Brain & Behavior

An Introduction to Behavioral Neuroscience

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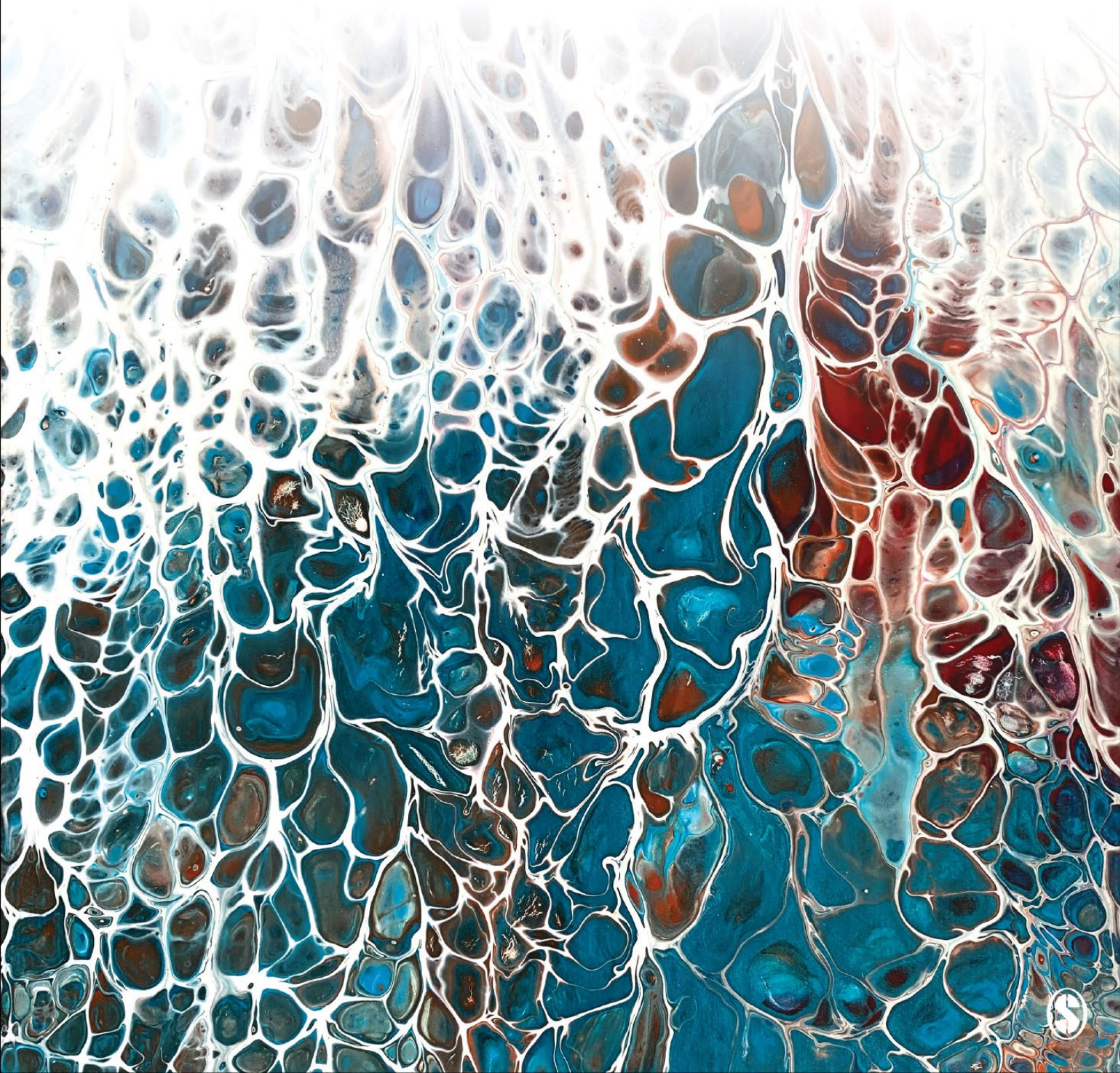
BOB GARRETT / GERALD HOUGH



Brain & Behavior

Sixth Edition

To my late wife, Duejean,
sons Geoffrey and Michael, and
grandchildren Evan, Naomi, and Talia.
—Bob Garrett

To my wife, Kerry,
thank you for being my partner in crime over the last three decades,
and for giving me the time to complete this edition.
—Gerald Hough

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An Introduction to Behavioral Neuroscience

Sixth Edition

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Preface

A Message From the Authors

> *Anyone who stops learning is old, whether at twenty or eighty. Anyone who keeps learning stays young. The greatest thing in life is to keep your mind young.*
>
> —Henry Ford

Flip through this book and you'll see that its pages are chock-full of facts and applications—just a sampling gleaned from a vast supply that grows too fast for any of us to keep up with and that becomes obsolete just as fast. But sifting through those facts and reporting them is neither the most difficult nor the most important function of a good textbook. A greater challenge is that most students fail to share their instructors' infatuation with learning; perhaps they lack the genes, or the parental role models, or just the idea that learning can be fun. At any rate, they can find a text like this intimidating, and it is the textbook's role to change their minds.

The colorful illustrations, case studies, and research vignettes may capture students' interest, but sparking interest alone is not enough. That's why we've adopted a big-picture approach in writing the text, one that marshals facts into explanations and discards the ones left standing around with nothing to do. When you put facts to work that way, you begin to see students look up and say, "That makes sense," or "I've always wondered about that, but I never thought of it that way," or "Now I understand what was going on with Uncle Edgar."

We believe education has the capacity to make a person healthy, happy, and productive, and it makes a society strong. Education realizes that promise when it leads people to inquire and to question—when they *learn how to learn*. When 45% of the public believes in ghosts, and politics has become a game played by shouting the loudest or telling the most convincing lie, education more than ever needs to teach young people to ask, "Where is the evidence?" and "Is that the only reasonable interpretation?"

To those who would teach and those who would learn, this book is for you.

To the Student

Brain & Behavior is our attempt to reach out to students, to beckon them into the fascinating world of behavioral neuroscience. These are exceptionally exciting times, comparable in many ways to the renaissance that thrust Europe from the Middle Ages into the modern world. According to the American neurologist Stanley B. Prusiner (n.d.),

> neuroscience is by far the most exciting branch of science because the brain is the most fascinating object in the universe. Every human brain is different—the brain makes each human unique and defines who he or she is.

We know of no scientific discipline with greater potential to answer the burning questions about ourselves than behavioral neuroscience. We hope this textbook will convey that kind of excitement as you read about discoveries that will revolutionize our understanding of what it means to be human, and how we got to where we are.

We want you to succeed in this course, but, more than that, we want you to learn more than you ever imagined you could and to go away with a new appreciation for the promise of behavioral neuroscience. So we have a few tips we want to pass along. First, try to sit near the front of the class, because those students usually get the best grades. That is probably because they stay more engaged and are encouraged to ask more questions, but to ask good questions, you should always read the text before you go to class. And so that you'll know where you're going before you begin to read, take a look at "After reading this chapter, you will be able to," then skim the chapter subheadings and read the summary at the end of the chapter.

Some special tips if you are using this text for an online course: First, make sure you ask questions of your instructor as you go through the material, and attend their virtual office hours! An online course is much more challenging—you are responsible for keeping up with the material on your own without the in-person reminders you'd normally get from a physical class. And when answering questions, make sure you document where you got your information; it is all too easy to simply copy and paste information without properly citing your sources. Finally, get into a study group with your fellow students. Not everybody understands the material with a single read-through, so discussing the content and exercises with your fellow students can help all of you grasp the complex concepts of behavioral neuroscience.

As you read, pay special attention to the text in blue; these are definitions of the most important terms, which are defined again in the glossary at the end of the book. Answer the Concept Check questions at the end of each section and the For Further Thought questions at the end of the chapter, and be sure to check your knowledge with Test Your Understanding. Then don't forget to look up some of the books and articles in For Further Reading; we selected these not only to increase your understanding of a particular topic but to be fun as well! Finally, the Student Resources site, at **edge.sagepub.com/garrett6e**, will provide you with a wealth of additional help. If you do all these things, you won't just do better in this course; you will leave saying, "I really got something out of that class!" And when it's time to take the GRE (or MCAT or VCAT), or talk to your doctor, or interview for a biomedical job, or simply read the Science section of the *New York Times*, you'll be using the knowledge you gained in this text.

We wrote *Brain & Behavior* with you in mind, so we hope you will let us know where we have done things right and, especially, where we have not. We wish you the satisfaction of discovery and knowledge as you read what we have written *for you*.

To the Instructor

A good textbook is all about teaching, but there is no teaching if there is no learning. Over the years, our students have taught us a great deal about what they need to help them learn. For one thing, we have realized how important it is for students to build on their knowledge throughout the course, so we have made several changes from the organization of other texts. First, the chapter on neuronal physiology precedes the chapter on the nervous system, because we believe that you can't begin to understand the brain until you know how its neurons work. And we reverse the usual order of the vision and audition chapters, because audition provides a friendlier context for introducing the basic principles of sensation and perception. The chapters on addiction, motivation, emotion, and sex follow the introduction to neurophysiology; this was done to build student motivation before tackling sensation and perception. Perhaps more significantly, some topics have been moved around among chapters so that they can be developed in a more behaviorally meaningful context. So we discuss language along with audition, the body senses with the mechanisms of movement, the sense of taste in the context of feeding behavior, and olfaction in conjunction with sexual behavior. Most unique, though, is the inclusion of a chapter on the biology of intelligence and another on consciousness. The latter is a full treatment of recent developments in the

field, rather than being limited to the usual topics of sleep and split-brain behavior. These two chapters strongly reinforce the theme that behavioral neuroscience is personally relevant and capable of addressing important questions.

Brain & Behavior has several features that will motivate students to learn and encourage them to take an active role in their learning. It engages the student with interest-grabbing opening vignettes, illustrative case studies, A Further Look features that take an intriguing step beyond the chapter content, and a Concept Check at the end of each section that serves as a reminder of the important ideas. At the end of each chapter, In Perspective emphasizes the importance and implications of what the student has just read, a summary helps organize that information, and Test Your Understanding questions assess the student's comprehension. For Further Reading suggestions guide the student in exploring the chapter's topics more fully. We have found over the years that students who use the study aids in a class are also the best performers in the course.

New in the Sixth Edition

When we published the fifth edition 3 years ago, we called it "the most ambitious revision of *Brain & Behavior* since the second"; the sixth rivals both of those. We consulted literally thousands of research articles and selected 516 of them in our effort to make sure *Brain & Behavior* has the most up-to-date coverage possible. To supplement this new information, we revised or replaced 70 illustrations and added a dozen new or revised animations. We replaced the three boxed features of previous editions with A Further Look and added content ranging from the challenge of regulating gene editing in the age of CRISPR (think CRISPR baby scandal and do-it-yourself kits), to communicative gestures humans share with apes, to a description of how actin motors help neurons inch forward during migration by "walking" microtubules along other microtubules.

As was the case in the fifth edition, genetics and neural connectivity dominate behavioral neuroscience research. As we point out in Chapter 14, fast, inexpensive genome-wide association studies have enabled hypothesis-free "gene snooping" that is turning up numerous gene locations but at the expense of requiring samples of 10,000 subjects to provide statistical protection against spurious "hits." Although hypoconnectivity has long been accepted as characteristic of many disorders, we are also finding hyperconnectivity in the same individuals, which is usually associated with more severe symptoms. However, in children with autism who had interhemispheric underconnectivity between the auditory areas, those with increased connections between the auditory cortex and the thalamus had fewer deficits in language, communication, and social behaviors.

Communication with the student has been foremost in the 18-year history of *Brain & Behavior*, and to that end, we have done extensive rewriting in this edition. Examples include the discussion of osmotic and hypovolemic thirst in Chapter 6 and the section on risk taking and decision making in Chapter 8. In addition, we added a new section in Chapter 5, The Hypothalamic Circuitry of Hunger, to better organize that information. As a part of improving communication, we have also tried to be especially mindful of language that might be offensive to our readers as we discuss gender-related issues and describe individuals with psychological disorders. We have always given special attention to applications of neuroscientific knowledge, particularly in the form of treatments. Three new experimental treatments, for example, attack addiction by interfering with drug-related memories—by blocking acetylcholine receptors, applying transcranial magnetic stimulation, or blocking reconsolidation with a single dose of ketamine during recall of alcohol-related memories. The prospects of gaining approval for three Alzheimer's drugs were revived after they appeared to fail in Phase 3 trials—when patients chose to continue the drug after one study was scrubbed and in two others when improvement was noted only in the control subjects, who were given minute "placebo" dosages.

With more than 500 added references, you can expect to see a number of new research findings and fresh ideas. A few highlights:

- There is new evidence that fathers who smoke pass gene mutations to their offspring, along with an increased risk of birth defects and childhood cancers and reduced fertility in the male offspring.
- Although the majority of epigenetic changes in obese individuals appear to be the result of obesity, brain characteristics such as cortical thinning are likely a hereditary component of obesity rather than a consequence of it.
- We've pointed out before that the Wernicke-Geschwind model is too simple; now we've added a new section, Beyond the Wernicke-Geschwind Model, that describes current knowledge.
- A breakthrough in stem cell therapy has enabled blind individuals to read at 60 to 80 words per minute.
- The idea presented in the fifth edition that infection rate accounts for national differences in intelligence is bolstered by two findings: IQ is negatively related to the number of hospitalizations for infection, and the immune response impairs brain plasticity and learning ability.
- A recently discovered "glymphatic system" transports cerebrospinal fluid among the brain cells during sleep to flush out toxins and debris, such as β-amyloid.

Acknowledgments

Revising a textbook like *Brain & Behavior* is incredibly hard work, and the sixth edition would not be possible without the help of many others. Kudos to acquisitions editor Abbie Rickard, content development editor Emma Newsom, and assistant content development editor Sam Rosenberg for their insights, their guidance, and their ability to keep us on schedule (almost). Thanks also to Laureen Gleason for her remarkable copyediting and gentleness in pointing out our many errors, to Ashley Brown for her enthusiasm and great care in managing the animations, and to Elizabeth Cruz for doggedly pursuing permissions for the material in our figures.

Bob has had a number of mentors along the way, to whom he is forever grateful. A few of those special people are Wayne Kilgore, who taught the joys of science along with high school chemistry and physics; Garvin McCain, who introduced him to the satisfactions of research; Roger Kirk, who taught him that anything worth doing is worth doing over and over until it's right; and Ellen Roye and Ouilda Piner, who shared their love of language. These dedicated teachers showed him that learning was his responsibility, and they shaped his life with their unique gifts and quiet enthusiasm. But of all of Bob's supporters, the most important was his late wife, Duejean; love and thanks to her for fond memories and for her patient understanding and her appreciation of how important this project has been to him.

For Gerald, becoming a coauthor on this textbook, which he has used in his classes over the past decade, is an amazing privilege. He hopes that the instructors and students who use this book find that the overall presentation and helpfulness in assisting in the learning process are unchanged from the previous editions. His background in behavioral neuroethology (a mouthful, for sure!) provides a background in understanding the neural bases of behavior. He would like to thank his academic mentors, who have helped him find his way in a complex scientific world: Erich Klinghammer at Wolf Park in Battle Ground, Indiana, sowed the seeds for a love of wolves and understanding behavior in naturalistic settings; Susan Volman at NIDA (formerly The Ohio State University) introduced him to the complexities of behavioral neuroscience through their investigation of how birds learn (and forget) songs at the neural

level; and Verner Bingman gave him the opportunity to develop as a scholar and mentor to his students at Bowling Green State University in Ohio. Finally, he would like to thank his colleagues at Rowan University, who provided valuable feedback and discussions on material in their areas of expertise: D. J. Angelone, Thomas Dinzeo, and Alison Krufka. He would also like to thank his family for letting him work on this important textbook: his wife of almost 30 years, Kerry; his teenage sons, Alexander and Benjamin; and his mother, Carole, who is finally living close to home.

In addition, the following reviewers gave generously of their time and expertise throughout the development of this text; they contributed immensely to the quality of *Brain & Behavior*:

First edition: Susan Anderson, University of South Alabama; Patrizia Curran, University of Massachusetts–Dartmouth; Lloyd Dawe, Cameron University; Tami Eggleston, McKendree College; James Hunsicker, Southwestern Oklahoma State University; Eric Laws, Longwood College; Margaret Letterman, Eastern Connecticut State University; Doug Matthews, University of Memphis; Grant McLaren, Edinboro University of Pennsylvania; Rob Mowrer, Angelo State University; Anna Napoli, University of Redlands; Robert Patterson, Washington State University; Joseph Porter, Virginia Commonwealth University; Jeffrey Stern, University of Michigan–Dearborn; Aurora Torres, University of Alabama in Huntsville; Michael Woodruff, East Tennessee State University; and Phil Zeigler, Hunter College.

Second edition: M. Todd Allen, University of Northern Colorado; Patricia A. Bach, Illinois Institute of Technology; Wayne Brake, University of California–Santa Barbara; Steven I. Dworkin, University of North Carolina; Sean Laraway, San Jose State University; Mindy J. Miserendino, Sacred Heart University; Brady Phelps, South Dakota State University; Susan A. Todd, Bridgewater State College; and Elizabeth Walter, University of Oregon.

Third edition: John A. Agnew, University of Colorado Boulder; Michael A. Bock, American International College; Rachel E. Bowman, Sacred Heart University; Jessica Cail, Pepperdine University; Mary Jo Carnot, Chadron State College; Cheryl A. Frye, The University at Albany–State University of New York; Rebecca L. M. Fuller, Catholic University of America; Cindy Gibson, Washington College; Bennet Givens, The Ohio State University; Robert B. Glassman, Lake Forest College; Gerald E. Hough, Rowan University; Joseph Nuñez, Michigan State University; and Kimberly L. Thomas, University of Central Oklahoma.

Fourth edition: John A. Agnew, University of Colorado Boulder; Ben Allen, University of Pittsburgh; Scott L. Decker, University of South Carolina; Carol L. DeVolder, St. Ambrose University; Jeff Dyche, James Madison University; Cindy Gibson, Washington College; Deirdre C. Greer, Columbus State University; William Meil, Indiana University of Pennsylvania; Samar Saade Needham, California State University, Long Beach; M. Foster Olive, Arizona State University; Catherine Powers Ozyurt, Bay Path College; Allen Salo, University of Maine at Presque Isle; Justin P. Smith, University of South Dakota; Gretchen Sprow, University of North Carolina at Chapel Hill; and Sandra Trafalis, San Jose State University.

Fifth edition: Kurt T. Choate, Northeastern State University; Andrea L. O. Hebb, Saint Mary's University; Bryant Horowitz, East Los Angeles College, California State University, Northridge, and The Chicago School of Professional Psychology; Dwight J. Kravitz, The George Washington University; and Lorenz S. Neuwirth, SUNY College at Old Westbury.

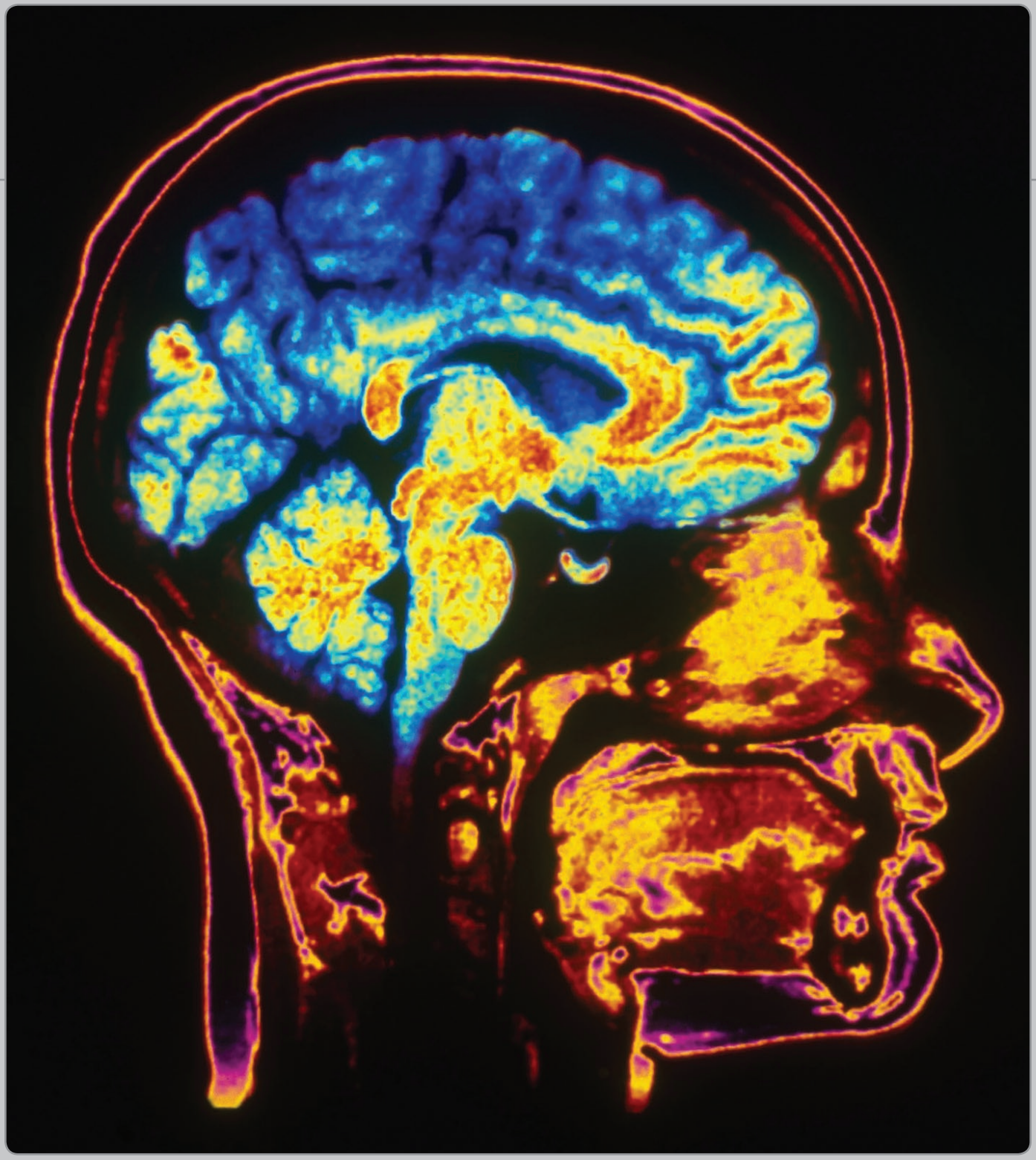
Sixth edition: Elizabeth Becker, St. Joseph's University; William Collins, Nova Southeastern University; Kelly Curtis, High Point University; Sharon Goyette, Bridgewater State University; Maxine Krengel, University of Massachusetts Boston; Linda Lockwood, Metropolitan State University of Denver; Karen Murphy, Duke University; Jim Paulus, Tabor College; and Leora Yetnikoff, College of Staten Island.

—Bob Garrett and Gerald Hough

About the Authors

Bob Garrett is a Visiting Scholar at California Polytechnic State University, San Luis Obispo. He was Professor of Psychology at DePauw University in Greencastle, Indiana, and held several positions there, including Chairperson of the Department of Psychology, Faculty Development Coordinator, and Interim Dean of Academic Affairs. He received his BA from the University of Texas at Arlington and his MA and PhD from Baylor University. He received further training in the Department of Physiology at Baylor University College of Medicine and at the Aeromedical Research Primate Laboratory, Holloman Air Force Base. Bob lives on a 3,200-acre ranch he shares with 48 other families in the hills outside San Luis Obispo. His sons, Geoffrey and Michael, and grandchildren, Evan, Naomi, and Talia, all live nearby.

Gerald (Jerry) Hough is an Associate Professor of Biological Sciences and Psychology at Rowan University in Glassboro, New Jersey. He received his BS from Purdue University and his MS and PhD from The Ohio State University. He also worked in the lab of Verner Bingman at Bowling Green State University. He has taught undergraduate and graduate courses on anatomy, animal behavior, research methods, psychopharmacology, cognitive neuroscience, physiology, and learning. He is an elected member of the American Ornithologists Union from his work on sparrows, pigeons, and Hawai'ian 'amakihi birds. He has served as the Undergraduate Advising Coordinator for Psychology, as the Chair of the IACUC, in curriculum development for the Cooper Medical School at Rowan University, and Negotiator and Vice President 1 of the American Federation of Teachers Local 2373 at Rowan University. His research focus is in the evolutionary and neural bases of spatial and communication behaviors in birds. Gerald; his wife, Kerry; their two sons; and his mother, Carole, live in lovely southern New Jersey.



Scott Camazine/Science Source

1 What Is Behavioral Neuroscience?

After reading this chapter, you will be able to

1.1 Define the mind-brain problem in behavioral neuroscience.

1.2 Describe the contributions of philosophers and scientists to the development of behavioral neuroscience as a field of study.

1.3 Identify the role of physiologists in the establishment of modern-day behavioral neuroscience.

1.4 Compare the relative contributions of genes and environment in the development of behavioral characteristics.

1.5 Critique the fixed nature of heredity in shaping behavior.

That device you carry in your pocket is a wonder of modern technology. It represents a very recent step in the evolution of long-distance communications, which began with smoke signals and drum beats and progressed through the telegraph, the wireless radio, and the landline telephone.

Mobile telephones appeared in vehicles in 1956, but a handheld mobile was not commercially available until 1983; dubbed the "brick," it weighed 1.75 pounds (0.79 kilograms) and cost $3,995 (Figure 1.1). Your 4- or 5-ounce phone operates over a vast cellular network to connect you to your friends and family and an estimated 5 billion people all around the world (there are actually more mobile devices on earth than there are people). Assuming you have a smartphone, you have access to many additional people by way of email, text, and video, as well as more than 1.8 billion websites on the Internet. Your phone also allows you to record memories in the form of notes and images, perform calculations, identify a tune or a flower, find your friends, and determine the best route for your road trip.

The brain has many similarities. An iPhone XR has around 7 trillion transistors (Shankland, 2018). The human brain contains about 80 billion neurons, but each of these in turn connects to thousands of others, forming a network of more than 100 trillion synapses (The Human Memory, 2019) where the brain's work is done. One computational neuroscientist estimates that the brain's storage capability rivals that of the Internet; as a psychologist put it, if the brain were a video recorder, it could store 2,500 GB of video information, which would take you about 300 *years* to watch

FIGURE 1.1 Lead Engineer Martin Cooper With the Motorola DynaTAC 8000X.

When the first handheld cellular phone came out in 1984, it cost $4,000 (about $10,000 today), had a battery that took 10 hours to charge, and only had 30 minutes of talk time.

Ted Soqui/Corbis Historical/Getty Images

(Reber, 2010). But storage of memories and information is only one of the brain's many tasks. The brain is organized into specialized subnetworks that orchestrate your body's 650 muscles and 206 bones, generate thought and make decisions, perform calculations, keep track of where you are and help you navigate around your world, tell you when and what to drink and eat, and provide your language capability and range of sensory capabilities. Like the cell phone, the brain has evolved over time and across species, but in this case, as its capability has grown, so has its size. Still, all its amazing power is packed into just 3 pounds of tissue that consumes the same amount of energy as a 20-watt light bulb!

Mobile phones came into their own in the last decade of the 20th century, in terms of both their capabilities—such as built-in cameras, Bluetooth connectivity, and augmented reality—and their popularity, indicated by more sales worldwide in 1998 than for cars and PCs combined. The period was also seminal for the awakening field of neuroscience, so much so that in the United States, it was designated as the Decade of the Brain. Planned as an effort to increase public awareness of the benefits of brain research, the Decade of the Brain was also a celebration of past achievements and a sober look at the future. At the threshold of a new millennium, we understood that we had an obligation to expand the horizons of human knowledge and advance the treatment of neurological diseases, emotional disorders, and addictions that cost the country a trillion dollars per year in care, lost productivity, and crime (Uhl & Grow, 2004). Since then, in the span of your lifetime, we have developed new treatments for depression, identified key genes responsible for the devastation of schizophrenia, developed agents that block addiction to drugs, found ways to slow the memory impairment of Alzheimer's, produced a map of the human genes, and literally peered into the brain itself to watch it work. These achievements seem remarkable for such a brief span of time, but, in fact, they have their roots in a 300-year scientific past and in 22 centuries of thought and inquiry before that. For that reason, we will spend a brief time examining those links to our past.

The Origins of Behavioral Neuroscience

? What is behavioral neuroscience, and how does it relate to psychology?

The term *neuroscience* identifies the subject matter of the investigation rather than the scientist's training. A neuroscientist may be a biologist, a physiologist, an anatomist, a neurologist, a biochemist, a psychologist, a psychiatrist—or even a computer scientist or a philosopher. Psychologists who work in the area of neuroscience specialize in *behavioral neuroscience*, the branch of psychology that studies the relationships between behavior and the body, particularly the brain. (*Behavioral neuroscience* is the more modern term for *biological psychology*; sometimes the term *biopsychology*, *psychobiology*, or *physiological psychology* is also used.) For psychologists, *behavior* has a very broad meaning, which includes not only overt acts but also internal events such as learning, thinking, and emotion. Behavioral neuroscientists attempt to answer questions such as "What changes in the brain when a person learns?"

"Why does one person develop depression and another, under similar circumstances, becomes anxious, while another seems unaffected?" "What is the physiological explanation for emotions?" "How do we recognize the face of a friend?" "How does the brain's activity result in consciousness?" Behavioral neuroscientists use a variety of research techniques to answer these questions, as you will see in Chapter 4. Whatever their area of study or their strategy for doing research, behavioral neuroscientists try to go beyond the mechanics of how the brain works to focus on the brain's role in behavior.

To really appreciate the impressive accomplishments of today's brain researchers, it is useful, perhaps even necessary, to understand the thinking and the work of their predecessors. Contemporary scientists stand on the shoulders of their intellectual ancestors, who made heroic advances with far less information and technology at their disposal than is available to today's undergraduate student.

Writers have pointed out that psychology has a brief history but a long past. What they mean is that thinkers have struggled with the questions of behavior and experience for more than two millennia, but psychology arose as a separate discipline fairly recently; the date most people accept is 1879, when Wilhelm Wundt (Figure 1.2) established the first psychology laboratory in Leipzig, Germany. But biological psychology would not emerge as a separate science until psychologists offered convincing evidence that the biological approach could answer significant questions about behavior. To do so, they would have to come to terms with an old philosophical question about the nature of the mind. Because the question forms a thread that helps us trace the development of behavioral neuroscience, we will orient our discussion around this issue.

Prescientific Psychology and the Mind-Brain Problem

This issue is usually called "the mind-body problem," but it is phrased differently here to place the emphasis squarely where it belongs—on the brain. The *mind-brain problem* deals with what the mind is and what its relationship is to the brain. There can be no doubt that the brain is essential to our behavior, but does the mind control the brain, or is it the other way around? Alternatively, are the mind and brain the same thing? How these questions are resolved affects how we ask all the other questions of neuroscience.

At the risk of sounding provocative, we argue that there is no such thing as *mind*. It exists only in the sense that, say, weather exists; weather is a concept used to include rain, wind, humidity, and related phenomena. We talk as if there is *a weather* when we say things like "The weather is interfering with my travel plans." But no one really thinks that there is *a weather*. Most, though not all, neuroscientists believe that we should think of the mind in the same way; it is simply the collection of things the brain does, such as thinking, sensing, planning, and feeling. But when we think, sense, plan, and feel, we get the compelling impression that there is *a mind* behind it all, guiding what we do and how we interpret our world. Most neuroscientists say this is just an illusion; the sense of mind is nothing more than an awareness of what the brain is doing. Mind, like weather, is just a concept; it is not a *something*; it does not *do* anything.

This position is known as monism, from the Greek *monos*, meaning "alone" or "single." *Monism* is the idea that the mind and the body consist of the same substance. Idealistic monists believe that everything is nonphysical mind, but most monists take the position that

FIGURE 1.2 Wilhelm Wundt (1832–1920).

Weltrundschau zu Reclams Universum 1902

the body and mind and everything else are physical; this view is called *materialistic monism*. The idea that the mind and the brain are separate is known as *dualism*. For most dualists, the body is material and the mind is nonmaterial. Most dualists also believe that the mind influences behavior by interacting with the brain.

? How do monists and dualists disagree on the mind-brain question?

This question did not originate with modern psychology. Ancient Egyptian texts about life after death support a dualistic perspective before two millennia BCE, and the Greek philosophers were debating it in the fifth century BCE (G. Murphy, 1949), when Democritus proposed that everything in the world was made up of atoms (*atomos*, meaning "indivisible"), his term for the smallest particle possible. Even the soul, which included the mind, was made up of atoms, so it, too, was material. Plato and Aristotle, considered the two greatest intellectuals among the ancient Greeks, continued the argument into the fourth century BCE. Plato was a dualist, whereas his monistic student Aristotle joined the body and soul in his attempt to explain memory, emotions, and reasoning.

Defending either position was not easy. The dualists had to explain how a nonphysical mind could influence a physical body, and monists had the task of explaining how the physical brain could account for mental processes such as perception and conscious experience. But the mind was not observable, and even the vaguest understanding of the nervous system was not achieved until the 1800s, so neither side had much ammunition for the fight.

Descartes and the Physical Model of Behavior

Scientists often resort to the use of models to understand whatever they are studying. A *model* is a proposed mechanism for how something works. Sometimes, a model is in the form of a theory, such as Charles Darwin's explanation that a species developed new capabilities because the capability enhanced the individual's survival and opportunity to reproduce. Other times, a model is a simpler organism, simulation, or system that scientists study in an attempt to understand a more complex one. For example, researchers have used the rat to model everything from learning to Alzheimer's disease in humans, and the computer has often been used to simulate models of cognitive processes. Historically, models tended to follow technological advancements in society, especially in early attempts to understand the nervous system. Though as we discuss in Chapter 2 with respect to human-exclusive processes, models will not duplicate the complexity of the human mind.

? What is a model in science, and how is it useful?

In the 17th century, the French philosopher and physiologist René Descartes (Figure 1.3a) used a hydraulic model to explain the brain's activity (Descartes, 1662/1984). Descartes's choice of a hydraulic model was influenced by his observation of the statues in the royal gardens at St. Germain. When a visitor stepped on certain tiles, the pressure forced water through tubes to the statues and made them move. Using this model, Descartes then reasoned that nerves were also hollow tubes. The fluid they carried was not water but what he called "animal spirits"; these flowed from the brain and inflated the muscles to produce movement. Sensations, memories, and other mental functions were produced as animal spirits flowed through "pores" in the brain. The animal spirits were pumped through the brain by the pineal gland (Figure 1.3b). Descartes's choice of the pineal gland (named because it resembled a pine cone) was based on his conclusion that it was at a perfect location to serve this function. Attached just below the two cerebral hemispheres by its flexible stalk, it appeared capable of bending at different angles to direct the flow of animal spirits into critical areas of the brain. It also was, to Descartes, the only part of the brain that was a single organ and not split into left and right sides (Berhouma, 2013). Thus, for Descartes, the pineal gland became the "seat of the soul," the place where the mind interacted with the body. Although Descartes assigned control to the mind, his unusual emphasis on the physical explanation of behavior foreshadowed the physiological approach that would soon follow.

Descartes lacked an understanding of how the brain and body worked, so he relied on a small amount of anatomical knowledge and a great deal of speculation. His hydraulic model not only represented an important shift in thinking it also illustrates how a model or a theory

FIGURE 1.3 Descartes (1596–1650) and the Hydraulic Model.

Descartes believed that behavior was controlled by animal spirits flowing through the nerves.

iStockphoto.com/traveler1116

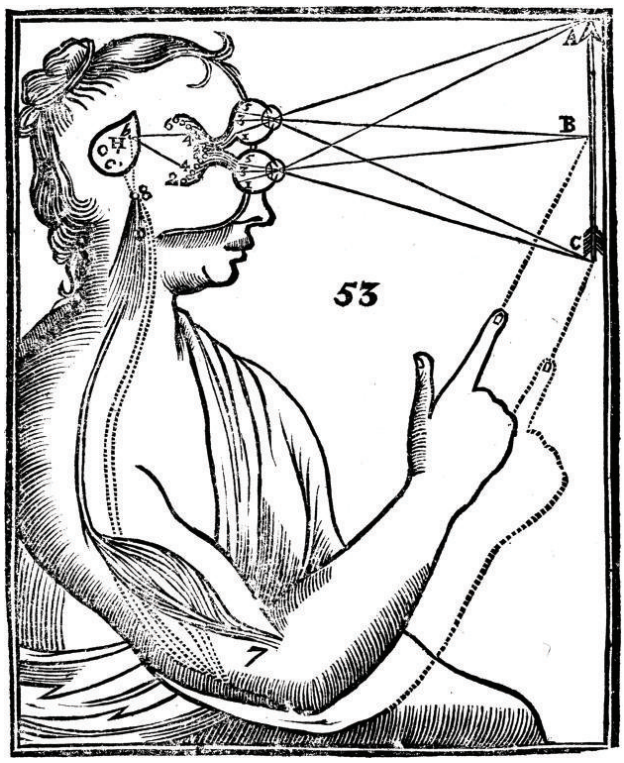


Photo 12/Contributor/Getty Images

can lead us astray, at least temporarily. Fortunately, this was the age of the Renaissance, a time not only of artistic expansion and world exploration but also of scientific curiosity. Thinkers began to test their ideas through direct observation and experimental manipulation as the Renaissance gave birth to science. In other words, they adopted the method of *empiricism*, which means that they gathered their information through observation rather than logic, intuition, or other means. Progress was slow, but two critically important principles would emerge as the early scientists ushered in the future.

Helmholtz and the Electrical Brain

In the late 1700s, the Italian physiologist Luigi Galvani showed that he could make a frog's leg muscle twitch by stimulating the attached nerve with electricity, even after the nerve and muscle had been removed from the frog's body. A century later in Germany, Gustav Fritsch and Eduard Hitzig (1870) produced movement in dogs by electrically stimulating their exposed brains. What these scientists showed was that animal spirits were not responsible for movement; instead, the cause was *nerves operated by electricity*! But the German physicist and physiologist Hermann von Helmholtz (Figure 1.4) demonstrated that nerves do not behave like wires conducting electricity. He was able to measure the speed of conduction in nerves, and his calculation of about 90 feet/second (27.4 meters/second) fell far short of the speed of electricity, which travels through wires at the speed of light (186,000 miles/second or 299,000 kilometers/second). It was obvious that researchers were dealing with a biological phenomenon and that the functioning of nerves and of the brain was open to scientific study. Starting from this understanding, Helmholtz's studies of vision and hearing gave "psychologists their first clear idea of what a fully mechanistic 'mind' might look like" (Fancher, 1979, p. 41). As

? What two discoveries furthered the early understanding of the brain?

FIGURE 1.4 Hermann von Helmholtz (1821–1894).

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FIGURE 1.5 Paul Broca (1824–1880).

Wikimedia Commons.

you will see in later chapters, Helmholtz's ideas were so insightful that even today we refer to his theories of vision and hearing as a starting point before describing the current ones.

The Localization Issue

The second important principle to come out of this period—localization—emerged over the first half of the 19th century. *Localization* is the idea that specific areas of the brain carry out specific functions. Fritsch and Hitzig's studies with dogs gave objective confirmation to physicians' more casual observations dating as far back as 17th-century BCE Egypt (Breasted, 1930), but it was two medical case studies that really grabbed the attention of the scientific community. In 1848, a railroad construction foreman named Phineas Gage was injured when a dynamite blast drove an iron tamping rod through his skull and the frontal lobes of his brain (see Chapter 3). Amazingly, he survived with little impairment of his intelligence, memory, speech, or movement. But he became irresponsible and profane and was unable to abide by social conventions (H. Damasio, Grabowski, Frank, Galaburda, & Damasio, 1994). Then, in 1861, the French physician Paul Broca (Figure 1.5) performed an autopsy on the brain of a man who had lost the ability to speak after a stroke. The autopsy showed that damage was limited to an area on the left side of his brain now known as Broca's area (Broca, 1861).

By the mid-1880s, additional observations like these had convinced researchers about localization. But a few brain theorists were already taking the principle of localization too far, and we should be on guard lest we make the same mistake. At the end of the 18th century, when interest in the brain's role in behavior was really heating up, the German anatomist Franz Gall had come up with an extreme and controversial theory of brain localization. According to *phrenology*, each of 35 different "faculties" of emotion and intellect—such as combativeness, inhabitiveness (love of home), calculation, and order—was located in a precise area of the brain (Spurzheim, 1908). Gall and his student Spurzheim determined this by feeling bumps on people's skulls and relating any protuberances to the individual's characteristics (Figure 1.6). Others, such as Karl Lashley (1929), took an equally extreme position at the other end of the spectrum; *equipotentiality* is the idea that the brain functions as an undifferentiated whole. According to this view, the extent of damage, not the location, determines how much function is lost.

Obviously, bumps on the skull have nothing to do with the size of the brain structures beneath, and most of the characteristics Gall and Spurzheim identified have no particular meaning at the physiological level. But we also know that the brain is not equipotential. The truth, as is often the case, lies somewhere between these two extremes.

Today's research tells us that functions are as much *distributed* as they are *localized*; behavior results from the interaction of many widespread areas of the brain. In later chapters, you will see examples of cooperative relationships among brain areas in language, visual perception, emotional behavior, motor control, and learning. In fact, you will learn that neuroscientists these days are less likely to ask where a function is located than to ask how the brain integrates activity from several areas into a single experience or behavior. Nevertheless, the

localizationists strengthened the monist position by showing that language, emotion, motor control, and so on are controlled by *relatively* specific locations in the brain (Figure 1.7). This meant that the mind ceased being *the explanation* and became *the phenomenon to be explained*.

Understand that the nature and the role of the mind are still debated in some quarters. For example, some neuroscientists believe that brain research will be unable to explain how a material brain can generate conscious experience and that this will spell the final doom of materialism. These nonmaterial neuroscientists interpret the brain changes that occur during behavior therapy as evidence of the mind changing the brain (J. M. Schwartz, Stoessel, Baxter, Martin, & Phelps, 1996; see Chapter 14). Of course, what material neuroscientists see is the brain changing the brain (Gefter, 2008). Neuroscience has been able to explain a great deal of behavior without any reference to a nonmaterial mind, and as you explore the rest of this text, you will begin to see why most brain scientists would describe themselves as material monists.

CONCEPT CHECK

Take a Minute to Check Your Knowledge and Understanding

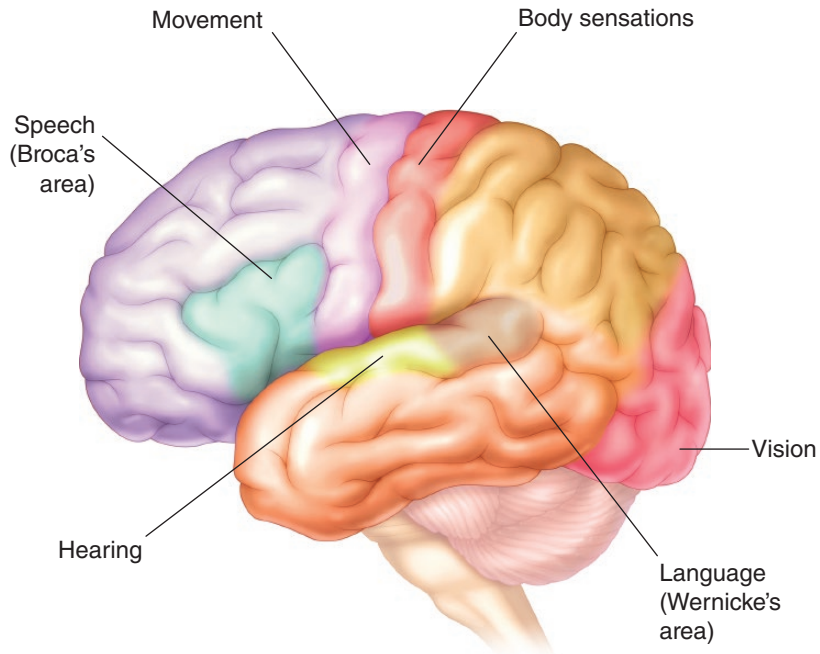
- What change in method separated science from philosophy?
- What were the important implications of the discoveries that nerve conduction is electrical and that specific parts of the brain have (more or less) specific functions?
- Where do scientists stand on the localization issue?

FIGURE 1.6 A Modern Reproduction of the Phrenologist L. M. Fowler's Map of the Brain.

Phrenologists believed that the psychological characteristics shown here were controlled by the respective brain areas.

Photo-Jope / Shutterstock Images

FIGURE 1.7 Some of the Brain's Functional Areas.



Nature and Nurture

A second extremely important issue in understanding the biological bases of behavior is the *nature versus nurture* question, or how important heredity is relative to environmental influences in shaping behavior. Like the mind-brain issue, this is one of the more controversial topics in psychology, at least as far as public opinion is concerned. The arguments are based on emotion and values almost as often as they appeal to evidence and reason. For example, some critics complain that attributing behavior to heredity is just a form of excusing actions for which the person or society should be held accountable. A surprising number of behaviors are turning out to have some degree of hereditary influence, so you will encounter this issue again in later chapters. Because there is so much confusion about heredity, we need to be sure you understand what it means to say that a behavior is hereditary before we go any further.

The Genetic Code

The *gene* is the biological unit that directs cellular processes and transmits inherited characteristics. Most genes are found on the chromosomes, which are located in the nucleus of each cell, but there are also a few genes in structures outside the nucleus, called mitochondria. Each body cell in a human has 46 chromosomes, arranged in 23 pairs (Figure 1.8). Each pair is identifiably distinct from every other pair. This is important, because genes for different functions are found on specific chromosomes. The chromosomes are referred to by number, except for the sex chromosomes; in mammals, females have two X chromosomes, while males typically have an X and a Y chromosome. Notice that the members of a pair of chromosomes are similar to each other, again with the exception that the Y chromosome is much shorter than the X chromosome.

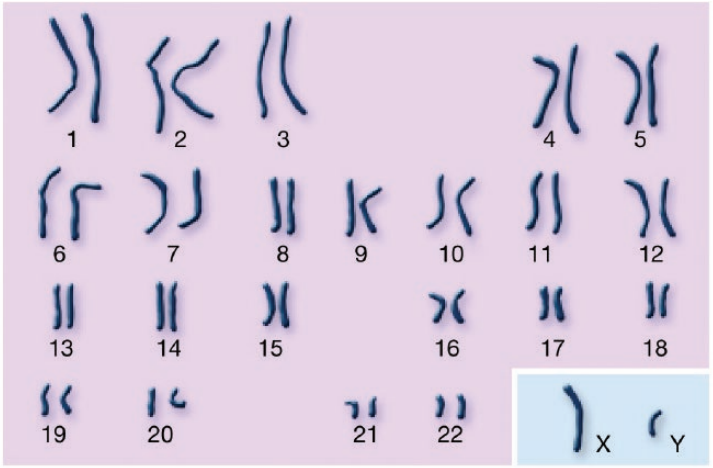
? How are characteristics inherited?

Unlike the body cells, the male's sperm cells and the female's ova (egg cells) each have 23 chromosomes. When these sex cells are formed by the division of their parent cells, the pairs of chromosomes separate, so that each daughter cell receives only one chromosome from each pair. When the sperm enters the ovum during fertilization, the chromosomes of the two cells merge to restore the number to 46. The fertilized egg, or *zygote*, then undergoes rapid cell division and development on its way to becoming a functioning organism. For the first eight weeks (in humans), the new organism is referred to as an *embryo*, and from then until birth as a *fetus*.

The mystery of how genes carry their genetic instructions began to yield to researchers in 1953, when James Watson and Francis Crick published a proposed structure for the deoxyribonucleic acid that genes are made of. *Deoxyribonucleic acid (DNA)* is a double-stranded chain of chemical molecules that looks like a ladder that has been twisted around itself; this is why DNA is often referred to as a *double helix* (Figure 1.9). Each rung of the ladder is composed of two of the four nucleotides adenine, thymine, guanine, and cytosine (A, T, G, C). The order in which these nucleotides appear on the ladder forms the code that carries all our genetic information. The four-letter alphabet these nucleotides provide is adequate to spell out the instructions for every structure and function in your body.

FIGURE 1.8 A Set of Human Chromosomes.

U.S. National Library of Medicine.



We only partially understand how genes control the development of the body and its activities, as well as how they influence many aspects of behavior. However, we do know that genes exert their influence in a deceptively simple manner: They provide the directions for making proteins. Some of these proteins are used in the construction of the body, and others are enzymes; enzymes act as catalysts, modifying chemical reactions in the body. It is estimated that humans differ among themselves in the sequences of nucleotides that make up our DNA by only about 0.5% (S. Levy et al., 2007); however, you will see throughout this text that this variation leads to enormous differences in development and behavior.

Because all but two of the chromosomes are paired, most genes are as well; a gene on one chromosome is paired with a gene for the same function on the other chromosome. The exception is that the shorter Y chromosome has only 1/25th as many genes as the X chromosome. Although paired genes have the same type of function, their effects often differ; these different versions of a gene are called *alleles*. In some cases, the effects of the two alleles blend to produce a result; for example, a person with the allele for type A blood on one chromosome and the allele for type B blood on the other will have type AB blood.

In other cases, one allele of a gene may be dominant over the other. A *dominant* allele will produce its effect regardless of which allele it is paired with on the other chromosome; a *recessive* allele will have an influence only when it is paired with the same allele. Figure 1.10 illustrates this point. In the example, note that one parent is *heterozygous* for the blood type B allele, which means that the two alleles are different; the other parent is heterozygous for the blood type A allele. The A and B alleles are dominant over the o allele; as a result, each blood type (A, B, AB, or O) has an equal chance (one in four) of occurring in an offspring. Individuals with the same *phenotype* (an observable characteristic such as blood type B) may differ by *genotype* (combinations of alleles such as B and B or B and o). You can see in the figure that type A and B parents have a one in four chance of having a child with different blood types, one of which will be *homozygous* (receiving two identical alleles) for the recessive o allele.

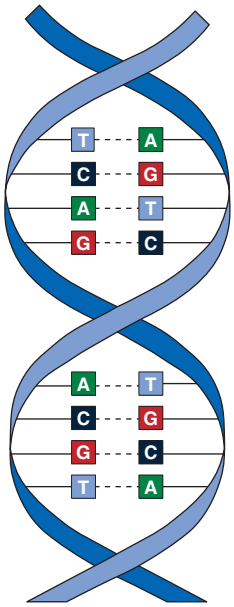
In the case of unpaired genes on the X chromosome, a recessive gene alone is adequate to produce an effect because it is not opposed by a dominant gene. A characteristic produced by an unpaired gene on the X chromosome is referred to as *X-linked*. With such a large discrepancy in the number of genes on the X and Y chromosomes, you can understand the potential for effects from X linkage. One example is that males are eight times more likely than females to have a deficiency in red-green color vision. See Chapter 10 for more on this deficiency.

Some characteristics—such as blood type and the degenerative brain disorder Huntington's disease—result from a single pair of genes, but many characteristics are determined by several genes; they are *polygenic*. Height is polygenic, and most behavioral characteristics such as intelligence and psychological disorders are also controlled by a large number of genes.

We have known from ancient times that animals could be bred for desirable behavioral characteristics, such as hunting ability or a mild temperament that made them suitable as pets. Darwin helped establish the idea that behavioral traits can be inherited in humans as well, but the idea fell into disfavor as an emphasis on learning as the major influence on behavior became increasingly fashionable. In the 1960s and 1970s, however, the tide of strict environmentalism began to ebb, and the perspective shifted toward a balanced view of the roles of nature and nurture (Plomin, Owen, & McGuffin, 1994). By 1992, the American Psychological Association was able to identify genetics as one of the themes that best represent the present and the future of psychology (Plomin & McClearn, 1993).

Of the behavioral traits that fall under genetic influence, intelligence is the most investigated. Most of the behavioral disorders, including alcoholism and drug addiction,

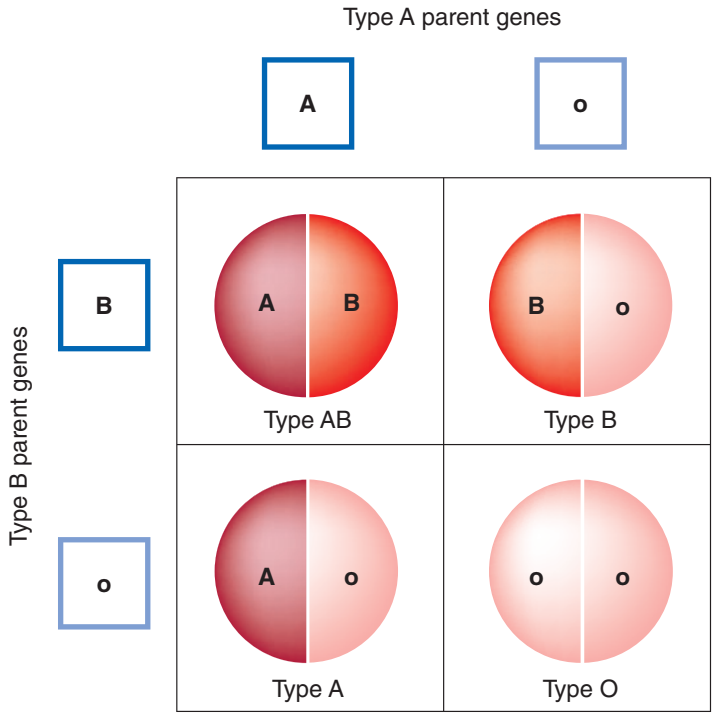
FIGURE 1.9 Structure of a Strand of DNA.



? Why do males more often show characteristics that are caused by recessive genes?

FIGURE 1.10 Blood Types in the Offspring of Heterozygous Parents.

The small boxes indicate the genes of the two parents; because A and B alleles are dominant over the o allele, the parents' blood types are A and B, respectively. Each offspring receives one allele from each parent; the circles show the four possible combinations of alleles (genotypes) in the offspring, each of which has an equal chance of occurring. The text under the circles indicates the blood types (phenotypes) of the offspring. Note that type O blood occurs only when the child receives two recessive o alleles.



schizophrenia, major mood disorders, and anxiety, are partially hereditary as well (McGue & Bouchard, 1998). The same can be said for some personality characteristics (T. J. Bouchard, 1994) and sexual orientation (J. M. Bailey & Pillard, 1991; J. M. Bailey, Pillard, Neale, & Agyei, 1993; Kirk, Bailey, Dunne, & Martin, 2000).

? What are some of the inheritable behaviors?

However, you should exercise caution in thinking about these genetic effects. Genes do not provide a script or instructions for behavior. They control the production of proteins; the proteins in turn affect the development of brain structures, the production of neurotransmitters and the receptors that respond to them, and the functioning of the glandular system. We will offer specific examples in later chapters, where we will discuss this topic in more depth.

The Human Genome Project

? What is the Human Genome Project, and how successful has it been?

After geneticists have determined that a behavior is influenced by genes, the next step is to discover which genes are involved. The various techniques for identifying genes boil down to determining whether people who share a particular characteristic also share a particular gene or genes that other people don't have. This task is extremely difficult if the researchers don't know where to look, because the amount of DNA is so great. However, the gene search received a tremendous boost in 1990, when a consortium of geneticists at 20 laboratories

around the world began a project to identify all the genes in our chromosomes, or the human *genome*.

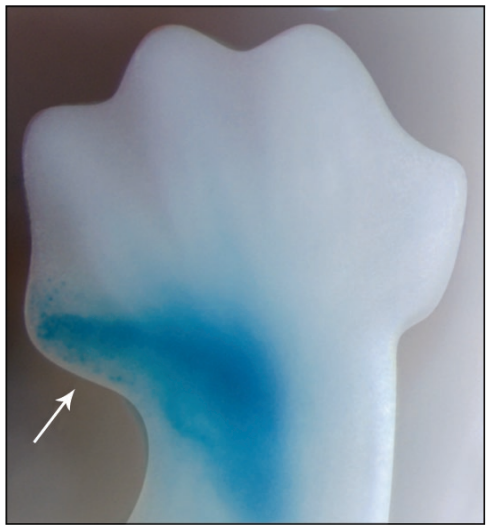
The goal of the *Human Genome Project* was to map the location of all the genes on the human chromosomes and to determine the genes' codes—that is, the order of bases within each gene. In 2000—just 10 years after the project began—the project group and a private organization simultaneously announced they had produced "rough drafts" (International Human Genome Sequencing Consortium, 2001; Venter et al., 2001); within another 5 years, the entire human genome had been sequenced (Gregory et al., 2006).

But when it comes to gene functioning, there is still more mystery than enlightenment. Only 21,000 of our genes—just 3% of our DNA—have turned out to be protein encoding (ENCODE Project Consortium, 2012). The lowly roundworm has 19,735 protein-coding genes (Hillier, Coulson, & Murray, 2005), so, clearly, the number of genes is not correlated with behavioral complexity. However, the amount of noncoding DNA—which we used to call "junk DNA"—*does* correlate with behavioral complexity (Andolfatto, 2005; Siepel et al., 2005). So what is important about "junk" DNA? Some of it is, in fact, nonfunctional, remnants left behind during evolution. But 80% of the non-protein-coding DNA is biochemically active. Much of it controls the functioning of other genes by altering *gene expression*—the translation of encoded information into the production of proteins (Pennacchio et al., 2006). For example, when a stretch of noncoding DNA known as *HACNS1*—which is unique to humans—is inserted into a mouse embryo, it turns on genes in the "forearm" and "thumb" (Figure 1.11; Prabhakar et al., 2008). DNA taken from the same area in chimpanzees and rhesus monkeys does not have that effect. The researchers speculate that the genes that *HACNS1* turns on led to the evolutionarily important dexterity of the human thumb.

FIGURE 1.11 Human Junk DNA Turns on Genes in a Mouse Embryo's Paw.

To determine where the DNA was having an effect, it was paired with a gene that produces a blue protein when activated. The blue area indicates that *HACNS1* is targeting genes in the area analogous to the human thumb.

From "Human-specific Gain of Function in a Developmental Enhancer," by S. Prabhakar et al, *Science*, 321, p. 1348. Reprinted with permission from AAAS.



A second question is what the genes do. The gene map doesn't answer that question, but it does make it easier to find the genes responsible for a particular disorder or behavior. For example, when geneticists were searching for the gene that causes Huntington's disease in the early 1980s, they found that most of the affected individuals in a large extended family shared a couple of previously identified genes with known locations on chromosome 4, whereas the disease-free family members didn't. This meant that the Huntington's gene was on chromosome 4 and near these two *marker* genes (Gusella et al., 1983). Actually finding the Huntington's gene still took another 10 years; now the gene map is dramatically reducing the time required to identify genes.

Identifying the genes and their functions will improve our understanding of human behavior and psychological as well as medical disorders. We will be able to treat disorders genetically, counsel vulnerable individuals about preventive measures, and determine whether a patient will benefit from a drug or have an adverse reaction, thus eliminating delays from trying one treatment after another.

Heredity: Destiny or Predisposition?

To many people, the idea that several, if not most, of their behavioral characteristics are hereditary implies that they are clones of their parents and their future is engraved in stone by their genes. This is neither a popular nor a comfortable view, and it creates considerable resistance to the concept of behavioral genetics. The view is also misleading; a hallmark of genetic influence is actually *diversity*.

GENES AND INDIVIDUALITY

Although family members do tend to be similar to each other, children share only half of their genes with each of their parents or with each other. A sex cell receives a random half of the parent's chromosomes; as a result, a parent can produce 2^{23}, or 8 million, different combinations of chromosomes. Add to this the uncertainty of which sperm will unite with which egg, and the number of genetic combinations that can be passed on to offspring rises to 60 or 70 trillion! So sexual reproduction increases individuality in spite of the inheritability of traits. This variability powers what Darwin (Figure 1.12) called *natural selection*, which means that those whose genes endow them with more adaptive capabilities are more likely to survive and transmit their genes to more offspring (Darwin, 1859).

? Do genes lock a person into a particular outcome in life?

The effects of the genes themselves are not rigid; they can be variable over time and circumstances. Genes are turned on and turned off, or their activity is upregulated and downregulated, so that they produce more or less of their proteins or different proteins at different times. If the activity of genes were constant, there would be no smoothly flowing sequence of developmental changes from conception to adulthood. A large number of genes change their functioning late in life, apparently accounting for many of the changes common to aging (Ly, Lockhart, Lerner, & Schultz, 2000), as well as the onset of diseases such as Alzheimer's (Breitner, Folstein, & Murphy, 1986). The functioning of some genes is even controlled by experience, which explains some of the changes in the brain that constitute learning (C. H. Bailey, Bartsch, & Kandel, 1996). For the past quarter century, researchers have puzzled over why humans are so different from chimpanzees, our closest relatives, considering that 95% to 98% of our DNA sequences are identical (R. J. Britten, 2002; M.-C. King & Wilson, 1975). Part of the answer appears to be that we differ more dramatically in which genes are *expressed*—actually producing proteins—in the brain (Enard et al., 2002).

Genes also have varying degrees of effects. Some determine the person's characteristics, whereas others only influence them. A person with the mutant form of the *huntingtin* gene *will* develop Huntington's disease, but most behavioral traits depend on many genes. For instance, a single gene will account for only a slight increase in intelligence or in the risk for schizophrenia. The idea of risk raises the issue of vulnerability and returns us to our original question, the relative importance of heredity and environment.

FIGURE 1.12 Charles Darwin (1809–1882).

From Origins, Richard Leakey and Roger Lewin.

HEREDITY, ENVIRONMENT, AND VULNERABILITY

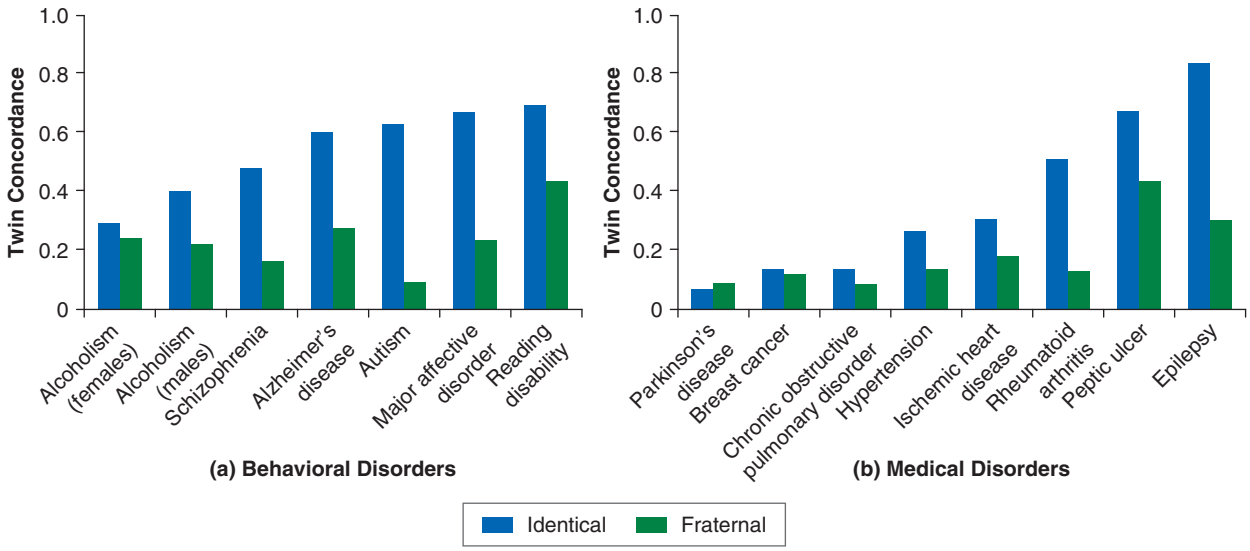
To assess the relative contributions of heredity and environment, we need to be able to quantify the two influences. *Heritability* is the percentage of the variation in a characteristic that can be attributed to genetic factors. There are various ways of estimating heritability of a characteristic. One technique involves a comparison of how often identical twins share the characteristic with how often fraternal twins share the characteristic. The reason for this comparison is that identical twins develop from a single egg and therefore have the same genes, while fraternal twins develop from separate eggs and share just 50% of their genes, like nontwin siblings. Heritability estimates are around 50% for intelligence (Devlin, Daniels, & Roeder, 1997), which means that about half of the population's differences in intelligence are due to heredity. Heritability has been estimated at 60% to 90% for schizophrenia (Tsuang, Gilbertson, & Faraone, 1991) and 40% to 50% for personality characteristics and occupational interests (Plomin et al., 1994). By way of comparison, the genetic influence on behavioral characteristics is typically stronger than it is for common medical disorders, as Figure 1.13 shows (Plomin et al., 1994).

Because about half of the differences in behavioral characteristics among people are attributable to heredity, approximately half are due to environmental influences. Keep in mind that heritability is not an

FIGURE 1.13 Twin Studies of Behavioral and Medical Disorders.

The concordance of (a) behavioral disorders and (b) medical disorders in identical and fraternal twins. Concordance is the proportion of twin pairs in which both twins have the disorder. Note the greater concordance in identical twins and the generally higher concordance for behavioral disorders than for medical disorders.

From "The Genetic Basis of Complex Human Behavior," by R. Plomin, M. J. Owen, and P. McGuffin, *Science*, 264, p. 1734. © 1994 American Association for the Advancement of Science. Reprinted with permission from AAAS.



absolute measure but tells us the proportion of variability that is due to genetic influence; the measure depends on the environmental circumstances of the group we're looking at as much as its genetic characteristics. For example, adoption studies tend to overestimate the heritability of intelligence, because adopting parents are disproportionately from the middle class. Because the children's adoptive environments are unusually similar, environmental influence will be lower and heritability higher than in the general population (McGue & Bouchard, 1998). Similarly, heritability will appear to be lower if we look only at a group of closely related individuals.

Researchers caution us that "we inherit dispositions, not destinies" (R. J. Rose, 1995, p. 648). This is because the influence of genes is only partial. This idea is formalized in the vulnerability model, which has been applied to disorders such as schizophrenia (Zubin & Spring, 1977). *Vulnerability* means that genes contribute a predisposition for a disorder, which may or may not exceed the threshold required to produce the disorder; environmental challenges such as neglect or emotional trauma may combine with a person's hereditary susceptibility to exceed that threshold. The general concept applies to behavior and abilities as well, though we wouldn't use the term *vulnerability* in those contexts. For example, the combination of genes a person receives determines a broad range for the person's potential intelligence; environmental influences then will determine where in that range the person's capability will fall. Psychologists no longer talk about heredity versus environment, as if the two are competing with each other for importance. Both are required, and they work together to make us what we are. As an earlier psychologist put it, "to ask whether heredity or environment is more important to life is like asking whether fuel or oxygen is more necessary for making a fire" (Woodworth, 1941, p. 1).

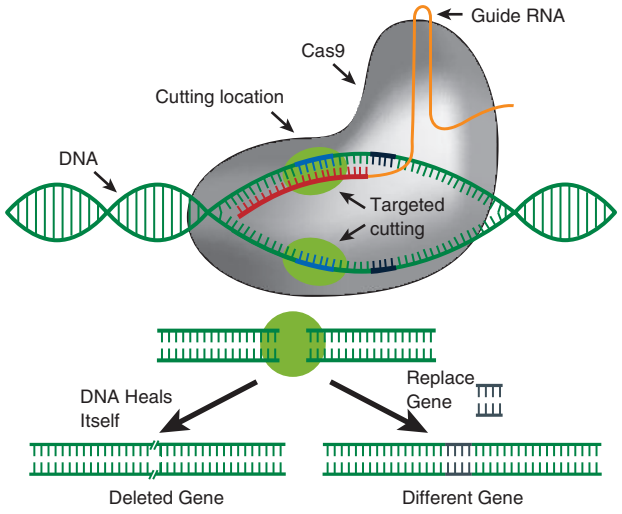
? What do we mean by "genetic predisposition"?

With an increasing understanding of genetics, we are now in the position to change our very being. This kind of capability carries with it a tremendous responsibility. The knowledge of our genetic makeup and the ready availability of genetic testing through companies such as AncestryDNA and 23andMe raise the question of whether it is better for a person to know about a risk that may never materialize, such as susceptibility to Alzheimer's disease.

In addition, many people worry that the ability to do genetic testing on our unborn children means that some parents will choose to abort a fetus because it has genes for a trait they consider undesirable (see A Further Look for more about genetic editing of fetal genes). Our ability to plumb the depths of the brain and of the genome is increasing faster than our grasp of either its implications or how to resolve the ethical questions that will arise. We will consider some of the ethical issues of genetic research in Chapter 4.

A FURTHER LOOK

CRISPR: A New Tool to Edit Genes



As we gain an increased understanding of the role, timing, and location of gene actions through efforts such as the Human Genome Project, it is only a matter of time before we will be routinely replacing defective genes in humans with healthy, functioning ones. Replacing or repairing a gene requires three key procedures at the DNA level: (1) identifying key genetic sequences that indicate the start and end of the defective DNA, (2) developing enzymes that can remove the DNA from the genome while leaving the rest of the genetic material intact, and, in some cases, (3) inserting an alternative form of DNA into the genome.

CRISPR stands for *clustered regularly interspaced short palindromic repeats*, which were discovered in bacteria. These repeats are fragments of previous viral infections that the bacterial cell uses to recognize and destroy similar invading viruses. Scientists employ various CRISPR-associated (Cas) proteins, which use an RNA sequence generated by the scientist as a guide to recognize DNA to be removed; the enzyme then acts like molecular scissors, cutting the ends of the DNA. The cell then patches the break or inserts replacement DNA carried by the Cas enzyme. This technology has the power to revolutionize our understanding of the genetic effects on physiology, behavior, and cognition, as well as to treat genetic diseases.

Though CRISPR is still in its infancy, its early successes have raised fears that this technique will eventually be used for editing human traits and creating designer babies. This fear was heightened in November 2018, when the Chinese scientist He Jiankui admitted that he had edited the genomes of two female embryos in an attempt to make them immune to HIV infection (Marchione, 2018). HIV viruses require the CCR5 receptor to enter white blood cells, and Dr. He was trying to replace the normal receptor gene with the gene for the CCR5 delta 32 receptor, which is HIV resistant. Although the technique was unsuccessful (the girls have one normal and one resistant gene, leaving them susceptible to HIV infection), the use of CRISPR technology on human embryos was universally condemned, and Dr. He was sentenced to 3 years in jail (Normile, 2019).

CONCEPT CHECK

Take a Minute to Check Your Knowledge and Understanding

- Why is it inappropriate to ask whether heredity or environment is more important for behavior?
- When we say that a person inherits a certain personality characteristic, what do we really mean?

- Explain how two parents who have the same characteristic produce children who are different from them in that characteristic. Use appropriate terminology.
- Explain how genes influence behavior.

In Perspective

In the first issue of the journal *Nature Neuroscience*, the editors observed that brain science still has a "frontier" feel to it. The excitement of exploration is real and tangible, and the discoveries and accomplishments are remarkable for such a young discipline. The successes come from many sources: the genius of our intellectual ancestors, the development of new technologies, the adoption of empiricism, and, we believe, a coming to terms with the concept of the mind. Evidence of all these influences will be apparent in the following chapters.

Behavioral neuroscience still has a long way to go. For all our successes, we do not fully understand what causes schizophrenia, exactly how the brain is changed by learning, or why some people are more intelligent than others. The 1990s was declared the Decade of the Brain; Torsten Wiesel (whose landmark research in vision you will read about later) scoffed at the idea of dedicating a decade to the brain as "foolish. . . . We need at least a century, maybe even a millennium" (as cited in Horgan, 1999, p. 18). As you read the rest of this book, keep in mind that you are on the threshold of that century's journey, that millennium of discovery.

CHAPTER SUMMARY

THE ORIGINS OF BEHAVIORAL NEUROSCIENCE

- Behavioral neuroscience (or biopsychology) developed out of physiology and philosophy as early psychologists adopted empiricism.
- Most psychologists and neuroscientists treat the mind as a product of the brain, believing that mental activity can be explained in terms of the brain's functions.
- Localization describes brain functioning better than equipotentiality, but a brain process is more likely to be carried out by a network of structures than by a single structure.

NATURE AND NURTURE

- We are learning that a number of behaviors are genetically influenced. One does not inherit a behavior itself, but genes influence structure and function in the brain and body in a way that influences behavior.
- Behavior is a product of both genes and environment. In many cases, genes produce a predisposition, and environment further determines the outcome.
- With the knowledge of the genome map, we stand on the threshold of unbelievable opportunity for identifying causes of behavior and diseases, but we face daunting ethical challenges as well.

STUDY RESOURCES

FOR FURTHER THOUGHT

- Why, in the view of most neuroscientists, is materialistic monism the more productive approach for understanding the functions of the mind? What will be the best test of the correctness of this approach?

- Scientists were working just as hard on the problems of the brain a half century ago as they are now. Why were the dramatic discoveries of recent years not made then?
- What are the implications of knowing what all the genes do and of being able to do a scan that will reveal which genes an individual has?
- If you were told that you had a gene that made it 50% likely that you would develop a certain disease later in life, what could you do with that knowledge?

TEST YOUR UNDERSTANDING

1. How would a monist and a dualist pursue the study of behavioral neuroscience differently?
2. What was the impact of the early electrical stimulation studies and the evidence that specific parts of the brain were responsible for specific behaviors?
3. The allele for type B blood is, like the one for type A, dominant over the allele for type O. Make a matrix like the one in Figure 1.10 to show the genotypes and phenotypes of the offspring of an AO parent and a BO parent.
4. A person has a gene that is linked with a disease but does not have the disease. We mentioned three reasons why this could occur; describe two of them.
5. Discuss the interaction between heredity and environment in influencing behavior, including the concept of vulnerability.

SELECT THE BEST ANSWER:

1. The idea that the mind and brain are both physical is known as
   a. idealistic monism.
   b. materialistic monism.
   c. idealistic dualism.
   d. materialistic dualism.
2. A model is
   a. an organism or a system used to understand a more complex one.
   b. a hypothesis about the outcome of a study.
   c. an analogy, not intended to be entirely realistic.
   d. a plan for investigating a phenomenon.
3. Descartes's most important contribution was in
   a. increasing knowledge of brain anatomy.
   b. suggesting the physical control of behavior.
   c. emphasizing the importance of nerves.
   d. explaining how movement is produced.
4. Helmholtz showed that
   a. nerves are not like electrical wires because they conduct too slowly.
   b. nerves operate electrically.
   c. nerves do not conduct animal spirits.
   d. language, emotion, movement, and so on depend on the activity of nerves.
5. In the mid-1800s, studies of brain-damaged patients convinced researchers that
   a. the brain's activity was electrical.
   b. the mind was not located in the brain.
   c. behaviors originated in specific parts of the brain.
   d. the pineal gland could not serve the role Descartes described.
6. Localization means that
   a. specific functions are found in specific parts of the brain.
   b. the most sophisticated functions are located in the highest parts of the brain.
   c. any part of the brain can take over other functions after damage.
   d. brain functions are located in widespread networks.
7. X-linked characteristics affect males more than females because
   a. the X chromosome is shorter than the Y chromosome.
   b. unlike males, females have only one X chromosome.
   c. the responsible gene is not paired with another gene on the Y chromosome.
   d. the male internal environment exaggerates effects of the genes.

8. Two parents are heterozygous for a dominant characteristic. They can produce a child with the recessive characteristic
   a. if the child receives a dominant gene and a recessive gene.
   b. if the child receives two recessive genes.
   c. if the child receives two dominant genes.
   d. under no circumstance.
9. The Human Genome Project has
   a. counted the number of human genes.
   b. made a map of the human genes.
   c. determined the functions of most genes.
   d. cloned most of the human genes.
10. Heritability is greatest for
    a. intelligence.
    b. occupational interest.
    c. personality.
    d. schizophrenia.
11. If we all had identical genes, the estimated heritability for a characteristic would be
    a. 0%.
    b. 50%.
    c. 100%.
    d. impossible to determine.

Answers:
1. b, 2. a, 3. b, 4. a, 5. c, 6. a, 7. c, 8. b, 9. b, 10. d, 11. a.

FOR MORE INFORMATION

The following journals are major sources of neuroscience articles (those that are not *open* access may require a subscription or university access). These may be of use to you as you progress through the textbook and your scholarly pursuits in behavioral neuroscience:

Brain and Behavior (open access)

Brain, Behavior, and Evolution

Frontiers in Neuroscience (open access; also see related journals under "18 Sections")

Journal of Neuroscience

Nature

Nature Neuroscience

Nature Reviews Neuroscience

New Scientist (for the general reader)

PLoS Biology and *PLoS Genetics* (open access)

Scientific American Mind (for the general reader)

The Scientist (for the general reader)

Trends in Neurosciences

General information sites:

BrainFacts (various topics in neuroscience)

Brain in the News (neuroscience news from media sources)

The Human Brain (a collection of brain-related articles published in the magazine *New Scientist*)

Neuroguide (a small but growing offering of resources)

Science Daily (latest developments in science; see "Mind & Brain" and "Health & Medicine")

FOR FURTHER READING

1. "The Emergence of Modern Neuroscience: Some Implications for Neurology and Psychiatry," by W. Maxwell Cowan, Donald H. Harter, and Eric R. Kandel (*Annual Review of Neuroscience*, 2000, *23*, 343–391), describes the emergence of neuroscience as a separate discipline in the 1950s and 1960s and describes some of its important accomplishments in understanding disorders.
2. Neuroscientist Michael Gazzaniga calls Mitchell Glickstein's *Neuroscience: A Historical Introduction* (MIT Press, 2014) "authoritative, highly readable, wonderfully illustrated, and just plain interesting."
3. *The Scientific American Brave New Brain*, by Judith Horstman (Jossey-Bass, 2010), describes how today's scientific breakthroughs will in the future help the blind see and help the deaf hear, allow our brains to repair and improve themselves, help us postpone the mental ravages of aging, and give the paralyzed control of prosthetic devices and machinery through brain waves.
4. *Behavioral Genetics*, by Valerie Knopik, Jenae Neiderhiser, John DeFries, and Robert Plomin (Worth, 2017, 7th ed.), is a textbook on that topic; another

text, *Evolutionary Psychology*, by William Ray (SAGE, 2013), takes a neuroscience approach to the evolution of behavior.

5. "Tweaking the Genetics of Behavior," by Dean Hamer (*Scientific American*, April 1999, 62–67), is a fanciful but thought-provoking story about a female couple in 2050 who have decided to have a child cloned and the decisions available to them for determining their baby's sex and her physical and psychological characteristics through genetic manipulation.

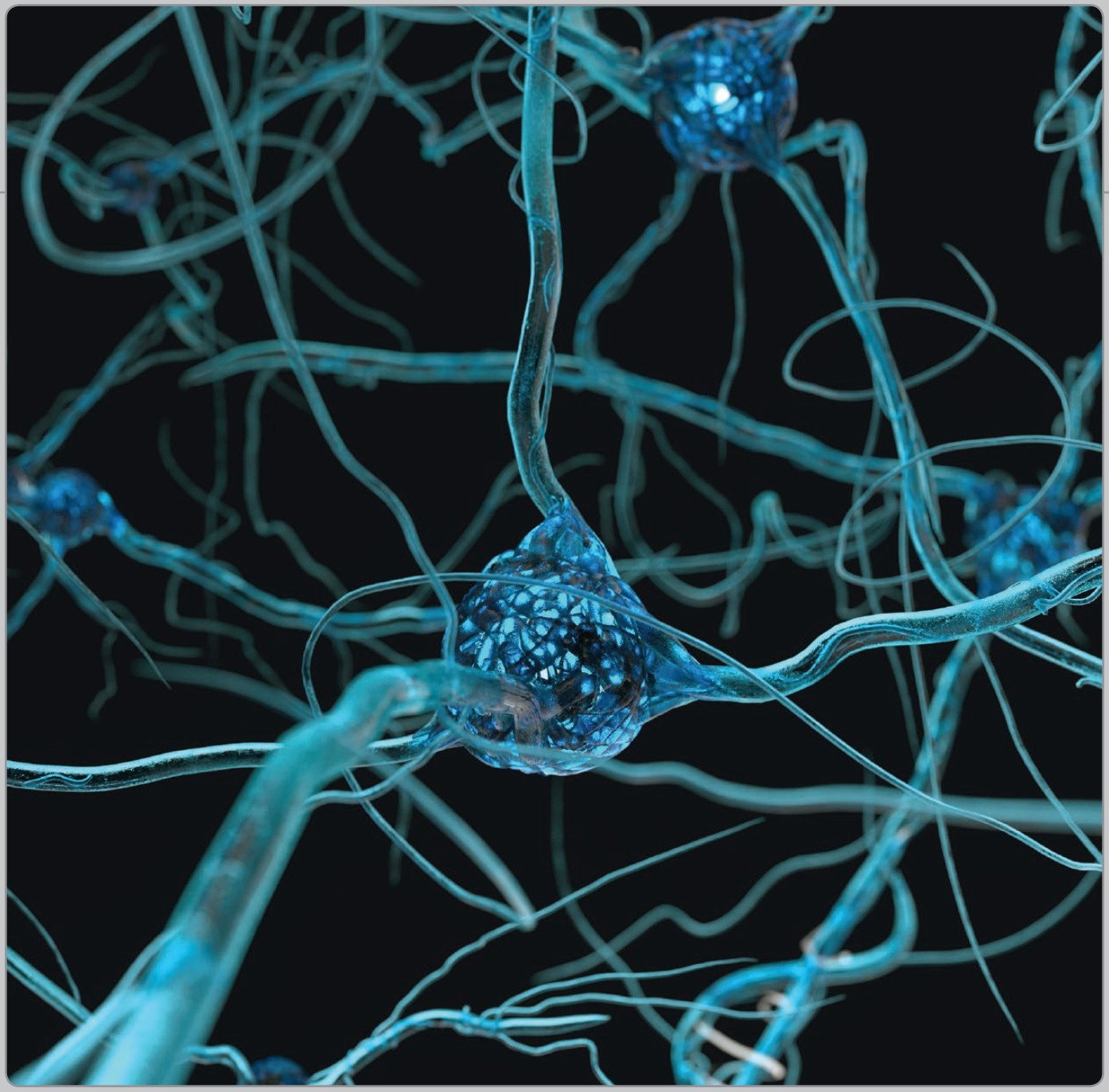
KEY TERMS

allele 9
behavioral neuroscience 2
deoxyribonucleic acid (DNA) 8
dominant 9
dualism 4
embryo 8
empiricism 5
equipotentiality 6
fetus 8
gene 8
gene expression 11
genome 11
genotype 9
heritability 12
heterozygous 9
homozygous 9
Human Genome Project 11
localization 6
materialistic monism 4
mind-brain problem 3
model 4
monism3
natural selection 12
nature versus nurture 8
phenotype 9
phrenology 6
polygenic 9
recessive 9
vulnerability 13
X-linked 9
zygote 8

Part I

Neural Foundations of Behavior

The Basic Equipment



Andriy Onufriyenko / Moment / Getty Images

2 Communication Within the Nervous System

After reading this chapter, you will be able to

2.1 Identify the cells of the nervous system.

2.2 Name the structures of neurons.

2.3 Compare the functions of sensory, motor, and interneurons.

2.4 Understand the roles of different types of glial cell.

2.5 Explain the roles of ions and the cell membrane in nervous system communication.

2.6 Explain how neurotransmitters are involved in communication between neural cells.

2.7 Discuss how neurons work together to generate your experiences of the world.

2.8 Illustrate the ways in which excitation and inhibition are important to the functioning of the nervous system.

Things were looking good for Jim and his wife. She was pregnant with their first child, and they had just purchased and moved into a new home. After the exterminating company treated the house for termites by injecting the pesticide chlordane under the concrete slab, Jim noticed that the carpet was wet and there was a chemical smell in the air. He dried the carpet with towels and thought no more about it, not realizing that chlordane can be absorbed through the skin. A few days later, he developed headaches, fatigue, and numbness. Worse, he had problems with memory, attention, and reasoning. His physician referred him to the toxicology research center of a large university medical school. His intelligence test score was normal, but the deficiencies he was reporting showed up on more specific tests of cognitive ability. Jim and his wife had to move out of their home; at work, he had to accept reduced responsibilities because of his difficulties in concentration and adapting to novel situations. The chlordane had not damaged the structure of his brain as you might suspect, but it had interfered with the functioning of the brain cells by impairing a mechanism called the sodium-potassium pump (Zillmer & Spiers, 2001). Jim's unfortunate case reminds us that the nervous system is as delicate as it is intricate. Only by understanding how it works will we be able to appreciate human behavior, to enhance human performance, and to treat behavioral problems such as drug addiction and psychosis.

FIGURE 2.1 Estimated Numbers of Neurons in the Brain and Spinal Cord.

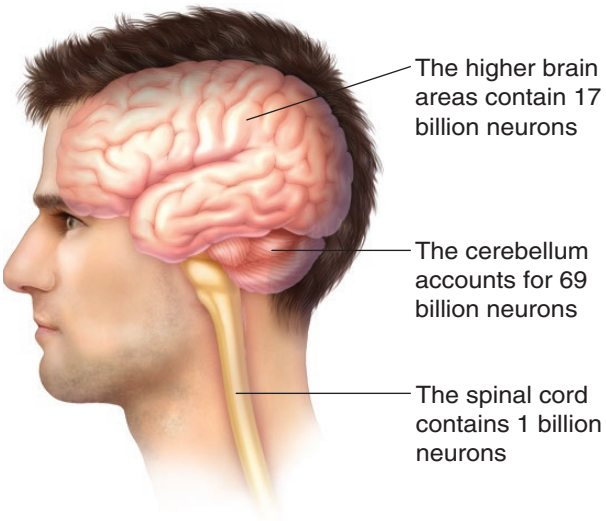
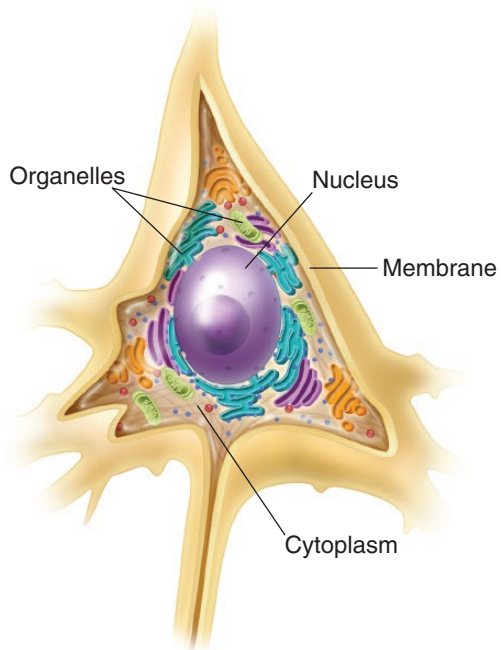


FIGURE 2.2 Cell Body (Soma) of a Neuron.

Part of the membrane has been removed to show interior features.



The Cells That Make Us Who We Are

To understand how the brain works, you must first have at least a basic understanding of the two categories of cells that carry messages back and forth in the brain and throughout the rest of the body. *Neurons* convey sensory information into the brain; carry out the operations involved in thought, feeling, and action; and transmit commands out to the body to control muscles and organs. It is estimated that there are about 86 billion neurons in the human brain (Figure 2.1; Azevedo et al., 2009). This means that there are more neurons in your brain than stars in our galaxy. But as numerous and as important as they are, neurons make up only half of the brain's cells (von Bartheld, Bahney, & Herculano-Houzel, 2016). There are also almost as many glial cells and, as we will see later in the chapter, they are almost as important.

Neurons

Neurons are responsible for all the things we do—our movements, our thoughts, our memories, and our emotions. It is difficult to believe that anything so simple as a cell can measure up to this task, and the burden is on the neuroscientist to demonstrate that this is true. As you will see, the neuron is deceptively simple in its action but impressively complex in its function.

BASIC STRUCTURE: THE MOTOR NEURON

First, let's look inside a neuron, because we want to show you that the neuron is a cell, very much like other cells in the body. Figure 2.2 is an illustration of the most prominent part of the neuron, the *cell body* or soma. The cell body is filled with a liquid called cytoplasm and contains a number of *organelles*. The largest of these organelles is the *nucleus*, which contains the cell's chromosomes. Other organelles are responsible for converting nutrients into fuel for the cell, constructing proteins and lipids, and removing waste materials. So far, this could be the description of any cell; now, let's look at the neuron's specializations that enable it to carry out its unique role. Figure 2.3 illustrates a typical neuron. We use "typical" guardedly here, because there are three major kinds of neurons and many variations within those types. The figure illustrates a *motor neuron*, which carries commands to the muscles and organs. It is particularly useful for demonstrating the structure and functions that all neurons have in common.

Dendrites are extensions that branch out from the cell body to receive information from other neurons. Their branching structure allows them to collect information from many neurons. The *axon* extends like a tail from the cell body and carries information to other locations, sometimes across great distances. The myelin sheath that wraps around the axon supports the axon and provides other benefits that we will consider later. Branches at the end of the axon culminate in swellings called *axon terminals*. The terminals contain chemical

? What are the parts of the neuron?

neurotransmitters, which the neuron releases to communicate with a muscle, an organ, or the next neuron in a chain. In our examples, we will talk as if neurons form a simple chain, with one cell sending messages to a single other neuron, and so on; in actuality, a single neuron receives input from many neurons and sends its output to many others.

Neurons are usually so small that they can be seen only with the aid of a microscope. The cell body is the largest part of the neuron, ranging from 0.005 to 0.1 millimeter (mm) in diameter in mammals. (In case you are unfamiliar with metric measurements, a millimeter is about the thickness of a dime.) Even the giant neurons of the squid, favored

FIGURE 2.3 Components of a Neuron.

The illustration is of a multipolar motor neuron.

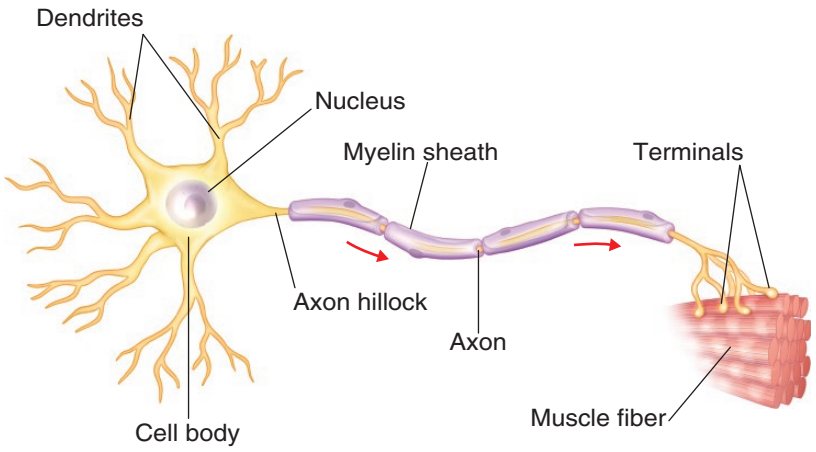
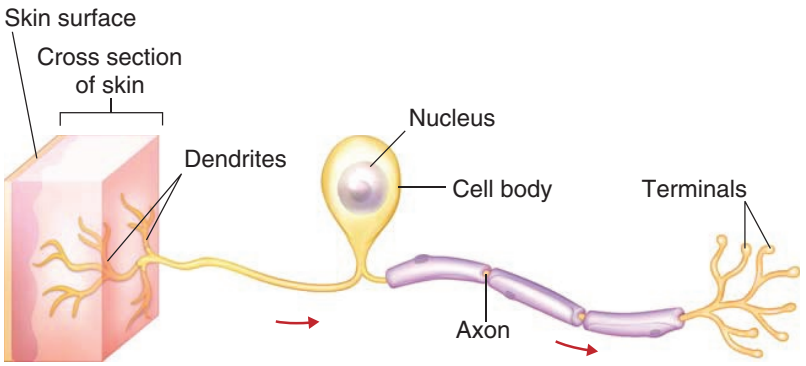


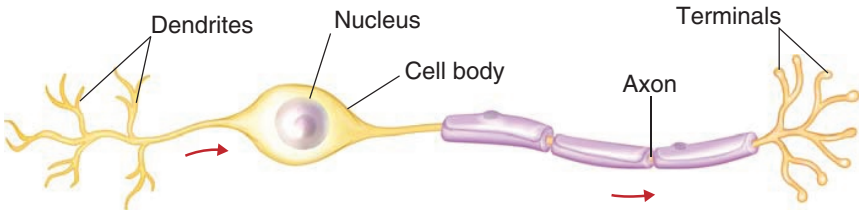
FIGURE 2.4 Sensory Neurons and an Interneuron.

Compare the location of the soma in relation to the dendrites and axon in these neurons and in the motor neuron.

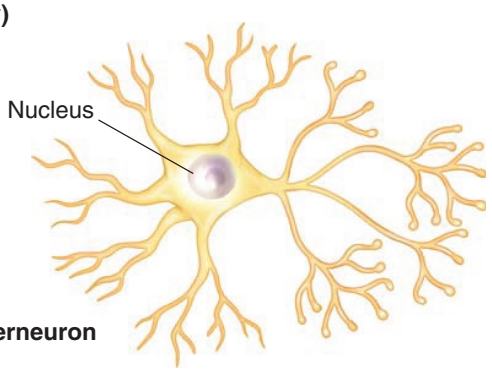
Carolina Hrejsa/Body Scientific Intl.



(a) Unipolar neuron (sensory)



(b) Bipolar neuron (sensory)



(c) Interneuron

by researchers for their conveniently large size, have axons that are only 1 mm in diameter. Typical axons are smaller; in mammals, they range from 0.002 to 0.02 mm in diameter. Axons may be as short as 0.1 mm or as long as 30 m in the blue whale (D. H. Smith, 2009).

OTHER TYPES OF NEURONS

The second type of neuron is the sensory neuron. *Sensory neurons* carry information from the body and the outside world into the brain and spinal cord. Motor and sensory neurons have the same components, but they are configured differently. A motor neuron's axon and dendrites extend in several directions from the cell body, which is why it is called a *multipolar* neuron. Sensory neurons can be either *unipolar* or *bipolar*. The sensory neuron in Figure 2.4a is called a unipolar neuron because the single short stalk from the cell body divides into two branches, with dendrites on one side and the axon and terminals on the other. (In the pseudounipolar subtype, both connections to the cell body are axons; that's because its sensory information must travel over a longer distance, from the periphery of the body to the spinal cord and the brain.) Bipolar neurons have an axon on one side of the cell body and a dendritic process on the other (Figure 2.4b). Motor and sensory neurons are specialized for transmission over long distances; their lengths are not shown here in the same scale as the rest of the cell.

The third type is neither motor nor sensory. *Interneurons* connect one neuron to another in the same part of the brain or spinal cord. Notice in Figure 2.4c that this neuron is also multipolar, but its axon appears to be missing; for some interneurons, this is so, and when they do have axons, they are often so short that they are indistinguishable from dendrites. Because interneurons make connections over very short distances, they do not need the long axons that characterize their motor and sensory counterparts. In the spinal cord, interneurons bridge sensory neurons and motor neurons to produce a reflex. In the brain, they connect adjacent neurons to carry out the complex processing that the brain is noted for. Considering the major roles they play, it should come as no surprise that interneurons are by far the most numerous neurons.

The different kinds of neurons operate similarly; they differ mostly in their shape, which fits them for their specialized tasks. We will examine how neurons work in the next few sections. The types of neurons and their characteristics are summarized in Table 2.1.

THE NEURAL MEMBRANE AND ITS POTENTIALS

The most critical factor in the neuron's ability to communicate is the membrane that encloses the cell. The membrane is exceptionally thin—only about 4 nanometers (billionths of a meter) thick—and is made up of lipid (fat) and protein (van Meer, Voelker, & Feigenson, 2008; Figure 2.5). Each lipid molecule has a "head" end and a "tail" end. The heads of the molecules are water soluble, so they are attracted to the seawater-like fluid around and inside cells. The tails are water insoluble, so they are repelled by the fluid. Therefore, as the heads orient toward the fluid and the tails orient away from the fluid, the molecules turn their tails toward each other and form a double-layer membrane.

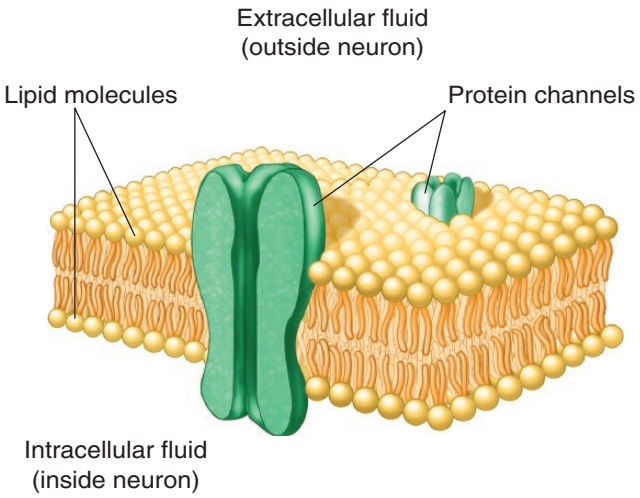
TABLE 2.1 The Major Types of Neurons.

TYPE	FUNCTION	FORM AND SOMA LOCATION	DESCRIPTION
Motor	Conducts messages from brain and spinal cord to muscles and organs	Multipolar; central nervous system	Axon, dendrites extend in several directions from cell body
Sensory	Carries information from body and world to brain and spinal cord	Unipolar; peripheral nervous system, cranial nerves	Single short stalk from cell body divides into two branches
		Bipolar; peripheral nervous system	Axon and dendritic processes are on opposite sides of cell body
Interneuron	Conducts information between neurons in same area	Multipolar; central nervous system	Has short or no axon; communicates locally (with nearby neurons)

The membrane not only holds a cell together but also controls the environment within and around the cell. Some molecules, such as water, oxygen, and most gases, can diffuse through the membrane freely. Many other substances are barred from crossing the membrane. Still others are allowed limited passage through protein channels (shown in the figure in green) that open and close under specific circumstances. This selective permeability contributes to the most fundamental characteristic of neurons, *polarization*, which means that there is a difference in electrical charge between the inside and outside of the neuron. A difference in electrical charge between two points, such as the poles of a battery or between the inside and outside of a neuron, is also called a *voltage*.

FIGURE 2.5 Cross Section of the Cell Membrane of a Neuron.

Notice how the lipid molecules form the membrane by orienting their heads toward the extracellular and intracellular fluids.



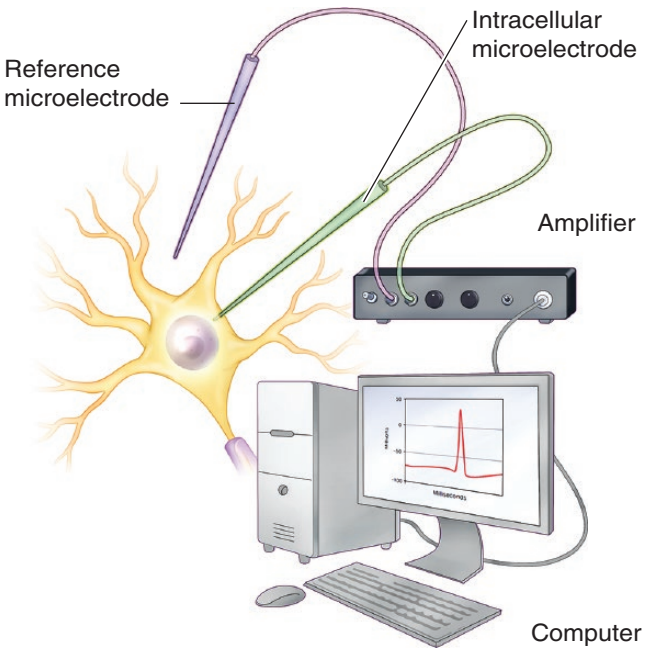
The Resting Potential. Just as you can measure the voltage of a battery, you can measure a neuron's voltage (Figure 2.6). By arbitrary convention, the voltage is expressed as a comparison of the inside of the neuron with the outside. The difference in charge between the inside and outside of the membrane of a neuron at rest is called the *resting potential*. This voltage is negative and varies anywhere from –40 to –80 millivolts (mV) in different neurons but is typically around –70 mV. You should understand that neither the inside of the neuron nor the outside has a voltage, because a voltage is a *difference* and is meaningful only in comparison with another location. Note that this voltage is quite small—the voltage of a standard 1.5-V battery is 25 times greater. No matter; we're moving information, and very little power is required.

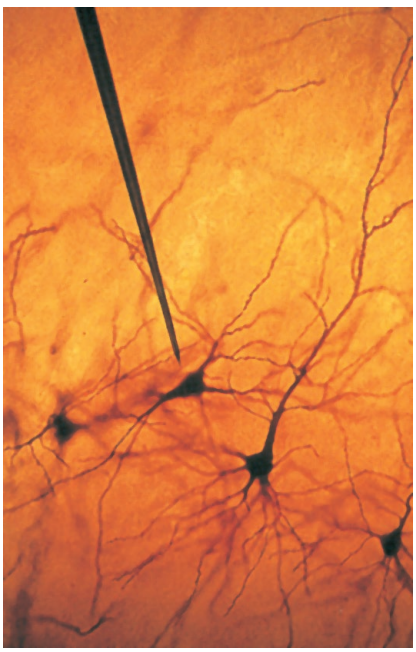
? What accounts for the resting potential?

The resting potential is due to the unequal distribution of electrical charges on the two sides of the membrane. The charges come from *ions*, atoms that have lost or gained one or more electrons.

FIGURE 2.6 Recording Potentials in a Neuron.

Potentials are being recorded in the axon of a neuron, with an electrode inside the cell and one in the fluid outside. Due to the size of neurons, the electrodes have microscopically small tips. On the right, a highly magnified view shows the size of a microelectrode relative to that of neurons. Electrodes for recording inside neurons are even smaller.

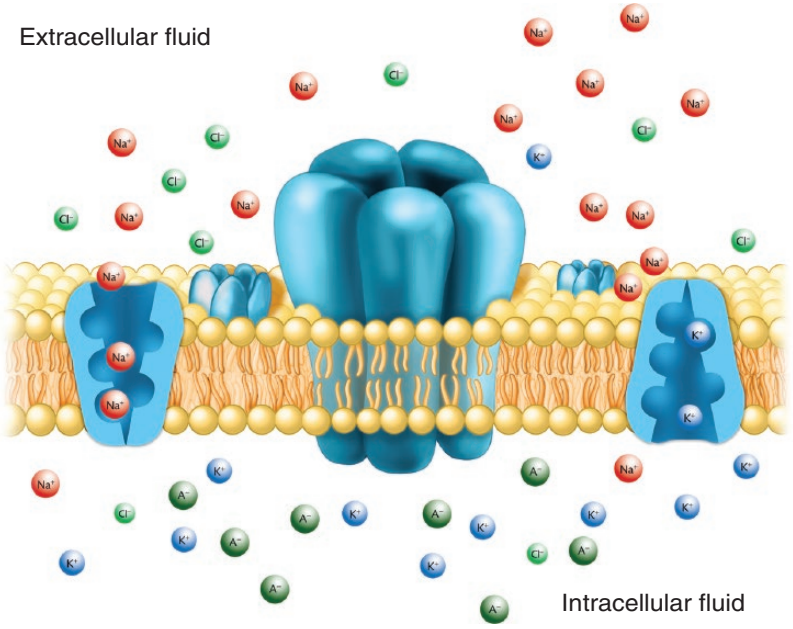




Right Photo: Bob Jacobs, Colorado College

FIGURE 2.7 Distribution of Ions Inside and Outside the Resting Neuron.

Ions on the outside are mostly Na^+ (red) and CL^- (green) ions; inside, the ions are mostly K^+ ions (blue) and organic anions (dark green). In the middle of the membrane is an ion channel, which is closed and not allowing ions through; on the left, a sodium-potassium pump is discharging three Na^+ ions outside the neuron, while on the right, an identical pump is returning two K^+ ions to the inside.



Sodium ions (Na^+) and potassium ions (K^+) are positively charged. Chloride ions (Cl^-) are negative, as are certain proteins and amino acids that make up the organic anions (A^-). The fluid outside the neuron contains mostly Na^+ and Cl^- ions, and the ions inside the neuron are mostly K^+ and A^- (Figure 2.7). The inside of the neuron has more negative ions than positive ions, whereas the ions on the outside are mostly positive, and this makes the resting potential negative.

If you remember from grade-school science that molecules tend to diffuse from an area of high concentration to one of low concentration, then you are probably wondering how this imbalance in ion distribution can continue to exist. In fact, two forces do work to balance the location of the ions. Because of the *force of diffusion*, ions tend to move through the membrane to the side where they are less concentrated. And as a result of *electrostatic pressure*, ions are repelled from the side that is similarly charged and attracted to the side that is oppositely charged.

In spite of these two forces, a variety of other influences keep the membrane polarized. Both forces would move the organic anions out, but they are too large to pass through the membrane. Their negative charge then repels the chloride ions, so the force of diffusion is unable to move those ions inside. As a result, the "real player" then becomes the potassium ions. Potassium's force of diffusion is stronger than its electrostatic pressure, and although the potassium and sodium channels are both closed during resting, potassium can slip through the membrane itself more readily than the other ions.

Another significant contributor to polarity is the *sodium-potassium pump*, which consists of large protein molecules that move sodium ions through the cell membrane to the outside and potassium ions back inside. It moves three sodium ions out for every two potassium ions it moves inside, which helps keep the inside of the membrane more negative than the outside. The pump's operation is a metabolic process, which means that it uses energy; in fact, it accounts for an estimated 40% of the neuron's energy expenditure. But you will soon see that this energy is well spent, because the resting potential stores the energy to power the action potential, the major signal in the nervous system.

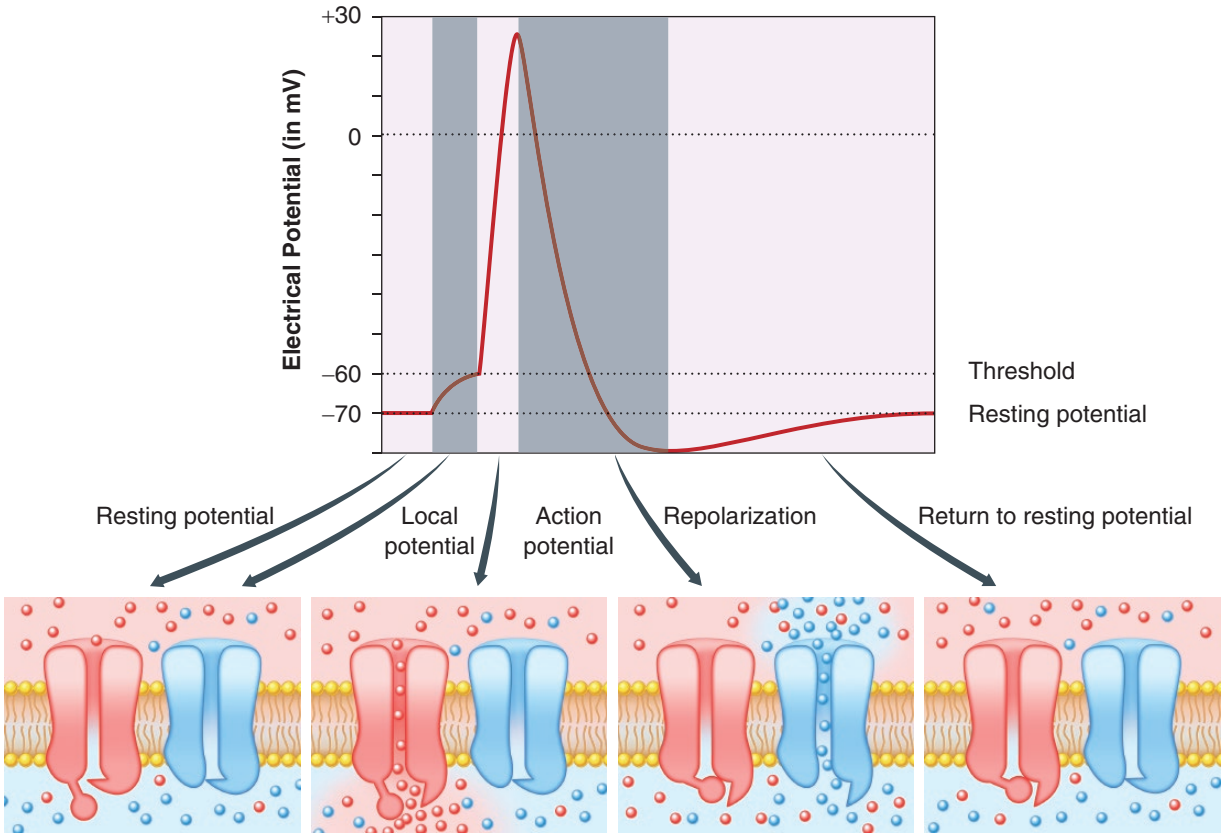
Ion Channels and Local Potentials. Before we move on, we need a better understanding of how the ion channels work. These are pores in the membrane formed by proteins, and they gate the flow of ions between the extracellular and intracellular fluids. Chemically gated channels can be opened by ligands (neurotransmitters or hormones), and electrically gated channels are opened by a change in the electrical potential of the membrane.

A neuron is usually stimulated by inputs that arrive on the neuron's dendrites and/or cell body from another neuron or from a sensory receptor. The effect may be excitatory or inhibitory, depending on the ligand and the characteristics of the receptors. An excitatory signal causes a slight partial depolarization, which means that the polarity in a small area of the membrane is shifted toward zero. This partial depolarization disturbs the ion balance in the adjacent membrane, so the disturbance flows down the dendrites and across

the cell membrane. This looks at first like the way the neuron might communicate its messages through the nervous system; however, because a partial depolarization is decremental—it dies out over distance—it is effective over only very short distances. For this reason, the partial depolarization is often called the *local potential*. The ion channels in the axon are electrically gated, and they have unique physical properties. If the local potential exceeds the threshold for activating those channels, typically about 10 mV more positive than the resting potential, it will initiate an action potential.

Action Potentials. The *action potential* is an abrupt depolarization of the membrane that allows the neuron to communicate over long distances. The voltage across the resting neuron membrane is stored energy, just as the term resting *potential* implies. Imagine countless sodium ions being held outside the neuron against the combined forces of diffusion and electrostatic pressure (Figure 2.8a). A stimulus that partially depolarizes a segment of membrane causes voltage-gated sodium ion channels to open; this allows nearby sodium ions to rush into the axon at a rate 500 times greater than normal (Figure 2.8b). They are propelled into the cell's interior so rapidly that the movement is often described as explosive. A small area

FIGURE 2.8 Ion Movement and Voltages During the Neural Impulse.



(a) Sodium channels (red) and potassium channels (blue) are closed and the membrane is at resting potential. Arrival of a local potential partially depolarizes the membrane but does not cause the channels to open unless it reaches threshold.

(b) As the local potential reaches the neuron's threshold, the sodium channels' activation gates open. Sodium ions (red) rush in, producing an action potential. The membrane in that area depolarizes and overshoots to positive.

(c) Sodium channels' inactivation gates close. Potassium channels' activation gates open; potassium ions (blue) move out, repolarizing the membrane. Polarity overshoots beyond resting potential.

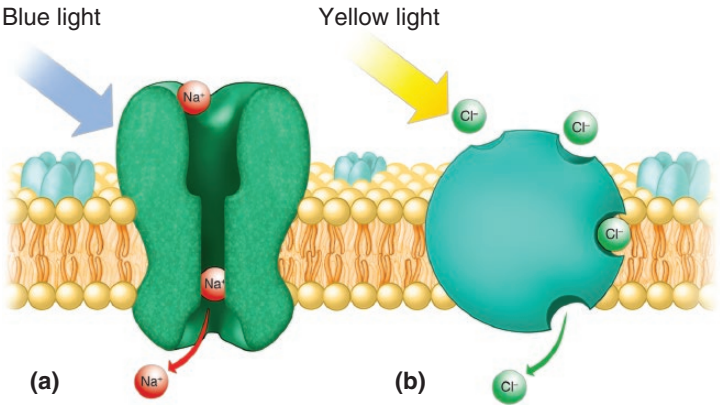
(d) Potassium channels close. The "excess" displaced ions drift away and the potential returns to resting level. (The sodium channel gates will return to their original state later.)

A FURTHER LOOK

Targeting Ion Channels

Modified Membrane Enables Light Control of Neuron Activity.

Stories of Brain & Behavior



(a) Blue light activates a channel from green algae; the channel allows positive ions to flow inward, triggering neural impulses. (b) Yellow light activates a chloride pump from bacteria; chloride ions hyperpolarize the neuron.

Source: Adapted from "Controlling Neural Circuits With Light," by M. Häusser and S. L. Smith, 2007, *Nature*, 446, 617–619 (Figure 1a, p. 617).

The Japanese delicacy fugu, or puffer fish, produces an exciting tingling sensation in the diner's mouth; improperly prepared, it causes numbness and weakness and, in some cases, a paralysis of the respiratory muscles that has claimed the lives of hundreds of culinary risk takers. The fish's natural poison, tetrodotoxin (TTX), blocks sodium channels and prevents neurons from firing (Siegelbaum & Kandel, 2013). Researchers are examining TTX as a potential replacement for opiate painkillers (Gorey, 2019; Nieto et al., 2012), so this dangerous toxin might lead to new treatments for chronic pain. Other *neurotoxins* (neuron poisons) are found in snake venoms, which block sodium, potassium (Benoit & Dubois, 1986; Fertuck & Salpeter, 1974), or calcium channels, and scorpion venom, which keeps sodium channels open, prolonging the action potential (Catterall, 1984; Chuang, Jaffe, Cribbs, Perez-Reyes, & Swartz, 1998; Pappone & Cahalan, 1987).

Interfering with neuron functioning can be useful, though; for example, most local anesthetics prevent neuron firing by blocking sodium channels (Ragsdale, McPhee, Scheuer, & Catterall, 1994), and some general anesthetics hyperpolarize the neuron by opening potassium channels and allowing the potassium ions to leak out (Nicoll & Madison, 1982; A. J. Patel et al., 1999). The cone snail of the South Seas can penetrate a wet suit with its proboscis and inject toxins that will kill a human in half an hour, but the various species' thousands of toxins that target sodium, potassium, or calcium channels or block neurotransmitter receptors are in demand by researchers developing pain relievers and drugs for preventing heart attacks and epilepsy (L. Nelson, 2004; Oliviera & Teichert, 2007).

An exciting new research strategy known as *optogenetics* allows researchers to create light-responsive channels (as well as receptors) in neurons so that they can be controlled by light. Different types of channels are triggered by different wavelengths of light, which allows the researcher either to accelerate or to inhibit firing. The procedure is being used to understand the circuitry in a variety of behaviors and brain processes and is showing potential for use in therapeutic procedures.

inside the membrane becomes fully depolarized to zero; the potential even overshoots to around +30 or +40 mV, making the interior at that location temporarily positive.

Just as abruptly as the neuron "fires," it begins to recover its resting potential. At the peak of the action potential, voltage sensors in the sodium channels detect the depolarization and close a gate, inactivating the channel and preventing further sodium ion influx (Catterall, 2010). The depolarization also causes voltage-gated potassium ion channels to open; the positive charge and the higher concentration of potassium ions inside the membrane combine to force potassium ions out. This outward flow of positive potassium ions lowers the axon voltage to its resting potential and sometimes a bit beyond (Figure 2.8c). In total, the action potential lasts about 1 millisecond (one thousandth of a second); the actual duration varies among individual neurons. (Obviously, these channels are what make the neuron operate; A Further Look (page 28) describes how they are exploited by nature and in research and medicine.)

Only a relatively few ions very near the two sides of the membrane have participated in the action potential; these dislocated ions quickly diffuse into the surrounding fluid, and the membrane potential returns to its resting level (Figure 2.8d). Eventually, though, the ions must be returned to their original locations, or the neuron cannot continue firing; the sodium-potassium pump takes care of this. (Perhaps you can see now why Jim was in such a bad way after his bout with chlordane.)

? What is the role of the sodium-potassium pump following an action potential?

The depolarization that occurs during the action potential triggers nearby sodium channels to open as well. Thus, a new action potential is triggered right next to the first one. That action potential in turn triggers another farther along, creating a chain reaction of action potentials that move through the axon; thus, a signal flows from one end of the neuron to the other. Nothing physically moves down the axon. Instead, a series of events occurs in succession along the axon's length, much as a line of dominoes standing on end knock each other over when you tip the first one. When the action potential reaches the terminals, they pass the signal on to the next neuron in the chain (or to an organ or a muscle). The transmission of signals from neuron to neuron is covered later; for now, the action potential needs to be examined a bit further.

The action potential differs in two important ways from the local potential that initiates it. First, the local potential is a *graded potential*, which means that it varies in magnitude with the strength of the stimulus that produced it. The action potential, by contrast, is *ungraded*; it operates according to the *all-or-none law*, which means that it occurs at full strength or it does not occur at all. A larger graded potential does not produce a larger action potential; like the fuse of a firecracker, the action potential depends on the energy stored in the neuron, in this case, due to the difference in ion concentrations between the two sides of the membrane. A second difference is that the action potential is *nondecremental*; it travels down the axon without any decrease in size, propagated anew and at full strength at each successive point along the way. The action potential thus makes it possible for the neuron to conduct information over long distances.

? How is an action potential different from a graded potential?

However, because the action potential is all-or-none, its size cannot carry information about the intensity of the initiating stimulus. One way stimulus intensity is represented is in the number of neurons firing. The voltage sensitivity of sodium channels varies among neurons, resulting in different thresholds; a more intense stimulus will recruit firing in neurons with higher thresholds and, therefore, in more neurons. There is, though, a way in which the individual neuron can encode stimulus strength, as you will see in the discussion of refractory periods.

REFRACTORY PERIODS

? What are the absolute and relative refractory periods?

If you remember a few paragraphs back, we stated that the flow of an action potential down the axon was like knocking down a line of dominoes. And just as you must go through and

reset the dominoes so that they can fall again, the ion channels must be reset before the neuron can fire again. During the action potential and initial recovery, the sodium ion channels are open and unresponsive to further stimulation, no matter how intense; this time is referred to as the *absolute refractory period*. This delay in responsiveness has two important effects. First, the 1- to 2-millisecond duration of the absolute refractory period limits how fast the neuron can generate new action potentials; a study of cortical *fast-spiking neurons* found maximal rates of 453 per second in humans, 611 in monkeys, and 342 in mice (B. Wang et al., 2016). Second, because the ion channels behind the action potential are still recovering, the impulse can propagate only down the axon toward the dendrites, not back toward the cell body. This makes neural transmission unidirectional, which has the secondary effect of preventing the neuron from "locking up." If recovery were immediate, activity would self-propagate in both directions from an ongoing action potential; this would result in impulses moving repeatedly back and forth along the axon, which would block the ability to respond to newly arriving messages.

At the end of the absolute refractory period, the sodium channels have closed, so the neuron is able to fire again. But the potassium channels remain open for an additional 3 or 4 milliseconds, and as potassium ions continue to exit the neuron, the polarity is driven slightly more negative than the resting potential (the "dip" in Figure 2.8). During the resulting *relative refractory period*, another action potential can be generated but only by a stronger-than-threshold stimulus. A stimulus that is slightly greater than this temporarily higher threshold will cause the neuron to fire again before the end of the relative refractory period; with progressively stronger stimuli, the neuron will fire increasingly earlier and, therefore, at a higher rate. Thus, the axon encodes stimulus intensity not in the size of its action potential but in its firing rate, an effect called the *rate law*.

Glial Cells

Glial cells are nonneural cells that provide a number of supporting functions to neurons. The name *glia* is derived from the Greek word for "glue," which gives you some idea of how the role of glial cells has been viewed in the past. However, glial cells do much more than hold neurons together. One of their most important functions is to increase the speed of conduction in neurons.

MYELINATION AND CONDUCTION SPEED

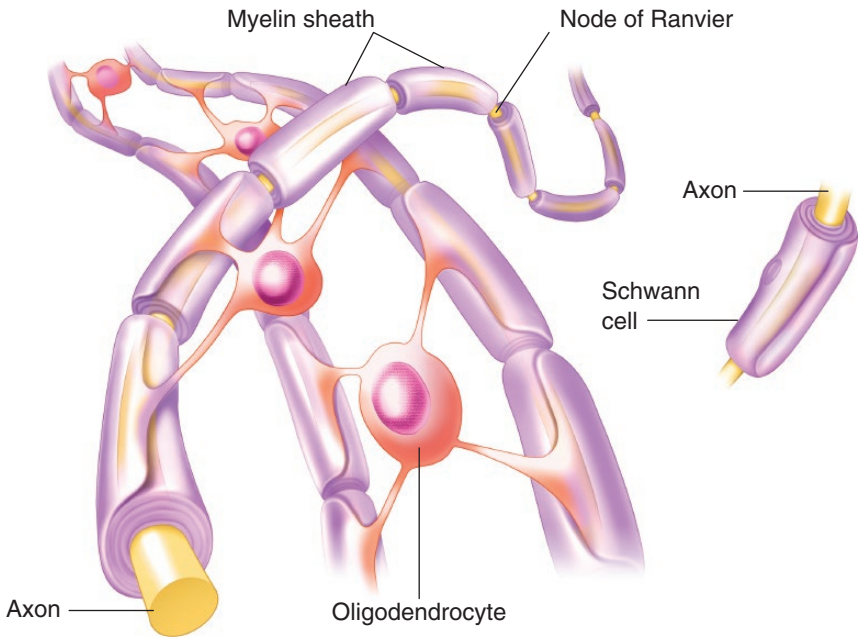
Survival depends in part on how rapidly messages can move through the nervous system, enabling the organism to pounce on its prey, outrun a predator, or process language quickly. The speed with which the fastest neurons conduct their impulses approaches 120 meters (m) per second (s), or about 270 miles per hour (435 km/hr). This seems fast, but the speed of electricity flowing through a wire, the analogy sometimes used to describe neural conduction, is up to 690 times faster. Because conduction speed is so critical to survival, strategies have evolved for increasing it. One way is to develop larger-diameter axons, which provide less resistance to the flow of electrical potentials. By evolving motor neurons with 0.5-mm-thick axons, the squid has achieved conduction speeds of 30 m/s, compared with 1 m/s in the smallest neurons.

? What are the functions of glial cells?

However, conduction speed increases not in direct proportion to axon size but closer to the square of the diameter (W. A. H. Rushton, 1951). To reach our four-times-greater maximum conduction speed of 120 m/s, our axons would have to be $4^2 = 16$ times larger than the squid axon, or 8 mm in diameter (the size of a large pea)! Obviously, your brain would be larger than you could carry around. In other words, if axon size were the only way to achieve fast conduction speed, *you* would not exist. Vertebrates (animals with backbones) have developed another solution, myelination. Two types of glial cells produce *myelin*, a fatty tissue that wraps around the axon (like a jellyroll) to insulate it from the surrounding fluid and from other neurons. Only the axon is covered, not the cell body. Myelin is produced in the brain and spinal cord by glial cells called *oligodendrocytes* and in the rest of the nervous system by

FIGURE 2.9 Oligodendrocytes Produce Myelin for Axons.

A single oligodendrocyte provides myelin for multiple segments of the axon and for multiple neurons. A Schwann cell covers only one segment of an axon.



Schwann cells (Figure 2.9). Almost 75% of the glial cells in the brain are myelin-producing oligodendrocytes (Pillay & Manger, 2007).

Because there are very few sodium channels under the myelin sheath, action potentials cannot occur there; conduction under myelinated areas is by local graded potential (Waxman & Ritchie, 1985). However, myelin appears in segments about 1 mm long, with a gap of one or two thousandths of a millimeter between segments; these gaps in the myelin sheath are called *nodes of Ranvier* (see Figure 2.9). At each node of Ranvier, where the membrane is exposed and there are plenty of sodium channels, the graded potential triggers an action potential. Action potentials thus appear to jump from node to node in a form of transmission called *saltatory conduction*.

This arrangement has three benefits. First, the insulating effect of myelin reduces an electrical effect of the membrane called capacitance. Because capacitance slows the movement of ions down the axon, the graded potential gets a big boost in speed. The overall effect of myelination is the equivalent of increasing the axon diameter 100 times (Koester & Siegelbaum, 2013). Second, the breaks in the myelination mean that the signal is regenerated by an action potential at every node of Ranvier. Third, myelinated neurons use much less energy because there is less work for the sodium-potassium pump to do.

Some diseases, such as multiple sclerosis, destroy myelin. As myelin is lost, the capacitance rises, reducing the distance that graded potentials can travel before dying out. The individual is worse off than if the neurons had never been myelinated; because there are few voltage-sensitive sodium channels under the myelin sheath (Ritchie & Rogart, 1977), action potentials may not be generated in the previously myelinated area. Therefore, conduction slows or stops in affected neurons.

OTHER GLIAL FUNCTIONS

There are several types of glial cells, and they make numerous contributions to neural functioning. During fetal development, *radial glia* form scaffolds that guide new neurons to their

FIGURE 2.10 Glial Cells Increase the Number of Connections Between Neurons.

Neurons were cultured for 5 days in (a) the absence of glial cells and (b) the presence of glia. The number of neurons was similar in both cultures; the greater density on the right is due to increased connections among both neurons.

Source: From F. W. Pfrieger and B. A. Barres, "Synaptic Efficacy Enhanced by Glial Cells In Vitro," *Science*, Vol. 277, p. 1684, 1997. Reprinted with permission from AAAS.

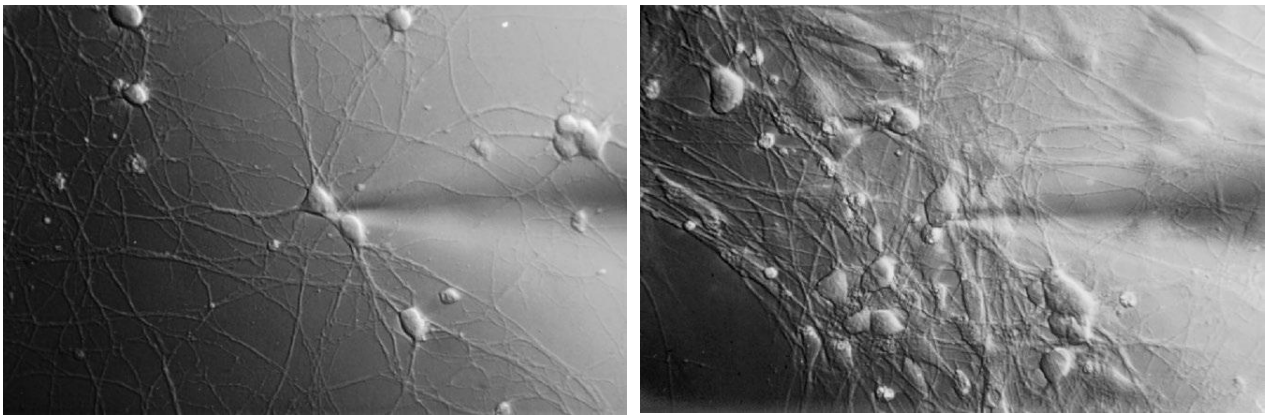
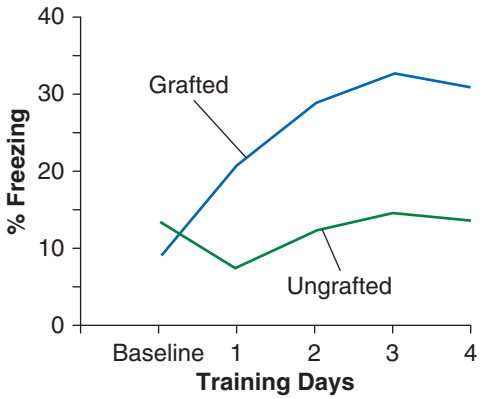


FIGURE 2.11 Human Glial Cells Enhance Conditioning in Mice.

Mice receiving brain grafts of human glial cells rapidly learned a fear response ("freezing" to a tone that signaled an upcoming electric shock), while ungrafted controls showed little or no improvement.

Source: Adapted from Figure 6B of "Forebrain Engraftment by Human Glial Progenitor Cells Enhances Synaptic Plasticity and Learning in Adult Mice," by Xiaoning Han et al., 2013, *Cell Stem Cell*, 12, p. 350.



destinations. Later on, *microglia* provide energy to neurons and respond to injury and disease by removing cellular debris. Neurons form seven times as many connections in the presence of the type of glia called *astrocytes*, and they start to lose their synapses if astrocytes are removed from the culture dish (Pfrieger & Barres, 1997; Ullian, Sapperstein, Christopherson, & Barres, 2001; see Figure 2.10). Astrocytes also appear to play a key role in learning, as Figure 2.11 demonstrates (X. Han et al., 2013; Suzuki et al., 2011). Later in this chapter, you will see that glial cells play a direct role in neural activity.

CONCEPT CHECK

Take a Minute to Check Your Knowledge and Understanding

- How is information conducted in the axon?
- How does the all-or-none law limit information transmission?
- What benefits do the refractory periods provide?
- How does myelin speed up conduction in axons?

How Neurons Communicate With Each Other

Before the late 1800s, microscopic examination suggested that the brain consisted of a continuous web called a reticulum. At that point, however, Camillo Golgi developed a new tissue-staining method that helped anatomists see individual neurons by randomly staining some entire cells without staining others (see the discussion of staining methods in Chapter 4).