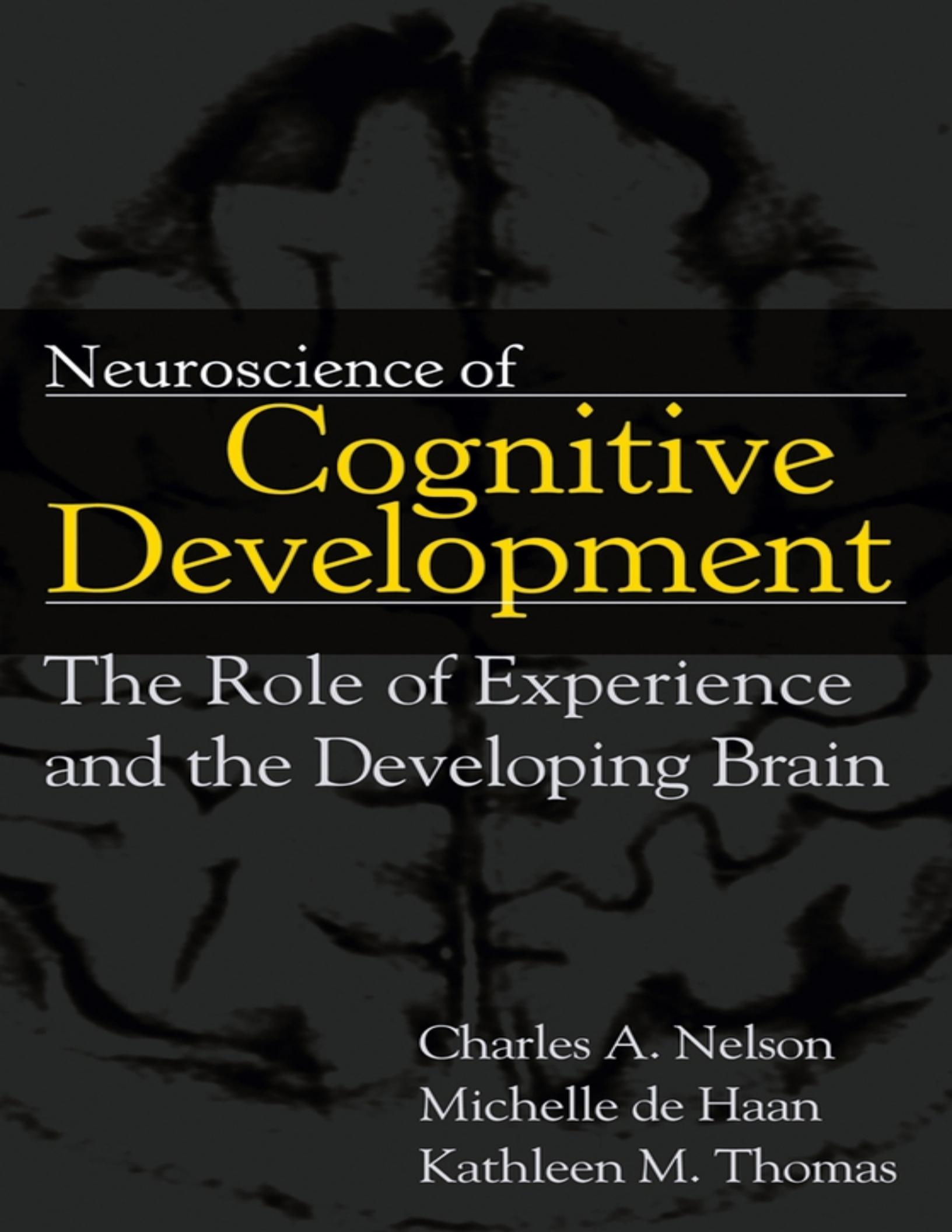
Neuroscience of
Cognitive Development
The Role of Experience and the Developing Brain
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Contents

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Preface

Our goal in writing this book is to introduce the reader to what is currently known about the neural bases of cognitive development. We begin by introducing a number of reasons why developmental psychologists might be interested in the neural bases of behavior (with particular reference to cognitive development). Having established the value of viewing child development through the lens of the developmental neurosciences, we provide an overview of brain development. This is followed by a discussion of how experience influences the developing—and when appropriate, developed—brain. Within this discussion on experience-dependent changes in brain development, we briefly touch on two issues we consider to be essential for all developmental psychologists: whether the mechanisms that underlie developmental plasticity differ from those that underlie adult plasticity, and more fundamentally, what distinguishes plasticity from development.

With this basic neuroscience background behind us, we next turn our attention to how one examines the neural bases of cognitive development—this will essentially be a tutorial on the methods employed by those working in developmental cognitive neuroscience. We begin this section with a brief historical tour, then move the discussion to behavioral (i.e., neuropsychological), anatomic (e.g., structural MRI), metabolic (e.g., functional MRI, functional Near Infrared Spectroscopy), and electrophysiological methods (e.g., event-related potentials).

Once we have concluded our discussion of methods, we turn our attention to specific content areas, limiting ourselves to domains in which there is a corpus of knowledge about the neural underpinnings of cognitive development. We include discussions of declarative and

nondeclarative memory and learning, spatial cognition, object recognition, social cognition, speech and language development, executive functions, and attention. We conclude the book with a brief discussion of the future of developmental cognitive neuroscience.

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Introduction

Why Should Developmental Psychologists Be Interested in the Brain?

Historical Background

Prior to the ascendancy of Piagetian theory, the field of cognitive development was dominated by behaviorism (for discussion, see Goldman-Rakic, 1987; Nelson & Bloom, 1997). Behaviorism eschewed the nonobservable, and therefore, the study of the neural bases of behavior, for the simple reason that neural processes could not be observed. (With the benefit of hindsight, this view always struck us as faulty logic because it failed to recognize that behavior was a product of physiology, and without understanding what *caused* behavior, the interpretation of the behavior itself would be incomplete.) Through the 1950s and 1960s, Piagetian theory gradually came to replace behaviorism as the dominant theory of cognitive development. However, despite a background in biology, Piaget and, subsequently, his followers primarily concerned themselves with developing a richly detailed cognitive architecture of the mind—albeit a brainless mind. We do not mean this in the pejorative sense, but rather, to reflect that the zeitgeist of the time was to develop elegant models of cognitive structures, with little regard for (a) whether such structures were biologically plausible, or (b) the neurobiological underpinnings of such structures. (And, of course, at this time there was no way to observe the living child's brain

directly.) Throughout the late 1970s and into the last decade of the twentieth century, neo- and non-Piagetian approaches came into favor. Curiously, a prominent theme of a number of investigators writing during this time was that of nativism. We say curiously because inherent in nativism is the notion of biological determinism, yet those touting a nativist perspective rarely if ever grounded their models and data in any kind of biological reality. It was not until the mid-1990s that neurobiology began to be inserted into a discussion of cognitive development, as reflected, for example, in Mark Johnson's eloquent contribution to the fifth edition of the *Handbook of Child Psychology* (Johnson, 1998). This perspective has become more commonplace, although the field of developmental cognitive neuroscience is still in its infancy. (For recent overviews of this field generally, see de Haan & Johnson, 2003, and Nelson & Luciana, 2001.) Moreover, our personal experience is that it is still not clear to many developmental psychologists why they should be interested in the brain. This is the topic to which we first direct our attention.

Our understanding of cognitive development will be improved as the mechanisms that underlie development are elucidated. This, in turn, should permit us to move beyond the descriptive, black box level to the level at which the actual cellular, physiologic, and eventually, genetic machinery will be understood—that is, the mechanisms that underlie development.

For example, a number of distinguished cognitive developmentalists and cognitive theorists have proposed or at least implied that elements of number concept (Wynn, 1992; Wynn, Bloom, & Chiang, 2002), object permanence (Baillargeon, 1987; Baillargeon, Spelke, & Wasserman, 1985; Spelke, 2000), and perhaps face recognition (Farah, Rabinowitz, Quinn, & Liu, 2000) reflect what we refer to as *experience-independent functions;* that is, they reflect in-

born “traits” (presumably coded in the genome) that require little if any experience in order to emerge. We see several problems with this perspective. First, these arguments seem biologically implausible. Such sophisticated cognitive abilities, if they were coded in the genome, would surely involve polygenic traits rather than reflect the action of a single gene. Given that we now know the human genome consists of approximately 30,000 genes, it seems highly unlikely that we could spare the genes to code for number concept, object permanence, or face recognition; after all, our existing complement of genes must be involved in a myriad of other events of more basic importance than subserving these aspects of cognitive development (such as the general operation of the body as a whole).

A second concern about this nativist perspective is that it is not particularly developmental. To say that something is “innate” essentially closes the door to any discussion of mechanism. More problematic is that genes do not “cause” behaviors; rather, genes express proteins that in turn work their magic through the brain. And, it seems unlikely that behaviors that are not absolutely essential to survival (of the species, not the individual) have been coded for in the genome, given the limited number of genes that are known to exist in the genome. Far more likely is that these behaviors are subserved by discrete or distributed neural circuits in the brain, and, these circuits, in turn, likely vary in the extent to which they depend on experience or activity for their subsequent elaboration (a topic we discuss in detail in Chapter 3).

Collectively, we wish to make three points. First, the value added by thinking of behavior in the context of neurobiology is that doing so provides a form of biological plausibility to our models of behavior (a point that we elaborate on later). Second, viewing behavioral development through the lens of neuroscience may shed new light on the mechanism(s) that

underlie behavior and behavioral development, thereby moving us beyond the level of description to the level of process. Third, when we insert the molecular biology of brain development into the equation, a more synthetic view of the child becomes possible—genes, brain, and behavior. This broader view permits us to move beyond simplistic notions of *gene-environment* interactions and instead talk about the ways that specific experiences influence specific neural circuits, which influence the expression of particular genes, which influence how the brain functions and how the child behaves.

Chapter 1

Brain Development and Neural Plasticity

A Précis to Brain Development

Before discussing the details of neural development, it is important to understand that brain development, at the species level, has been shaped over many thousands of generations by selective pressures that drive evolution. According to Knudsen (2003a), this portion of biological inheritance is responsible for nearly all of the genetic influences that shape the development and function of the nervous system, the majority of which have proven to be adaptive for the success of any given species. These influences determine both the properties of individual neurons and the patterns of neural connections. As a result, these selective pressures delimit an individual's cognitive, emotional, sensory, and motor capabilities.

There is, however, a small portion of biological inheritance that is unique to the individual and results from the novel combination of genes that the child receives from the parents. Because there is no history to this gene pattern, any new phenotype that is produced has never been subjected to the forces of natural selection and is unlikely to confer any selective advantage for that individual. However, this small portion of biological inheritance is particularly important for driving evolutionary change, as novel combinations of genes or mutations that do confer a

selective advantage will increase in the gene pool, while those that result in maladaptive phenotypes will die out (Knudsen, personal communication).

The brain develops according to a complex array of genetically programmed influences. These include both molecular and electrical signals that arise spontaneously in growing neural networks. By “spontaneously,” we mean signals that are inherent in the circuitry and are entirely independent of any outside influence. These molecular and electrical signals establish neural pathways and patterns of connections that are remarkably precise, and that make it possible for animals to carry out discrete behaviors beginning immediately after birth. They also underlie instinctive behaviors that may appear much later in life, often associated with emotional responses, foraging, reproduction (sex would fall under a social interaction), and social interactions. Beyond the scope of this chapter, but certainly worth investigating, is a consideration of which human behaviors fall into this category of “instinctive.” Our bias is that these are most likely going to be behaviors that have enormous implications for survival or reproductive fitness, such as the ability to experience fear in order to recognize a predator or to experience pleasure and, conversely, the reduction of displeasure in order to become attached to a caregiver. We should also acknowledge that it is extraordinarily difficult to study such behaviors in humans because the experimental manipulations that would need to be performed would be unethical (they would generally require selective deprivation). Hence our reluctance to claim that certain behaviors are “innate.”

To return to our discussion of nativism, there is no question that our genetic makeup has an enormous influence over who we are. To a large extent, human characteristics reflect evolutionary learning, which is exhibited in patterns of neural connections and interactions that have been shaped

adaptively by evolution over thousands of generations. In addition to adaptive capacities, however, genetic mutations also can lead to *deficits* in brain function, such as impairments of sensation, cognition, emotion, and/or movement. We provide examples of both in subsequent sections of this chapter.

Genes specify the properties of neurons and neural connections to different degrees in different pathways and at different levels of processing. On the one hand, the extent of genetic determination reflects the degree to which the information processed at a particular connection is predictable from one generation to the next. On the other hand, because many aspects of an individual's world are not predictable, the brain's circuitry must rely on experience to customize connections to serve the needs of the individual. Experience shapes these neural connections and interactions but always within the constraints imposed by genetics.

BRAIN DEVELOPMENT

The construction and development of the human brain occurs over a very protracted period of time, beginning shortly after conception and depending on how we view the end of development, continuing through at least the end of adolescence (for overviews, see Figure 1.1 and Table 1.1). Before discussing brain development per se, we must first provide some background to embryology in general.

Figure 1.1 Overview to human brain development, beginning the 15th prenatal week and continuing to term and then the adult. This figure illustrates the dramatic changes (in surface structure) the brain undergoes during the 9 months of gestation. Source: *From* Central Nervous System, *by O. E. Millhouse and S. Stensaas, n.d. Retrieved June 6, 2005, from http://www.medlib.med.utah.edu/kw/sol/sss/subj2.html.*

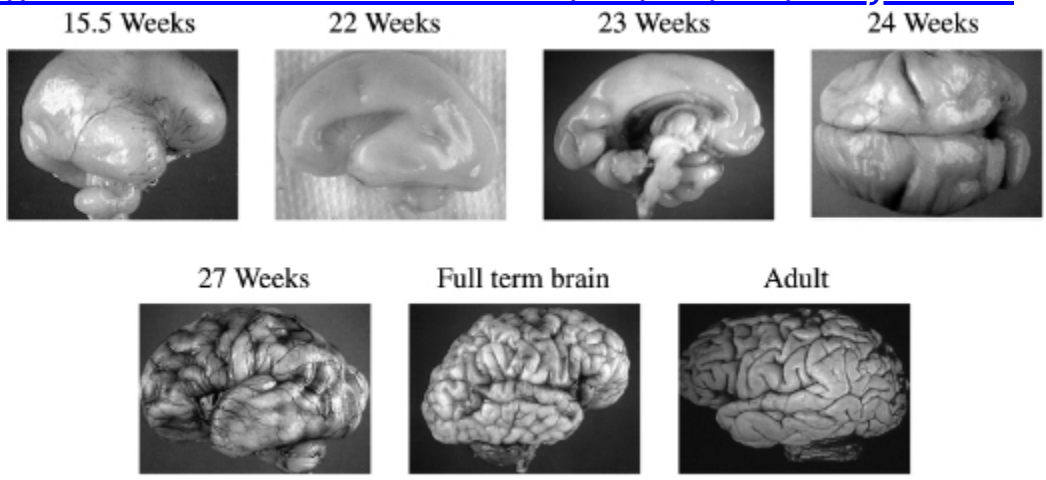


Table 1.1 Neurodevelopmental Timeline from Conception through Adolescence

Developmental Event	Timeline	Overview of Developmental Event
Neurulation	18–24 prenatal days	Cells differentiate into one of three layers: endoderm, mesoderm and ectoderm, which then form the various organs in the body. The neural tube (from which the CNS is derived) develops from the ectoderm cells; the neural crest (from which the ANS is derived) lies between the ectodermal wall and the neural tube.
Neuronal migration	6–24 prenatal weeks	Neurons migrate at the ventricular zone along radial glial cells to the cerebral cortex. The Neurons migrate in an inside-out manner, with later generations of cells migrating through previously developed cells. The cortex develops into six layers.

Developmental Event	Timeline	Overview of Developmental Event
Synaptogenesis	3rd trimester–adolescence	Neurons migrate into the cortical plate and extend apical and basilar dendrites. Chemical signals guide the developing dendrites toward their final location, where synapses are formed with projections from subcortical structures.
		These connections are strengthened through neuronal activity, and connections with very little activity are pruned.
Postnatal neurogenesis	Birth–adulthood	The development of new cells in several brain regions, including:
		—Dentate gyrus of the hippocampus
		—Olfactory bulb
		—Possibly cingulated gyrus; regions of parietal cortex
Myelination	3rd trimester–middle age	Neurons are enclosed in a myelin sheath, resulting in an increased speed of action potentials.
Gyrification	3rd trimester–adulthood	The smooth tissue of the brain folds to form gyri and sulci.
Structural development of the prefrontal cortex	Birth–late adulthood	The prefrontal cortex is the last structure to undergo gyrification during uterine life. The synaptic density reaches its peak at 12 months, however, myclination of this structure continues into adulthood.
Neurochemical development of the prefrontal cortex	Uterine life–adolescence	All major neurotransmitter systems undergo initial development during uterine life and are present at birth. Systems do not reach full maturity until late adulthood.

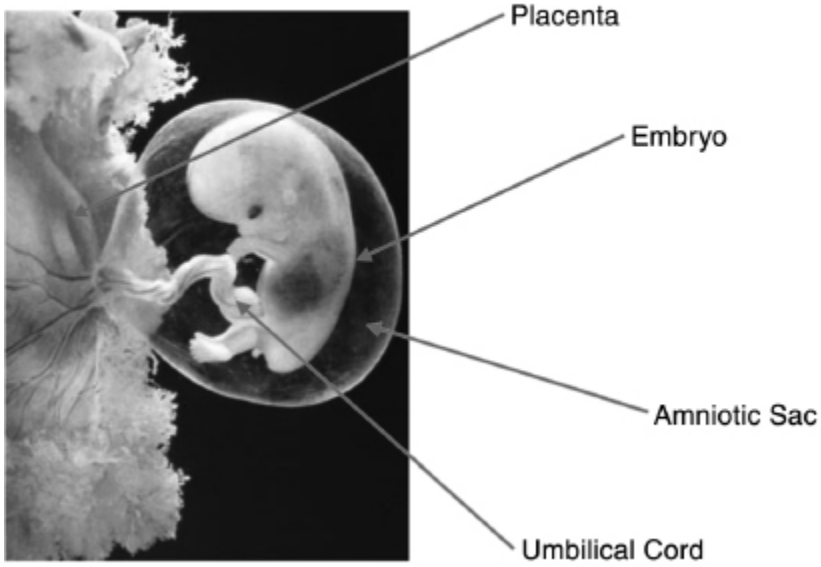
Source: From “Neurobiological Development during Childhood and Adolescence,” by T. White and C. A. Nelson, in *Schizophrenia in Adolescents and Children: Assessment, Neurobiology, and Treatment,* R. Findling and S. C. Schulz (Eds.), 2004, Baltimore, MD: Johns Hopkins University Press.

Embryonic Origins of Brain Tissue

Immediately after conception the two-celled zygote rapidly begins to divide into a many-celled organism. Approximately 1 week after conception has occurred, 100 cells have been formed (this clump of cells is referred to as a blastocyst). A series of molecular changes occur that lead to the rearrangement of these cells, with the subsequent creation of an inner and an outer cell mass. The inner mass (embryoblast) will give rise to the embryo itself, whereas the outer mass (trophoblast) will eventually give rise to all of the supporting tissues, such as the amniotic sac, placenta, and umbilical cord (see Figure 1.2).

Figure 1.2 As described in the text, the blastocyst is created by the mitotic process the zygote undergoes following conception. The blastocyst proper divides into an inner and outer layer, with the latter giving rise to the support structures (e.g., amniotic sac, umbilical cord, and placenta), whereas the former give rise to the embryo itself. Source: *From* Introduction to Child Development (*6th ed.), by J. P. Dworetzky, 1996, St. Paul, MN: West Publishing Company.*

Brain Development



Over the course of the next weeks, the cells comprising the embryo itself undergo a transformation, forming inner,

middle, and outer layers. The inner layer of the embryo will go on to develop into the epithelial lining of the gastrointestinal and respiratory tracts; the parenchyma (outside portion) of the tonsils, thyroid gland, parathyroid glands, thymus, liver, and pancreas; the epithelial lining of the urinary bladder and most of the urethra; and the epithelial lining of the tympanic cavity, tympanic antrum, and auditory tube. Among others, the middle layer gives rise to cartilage, bone, connective tissue; striated and smooth muscles; heart, blood and lymph vessels, and cells; kidneys; gonads (ovaries and testes), and genital ducts; the membranes lining the body cavities (e.g., pericardial); and spleen. Finally, the outer layer of the embryo gives rise to the central (brain and spinal cord) and peripheral nervous system; the sensory epithelia of eye, ear, and nose; epidermis (or skin) and its appendages (hair and nails); mammary glands; pituitary gland and subcutaneous glands; enamel of the teeth; spinal, cranial, and autonomic ganglia; pigment cells of the dermis; the membranes covering the brain and spinal cord (meninges). The outer-most layer is the focus of attention in this book.

STAGES OF BRAIN DEVELOPMENT

Neural Induction and Neurulation

The process of transforming the undifferentiated tissue lining the dorsal side of the ectoderm (the outermost layer of the embryo) into nervous system tissue is referred to as neural *induction.* In contrast, the dual processes called primary and secondary *neurulation* further differentiate of

this neural tissue into the brain and the spinal cord respectively (for recent review of neural induction and neurulation, see Lumsden & Kintner, 2003).

As Figures 1.3 and 1.4 illustrate, a thin layer of undifferentiated tissue is gradually transformed into an increasingly thick layer of tissue that will become the *neural plate.* Chemical agents collectively referred to as *transforming growth factors* are responsible for the subsequent transformation of this undifferentiated tissue into nervous system tissue (Murloz-Sanjuan & Brivanfou, 2002). Morphologically this is marked by a shift from the neural plate to the neural tube. The neural plate buckles, forming a crease down its longitudinal axis. The tissue then folds inward, the edges rise up, and a tube is formed. This process begins on approximately day 22 of gestation (Keith, 1948), with the tube fusing first at the midsection and progressing outward in either direction until approximately day 26 (Sidman & Rakic, 1982). The rostral portion of the tube eventually forms the brain and the caudal portion develops into the spinal cord (see Figure 1.4).

Figure 1.3 As discussed in the text, the inner cell mass gives rise to the embryo, which in turn differentiates into inner, middle, and outer layers. The central nervous system (CNS) is derived from the outer layer (ectoderm). Source: *From* The Development of Children, *(3rd ed.), by M. Cole and S. R. Cole, 1996, New York: W.H. Freeman and Company.*

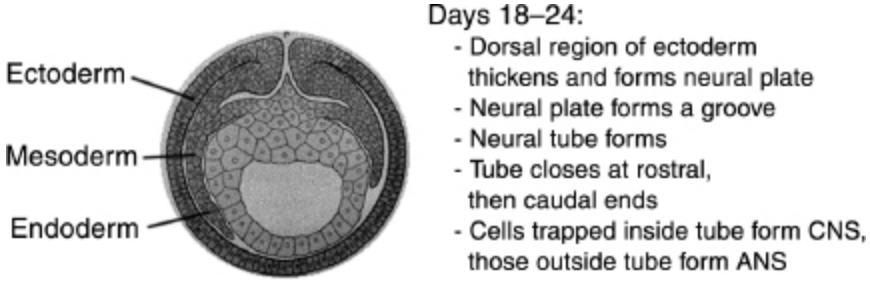
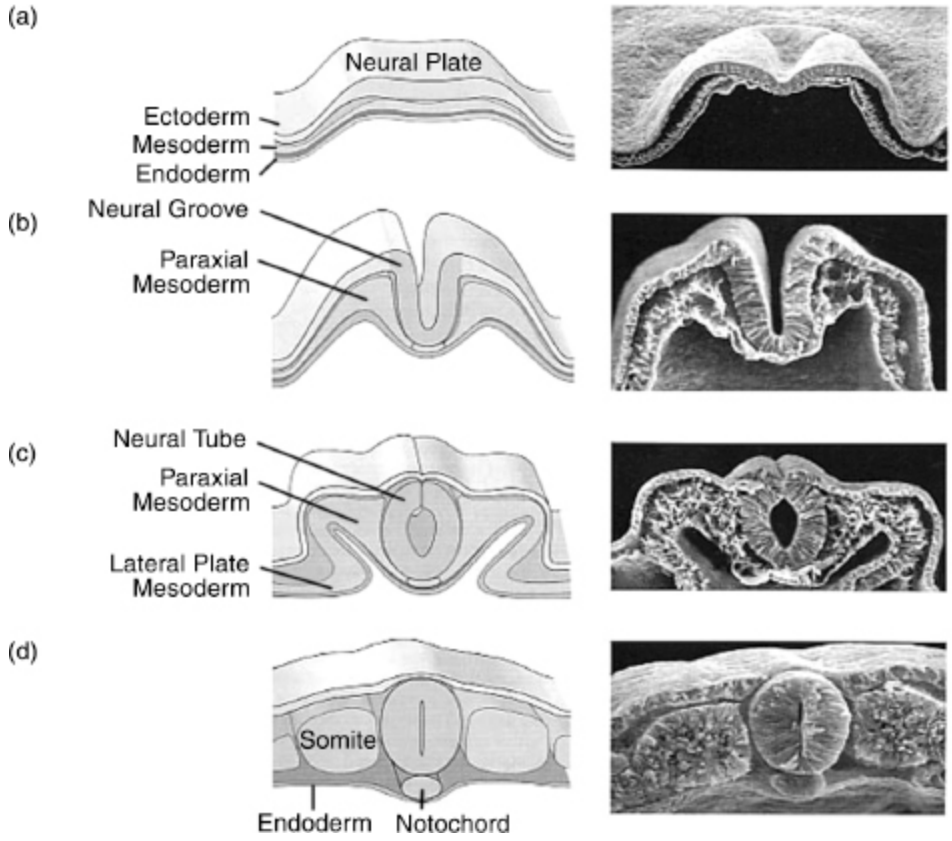


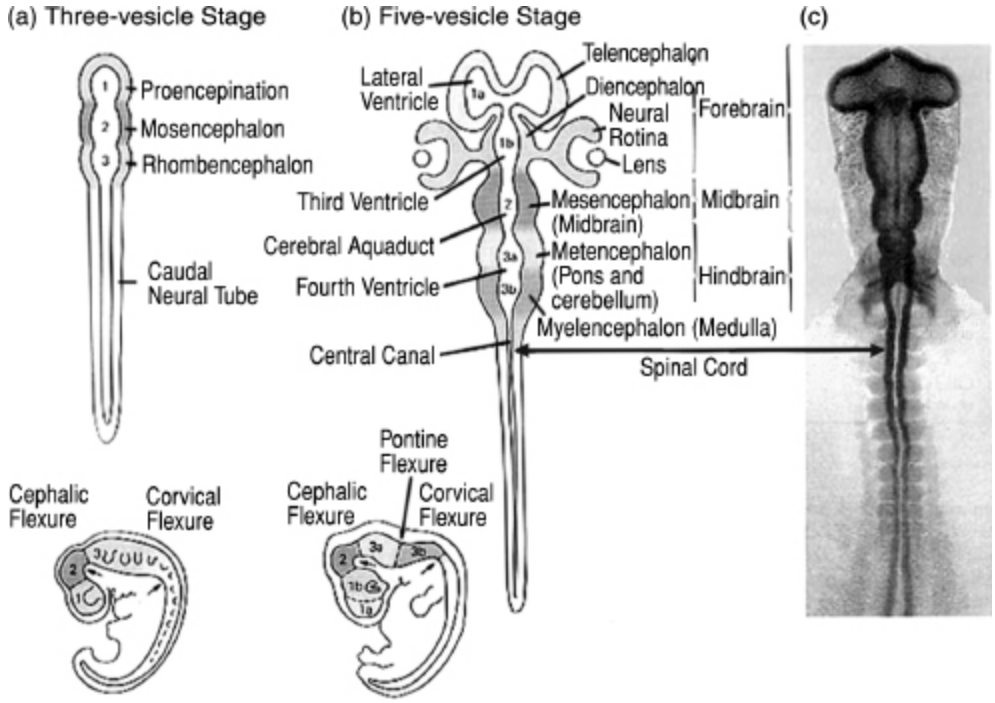
Figure 1.4 The formation of the neural tube, illustrated in cartoon form on the left side of the page and an electron micrograph on the right. Moving from top to bottom shows the initial formation of the neural plate followed by the neural groove followed by the closure of the grove to form the neural tube. Source: *From "Induction and Patterning of the Nervous System" (p. 1020), by T. M. Jessell and J. R. Sanes, in* Principles of Neuroscience, *4th ed., E. R. Kandel, J. H. Schwartz, and T. M. Jessell (Eds.), 2000, New York: McGraw-Hill.*



It is the cells trapped inside the tube that typically go on to comprise the central nervous system; however, there is a cluster of cells trapped between the outside of the neural tube and the dorsal portion of the ectodermal wall (see Figure 1.5) that is referred to as the neural crest. Neural crest cells also contribute to the central nervous system; these cells typically go on to develop into the autonomic nervous system (the elements of the nervous system that

regulate autonomic functions such as respiration, heart rate, and so on).

Figure 1.5 As described in the text, once the neural tube has closed, three vesicles form—the forebrain, midbrain and hindbrain. Each of these vesicles is subsequently elaborated, as is illustrated in panels B and C. Source: *From "Induction and Patterning of the Nervous System" (p. 1020), by T. M. Jessell and J. R. Sanes, in* Principles of Neuroscience, *4th ed., E. R. Kandel, J. H. Schwartz, and T. M. Jessell (Eds.), 2000, New York: McGraw-Hill.*



A fair amount is now known about the genes that regulate many aspects of brain development, including neurulation. Much of this knowledge is based on studies of invertebrates and vertebrates, in which alterations in morphogenesis are observed after genes are selectively deleted ("knock-out") or in a more recently developed method, added ("knock-in"). Because humans share more than 61% of their genes with fruit flies and 81% with mice, there is some basis for generalization of this information. Of course, not everything we know is based on animal models: Increasingly our

knowledge of the molecular biology of brain development is based on careful genetic analysis of nervous system tissue that has failed to develop correctly.

The patterning of the neuroaxis (i.e., head to tail) is for the most part completed by about the 5th prenatal week in humans. Based on mouse studies, many of the transcription factors[1] responsible for this process are now known. As reviewed by Levitt (2003), some of the genes involved in dorsal patterning include members of the *emx, pax,* and *ihx* families of genes, whereas *nkx* and *dlx* gene families may play a role in ventral patterning.

Atypical Development. Unfortunately, errors do occur in neural induction and neurulation. *Neural tube defects* are disorders of primary neurulation, which means that in one way or another the tube has failed to close as it should. Such failure can be complete or partial. An example of a complete failure is *Craniorachischisis Totalis,* which is incompatible with life. Examples of partial failure include a*nencephaly* (when the anterior portion of the neural tube fails to close completely), *holoprosencephaly* (when a single, undifferentiated forebrain develops, rather than a forebrain that has two halves), and most commonly, *Myelomeningocele* or *spina bifida* (where the posterior portion of the neural tube fails to close normally). Holoprosencephaly appears to be due to mutations in a transcription factor called sonic hedgehog (*ZIC2* genes; e.g., Brown et al., 1998), whereas Myelomeningocele may be due to mutations in the *Pax1* gene (Hof et al., 1996). Importantly, neural tube defects generally have been associated with a deficiency of folic acid, and indeed, supplementing the diet of women with this nutrient before and during pregnancy appears to have reduced the incidence of these disorders in the general population.

Proliferation

Once the neural tube has closed, cell division leads to a massive proliferation of new neurons (*neurogenesis*), generally beginning in the 5th prenatal week and peaking between the 3rd and 4th prenatal months (Volpe, 2000; for review, see Bronner-Fraser & Hatten, 2003). The term *massive* barely captures this process. It has been estimated, for example, that at its peak, several hundred thousand new nerve cells are generated *each minute* (Brown, Keynes, & Lumsden, 2001). Proliferation begins in the innermost portion of the neural tube, referred to as the ventricular zone (Chenn & McConnell, 1995), a region that is derived from the subependeymal location that lines the neural tube. In a process called *interkinetic nuclear migration,* new neural cells travel back and forth between the inner and outer portions of the ventricular zone. During the so-called S phase of cell division (mitosis), the new cell first travels toward the outer portion of the ventricular zone where DNA is synthesized, creating a duplicate copy of the cell. Once the S phase has been completed, the cell migrates downward toward the innermost portion of the ventricular zone where it divides into two cells (for a generally accessible description of these phases, see Takahashi, Nowakowski, & Caviness, 2001). Each of these new cells then begins the process again. As cells divide, a new zone is created, the marginal zone, which contains processes (axons and dendrites) from the cells of the ventricular zone. During the second phase of proliferation, neurons actually begin to form. However, for each dividing cell, only one daughter cell will continue to divide; it is the nondividing cell that goes on to migrate to its final destination (Rakic, 1988; see discussion that follows).

Before turning to disorders of proliferation, we wish to make three final points. First, with the exception of cells that comprise the olfactory bulb, the dentate region of the hippocampus, and possibly regions of the neocortex,