.

The common inclusionary factor among the children in this population was the documented injury to a circumscribed region of the brain. Children were excluded from the study if there was evidence of multiple lesions, disorders with potential of more global damage such as congenital viral infection, maternal drug or alcohol abuse, bacterial meningitis, encephalitis, severe anoxia, or chronic lesions such as tumor or arteriovenus malformation. Within the population, children were classified by site of lesion; that is, whether lesion is on the left or right side of the brain and which lobe or lobes are involved. Finally, on gross assessment, the children in the population do well behaviorally, both individually and as a group. They typically score within the normal range on standardized IQ measures and attend public schools.

Language

The studies of language acquisition in the FL population began with the earliest stages of acquisition and extended well into the school-age period. The studies be-

gan with a model of early deficit that mirrored those observed in adults with focal brain injury. Very generally, it was predicted that children with LH injury would have more pronounced deficits than children with RH injury. Within the LH group, it was predicted that production deficits would be associated with anterior injury, and comprehension deficits with posterior injury. Data from this first large prospective study of language acquisition provided the opportunity to document the process of language acquisition following early insult to different brain regions. The profiles that have emerged from this prospective approach to the study of language in this population have been both surprising and intriguing (for recent review of these findings, see Stiles et al., 1998). They provide insight into the issues of specification of deficit and functional recovery.

The first major finding from this study was the pervasiveness of language acquisition deficits in the FL population. The substantial majority of children in the population were delayed in early language acquisition. Delay was associated with lesions to widely distributed brain regions. Furthermore, the association between the pattern of deficit and the site of the lesion did not correspond to typical profiles in adults. In the earliest stages of language acquisition between about 10 and 17 months, receptive deficits were more common in children with RH injury than with LH injury. These children were also delayed in the production of communicative gestures. During this period, children with left temporal (LT) injury were delayed in word production but performed within the normal range on comprehension and gesture. This profile among the children with LT injury contradicts the profile of deficit observed in adults with left posterior injury. Among adults, production is typically spared, whereas comprehension is impaired.

Between 19 and 31 months, children with LT injury were delayed in expressive vocabulary and early grammar production. Delays in vocabulary and grammar were also noted in children with either left or right frontal involvement. Delays in grammar persisted through about 42 months in children with LT injury. However, by this time, children with frontal injury fell within the normal range. By the time children in this population reached age 5, there was little evidence of language impairment, at least for the basic features of language production and comprehension. Children fell within the normal range and appeared to have mastered the basic semantic and morphosyntactic structures of their language.

However, recent data from older children with focal brain injury indicate persistent, subtle disorders in the use of language, which persists well into the school-age period. In a study of narrative discourse, Reilly (Reilly, Bates, & Marchman, 1998) reported that children with RH and LH lesions showed comparable delays in both the use of morphosyntactic structures and in the understanding of narrative structure. Narratives provide a complex discourse context in which to examine narrative skills as well as the expression of language and affect. In the basic narrative task, the children were asked to look through a wordless picture book, *Frog, Where Are You?* (Mayer, 1969), and then, while looking at the book, to tell

the story to an adult. Analyses focused on different levels of narrative production: (a) microstructures—morphology and syntax, (b) macrostructures—narrative components and theme, and (c) affective expression in the form of evaluation and affective prosody. Stories from 31 children ranging in age from 3 years, 7 months to 9 years, 4 months and including 13 with RH damage (RHD) and 18 with LH damage (LHD) were analyzed. Age-related changes in aspects of lexical production, morphological errors, syntactic complexity, and narrative complexity are typically observed across the school-age period. In every domain, except the lexical production, children with focal brain injury (as a group) were delayed relative to age-matched normal controls.

In contrast to the global lag displayed by the school-age FL group, the four younger children (ages three years, 7 months–5 years, 0 months) with RHD scored well within the normal range for their age in the frequency and diversity of complex syntax. However, the RHD children in the older group (over 5 years, 0 months) were no different from older children with damage on the left, and both FL groups performed significantly below normal controls. There was also a significant interaction between age and presence or absence of LT damage in morphological errors and in syntactic diversity, suggesting a specific effect of LT damage on grammatical development prior to (but not after) age 5. Because these interactions between age and lesion site are based on small samples, and because so few effects emerged across a large number of comparisons, they are presented with a strong note of caution. On the other hand, these data are consonant with those of Bates et al. (1997) on the emergence of grammar between 10 and 44 months of age. These investigators found no significant differences between LHD and RHD children per se on any measure of language production, but they did find significant delays in both vocabulary and grammar in children whose injuries involve the LT cortex. The narrative data presented here suggest that this particular correlation between language symptoms and lesion site may continue up to age 5, but it does not appear among the older children, leading to the hypothesis that region-specific effects on language development have been resolved by 5 to 6 years of age—presumably due to the emergence of alternative forms of brain organization for language. It is interesting that this is also the point at which the basic structures of morphology and grammar have been acquired in children who are developing on a normal schedule.

Spatial Cognition

The studies of spatial cognition have focused on a particular basic aspect of spatial processing—spatial pattern analysis. Spatial analysis is defined as the ability to specify both the parts and the overall configuration of a pattern. Thus, it involves both the ability to segment a pattern into a set of constituent parts and the ability to

integrate those parts into a coherent whole. Studies with adults have shown that different patterns of spatial deficit are associated with LH and RH lesions (e.g., Arena & Gainotti, 1978; Delis, Kiefner, & Fridlund, 1988; Delis, Kramer, & Kiefner, 1988; Delis, Robertson, & Efron, 1986; Gainotti & Tiacci, 1970; McFie & Zangwill, 1960; Piercy, Hecaen, & De Ajuriaguerra, 1960; Ratcliff, 1982; Swindell, Holland, Fromm, & Greenhouse, 1988; Warrington, James, & Kinsbourne, 1966). Injury to the left posterior brain region results in disorders involving difficulty defining the parts of a spatial array, whereas patients with right posterior lesions have difficulty with the configural aspects of spatial pattern analysis. In contrast to the findings of the studies of language acquisition, disorders of spatial analytic processing analogous to those reported for adults have been identified in these studies of young children with early focal brain injury. These deficits tend to be less marked among children than adults, but the association between the site of the lesion and the specific disorder are quite similar (for recent review, see Stiles et al., 1998).

Construction tasks have been a major source of data on patterns of impairment in the FL population. A recent modeling study with 3- to 6-year-old children (Stiles, Stern, Trauner, & Nass, 1996) showed evidence of impairment among children with both RH and LH injury. Children with LH injury initially showed delay on the task, producing simplified constructions. By the time they were 4 years old, most of the children were able to produce accurate copies of the target constructions; however, the procedures they used in copying the forms were greatly simplified. This dissociation between product and process persisted at least through age 6, when testing on this task was terminated. Children with RH injury were initially delayed on this task. Like the 3-year-olds with LH injury, they produced only simple constructions. At about age 4, they began to produce more complex constructions, but they were disordered and poorly configured. However, the procedures the children used to generate their ill-formed constructions were comparable to age-matched controls. By the time these children were 6 years old, they were able to copy the targets accurately, but like their LH injured peers, they now used simplified procedures. This study provides evidence of both impairment and development. Close examination of process suggests persistent deficit.

The development of compensatory strategies was further explored in a study of free drawing. These tasks extended the age range of the investigation by focusing on children in the school-age period. This study of drawing showed that young children with RH injury have considerable difficulty drawing organized pictures (Stiles-Davis, Janowsky, Engel, & Nass, 1988). At about age 5, their drawings are typically disorganized. The children produce the parts of objects, but they fail to organize them systematically on the page. However, these longitudinal studies have shown considerable improvement with age. This study of graphic formula production suggested that a specific compensatory strategy could account for this

pattern of change. Reliance was tested on graphic formulas using a task developed by Karmilloff-Smith (1990) in which children were asked to first draw a house and then an impossible house (Stiles, Trauner, Engel, & Nass, 1997). The typical response among normal children and among children with LH injury was to distort the spatial configuration of the house. However, in this longitudinal sample of six RH children tested every 6 to 12 months for a period from 3 to 6 years, configural distortion was not used. Instead, the children used a variety of nonconfigurational solutions for solving the problem. These findings suggest that even when output appears normal, more detailed analyses can reveal evidence of compensatory strategies and continuing deficit.

Data from two other copying tasks are consistent with the findings previously reported. Children showed initial impairment on both a memory reproduction task using hierarchically organized forms and on the copying version of the Rey-Osterrieth Complex Figure (Osterrieth, 1944; Rey, 1941). On the hierarchical forms task, children were asked to reproduce from memory a series of hierarchically organized patterns (see Figure 2). Each pattern had two levels of pattern structure: the local elements and the more global integrated whole. Studies of adult stroke patients using these kinds of stimuli have shown that patients with LH injury have difficulty reproducing the local level elements, whereas patients with RH injury have difficulty with the global level pattern. Consistent with data from adults, children with LH injury had difficulty remembering the local level elements, whereas the children with RH injury appear to remember the global structure, but have difficulty reproducing it accurately.

This study of performance on the Rey-Osterrieth Complex Figure (Osterrieth, 1944; Rey, 1941) task used a new measure for scoring the procedures by which children attempt to reproduce the form (Akshoomoff & Stiles, 1995a, 1995b). The measure provides a systematic account of normal patterns of developmental change in the school-age period. These analyses included longitudinal data from 18 FL children between the ages of 6 and 13 (Akshoomoff, Feroleto, Doyle, & Stiles, 2000; see also Akshoomoff & Stiles, in press). The drawings from the younger children were sparser and less accurate than normal children the same age. However, there were no striking differences between the young children with early LH and RH injury (see Figure 3). It appears that the ability to identify the elements of a spatial form and to integrate those parts is necessary for this task, thus a deficit in either aspect of spatial analysis affects performance. With development, performance improved and the children were able to produce recognizable copies of the Rey-Osterrieth Complex Figure form. However, analysis of the procedures they used indicated continuing spatial impairment. Across the school-age period, the children used the simplest and least sophisticated procedural strategy to copy the form.

The construction tasks reviewed here present a common, converging profile of development following early focal brain injury. For each task, there was initially
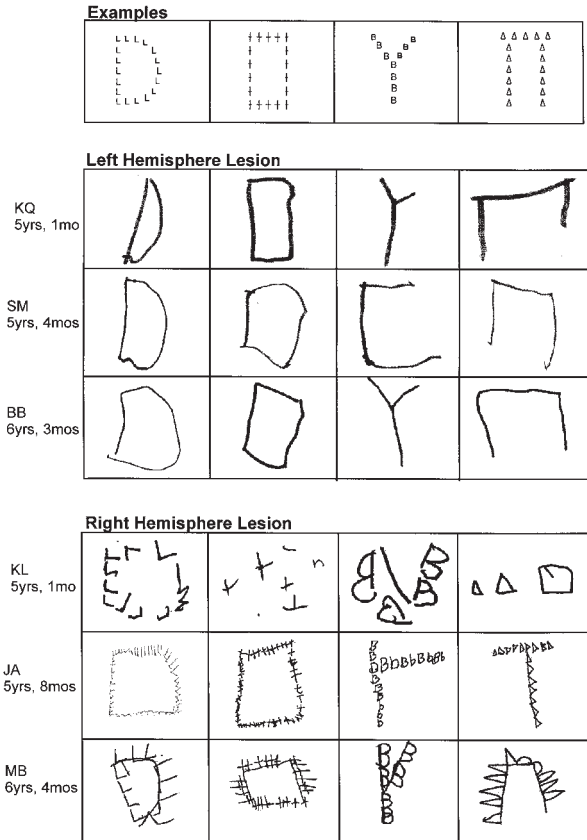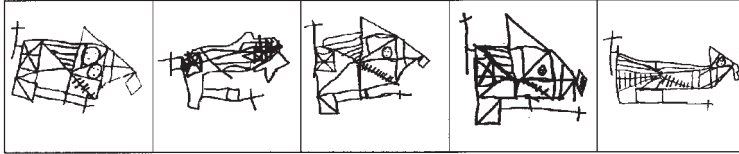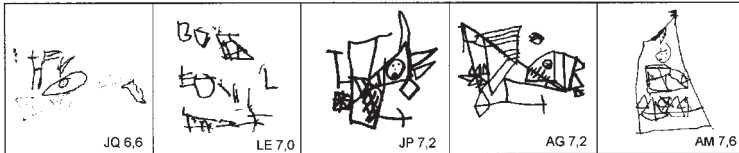
FIGURE 2   Children with either left hemisphere (LH) or right hemisphere (RH) injury were asked to reproduce the model hierarchical forms from memory. LH injury results in difficulty reproducing the parts, or local elements of the forms, whereas RH injury results in greater difficulty reproducing the larger, or global, configuration.

evidence of marked deficit, and the associations of deficit to lesion site were consistent with adult patterns. With development, performance improved and the children's output, the products of their construction efforts, became indistinguishable from normal. However, there is consistent evidence that the processes by which children generate their constructions are not developing normally. This pattern is evident from preschool through the school-age period. Thus, although performance improves with development, the data indicate that the processes underlying improved performance on these tasks may diverge from normal. These deficits in process provide evidence of persistent spatial cognitive deficits in this population of children.

Normal - 6yr

Left Hemisphere Lesion

JQ 6,6   LE 7,0   JP 7,2   AG 7,2   AM 7,6

Right Hemisphere Lesion

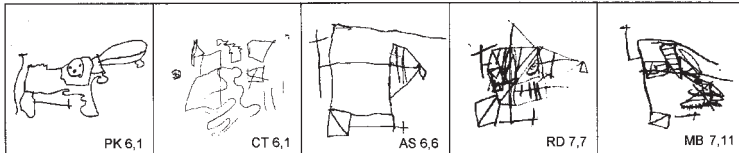PK 6,1   CT 6,1   AS 6,6   RD 7,7   MB 7,11

FIGURE 3   Children with either left hemisphere or right hemisphere injury were asked to copy the Rey Osterreith Complex Figure. As these examples show, injury to either hemisphere results in difficulty reproducing the complicated pattern. With development, the accuracy of the children's copies improves, but their strategy for reproducing the pattern remains piecemeal until well into the teenage years.

Affect

This study of affective development has focused on two aspects of emotional behavior. The first is affective facial expression. This study focused on the earliest phase of development, examining production of facial affect among children in the first and second year of life. The second area of investigation is the comprehension of affective prosody. This study examined possible dissociations in responses to linguistic and affective prosody in school-age children.

By their first birthday, children are fluent affective communicators. The development of affective facial expression in infants with focal brain damage thus provides a promising area in which to investigate the developing neural substrates of emotions as well as to ascertain the degree to which the infant brain is specified for particular behavioral functions. To this end, both positive and negative affective expression in 12 infants (6–24 months) with prenatal or perinatal unilateral focal brain damage (6 RHD and 6 LHD) and their age- and gender-matched controls (Reilly, Stiles, Larsen, & Trauner, 1995) were examined. Infants were videotaped in free and semistructured tasks with the mother and with an experimenter, and interactions were microanalytically coded, including the use of Ekman and Friesen's Facial Action Coding System (Ekman & O'Sullivan, 1988). These results from the

cross-sectional data demonstrate a consistent pattern of affective expression: both normal infants and babies with posterior LHD exhibit the full range of affective expressions appropriate to the elicited situations. In contrast, the infants with RHD, especially those with posterior involvement, showed marked affective impairment to positive, but not to negative, stimulation. It is interesting to note that longitudinal data from the 1 infant with isolated right frontal damage showed no such impairment, whereas comparable data from the infant with left frontal damage showed enhanced negative affect and depressed positive affect. Overall, these data are consistent with the adult neuropsychological findings that the RH plays a critical role in affective expression (Blonder, Burns, Bowers, Moore, & Heilman, 1993; Borod, Koff, Lorch, & Nicholas, 1985) and the electrophysiological studies of Fox and Davidson (1988; Fox, 1994), which implicate the frontal lobes in the mediation of approach or avoidant emotions. The findings expressed in this article are dramatic in that they provide evidence dating to the middle of the first year of life and suggest that for affective facial expression, the infant brain shows functional specification early on.

In adults, damage to the RH produces deficits in the comprehension and expression of affective meaning in language. LH damage may cause difficulty with the understanding and use of the more linguistic aspects of nonverbal communication. Prior to the work reported here, no similar studies had been reported of individuals who suffered early unilateral brain damage. In this study, comprehension and expression of affective and linguistic prosody were tested in individuals with documented unilateral brain damage of prenatal or perinatal onset, as well as in matched controls. Fifty-six individuals participated in the study. Of these, 28 participants had a single, unilateral focal brain lesion, each documented by a neuroimaging procedure. Thirteen individuals had LH lesions (age range: 6.0–15.58 years, $M = 8.8 \pm 3.0$), and 15 had RH lesions (age range: 5.5–20.33 years, $M = 11.5 \pm 5.1$). The results of this study showed that the RH lesion group demonstrated difficulty on tasks involving comprehension and expression of affective prosody, and to a lesser extent on tests of linguistic prosody. Individuals with LH lesions performed more poorly than controls on tests of linguistic, but not affective, prosody. These findings indicate that even after very early unilateral brain damage, prosodic deficits similar to those found in adults can be demonstrated. The findings are consistent with the findings from the study of affective facial expression and provide further evidence that there are limitations on the extent to which the developing brain can reorganize after early injury.

Summary.   These longitudinal studies of the effects of early brain injury present a different view of development than that offered by the traditional neuropsychological accounts. Across domains, evidence of initial deficit was found; in each domain, developmental change was observed. However, the devel-

opmental profiles vary widely across domain in terms of both the persistence and magnitude of deficit and in the consistency with which the mapping of specific deficit to lesion site corresponds to adult profiles. There is no simple or uniform pattern of deficit and recovery that can be captured by the traditional models of sparing, crowding, or redundancy.

In the early stages of acquisition, language is not spared. It is affected by lesions to widely distributed brain regions; indeed it is affected by lesions to areas that do not typically affect adult language. The nature of the deficits also diverges from the adult models. For example, children with left posterior injury show evidence of production, but not comprehension deficits, thus contradicting the adult model. These data suggest that the acquisition of language depends on different neural systems than those used by proficient language users. Event-related potential studies of early language processing support this view. Neville, Nicol, Barss, Forster, and Garrett (1991) showed that widely distributed, bilateral brain areas are activated during lexical processing in normally developing 13-month-olds with limited production vocabularies. With development, specifically following the vocabulary burst at about 20 months, the activation profiles change dramatically and much more closely resemble the predominantly LH patterns observed in adults. These data suggest that early language acquisition relies on a wide array of brain areas, and this could account for the ubiquitous patterns of language deficit in the FL population. Initially, there does not appear to be well-defined sites for language processing, rather localization of the system for linguistic processing appears to emerge with development and may be defined by computation biases in the neural system. With development, language among children in the FL population improves markedly, such that by the end of the preschool period the children master the basic lexical and morphosyntactic structures of their language. There is continuing evidence of subtle impairment in their narrative discourse. However, these profiles are no longer specific to site of lesion, rather evidence of subtle language decrement is evident across the population. This developmental profile is consistent with an account of a language system that is emergent and to some extent self-organizing. This account does not require preferential sparing of language following early brain injury. Rather, in the normal course of development, the neural substrate for language is not initially well-specified. As a result, widely distributed brain regions participate in language acquisition, and thus, lesions to many different brain areas can impair language acquisition. This initial distribution of processing may also provide options, which allow for the development of alternative patterns of neural mediation for language. Thus, initial underspecification of the neural substrate for language may account for the patterns of deficit and development observed following early injury.

Data from spatial-analytic processing present a very different profile. Children show evidence of subtle and persistent deficit following early brain injury. The mapping of site of injury to functional deficit is consistent with adult profiles.

Across spatial construction tasks, the developmental data are consistent with a model of compensation against a backdrop of persistent, well-specified, but subtle deficit. It should be noted that spatial deficits observed in children with LH injury do not require a linguistic crowding account. A wealth of recent data from both normal and patient studies demonstrate that spatial analytic processing is bilaterally mediated. Normal processing of information in visual arrays depends on inferior temporal regions in both hemispheres (Martinez et al., 1997). Processing functions in the two hemispheres are different, and different patterns of spatial deficit should be evident following LH and RH injury. Thus, the children with LH injury do show spatial deficits, but it is not necessary to postulate a RH linguistic crowding effect to account for them. Indeed, the specific nature of impairment in these children is consistent with injury to the LH spatial processing system. Functional imaging data from a case study of a child with early left parietal temporal involvement confirms this suggestion (Stiles, 1998). This child showed consistent RH activation in both the global and the local processing conditions.

The profiles of affective impairment and development following early injury are consistent with those observed for spatial analytic processing. From the first year of life, children manifest evidence of affective deficit, and the correspondence between site of lesion and behavioral disorder is consistent with those observed among adults. The persistence of affective deficits is suggested by the studies of production and comprehension of affective prosody. During the school-age period, children with focal brain injury present with patterns of prosodic deficit that is consistent with adult profiles. Specifically, linguistic prosody is more affected than affective prosody among children with LH injury, whereas the reverse profile holds for children with RH injury.

Extending the arguments previously outlined, the cross-domain differences observed between linguistic, spatial analytic, and affective processing may be related to the initial specificity of the neural system for the different functions. Spatial information processing and, arguably, affective processing are phylogenetically older functions than language processing, and their neural substrates may be much more highly specified and constrained. Thus, there is less capacity to achieve an alternative solution to the problem of processing spatial or affective information. However, it is also clear that the effects of early injury on spatial and affective processing are markedly attenuated relative to those of later injury. This suggests that the capacity for reorganization and functional compensation is retained within these more constrained systems.

CONCLUSION

The data presented in this article represent an alternative to the traditional neuropsychological account of early brain plasticity. The profiles of development observed in these longitudinal data can be accounted for by the same mechanisms

that underlie normal brain development. It is not necessary to postulate special mechanisms such as selective preservation or crowding to account for the kinds of changes observed following early brain injury. In both normal brain development and in development following early injury, there are basic, biological constraints on the ways in which neural systems can develop (e.g., Allendoerfer & Schatz, 1994; Flanagan & Vanderhaeghen, 1998; Goodman, 1996). However, the fact that there are constraints does not mean that development proceeds as a passive unfolding of predetermined systems, or even as well-defined systems awaiting an external trigger. Neural development is an active, reciprocal process. The construct of functional plasticity refers to the dynamic and adaptive processes that underlie brain development and function. The normally developing brain is dynamic and plastic. Initially, there is a profusion of connections throughout the brain. With development, many of these early connections are withdrawn, whereas others are retained. This selective retention process is presumed to be the product of competitive processes that are driven to a large extent by input. The structure and organization of the mature normal brain is the product of these plastic, competitive processes. Furthermore, the capacity for plastic change is never completely lost. A large number of animal studies have shown that, across a range of mammalian species, patterns of neural connectivity in the adult organism are altered by change in input to the system. Recent work suggests that experience can even affect the survival of new neurons in the adult brain. By this account, plasticity is a central feature of brain development and learning; it is not a system response to pathological insult.

When plasticity is viewed as a necessary part of brain development, rather than a possible alternative in the case of early insult, a very different perspective on the effects of early brain injury on development emerges. The developing brain is a dynamic, responsive, and to some extent self-organizing, system. Early injury constitutes a perturbation of normal development. Specific neural resources are lost, and there should be consequent impairment of the system; and that is precisely what is observed in language, visuospatial, and affective processing. However, it is also a developing system and, therefore, a system with an exuberance of resources, the fate of which are determined in large measure by input. Thus, the magnitude and duration of the initial impairment may well depend on a range of factors, such as the timing of insult, extent and location of injury, and specificity of the neural substrate for the function under consideration. Early damage to the neural substrate insures that neural organization will differ from that observed following normal development, but the processes by which that organization is achieved need not be fundamentally different.

ACKNOWLEDGMENTS

REFERENCES

Akshoomoff, N. A., Feroleto, C. C., Doyle, R. E., & Stiles, J. (2000). *The impact of early unilateral brain injury on perceptual organization and visual memory.* Manuscript submitted for publication.

Akshoomoff, N. A., & Stiles, J. (1995a). Developmental trends in visuospatial analysis and planning: I. Copying a complex figure. *Neuropsychology, 9,* 364–377.

Akshoomoff, N. A., & Stiles, J. (1995b). Developmental trends in visuospatial analysis and planning: II. Memory for a complex figure. *Neuropsychology, 9,* 378–389.

Akshoomoff, N. A., & Stiles, J. (in press). Children's performance on the Rey-Osterrieth Complex Figure and the development of spatial analysis. In J. Knight & E. Kaplan (Eds.), *The handbook of Rey-Osterrieth Complex Figure usage: Clinical research and application.*

Allendoerfer, K. L., & Schatz, C. J. (1994). The subplate, a transient neocortical structure: Its role in the development of connections between thalamus and cortex. *Annual Review of Neuroscience, 17,* 185–218.

Almli, C. R., & Finger, S. (1984). *Early brain damage. Volume 1: Research orientations and clinical observations.* Orlando, FL: Academic.

Angelucci, A., Clasca, F., Bricolo, E., Cramer, K. S., & Sur, M. (1997). Experimentally induced retinal projections to the ferret auditory thalamus: Development of clustered eye-specific patterns in a novel target. *The Journal of Neuroscience, 17,* 2040–2055.

Arena, R., & Gainotti, G. (1978). Constructional apraxia and visuoperceptive disabilities in relation to laterality of cerebral lesions. *Cortex, 14,* 463–473.

Bachevalier, J., & Mishkin, M. (1994). Effects of selective neonatal temporal lobe lesions on visual recognition memory in rhesus monkeys. *The Journal of Neuroscience, 14,* 2128–2139.

Bates, E. A., Thal, D., Trauner, D., Fenson, J., Aram, D., Eisele, J., & Nass, R. (1997). From first words to grammar in children with focal brain injury. *Developmental Neuropsychology, 13,* 275–343.

Bennett, E. L., Rosenzweig, M. R., & Diamond, M. C. (1969). Rat brain: Effects of environmental enrichment on wet and dry weights. *Science, 163,* 825–826.

Blonder, L., Burns, A. F., Bowers, D., Moore, R. W., & Heilman, K. M. (1993). Right hemisphere facial expressivity during natural conversation. *Brain and Cognition, 21,* 44–56.

Borod, J. C., Koff, E., Lorch, M. P., & Nicholas, M. (1985). Channels of emotional expression in patients with unilateral brain damage. *Archives of Neurology, 42,* 345–348.

Buonomano, D. V., & Merzenich, M. M. (1998). Cortical plasticity: From synapses to maps. *Annual Review of Neuroscience, 21,* 149–186.

Changeux, J. P., & Danchin, A. (1976). Selective stabilization of developing synapses as a mechanism for the specification of neuronal networks. *Nature, 264,* 705–712.

Cowan, W. M., Fawcett, J. W., O'Leary, D. D., & Stanfield, B. B. (1984). Regressive events in neurogenesis. *Science, 225,* 1258–1265.

Crair, M. C., Gillespie, D. C., & Stryker, M. P. (1998). The role of visual experience in the development of columns in cat visual cortex. *Science, 279,* 566–570.

Delis, D. C., Kiefner, M. G., & Fridlund, A. J. (1988). Visuospatial dysfunction following unilateral brain damage: Dissociations in hierarchical hemispatial analysis. *Journal of Clinical and Experimental Neuropsychology, 10,* 421–431.

Delis, D. C., Kramer, J. H., & Kiefner, M. G. (1988). Visuospatial functioning before and after commissurotomy: Disconnection in hierarchical processing. *Archives of Neurology, 45,* 462–465.

Delis, D. C., Robertson, L. C., & Efron, R. (1986). Hemispheric specialization of memory for visual hierarchical stimuli. *Neuropsychologia, 24,* 205–214.

Dennis, M. (1980). Capacity and strategy for syntactic comprehension after left or right hemidecortication. *Brain and Language, 10,* 287–317.

Dennis, M., & Kohn, B. (1975). Comprehension of syntax in infantile hemiplegics after cerebral hemidecortication: Left-hemisphere superiority. *Brain and Language, 2,* 472–482.

Dennis, M., Lovett, M., & Wiegel-Crump, C. A. (1981). Written language acquisition after left or right hemidecortication in infancy. *Brain and Language, 12,* 54–91.

Dennis, M., & Whitaker, H. A. (1976). Language acquisition following hemidecortication: Linguistic superiority of the left over the right hemisphere. *Brain and Language, 3,* 404–433.

Dennis, M., & Whitaker, H. A. (1977). Hemispheric equipotentiality and language acquisition. In S. J. Segalowitz & F. A. Gruber (Eds.), *Language development and neurological theory* (pp. 93–106). New York: Academic.

Ekman, P., & O'Sullivan, M. (1988). The role of context in interpreting facial expression: Comment on Russel and Fehr (1987). *Journal of Experimental Psychology: General, 117,* 86–88.

Finger, S., LeVere, T. E., Almli, R., & Stein, D. G. (1988). *Brain injury and recovery: Theoretical and controversial issues.* New York: Plenum.

Flanagan, J. G., & Vanderhaeghen, P. (1998). The ephrins and EPH receptors in neural development. *Annual Review of Neuroscience, 21,* 309–345.

Fox, N. (1994). Dynamic cerebral processes underlying emotion regulation. *The Development of Emotion Regulation: Monographs of the Society for Research in Child Development, 59*(2–3, Serial No. 240).

Fox, N. A., & Davidson, R. J. (1988). Patterns of brain electrical activity during facial signs of emotion in 10-month-old infants. *Developmental Psychology, 24,* 230–236.

Gainotti, G., & Tiacci, C. (1970). Patterns of drawing disability in right and left hemispheric patients. *Neuropsychologia, 8,* 379–384.

Gilbert, C. D. (1996). Plasticity in visual perception and physiology. *Current Opinion in Neurobiology, 6,* 269–274.

Gilbert, C. D., & Wiesel, T. N. (1992). Receptive field dynamics in adult primary visual cortex. *Nature, 356,* 150–152.

Goldman, P. S. (1971). Functional development of the prefrontal cortex in early life and the problem of neuronal plasticity. *Experimental Neurology, 32,* 366–387.

Goldman, P. S. (1974). An alternative to developmental plasticity: Heterology of CNS structures in infants and adults. In D. G. Stein, J. J. Rosen, & N. Butters (Eds.), *Plasticity and recovery of function in the central nervous system* (pp. 149–174). New York: Academic.

Goldman, P. S., Rosvold, H. E., & Mishkin, M. (1970). Selective sparing of function following prefrontal lobectomy in the infant monkey. *Experimental Neurology, 29,* 221–226.

Goodman, C. S. (1996). Mechanisms and molecules that control growth cone guidance. *Annual Review of Neuroscience, 19,* 341–377.

Gottlieb, G. (1992). *Individual development and evolution. The genesis of novel behavior.* New York: Oxford University Press.

Gottlieb, G., Wahlsten, D., & Lickliter, R. (1997). The significance of biology for human development: A developmental psychobiological systems view. In R. Lerner (Ed.), *Handbook of child psychology: Vol. 1, Theoretical models of human development* (5th ed.). New York: Wiley.

Gould, E., Reeves, A. J., Fallah, M., Tanapat, P., Gross, C. G., & Fuchs, E. (1999). Hippocampal neurogenesis in adult Old World primates. *Proceedings of the National Academy of Sciences, USA, 96,* 5263–5267.

Greenough, W. T., & Chang, F. F. (1989). Plasticity of synapse structure and pattern in the cerebral cortex. *Cerebral Cortex, 7,* 391–440.

Hebb, D. O. (1947). The effects of early experience on problem solving at maturity. *American Psychologist, 2,* 306–307.

Hubel, D. H., & Wiesel, T. N. (1967). Cortical and callosal connections concerned with the vertical meridian of visual fields in the cat. *Journal of Neurophysiology, 30,* 1561–1573.

Hubel, D. H., & Wiesel, T. N. (1970). The period of susceptibility to the psychological effects of unilateral eye closure in kittens. *Journal of Physiology, 206,* 419–436.

Hubel, D. H., Wiesel, T. N., & LeVay, S. (1977). Plasticity of ocular dominance columns in monkey striate cortex. *Philosophical Transactions of the Royal Society of London, Series B: Biological Sciences, 278,* 377–409.

Huttenlocher, P. R. (1990). Morphometric study of human cerebral cortex development. *Neuropsychologia, 28,* 517–527.

Huttenlocher, P. R., & Dabholkar, A. S. (1997). Regional differences in synaptogenesis in human cerebral cortex. *The Journal of Comparative Neurology, 387,* 167–178.

Huttenlocher, P. R., de Courten, C., Garey, L. J., & Van der Loos, H. (1982). Synaptogenesis in human visual cortex—evidence for synapse elimination during normal development. *Neuroscience Letters, 33,* 247–252.

Janowsky, J. S. (1993). The development and neural basis of memory systems. In M. Johnson (Ed.), *Brain development and cognition: A reader* (pp. 665–678). Cambridge, MA: Blackwell.

Jones, T. A., Kleim, J. A., & Greenough, W. T. (1996). Synaptogenesis and dendritic growth in the cortex opposite unilateral sensorimotor cortex damage in adult rats: A quantitative electron microscopic examination. *Brain Research, 733,* 142–148.

Jones, T. A., Klintsova, A. Y., Kilman, V. L., Sirevaag, A. M., & Greenough, W. T. (1997). Induction of multiple synapses by experience in the visual cortex of adult rats. *Neurobiology of Learning and Memory, 68,* 13–20.

Kaas, J. H. (1991). Plasticity of sensory and motor maps in adult mammals. *Annual Review of Neuroscience, 14,* 137–167.

Kaas, J. H., Krubitzer, L. A., Chino, Y. M., Langston, A. L., Polley, E. H., & Blair. N. (1990). Reorganization of retinotopic cortical maps in adult mammals after lesions of the retina. *Science, 248,* 229–231.

Karmilloff-Smith, A. (1990). Constraints on representational change: Evidence from children's drawing. *Cognition, 34,* 57–83.

Kempermann, G., & Gage, F. H. (1998). Closer to neurogenesis in adult humans. *Nature Medicine, 4,* 555–556.

Kempermann, G., Kuhn, H. G., & Gage, F. H. (1997). More hippocampal neurons in adult mice living in an enriched environment. *Nature, 386,* 493–495.

Kennard, M. A. (1936). Age and other factors in motor recovery from precentral lesions in monkeys. *American Journal of Physiology, 115,* 138–146.

Kennard, M. A. (1938). Reorganization of motor function in the cerebral cortex of monkeys deprived of motor and premotor areas in infancy. *Journal of Neurophysiology, 1,* 477–496.

Kennard, M. A. (1942). Cortical reorganization of motor function. Studies on series of monkeys of various ages from infancy to maturity. *Archives of Neurology and Psychiatry, 48,* 227–240.

Kohn, B., & Dennis, M. (1974). Selective impairments of visuospatial abilities in infantile hemiplegics after right cerebral hemidecortication. *Neuropsychologia, 12,* 505–512.

Kolb, B. (1987). Recovery from early cortical damage in rats. I. Differential behavioral and anatomical effects of frontal lesions at different ages of neural maturation. *Behavioral Brain Research, 25,* 205–220.

Kolb, B. (1995). *Brain plasticity and behavior*. Hillsdale, NJ: Lawrence Erlbaum Associates, Inc.

Kolb, B., & Elliot, W. (1987). Recovery from early cortical damage in rats. II. Effects of experience on anatomy and behavior following frontal lesions at 1 or 5 days of age. *Behavioral Brain Research, 26,* 47–56.

Kolb, B., Mackintosh, A., Sutherland, R. J., & Whishaw, I. Q. (1984). Evidence for anatomical but not functional asymmetry in the hemidecorticate rat. *Behavioral Neuroscience, 96,* 44–58.

Kolb, B., Sutherland, R. J., & Whishaw, I. Q. (1983). Neonatal hemidecortication or frontal cortex abla-
tion produce similar behavioral sparing but opposite effects on morphogenesis of remaining cortex.
Behavioral Neuroscience, 97, 154–158.

Kolb, B., & Tomie, J. (1988). Recovery form early cortical damage in rats. IV. Effects of
hemidecortication at 1, 5, or 10 days of age. *Behavioral Brain Research, 28,* 259–274.

Kolb, B., & Whishaw, I. Q. (1989). Plasticity in the neocortex: Mechanisms underlying recovery from
early brain damage. *Progress in Neurobiology, 32,* 235–276.

Krashen, S. D. (1973). Lateralization, language learning, and the critical period: Some new evidence.
Language Learning, 23, 63–74.

Lenneberg, E. H. (1967). *Biological foundations of language.* New York: Wiley.

LeVay, S., Wiesel, T. N., & Hubel, D. H. (1980). The development of ocular dominance columns in nor-
mal and visually deprived monkeys. *Journal of Comparative Neurology, 191,* 1–51.

Malkova, L., Mishkin, M., & Bachevalier, J. (1995). Long-term effects of selective neonatal temporal
lobe lesions on learning and memory in monkeys. *Behavioral Neuroscience, 109,* 212–226.

Martinez, A., Moses, P., Frank, L., Buxton, R., Wong, E., & Stiles, J. (1997). Hemispheric asymmetries
in global and local processing: Evidence from fMRI. *Neuroreport, 8,* 1685–1689.

Mayer, M. (1969). *Frog, where are you?* New York: Dial Press.

McFie, J., & Zangwill, O. L. (1960). Visual-constructive disabilities associated with lesions of the left
cerebral hemisphere. *Brain, 83,* 243–260.

Merzenich, M. M., & Jenkins, W. M. (1995). Cortical plasticity, learning, and learning dysfunction. In
B. Julesz & I. Kovacs (Eds.), *Maturational windows and adult cortical plasticity* (pp. 247–264).
Reading, MA: Addison-Wesley.

Merzenich, M. M., Kaas, J. H., Wall, J., Nelson, R. J., Sur, M., & Felleman, D. (1983). Topographic re-
organization of somatosensory cortical areas 3b and 1 in adult monkeys following restricted
deafferentation. *Neuroscience, 8,* 33–55.

Merzenich, M. M., Kaas, J. H., Wall, J., Sur, M., Nelson, R. J., & Felleman, D. (1983). Progression of
changes following median nerve section in the cortical representation of the hand in areas 3b and 1 in
adult owl and squirrel monkeys. *Neuroscience, 10,* 639–665.

Mishkin, M. (1982). A memory system in the monkey. *Philosophical Transactions of the Royal Society
of London, 298,* 85–95.

Mogilner, A., Grossman, J. A., Ribary, U., Joliot, M., Volkmann, J., Rapaport, D., Beasley, R. W., &
Llinas, R. R. (1993). Somatosensory cortical plasticity in adult humans revealed by
magnetoencephalography. *Proceedings of the National Academy of Sciences, USA, 90,* 3593–3597.

Morris, R. G. M. (1980). Spatial localization does not require the presence of local cues. *Learning and
Motivation, 12,* 239–261.

Neville, H. J., Nicol, J. L., Barss, A., Forster, K. I., & Garrett, M. F. (1991). Syntactically based sentence
processing classes: Evidence from event-related brain potentials. *Journal of Cognitive Neurosci-
ence, 3,* 151–165.

Neville, H. J., Schmidt, A., & Kutas, M. (1983). Altered visual-evoked potentials in congenitally deaf
adults. *Brain Research, 266,* 127–132.

O'Leary, D. D. M., & Stanfield, B. B. (1989). Selective elimination of axons extended by developing
cortical neurons is dependent on regional locale: Experiments utilizing fetal cortical transplants.
Journal of Neuroscience, 9, 2230–2246.

Oppenheim, R. W. (1985). Naturally occurring cell death during neural development. *Trends in Neuro-
science, 8,* 487–493.

Osterrieth, P. A. (1944). The Complex Figure Copy Test. *Archives de Psychologie, 30,*
206–353.

Pallas, S. L., Roe, A. W., & Sur, M. (1990). Visual projections induced into the auditory pathway of fer-
rets. I. Novel inputs to primary auditory cortex (AI) from the LP/pulvinar complex and the topogra-
phy of the MGN-AI projection. *Journal of Comparative Neurology, 298,* 50–68.

Piercy, M., Hecaen, H., & De Ajuriaguerra, J. (1960). Constructional apraxia associated with unilateral cerebral lesions: Left and right sided cases compared. *Brain, 83,* 225–242.

Purves, D. (1988). *Body and brain, a trophic theory of neural connections.* Cambridge, MA: Harvard University Press.

Quartz, S. R., & Sejnowski, T. J. (1997). The neural basis of cognitive development: A constructivist manifesto. *Behavioral and Brain Sciences, 20,* 537–596.

Ramachandran, V. S. (1993). Behavioral and magnetoencephalographic correlates of plasticity in the adult human brain. *Proceedings of the National Academy of Sciences, 90,* 10413–10420.

Ramachandran, V. S., Rogers-Ramachandran, D., & Stewart, M. (1992). Perceptual correlates of massive cortical reorganization. *Science, 258,* 1159–1160.

Ramachandran, V. S., Stewart, M., & Rogers-Ramachandran, D. (1992). Perceptual correlates of massive cortical reorganization. *Neuroreport, 3,* 583–586.

Rasmussen, T., & Milner, B. (1977). The role of early left-brain injury in determining lateralization of cerebral speech functions. *Annals of the New York Academy of Sciences, 299,* 355–369.

Ratcliff, G. (1982). Disturbances of spatial orientation associated with cerebral lesions. In M. Potegal (Ed.), *Spatial abilities: Development and physiological foundations* (pp. 301–331). New York*:* Academic.

Reilly, J. S., Bates, E. A., & Marchman, V. A. (1998). Narrative discourse in children with early focal brain injury. *Brain and Language, 61,* 335–375

Reilly, J. S., Stiles, J., Larsen, J., & Trauner, D. (1995). Affective facial expression in infants with focal brain damage. *Neuropschologia, 33,* 83–99.

Rey, A. (1941). Psychological examination of traumatic encephalopathy. *Archives de Psychologie, 28,* 286–340.

Rosenzweig, M. R., & Bennett, E. L. (1972). Cerebral changes in rats exposed individually to an enriched environment. *Journal of Comparative and Physiological Psychology, 80,* 304–313.

Rosenzweig, M. R., Krech, D., Bennett, E. L., & Diamond, M. C. (1962). Effects of environmental complexity and training on brain chemistry and anatomy: A replication and extension. *Journal of Comparative and Physiological Psychology, 55,* 429–437.

Rosenzweig, M. R., Krech, D., Bennett, E. L., & Zolman, J. F. (1962). Variation in environmental complexity and brain measures. *Journal of Comparative and Physiological Psychology, 55,* 1092–1095.

Rosenzweig, M. R., Love, W., & Bennett, E. L. (1968). Effects of a few hours a day of enriched experience on brain chemistry and brain weights. *Physiology and Behavior, 3,* 819–825.

Schwaber, M. K., Garraghty, P. E., & Kaas, J. H. (1993). Neuroplasticity of the adult primate auditory cortex following cochlear hearing loss. *The American Journal of Otology, 14,* 252–258.

Stiles, J. (1998, September). *Spatial analytic processing following pre- or perinatal focal brain injury: Profiles of deficit and development.* Paper presented at the European Research Conference on Brain Development and Cognition in Human Infants: Development and Functional Specialization of the Cortex, Sant Feliu de Guixols, Spain.

Stiles, J., Bates, E. A., Thal, D., Trauner, D., & Reilly, J. (1998). Linguistic, cognitive, and affective development in children with pre- and perinatal focal brain injury: A ten-year overview from the San Diego Longitudinal Project. In C. Rovee-Collier, L. P. Lipsitt, & H. Hayne (Eds.), *Advances in infancy research* (pp. 131–163). Stamford, CT: Ablex.

Stiles, J., Stern, C., Trauner, D., & Nass, R. (1996). Developmental change in spatial grouping activity among children with early focal brain injury: Evidence from a modeling task. *Brain and Cognition, 31,* 46–62.

Stiles, J., Trauner, D., Engel, M., & Nass, R. (1997). The development of drawing in children with congenital focal brain injury: Evidence for limited functional recovery. *Neuropsychologia, 35,* 299–312.

Stiles-Davis, J., Janowsky, J., Engel, M., & Nass, R. (1988). Drawing ability in four young children with congenital unilateral brain lesions. *Neuropsychologia, 26,* 359–371.

St. James-Roberts, I. (1979). Neurological plasticity, recovery from brain insult, and child development. *Advances in Child Development and Behavior, 14,* 253–319.

Sur, M., Garraghty, P. E., & Roe, A. W. (1988). Experimentally induced visual projections into auditory thalamus and cortex. *Science, 242,* 1437–1441.

Swindell, C. S., Holland, A. L., Fromm, D., & Greenhouse, J. B. (1988). Characteristics of recovery of drawing ability in left and right brain-damaged patients. *Brain and Cognition, 7,* 16–30.

Teuber, H. L. (1974). Why two brains? In F. O. Schmidt & F. G. Worden (Eds.), *The neurosciences, third study program* (pp. 71–74). Cambridge, MA: MIT Press.

Warrington, E. K., James, M., & Kinsbourne, M. (1966). Drawing disability in relation to laterality of cerebral lesion. *Brain, 89,* 53–82.

Webster, M. J., Bachevalier, J., & Ungerleider, L. G. (1994). Connections of inferior temporal areas TE and TEO with parietal and frontal cortex in macaque monkeys. *Cerebral Cortex, 5,* 470–483.

Webster, M. J., Bachevalier, J, & Ungerleider, L. G. (1995). Transient subcortical connections of inferior temporal areas TE and TEO in infant macaque monkeys. *The Journal of Comparative Neurology, 352,* 213–226.

Webster, M. J., Ungerleider, L. G., & Bachevalier, J. (1991). Connections of inferior temporal areas TE and TEO with medial temporal-lobe structures in infant and adult monkeys. *The Journal of Neuroscience, 11,* 1095–1116.

Wiesel, T. N. (1982). Postnatal development of the visual cortex and the influence of environment. *Nature, 299,* 583–591.

Wiesel, T. N., & Hubel, D. H. (1963a). Receptive fields of cells in striate cortex of very young, visually inexperienced kittens. *Journal of Neurophysiology, 26,* 994–1002.

Wiesel, T. N., & Hubel, D. H. (1963b). Single-cell responses in striate cortex of kittens deprived of vision in one eye. *Journal of Neurophysiology, 26,* 1003–1017.

Wiesel, T. N., & Hubel, D. H. (1965a). Comparison of the effects of unilateral and bilateral eye closure on cortical unit responses in kittens. *Journal of Neurophysiology, 28,* 1029–1040.

Wiesel, T. N., & Hubel, D. H. (1965b). Extent of recovery from the effects of visual deprivation in kittens. *Journal of Neurophysiology, 28,* 1060–1072.

Witelson, S. F. (1985). On hemisphere specialization and cerebral plasticity from birth: Mark II. In C. T. Best (Ed.), *Hemispheric function and collaboration in the child* (pp. 33–77). San Diego, CA: Academic.

Woods, B. T., & Carey, S. (1978). Language deficits after apparent clinical recovery from childhood aphasia. *Annuals of Neurology, 6,* 405–409.