CHAPTER 7

How Does the Brain Develop?

Perspectives on Brain Development
Mr. Higgins Builds a House
Linking Brain and Behavioral Development

The Development of the Child's Brain
The Gross Development of the Human Nervous System
The Origins of Neurons and Glia
The Growth and Development of Neurons
Focus on Disorders: Cerebral Palsy
Glial Development

Correlating Behavior with Brain Development
Motor Behaviors
Language Development
The Development of Problem-Solving Ability

Brain Development and the Environment
Experience and Cortical Organization
Experience and Neural Connectivity
Critical Periods for Experience and Brain Development
Abnormal Experience and Brain Development
Focus on Disorders: Romanian Orphans
Hormones and Brain Development
Injury and Brain Development
Other Kinds of Abnormal Brain Development
Focus on Disorders: Schizophrenia
Mental Retardation

How Do Any of Us Develop a Normal Brain?

Myrleen F. Cate/Photo Network/Picture Quest
Oliver Meckes/Ottawa/Photo Researchers

A monarch butterfly begins life as a fertilized egg and develops into a caterpillar. After a time, the caterpillar spins a cocoon, inside of which it lives as it undergoes a process that transforms it into a butterfly. The stages of development in the life cycle of a monarch butterfly are collectively called metamorphosis and are shown in Figure 7-1. Consider how formidable this insect's development is. First, the egg must develop a body, including a nervous system. This nervous system has to produce caterpillar-like movements and control the animal's feeding apparatus, which is designed for munching leaves. Then, during metamorphosis, the original nervous system has to be reconstructed to control the flight, feeding, and reproductive behaviors of a butterfly. The addition of flying behavior is remarkable because it requires the use of entirely different muscles from those used in crawling. Furthermore, adult monarch butterflies fly very long distances in their annual migration and must navigate to the correct geographical location. In contrast, the caterpillar's main challenge is to find an appropriate food source as it crawls slowly around in a limited area. It seems that a caterpillar would need a major overhaul of its brain to control the completely reconfigured body and brand-new behaviors that go with being a butterfly.

We humans do not metamorphose into a different life form in the course of our development, but the developmental problems that we face are similar to those of the monarch. We also begin life as a fertilized egg that develops a body and a nervous system. When we are born, however, we are not able to fend for ourselves. Human offspring are virtually helpless for an extended period of time. The behavioral demands on the brain of a newborn include relatively simple actions such as searching for and recognizing a nipple with which to feed and signaling hunger or discomfort to caregivers. But soon a human infant undergoes an enormous transformation. The child's brain becomes able to control a variety of new behaviors such as crawling and, later, walking, eating solid foods, using tools, and learning a language. At school age, the child's brain becomes able to formulate complex ideas, solve challenging problems, and remember large quantities of information. And changes in a person's nervous system do not end with graduation from college. As the adult brain begins to age in the third decade of life, it starts to lose cells and grows few new ones. The loss forces the middle-aged brain to reconstruct some of its parts to forestall the effects of aging. Brain development, then, is a continuous process that is central to our functioning. Changes in the brain allow us to adapt to the environment throughout our life cycle.

This chapter answers many questions about the development of the human brain. How did your brain manage to develop from a single embryonic cell into an organ made up of billions of cells? This question parallels one asked in Chapter 1—namely, how did the brain evolve from a small and simple organ into a large and

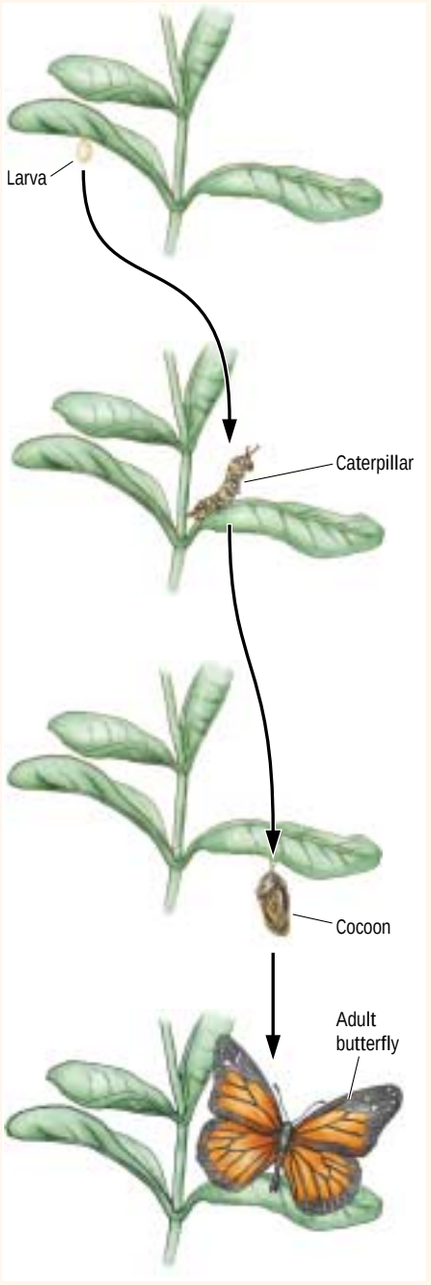


Figure 7-1
In metamorphosis, the nervous system of the monarch butterfly must undergo significant changes as the insect develops from a larva into a caterpillar into a butterfly.

highly complex one? When we consider that there are many kinds of neurons and glia and that they must be located in specific nuclei, layers, and so on, we are left wondering how all this complicated architecture is accomplished. Is there a blueprint of some sort and, if so, where does it come from and how is it read? Is there any relation between brain development and behavioral development? And how do our experiences influence the development of the brain? You will soon learn that the brain's development is affected by many factors, some of which can lead to abnormalities. When you become aware of how many influences on brain development there are, you may wonder how so many people end up with a normal brain.

PERSPECTIVES ON BRAIN DEVELOPMENT

To begin to understand how the brain is constructed, we start with an analogy of building a house. Do not take this analogy too literally. It is used here simply as a way of introducing the topic of brain development and some important principles related to it.

Mr. Higgins Builds a House

Mr. Higgins finds a picture of his dream house in a magazine and decides to build it himself. The house has a basement, which contains the furnace, a hot-water tank, and other essential machinery. The first floor accommodates a kitchen, a bathroom, and a general living area. The second story contains a master bedroom and Mr. Higgins's den. The den is extremely important, because it is here that Mr. Higgins will work as a mystery book writer.

Mr. Higgins quickly discovers that houses do not just materialize; they go through several stages of development. First, Mr. Higgins orders a blueprint. The blueprint outlines the house's structure and ensures that everyone taking part in its construction is building the same house. The construction process begins with the laying of a concrete foundation. At this point, however, Mr. Higgins starts to realize that the blueprint is not as detailed as it first appeared. It specifies where the walls and pipes and plugs will be, but it does not always say exactly what materials to use where. Thus, the choice of a particular kind of plywood or a particular type of nail or screw is often more or less random within certain limitations. Similarly, the blueprint specifies that there should be connections between certain circuits in the power box and certain fixtures or plugs, but it does not detail the precise route that the connecting wires should take. Mr. Higgins also finds that the blueprint does not specify the precise order in which tasks should be done. He knows that the foundation has to be finished first, the subfloor next, and the walls framed after that. But what comes then is largely left to his discretion, except where a certain sequence is required to make something work (for example, the electrical wiring must be installed before the walls are closed in.) Given how many options are open to him in building the house, Mr. Higgins realizes that his version of the building will undoubtedly be different from anyone else's.

Franklin Avery/Liaison International

Much the same problems are encountered in building a brain. Like a house, a brain is constructed in levels, each one with a different function. And, just as house plans are written in the form of a blueprint, the

plans for a brain are encoded in genes. As Mr. Higgins learned, architects do not specify every detail in a blueprint; nor do genes include every instruction for how a brain is assembled and wired. The process of building a brain is just too complex to be encoded entirely and precisely in genes. For this reason, the fate of billions of brain cells is left partly open, especially when it comes to the massive undertaking of forming appropriate connections between cells.

If the structure and fate of each brain cell are not specified in advance, what factors do control brain development? Many factors are at work, including special molecules, such as hormones. Brain development is also influenced by the experiences that people have both in the womb and after they are born. We return to these influences later in this chapter, after examining the major stages in brain development. But first we explore how scientists go about studying the interconnected processes of brain and behavioral development.

Linking Brain and Behavioral Development

In the course of development, changes take place both in the brain and in behavior. Scientists assume that these two lines of development are closely linked. As the brain develops, neurons become more and more intricately connected, and these increasingly complex interconnections underlie increased behavioral complexity.

We can study the relation between brain and behavioral development in three basic ways. First, we can look at the structural development of the nervous system and correlate it with the emergence of specific behaviors. For example, we can link the development of certain brain structures to the development of, say, grasping or crawling in infants. As the brain structures develop, their functions emerge; these functions are manifested in behaviors that we can observe.

Structures that develop quickly exhibit their functions sooner than structures that develop more slowly. Because the human brain continues to develop well into adolescence, you should not be surprised that some behavioral abilities emerge rather late in development. For example, the frontal lobes continue to develop well into adolescence, reaching maturity at about 16 years of age. It follows that certain behaviors controlled by the frontal lobes also are slow to develop.

Perhaps the best example is the ability to understand the nuances of social interaction, which is a function of the frontal lobes. One way to test a person's understanding of social interaction is illustrated in Figure 7-2. The person looks at a cartoon scene and is asked to mimic the facial expression appropriate for the face that is blank. Adults have no difficulty with this task, but children are very poor at producing the right expression. The ability does not emerge until midadolescence. It is not that children have trouble producing facial expressions; they do so spontaneously at a very early age. What they lack is an adultlike ability to interpret what a particular social interaction means, because brain structures that play an important role in this ability are very late to mature. Children therefore make many social gaffes and are often unable to grasp all the nuances of a social situation. Behaviors that seem simple to us, such as a wink or a flirtatious look, are incomprehensible to children. Children, then, are not miniature adults who simply need to learn the "rules" of adult behavior. The brain of a child is very different from that of an adult, and the brains of children at different ages are really not comparable either.

Figure 7-2

This task of social perception is one that children have great difficulty in accomplishing. The task is to mimic the facial expression that is most appropriate for the blank in the drawing.

Adapted from "Developmental Changes in the Recognition and Comprehensional Expression: Implications for Frontal Lobe Function," by B. Kolb, B. Wilson, and L. Taylor, 1992, *Brain and Cognition*, *20*, p. 77.

The second way to examine the relation between brain and behavioral development is to turn our sequence of observations around. First we scrutinize behavior for the emergence of new abilities, and then we make inferences about underlying neural maturation. For example, as language emerges in the young child, we expect to find corresponding changes in neural structures that control language. In fact, this is what we do find. At birth, children do not speak, and even extensive speech training would not enable them to do so. The neural structures that control speech are not yet mature enough. As language emerges, we can conclude that the speech-related structures in the brain are undergoing the necessary maturation. The same reasoning can be applied to frontal-lobe development. As frontal-lobe structures mature in adolescence, we look for related changes in behavior, but we can also do the reverse: because we observe new abilities emerging in the teenage years, we infer that they must be controlled by late-maturing neural structures.

The third way to study the relation between brain and behavioral development is to identify and study factors that influence both. From this perspective, the mere emergence of a certain fully developed brain structure is not enough; we must also know the events that shape how that structure functions and produce certain kinds of behaviors. Some of the events that influence brain function are sensory experience, injuries, and the actions of hormones and abnormal genes. Logically, if behavior is influenced by one of these experiences, then structures in the brain that are changed by that experience are responsible for the behavioral outcomes. For example, we might study how the abnormal secretion of a hormone affects both a certain brain structure and a certain behavior. We can then infer that, because the observed behavioral abnormality results from the abnormal functioning of the brain structure, that structure must normally play some role in controlling the behavior.

By applying each of these three approaches to the study of brain and behavioral development, we can shed much light on the nature of brain organization and function. We begin by considering the anatomical development of the child's brain. We then explore the behavioral correlates of brain development. Finally, we explore some factors that influence the development of both the brain and behavior.

In Review

Brain development can be approached from three different perspectives. First, the structural development can be studied and correlated with the emergence of behavior. Second, behavioral development can be analyzed and predictions can be made about what underlying circuitry must be emerging. Finally, those factors that influence brain and behavioral development, such as an injury to the brain, can be studied. In this last approach, the idea is that events that alter behavioral development should similarly alter structural development.

THE DEVELOPMENT OF THE CHILD'S BRAIN

Some 2000 years ago the Roman philosopher Seneca proposed that a human embryo was a miniature person. According to him, the task of development was simply to grow bigger. This idea, known as *preformation*, was so appealing that, until fairly recently, it was widely believed to be true. In fact, even with the development of the microscope, the appeal of preformation was so strong that biologists claimed to be able to see microscopic horses in horse semen.

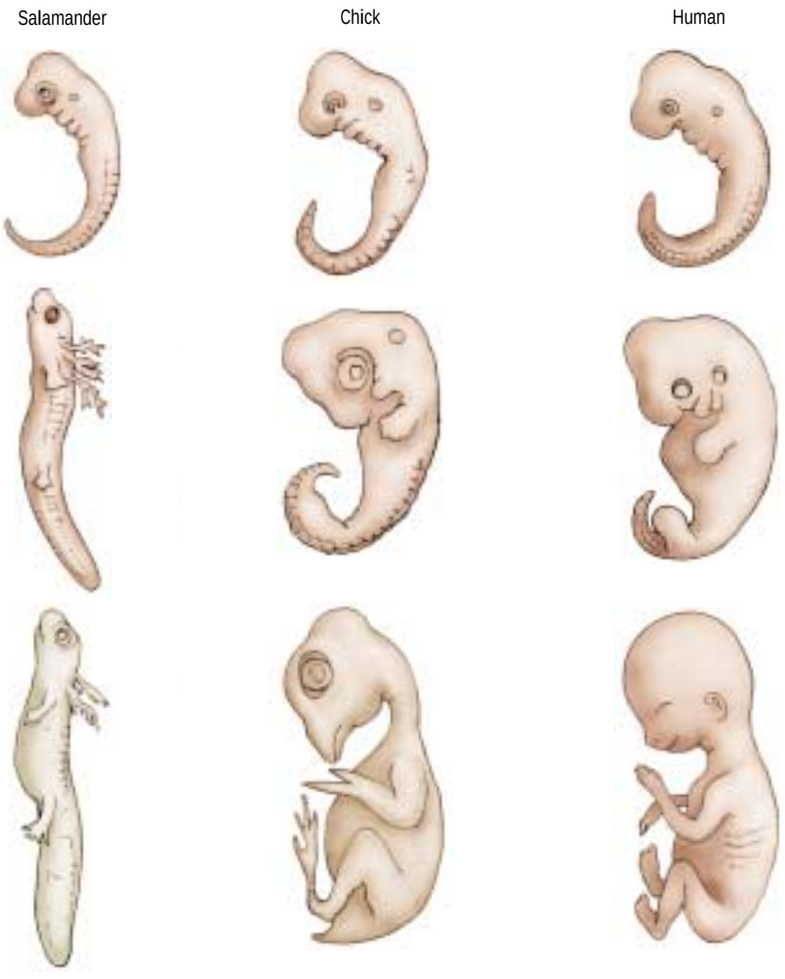


Figure 7-3

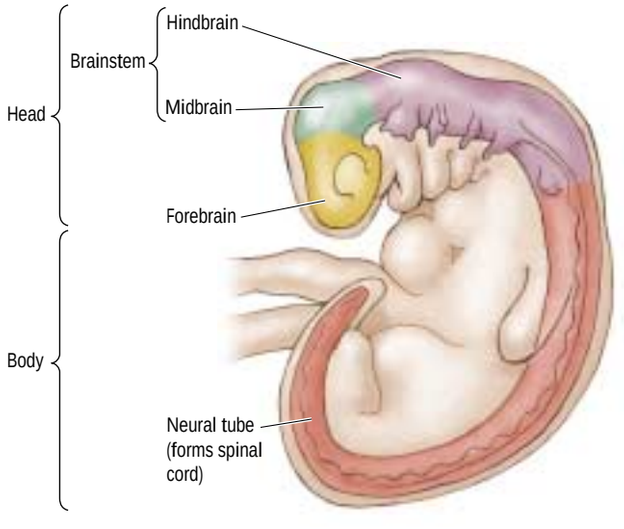
The similarity of embryos of different species is striking in the earliest stages of development, as these salamander, chick, and human embryos show. This similarity led to the conclusion that embryos are not miniature versions of adults.

By the middle of the nineteenth century, the idea of preformation began to wane as people realized that embryos looked nothing like the adults that they become. In fact, it was obvious that embryos of different species more closely resembled one another than their respective parents. Figure 7-3 shows the striking similarity in the early embryos of species as diverse as salamanders, chickens, and humans. Early in development, all species have a similar-looking primitive head, which is a region with bumps or folds, and all possess a tail. It is only as the embryo develops that it acquires the distinctive characteristics of its species. The similarity of young embryos is so great that many nineteenth-century biologists saw it as evidence for Darwin's view that vertebrates arose from a common ancestor millions of years ago.

Although not shown in Figure 7-3, embryos are structurally similar in their nervous systems as well as in their bodies. Figure 7-4 reveals that the nervous system of a young vertebrate embryo always has three regions: the forebrain, the brainstem (with the midbrain and hindbrain clearly visible), and the remaining neural tube, which forms the spinal cord. Where do these three regions come from? We can answer this question by tracing events as the embryo matures.

Figure 7-4

The basic brain regions of the forebrain, the midbrain, and the hindbrain are visible at about 28 days, as is the remaining neural tube, which will form the spinal cord.



Neural plate. The thickened region of the ectodermal layer that gives rise to the neural tube.

Neural tube. A structure in the early stage of brain development from which the brain and spinal cord develop.

The Gross Development of the Human Nervous System

At the time an egg is fertilized by a sperm, a human zygote consists of just a single cell. But this cell soon begins to divide; by the 15th day, the embryo resembles a fried egg. It is made of several sheets of cells with a raised area in the middle, as shown in Figure 7-5. The raised area is called the *primitive body*. By 3 weeks after conception, there is primitive neural tissue, known as the neural plate, which is part of the outermost layer of embryonic cells. The neural plate first folds to form a groove, called the *neural groove*, as illustrated in Figure 7-6. The neural groove then curls to form the neural tube, much as a flat sheet of paper can be curled to make a cylinder. Micrographs of the neural tube closing in a mouse embryo can be seen in Figure 7-7. The cells that form the neural tube can be thought of as the "nursery" for the rest of the nervous system. The open region in the center of the tube remains open and becomes the brain's ventricles and the spinal canal.

Visit the Web site at **www.worthpublishers.com/kolb/chapter7** to link to visual tours of human fetal development.

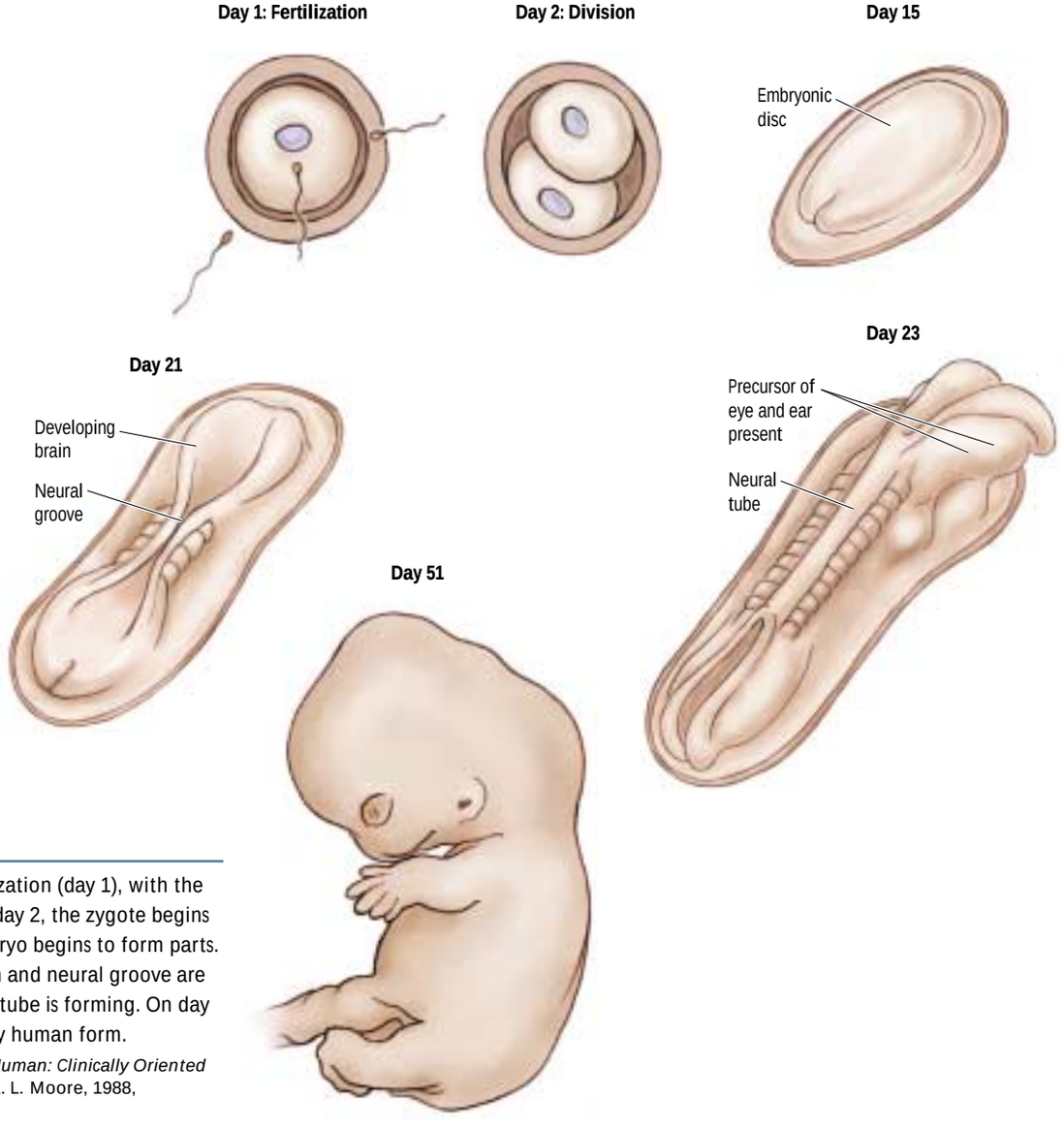
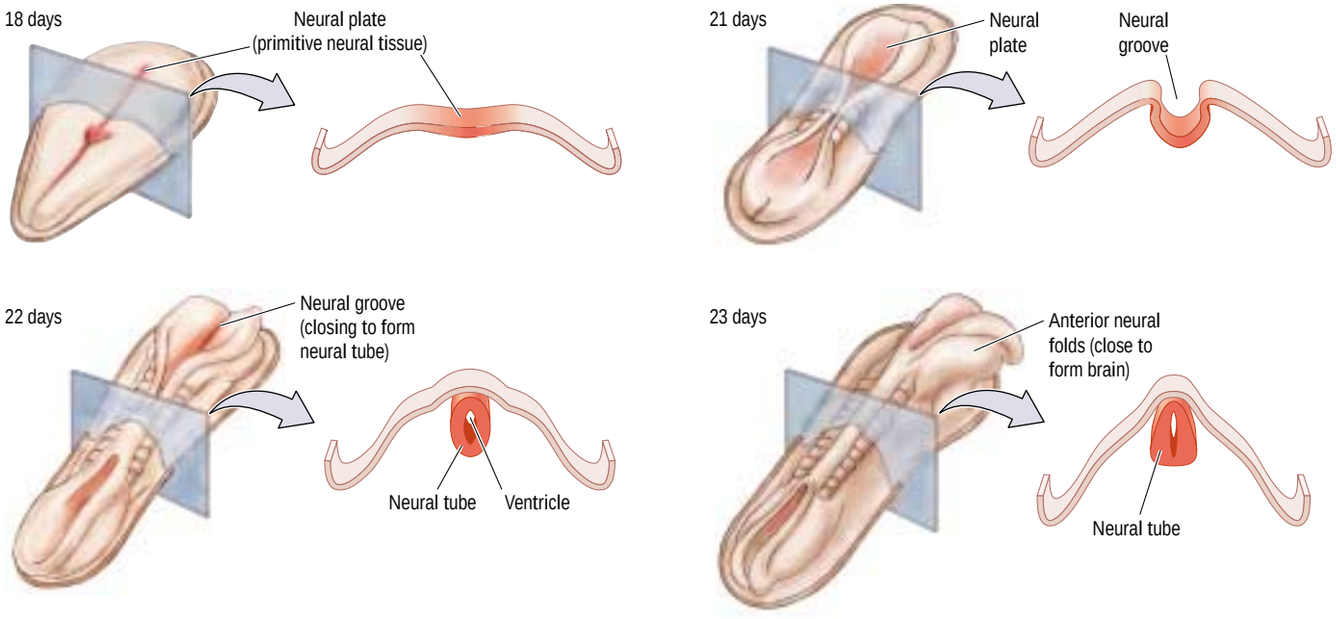
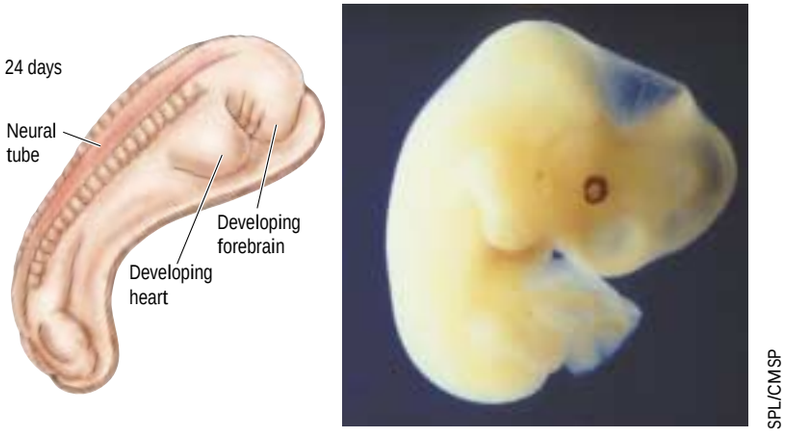


Figure 7-5

Development begins at fertilization (day 1), with the formation of the zygote. On day 2, the zygote begins to divide. On day 15, the embryo begins to form parts. On day 21, the primitive brain and neural groove are visible. On day 23, the neural tube is forming. On day 51, the embryo has a distinctly human form.

Adapted from *The Developing Human: Clinically Oriented Embryology* (4th ed., p. 61), by K. L. Moore, 1988, Philadelphia: Saunders.





SPL/CMSP

Figure 7-6

In the formation of the neural tube, the precursor of the nervous system, a long depression (the neural groove) is first formed in the neural plate. The neural plate collapses inward, forming a tube along the length of the dorsal surface of the embryo. The embryo is shown in a photograph at 24 days.

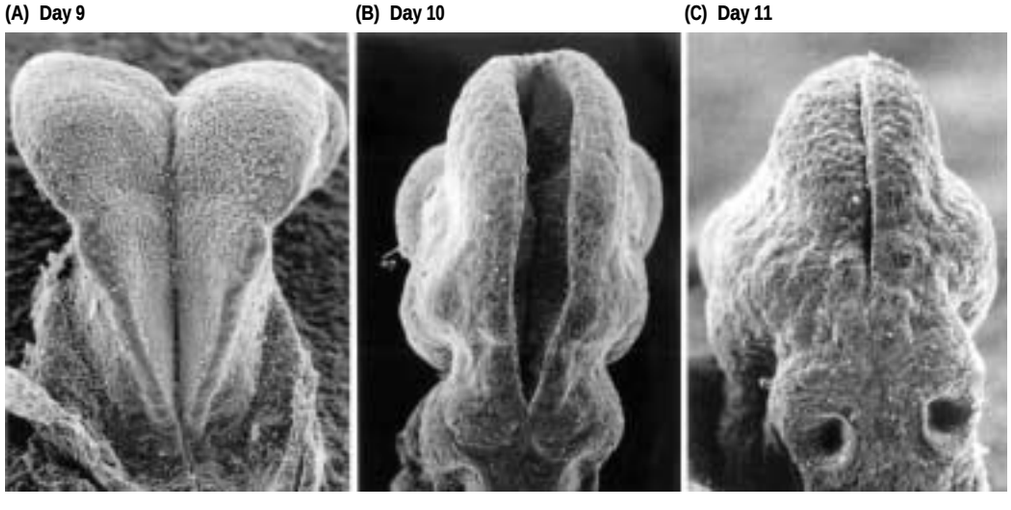


Figure 7-7

Scanning electron micrographs show the closing of the neural tube in a mouse embryo.

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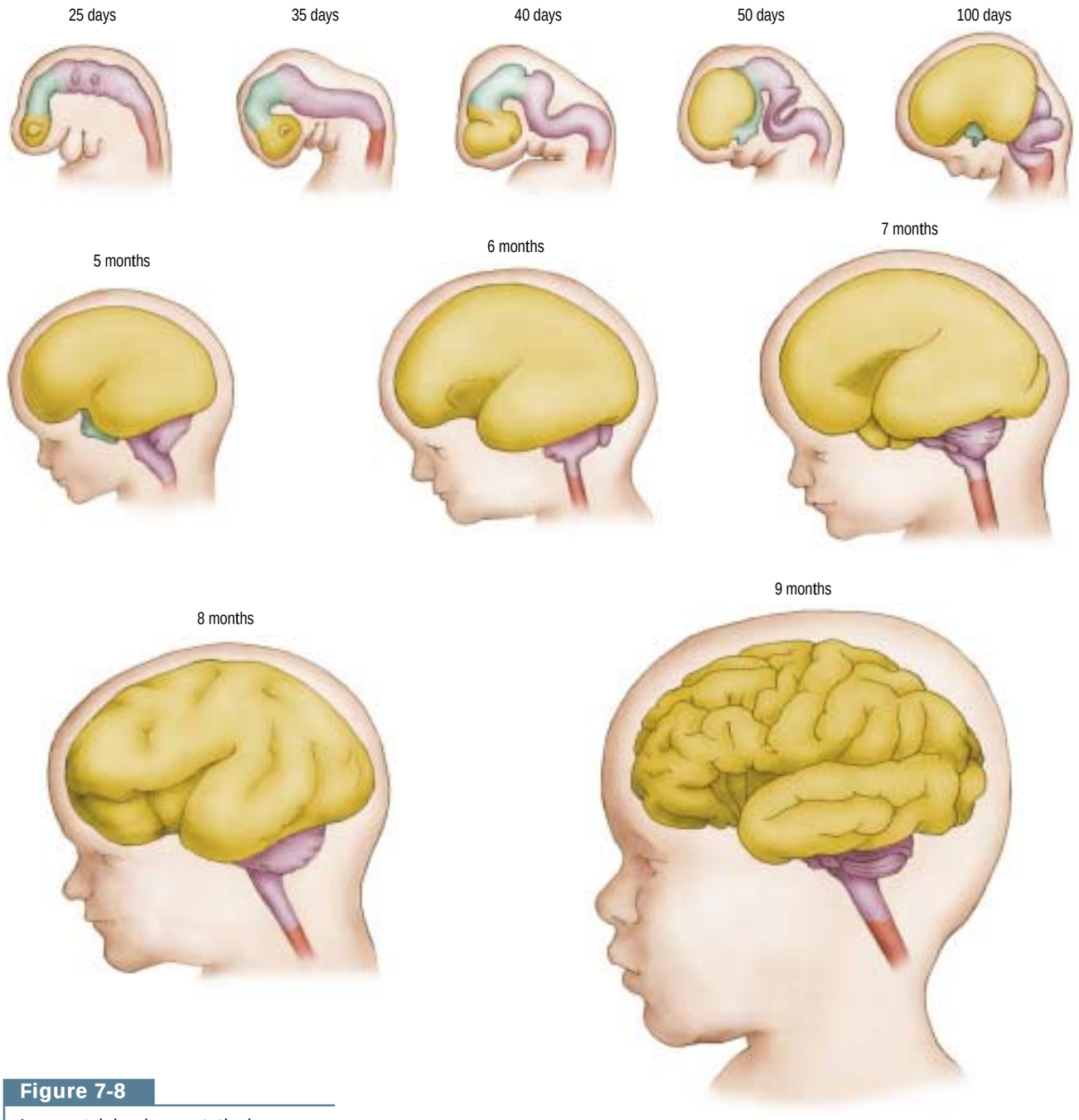


Figure 7-8

In prenatal development, the human brain undergoes a series of embryonic and fetal stages. Refer to Figure 7-4 for identification of the various parts of the nervous system.

Adapted from "The Development of the Brain," by W. M. Cowan, 1979, *Scientific American*, *241*(3), p. 116.

The body and the nervous system change rapidly in the next 3 weeks of development. By 7 weeks (or 49 days), the embryo begins to resemble a miniature person, as can be seen in Figure 7-5. Figure 7-8 shows that the brain looks distinctly human by about 100 days after conception, but it does not begin to form gyri and sulci until about 7 months. By the end of the 9th month, the brain has the gross appearance of the adult human brain, even though its cellular structure is different.

Another developmental process, shown in Figure 7-9, is sexual development. Although the genitals begin to form in the 7th week after conception, they appear identical in the two sexes at this early stage. There is not yet any *sexual dimorphism*, or

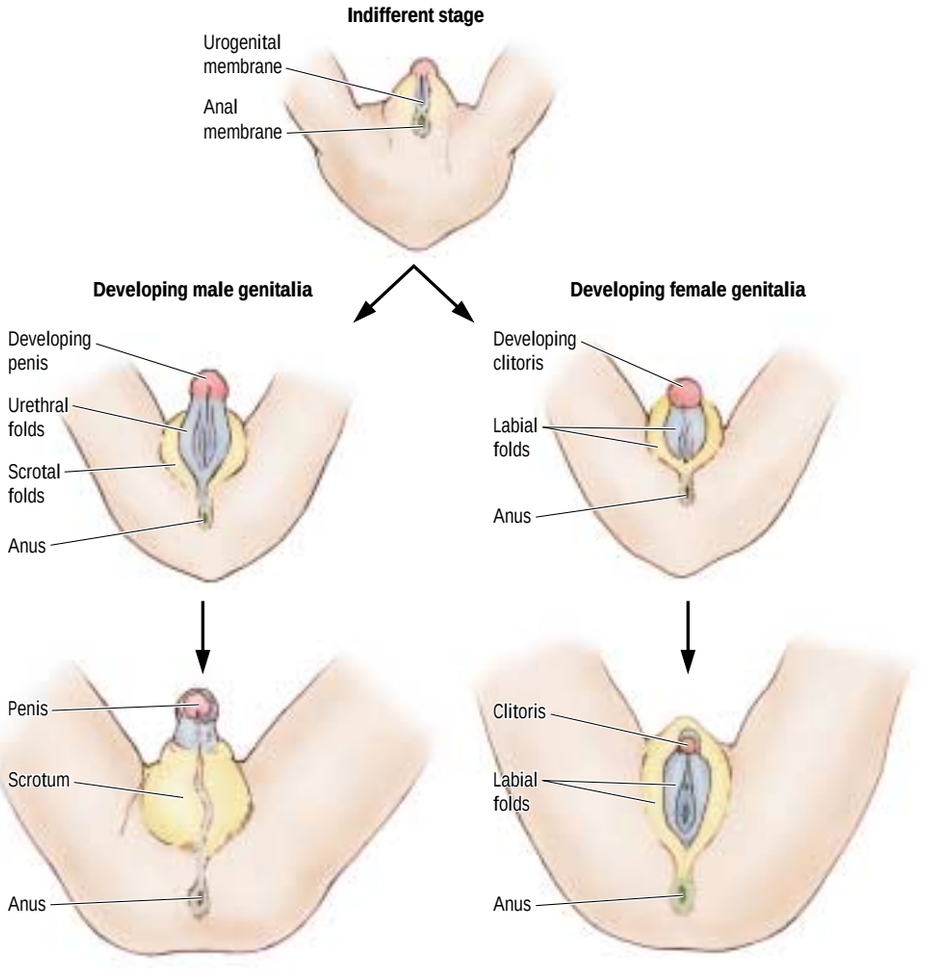


Figure 7-9

Sexual differentiation in the human infant. Early in development (indifferent stage), the human male and female embryos are identical. In response to testosterone in male embryos, the genitalia begin to develop into the male structure at about 60 days. In the absence of testosterone, the female structure emerges. Parallel changes take place in the brain in response to the absence or presence testosterone.

structural difference between the two sexes. Then, about 60 days after conception, male and female genitals start to become distinguishable. But what does this sexual differentiation have to do with brain development? The answer is that sexual differentiation is stimulated by the presence of the hormone testosterone in male embryos. Testosterone changes the genetic activity of certain cells, most obviously those that form the genitals. However, genital cells are not the only cells influenced by testosterone. The brain also has cells that respond to this hormone, so certain regions of the embryonic brain also may begin to show sexual dimorphism, beginning about 60 days after conception.

The Origins of Neurons and Glia

The cells lining the neural tube, the nursery for the brain, are known as neural stem cells. A stem cell is a cell with an extensive capacity for self-renewal. It divides and produces two stem cells, which both can divide again. In adulthood, one stem cell dies after division, leaving a constant number of dividing stem cells. In an adult, the neural stem cells line the ventricles and thus form what is called the ventricular zone.

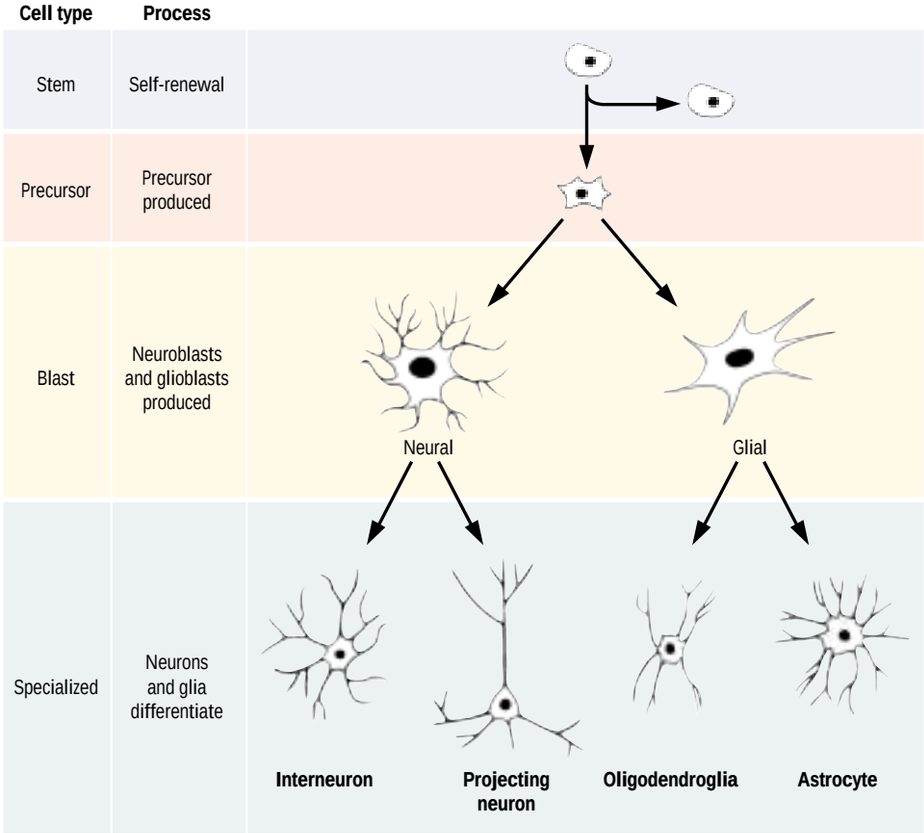
If lining the ventricles were all that stem cells did throughout the decades of a human life, they would seem like odd kinds of cells to possess. But stem cells also have

Neural stem cells. Cells that give rise to all neurons in the nervous system.

Ventricular zone. The zone surrounding the ventricles in which stem cells reside.

Figure 7-10

Cells in the brain begin as multipotential stem cells, which become precursor cells, which become blasts, which finally develop into specialized neurons or glia.



another function: they give rise to so-called progenitor (precursor) cells. These progenitor cells also can divide and, as shown in Figure 7-10, they eventually produce nondividing cells known as neuroblasts and glioblasts. In turn, neuroblasts and glioblasts become neurons and glia when they mature. Neural stem cells, then, are the cells that give rise to all the many specialized cells of the brain and spinal cord.

Sam Weiss and his colleagues (1996) discovered that stem cells remain capable of producing neurons and glia not just into early adulthood, but even in an aging brain. This discovery is important because it implies that neurons that die in an adult brain should be replaceable. We do not yet know how to instruct stem cells to carry out this replacement process, however. Consequently, injury to central nervous system tissue usually remains permanent.

An important question in the study of brain development is how cells are generated to form stem cells, progenitor cells, neuro- and glioblasts, and finally neurons and glia. In other words, how does a cell "know" to become a neuron rather than a skin cell? Recall that each human cell has 23 chromosome pairs containing the approximately 100,000 genes of the human genome. In each cell, certain genes are "turned on" by a signal, and those genes then produce a particular cell type. "Turned on" means that a formerly dormant gene becomes activated, which results in the cell making a specific kind of protein. You can easily imagine that certain types of proteins are needed to produce skin cells, whereas other types of proteins are needed for neurons. The specific signals for turning on genes are largely unknown, but these signals are probably chemical. Thus, the chemical environment of a cell in the brain is different from that of a cell forming skin, and so different genes in these cells are activated, producing different proteins and different cell types. The different chemical environments needed to trigger this cellular differentiation could be caused by the activity of other

Progenitor cell. A cell that is derived from a stem cell and acts as a precursor cell that migrates and produces a neuron or a glial cell.

Neuroblast. A progenitor cell that gives rise to all the different types of neurons.

Glioblast. A progenitor cell that gives rise to different types of glial cells.

neighboring cells or by chemicals, such as hormones, that are transported in the bloodstream.

You can see that the differentiation of stem cells into neurons must require a series of signals and the resulting activation of genes. A chemical signal must induce the stem cells to produce progenitor cells, and then another chemical signal must induce the progenitor cells to produce either neuroblasts or glioblasts. Finally, a chemical signal, or perhaps even a set of signals, must induce the genes to make a neuron or a particular type of neuron.

One class of compounds that signal cells to develop in particular ways comprises so-called neurotrophic factors. By removing stem cells from the brain of an animal and placing those cells in solutions that keep them alive, researchers can study how neurotrophic factors function. When one compound, known as *epidermal growth factor* (EGF), is added to the cell culture, it stimulates stem cells to produce progenitor cells. Another compound, *basic fibroblast growth factor* (bFGF), stimulates progenitor cells to produce neuroblasts. At this point, the destiny of a given neuroblast is not predetermined. A neuroblast can become any type of neuron if it receives the right chemical signal. The body relies on a "general-purpose neuron" that, when exposed to certain neurotrophic factors, matures into the specific type of cell that the nervous system requires in a particular location. This process makes brain development simpler than it would be if each different kind of cell, and the number of cells of each type, had to be precisely specified in an organism's genes. In the same way, building a house from "all-purpose" two-by-fours that can be cut to any length as needed is easier than specifying in a blueprint a precise number of precut pieces of lumber that can be used only in a certain location.

Neurotrophic factors. A class of compounds that act to support growth and differentiation in developing neurons and may act to keep certain neurons alive in adulthood.

The Growth and Development of Neurons

In humans, approximately 10^9 cells are needed to form just the cortex of a single hemisphere. To produce such a large number of cells, about 250,000 neurons must be born per minute at the peak of brain development. But, as Table 7-1 shows, this rapid formation of neurons and glia is just the first step in the growth of a brain. These cells must travel to their correct locations (a process called *migration*), they must differentiate into the right type of neuron or glial cell, and the neurons must grow dendrites and axons and subsequently form synapses. It may surprise you to learn that the brain must also prune back unnecessary cells and connections, sculpting itself according to the experiences and needs of the particular person. In the following subsections, we will consider each of these stages in brain development. We will focus our attention on the development of the cerebral cortex because more is known about cortical development than about the development of any other area of the human brain. However, the developmental principles derived from our examination of the cortex apply to other brain regions as well.

Table 7-1 The Stages of Brain Development

1. Cell birth (neurogenesis; gliogenesis)
2. Cell migration
3. Cell differentiation
4. Cell maturation (dendrite and axon growth)
5. Synaptogenesis (formation of synapses)
6. Cell death and synaptic pruning
7. Myelogenesis (formation of myelin)

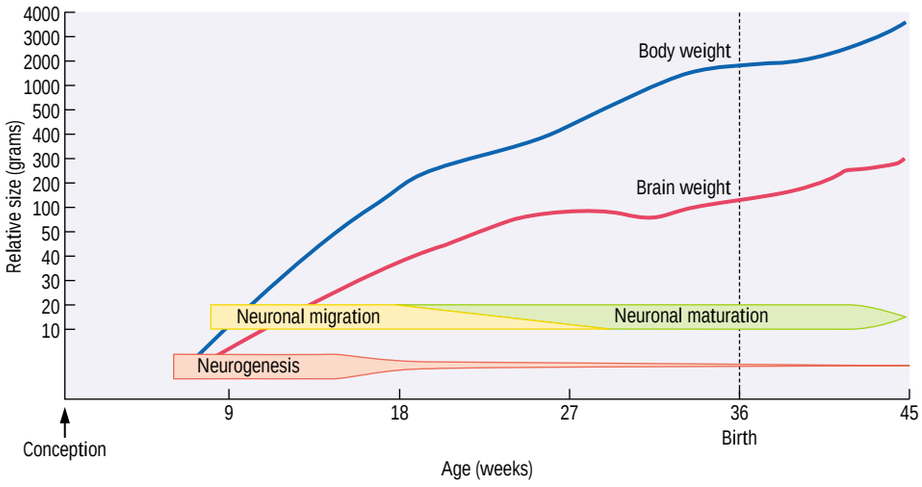


Figure 7-11

The major developmental events in the ontogenesis of the human cerebral cortex. The cortex begins to form at about 6 weeks, with neurogenesis largely complete by 20 weeks. Neural migration begins at about 8 weeks and is largely complete by about 29 weeks. Neuron maturation, including axon and dendrite growth, begins at about 20 weeks and continues until well after birth. Both brain and body weight grow rapidly, and in parallel, during the prenatal period.

Adapted from "Pathogenesis of Late-Acquired Leptomeningeal Heterotopias and Secondary Cortical Alterations: A Golgi Study," by M. Marin-Padilla, in *Dyslexia and Development: Neurobiological Aspects of Extraordinary Brains* (p. 66), edited by A. M. Galaburda, 1993, Cambridge, MA: Harvard University Press.

NEURAL GENERATION, MIGRATION, AND DIFFERENTIATION

In humans, as in other vertebrates, the brain begins as part of the neural tube, the part that contains the cells from which the brain will form. Figure 7-11 shows that the generation of the cells that will eventually form the cortex begins about 7 weeks after conception and is largely complete by 20 weeks. In other words, the process of forming neurons (called *neurogenesis*) is largely finished by about 5 months of gestation, approximately the time at which prematurely born infants have some chance of surviving.

During the next 4 months, until full-term birth, the brain is especially delicate and is extremely vulnerable to injury or trauma, including asphyxia, as explained in "Cerebral Palsy" on page 248. Apparently, the brain can more easily cope with injury during the time of neuron generation than it can during the time of cell migration or differentiation. One reason may be that, when neurogenesis has stopped, it is very hard to start it again. If neurogenesis is still progressing, it may be possible to make more neurons to replace injured ones or perhaps existing neurons can be allocated differently. The same is true in supplying the lumber for a house. If some of the lumber is damaged during milling, it is possible to make more to replace the damaged pieces. But if the lumber is damaged in transit or on site, it is not so easy to replace, especially if the mill is closed. Replacement is even more difficult if the lumber has already has been cut to size for a specific use.

Cell migration begins shortly after the first neurons are generated, but it continues for about 6 weeks after neurogenesis is complete. At this point, the process of cell differentiation, in which neuroblasts become specific types of neurons, begins. Cell differentiation is essentially complete at birth, although neuron maturation, which includes the growth of dendrites, axons, and synapses, goes on for years and, in some parts of the brain, may continue into adulthood.

As you learned in Chapter 2, the cortex is organized into various areas that are distinctly different from each other in their cellular makeup. How is this arrangement of differentiated areas created during development? Pasko Rakic and his colleagues have been finding answers to this question for the past 30 years. Apparently, the ventricular zone contains a primitive map of the cortex that predisposes cells formed in a certain ventricular region to migrate to a certain cortical location. For example, one region of the ventricular zone may produce cells destined to migrate to the visual cortex, whereas another region produces cells destined to migrate to the frontal lobes.

But how do the cells know where these different parts of the cortex are located? This problem is solved by having a road of sorts for the cells to follow. The road is made up of cells known as radial glial cells; a radial glial cell has a fiber that extends from the ventricular zone to the surface of the cortex, as illustrated in Figure 7-12. The cells from a given region of the ventricular zone need only follow the glial road and they will end up in the right location. The advantage of this system is that, as the brain grows, the glial fibers stretch but they still go to the same place. Figure 7-12 also shows a cell that is migrating perpendicularly to the radial glial fibers. Although most cortical neurons follow the radial glial fibers, a small number of neurons appear to migrate by seeking some type of chemical signal. We do not yet know why these cells function in this different way.

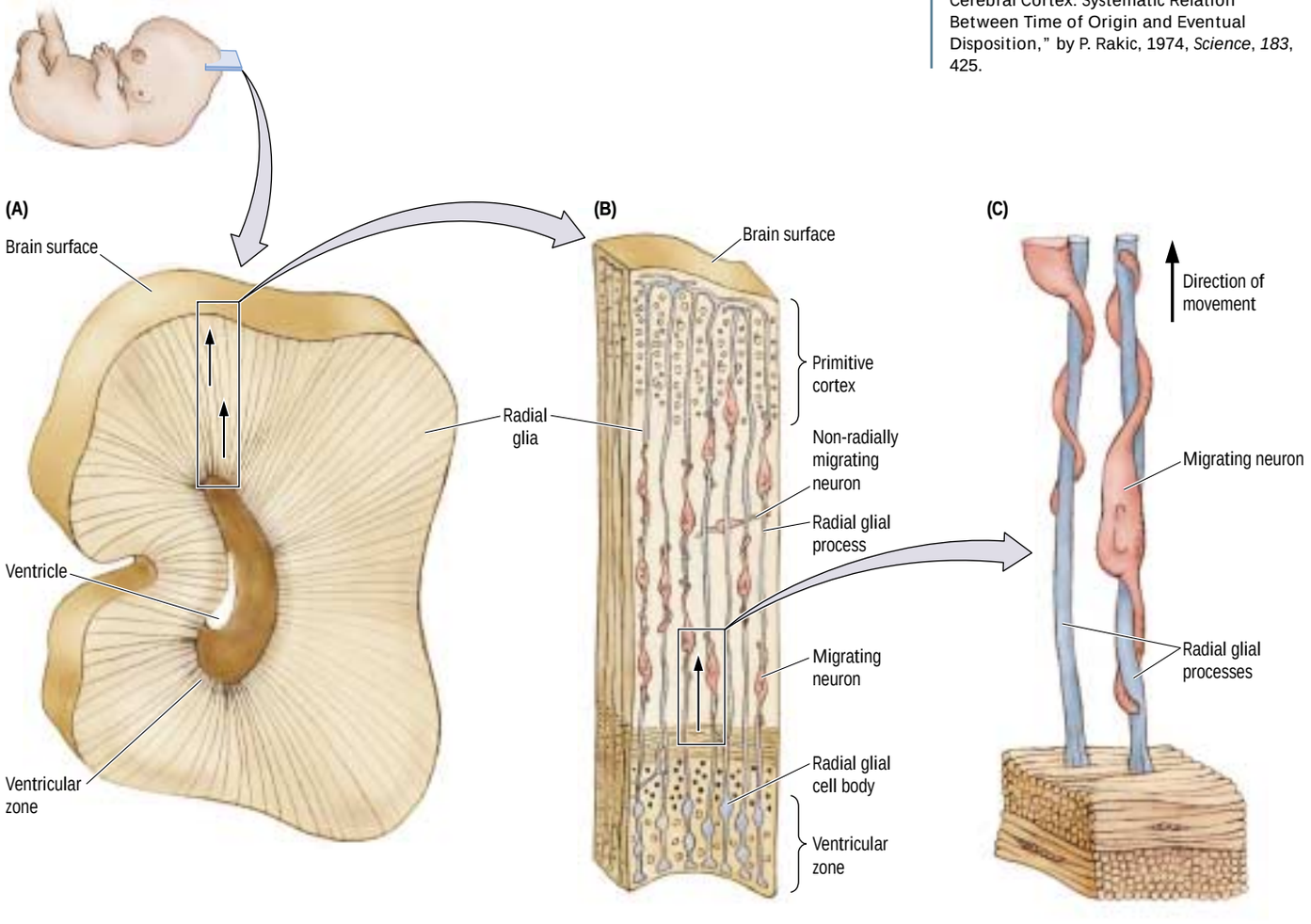
Perhaps the most obvious characteristic of the cortex is its layered appearance, also discussed in Chapter 2. The layers develop from the inside out, much like adding layers to a ball. The neurons of layer VI, which is the innermost layer, migrate to their locations first, followed by those destined for layer V, and so on. In this way, successive waves of neurons pass earlier-arriving neurons to assume progressively more exterior positions in the cortex. The formation of the cortex is a bit like building the ground floor of a house first, then the second floor, and so on, until you reach the roof. The materials needed to build higher floors must pass through lower floors to get to their destinations.

Radial glial cells. Cells that form miniature "highways" that provide pathways for migrating neurons to follow to their appropriate destinations.

Figure 7-12

(A) The map for the cortex is hypothesized to be represented in the ventricular zone. **(B)** Radial glial fibers extend from the ventricular zone to the cortical surface. **(C)** Neurons migrate along the radial glial fibers, which take them from the protomap in the ventricular zone to the respective region in the cortex.

Adapted from "Neurons in Rhesus Monkey Cerebral Cortex: Systematic Relation Between Time of Origin and Eventual Disposition," by P. Rakic, 1974, *Science*, *183*, 425.



Focus on Disorders

Cerebral Palsy

We first encountered Patsy when she took our introductory course on brain and behavior. She walked with a peculiar shuffle; her handwriting was almost illegible; and her speech was at times almost unintelligible. She got an A in the course. Patsy had cerebral palsy.

It was William Little, an English physician, who first noticed in 1853 that difficult or abnormal births could lead to later motor difficulties in children. The disorder that Little described was cerebral palsy, although it has also been called Little's disease. Cerebral palsy is relatively common worldwide, with an incidence estimated to be 1.5 in every 1000 births. Among surviving babies who weigh less than 2.5 kilograms at birth, the incidence is much higher—about 10 in every 1000.

The most common cause of cerebral palsy is birth injury, especially due to anoxia, a lack of oxygen. Anoxia may result from a defect in the placenta, the organ that allows oxygen and nutrients to pass from mother to child, or it may be caused by an entanglement of the umbilical cord during birth, which may reduce the oxygen supply to the infant. Other causes include infections, hydrocephalus, seizures, and prematurity. All produce a defect in the immature brain either before, during, or just after birth.

Most children with cerebral palsy appear normal in the first few months of life but, as the nervous system develops, the motor disturbances become progressively more noticeable. The most common symptom, which afflicts about half of those affected, is spasticity, or exaggerated contraction of muscles when they are stretched. Not surprisingly, spasticity often interferes with other motor functions. For example, people with cerebral palsy may have an odd gait, sometimes dragging one foot. A second common symptom is dyskinesia, or involuntary extraneous movements. Examples are tremors and uncontrollable jerky twists, called athetoid movements, which often occur during activities such as walking. A third common symptom is rigidity, or resistance to passive movement. For example, the patient's fingers may resist being moved passively by an examiner, even though the person is able to move the fingers voluntarily. In addition to these motor symptoms, people with cerebral palsy are at risk for retardation, although many of them, Patsy included, function at a high intellectual level and earn college and postgraduate degrees.

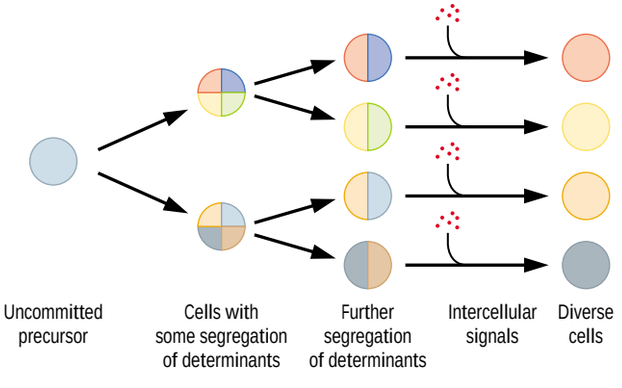


Figure 7-13

Precursor cells have an unlimited cell-fate potential but, as they develop, they become increasingly committed to a particular cell type.

One thing that facilitates the building of a house is that each new story has a blueprint-specified dimension, such as 8 feet high. But how do neurons determine how thick a cortical layer should be? This is a tough question, especially when you consider that the layers of the cortex are not all the same thickness. Probably the answer is partly related to timing. Cells that are destined to be located in a certain layer are generated at a certain time in the ventricular zone, and so they migrate together in that particular time frame. The mechanisms that govern this timing are not yet understood, however. In addition, there are likely some local environmental signals—chemicals produced by other cells—that also influence the way in which cells form layers in the cortex. These signals progressively restrict the choice of traits that a cell can express, as illustrated in Figure 7-13. Thus, the emergence of distinct types of cells in the brain does not result from the unfolding of a specific genetic program. Instead, it is due to the interaction of genetic instructions, timing, and local signals from other cells.

NEURAL MATURATION

After neurons have migrated to their final destinations and differentiated into specific neuron types, they must begin the process of growing dendrites to provide the surface area for synapses with other cells. They must also extend their axons to appropriate targets to initiate the formation of other synapses. These processes are part of neural maturation.

Two events take place in the development of a dendrite: dendritic *arborization* (branching) and the growth of dendritic spines. As illustrated in Figure 7-14, dendrites begin as individual processes protruding from the cell body. Later, they develop increasingly complex extensions that look much like the branches of trees visible in winter; that is, they undergo arborization. The dendritic branches then begin to form spines, which are the location of most synapses on the dendrites.

Although dendritic development begins prenatally in humans, it continues for a long time after birth, as Figure 7-14 shows. Dendritic growth proceeds at a relatively slow rate, on the order of micrometers per day. This rate contrasts with that for the development of axons, which grow on the order of a millimeter per day. The disparate developmental rates of axons and dendrites are important because the faster-growing axon can contact its target cell before the dendrites of that cell are completely formed. In this way, the axon may play a role in dendritic differentiation.

The development of an axon presents a significant "engineering" problem because the axon must find its way through a complex cellular terrain to make appropriate connections that may be millimeters or even centimeters away. Such a task could not possibly be specified in a rigid genetic program. Rather, the formation of axonic connections is guided by various molecules that attract or repel the developing axon.

Santiago Ramón y Cajal in the early twentieth century was the first to describe this developmental process. He called the growing tips of axons **growth cones.** Figure 7-15 shows that, as these growth cones extend, they send out shoots that are similar to fingers reaching out to find a pen on a cluttered desk. When one shoot, known as a **filopod** (plural, *filopodia*), reaches an appropriate target, the others follow. The growth cones are responsive to two types of cues. One cue consists of a variety of cell-manufactured molecules that either lie on the cell surface or are secreted into the space between cells. Some of these molecules provide a surface to which the

Growth cone. The growing tip of an axon.

Filopod. A process at the end of a developing axon that reaches out to search for a potential target.

Click on your CD to review the structure of dendrites. Find the area on the structure of a neuron in the module on Neural Communication.

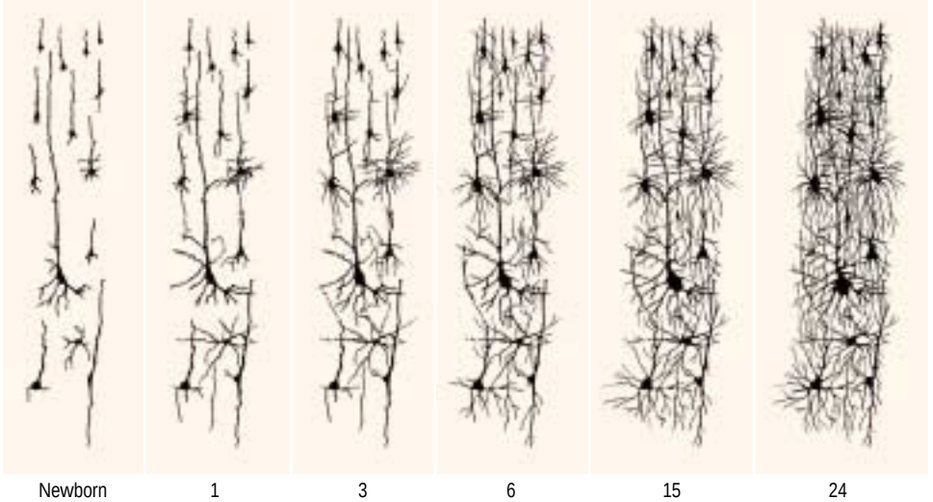


Figure 7-14

In postnatal differentiation of the human cerebral cortex around Broca's area, the neurons begin with simple dendritic fields, which become progressively more complex until a child reaches about 2 years of age.

Adapted from *Biological Foundations of Language* (pp. 160–161), by E. Lenneberg, 1967, New York: Wiley.

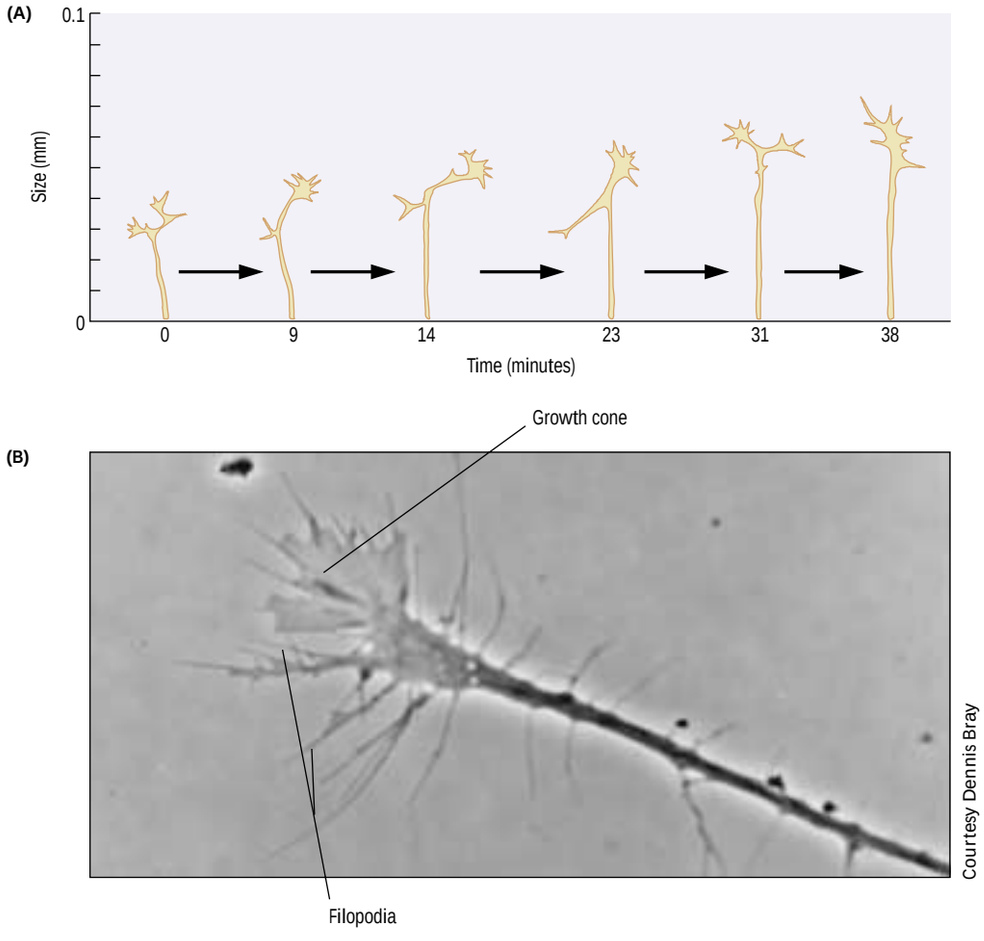


Figure 7-15

At the tip of this axon growing in culture is a growth cone that sends out filopodia seeking specific molecules that will guide axon direction. At top are drawings showing the growth in the axon tip over time. The growth cone is at the end of the axon.

growth cones can adhere and are thus called cell-adhesion molecules (CAMs), whereas others serve to attract or repel the growth cones. The second cue to which growth cones respond is chemicals, known as tropic molecules, that are produced by the targets being sought by the axons. (*Tropic* molecules, which guide axons, should not be confused with the *trophic* molecules that support the growth of neurons and their processes.) These tropic molecules essentially tell growth cones to "come over here." They likely also tell other growth cones seeking different targets to "keep away." Although Ramón y Cajal predicted the presence of tropic molecules more than 100 years ago, they have proved difficult to find. Only one group of tropic molecules, known as netrins (from Sanskrit meaning "to guide"), has so far been identified. Given the enormous number of connections in the brain and the great complexity in wiring them, it seems likely that many other types of tropic molecules are still to be found.

SYNAPTIC DEVELOPMENT

The number of synapses in the human cerebral cortex is staggering, on the order of 10^{14}. This huge number could not possibly be determined by a genetic program that assigns each synapse a specific location. Instead, it is more likely that only the general outlines of neural connections in the brain are predetermined. The vast array of specific synaptic contacts is then guided into place by a variety of cues and signals.

In humans, simple synaptic contacts exist in the fifth gestational month. By the seventh gestational month, synaptic development on the deepest cortical neurons is extensive. After birth, the number of synapses increases rapidly. In the visual cortex,

Cell-adhesion molecule (CAM). A chemical to which specific cells can adhere, thus aiding in migration.

Tropic molecule. A signaling molecule that attracts or repels growth cones.

Netrins. A class of tropic molecules.

synaptic density almost doubles between age 2 months and age 4 months and then continues to increase until age 1 year.

CELL DEATH AND SYNAPTIC PRUNING

Perhaps the most surprising events in vertebrate brain development are cell death and synaptic pruning. These terms mean that there is first an overproduction of neurons and synapses and then a subsequent loss of them. For example, as already stated, the number of synapses in the visual cortex increases rapidly after birth, reaches a peak at about 1 year, and begins to decline as the brain apparently prunes out unnecessary or incorrect synapses. The graph in Figure 7-16 plots this rise and fall in synaptic density. Pasko Rakic estimated that, at the peak of synapse loss in humans, as many as 100,000 synapses may be lost per second. We can only wonder what the behavioral consequence of this rapid synaptic loss might be. It is probably no coincidence that children seem to change moods and behaviors quickly.

How does the brain accomplish this elimination of neurons? The simplest explanation is competition, sometimes referred to as neural Darwinism. Charles Darwin believed that the key to evolution was the production of variation in the traits that a species possesses. Certain traits can then be selected by the environment for their favorableness in aiding survival. According to a Darwinian perspective, then, more animals are born than can survive to adulthood, and environmental pressures "weed out" the less fit ones. Similar pressures cause neural Darwinism.

But what exactly is causing this weeding out of cells in the brain? It turns out that, when neurons form synapses, they become somewhat dependent on their targets for survival. In fact, if deprived of synaptic targets, they eventually die. This neuron death occurs because target cells produce signaling molecules—the neurotrophic factors that we encountered earlier—that are absorbed by the axon terminals and function to regulate neuronal survival. If many neurons are competing for a limited amount of a neurotrophic factor, only some of those neurons can survive. The death of neurons deprived of a neurotrophic factor is different from the cell death caused by injury or disease. It seems that, when neurons are deprived of a neurotrophic factor,

Neural Darwinism. The idea that the process of cell death and synaptic pruning is not random but is the outcome of competition between neurons for connections and metabolic resources.

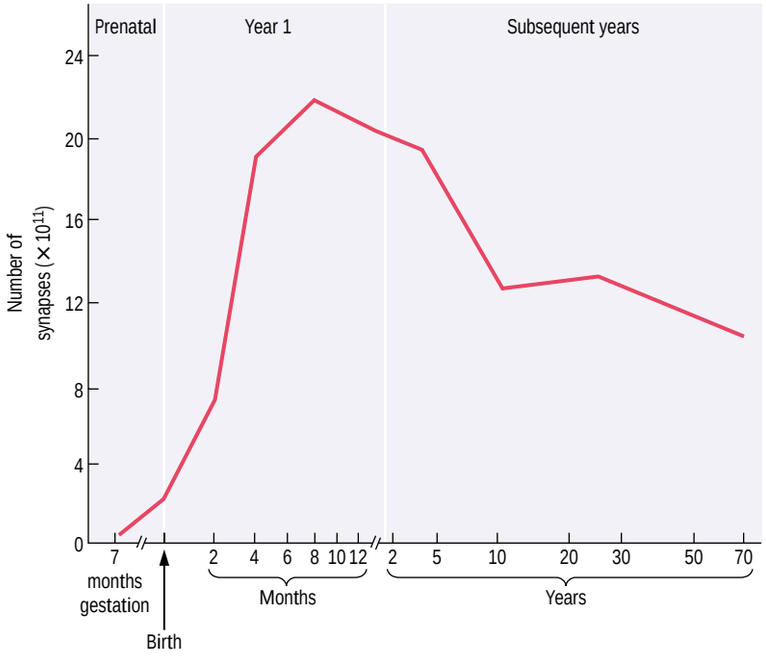


Figure 7-16

This estimate of the total number of synapses in the human visual cortex as a function of age shows that the synapse number rises rapidly, peaking at about 1 year. Then the number declines until about 10 years of age, at which point synapse number levels off until early adulthood, when it begins to drop again.

Adapted from "Synaptogenesis in Human Cerebral Cortex," by P. R. Huttenlocher, in *Human Behavior and the Developing Brain* (p. 142), edited by G. Dawson and K. W. Fischer, 1994, New York: Guilford Press.

Apoptosis. Cell death that is genetically programmed.

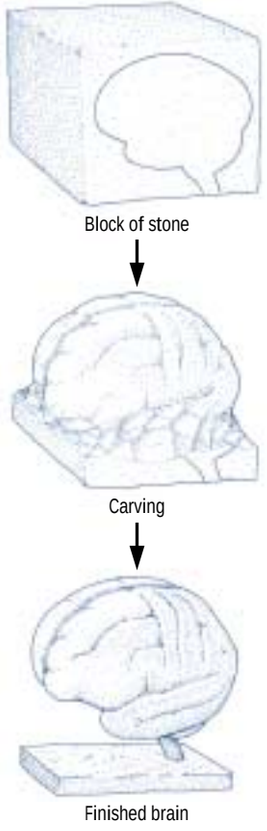
certain genes are "turned on" that result in a message for the cell to die. This process is called apoptosis.

Apoptosis accounts for the death of overabundant neurons, but it does not account for the pruning of synapses from cells that survive. In 1976, the French neurobiologist Jean-Pierre. Changeux proposed a theory for synapse loss that also is based on competition. According to Changeux, synapses persist into adulthood only if they have become members of functional neural networks. If they have not, they are eventually eliminated from the brain.

An example will help explain this mechanism of synaptic pruning. Consider neural input to the midbrain from the eyes and ears. The visual input goes to the superior colliculus, and the auditory input goes to the inferior colliculus. Some errant axons from the auditory system will likely end up in the visual midbrain and form synapses with the same cells as those connected to axons coming from the visual pathway. However, the auditory axons are not part of functional networks in this location. Whereas inputs from an eye are apt to be active at the same time as one another, inputs from an ear are unlikely to be active along with the visual ones. The presence of simultaneous electrical activity in a set of visually related synapses leads to the formation of a neural circuit comprising those synapses. In contrast, the errant auditory inputs, because they are not active at the same time as the visual inputs, become unstable and are eventually eliminated. We can speculate that factors such as hormones, drugs, and experience would influence the formation of active neural circuits and thus influence the processes of synapse stabilization and pruning. In fact, as you will see shortly, experience can have truly massive effects on the organization of the nervous system.

Richard Tees Janet Werker

In addition to outright errors in synapse formation that give rise to synaptic pruning, more subtle changes in neural circuits may trigger the same process. An instance of this accounts for the findings of Janet Werker and Richard Tees (1992), who studied the ability of infants to discriminate speech sounds taken from widely disparate languages, such as English, Hindi (from India), and Salish (a Native American language). Their results showed that young infants can discriminate speech sounds of different languages without previous experience, but their ability to do so declines over the first year of life. One explanation of this declining ability is that synapses encoding speech sounds not normally encountered in the infant's daily environment are not active simultaneously with other speech-related synapses. As a result, they become unstable and are eliminated.



Synapse elimination is quite extensive. Peter Huttenlocher (1994) estimated it to be on the order of 42 percent of all synapses in the human cortex. Synapse elimination is much less extensive in smaller-brained animals, however. In the rat cortex, it is about 10 percent, and, in the cat cortex, about 30 percent. The reason for these differences may be that, the larger the brain, the more difficult it is to make precise connections and so the greater the need for synaptic pruning. Synaptic pruning may also allow the brain to adapt more flexibly to environmental demands. Human cultures are probably the most diverse and complex environments with which any animal must cope. Perhaps the flexibility in cortical organization that is achieved by the mechanism of selective synaptic pruning is a necessary precondition for developing this kind of environment. It may also be a precursor to disputes related to different perceptions of the world.

The value of cell death and synaptic pruning can be seen through an analogy. If you wanted to make a statue, you could do so either by starting with grains of sand and gluing them together to form the desired shape or by starting with a block of stone and chiseling the unwanted pieces away. Sculptors consider the second route much easier. They start with more than they need and eliminate the excess. So does

the brain. It makes too many neurons and too many connections and then gets rid of the unessential ones. The "chisel" in the brain could be of several forms, including a genetic signal, experience, reproductive hormones, and stress.

Glial Development

The birth of astrocytes and oligodendrocytes begins after most neurons are born and continues throughout life. As you know from Chapter 3, oligodendroglia form the myelin that surrounds axons in the spinal cord and brain. Although axons can function before they are encased by myelin, normal adult function is attained only after myelination is complete. Consequently, myelination is useful as a rough index of cerebral maturation.

In the early 1920s, Paul Flechsig noticed that myelination of the cortex begins just after birth and continues until nearly 18 years of age. He also noticed that some cortical regions were myelinated by age 3 to 4 years, whereas others showed virtually no myelination at that time. Figure 7-17 shows one of Flechsig's maps of the brain, with areas shaded according to the age at which myelination takes place. Flechsig hypothesized that the earliest-maturing areas control relatively simple movements or sensory analyses, whereas the late-myelinating areas control the highest mental functions.

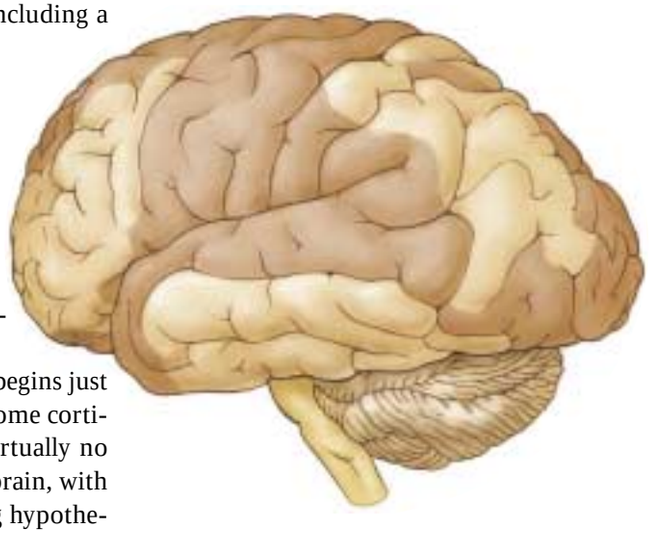


Figure 7-17

A map of how myelination progresses in the human cortex, based on Flechsig's research. The light-colored zones are very late to myelinate, which led Flechsig to propose that they are qualitatively different in function from those that mature earlier.

In Review

Brain development begins with the growth of the first neural stem cell in the third week of embryonic development. The nervous system begins as a sheet of cells that folds to become a tube, known as the neural tube. Brain formation then proceeds rapidly; by about 100 days after conception, the brain begins to look human in form. The neurons and glia of the brain develop through a series of seven stages: birth, migration, differentiation, maturation, synaptic formation, death, and myelination. Neurons begin to process information before they are completely mature, but their activity is much simpler than it will be with full maturation. Behavioral development is therefore constrained by the maturation of brain cells. For example, although infants and children are capable of complex movements, it is not until the completion of myelin formation in adolescence that adult levels of coordination and fine motor control are reached. By studying how the nervous system develops and matures, we are able to make predictions about when behaviors will emerge. Conversely, by studying the stages of behavioral development, we can make predictions about developments taking place in the brain.

CORRELATING BEHAVIOR WITH BRAIN DEVELOPMENT

It is reasonable to assume that, as a particular brain area matures, a person exhibits behaviors corresponding to that particular mature brain structure. The strongest advocate of this view has been Eric Lenneberg, who, in 1967, published a seminal book titled *Biological Foundations of Language*. A principal theme of this book is that children's acquisition of language is tied to the development of the critical language areas in the cerebral cortex. This idea immediately stimulated debate over the merits of correlating brain and behavioral development. Now, 30-some years later, the relation between brain development and behavior is widely accepted, although the influence of experience and learning on behavior is still considered critical. Psychologists believe

that behaviors cannot emerge until the neural machinery for them has developed, but, when that machinery is in place, related behaviors develop quickly and are shaped significantly by experience. The new behaviors then alter brain structure by the processes of neural Darwinism presented earlier. Researchers have studied these interacting changes in the brain and behavior, especially in regard to the emergence of motor skills, language, and problem solving in children. We will explore each of these topics separately.

Motor Behaviors

Link to the Web site at **www.worthpublishers.com/kolb/chapter7** to see some more examples of motor development during childhood.

The development of locomotion in human infants is easy to observe. At first, babies are unable to move about independently but, eventually, they learn to crawl and then to walk. Other motor skills develop is less obvious but no less systematic ways. For example, Tom Twitchell studied and described the development of the ability to reach for and grasp objects. This development progresses in a series of stages, illustrated in Figure 7-18. Shortly after birth, an infant is capable of flexing the joints of an arm in such a way that he or she could scoop something toward the body, but, at this age, infants do not seem to direct their arm movements toward any specific thing. Then, between 1 and 3 months of age, a baby begins to orient a hand toward an object that the hand has touched and gropes to hold that object. For example, if the baby's hand touches a stick, the fingers will flex to grasp it. At this stage, however, all the fingers flex together. Between 8 and 11 months, infants' grasping becomes more sophisticated as the "pincer grasp," which uses the index finger and the thumb, develops. The pincer grasp is a significant development because it allows babies to make the very precise finger movements needed to manipulate small objects. What we see, then, is a sequence in the development of grasping: first scooping, then grasping with all of the fingers, and then grasping by using independent finger movements.

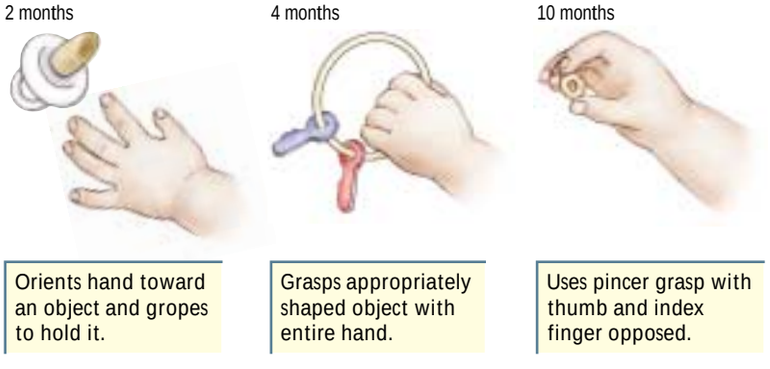


Figure 7-18

Development of the grasping response of infants.

Adapted from "The Automatic Grasping Response of Infants," by T. E. Twitchell, 1965, *Neuropsychologia*, 3, p. 251.

If the development of increasingly well-coordinated grasping depends on the emergence of certain neural machinery, anatomical changes in the brain should accompany the emergence of these behaviors. Probably many such changes take place, especially in the development of dendritic arborizations. However, a correlation between myelin formation and the ability to grasp has been found. In particular, a group of axons from motor-cortex neurons becomes myelinated at about the same time that reaching and grasping with the whole hand develop. Similarly, another group of motor-cortex neurons, which are known to control finger movements, becomes myelinated at about the time that the pincer grasp develops.

We can now make a simple prediction. If specific motor-cortex neurons are essential for adultlike grasping movements to emerge, removal of those neurons should make an adult's grasping ability similar to that of a young infant, which is in fact what happens. One of the classic symptoms of damage to the motor cortex is the permanent loss of the pincer grasp.

Visit the CD to review myelination of axons and how this process affects neural transmission. Find the area on the conduction of the action potential in the module on Neural Communication.

Language Development

The acquisition of speech follows a gradual series of developments that has usually progressed quite far by the age of 3 or 4. According to Lenneberg, children reach certain important speech milestones in a fixed sequence and at relatively constant chronological ages. These milestones are summarized in Table 7-2.

Table 7-2 Postnatal Development of Basic Language Functions

Approximate age	Basic social and language functions
Birth	Comforted by sound of human voice; most common utterances are discomfort and hunger cries
6 weeks	Responds to human voice and makes cooing and pleasure noises; cries to gain assistance
2 months	Begins to distinguish different speech sounds; cooing becomes more guttural or "throaty"
3 months	Orients head to voices; makes a vocal response to others' speech; begins babbling, or chanting various syllabic sounds in a rhythmic fashion
4 months	Begins to vary pitch of vocalizations; imitates tones
6 months	Begins to imitate sounds made by others
9 months	Begins to convey meaning through intonation, using patterns that resemble adult intonations
12 months	Starts to develop a vocabulary; a 12-month-old may have a 5–10 word vocabulary that will double in the next 6 months
24 months	Vocabulary expands rapidly and can be approximately 200–300 words; names most common everyday objects; most utterances are single words
36 months	Has 900–1000 word vocabulary; 3- to 4-word simply constructed sentences (subject and verb); can follow two-step commands
4 years	Has a vocabulary of more than 1500 words; asks numerous questions; sentences become more complex
5 years	Typically has a vocabulary of approximately 1500–2200 words; discusses feelings; the average 5- to 7-year-old has acquired a slow but fluent ability to read; handwriting also likely to be slow
6 years	Speaks with a vocabulary of about 2600 words; understands 20,000–24,000 words; uses all parts of speech
Adult	Has 50,000+ word vocabulary by 12 years old

Adapted from "Development of the Child's Brain and Behavior," by B. Kolb and B. Fantie, in *Handbook of Clinical Child Neuropsychology* (2nd ed, p. 29), edited by C. R. Reynolds and E. Fletcher-Janzen, New York: Plenum.

Although there is a general parallel between language development and the development of motor capacities, language development depends on more than just the ability to make controlled movements of the mouth, lips, and tongue. Precise movements of the muscles controlling these body parts develop well before children can speak. Furthermore, even when children have sufficient motor skill to articulate most words, their vocabulary does not rocket ahead, but rather progresses gradually. A small proportion of children (about 1 percent) have normal intelligence and normal motor-skill development, and yet their speech acquisition is markedly delayed. Such children may not begin to speak in phrases until after age 4, despite an apparently normal environment and the absence of any obvious neurological signs of brain damage. Because the timing of the onset of speech appears to be so universal in the remaining 99 percent of children across all cultures, it seems likely that there is something different in the brain maturation of a child with late language acquisition. But it is hard to specify what that difference is. Because language onset is usually between ages 1 and 2 and language acquisition is largely complete by age 12, the best strategy is to consider how the cortex is different before and after these two age milestones.

By 2 years of age, cell division and migration are complete in the language zones of the cerebral cortex. The major changes that take place between the ages of 2 and 12 are in the interconnections of neurons and the myelination of the speech zones. The

changes in dendritic complexity in these areas are among the most impressive in the brain. As illustrated in Figure 7-13, the axons and dendrites of the speech zone called Broca's area are simple at birth but become dramatically more dense between 15 and 24 months of age. This development correlates with an equally dramatic change in language ability, given that this age is when a baby's vocabulary starts to expand rapidly. We can therefore infer that language development may be constrained, at least in part, by the maturation of language areas in the cortex. Individual differences in the speed of language acquisition may be accounted for by differences in this neural development. Children with early language abilities may have early maturation of the speech zones, whereas children with delayed language onset may have later speech-zone maturation.

The Development of Problem-Solving Ability

The first person to try to identify stages of cognitive development was the Swiss psychologist Jean Piaget. He realized that the behavior of children could be used to make inferences about their understanding of the world. For example, a baby who lifts a cloth to retrieve a hidden toy is showing an understanding that objects continue to exist even when out of sight. This understanding, called the concept of *object permanence*, is revealed by the behavior of the infant in the upper photographs of Figure 7-19. An absence of understanding also can be seen in children's behavior, as shown by the actions of the 5-year-old girl in the lower photographs of Figure 7-19. She was shown two beakers with identical volumes of liquid in each, and then watched as one beaker's liquid was poured into a skinnier beaker. When asked which beaker contained more

Doug Goodman/Monkmeyer

Courtesy Don and Sandy Hockenbury

Figure 7-19

Stages of cognitive development. (*Top*) The infant illustrates that she understands that things continue to exist when they are out of sight. (*Bottom*) This girl does not yet understand the principle of conservation of volume. Beakers with identical volumes seem to hold different amounts.

Table 7-3 Piaget's Stages of Cognitive Development

Typical age range	Description of the stage	Developmental phenomena
Birth to 18–24 months	*Stage I: Sensorimotor* Experiences the world through senses and actions (looking, touching, mouthing)	Object permanence Stranger anxiety
About 2–6 years	*Stage II: Preoperational* Represents things with words and images but lacks logical reasoning	Pretend play Egocentrism Language development
About 7–11 years	*Stage III: Concrete operational* Thinks logically about concrete events; grasps concrete analogies and performs arithmetical operations	Conservation Mathematical transformations
About 12+ years	*Stage IV: Formal operational* Reasons abstractly	Abstract logic Potential for mature moral reasoning

liquid, she pointed to the taller, skinnier beaker, not understanding that the amount of liquid remains constant despite the difference in appearance. An understanding of this principle, called *conservation of liquid volume*, is not displayed until about age 7.

By studying children engaged in such tasks, Piaget concluded that cognitive development is a continuous process. Children's strategies for exploring the world, and their understanding of it, are constantly changing. These changes are not simply the result of acquiring specific pieces of new knowledge. Rather, at certain points in development, fundamental changes take place in the organization of a child's strategies for learning about the world, and with these changes come new understandings.

Piaget identified four major stages of cognitive development, which are summarized in Table 7-3. Stage I is the sensorimotor period, from birth to about 18 to 24 months of age. During this time, babies learn to differentiate themselves from the external world, they come to realize that objects exist even when out of sight, and they gain some understanding of cause-and-effect relations. Next is stage II, the preoperational period, from age 2 to 6 years. This stage is when children become able to form mental representations of things in their world and to represent those things in words and drawings. Stage III is the period of concrete operations, from age 7 to 11 years. At this stage, children are able to mentally manipulate concrete ideas such as volumes of liquid and dimensions of objects. Finally, stage IV is the period of formal operations, which is reached after age 11. The child is now able to reason in the abstract, not just in concrete terms.

If we take Piaget's stages as rough approximations of qualitative changes that take place in children's thinking as they grow older, we can ask what changes in the brain might underlie them. One place to look for brain changes is in the relative rate of brain growth. After birth, the brain does not grow uniformly; rather, it tends to increase its mass during irregularly occurring periods commonly called growth spurts. In his analysis of brain-to-body-weight ratios, Herman Epstein found consistent spurts in brain growth between 3 and 10 months (accounting for an increase of 30 percent in brain weight by the age of 1½ years) as well as from the ages of 2 to 4, 6 to 8, 10 to 12, and 14 to 16+ years. The increments in brain weight were from about 5 to 10 percent in each of these 2-year periods. The brain growth takes place without a concurrent increase in the number of neurons, so it is most likely due to the growth of glial cells and synapses. Although synapses themselves would be unlikely to add much weight to the brain, the growth of synapses is accompanied by increased metabolic demands, which cause neurons to become larger, new blood vessels to form, and new astrocytes to be produced.

Growth spurt. A sudden growth in development that lasts for a finite time.

We would expect such an increase in the complexity of the cortex to generate more complex behaviors, so we might predict that there would be significant, perhaps qualitative, changes in cognitive function during each of the growth spurts. The first four brain-growth spurts coincide nicely with the four main stages of cognitive development described by Piaget. This correspondence suggests that there may be significant alterations in neural functioning with the onset of each of Piaget's stages. At the same time, differences in the rate of brain development or perhaps in the rate at which specific groups of neurons mature may account for individual differences in the age at which the various cognitive advances that Piaget identified emerge. Although Piaget did not identify a fifth stage of cognitive development in later adolescence, the presence of a growth spurt then implies that there may, in fact, be one.

One difficulty in linking brain-growth spurts to cognitive development is that growth spurts are superficial measures of changes taking place in the brain. We need to know what neural events are contributing to brain growth and just where they are taking place. A way to find this out is to observe children's attempts to solve specific problems that are diagnostic of damage to discrete brain regions in adults. If children perform a particular task poorly, then whatever brain region regulates the performance of that task in adults must not yet be mature in children. Similarly, if children can perform one task but not another, the tasks apparently require different brain structures and these structures mature at different rates.

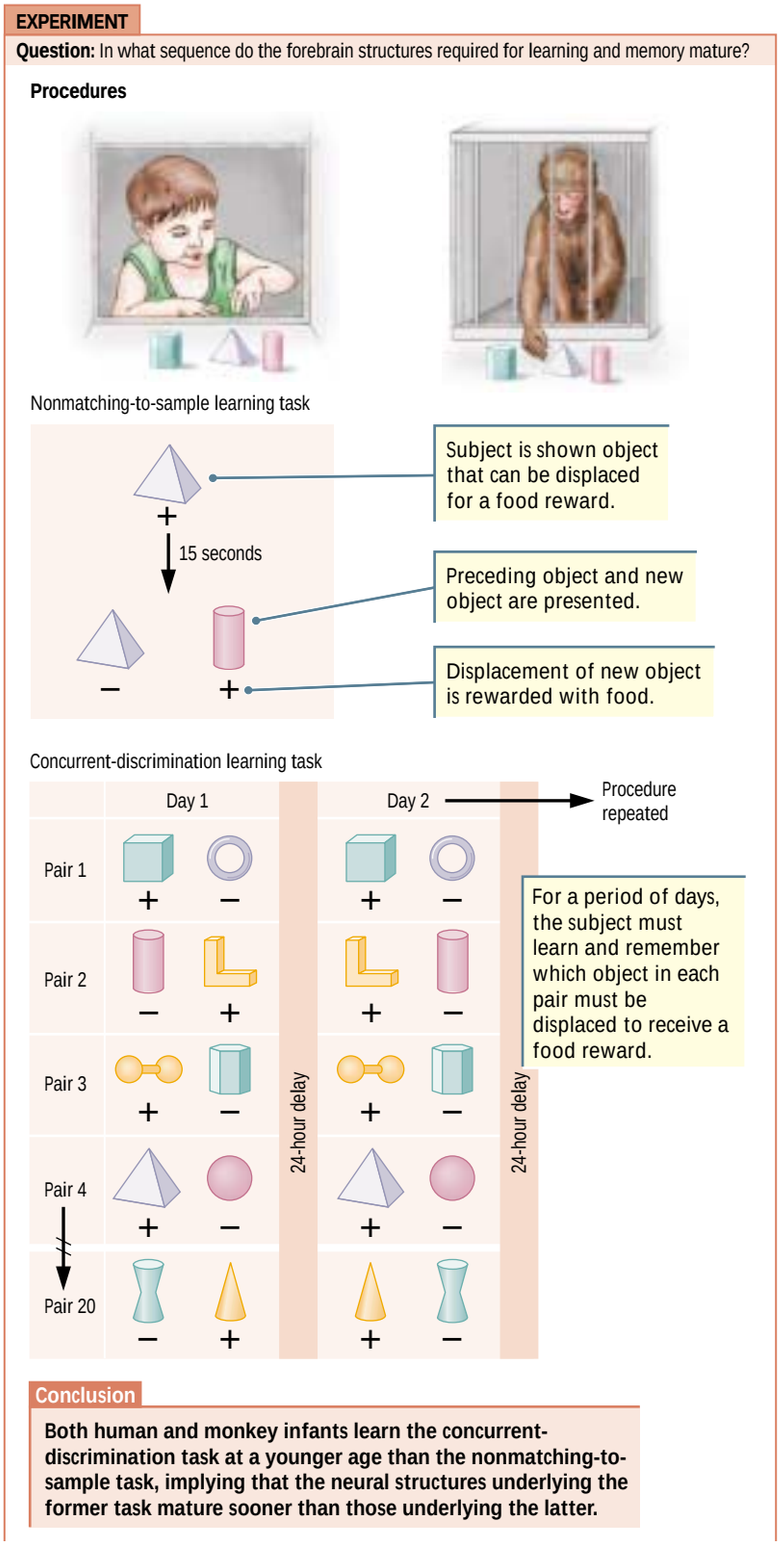


Figure 7-20

An experiment designed to show the order in which forebrain structures involved in learning and memory mature. In these versions of the Wisconsin General Test Apparatus, the subject's task is to displace an object to reveal a food reward. The non matching-to-sample task requires maturation of the temporal lobes, while the concurrent-discrimination task requires maturation of the basal ganglia. Both human and monkey infants learn the concurrent task at a younger age than the matching task, implying that the neural structures underlying the former type of learning mature sooner than those underlying the latter.

Adapted from "Object Recognition Versus Object Discrimination: Comparison Between Human Infants and Infant Monkeys," by W. H. Overman, J. Bachevalier, M. Turner, and A. Peuster, 1992, *Behavioral Neuroscience*, *106*, p. 18.

Bill Overman and Jocelyn Bachevalier used this logic to study the development of forebrain structures required for learning and memory in young children and monkeys. Figure 7-20 shows the tests that they presented to their subjects. The first task was simply to learn to displace an object to obtain a food reward. When the subjects had learned this task, they were trained in two more tasks that are believed to measure the functioning of the temporal lobes and the basal ganglia, respectively. In the first of these two additional tasks, the subjects were shown an object, which they could displace to receive a food reward. After a brief (15-second) delay, two objects were presented: the first object and a novel object. The subjects then had to displace the novel object to obtain the food reward. This task, called *nonmatching to sample*, is thought to measure object recognition, which is a function of the temporal lobes. The subject can find the food only by recognizing the original object and *not* choosing it. In the second of the two additional tasks, the subjects were presented with a pair of objects and had to learn that one object in that pair was always associated with a food reward, whereas the other object was never rewarded. The task was made more difficult by sequentially giving the subjects 20 different object pairs. Each day, they were presented with one trial per pair. This task, called *concurrent discrimination*, is thought to measure trial-and-error learning of specific object information, which is a function of the basal ganglia.

Bill Overman

Adults easily solve both tasks, but they say that the concurrent task is more difficult because it requires remembering far more information than the nonmatching-to-sample task. The key question developmentally is whether there is a difference in the age at which children (or monkeys) can solve these two tasks. It turns out that children can solve the concurrent task by about 12 months of age, but not until about 18 months of age can they solve what most adults believe to be the easier task. These results imply that the basal ganglia, which is the critical site for the concurrent-discrimination task, mature more quickly than the temporal lobe, which is the critical region for the nonmatching-to-sample task.

In Review

As children develop, increasingly mature behaviors emerge in a predictable sequence. This behavioral development is probably related to neural changes in the brain. For example, as the cortex and basal ganglia develop, different motor abilities and cognitive capacities emerge. As you will see in the next section, these developing behaviors are shaped not only by the emergence of brain structures but also by the experiences that each person has.

BRAIN DEVELOPMENT AND THE ENVIRONMENT

Brain plasticity. The capacity of the brain to change in response to chemicals, activity, or experience.

Brain plasticity refers to the lifelong changes in the structure of the brain that accompany experience. This term suggests that the brain is pliable, like plastic, and can be molded into different forms, at least at the microscopic level. Brains exposed to different environmental experiences are molded in different ways. Culture is part of the human environment, so culture helps to mold the human brain. We would therefore expect people in different cultures to acquire differences in brain structure that would have a lifelong effect on their behavior.

The brain is plastic not only in response to external events but also in response to events within a person's body, including the effects of hormones, injury, and abnormal

genes. The developing brain early in life is especially responsive to these internal factors, which in turn alter the way that the brain reacts to external experiences. In this section, we explore a whole range of environmental influences on brain development, including both external and internal ones. We start with the question of exactly how experience manages to alter brain structure.

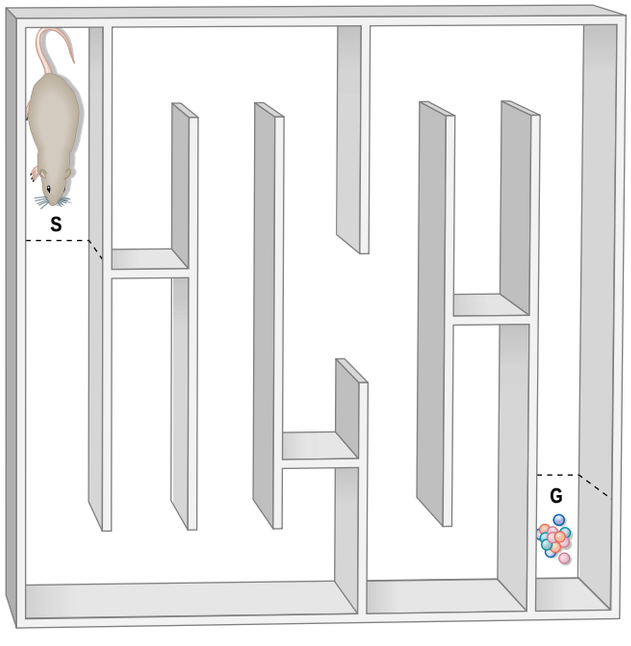
Experience and Cortical Organization

Researchers can study the effects of experience on the brain and behavior by placing laboratory animals in different environments and observing the results. In one of the earliest such studies, Donald Hebb took one group of young laboratory rats home and let them grow up in his kitchen. A control group grew up in standard laboratory cages at McGill University. The "home rats" had many experiences that the caged rats did not, including being chased with a broom by Hebb's less-than-enthusiastic wife. Subsequently, Hebb gave all the rats a rat-specific "intelligence test" that consisted of learning to solve a series of mazes, collectively known as *Hebb-Williams mazes*. An example of a Hebb-Williams maze is shown in Figure 7-21. The home rats performed far better on these tasks than the caged rats did. Hebb therefore concluded that intelligence must be influenced by experience.

On the basis of his research, Hebb reasoned that people reared in stimulating environments would maximize their intellectual development, whereas people raised in impoverished environments would not reach their intellectual potential. Although this seems to be a logical conclusion, there is a problem in defining what stimulating and impoverished environments are. People living in slums with little education are not in what we would normally call an enriched setting, but that does not necessarily mean that the environment offers no cognitive stimulation or challenge. Certainly, people raised in this setting would be better adapted for survival in a slum than people raised in upper-class homes. Does this make them more intelligent in a certain way? Perhaps. In contrast, slum dwellers are not likely to be well adapted for college life, which was probably closer to what Hebb had in mind when he referred to such an environment as limiting intellectual potential. Indeed, it was Hebb's logic that led to the development of preschool television programs such as *Sesame Street*, which tried to provide a form of enrichment for children who would otherwise have little preschool exposure to reading.

Figure 7-21

In this version of the Hebb-Williams maze, a rat is placed in the start box (S) and must learn to find the food in the goal box (G). The walls of the maze can be moved to create new problems. Rats raised in complex environments solve such mazes much more quickly than do rats raised in standard laboratory cages.



The idea that early experience can change later behavior seems sensible enough, but we are left with the question of why experience should make such a difference. One reason is that experience changes the structure of neurons in the brain, especially in the cortex. Neurons in the brains of animals raised in complex environments, such as the environment shown in Figure 7-22, are larger and have more synapses than do those of animals reared in barren cages. Presumably, the increased number of synapses results from increased sensory processing in a complex and stimulating environment. There are also more (and larger) astrocytes in the brains of animals raised in complex settings.

Although complex-rearing studies do not address the effects of human culture directly, it is easy to make predictions about human development on the basis of their findings. We know that experience can modify the brain, so we can predict that different experiences might modify the brain differently, which seems to be the case in language development. Recall that exposure to different languages in infancy alters a child's subsequent ability to dis-

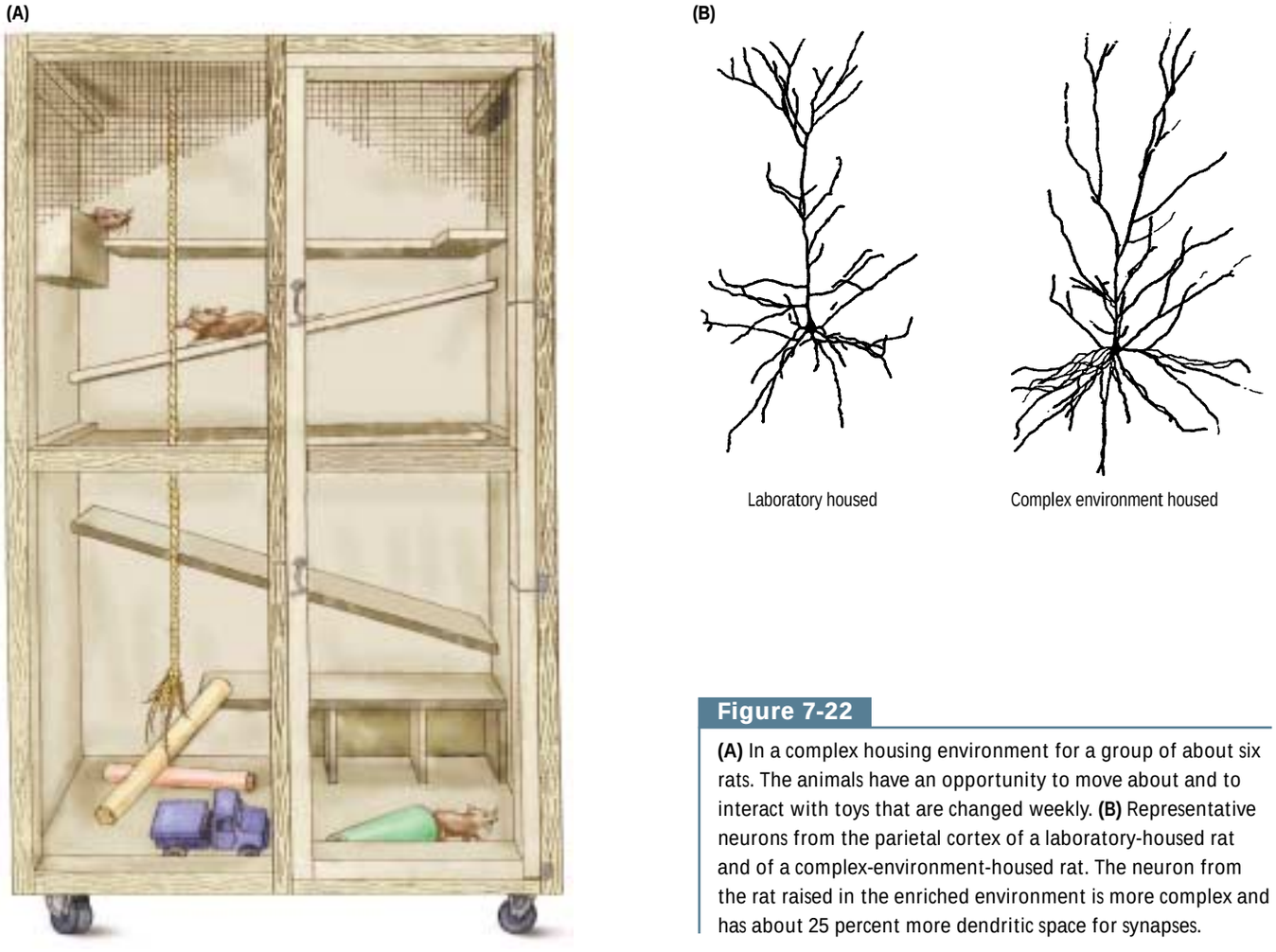


Figure 7-22

(A) In a complex housing environment for a group of about six rats. The animals have an opportunity to move about and to interact with toys that are changed weekly. **(B)** Representative neurons from the parietal cortex of a laboratory-housed rat and of a complex-environment-housed rat. The neuron from the rat raised in the enriched environment is more complex and has about 25 percent more dendritic space for synapses.

criminate language-specific speech sounds. A similar process is likely to occur for music. People exposed to Western music since childhood usually find Eastern music peculiar, even nonmusical, on first encountering it when they are adults. Presumably, cells in the language- and music-analysis systems of the auditory cortex are altered by early experience and lose much of their plasticity in adulthood.

This loss of plasticity does not mean that the human brain becomes fixed and unchangeable in adulthood, however. There is little doubt that the brains of adults are influenced by exposure to new environments and experiences, although probably more slowly and less extensively than the brains of children are. Animal studies have shown plasticity in the adult brain. In fact, there is evidence that the brain is affected by experience well into old age, which is good news for those of us who are no longer children.

Experience and Neural Connectivity

If experience can influence the structure of the cerebral cortex after a person is born, can it also do so prenatally? It can. This prenatal influence of experience is very clearly illustrated in studies of the developing visual system.

Consider the problem of connecting the eyes to the rest of the visual system. The problem can be understood with a simple analogy. Imagine that students in a large lecture hall are each viewing the front of the room (the visual field) through a small

Chemoaffinity hypothesis. The idea that cells or their axons and dendrites are drawn toward a signaling chemical that indicates the correct direction in which to go.

Amblyopia. A condition in which vision in one eye is reduced as a result of disuse; usually caused by a failure of the two eyes to point in the same direction.

cardboard tube, such as that for a paper-towel roll. If each student looks directly ahead, he or she will each see only a small bit of the visual field. This is essentially how the photoreceptors in the eyes act. Each of these cells sees only a small bit of the visual field. The problem is to put all the bits together to form a complete picture. To do so, receptors that see adjacent views (analogous to students sitting side by side) must send their information to adjacent regions in the various parts of the brain's visual system, such as the midbrain. How do they accomplish this feat?

Roger Sperry suggested that specific molecules exist in different cells in the various regions of the midbrain, giving each cell a distinctive chemical identity. Each cell, in other words, has an identifiable biochemical label. This idea is called the chemoaffinity hypothesis. Presumably, incoming axons seek out a specific chemical, such as the tropic factors discussed earlier, and consequently land in the correct general region of the midbrain. Many experiments have shown this process to take place. But the problem is that chemical affinity "directs" incoming axons to only the general location in which they need to be. To return to our two adjacent retinal cells, how do they now place themselves in the *precisely* correct position?

This fine-tuning of placement is believed to be activity dependent. Because adjacent receptors tend to be activated at the same time, they tend to form synapses on the same neurons in the midbrain, after chemoaffinity has drawn them to a general midbrain region. This process is shown in Figure 7-23. Neurons A and G are unlikely to be activated by the same stimulus and so they seldom fire synchronously. Neurons A and B, in contrast, are apt to be activated by the same stimuli, as are B and C. Through this simultaneous activity, cells eventually line up correctly in the connections that they form.

Now consider what happens to axons coming from different eyes. Although the inputs from the two eyes may be active simultaneously, the activity of cells in the same eye are more likely to be active together than are cells in different eyes. The net effect is that inputs from the two eyes tend to organize themselves into bands, or columns, that represent the same region of space in each of the eyes, as shown in Figure 7-24. The formation of these segregated bands therefore depends on the patterns of coinciding electrical activity on the incoming axons.

The importance of coinciding electrical activity and the formation of neural columns in the brain are demonstrated beautifully in a clever experiment by Martha Constantine-Paton. She knew that, because the optic nerves of frogs are completely crossed, the optic tectum on each side has input from only one eye. She wondered what would happen if a third eye were transplanted in the embryonic frog head. Probably this eye would send connections to one of the tecta, which would now have to accommodate to the new input. This accommodation is exactly what happened, as shown in Figure 7-25.

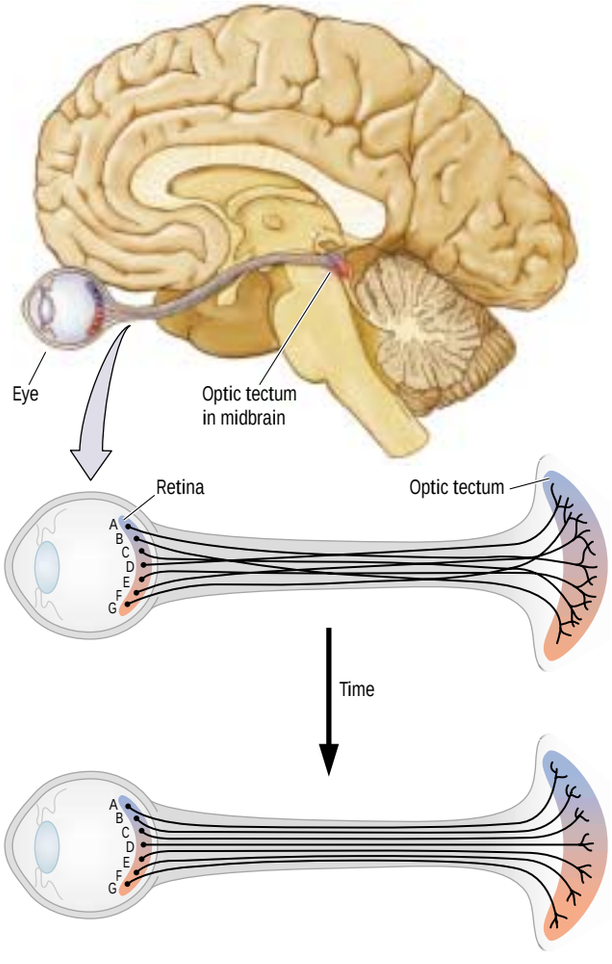


Figure 7-23

Experience has a role in organizing connections in the brain. Various neurons (labeled A–G) project from the retina to the tectum. The activities of adjacent neurons (for example, C and D) are more likely to coincide than the activities of neurons that are far apart (for example, A and G). As a result, the adjacent neurons are more likely to establish permanent synapses on the same tectal neurons. Axons grow to the approximate location in the tectum by using chemical signals (*top*), but there is a lack of precision. The connections are made more precise by the correlated activity.

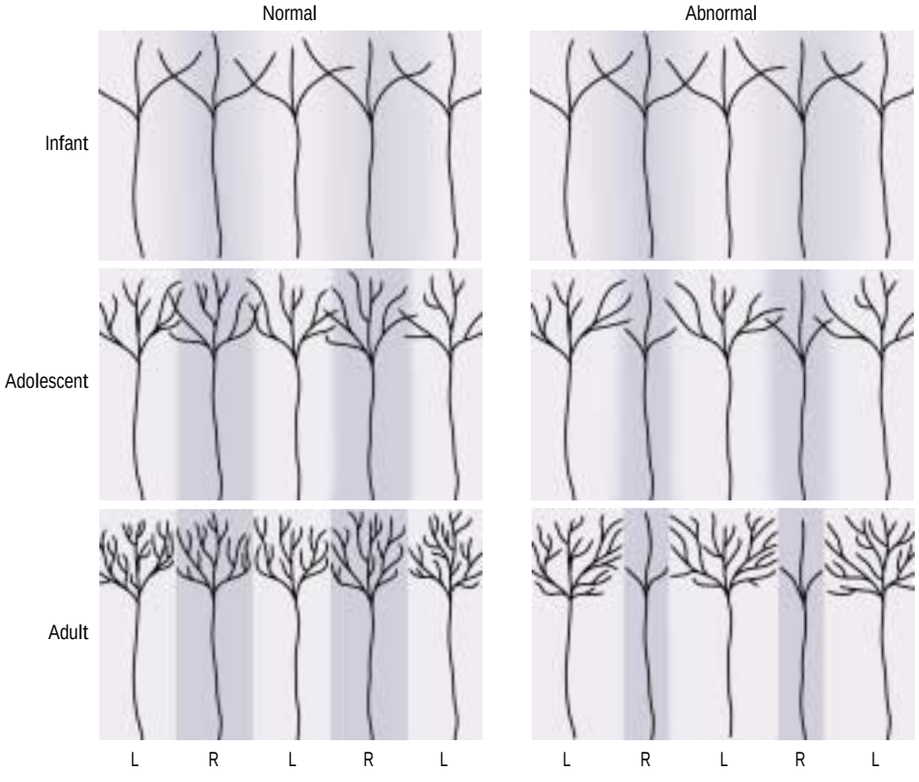


Figure 7-24

In the postnatal development of ocular dominance columns in the cat, axons enter the cortex where they grow large terminal arborizations. In infancy, the projections of both eyes overlap (L, left eye; R, right eye). In adulthood, a nonoverlapping pattern of terminal arborizations from each of the eyes is normal. If one eyelid of a kitten is sewn shut during a critical week of development, the terminations from that eye retract and those from the open eye expand.

The new eye sent connections to one of the tecta, which produced competition with one of the ungrafted eyes sending axons there. This competition resulted in the formation of one neural column for each eye. We can only imagine what this frog made of the world with its three eyes.

To summarize, the details of neural connections are modified by experience. An organism's genetic blueprint is vague regarding exactly which connections in the brain go to exactly which neurons. It is experience that fine-tunes neural connectivity. If experience is abnormal, such as would happen if one eye were covered during development, then the connections will not be guided appropriately by experience. In fact, this is exactly what happens to children who have a "lazy eye." The visual input from the lazy eye does not contribute to the fine-tuning of connections as it should, so the details of those connections do not develop normally. The result is a loss of sharpness in vision known as amblyopia.

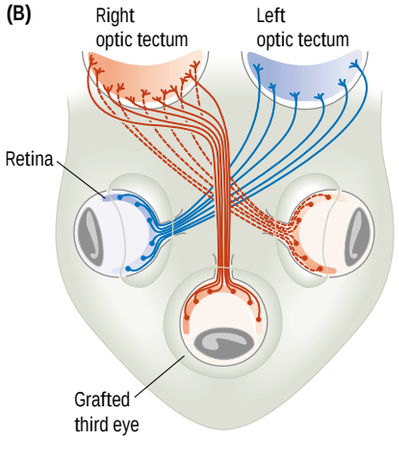
Figure 7-25

(A) The third eye of this three-eyed frog was grafted into the frog embryo. **(B)** The third eye forms connections with one optic tectum, in this case the right. Because the connections of the third eye are shared with another eye, these two eyes compete for synaptic space. This competition leads to the formation of alternating bands of connections.

(A)

From Martha Constantine-Paton and Margaret I. Law, "Eye Specific Termination Bands in Tecta of Three-Eyed Frogs," *Science*, November 10, 1978, vol. 202, pp. 639–641. ©1978 by the American Association for the Advancement of Science.

(B)



Critical period. A period in development during which some event has a long-lasting influence on the brain; often referred to as a sensitive period.

Imprinting. The process in which an animal is predisposed to learning an attachment to objects or animals at a critical period in development.

Critical Periods for Experience and Brain Development

There seem to be particular times in the course of brain development when specific experiences are especially important for normal development. In kittens, for example, the effect of suturing one eye closed has the most disruptive effect on cortical organization between 30 and 60 days after birth. A period during which brain development is most sensitive to a specific experience is often called a critical period. The absence of the appropriate sensory experience during a critical period may result in abnormal brain development, leading to abnormal behavior that endures even into adulthood.

Richard Tees offered an analogy to help explain the concept of critical periods. He pictured the developing animal as a little train traveling past an environmental setting, perhaps the Rocky Mountains. All the windows are closed at the beginning of the journey (prenatal development), but, at particular stages of the trip, the windows in certain cars open, exposing the occupants (different parts of the brain) to the outside world. Some windows open to expose the brain to specific sounds, others to certain smells, others to particular sights, and so on. This exposure affects the brain's development and, in the absence of any exposure through an open window, that development is severely disturbed. As the journey continues, the windows become harder to open until, finally, they are permanently closed. This closure does not mean that the brain can no longer change, but changes become much harder to induce. Now, imagine two different trains, one headed through the Rocky Mountains and another, the Orient Express, traveling across eastern Europe. The "views" from the windows are very different, and the effects on the brain are correspondingly different. In other words, not only is the brain altered by the experiences that it has during a critical period, but the particular kinds of experiences encountered matter, too.

Figure 7-26

The ethologist Konrad Lorenz is being followed by goslings that imprinted on him. Because he was the first "object" that the geese experienced after hatching, he became their "mother."

Thomas D. McAvoy/Time Magazine

An extensively studied behavior that relates to the concept of critical periods is imprinting. In imprinting, an animal learns, during a critical period, to restrict its social preferences to a specific class of objects, usually the members of its own species. In birds, such as chickens or waterfowl, the critical period for imprinting is often shortly after hatching. Normally, the first moving object that a young hatchling sees is one of its parents or a sibling, so the hatchling's brain appropriately imprints to its own species. This appropriate imprinting is not inevitable, however. Konrad Lorenz demonstrated that, if the first animal or object that baby goslings encounter is a human, the goslings imprint to the human as though it were their mother. Figure 7-26 shows a flock of goslings that imprinted to Lorenz and followed him about wherever he went. This incorrect imprinting has long-term consequences for the hatchlings, which will often direct their subsequent sexual behavior inappropriately toward humans. For instance, a Barbary dove that had become imprinted to Lorenz directed its courtship toward his hand and even tried to copulate with the hand if it were held in a certain orientation. Interestingly, birds inappropriately imprint not just to humans, but to inanimate objects, too, especially if they are moving. Chickens have been induced to imprint to a milk bottle sitting on the back of a toy train that was moving around a track. But the brain is not entirely "clueless" when it comes to selecting a target to which to imprint. Given a choice, young chicks choose a real chicken to which to imprint over any other stimulus.

The fact that imprinting is rapid and has permanent behavioral consequences suggests that, during imprinting, the brain makes a rapid change of some kind, probably a structural change, given the permanence of the new behavior. Gabriel Horn and his colleagues at Cambridge University tried to identify this change in the brains of chicks during imprinting. Apparently, the change takes place in a specific region of the forebrain, known as the IMHV. The results of electron microscopic studies show that the synapses in this region enlarge with imprinting. Imprinting, then, seems to be a good model for studying brain plasticity during development, in part because the changes are rapid, are related to specific experience, and are localized.

Abnormal Experience and Brain Development

If complex experiences can stimulate brain growth and influence later behavior, it seems likely that severely restricted experiences might retard both brain growth and behavior. To study the effects of such restrictions, Donald Hebb and his colleagues placed Scottish terriers in a dark environment with as little stimulation as possible and compared their behavior with that of dogs raised in a normal environment. When the dogs raised in the impoverished environment were later removed from that environment, their actions were very unusual. They showed virtually no reaction to people or other dogs, and they appeared to have lost their sense of pain. Even sticking pins in them produced no response. When given a dog version of the Hebb-Williams intelligence test for rats, these dogs performed very poorly and were unable to learn some tasks that dogs raised in more stimulating settings could learn easily.

The results of subsequent studies have shown that depriving young animals specifically of visual input or even of maternal contact has devastating consequences for their behavioral development and, presumably, for the development of the brain. For instance, Austin Riesen and his colleagues extensively studied animals raised in the dark and found that, even though the animals' eyes still work, they may be functionally blind after early visual deprivation. The absence of visual stimulation results in an atrophy of dendrites on cortical neurons, which is essentially the opposite of the results observed in the brains of animals raised in complex and stimulating environments.

Not only does the absence of specific sensory inputs adversely affect brain development, so do more complex kinds of abnormal experiences. This can be seen in the retarded intellectual development of children raised in dreadful circumstances in Romanian orphanages, as described in "Romanian Orphans" on page 266. In the 1950s, Harry Harlow began the first systematic laboratory studies of analogous deprivation in laboratory animals. Harlow showed that infant monkeys raised without maternal (or paternal) contact have grossly abnormal intellectual and social behaviors in adulthood. Harlow separated baby monkeys from their mothers shortly after birth and raised them in individual cages. Perhaps the most stunning effect was that, in adulthood, these animals were totally unable to establish normal relations with other animals. Unfortunately, Harlow did not analyze the brains of the deprived monkeys. We would predict atrophy of cortical neurons, especially in the frontal-lobe regions known to be related to normal social behavior.

The importance of the environment in brain development cannot be overemphasized. Children exposed to impoverished environments or to abuse or neglect can be expected to be at a serious disadvantage later in life. Although it is often thought that children can succeed in school and in life *if they really want to*, it is clear that abnormal developmental experiences can alter the brain irrevocably. As a society, we cannot be complacent about the environments to which our children are exposed.

Romanian Orphans

Focus on Disorders

In the 1970s, the Communist regime then governing Romania outlawed all forms of birth control and abortion. The natural result was thousands of unwanted pregnancies. More than 100,000 unwanted children were placed in orphanages where the conditions were appalling. Children had virtually no environmental stimulation. In most instances, they were confined to cots. There were few, if any, playthings and virtually no personal interaction with caregivers. Bathing often consisted of being hosed down with cold water. After the Communist government fell and the outside world was able to intervene, hundreds of these children were rescued and placed in adoptive homes throughout the world, especially in the United States, Canada, and the United Kingdom.

There have now been several studies of the fate of these severely deprived children (see Ames, 1997; Rutter et al., 1998). When the children arrived in their new homes, they were in a poor physical state. They were malnourished; they had chronic respiratory and intestinal infections; and they were severely developmentally impaired. A British study by Michael Rutter and his colleagues found them to be two standard deviations below age-matched children for weight, height, and head circumference. Assessments with the use of scales of motor and cognitive development showed most of the children to be in the retarded range.

The improvement in these children in the first 2 years after placement in their adoptive homes was nothing short of spectacular. Average height and weight became nearly normal, although head circumference remained below normal. (Head circumference can be taken as a very rough measure of brain size.) Many of the children were now in the normal range of motor and cognitive development. A significant number, however, were still considered retarded. Why were there individual differences in recovery from the past deprivation?

The key factor in predicting recovery was age at adoption. Those children adopted before 6 months of age did significantly better than those adopted later. In a Canadian study by Elenor Ames, Romanian orphans who were adopted before 4 months of age had an average Stanford-Binet IQ of 98 when tested at 4½ years of age. In comparison, age-matched Canadian controls had an average IQ of 109, whereas Romanian children adopted at a median age of 19 months had an average IQ of only 90. Brain-imaging studies showed the children adopted at an older age to have smaller-than-normal brains. Although there are no formal

Hormones and Brain Development

The determination of sex is largely genetic. In mammals, the Y chromosome present in males controls the process by which an undifferentiated primitive gonad develops into testes, as illustrated in Figure 7-9. The testes subsequently secrete testosterone, which stimulates the development of male reproductive organs and, during puberty, the growth of male secondary sexual characteristics.

Gonadal hormones also influence the development of neurons. Testosterone is released in males during a brief period in the course of brain development, and it subsequently acts to alter the brain, much as it alters the sex organs. This process is called masculinization. Just as testosterone does not affect all body organs, it does not affect all regions of the brain. It does, however, affect many brain regions and in many different ways. For instance, it affects the number of neurons formed in certain brain areas, reduces the number of neurons that die, increases cell growth, increases or reduces dendritic branching, increases or reduces synaptic growth, and regulates the activity of synapses. As a result of these effects due to exposure to testosterone, a male brain and a female brain are not the same.

Masculinization. A process by which exposure to androgens alters the brain, rendering it "malelike."

studies of large groups of these children as they approach adolescence, anecdotal reports of individual children who were adopted at an older age and are now adolescents indicate continuing problems. Some of these youngsters have significant learning disabilities in school, suffer from hyperactivity, and have not developed normal patterns of social interaction.

The inescapable conclusion emerging from the Romanian orphanage experience is that the brain may be able to recover from a brief period of extreme deprivation in early infancy, but periods longer than 6 months produce significant abnormalities in brain development that cannot be completely repaired. This conclusion is supported by the case study of an American girl named Genie, who experienced severe social and experiential deprivation as well as chronic malnutrition at the hands of her psychotic father (see Curtis, 1978). She was discovered at the age of 13, after having spent much of her life in a closed room, during which time she was punished for making any noise. After her rescue, she, too, showed rapid growth and cognitive development, although her language development remained severely retarded.

To summarize, studies of the Romanian orphans, of orphans from other highly impoverished settings, and of cases such as that of Genie make it clear that the developing brain requires stimulation for normal development. Although the brain may be able to catch up after a short period of deprivation, more than a few months of severe deprivation results in a smaller-than-normal brain and associated behavioral abnormalities, especially in cognitive and social skills.

Johnson/Gamma-Liaison

The situation depicted in this photo was not unusual for Romanian orphans in the 1970s and 1980s: children were housed and clothed, but had no other forms of stimulation, either from caregivers or an enriched environment. Studies on this population have shown that the lack of stimulation has hampered normal brain development.

It was once believed that testosterone's effects on brain development were not all that important, because this hormone was thought to primarily influence regions of the brain regarding sexual behavior, not regions of "higher" functions. We now know that this belief is false. Testosterone changes the structure of cells in many regions of the cortex, with diverse behavioral consequences that include influences on cognitive processes.

Consider one example. Jocelyn Bachevalier trained infant male and female monkeys in the concurrent-discrimination task described earlier, in which the subject has to learn which of two objects in a series of object pairs conceals a food reward. In addition, Bachevalier trained the animals in another task, known as *object-reversal learning*. The task here is to learn that one particular object always conceals a food reward, whereas another object never does. After this pattern has been learned, the reward contingencies are reversed so that the particular object that has always been rewarded is now never rewarded, whereas the formerly unrewarded object now conceals the reward. When this new pattern has been learned, the contingencies are reversed again, and so on, for five reversals. Bachevalier found that 2½-month-old male monkeys

were superior to female monkeys on the object-reversal task, but females did better on the concurrent task. Apparently, the different brain areas required for these two tasks matured at different rates in the male and female monkeys. Bachevalier later tested additional male monkeys whose testes had been removed at birth and so were no longer exposed to testosterone. These animals performed like females on the tasks, implying that testosterone was influencing the rate of brain development in areas related to certain cognitive behaviors.

Bachevalier and her colleague Bill Overman then repeated the experiment, this time using as their subjects children from 15 to 30 months old. The results were the same: boys were superior at the object-reversal task and girls were superior at the concurrent task. There were no such male–female differences in performance among older children (32–55 months of age). Presumably, by this older age, the brain regions required for each task had matured in both boys and girls. At the earlier age, however, gonadal hormones seemed to be influencing the rate of maturation in certain regions of the brain, just as they had in the baby monkeys.

Although the biggest effects of gonadal hormones may be during early development, their role is by no means finished at the end of childhood. Gonadal hormones (including both testosterone and estrogen, the latter of which is produced in large quantities by the ovaries in females) continue to influence the structure of the brain throughout an animal's life. In fact, removal of the ovaries in middle-aged laboratory rats leads to marked growth of dendrites and the production of more glial cells in the cortex. This finding of widespread neural change in the cortex associated with loss of estrogen has implications for the treatment of postmenopausal women.

Gonadal hormones also affect how the brain responds to events in the environment. For instance, among rats housed in complex environments, males show more dendritic growth in neurons of the visual cortex than do females (see Juraska, 1990). In contrast, females housed in this setting show more dendritic growth in the frontal cortex than do males. Apparently, the same experience can affect the male and female brain differently owing to the mediating influence of gonadal hormones. This finding means that, as females and males develop, their brains continue to become more and more different from each other. It is much like coming to a fork in a road. Once having chosen to go down one path, your direction of travel is forever changed as the roads diverge and become increasingly farther apart.

To summarize, gonadal hormones alter the basic development of neurons, shape the nature of experience-dependent changes in the brain, and influence the structure of neurons throughout our lifetime. These effects of sex hormones need to be considered by those who believe that behavioral differences between males and females are solely the result of environmental experiences. In part, it is true that environmental factors exert a major influence. But one reason that they do may be that male and female brains are different to start with, and even the same events, when experienced by structurally different brains, may lead to different effects on the brain. In our view, the important task is not to deny the presence of sex differences in brain organization and function, but rather to understand the degree to which those neurological differences contribute to observed differences in behavior.

Injury and Brain Development

If the brain is damaged in the course of development, is it irrevocably altered? In the 1930s, Donald Hebb studied children with major birth-related injuries to the frontal lobes and found that such children had severe and permanent behavioral abnormalities in adulthood. He concluded that severe brain damage early in life can

alter the subsequent development of the rest of the brain, leading to chronic behavioral disorders.

To what extent have other studies confirmed Hebb's conclusion? There are few anatomical studies of humans with early brain injuries, but we can make some general predictions from the study of laboratory animals. In general, early brain injuries do produce abnormal brains, especially at certain critical periods of development. For humans, the worst time appears to be during the last half of the intrauterine period and the first couple of months after birth. Rats that suffer injuries at a comparative time have significantly smaller brains than normal, and their cortical neurons show a generalized atrophy relative to normal brains, as illustrated in Figure 7-27. Behaviorally, these animals appear cognitively retarded, deficient in a wide range of skills.

The effect of injury to the developing brain is not always devastating, however. For example, we have known for more than 100 years that children with brain injuries in the first couple of years after birth almost never have the severe language disturbances common to adults with equivalent injuries. Animal studies help explain why. Whereas damage to the brain in the period comparable to the last few months of gestation in humans produces widespread cortical atrophy, damage at a time roughly comparable to age 6 months to 2 years in humans actually produces more dendritic development, as also seen in Figure 7-27. Furthermore, these animals show dramatic recovery of functions, implying that the brain has a capacity during development to compensate for injury.

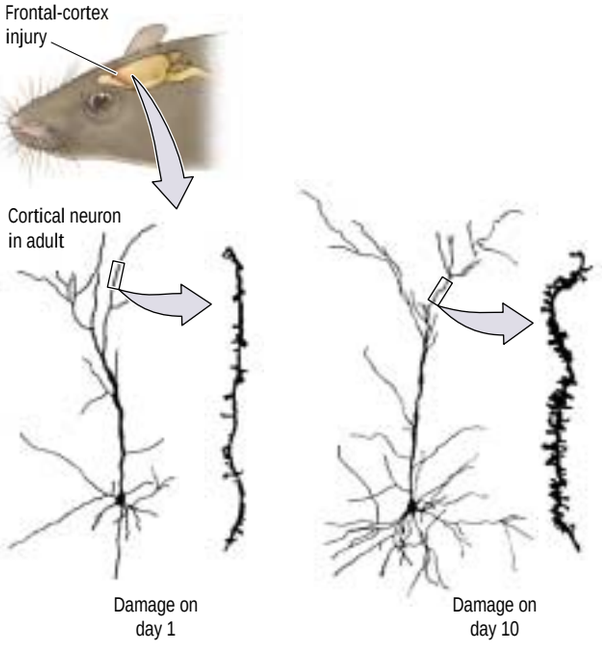


Figure 7-27

Cortical injury at different times in the course of development has different anatomical and behavioral consequences. In the rat, damage to the frontal cortex on the day of birth leads to the development of cortical neurons with simple dendritic fields and a sparce growth of spines. In contrast, damage to the frontal cortex at 10 days of age leads to the development of cortical neurons with expanded dendritic fields and denser spines than normal.

Adapted from "Possible Anatomical Basis of Recovery of Function After Neonatal Frontal Lesions in Rats," by B. Kolb and R. Gibb, 1993, *Behavioral Neuroscience*, *107*, p. 808.

Other Kinds of Abnormal Brain Development

The nervous system need not be damaged by external forces for it to develop abnormally. For instance, many genetic abnormalities are believed to result in abnormalities in the development and, ultimately, the structure of the brain. You may have heard of *spina bifida*, a condition in which the genetic blueprint goes awry and the neural tube does not close completely, leading to an incompletely formed spinal cord. After birth,

Anencephaly. Failure of the forebrain to develop.

children with spina bifida usually have serious motor problems because of this spinal-cord abnormality. But imagine what would happen if some genetic abnormality caused the front end of the neural tube not to close properly. Because the front end of the neural tube forms the brain, this failure would result in gross abnormalities in brain development. Such a condition exists and is known as **anencephaly**. Infants affected by this condition die soon after birth.

Abnormal brain development can be much subtler than anencephaly. For example, if cells do not migrate to their correct locations and these mispositioned cells do not subsequently die, they can disrupt brain function and may lead to disorders ranging from seizures to schizophrenia (see "Schizophrenia" below). There are also a variety of conditions in which neurons fail to differentiate normally. In certain cases, the

Schizophrenia

Focus on Disorders

When Mrs. T. was 16 years old, she began to experience her first symptom of schizophrenia: a profound feeling that people were staring at her. These bouts of self-consciousness soon forced her to end her public piano performances. Her self-consciousness led to withdrawal, then to fearful delusions that others were speaking about her behind her back, and finally to suspicions that they were plotting to harm her. At first Mrs. T.'s illness was intermittent, and the return of her intelligence, warmth, and ambition between episodes allowed her to complete several years of college, to marry, and to rear three children. She had to enter a hospital for the first time at age 28, after the birth of her third child, when she began to hallucinate.

Now, at 45, Mrs. T. is never entirely well. She has seen dinosaurs on the street and live animals in her refrigerator. While hallucinating, she speaks and writes in an incoherent, but almost poetic way. At other times, she is more lucid, but even then the voices she hears sometimes lead her to do dangerous things, such as driving very fast down the highway in the middle of the night, dressed only in a nightgown. . . . At other times and without any apparent stimulus, Mrs. T. has bizarre visual hallucinations. For example, she saw cherubs in the grocery store. These experiences leave her preoccupied, confused, and frightened, unable to perform such everyday tasks as cooking or playing the piano. (Gershon & Rieder, 1992, p. 127)

Schizophrenia is obviously an extraordinary disorder, with symptoms that are hard to generalize. It has always been easier to identify schizophrenic behavior than to define what schizophrenia is. Perhaps the one universally accepted criterion for diagnosing schizophrenia is the absence of other neurological disturbances or affective disorders that could cause a person to lose touch with reality. This is a definition by default. Other authors have emphasized the presence of bizarre hallucinations and disturbances of thought, much like those displayed by Mrs. T. However, the symptoms of schizophrenia are heterogeneous, suggesting that the biological abnormalities vary from person to person.

In 1913, Emil Kraepelin first proposed that schizophrenia follows a progressively deteriorating course with a dismal final outcome. This opinion about the disorder was dominant through most of the twentieth century. Today, however, a consensus is emerging that this view is probably incorrect. Most patients appear to stay at a fairly stable level after the first few years of displaying schizophrenic symptoms, with little evidence of a decline in neuropsychological functioning. The symptoms come and go, much as for Mrs. T., but the severity is relatively constant after the first few episodes.

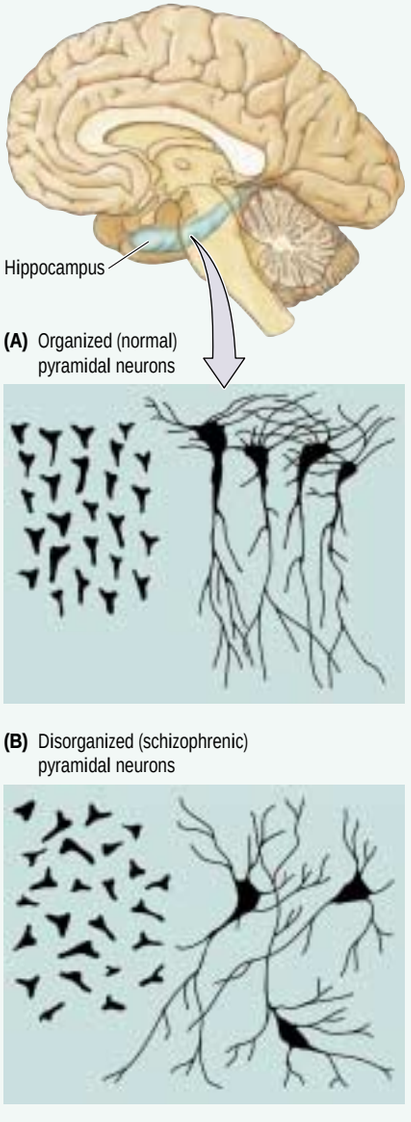
neurons fail to produce long dendrites or spines. As a result, connectivity in the brain is abnormal, leading to retardation. The opposite condition also is possible: neurons continue to make dendrites and form connections with other cells to the point at which these neurons become extraordinarily large. The functional consequences of all the newly formed connections can be devastating. Excitatory synapses in the wrong location effectively short-circuit a neuron's function.

One curious consequence of abnormal brain development is that the behavioral effects may emerge only as the brain matures and the maturing regions begin to play a greater role in behavior. This consequence is especially true of frontal-lobe injuries. The frontal lobes continue to develop into adolescence, and often not until adolescence do the effects of frontal-lobe abnormalities begin to be noticed. Schizophrenia

To learn more about abnormal brain development, visit the Web site at **www.worthpublishers.com/kolb/chapter7.**

Numerous studies have investigated the brains of schizophrenics, both in autopsies and in MRI and CT scans. Although the results vary, most agree that schizophrenics have brains that are lighter than normal and that have enlarged ventricles. There are also suggestions that schizophrenics have both smaller frontal lobes (or at least a reduction in the number of neurons in the prefrontal cortex) and thinner parahippocampal gyri. One of the most interesting discoveries is that of Joyce Kovelman and Arnold Scheibel (1984), who found pronounced abnormalities in the orientation of neurons in the hippocampi of schizophrenics. Rather than the consistently parallel orientation of neurons in this region characteristic of normal brains, the schizophrenics had a more haphazard organization, as shown in the accompanying drawing.

There is increasing evidence that the abnormalities observed in schizophrenic brains are associated with disturbances of brain development. William Bunney and his colleagues (1997) suggest that at least a subgroup of schizophrenics experience either environmental insults or some type of abnormal gene activity in the fourth to sixth month of fetal development. These events are thought to result in abnormal cortical development, particularly in the frontal lobes. Later in adolescence, as the frontal lobes complete development, the person begins to experience symptoms of this abnormal prior development.



Examples of pyramidal cell orientation from the hippocampus of **(A)** a normal brain and **(B)** a schizophrenic brain. In the schizophrenic brain these pyramidal neurons are much more disorganized.

Adapted from "A Neurohistologic Correlate of Schizophrenia," by J. A. Kovelman and A. B. Scheibel, 1984, *Biological Psychiatry*, *19*, p. 1613.

is a disease that is characterized by slow development, usually not becoming obvious until late adolescence. The schizophrenic brain has many abnormalities, some of which are in the frontal lobes.

Mental Retardation

Mental retardation refers to an impairment in cognitive functioning that accompanies abnormal brain development. Mental retardation may range in severity from mild, allowing an almost normal life style, to severe, requiring constant care. As summarized in Table 7-4, mental retardation can result from chronic malnutrition, genetic abnormalities such as Down's syndrome, hormonal abnormalities, brain injury, or neurological disease. Different causes produce different abnormalities in brain organization, but the critical similarity across all types of retardation is that the brain is not normal.

Table 7-4 Causes of Mental Retardation

Cause	Example mechanism	Example condition
Genetic abnormality	Error of metabolism	Phenylketonuria (PKU)
	Chromosomal abnormality	Down's syndrome
Abnormal embryonic development	Exposure to a toxin	Fetal alcohol syndrome
Prenatal disease	Infection	Rubella (also called German measles)
Birth trauma	Anoxia (oxygen deprivation)	Cerebral palsy
Malnutrition	Abnormal brain development	Kwashiorkor
Environmental abnormality	Sensory deprivation	Children in orphanages

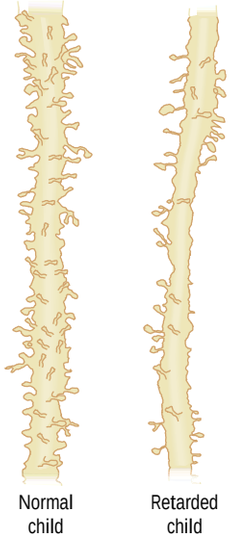


Figure 7-28

Representative dendritic branches from cortical neurons in a normal child (*left*) and a retarded child (*right*). The dendrite branch from the retarded child has fewer spines.

Adapted from "Dendritic Spine 'Dysgenesis' and Mental Retardation," by D. P. Purpura, 1974, *Science*, *186*, p. 1127.

A study by Dominique Purpura provides an example of one of the few systematic investigations of the brains of retarded children. Purpura used Golgi stain to examine neurons of children who had died from accident or disease unrelated to the nervous system. When he examined the brains of children with various forms of retardation, he found that the dendrites were stunted in growth and the spines were very sparse, as illustrated in Figure 7-28. The simple structure of these neurons was probably indicative of a marked reduction in the number of connections in the brain, which presumably caused the retardation. Variation in both the nature and the extent of neuronal abnormality in different children would lead to different behavioral syndromes.

In Review

The brain is plastic during its development and can therefore be molded by experience into different forms, at least at the microscopic level. The sensitivity of the brain to experience varies with time, however. There are critical periods in the course of development when different parts of the brain are particularly sensitive to different experiences. Not only is the brain plastic in response to external events, but it is changed by internal events as well, including the effects of hormones, injury, and abnormal genes. If experiences are abnormal, then the brain's development is abnormal, possibly leading to disorders such as mental retardation or schizophrenia.

HOW DO ANY OF US DEVELOP A NORMAL BRAIN?

When we look at the complexity of the brain, the less-than-precise process of brain development, and the large number of factors that can influence it, we are left marveling at how so many of us end up with brains that pass for "normal." After all, we must all have had neurons that migrated to wrong locations, made incorrect connections, and were exposed to viruses or other harmful substances. If the brain were as fragile as it might seem, it would be almost impossible to end up with a normal brain.

Apparently, animals have evolved a substantial capacity to repair minor abnormalities in brain development. Most people have developed in the range that we call "normal" because the human brain's plasticity and regenerative powers are successful in overcoming minor developmental deviations. Recall that one stage in brain development consists of cell death and synaptic pruning. By initially overproducing neurons and synapses, the brain has the capacity to correct any errors that might have arisen accidentally.

These same plastic properties of the brain later allow us to cope with the ravages of aging. Neurons are dying throughout our lifetimes and, by age 50, we ought to be able to see significant effects of all of this cell loss, especially considering the cumulative results of exposure to environmental toxins, drugs, closed head injuries, and so on. But this is not what happens. Although teenagers may not believe it, very few 50-year-olds are demented. By most criteria, the 50-year-old who has been intellectually active throughout adulthood is likely to be much wiser than the 18-year-old whose brain has lost relatively few neurons. Clearly, we must have some mechanism to compensate for loss and minor injury to our brain cells. This capacity for plasticity and change is one of the most important characteristics of the human brain, not only during development but through the rest of life as well. We return to this idea in Chapter 13.

SUMMARY

1. *What are the stages of neural development?* The process of brain maturation is long, lasting until 16 or 18 years of age. Neurons, the elementary components of the brain, are born, develop a neuronal phenotype, migrate, and, as their processes elaborate, establish connections with other neurons. Because the brain contains such a large number of cells, and an even larger number of connections, the brain produces more neurons and connections than it needs and then prunes back to a stable adult level.
2. *How does behavior develop?* The infant and child go through stages of behavioral development that are similar in children across all cultural spectrums. For example, as infants develop, motor behaviors emerge in a predictable sequence. Infants first make clumsy movements towards objects but they are poorly directed. By about 4 months, the motor system has matured sufficiently so that the infant can grasp objects with the whole hand, and by around 11 months children are able to make pincer grasps to pick up objects like pencils. Other motor behaviors emerge over the ensuing months and years, such as walking, throwing, catching, and so on. Similarly, cognitive behaviors emerge through a series of stages in which children acquire principles that allow them to solve problems. Researchers such as Jean Piaget have identified and characterized four or more distinct stages of cognitive development, each of which can be identified by special behavioral tests.
3. *How do behavioral and neural maturation relate to one another?* The emergence of behaviors is correlated with the development of the neural systems that produce the behaviors. Behavioral and cognitive capacities follow a similar sequence of development from the rudimentary to the complex. The relationship between

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■ **www.ucpa.org.**

Learn more about cerebral palsy at the home page of United Cerebral Palsy.

On your CD-ROM you'll be able to quiz yourself on your comprehension of the chapter. The module on Neural Communication also provides important review on the neural structure.

brain structure and function can be inferred by matching the developmental timetables of brain anatomy and physiology with that of behavior. For example, motor behaviors emerge in synchrony with the maturation of motor circuits in the cerebral cortex, basal ganglia, and cerebellum, as well as in the connections from these areas to the spinal cord. Similar correlations between behavioral emergence and neuronal development can be seen in the development of other behaviors, including cognitive behaviors. For example, different types of memory abilities emerge as circuits in the frontal and temporal lobes mature.

4. *What factors influence neural maturation?* The brain is modifiable during its development and the structure of neurons and their connections can be molded by various factors throughout the period of development. These factors include external events, gonadal hormones, and injury. The sensitivity of the brain to these factors varies with time as there are periods during the course of development when different brain regions are particularly sensitive to different events. If experiences are abnormal, then the brain's development is abnormal, as well, and can lead to disorders such as retardation.
5. *How sensitive is the developing brain to injury?* Perturbations of the brain during development, such as from anoxia, trauma, or toxins can significantly alter brain development and result in severe behavioral abnormalities including retardation and cerebral palsy. The brain does have a substantial capacity to repair or correct minor abnormalities, however, allowing most people to develop a normal behavioral repertoire.

KEY TERMS

amblyopia, p. 263
anencephaly, p. 270
apoptosis, p. 252
brain plasticity, p. 259
cell-adhesion molecule (CAM), p. 250
chemoaffinity hypothesis, p. 262
critical period, p. 264
filopod, p. 249
glioblast, p. 244
growth cone, p. 249
growth spurt, p. 257
imprinting, p. 264
masculinization, p. 266
netrins, p. 250
neural Darwinism, p. 251
neural plate, p. 240
neural stem cells, p. 243
neural tube, p. 240
neuroblast, p. 244
neurotrophic factors, p. 245
progenitor cells, p. 244
radial glial cells, p. 247
tropic molecules, p. 250
ventricular zone, p. 243

REVIEW QUESTIONS

1. Describe the gross development of the nervous system. Summarize and explain the steps in brain development.
2. What roles do different factors such as molecules, genetics, and experience play in development?
3. How does behavioral development relate to neural development?
4. How does experience affect brain development?

FOR FURTHER THOUGHT

1. Experience plays an important role in brain development. How might an interaction between sex and environment account for behavioral differences in adulthood?

2. How can the principles of behavioral development help to explain why each brain is unique?

RECOMMENDED READING

Edelman, G. M. (1987). *Neural darwinism: The theory of neuronal group selection*. New York: Basic Books. You have heard of Darwinism and the idea of survival of the fittest. Edelman applies this Darwinian concept to the nervous system's shedding of neurons in the course of development and throughout a person's lifetime. Although not universally accepted, the ideas in the book are amusing to read.

Greenough, W. T., & Chang, F. F. (1988). Plasticity of synapse structure and pattern in the cerebral cortex. In A. Peters and E. G. Jones (Eds.), *Cerebral cortex: Vol. 7. Development and maturation of the cerebral cortex* (pp. 391–440). New York: Plenum. Greenough is one of the world leaders in the study of experience-dependent change in the nervous system. This chapter not only provides a nice historical review, but also lays out seminal ideas on the developmental plasticity of the nervous system.

Hebb, D. O. (1949). *The organization of behavior*. New York: Wiley. Although 1949 may seem like a long time ago for a book to be still relevant today, Hebb's book may be the most important single volume on brain and behavior. It was the first serious attempt to outline a neuropsychological theory of how the brain could produce behavior and, especially, thought. Development is an important theme in the book because Hebb believed that experience plays an essential role in developing the cognitive and neural structures necessary for adulthood. This book is mandatory reading for any student going on to graduate school in behavioral neuroscience.

Michel, G. F., & Moore, C. L. (1995). *Developmental psychobiology*. Cambridge, MA: MIT Press. Most neural development books are thin on behavioral development, but this book strikes a nice balance in its analysis of both brain and behavioral development.

Purves, D., & Lichtman, J. W. (1985). *Principles of neural development*. Sunderland, MA: Sinauer. Although not primarily about the development of the cortex, the book provides sufficient background to enable a thorough understanding of the principles that guide nervous system development.