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NEUROSCIENCE

Exploring the Brain

Fourth Edition

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NEUROSCIENCE

EXPLORING THE BRAIN

NEUROSCIENCE
EXPLORING THE BRAIN

FOURTH EDITION

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Marketing Manager: Shauna Kelley
Prepress Vendor: Absolute Service, Inc.

Fourth Edition

9 8 7 6 5 4 3 2 1

Printed in China

Library of Congress Cataloging-in-Publication Data

Bear, Mark F., author.
Neuroscience : exploring the brain / Mark F. Bear, Barry W. Connors, Michael A. Paradiso. — Fourth edition.
p. ; cm.
Includes bibliographical references and index.
ISBN 978-0-7817-7817-6 (hardback : alk. paper)
I. Connors, Barry W., author. II. Paradiso, Michael A., author. III. Title.
[DNLM: 1. Brain. 2. Neurosciences. 3. Spinal Cord. WL 300]
QP355.2
612.8—dc23
2014047026

LWW.com

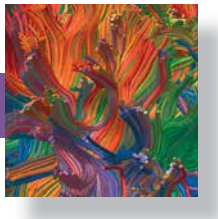
DEDICATION

Anne, David, and Daniel
Ashley, Justin, and Kendall

Brian and Jeffrey

Wendy, Bear, and Boo

PREFACE



THE ORIGINS OF *NEUROSCIENCE: EXPLORING THE BRAIN*

For over 30 years, we have taught a course called Neuroscience 1: An Introduction to the Nervous System. "Neuro 1" has been remarkably successful. At Brown University, where the course originated, approximately one out of every four undergraduates takes it. For a few students, this is the beginning of a career in neuroscience; for others, it is the only science course they take in college.

The success of introductory neuroscience reflects the fascination and curiosity everyone has for how we sense, move, feel, and think. However, the success of our course also derives from the way it is taught and what is emphasized. First, there are no prerequisites, so the elements of biology, chemistry, and physics required for understanding neuroscience are covered as the course progresses. This approach ensures that no students are left behind. Second, liberal use of commonsense metaphors, real-world examples, humor, and anecdotes remind students that science is interesting, approachable, exciting, and fun. Third, the course does not survey all of neurobiology. Instead, the focus is on mammalian brains and, whenever possible, the human brain. In this sense, the course closely resembles what is taught to most beginning medical students. Similar courses are now offered at many colleges and universities by psychology, biology, and neuroscience departments.

The first edition of *Neuroscience: Exploring the Brain* was written to provide a suitable textbook for Neuro 1, incorporating the subject matter and philosophy that made this course successful. Based on feedback from our students and colleagues at other universities, we expanded the second edition to include more topics in behavioral neuroscience and some new features to help students understand the structure of the brain. In the third edition, we shortened chapters when possible by emphasizing principles more and details less and made the book even more user-friendly by improving the layout and clarity of the illustrations. We must have gotten it right because the book now ranks as one of the most popular introductory neuroscience books in the world. It has been particularly gratifying to see our book used as a catalyst for the creation of new courses in introductory neuroscience.

NEW IN THE FOURTH EDITION

The advances in neuroscience since publication of the third edition have been nothing short of breathtaking. The elucidation of the human genome has lived up to its promise to "change everything" we know about our brains. We now have insight into how neurons differ at the molecular level, and this knowledge has been exploited to develop revolutionary technologies to trace their connections and interrogate their functions. The genetic basis for many neurological and psychiatric diseases has been revealed. The methods of genetic engineering have made it possible to create animal models to examine how genes and genetically defined circuits contribute to brain function. Skin cells derived from patients have

been transformed into stem cells, and these have been transformed into neurons that reveal how cellular functions go awry in diseases and how the brain might be repaired. New imaging and computational methods now put within reach the dream of creating a "wiring diagram" for the entire brain. A goal for the fourth edition was to make these and other exciting new developments accessible to the first-time neuroscience student.

We authors are all active neuroscientists, and we want our readers to understand the allure of brain research. A unique feature of our book is the *Path of Discovery* boxes, in which famous neuroscientists tell stories about their own research. These essays serve several purposes: to give a flavor of the thrill of discovery; to show the importance of hard work and patience, as well as serendipity and intuition; to reveal the human side of science; and to entertain and amuse. We have continued this tradition in the fourth edition, with contributions from 26 esteemed scientists. Included in this illustrious group are Nobel laureates Mario Capecchi, Eric Kandel, Leon Cooper, May-Britt Moser, and Edvard Moser.

AN OVERVIEW OF THE BOOK

Neuroscience: Exploring the Brain surveys the organization and function of the human nervous system. We present material at the cutting edge of neuroscience in a way that is accessible to both science and nonscience students alike. The level of the material is comparable to an introductory college text in general biology.

The book is divided into four parts: Part I, Foundations; Part II, Sensory and Motor Systems; Part III, The Brain and Behavior; and Part IV, The Changing Brain. We begin Part I by introducing the modern field of neuroscience and tracing some of its historical antecedents. Then we take a close look at the structure and function of individual neurons, how they communicate chemically, and how these building blocks are arranged to form a nervous system. In Part II, we go inside the brain to examine the structure and function of the systems that serve the senses and command voluntary movements. In Part III, we explore the neurobiology of human behavior, including motivation, sex, emotion, sleep, language, attention, and mental illness. Finally, in Part IV, we look at how the environment modifies the brain, both during development and in adult learning and memory.

The human nervous system is examined at several different scales, ranging from the molecules that determine the functional properties of neurons to the large systems in the brain that underlie cognition and behavior. Many disorders of the human nervous system are introduced as the book progresses, usually within the context of the specific neural system under discussion. Indeed, many insights into the normal functions of neural systems have come from the study of diseases that cause specific malfunctions of these systems. In addition, we discuss the actions of drugs and toxins on the brain using this information to illustrate how different brain systems contribute to behavior and how drugs may alter brain function.

Organization of Part I: Foundations (Chapters 1–7)

The goal of Part I is to build a strong base of general knowledge in neurobiology. The chapters should be covered sequentially, although Chapters 1 and 6 can be skipped without a loss of continuity.

In Chapter 1, we use an historical approach to review some basic principles of nervous system function and then turn to the topic of how neuroscience research is conducted today. We directly confront the ethics of neuroscience research, particularly that which involves animals.

In Chapter 2, we focus mainly on the cell biology of the neuron. This is essential information for students inexperienced in biology, and we find that even those with a strong biology background find this review helpful. After touring the cell and its organelles, we go on to discuss the structural features that make neurons and their supporting cells unique, emphasizing the correlation of structure and function. We also introduce some of the feats of genetic engineering that neuroscientists now use routinely to study the functions of different types of nerve cell.

Chapters 3 and 4 are devoted to the physiology of the neuronal membrane. We cover the essential chemical, physical, and molecular properties that enable neurons to conduct electrical signals. We discuss the principles behind the revolutionary new methods of optogenetics. Throughout the chapter, we appeal to students' intuition by using a commonsense approach, with a liberal use of metaphors and real-life analogies.

Chapters 5 and 6 cover interneuronal communication, particularly chemical synaptic transmission. Chapter 5 presents the general principles of chemical synaptic transmission, and Chapter 6 discusses the neurotransmitters and their modes of action in greater detail. We also describe many of the modern methods for studying the chemistry of synaptic transmission. Later chapters do not assume an understanding of synaptic transmission at the depth of Chapter 6, however, so this chapter can be skipped at the instructor's discretion. Most coverage of psychopharmacology appears in Chapter 15, after the general organization of the brain and its sensory and motor systems have been presented. In our experience, students wish to know where, in addition to how, drugs act on the nervous system and behavior.

Chapter 7 covers the gross anatomy of the nervous system. Here we focus on the common organizational plan of the mammalian nervous system by tracing the brain's embryological development. (Cellular aspects of development are covered in Chapter 23.) We show that the specializations of the human brain are simple variations on the basic plan that applies to all mammals. We introduce the cerebral cortex and the new field of connectomics.

Chapter 7's appendix, An Illustrated Guide to Human Neuroanatomy, covers the surface and cross-sectional anatomy of the brain, the spinal cord, the autonomic nervous system, the cranial nerves, and the blood supply. A self-quiz will help students learn the terminology. We recommend that students become familiar with the anatomy in the guide before moving on to Part II. The coverage of anatomy is selective, emphasizing the relationship of structures that will be covered in later chapters. We find that students love to learn the anatomy.

Organization of Part II: Sensory and Motor Systems (Chapters 8–14)

Part II surveys the systems within the brain that control sensation and movement. In general, these chapters do not need to be covered sequentially, except for Chapters 9 and 10 on vision and Chapters 13 and 14 on the control of movement.

We chose to begin Part II with a discussion of the chemical senses—smell and taste—in Chapter 8. These are good systems for illustrating the general principles and problems in the encoding of sensory information, and the transduction mechanisms have strong parallels with other systems.

Chapters 9 and 10 cover the visual system, an essential topic for all introductory neuroscience courses. Many details of visual system organization are presented, illustrating not only the depth of current knowledge but also the principles that apply across sensory systems.

Chapter 11 explores the auditory system, and Chapter 12 introduces the somatic sensory system. Audition and somatic sensation are such important parts of everyday life; it is hard to imagine teaching introductory neuroscience without discussing them. The vestibular sense of balance is covered in a separate section of Chapter 11. This placement offers instructors the option to skip the vestibular system at their discretion.

In Chapters 13 and 14, we discuss the motor systems of the brain. Considering how much of the brain is devoted to the control of movement, this more extensive treatment is clearly justified. However, we are well aware that the complexities of the motor systems are daunting to students and instructors alike. We have tried to keep our discussion sharply focused, using numerous examples to connect with personal experience.

Organization of Part III: The Brain and Behavior (Chapters 15–22)

Part III explores how different neural systems contribute to different behaviors, focusing on the systems where the connection between the brain and behavior can be made most strongly. We cover the systems that control visceral function and homeostasis, simple motivated behaviors such as eating and drinking, sex, mood, emotion, sleep, consciousness, language, and attention. Finally, we discuss what happens when these systems fail during mental illness.

Chapters 15–19 describe a number of neural systems that orchestrate widespread responses throughout the brain and the body. In Chapter 15, we focus on three systems that are characterized by their broad influence and their interesting neurotransmitter chemistry: the secretory hypothalamus, the autonomic nervous system, and the diffuse modulatory systems of the brain. We discuss how the behavioral manifestations of various drugs may result from disruptions of these systems.

In Chapter 16, we look at the physiological factors that motivate specific behaviors, focusing mainly on recent research about the control of eating habits. We also discuss the role of dopamine in motivation and addiction, and we introduce the new field of "neuroeconomics." Chapter 17 investigates the influence of sex on the brain, and the influence of the brain on sexual behavior. Chapter 18 examines the neural systems believed to underlie emotional experience and expression, specifically emphasizing fear and anxiety, anger, and aggression.

In Chapter 19, we investigate the systems that give rise to the rhythms of the brain, ranging from the rapid electrical rhythms during sleep and wakefulness to the slow circadian rhythms controlling hormones, temperature, alertness, and metabolism. We next explore aspects of brain processing that are highly developed in the human brain. Chapter 20 investigates the neural basis of language and Chapter 21 discusses changes in brain activity associated with rest, attention, and consciousness. Part III ends with a discussion of mental illness in Chapter 22. We introduce the promise of molecular medicine to develop new treatments for serious psychiatric disorders.

Organization of Part IV: The Changing Brain (Chapters 23–25)

Part IV explores the cellular and molecular basis of brain development and learning and memory. These subjects represent two of the most exciting frontiers of modern neuroscience.

Chapter 23 examines the mechanisms used during brain development to ensure that the correct connections are made between neurons. The cellular aspects of development are discussed here rather than in Part I

for several reasons. First, by this point in the book, students fully appreciate that normal brain function depends on its precise wiring. Because we use the visual system as a concrete example, the chapter must also follow a discussion of the visual pathways in Part II. Second, we survey aspects of experience-dependent development of the visual system that are regulated by behavioral state, so this chapter is placed after the early chapters of Part III. Finally, an exploration of the role of the sensory environment in brain development in Chapter 23 is followed in the next two chapters by discussions of how experience-dependent modifications of the brain form the basis for learning and memory. We see that many of the mechanisms are similar, illustrating the unity of biology.

Chapters 24 and 25 cover learning and memory. Chapter 24 focuses on the anatomy of memory, exploring how different parts of the brain contribute to the storage of different types of information. Chapter 25 takes a deeper look into the molecular and cellular mechanisms of learning and memory, focusing on changes in synaptic connections.

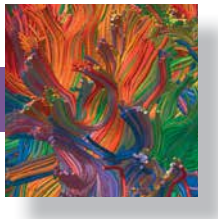
HELPING STUDENTS LEARN

Neuroscience: Exploring the Brain is not an exhaustive study. It is intended to be a readable textbook that communicates to students the important principles of neuroscience clearly and effectively. To help students learn neuroscience, we include a number of features designed to enhance comprehension:

- **Chapter Outlines and Introductory and Concluding Remarks.** These elements preview the organization of each chapter, set the stage, and place the material into broader perspective.
- **Of Special Interest Boxes.** These boxes are designed to illuminate the relevance of the material to the students' everyday lives.
- **Brain Food Boxes.** More advanced material that might be optional in many introductory courses is set aside for students who want to go deeper.
- **Path of Discovery Boxes.** These essays, written by leading researchers, demonstrate a broad range of discoveries and the combination of hard work and serendipity that led to them. These boxes both personalize scientific exploration and deepen the reader's understanding of the chapter material and its implications.
- **Key Terms and Glossary**. Neuroscience has a language of its own, and to comprehend it, one must learn the vocabulary. In the text of each chapter, important terms are highlighted in boldface type. To facilitate review, these terms appear in a list at the end of each chapter in the order in which they appeared in the text, along with page references. The same terms are assembled at the end of the book, with definitions, in a glossary.
- **Review Questions.** At the end of each chapter, a brief set of questions for review are specifically designed to provoke thought and help students integrate the material.
- **Further Reading.** We include a list of several recent review articles at the end of each chapter to guide study beyond the scope of the textbook.
- **Internal Reviews of Neuroanatomical Terms.** In Chapter 7, where nervous system anatomy is discussed, the narrative is interrupted periodically with brief self-quiz vocabulary reviews to enhance understanding. In Chapter 7's appendix, an extensive self-quiz is provided in the form of a workbook with labeling exercises.

- **References and Resources.** At the end of the book, we provide selected readings and online resources that will lead students into the research literature associated with each chapter. Rather than including citations in the body of the chapters, where they would compromise the readability of the text, we have organized the references and resources by chapter and listed them at the end of the book.
- **Full-Color Illustrations.** We believe in the power of illustrations—not those that "speak a thousand words" but those that each make a single point. The first edition of this book set a new standard for illustrations in a neuroscience text. The fourth edition reflects improvements in the pedagogical design of many figures from earlier editions and includes many superb new illustrations as well.

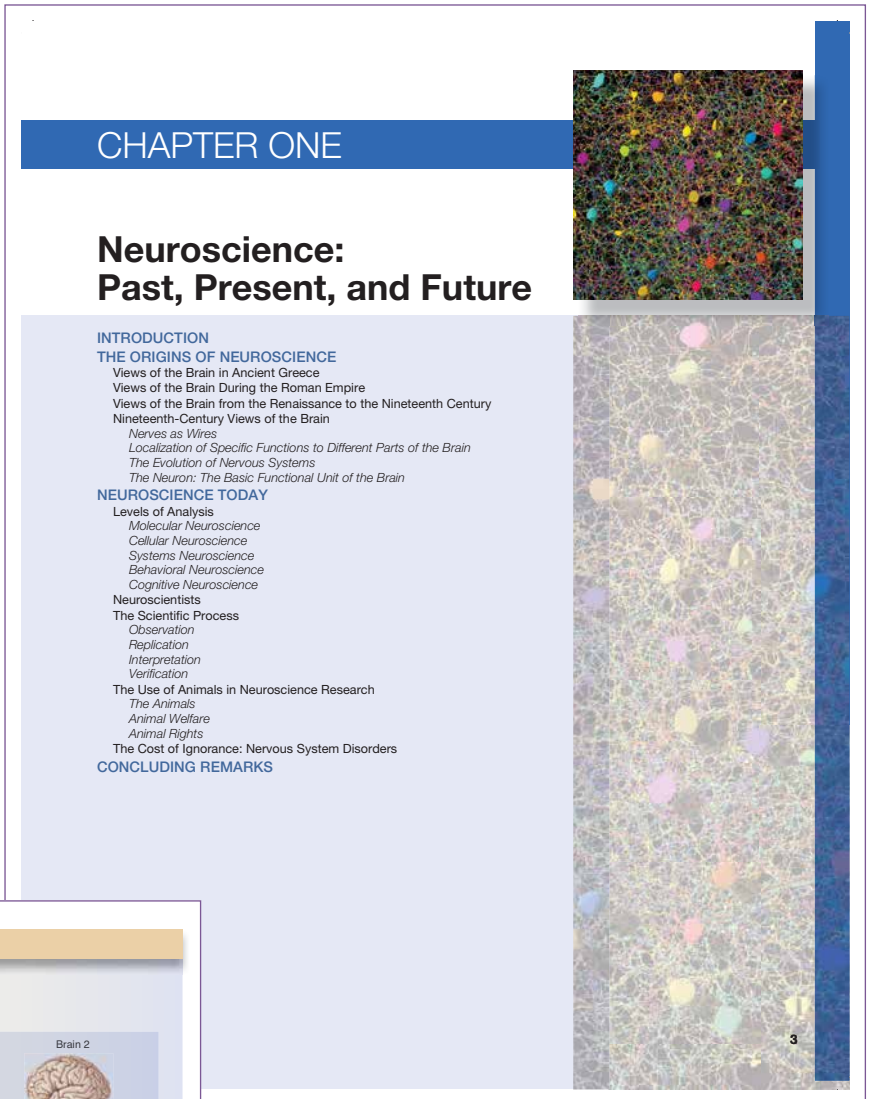
USER'S GUIDE



Succeed in your course and discover the excitement of the dynamic, rapidly changing field of neuroscience with this fourth edition of ***Neuroscience: Exploring the Brain***. This user's guide will help you discover how to best use the features of this book.

Chapter Outline

This "road map" to the content outlines what you will learn in each chapter and can serve as a valuable review tool.



CHAPTER ONE

Neuroscience: Past, Present, and Future

3

BOX 2.2 BRAIN FOOD

Expressing One's Mind in the Post-Genomic Era

Sequencing the human genome was a truly monumental achievement, completed in 2003. The Human Genome Project identified all of the approximately 25,000 genes in human DNA. We now live in what has been called the "post-genomic era," in which information about the genes expressed in our tissues can be used to diagnose and treat diseases. Neuroscientists are using this information to tackle long-standing questions about the biological basis of neurological and psychiatric disorders as well as to probe deeper into the origins of individuality. The logic goes as follows. The brain is a product of the genes expressed in it. Differences in gene expression between a normal brain and a diseased brain, or a brain of unusual ability, can be used to identify the molecular basis of the observed symptoms or traits.

The level of gene expression is usually defined as the number of mRNA transcripts synthesized by different cells and tissues to direct the synthesis of specific proteins. Thus, the analysis of gene expression requires comparing the relative abundance of various mRNAs in the brains of two groups of humans or animals. One way to perform such a comparison is to use DNA *microarrays*, which are created by robotic machines that arrange thousands of small spots of synthetic DNA on a microscope slide. Each spot contains a unique DNA sequence that will recognize and stick to a different specific mRNA sequence. To compare the gene expression in two brains, one begins by collecting a sample of mRNAs from each brain. The mRNA of one brain is labeled with a chemical tag that fluoresces green, and the mRNA of the other brain is labeled with a tag that fluoresces red. These samples are then applied to the microarray. Highly expressed genes will produce brightly fluorescent spots, and differences in the relative gene expression between the brains will be revealed by differences in the color of the fluorescence (Figure A).

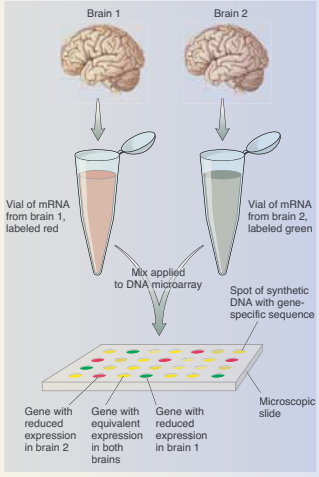


Figure A
Profiling differences in gene expression.

Brain Food Boxes

Want to expand your understanding? These boxes offer optional advanced material so you can expand on what you've learned.

BOX 16.2 OF SPECIAL INTEREST

Marijuana and the Munchies

A well-known consequence of marijuana intoxication is stimulation of appetite, an effect known by users as "the munchies." The active ingredient in marijuana is D^9-tetrahydrocannabinol (THC), which alters neuronal functions by stimulating a receptor called cannabinoid receptor 1 (CB1). CB1 receptors are abundant throughout the brain, so it is overly simplistic to view these receptors as serving only appetite regulation. Nevertheless, "medical marijuana" is often prescribed (where legal) as a means to stimulate appetite in patients with chronic diseases, such as cancer and AIDS. A compound that inhibits CB1 receptors, rimonabant, was also developed as an appetite suppressant. However, human drug trials had to be discontinued because of psychiatric side effects. Although this finding underscores the fact that these receptors do much more than mediate the munchies, it is still of interest to know where in the brain CB1 receptors act to stimulate appetite. Not surprisingly, the CB1 receptors are associated with neurons in many regions of the brain that control feeding, such as the hypothalamus, and some of the orexigenic effects of THC are related to changing the activity of these neurons. However, neuroscientists were surprised to learn in 2014 that much of the appetite stimulation comes from enhancing the sense of smell, at least in mice. Collaborative research conducted by neuroscientists in France and Spain, countries incidentally known for their appreciation of good tastes and smells, revealed that activation of CB1 receptors in the olfactory bulb increases odor detection and is necessary for the increase in food intake stimulated in hungry mice by cannabinoids.

In Chapter 8, we discussed how smells activate neurons in the olfactory bulb which, in turn, relay information to the olfactory cortex. The cortex also sends feedback projections to the bulb that synapse on inhibitory interneurons called *granule cells*. By activating the inhibitory granule cells, this feedback from the cortex dampens ascending olfactory activity. These corticofugal synapses use glutamate as a neurotransmitter. The brain's own endocannabinoids (anandamide and 2-arachidonoylglycerol) are synthesized under fasting conditions, and they inhibit glutamate release by acting on CB1 receptors on the corticofugal axon terminals. Reducing granule cell activation by glutamate in the bulb has the net effect of enhancing the sense of smell (Figure A). It remains to be determined if the munchies arise from enhanced olfaction in marijuana users, but a simple experiment, such as holding your nose while eating, confirms that much of the hedonic value of food derives from the sense of smell.

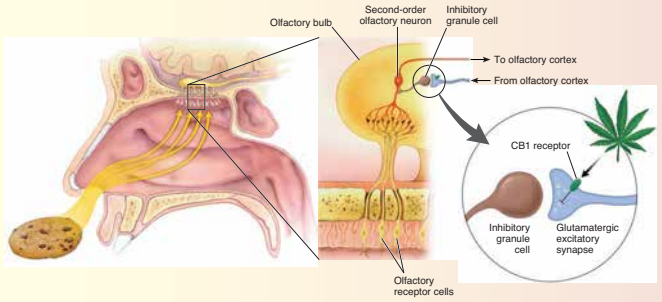


Figure A
Activation of CB1 receptors by THC, the psychoactive ingredient in marijuana, enhances olfaction by suppressing the release of glutamate from corticofugal inputs to inhibitory granule cells in the olfactory bulb. (Source: Adapted from Soria-Gomez et al., 2014.)

Of Special Interest Boxes

Wondering how key concepts appear in the real world? These boxes complement the text by showing some of the more practical applications of concepts. Topics include brain disorders, human case studies, drugs, new technology, and more.

BOX 2.3 PATH OF DISCOVERY

Gene Targeting in Mice

by Mario Capecchi

How did I first get the idea to pursue gene targeting in mice? From a simple observation. Mike Wigler, now at Cold Spring Harbor Laboratory, and Richard Axel, at Columbia University, had published a paper in 1979 showing that exposing mammalian cells to a mixture of DNA and calcium phosphate would cause some cells to take up the DNA in functional form and express the encoded genes. This was exciting because they had clearly demonstrated that exogenous, functional DNA could be introduced into mammalian cells. But I wondered why their efficiency was so low. Was it a problem of delivery, insertion of exogenous DNA into the chromosome, or expression of the genes once inserted into the host chromosome? What would happen if purified DNA was directly injected into the nucleus of mammalian cells in culture?

To find out, I converted a colleague's electrophysiology station into a miniature hypodermic needle to directly inject DNA into the nucleus of a living cell using mechanical micromanipulators and light microscopy (Figure A). The procedure worked with amazing efficiency (Capecchi, 1980). With this method, the frequency of successful integration was now one in three cells rather than one in a million cells as formerly. This high efficiency directly led to the development of transgenic mice through the injection and random integration of exogenous DNA into chromosomes of fertilized mouse eggs, or zygotes. To achieve the high efficiency of expression of the exogenous DNA in the recipient cell, I had to attach small fragments of viral DNA, which we now understand to contain enhancers that are critical in eukaryotic gene expression.

But what fascinated me most was our observation that when many copies of a gene were injected into a cell nucleus, all of these molecules ended up in an ordered head-to-tail arrangement, called a *concatemer* (Figure B). This was astonishing and could not have occurred as a random event. We went on to unequivocally prove that homologous recombination, the process by which chromosomes share genetic information during cell division, was responsible for the incorporation of the foreign DNA (Folger et al., 1982). These experiments demonstrated that all mammalian somatic cells contain a very efficient machinery for swapping segments of DNA that have similar sequences of nucleotides. Injection of a thousand copies of a gene sequence into the nucleus of a cell resulted in chromosomal insertion of a concatemer containing a thousand copies of that sequence, all oriented in the same direction. This simple observation directly led me to

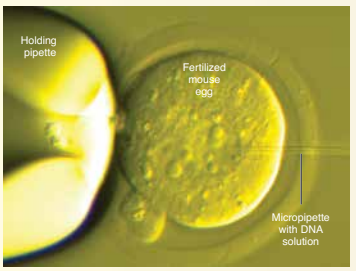


Figure A
Fertilized mouse egg receiving an injection of foreign DNA. (Image courtesy of Dr. Peimin Qi, Division of Comparative Medicine, Massachusetts Institute of Technology.)

Path of Discovery Boxes

Learn about some of the superstars in the field with these boxes. Leading researchers describe their discoveries and achievements and tell the story of how they arrived at them.

the anatomical study of brain cells had to await a method to harden the tissue without disturbing its structure and an instrument that could produce very thin slices. Early in the nineteenth century, scientists discovered how to harden, or "fix," tissues by immersing them in formaldehyde, and they developed a special device called a *microtome* to make very thin slices.

These technical advances spawned the field of **histology**, the microscopic study of the structure of tissues. But scientists studying brain structure faced yet another obstacle. Freshly prepared brain tissue has a uniform, cream-colored appearance under the microscope, with no differences in pigmentation to enable histologists to resolve individual cells. The final breakthrough in neurohistology was the introduction of stains that selectively color some, but not all, parts of the cells in brain tissue.

One stain still used today was introduced by the German neurologist Franz Nissl in the late nineteenth century. Nissl showed that a class of basic dyes would stain the nuclei of all cells as well as clumps of material surrounding the nuclei of neurons (Figure 2.1). These clumps are called *Nissl bodies*, and the stain is known as the **Nissl stain**. The Nissl stain is extremely useful for two reasons: It distinguishes between neurons and
rrangement, or **cytoarchi-**
e brain. (The prefix *cyto-* is
f cytoarchitecture led to the
pecialized regions. We now
nction.

The Nucleus. Its name derived from the Latin word for "nut," the **nucleus** of the cell is spherical, centrally located, and about 5–10 μm across. It is contained within a double membrane called the *nuclear envelope*. The nuclear envelope is perforated by pores about 0.1 μm across.

Within the nucleus are **chromosomes** which contain the genetic material **DNA** (**deoxyribonucleic acid**). Your DNA was passed on to you from your parents and it contains the blueprint for your entire body. The DNA in each of your neurons is the same, and it is the same as the DNA in the cells of your liver and kidney and other organs. What distinguishes a neuron from a liver cell are the specific parts of the DNA that are used to assemble the cell. These segments of DNA are called **genes**.

Each chromosome contains an uninterrupted double-strand braid of DNA, 2 nm wide. If the DNA from the 46 human chromosomes were laid out straight, end to end, it would measure more than 2 m in length. If we were to compare this total length of DNA to the total string of letters that make up this book, the genes would be analogous to the individual words. Genes are from 0.1 to several micrometers in length.

The "reading" of the DNA is known as **gene expression**. The final product of gene expression is the synthesis of molecules called **proteins**, which exist in a wide variety of shapes and sizes, perform many different functions, and bestow upon neurons virtually all of their unique characteristics. **Protein synthesis**, the assembly of protein molecules, occurs in the cytoplasm. Because the DNA never leaves the nucleus, an intermediary must carry the genetic message to the sites of protein synthesis in the cytoplasm. This function is performed by another long molecule called

KEY TERMS

Introduction
neuron (p. 24)
glial cell (p. 24)

The Neuron Doctrine
histology (p. 25)
Nissl stain (p. 25)
cytoarchitecture (p. 25)
Golgi stain (p. 26)
cell body (p. 26)
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dendritic spine (p. 46)

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unipolar neuron (p. 46)
bipolar neuron (p. 46)
multipolar neuron (p. 46)
stellate cell (p. 46)
pyramidal cell (p. 46)
spiny neuron (p. 46)
aspinous neuron (p. 46)
primary sensory neuron (p. 48)
motor neuron (p. 48)
interneuron (p. 48)
green fluorescent protein (GFP) (p. 48)

Glia
astrocyte (p. 49)
oligodendroglial cell (p. 49)
Schwann cell (p. 49)
myelin (p. 49)
node of Ranvier (p. 49)
ependymal cell (p. 52)
microglial cell (p. 52)

Key Terms
Appearing in bold throughout the text, key terms are also listed at the end of each chapter and defined in the glossary. These can help you study and ensure you've mastered the terminology as you progress through your course.

REVIEW QUESTIONS

1. State the neuron doctrine in a single sentence. To whom is this insight credited?
2. Which parts of a neuron are shown by a Golgi stain that are not shown by a Nissl stain?
3. What are three physical characteristics that distinguish axons from dendrites?
4. Of the following structures, state which ones are unique to neurons and which are not: nucleus, mitochondria, rough ER, synaptic vesicle, Golgi apparatus.
5. What are the steps by which the information in the DNA of the nucleus directs the synthesis of a membrane-associated protein molecule?
6. Colchicine is a drug that causes microtubules to break apart (depolymerize). What effect would this drug have on anterograde transport? What would happen in the axon terminal?
7. Classify the cortical pyramidal cell based on (1) the number of neurites, (2) the presence or absence of dendritic spines, (3) connections, and (4) axon length.
8. Knowledge of genes uniquely expressed in a particular category of neurons can be used to understand how those neurons function. Give one example of how you could use genetic information to study a category of neuron.
9. What is myelin? What does it do? Which cells provide it in the central nervous system?

Review Questions
Test your comprehension of each of the chapter's major concepts with these review questions.

FURTHER READING

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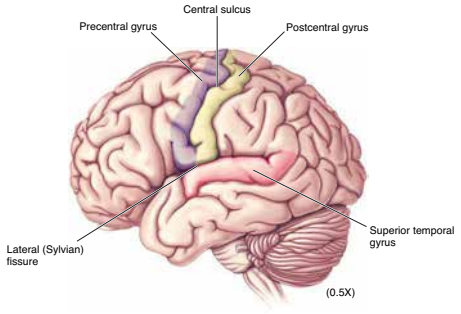
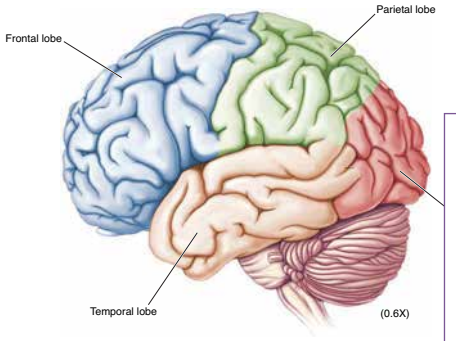
Further Reading
Interested in learning more? Recent review articles are identified at the end of each chapter so you can delve further into the content.

(b) Selected Gyri, Sulci, and Fissures. The cerebrum is noteworthy for its convoluted surface. The bumps are called *gyri*, and the grooves are called *sulci* or, if they are especially deep, fissures. The precise pattern of gyri and sulci can vary considerably from individual to individual, but many features are common to all human brains. Some of the important landmarks are labeled here. Notice that the postcentral gyrus lies immediately posterior to the central sulcus, and that the precentral gyrus lies immediately anterior to it. The neurons of the postcentral gyrus are involved in somatic sensation (touch; Chapter 12), and those of the precentral gyrus control voluntary movement (Chapter 14). Neurons in the superior temporal gyrus are involved in audition (hearing; Chapter 11).



(c) Cerebral Lobes and the Insula. By convention, the cerebrum is subdivided into lobes named after the bones of the skull that lie over them. The central sulcus divides the frontal lobe from the parietal lobe. The temporal lobe lies immediately ventral to the deep lateral (Sylvian) fissure. The occipital lobe lies at the very back of the cerebrum, bordering both parietal and temporal lobes. A buried piece of the cerebral cortex, called the *insula* (Latin for "island"), is revealed if the margins of the lateral fissure are gently pulled apart (inset). The insula borders and separates the temporal and frontal lobes.



An Illustrated Guide to Human Neuroanatomy

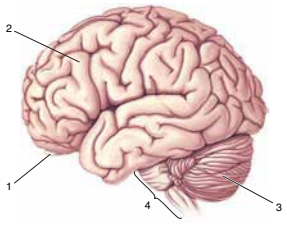
This appendix to Chapter 7 includes an extensive self-quiz with labeling exercises that enable you to assess your knowledge of neuroanatomy.

SELF-QUIZ

This review workbook is designed to help you learn the neuroanatomy that has been presented. Here, we have reproduced the images from the Guide; however, instead of labels, numbered leader lines (arranged in a clockwise fashion) point to the structures of interest. Test your knowledge by filling in the appropriate names in the spaces provided. To review what you have learned, quiz yourself by putting your hand over the names. Experience has shown that this technique greatly facilitates the learning and retention of anatomical terms. Mastery of the vocabulary of neuroanatomy will serve you well as you learn about the functional organization of the brain in the remainder of the book.

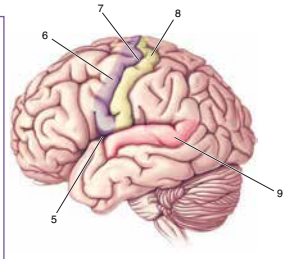
The Lateral Surface of the Brain

(a) Gross Features



1. _____
2. _____
3. _____
4. _____

(b) Selected Gyri, Sulci, and Fissures



5. _____
6. _____
7. _____
8. _____
9. _____

Self-Quiz

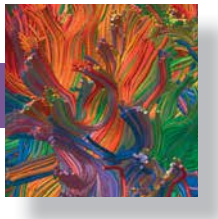
Found in Chapter 7, these brief vocabulary reviews can help enhance your understanding of nervous system anatomy.

SELF-QUIZ

Take a few moments right now and be sure you understand the meaning of these terms:

anterior	ventral	contralateral
rostral	midline	midsagittal plane
posterior	medial	sagittal plane
caudal	lateral	horizontal plane
dorsal	ipsilateral	coronal plane

ACKNOWLEDGMENTS



Back in 1993, when we began in earnest to write the first edition of this textbook, we had the good fortune to work closely with a remarkably dedicated and talented group of individuals—Betsy Dilernia, Caitlin and Rob Duckwall, and Suzanne Meagher—who helped us bring the book to fruition. Betsy continued as our developmental editor for the first three editions. We attribute much of our success to her extraordinary efforts to improve the clarity and consistency of the writing and the layout of the book. Betsy's well-deserved retirement caused considerable consternation among the author team, but good fortune struck again with the recruitment of Tom Lochhaas for this new edition. Tom, an accomplished author himself, shares Betsy's attention to detail and challenged us to not rest on our laurels. We are proud of the fourth edition and very grateful to Tom for holding us to a high standard of excellence. We would be remiss for not thanking him also for his good cheer and patience despite a challenging schedule and occasionally distracted authors.

It is noteworthy that despite the passage of time—*21 years!*—we were able to continue working with Caitlin, Rob, and Suzanne in this edition. Caitlin's and Rob's Dragonfly Media Group produced the art, with help and coordination from Jennifer Clements, and the results speak for themselves. The artists took our sometimes fuzzy concepts and made them a beautiful reality. The quality of the art has always been a high priority for the authors, and we are very pleased that they have again delivered an art program that ensures we will continue to enjoy the distinction of having produced the most richly illustrated neuroscience textbook in the world. Finally, we are forever indebted to Suzanne, who assisted us at every step. Without her incredible assistance, loyalty, and dedication to this project, the book would never have been completed. That statement is as true today as it was in 1993. Suzanne, you are—still—the best!

For the current edition, we have the pleasure of acknowledging a new team member, Linda Francis. Linda is an editorial project manager at Lippincott Williams & Wilkins, and she worked closely with us from start to finish, helping us to meet a demanding schedule. Her efficiency, flexibility, and good humor are all greatly appreciated. Linda, it has been a pleasure working with you.

In the publishing industry, editors seem to come and go with alarming frequency. Yet one senior editor at Lippincott Williams & Wilkins stayed the course and continued to be an unwavering advocate for our project: Emily Lupash. We thank you Emily and the entire staff under your direction for your patience and determination to get this edition published.

We again would like to acknowledge the architects and current trustees of the undergraduate neuroscience curriculum at Brown University. We thank Mitchell Glickstein, Ford Ebner, James McIlwain, Leon Cooper, James Anderson, Leslie Smith, John Donoghue, Bob Patrick, and John Stein for all they did to make undergraduate neuroscience great at Brown. Similarly, we thank Sebastian Seung and Monica Linden for their innovative contributions to introductory neuroscience at the Massachusetts Institute of Technology. Monica, who is now on the faculty

of Brown's Department of Neuroscience, also made numerous suggestions for improvements in the fourth edition of this book for which we are particularly grateful.

We gratefully acknowledge the research support provided to us over the years by the National Institutes of Health, the Whitehall Foundation, the Alfred P. Sloan Foundation, the Klingenstein Foundation, the Charles A. Dana Foundation, the National Science Foundation, the Keck Foundation, the Human Frontiers Science Program, the Office of Naval Research, DARPA, the Simons Foundation, the JPB Foundation, the Picower Institute for Learning and Memory, the Brown Institute for Brain Science, and the Howard Hughes Medical Institute.

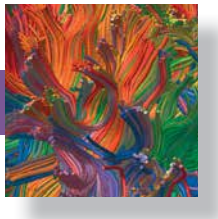
We thank our colleagues in the Brown University Department of Neuroscience and in the Department of Brain and Cognitive Sciences at MIT for their ongoing support of this project and helpful advice. We thank the anonymous but very helpful colleagues at other institutions who gave us comments on the earlier editions. We gratefully acknowledge the scientists who provided us with figures illustrating their research results and, in particular, Satrajit Ghosh and John Gabrieli of MIT for providing the striking image that appears on the cover of the new edition (to learn about the image, see p. xxi). In addition, many students and colleagues helped us to improve the new edition by informing us about recent research, pointing out errors in earlier editions, and suggesting better ways to describe or illustrate concepts. Special thanks to Peter Kind of the University of Edinburgh and Weifeng Xu of MIT.

We are very grateful to our many colleagues who contributed "Path of Discovery" stories. You inspire us.

We thank our loved ones, not only for standing by us as countless weekends and evenings were spent preparing this book, but also for their encouragement and helpful suggestions for improving it.

Finally, we wish to thank the thousands of students we have had the privilege to teach neuroscience over the past 35 years.

PATH OF DISCOVERY AUTHORS



Floyd Bloom, M.D.
Scripps Research Institute
La Jolla, California
Exploring the Central Noradrenergic Neurons

Mario Capecchi, Ph.D.
University of Utah
Howard Hughes Medical Institute
Salt Lake City, Utah
Gene Targeting in Mice

Leon N Cooper, Ph.D.
Brown University
Providence, Rhode Island
Memories of Memory

Timothy C. Cope, Ph.D.
Wright State University
Dayton, Ohio
Nerve Regeneration Does Not Ensure Full Recovery

Antonio Damasio, Ph.D.
University of Southern California
Los Angeles, California
Concepts and Names in Everyday Science

Nina Dronkers, Ph.D.
University of California
Davis, California
Uncovering Language Areas of the Brain

Geoffrey Gold, Ph.D.
Monell Chemical Senses Center
Philadelphia, Pennsylvania
Channels of Vision and Smell

Kristen M. Harris, Ph.D.
University of Texas
Austin, Texas
For the Love of Dendritic Spines

Thomas Insel, M.D., Director
United States National Institute of Mental Health
Rockville, Maryland
Bonding with Voles

Stephanie R. Jones, Ph.D.
Brown University
Providence, Rhode Island
The Puzzle of Brain Rhythms

Eric Kandel, M.D.
Columbia University
Howard Hughes Medical Institute
New York, New York
What Attracted Me to the Study of Learning and Memory in Aplysia?

Nancy Kanwisher, Ph.D.
Massachusetts Institute of Technology
Cambridge, Massachusetts
Finding Faces in the Brain

Julie Kauer, Ph.D.
Brown University
Providence, Rhode Island
Learning to Crave

Christof Koch, Ph.D.
Allen Institute for Brain Science
Seattle, Washington
Tracking the Neuronal Footprints of Consciousness

Helen Mayberg, M.D.
Emory University School of Medicine
Atlanta, Georgia
Tuning Depression Circuits

James T. McIlwain, M.D.
Brown University
Providence, Rhode Island
Distributed Coding in the Superior Colliculus

Chris Miller, Ph.D.
Brandeis University
Howard Hughes Medical Institute
Waltham, Massachusetts
Feeling Around Inside Ion Channels in the Dark

Edvard Moser, Ph.D., and May-Britt Moser, Ph.D.
Kavli Institute for Neural Systems
University of Science and Technology
Trondheim, Norway
How the Brain Makes Maps

Georg Nagel, Ph.D.
University of Würzburg
Würzburg, Germany
The Discovery of the Channelrhodopsins

Donata Oertel, Ph.D.
University of Wisconsin School of Medicine and Public Health
Madison, Wisconsin
Capturing the Beat

Pasko Rakic, M.D., Ph.D.
Yale University School of Medicine
New Haven, Connecticut
Making a Map of the Mind

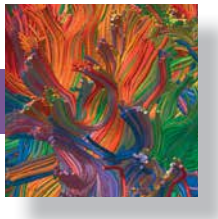
Sebastian Seung, Ph.D.
Princeton University
Princeton, New Jersey
Connecting with the Connectome

Solomon H. Snyder, M.D.
The Johns Hopkins University School of Medicine
Baltimore, Maryland
Finding Opiate Receptors

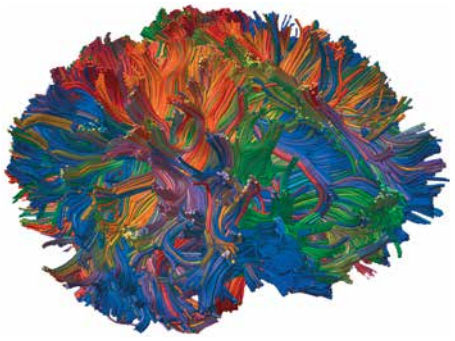
David Williams, Ph.D.
University of Rochester
Rochester, New York
Seeing Through the Photoreceptor Mosaic

Thomas Woolsey, M.D.
Washington University School of Medicine
St. Louis, Missouri
Cortical Barrels

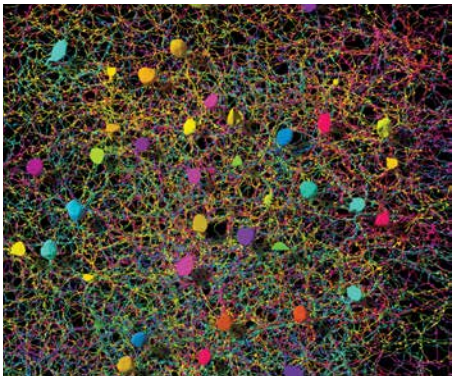
IMAGES



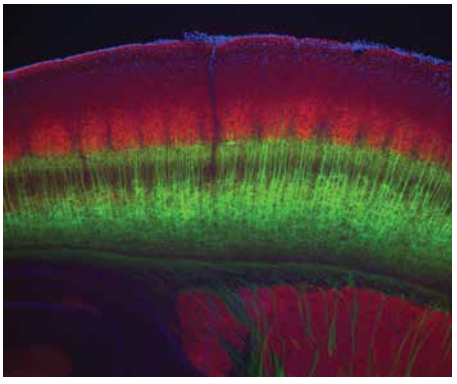
Cover: An image of a living human brain acquired by magnetic resonance tomography to reveal the diffusion of water molecules. Water diffusion in the brain occurs preferentially along bundles of axons. Axons are the "wires" of the nervous system and conduct electrical impulses generated by brain cells. Thus, this image reveals some of the paths of long-range communication between different parts of the brain. The image, acquired at the Athinoula A. Martinos Center for Biomedical Imaging at the Massachusetts Institute of Technology, was processed by a computer algorithm to display bundles of axons traveling together as pseudo-colored noodles. The colors vary depending on the direction of water diffusion. (Source: Courtesy of Satrajit Ghosh and John Gabrieli, McGovern Institute for Brain Research and Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology.)

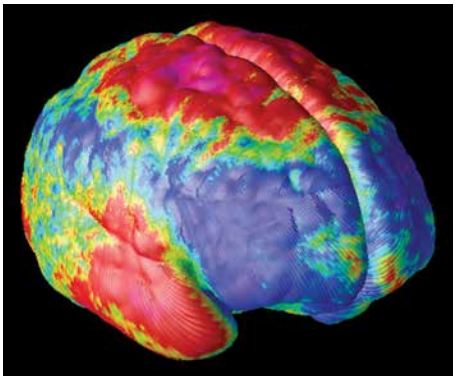


Part One Chapter Opener: Neurons and their neurites. Serial images were taken using an electron microscope of a small piece of the retina as thin slices were shaved off. Then, a computer algorithm, aided by thousands of people worldwide playing an online game called EyeWire, reconstructed each neuron and their synaptic connections—the "connectome" of this volume of tissue. In this image, the neurons are pseudo-colored by the computer, and their neurites, the axons and dendrites from each cell, are displayed in their entirety. (Source: Courtesy of Sebastian Seung, Princeton University, and Kris Krug, Pop Tech.)

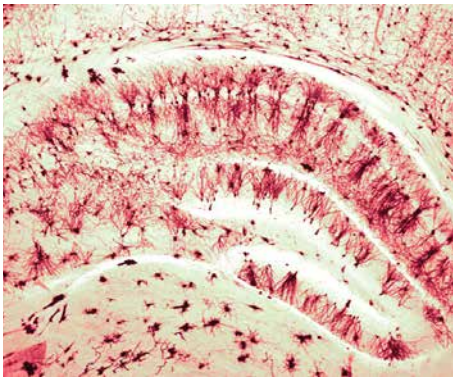


Part Two Chapter Opener: The mouse cerebral cortex. The cerebral cortex lies just under the skull. It is critical for conscious sensory perception and voluntary control of movement. The major subcortical input to the cortex arises from the thalamus, a structure that lies deep inside the brain. Stained red are thalamic axons that bring to the cortex information about the whiskers on the animal's snout. These are clustered into "barrels" that each represent a single whisker. The neurons that project axons back to the thalamus have been genetically engineered to fluoresce green. Blue indicates the nuclei of other cells stained with a DNA marker. (Source: Courtesy of Shane Crandall, Saundra Patrick, and Barry Connors, Department of Neuroscience, Brown University.)



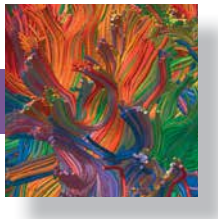


Part Three Chapter Opener: Gray matter loss in the cerebral cortex of adolescents with schizophrenia. Schizophrenia is a severe mental illness characterized by a loss of contact with reality and a disruption of thought, perception, mood, and movement. The disorder typically becomes apparent during adolescence or early adulthood and persists for life. Symptoms may arise in part from shrinkage of specific parts of the brain, including the cerebral cortex. High-resolution magnetic resonance imaging of the brains of adolescents with schizophrenia has been used to track the location and progression of tissue loss. In this image, the regions of gray matter loss are color coded. Severe tissue loss, up to 5% annually, is indicated in red and pink. Regions colored blue are relatively stable over time. (Source: Courtesy of Arthur Toga and Paul Thompson, Keck School of Medicine, University of Southern California.)

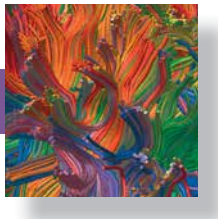


Part Four Chapter Opener: Neurons of the hippocampus. The hippocampus is a brain structure that is critical for our ability to form memories. One way that information is stored in the brain is by modification of synapses, the specialized junctions between the axons of one neuron and the dendrites of another. Synaptic plasticity in the hippocampus has been studied to reveal the molecular basis of memory formation. This image shows the neurites of a subset of hippocampal neurons using a time honored method introduced in 1873 by Italian scientist Emilio Golgi. (Source: Courtesy of Miquel Bosch and Mark Bear, The Picower Institute for Learning and Memory and Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology.)

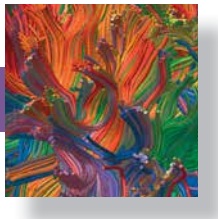
CONTENTS IN BRIEF



EXPANDED CONTENTS



LIST OF BOXES

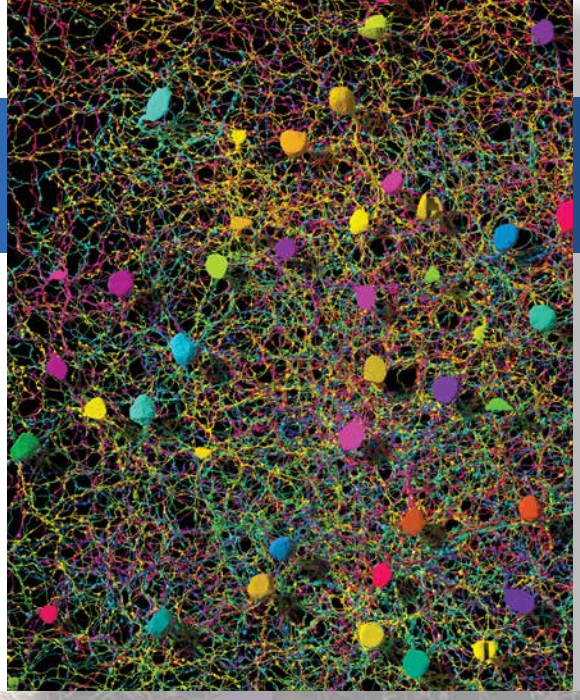


BRAIN FOOD

OF SPECIAL INTEREST

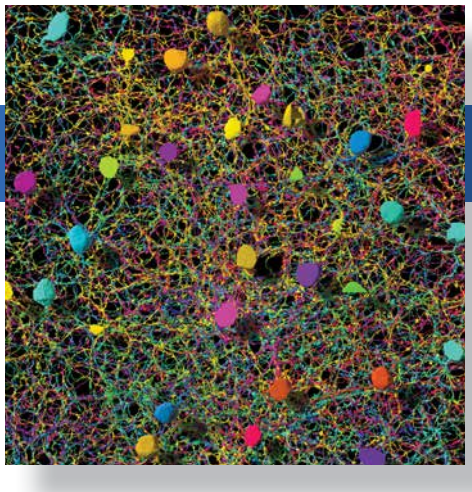
PATH OF DISCOVERY

PART ONE

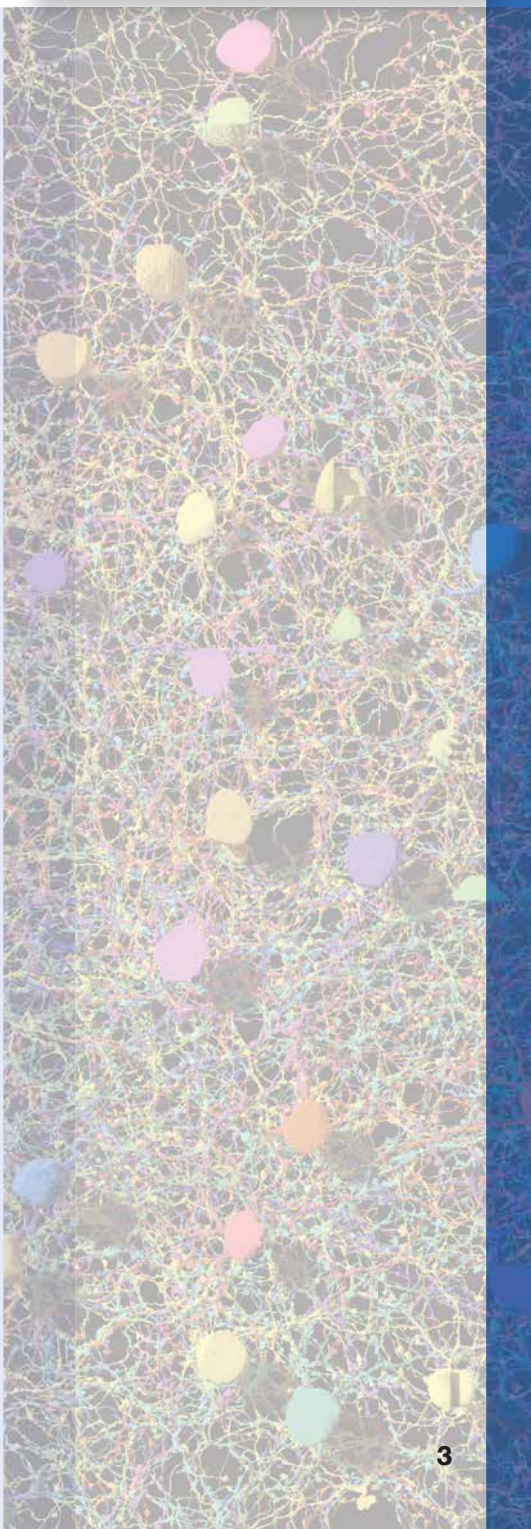


Foundations

CHAPTER ONE



Neuroscience: Past, Present, and Future



INTRODUCTION

Men ought to know that from nothing else but the brain come joys, delights, laughter and sports, and sorrows, griefs, despondency, and lamentations. And by this, in an especial manner, we acquire wisdom and knowledge, and see and hear and know what are foul and what are fair, what are bad and what are good, what are sweet and what are unsavory. . . . And by the same organ we become mad and delirious, and fears and terrors assail us. . . . All these things we endure from the brain when it is not healthy. . . . In these ways I am of the opinion that the brain exercises the greatest power in the man.

—Hippocrates, *On the Sacred Disease* (Fourth century B.C.E.)

It is human nature to be curious about how we see and hear; why some things feel good and others hurt; how we move; how we reason, learn, remember, and forget; and the nature of anger and madness. Neuroscience research is unraveling these mysteries, and the conclusions of this research are the subject of this textbook.

The word "neuroscience" is young. The Society for Neuroscience, an association of professional neuroscientists, was founded only relatively recently in 1970. The study of the brain, however, is as old as science itself. Historically, the scientists who devoted themselves to an understanding of the nervous system came from different scientific disciplines: medicine, biology, psychology, physics, chemistry, mathematics. The neuroscience revolution occurred when scientists realized that the best hope for understanding the workings of the brain would come from an interdisciplinary approach, a combination of traditional approaches to yield a new synthesis, a new perspective. Most people involved in the scientific investigation of the nervous system today regard themselves as neuroscientists. Indeed, while the course you are now taking may be sponsored by the psychology or biology department at your university or college and may be called biopsychology or neurobiology, you can bet that your instructor is a neuroscientist.

The Society for Neuroscience is one of the largest and fastest growing associations of professional scientists. Far from being overly specialized, the field is as broad as nearly all of natural science, with the nervous system serving as the common point of focus. Understanding how the brain works requires knowledge about many things, from the structure of the water molecule to the electrical and chemical properties of the brain to why Pavlov's dog salivated when a bell rang. This book explores the brain with this broad perspective.

We begin the adventure with a brief tour of neuroscience. What have scientists thought about the brain over the ages? Who are the neuroscientists of today, and how do they approach studying the brain?

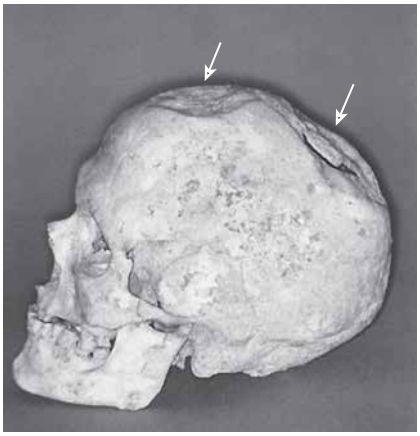
THE ORIGINS OF NEUROSCIENCE

You probably already know that the nervous system—the brain, spinal cord, and nerves of the body—is crucial for life and enables you to sense, move, and think. How did this view arise?

Evidence suggests that even our prehistoric ancestors appreciated that the brain was vital to life. The archeological record includes many hominid skulls, dating back a million years and more, that bear signs of fatal cranial damage likely inflicted by other hominids. As early as 7000 years ago, people were boring holes in each other's skulls (a process called

trepanation), evidently with the aim not to kill but to cure (Figure 1.1). These skulls show signs of healing after the operation, indicating that this procedure had been carried out on live subjects rather than being a ritual conducted after death. Some individuals apparently survived multiple skull surgeries. What those early surgeons hoped to accomplish is not clear, although it has been speculated that this procedure may have been used to treat headaches or mental disorders, perhaps by giving the evil spirits an escape route.

Recovered writings from the physicians of ancient Egypt, dating back almost 5000 years, indicate that they were well aware of many symptoms of brain damage. However, it is also very clear that the heart, not the brain, was considered to be the seat of the soul and the repository of memories. Indeed, while the rest of the body was carefully preserved for the afterlife, the brain of the deceased was simply scooped out through the nostrils and discarded! The view that the heart was the seat of consciousness and thought was not seriously challenged until the time of Hippocrates.



▲ FIGURE 1.1
Evidence of prehistoric brain surgery. This skull of a man over 7000 years old was surgically opened while he was still alive. The arrows indicate two sites of trepanation. (Source: Alt et al., 1997, Fig. 1a.)

Views of the Brain in Ancient Greece

Consider the idea that the different parts of your body look different because they serve different purposes. The structures of the feet and hands are very different, for example, because they perform very different functions: We walk on our feet and manipulate objects with our hands. Thus, there appears to be a very clear *correlation between structure and function*. Differences in appearance predict differences in function.

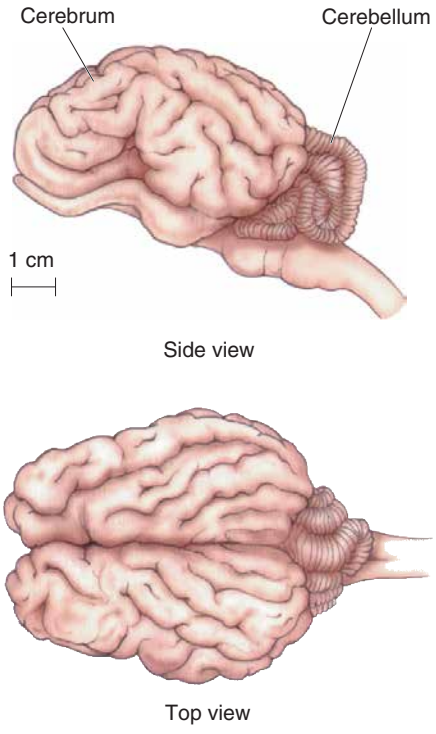
What can we glean about function from the structure of the head? Quick inspection and a few simple experiments (like closing your eyes) reveal that the head is specialized for sensing the environment with the eyes and ears, nose, and tongue. Even crude dissection can trace the nerves from these organs through the skull into the brain. What would you conclude about the brain from these observations?

If your answer is that the brain is the organ of sensation, then you have reached the same conclusion as several Greek scholars of the fourth century B.C.E. The most influential scholar was Hippocrates (460–379 B.C.E.), the father of Western medicine, who believed that the brain was not only involved in sensation but was also the seat of intelligence.

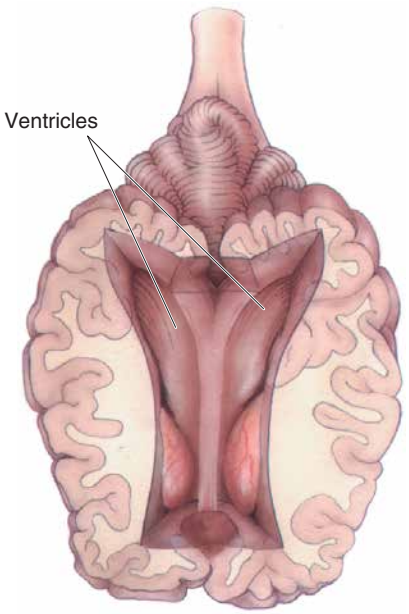
This view was not universally accepted, however. The famous Greek philosopher Aristotle (384–322 B.C.E.) clung to the belief that the heart was the center of intellect. What function did Aristotle reserve for the brain? He believed it was a radiator for cooling blood that was overheated by the seething heart. The rational temperament of humans was thus explained by the large cooling capacity of our brain.

Views of the Brain During the Roman Empire

The most important figure in Roman medicine was the Greek physician and writer Galen (130–200 C.E.), who embraced the Hippocratic view of brain function. As physician to the gladiators, he must have witnessed the unfortunate consequences of spine and brain injuries. However, Galen's opinions about the brain were probably influenced more by his many careful animal dissections. Figure 1.2 is a drawing of the brain of a sheep, one of Galen's favorite subjects. Two major parts are evident: the *cerebrum* in the front and the *cerebellum* in the back. (The structure of the brain is described in Chapter 7.) Just as we can deduce function



▲ FIGURE 1.2
The brain of a sheep. Notice the location and appearance of the cerebrum and the cerebellum.



▲ FIGURE 1.3
A dissected sheep brain showing the ventricles.

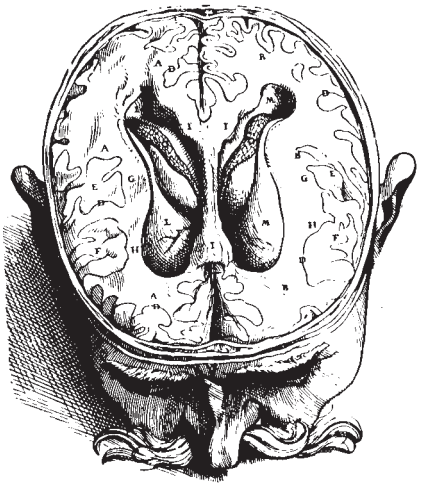
from the structure of the hands and feet, Galen tried to deduce function from the structure of the cerebrum and the cerebellum. Poking the freshly dissected brain with a finger reveals the cerebellum is rather hard and the cerebrum rather soft. From this observation, Galen suggested that the cerebrum must receive sensations while the cerebellum must command the muscles. Why such a distinction? He recognized that to form memories, sensations must be imprinted in the brain. Naturally, this must occur in the doughy cerebrum.

As improbable as his reasoning may seem, Galen's deductions were not that far from the truth. The cerebrum, in fact, is largely concerned with sensation and perception, and the cerebellum is primarily a movement control center. Moreover, the cerebrum is a repository of memory. We will see that this is not the only example in the history of neuroscience in which the right general conclusions were reached for the wrong reasons.

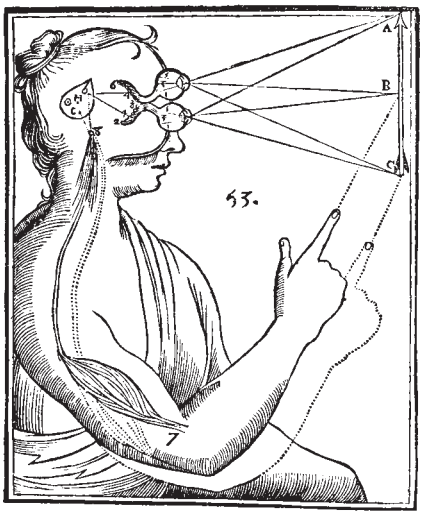
How does the brain receive sensations and move the limbs? Galen cut open the brain and found that it is hollow (Figure 1.3). In these hollow spaces, called *ventricles* (like the similar chambers in the heart), there is fluid. To Galen, this discovery fit perfectly with the prevailing theory that the body functioned according to a balance of four vital fluids, or humors. Sensations were registered and movements initiated by the movement of humors to or from the brain ventricles via the nerves, which were believed to be hollow tubes, like the blood vessels.

Views of the Brain from the Renaissance to the Nineteenth Century

Galen's view of the brain prevailed for almost 1500 years. During the Renaissance, the great anatomist Andreas Vesalius (1514–1564) added more detail to the structure of the brain (Figure 1.4). However, the ventricular theory of brain function remained essentially unchallenged. Indeed, the whole concept was strengthened in the early seventeenth century, when French inventors built hydraulically controlled mechanical devices. These devices supported the notion that the brain could be machinelike in its function: Fluid forced out of the ventricles through the nerves might literally "pump you up" and cause the movement of the limbs. After all, don't the muscles bulge when they contract?



▶ FIGURE 1.4
Human brain ventricles depicted during the Renaissance. This drawing is from *De humani corporis fabrica* by Vesalius (1543). The subject was probably a decapitated criminal. Great care was taken to be anatomically correct in depicting the ventricles. (Source: Finger, 1994, Fig. 2.8.)

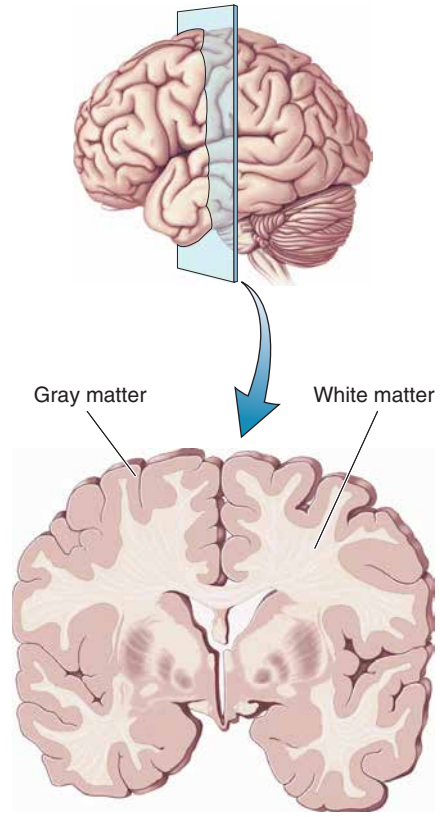


◀ FIGURE 1.5
The brain according to Descartes.
This drawing appeared in a 1662 publication by Descartes, who thought that hollow nerves from the eyes projected to the brain ventricles. The mind influenced the motor response by controlling the pineal gland (H), which worked like a valve to control the movement of animal spirits through the nerves that inflated the muscles. (Source: Finger, 1994, Fig. 2.16.)

A chief advocate of this fluid–mechanical theory of brain function was the French mathematician and philosopher René Descartes (1596–1650). Although he thought this theory could explain the brain and behavior of other animals, Descartes believed it could not possibly account for the full range of *human* behavior. He reasoned that unlike other animals, people possess intellect and a God-given soul. Thus, Descartes proposed that brain mechanisms control only human behavior that is like that of the beasts. Uniquely human mental capabilities exist outside the brain in the "mind." Descartes believed that the mind is a spiritual entity that receives sensations and commands movements by communicating with the machinery of the brain via the pineal gland (Figure 1.5). Today, some people still believe that there is a "mind–brain problem," that somehow the human mind is distinct from the brain. However, as we shall see in Part III, modern neuroscience research supports a different conclusion: The mind has a physical basis, which is the brain.

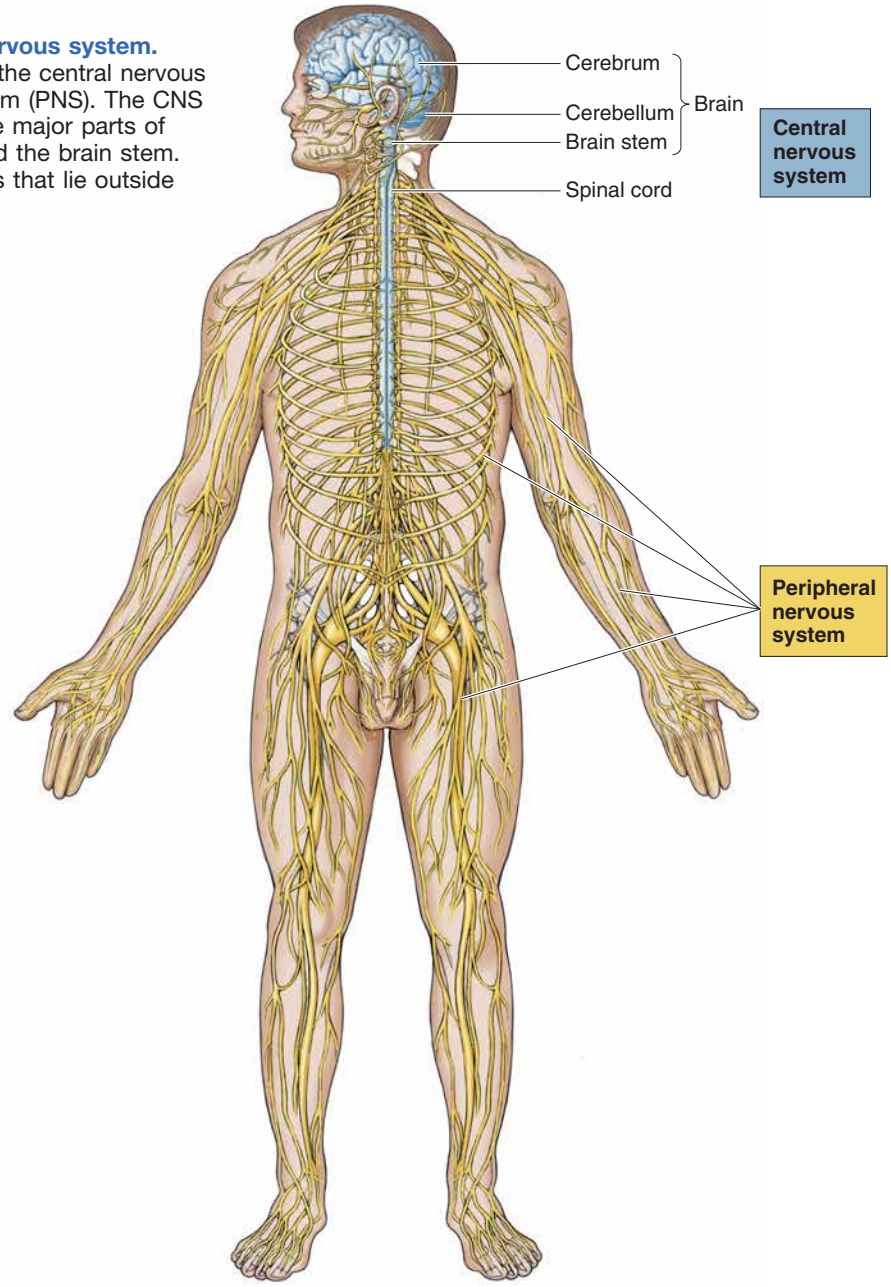
Fortunately, other scientists during the seventeenth and eighteenth centuries broke away from the traditional focus on the ventricles and began examining the brain's substance more closely. They observed, for example, two types of brain tissue: the *gray matter* and the *white matter* (Figure 1.6). What structure–function relationship did they propose? White matter, because it was continuous with the nerves of the body, was correctly believed to contain the fibers that bring information to and from the gray matter.

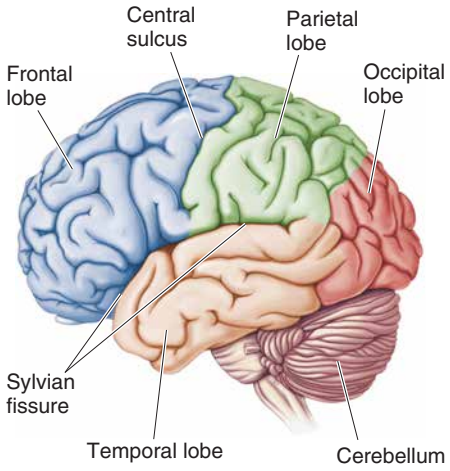
By the end of the eighteenth century, the nervous system had been completely dissected and its gross anatomy described in detail. Scientists recognized that the nervous system has a central division, consisting of the brain and spinal cord, and a peripheral division, consisting of the network of nerves that course through the body (Figure 1.7). An important breakthrough in neuroanatomy came with the observation that the same general pattern of bumps (called *gyri*) and grooves (called *sulci* and *fissures*) can be identified on the surface of the brain in every individual (Figure 1.8). This pattern, which enables the parceling of the cerebrum into *lobes*, led to speculation that different functions might be localized to the different bumps on the brain. The stage was now set for the era of cerebral localization.



▲ FIGURE 1.6
White matter and gray matter.
The human brain has been cut open to reveal these two types of tissue.

▶ FIGURE 1.7
The basic anatomical subdivisions of the nervous system. The nervous system consists of two divisions, the central nervous system (CNS) and the peripheral nervous system (PNS). The CNS consists of the brain and spinal cord. The three major parts of the brain are the cerebrum, the cerebellum, and the brain stem. The PNS consists of the nerves and nerve cells that lie outside the brain and spinal cord.





▲ FIGURE 1.8
The lobes of the cerebrum. Notice the deep Sylvian fissure, dividing the frontal lobe from the temporal lobe, and the central sulcus, dividing the frontal lobe from the parietal lobe. The occipital lobe lies at the back of the brain. These landmarks can be found on all human brains.

Nineteenth-Century Views of the Brain

Let's review how the nervous system was understood at the end of the eighteenth century:

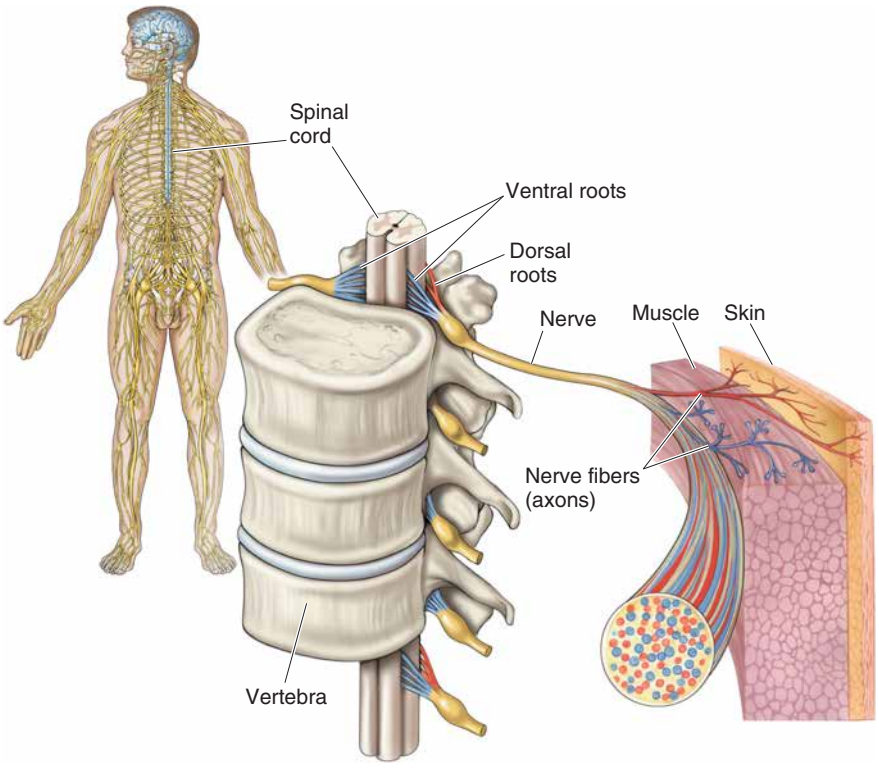
- Injury to the brain can disrupt sensations, movement, and thought and can cause death.
- The brain communicates with the body via the nerves.
- The brain has different identifiable parts, which probably perform different functions.
- The brain operates like a machine and follows the laws of nature.

During the next 100 years, more would be learned about the function of the brain than had been learned in all of previous recorded history. This work provided the solid foundation on which modern neuroscience rests. Now we'll look at four key insights gained during the nineteenth century.

Nerves as Wires. In 1751, Benjamin Franklin published a pamphlet titled *Experiments and Observations on Electricity*, which heralded a new understanding of electrical phenomena. By the turn of the century, Italian scientist Luigi Galvani and German biologist Emil du Bois-Reymond had shown that muscles can be caused to twitch when nerves are stimulated electrically and that the brain itself can generate electricity. These discoveries finally displaced the notion that nerves communicate with the brain by the movement of fluid. The new concept was that the nerves are "wires" that conduct electrical signals to and from the brain.

Unresolved was whether the signals to the muscles causing movement use the same wires as those that register sensations from the skin. Bidirectional communication along the same wires was suggested by the observation that when a nerve in the body is cut, there is usually a loss of both sensation and movement in the affected region. However, it was also known that within each nerve of the body there are many thin filaments, or *nerve fibers*, each one of which could serve as an individual wire carrying information in a different direction.

This question was answered around 1810 by Scottish physician Charles Bell and French physiologist François Magendie. A curious anatomical fact is that just before the nerves attach to the spinal cord, the fibers divide into two branches, or roots. The dorsal root enters toward the back of the spinal cord, and the ventral root enters toward the front (Figure 1.9). Bell tested the possibility that these two spinal roots carry information in different directions by cutting each root separately and observing the consequences in experimental animals. He found that cutting only the ventral roots caused muscle paralysis. Later, Magendie was able to show that the dorsal roots carry sensory information into the spinal cord. Bell and Magendie concluded that within each nerve is a mixture of many wires, some of which bring information into the brain and spinal cord and others that send information out to the muscles. In each



◀ FIGURE 1.9
Spinal nerves and spinal nerve roots. Thirty-one pairs of nerves leave the spinal cord to supply the skin and the muscles. Cutting a spinal nerve leads to a loss of sensation and a loss of movement in the affected region of the body. Incoming sensory fibers (*red*) and outgoing motor fibers (*blue*) divide into spinal roots where the nerves attach to the spinal cord. Bell and Magendie found that the ventral roots contain only motor fibers and the dorsal roots contain only sensory fibers.