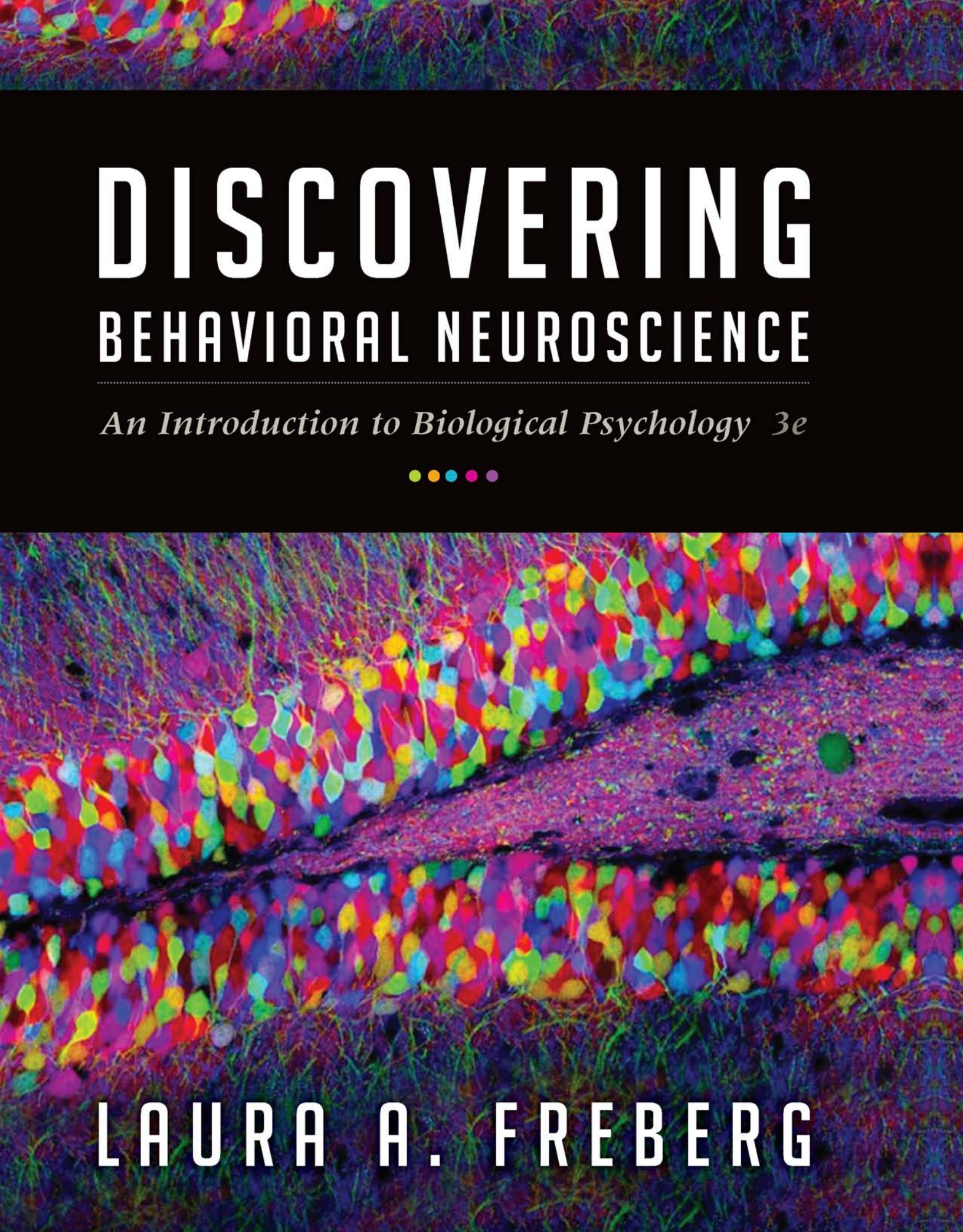

DISCOVERING BEHAVIORAL NEUROSCIENCE

An Introduction to Biological Psychology 3e

LAURA A. FREBERG

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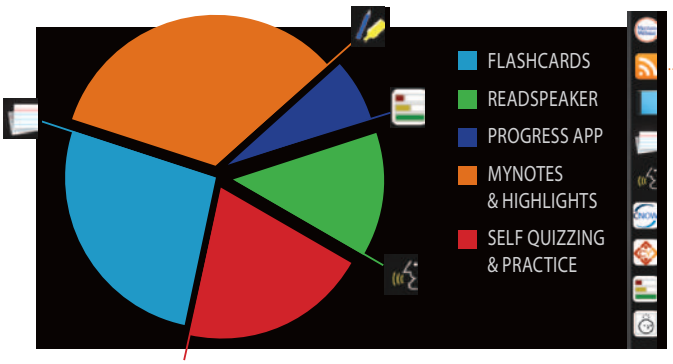

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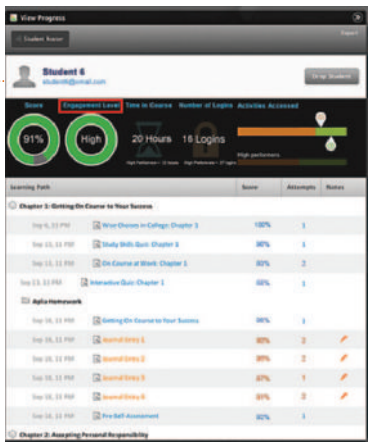

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AN INTRODUCTION TO BIOLOGICAL PSYCHOLOGY

Third Edition

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California Polytechnic State University,
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***Discovering Behavioral Neuroscience: An Introduction to Biological Psychology*, Third Edition**
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TO MY FAMILY
Roger, Kristin, Karen, and Karla

About the Author

Laura A. Freberg is Professor of Psychology at California Polytechnic State University, San Luis Obispo, where she teaches courses in Introductory Psychology, Biological Psychology, and Sensation and Perception. With John Cacioppo of the University of Chicago, Laura is the co-author of two editions of *Discovering Psychology: The Science of Mind* for Cengage Learning.

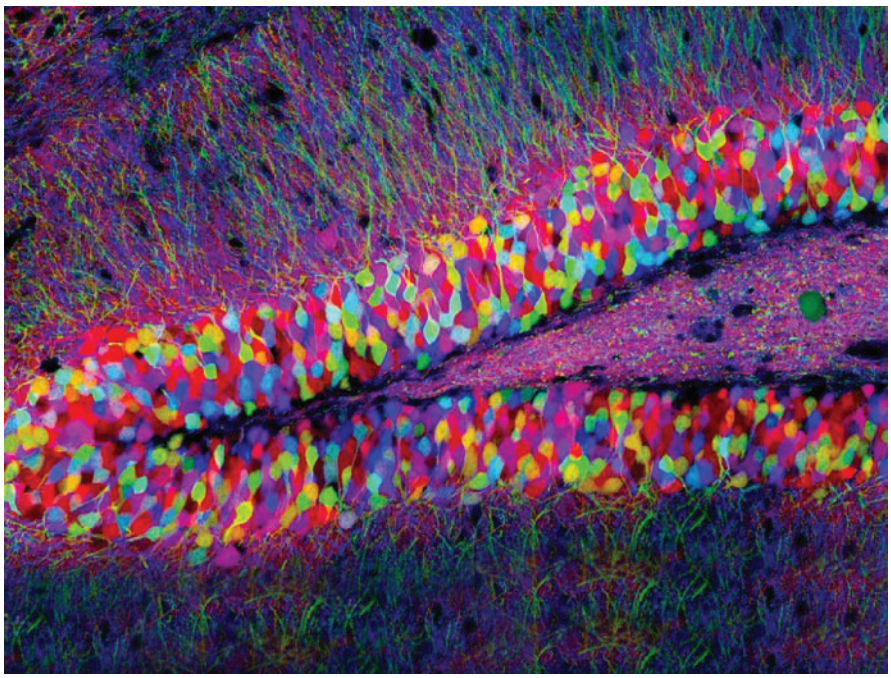
Laura completed her undergraduate and graduate studies at UCLA, where her thinking about psychology was shaped by Eric Holman, John Garcia, O. Ivar Lovaas, Larry Butcher, Jackson Beatty, John Libeskind, Donald Novin, Frank Krasne, and F. Nowell Jones. She was privileged to study neuroanatomy with Arnold Scheibel, and investigated the effects of psychoactive drugs on learning and memory under the direction of Murray Jarvik and Ronald Siegel in the UCLA Neuropsychiatric Institute. As a capstone to her education, Laura completed her dissertation with Robert Rescorla, then at Yale University.

Laura's teaching career began when she taught her first college course at Pasadena City College at the age of 23 while still a graduate student at UCLA. Recently, to better understand the needs of the online education community, she also began teaching for Argosy University Online, including courses in Social Psychology, Sensation/Perception, Cognitive Psychology, Statistics, Research Methods, and Writing in Psychology. She has received Faculty Member of the Year recognition from Cal Poly Disabilities Resource Center three times (1991, 1994, and 2009) for her work with students with disabilities. She enjoys using technology and social media in the classroom and is a Google Glass Explorer. Laura serves as the Content Expert Writer for Psychology for Answers.com. and enjoys collaborating with daughters Kristin Saling (Systems Engineering—U.S. Military Academy at West Point) and Karen Freberg (Communications—University of Louisville) on a variety of research projects in crisis management and public relations as well as in psychology. She serves as the Bylaws and Archives Committee Chair for the Society for Social Neuroscience and is a member of the editorial board for *Leadership Quarterly*.

In her spare time, Laura enjoys family time with her husband, Roger, their youngest daughter Karla, who has autism spectrum disorder, and an active menagerie including an Australian shepherd, two cats, and three parakeets. She usually writes while consuming vast quantities of Gevalia coffee and listening to the Rolling Stones (which might be apparent in the book's writing style), and she has been known to enjoy college football, Harley Davidsons, episodes of *Game of Thrones* that do not feature weddings, and *Sherlock*. Her ringtone is from Nintendo's *Legend of Zelda*.

About the Cover

If you are familiar with the first and second editions of this textbook, you know that we like to pick colorful visuals that portray the biology behind the behavior. For this third edition, we selected an image of a "brainbow" of the hippocampus of a transgenic mouse. Brainbows are constructed by promoting the expression of different ratios of red, green, and blue fluorescent proteins by individual neurons. This imaging process has assisted researchers interested in mapping the connectome, or the neural connections of the brain. The brainbow technique was developed in 2007 by researchers under the direction of Joshua Sanes and Jeff Lichtman.



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Preface

> "… in teaching, you must simply work your pupil into such a state of interest in what you are going to teach him that every other object of attention is banished from his mind; then reveal it to him so impressively that he will remember the occasion to his dying day; and finally fill him with devouring curiosity to know what the steps in connection with the subject are."
>
> —William James (1899, p. 10)

James's goals for the classroom instructor might seem lofty to some, but many of us who teach neuroscience have enjoyed the peak experience of seeing students "turn on" to the material in just the way James describes.

This is an exciting time to be a neuroscientist. Every day, science newsfeeds announce some new and dramatic breakthroughs in our knowledge about the nervous system and the human mind. Important questions raised in the past now have definitive answers. In 1890, James commented that "blood very likely may rush to each region of the cortex according as it is most active, but of this we know nothing" (vol. 1, p. 99). With today's technology, it is safe to say we now know much more than "nothing" about this phenomenon James described.

Much has changed in the field of neuroscience since our first edition of this textbook in 2006. More than half of the four-year universities in the United States now offer bachelors degrees in neuroscience, and most offer at least a minor in the discipline. Neuroscience reflects a general academic trend of the 21st century, in which the walls separating specializations are giving way to new, transdisciplinary research teams, courses, and educational programs. In recognition of these changes, we have decided to modify the title of the third edition of this textbook from *Discovering Biological Psychology* to *Discovering Behavioral Neuroscience: An Introduction to Biological Psychology.* A greater emphasis on the neurosciences in general is also achieved by renaming some chapter titles. Psychology, of course, still provides a foundation for the study of behavioral neuroscience, as without the ability to ask the right questions about behavior and mental processes, all of the technology on the planet wouldn't do us much good. Our current behavioral neuroscience students, however, are just as likely to be preparing for careers in the health professions, biomedical engineering, or even scientific journalism as they are in psychology.

A major reflection of the transdisciplinary approach exemplified by the neurosciences is the inclusion of psychology and behavioral neuroscience content in the revised edition of the Medical College Admission Test (MCAT) beginning in 2015. One hundred years ago, the leading killers of humans were infectious diseases. Today's top killers—heart disease, diabetes, and cancer—have far stronger relationships with behavior, not only in their causes but also in their treatments. A simple five-minute conversation with a health professional about the need to quit smoking is sufficient to lead to abstention for one year by 2 percent of patients (Law & Tang, 1995). This might not sound like much, but given the 20 percent or so of American adults who smoke and the billions of dollars their healthcare and lost productivity represent, the stakes are very high. Imagine what could be accomplished by healthcare providers who have a deep understanding of learning, motivation, and social influences on behavior. In response to these and similar trends, the current edition of the textbook explores relevant applications to students pursuing fields of study other than psychology whenever these are relevant.

This third edition continues and expands upon the goals of the previous two:

- To provide challenging, very current content in a student-friendly, accessible form.
- To stimulate critical thinking about neuroscience by presenting controversial and cutting-edge material.
- To promote active student engagement and excitement about the neurosciences.
- To integrate across chapters rather than treating them as stand-alone modules; to encourage students to see the connections among the topics. For example, connections are made between glutamate as a chemical messenger, its role in learning, the effects of psychoactive drugs on glutamate, its role in psychosis, and its importance to the causes and treatments of stroke and epilepsy.

Pedagogical Features

We realize that a course in behavioral neuroscience can be challenging for many students, particularly those who are underprepared for science courses. To make the process of mastering behavioral neuroscience concepts easier, we have included the following features:

- **Accessible Writing Style** Many textbooks are classified by "level," but it is my opinion that the most complex topics can be mastered by students across a wide range of preparation if the writing style is clear. Students and instructors from the community college through the top R1 universities have kindly complimented me on the accessible writing style used in this textbook. The textbook is also widely adopted in non-English-speaking countries, which suggests that the writing style is manageable for those for whom English is not a first language.
- **Clear, Large, Carefully Labeled Illustrations** Our medical-quality anatomical illustrations help students visualize the structures and processes discussed in each part of the textbook. Behavioral neuroscience is similar to geography in its highly visual nature, and both fields require more visual aids than most other courses. The illustrations in the textbook are augmented by a set of online animations that help the student grasp processes over time, such as the propagation of action potentials down the length of an axon.
- **Learning Objectives and Chapter Outlines** Each chapter begins with a concise set of learning objectives designed to tap into higher levels of Bloom's taxonomy, as well as an outline of the chapter's content. These features assist students in planning their learning and in becoming familiar with main terms and concepts to be covered.
- **Margin Glossaries** We regularly provide margin definitions for many difficult terms. Unlike many textbooks, we do not restrict margin definitions to keyterms only. In the electronic forms of the book, these take the form of pop-up definitions, with which students are familiar from their online searching experience.
- **Keyterms** We provide a concise list of keyterms to help students focus their learning. Behavioral neuroscience can often seem more like a foreign language course than a science course, and students benefit from guidance regarding which terms should be prioritized.
- **Interim Summaries** Each chapter features two to three interim summaries where students can catch their breath and check their mastery of the material before proceeding. These summaries feature summary points keyed to the learning objectives listed at the beginning of each chapter as well as review questions. Most interim summaries also include a helpful table that pulls together key concepts from the previous section in one convenient place.

- **Chapter Integration** To emphasize how the material fits together and to promote elaborative rehearsal, we make references to other chapters relevant to the topic at hand. In the electronic form of the textbook, these will take the form of hyperlinks. This will allow the reader to refer to other parts of the book as review if necessary before proceeding to new material.
- **Chapter Review** At the end of each chapter, the student will find some thought questions that can also serve as essay or discussion prompts. The Chapter Reviews also include the list of keyterms.
- **Practice Tests** In the electronic version of the textbook (see the description of MindTap), practice tests will be available for each main heading with a comprehensive practice test at the end of each chapter.

New Features for the Third Edition

Students have told me that the narrative of the textbook is "packed," and that skimming paragraphs is usually a recipe for disaster, as each sentence "counts." In defense, I respond that we have so much to say and so little room to say it in that there is little space for "fluff." At the same time, psychological science shows that spaced learning is superior to massed learning, so it is a good idea to provide regular breaks in the narrative to allow students to catch their breath and digest what they have read. We like to think of these breaks as cool stepping-stones in the flow of lava.

One type of break that we used in the previous editions and continue here in the third is the use of interim summaries that include section summary points and review questions. Most also feature tables that pull together chunks of material in a way that makes it easy to learn. Any complex field like the neurosciences entails a bit of simple, rote memorization to form a foundation for later analysis and critical thinking. The more quickly we can bring students up to speed on the basics, the faster we can move on to higher levels of discussion. Chapter summaries include thought questions designed to push students to think more actively and deeply about what they have read.

In addition to the interim and chapter summaries, each chapter of the third edition includes four types of features. We recognize that "boxing" material often encourages students to overlook content unless expressly instructed to read the boxes, but we trust instructors to use these in ways consistent with their personal style. Obviously, we hope that the content is sufficiently engaging that students will read the material regardless of "what's on the test."

- **Thinking Ethically** features introduce controversial, contemporary questions that require the students to use the information in the chapter in critical ways. Our students will graduate to become community leaders, and they need to be able to think ethically about future cultural choices related to the neurosciences. For example, this feature in Chapter 1 follows a discussion of brain imaging technology with questions about the potential use of brain imaging as a "lie detection" technology.
- **Connecting to Research** features highlight either classic or very contemporary single studies in behavioral neuroscience. This provides students with a "soft" segue into the scholarly literature, which might otherwise seem somewhat intimidating. The feature emphasizes the type of critical thinking and creativity required to advance science. For example, this feature in Chapter 2 describes the re-analysis of Phineas Gage's brain damage using a connectome approach.
- **Behavioral Neuroscience Goes to Work** features expose students to some of the many real-world career paths that relate to behavioral neuroscience. In my experience, many students are unaware of a number of these options. They love the material but have no idea how they can meld this passion with their need to find employment. In this feature in Chapter 5, we describe the role of the genetics counselor, whose insights will be increasingly important as the public obtains

more information about personal genotypes. As a bridge between biological sciences and the counseling professions, this career has become increasingly popular with my students. At least half a dozen who are now enrolled or who have completed genetics counseling master's degrees attribute their career choice to my "selling" this concept in class.

- **Building Better Health** features provide an additional opportunity for students to think critically about behavioral neuroscience in the context of real-world health problems. Do gluten-free diets relieve symptoms of autism spectrum disorder? How well do smartphone sleep apps work? How do you recognize the signs of a stroke?

New Content for the Third Edition

This new edition contains many hundreds of new citations to reflect the advances in the field that have occurred since the previous edition went to press. One of the major sources of change was the publication of DSM-5 in May 2013. The discussion of movement disorders, neurocognitive disorders, and psychological disorders has been updated to match changes made by DSM-5 in terminology and organization.

Illustrations have also been updated to reflect the new content. Because space is so precious, illustrations are viewed as "teachable moments" that expand on or further explain the narrative rather than redundant, "pretty" placeholders. We are especially proud of our medical-quality anatomical illustrations, which have been the source of much positive feedback through the previous editions.

Space does not permit me to provide an exhaustive list of the updates, but here are some of the chapter-by-chapter highlights:

Chapter 1 What Is Behavioral Neuroscience?

- Updated definitions of neuroscience and behavioral neuroscience
- Updated methods section including a description of optogenetics
- Added description of the analysis of epigenetics

Chapter 2 Functional Neuroanatomy and the Evolution of the Nervous System

- Clarified use of anatomical directional terms
- Expanded discussion of embryological divisions of the brain, including organizational table
- Expanded discussion of the parts of the basal ganglia
- Added section on the enteric nervous system
- Added section on the endocrine system

Chapter 3 Neurophysiology: The Structure and Function of the Cells of the Nervous System

- Re-ordered discussion of glia and neurons to improve transition from discussions of neural structure to neural function
- Introduction of concept of axonal varicosities.
- Introduction of distinction between directed and nondirected synapses

Chapter 4 Psychopharmacology

- Clarified use of neurotransmitter, neuromodulator, and neurohormone terms in conjunction with directed and nondirected synapses
- Updated discussion of gasotransmitters
- Added discussion of histamine to the indoleamines
- Expanded discussion of dopaminergic pathways to include the mesostriatal and mesolimbocortical pathways and pathways originating in the hypothalamus
- Expanded discussion of receptor subtypes
- Added discussion of glycine
- Updated discussion of mode of action of methamphetamine and MDMA

Chapter 5 Genetics and the Development of the Human Brain

- Added discussion of copy-number variations (CNVs)
- Added section on epigenetics, including discussion of histone modification and DNA methylation
- Updated discussion of role of astrocytes in synapse formation and pruning
- Expanded discussion of enriched environments
- Expanded section on the brain in adolescence and adulthood, emphasizing healthy brain aging

Chapter 6 Vision

- Added general section introducing concepts of sensation, perception, transduction, and top-down/bottom-up processing
- Distinguished between diffuse and midget bipolar cells in the retina
- Added section on cortical mapping of the visual field
- Added description of akinetopsia

Chapter 7 Nonvisual Sensation and Perception

- Updated and expanded discussion of loudness perception
- Updated section on cochlear implants
- Expanded and clarified discussion of the gate theory of pain
- Expanded discussion of the chemical senses

Chapter 8 Movement

- Added subtypes of muscle spindle fibers and their relationships with Ia and group II sensory fibers
- Updated section on planning of movement
- Updated discussion of mirror systems
- Updated discussion of the causes and treatments for movement disorders, and in particular Parkinson's disease and Huntington's disease

Chapter 9 Homeostasis and Motivation

- Increased coverage of hyperthermia related to MDMA and serotonin syndrome
- Expanded explanation of the preoptic area and temperature regulation

- Updated information about why we stop drinking
- Updated discussion of obesity
- Updated discussion of disordered eating to be consistent with DSM-5, including section on new binge-eating disorder

Chapter 10 Sexual Behavior

- Updated discussion of sex chromosome variations, including mosaic karyotypes
- Expanded discussion of intersex and gender dysphoria
- Increased emphasis on organizing and activating roles of sex hormones in development
- Updated discussion of biomarkers for prenatal hormone environment
- Updated discussion of sexual dimorphism in the brain
- Expanded section on gender differences in behavior and cognition
- Added section on gender identity and transsexuality
- Expanded discussion on sexual orientation
- Updated section on male contraception
- Updated section on attraction, romantic love, and sexual desire
- Updated section on sexual dysfunction and its treatment

Chapter 11 Biorhythms

- Expanded discussion of the effects of artificial lighting on circadian rhythms
- Added discussion of gamma band activity
- Added discussion of default mode network (DMN) and its relationship to levels of consciousness
- Updated section on sleep–wake disorders to conform to DSM-5

Chapter 12 Learning and Memory

- Reorganized chapter material into sections on learning at the synapse and learning involving brain structures and circuits
- Updated information about short-term and long-term learning at the synapse
- Added information on operant conditioning in *Aplysia*
- Added information about extinction learning
- Expanded and updated section on long-term potentiation (LTP)
- Expanded and updated section on the biochemistry of memory
- Updated sections on the effects of stress and healthy aging on memory

Chapter 13 Hemispheric Asymmetry, Language, and Intelligence

- Updated discussion of lateralization to include lateralization "hubs"
- Expanded discussion of the advantages and development of lateralization
- Added section on lateralization, psychological disorders, and disease
- Updated and expanded discussion of gesture and language
- Updated and expanded discussion of multilingualism, including its contribution to cognitive reserve

- Added discussion of dual stream models of language
- Updated discussion of epigenetics and intelligence

Chapter 14 Emotion, Reward, Aggresssion, and Stress

- Expanded discussion of somatic markers
- Updated discussion of roles of amygdala, insula, basal ganglia, and anterior cingulate cortex to emotional processing
- Updated and expanded discussion of mesostriatal pathway, reward, and addiction
- Expanded and updated discussion of epigenetics and aggression
- Distinguished between roles of the sympathetic adrenal-medullary (SAM) system and the HPA axis in responses to stress
- Added section on epigenetics and stress
- Updated section on stress and health

Chapter 15 Neuropsychology

- Reorganized chapter to begin with a discussion of neuropsychology
- Updated and expanded section on neuropsychological assessment
- Updated terms such as neurocognitive disorder to maintain consistency with DSM-5
- Updated and greatly expanded coverage of Alzheimer's disease, which was moved here from Chapter 5 in 2e
- Expanded coverage of traumatic brain injury (TBI) to differentiate between combat-related blast injuries and other types of TBI
- Updated discussion of treatment of TBI
- Added section on substance/medication-induced neurocognitive disorder
- Updated section on HIV-associated neurocognitive disorder
- Updated and expanded section on recovery and treatment of neurocognitive disorders, including discussion of cognitive reserve and "Wii-hab"

Chapter 16 Psychopathology

- Updated the ordering of topics, new terminology, and new diagnostic criteria for all disorders to maintain consistency with DSM-5
- Discussed new research identifying common susceptibility genes for schizophrenia, bipolar disorder, autism spectrum disorder, attention deficit disorder, and major depressive disorder
- Updated discussion of the prevalence, causes, and brain correlates of autism spectrum disorder and attention deficit hyperactivity disorder
- Updated discussion of genetic, biochemical, and brain correlates of schizophrenia
- Introduced the concept of oxidative stress as a correlate of bipolar disorder
- Expanded the discussion of biochemical correlates of major depressive disorder
- Expanded and updated section on posttraumatic stress disorder (PTSD) and the roles of the hippocampus and anterior cingulate cortex in particular
- Discussed the relationship between psychopathy and antisocial personality disorder within the context of DSM-5
- Expanded discussion of biological correlates and treatment of antisocial personality disorder

MindTap

MindTap Psychology for Freberg's *Discovering Behavioral Neuroscience: An Introduction to Biological Psychology,* 3rd edition, is a personalized teaching experience with relevant assignments that guide students to analyze, apply, and improve thinking, allowing you to measure skills and outcomes with ease.

The *Discovering Behavioral Neuroscience* MindTap:

- Delivers assessment and content that moves students into higher-order thinking
- Provides evidence of student performance and a targeted delivery of assets to better engage and further demonstrate concepts both in and out of class
- Provides secure online testing comprised of evidence-based, standard assessment items to ensure students are performing based on their whole learning experience
- Provides first-rate animations and simulated lab experiences that illustrate biological processes

While other publishers offer homework-based solutions that focus on knowledge and comprehension, the *Discovering Behavioral Neuroscience* MindTap learning path includes resources that move students through Bloom's taxonomy utilizing formative and summative assessment and first-class videos, animations, and virtual labs.

Instructor Ancillaries

To further serve the needs of faculty, I have paid close attention to the production of useful ancillaries. As tempting as it was to farm these out in the interests of time and sanity, I have been personally involved with the production of animations as well as the construction of more than 3,000 questions for the Test Bank. Many of these questions have been piloted in my own classes. My questions reflect past collaboration with consultants who specialize in test construction for higher education, and I think you will find them a refreshing change from the usual test banks supplied with textbooks. The following ancillaries give instructors the tools to present course materials according to individual preference:

- ***Instructor's Resource Manual:*** Save time, streamline your course preparation, and get the most from the text by preparing for class more quickly and effectively. The Instructor's Resource Manual contains sample lecture outlines, ideas for classroom demonstrations and handouts, and suggestions for using outside resources in the classroom.
- ***Cengage Learning Testbank Powered by Cognero:*** This is a flexible, online system that allows you to: import, edit, and manipulate content from the text's test bank or elsewhere, including your own favorite test questions; create multiple test versions in an instant; and deliver tests from your LMS, your classroom, or wherever you want.
- ***PowerPoints***: This one-stop lecture and class preparation tool contains ready-to-use Microsoft PowerPoint slides and allows you to assemble, edit, publish, and present custom lectures for your course. Our PowerPoints let you bring together text-specific lecture outlines along with videos, animations based on the art program, or your own materials—culminating in a powerful, personalized, media-enhanced presentation.
- ***The Instructors' Website:*** Log on to the password-protected site to access a wide range of resources, such as electronic versions of the instructor's manual, PowerPoint slides, and more.

Acknowledgments

I view this text as a work in progress. Please take a moment to share your thoughts and suggestions with me: lfreberg@calpoly.edu. You can also find me on Facebook and on my blog: http://www.laurafreberg.com/blog.

I am enormously grateful for the team that Cengage assembled to help make this book a reality. First, I would like to thank my professional colleagues who reviewed the many drafts of the current edition:

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Marcello Spinella *Richard Stockton College of New Jersey*

The many instructors who responded to market research surveys and interviews over the past several years have also contributed greatly to the text and its ancillaries.

I would like to give a special thank you to several colleagues. ***Skirmantis Janusonis*** of the University of California, Santa Barbara, has provided not only encouragement but gentle suggestions for improved accuracy. Skirmantis kindly provided me with an opportunity to photograph some of his human brains (one appears in Chapter 1) and he shared an image of his fantastic dissection of the hippocampus for us to use in Chapter 2. ***Simon LeVay*** is not only a gifted researcher but a truly elegant writer. His careful review of the chapter on sexual behavior for the first edition is deeply appreciated. I am indebted to Simon for pointing out many important studies included in the sections on sexual orientation and gender differences in cognition. ***Marie Banich*** at the University of Colorado at Boulder provided her expert opinions on the art program, and ***Gayle Brosnan-Watters*** at Arizona Christian University contributed many helpful suggestions as a reviewer and while working with me on the third edition of the Test Bank. ***John Cacioppo*** of the University of Chicago generously shared his considerable insight into the social aspects of neuroscience. ***Konstantinos Priftis*** of the University of Padova supplied several helpful corrections to the second edition. ***Robert Matchock*** of the University of Pennsylvania, Altoona, has been a friendly voice of encouragement beginning with the first edition. The late ***Larry Butcher*** of UCLA, one of my former professors, provided valuable assistance in the fine-tuning of my cholinergic pathway image in Chapter 4. ***Rick Howe*** and the students and faculty of the psychology department at College of the Canyons in California not only took the time to meet with me to share their reactions to the first edition but fed me cookies as well.

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Finally, I would like to thank my family for their patience and support. Roger, my husband of 43 years, read every word, helped me choose photos, and even contributed some of our original sketches when I had trouble articulating what I wanted to show. My daughters, Kristin, Karen, and Karla, frequently offered their encouragement and perspectives. I am very much indebted to all.

Laura A. Freberg

CHAPTER 1

What Is Behavioral Neuroscience?

Learning Objectives

L01 Classify the subfields of neuroscience, and explain how behavioral neuroscience fits within the field.

L02 Interpret the significance of the major historical highlights in the study of the nervous system.

L03 Differentiate the brain imaging technologies, including CT, PET, SPECT, MRI, fMRI, and DTI.

L04 Assess the use of histological, recording, stimulation, lesion, optogenetics, and biochemical methods in behavioral neuroscience.

L05 Discuss the relative strengths and weaknesses of twin studies, adoption studies, and the investigation of epigenetics for understanding behavior.

L06 Evaluate the ethical standards used to protect human and animal research participants.

Chapter Outline

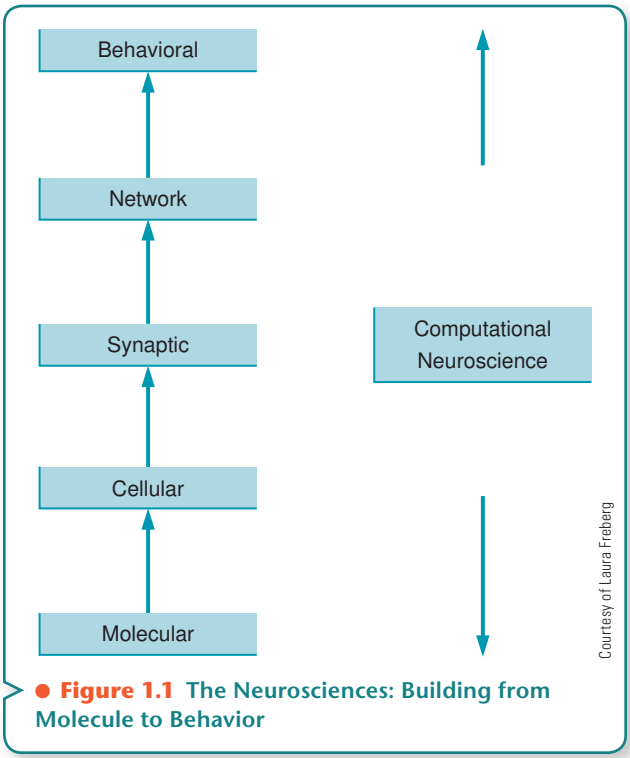
Neuroscience as an Interdisciplinary Field

Neuroscience is the scientific study of the brain and nervous system, in health and in disease (UCLA, 2008). Neuroscientists strive to understand the functions of the brain and nervous system across a number of levels of analysis, using molecular, cellular, synaptic, network, computational, and behavioral approaches. You might think of this field as analogous to Google Earth. We can zoom in to see the tiniest detail and then zoom back out again to see the "big picture."

Beginning at the most microscopic level, the molecular neuroscientist explores the nervous system at the level of the molecules that serve as its building blocks. We will cover their work in our chapters on neural cell physiology (Chapter 3) and psychopharmacology (Chapter 4). Starting with DNA and RNA and the proteins resulting from gene expression, the molecular neuroscientist attempts to understand the chemicals that build the system and make neural functioning possible.

Zooming out just a bit from the molecular level of analysis, we find the cellular neuroscientist hard at work outlining the structure, physiological properties, and functions of single cells found within the nervous system. These isolated cells would be of no use unless they could forge connections, which they do at junctions we call synapses. Synaptic neuroscience examines the strength and flexibility of neural connections, which underlie complex processes such as learning and memory.

Beyond the single synapse, we find that interconnected neurons form pathways or networks. In contemporary neuroscience, we are seeing a move away from the idea that "this structure engages in this function" to ideas that more accurately reflect neural networks that have been identified. We are more likely to say that "this structure participates in a network connecting these other structures to engage in this type of processing."



● **Figure 1.1 The Neurosciences: Building from Molecule to Behavior**

Zooming out perhaps to the most global point of view, we find **behavioral neuroscience**, also known as **biological psychology**, which is the primary focus of this textbook. Behavioral neuroscientists use all of the previous levels of analysis, from the molecular up through the network, in their efforts to understand the biological correlates of behavior. Like the neurosciences in general, behavioral neuroscience looks at the activity of the nervous system in health and in cases of illness or injury. Subspecialties within behavioral neuroscience include cognitive neuroscience, or the study of the biological correlates of information processing, learning and memory, decision making, and reasoning. Social neuroscience explores the interactions between the nervous system and our human social environment and behavior.

Computational neuroscience runs parallel to the types of neuroscience described so far, but draws from computer science, electrical engineering, mathematics, and physics to produce models of the nervous system from the molecular up through the behavioral levels of analysis. The predictions from these computational models can then be tested against living systems, forming a cooperative symbiosis with researchers in other areas of neuroscience.

These different levels of analysis complement each other rather than compete with one another. Because of the diversity of skills needed to pursue each of these approaches, neuroscience is an essentially interdisciplinary field of study, reaching across traditional academic departments of biology, chemistry, psychology, medicine, mathematics, physics, engineering, and computer science.

The need for better understanding of the nervous system has never been greater. The Society for Neuroscience (2012) reported that neurological illnesses impact one out of

neuroscience The scientific study of the brain and nervous system in health and in disease.
behavioral neuroscience/ biological psychology The study of the biological foundations of behavior, emotions, and mental processes.

Behavioral Neuroscience GOES TO WORK

WHAT CAN I DO WITH A DEGREE IN NEUROSCIENCE?

One of the pleasures of teaching courses in behavioral neuroscience occurs when a student suddenly falls in love with the field. "This is for me," the student might say, but the question that usually follows is "But how can I make a living doing this?" The answers to this question are as diverse as the field. Because neuroscience is so broad, opportunities can be found down many different paths.

Like many other fields, neuroscience has more opportunities for people with more education. Many practicing neuroscientists have medical degrees, PhDs, or even both. This does not mean that jobs are unavailable for students with undergraduate degrees, however. Students with undergraduate degrees can be employed as research assistants in pharmaceutical firms, universities, and government agencies. Some neuroscience graduates work in substance abuse counseling or in mental health facilities. Neuroscience is used in some unexpected places as well. A growing trend in advertising agencies is to use brain imaging and other technologies to gauge public reactions to advertising. Web designers use eye-tracking technology to assess whether a person "sees" and processes the important features of a webpage.

The ongoing burst in neuroscience technologies is likely to continue to shape the field, and additional opportunities are likely to emerge. In the meantime, any student interested in neuroscience would benefit from gaining the best possible skills in general science, research methods, mathematics, and statistics.

six Americans annually at a cost of more than $500 billion for treatment, which does not include the cost of disability. Delaying the onset of Alzheimer's disease on an average of five years would save the United States $50 billion in annual health care costs. Connections between biology and behavior are not just relevant to neurological disease, but inform our understanding of health in general. Compared to 100 years ago, when most people died from infectious diseases, today's killers (cancer, diabetes, heart disease) are tightly linked to behavior. Reflecting recognition of the role of behavior in illness, the standardized Medical College Admission Test (MCAT) for medical school applicants contains a significant number of questions about psychology and behavioral neuroscience.

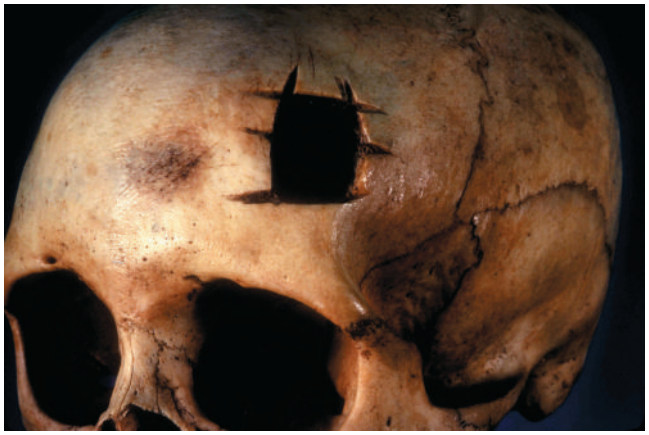
Illness is only part of the human equation. We also need to understand how the nervous system responds in typical ways to promote well-being, including better relationships, better parenting, better child development, and better thinking and learning. Through improved understanding of the nervous system and its interactions with behavior, scientists and practitioners will be more thoroughly prepared to tackle the significant challenges to health and well-being faced by contemporary world populations.

Historical Highlights in Neuroscience

The history of neuroscience parallels the development of tools for studying the nervous system. Early thinkers were limited in their understanding of the structures and functions of the nervous system by lack of scientific methods and technologies and by religious prohibitions regarding autopsy.

Ancient Milestones in Understanding the Nervous System

Our earliest ancestors apparently had at least a rudimentary understanding about the brain's essential role in maintaining life. Archaeological evidence of brain surgery suggests that as long as 7,000 years ago, people tried to cure others by drilling holes in the skull, a process known as trephining or trepanation. Because some skulls have been located that show evidence of healing following the drilling procedure, we can assume that the patient lived through the procedure and that this was not a



Courtesy San Diego Museum of Man

● **Figure 1.2 Prehistoric Brain Surgery** As far back in history as 7,000 years ago, people used trepanation (trephining), or the drilling of holes in the skull, perhaps to cure "afflictions" such as demonic possession. Regrowth around some of the holes indicates that at least some of the patients survived the procedure. More recently, trephining has resurfaced as a DIY (do it yourself) process, possibly as a type of self-injurious behavior.

postmortem ritual. What is less clear is the intent of such surgeries. Possibly, these early surgeons hoped to release demons or relieve feelings of pressure (Clower & Finger, 2001).

The *Edwin Smith Surgical Papyrus* represents the oldest known medical writing in history, yet features many sophisticated observations (Breasted, 1930). The Egyptian author of the *Papyrus* clearly understood that paralysis and lack of sensation in the body resulted from nervous system damage. Cases of nervous system damage were usually classified as "an ailment not to be treated," indicating the author's understanding of the relatively permanent damage involved.

Building on the knowledge taken from ancient Egypt, the Greek scholars of the fourth century BCE proposed that the brain was the organ of sensation. Hippocrates (460–379 BCE) correctly identified epilepsy as originating in the brain, although the most obvious outward signs of the disorder were muscular convulsions (see Chapter 15). Galen (130–200 CE), a Greek physician serving the Roman Empire, made careful dissections of animals (and we suspect of the mortally wounded gladiators in his care as well). Galen believed erroneously that the ventricles played an important role in transmitting messages to and from the brain, an error that influenced thinking about the nervous system for another 1,500 years (Aronson, 2007).

The Dawn of Scientific Reasoning

The French philosopher René Descartes (1596–1650) argued in favor of **mind–body dualism**. For Descartes and other dualists, the mind is neither physical nor accessible to study through the physical sciences. In contrast, the modern neurosciences are based on **monism** rather than dualism. The monism perspective proposes that the mind is the result of activity in the brain, which can be studied scientifically. Descartes's ideas were very influential, and even today some people struggle with the idea that factors such as personality, memory, and logic simply represent the activity of neurons in the brain. Later in the chapter, the discussion of research ethics presents another legacy of Descartes's ideas. Because many shared his view of animals as mechanical, not sentient, beings, experiments were carried out on animals that seem barbaric to many modern thinkers.

Between 1500 and 1800, scientists made considerable progress in describing the structure and function of the nervous system. The invention of the light microscope by Anton van Leeuwenhoek in 1674 opened up a whole new level of analysis. Work by Luigi Galvani and Emil du Bois-Reymond established electricity as the mode of communication used by the nervous system. British physiologist Charles Bell (1774–1842) and French physiologist François Magendie (1783–1855) demonstrated that information traveled in one direction, not two, within sensory and motor nerves.

mind–body dualism A philosophical perspective put forward by René Descartes in which the body is mechanistic, whereas the mind is separate and nonphysical.

monism A philosophical perspective characteristic of the neurosciences in which the mind is viewed as the product of activity in the brain.

Modern Neuroscience Begins

As late as the beginning of the 20th century, many scientists, including Italian researcher Camillo Golgi, continued to support the concept of the nervous system as a vast, interconnected network of continuous fibers. Others, including the Spanish anatomist Santiago Ramón y Cajal, argued that the nervous system was composed of an array of separate, independent cells. Cajal's concept is known as the Neuron Doctrine. Golgi

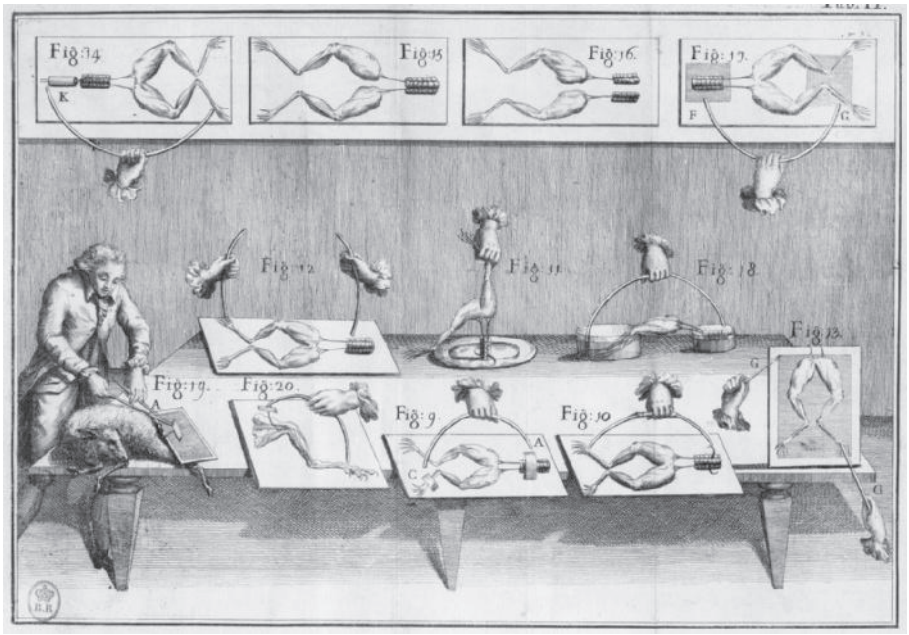
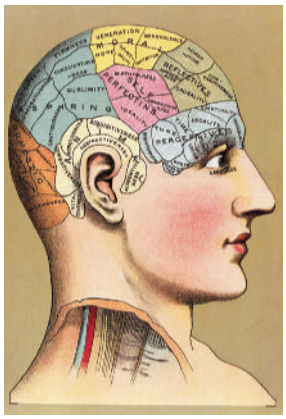


Photo by Time Life Pictures/Mansell/Time Life Pictures/Getty Images

● **Figure 1.3 Luigi Galvani Demonstrated a Role for Electricity in Neural Communication** This engraving illustrates the basement laboratory of Luigi Galvani, where his experiments with frogs helped establish understanding of the electrical nature of neural communication.

and Cajal shared the Nobel Prize for their work in 1906. Ironically, Cajal used a stain invented by Golgi to prove that Golgi was incorrect.

The road to our current understanding of the nervous system has not been without its odd turns and dead ends. The notion that certain body functions are controlled by certain areas of the brain, called localization of function, began with an idea proposed by Franz Josef Gall (1758–1828) and elaborated by Johann Gasper Spurzheim (1776–1832). These otherwise respectable scientists proposed a "science" of **phrenology** that maintained that the structure of an individual's skull could be correlated with his or her individual personality characteristics and abilities. A phrenologist could "read" a person's character by comparing the bumps on his or her skull to a bust showing the supposed location of each trait. Although misguided, Gall and Spurzheim's work did move us away from the metaphysical, nonlocalized view of the brain that had persisted from the time of Descartes. Instead, Gall and Spurzheim proposed a more modern view of the brain as the organ of the mind, composed of interconnected, cooperative, yet relatively independent functional units.



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● **Figure 1.4 Phrenology Bust** Franz Josef Gall and his followers used busts like this one to identify traits located under different parts of the skull. Bumps on the skull were believed to indicate that the underlying trait had been "exercised." Although Gall's system was an example of very bad science, the underlying principle that functions could be localized in the brain turned out to be valuable.

Further evidence in support of localization of function in the brain began to accumulate. In the mid-1800s, a French physician named Paul Broca correlated the damage he observed in patients with their behavior and concluded that language functions were localized in the brain (see Chapter 13). Gustav Theodor Fritsch and Eduard Hitzig (1870/1960) described how electrically stimulating the cortex of a rabbit and a dog produced movement on the opposite side of the body. Localization of function in the brain became a generally accepted concept.

The founding of modern neuroscience has often been attributed to the British neurologist John Hughlings Jackson (1835–1911). Hughlings Jackson proposed that the nervous system was organized as a hierarchy, with simpler processing carried out by lower levels and more sophisticated processing carried out by the higher levels, such as the cerebral cortex. We meet Hughlings Jackson again in Chapter 15, in which his contributions to the understanding of epilepsy will be discussed.

Progress in the neurosciences over the past 100 years accelerated rapidly as new methods became available for studying the nervous system. Charles Sherrington not only coined the term *synapse* (defined as the point of communication between two neurons), but also conducted extensive research on reflexes and the motor systems of the brain (see Chapter 8). Otto Loewi demonstrated chemical signaling at the synapse (see Chapter 3),

phrenology The misguided effort to correlate character traits with bumps in the skull.

using an elegant research design that he claims came to him while asleep. Sir John Eccles, Bernard Katz, Andrew Huxley, and Alan Hodgkin furthered our understanding of neural communication. You will meet many more contemporary neuroscientists as you read the remainder of this text. The ranks of neuroscientists continue to grow, with membership in the Society for Neuroscience expanding from 500 members in 1969 to more than 42,000 members in 90 countries as of 2014 (Society for Neuroscience).

INTERIM SUMMARY 1.1

Highlights in the Neuroscience Timeline

Historical Period	Significant Highlights and Contributions
Ca. 3000 BCE	• Egyptians discard brain during mummification process; however, published case studies indicate accurate observations of neural disorders.
Ca. 400 BCE–200 CE	• Hippocrates recognizes that epilepsy is a brain disease. • Galen makes accurate observations from dissection; however, he believed erroneously that fluids transmitted messages.
1600–1800	• René Descartes suggests mind-body dualism. • Anton van Leeuwenhoek invents the light microscope. • Galvani and du Bois-Reymond discover that electricity transmits messages in the nervous system.
1800–1900	• Bell and Magendie determine that neurons communicate in one direction and that sensation and movement are controlled by separate pathways. • Gall and Spurzheim make inaccurate claims about phrenology, but their notion of localization of function in the nervous system is accurate. • Paul Broca discovers localization of speech production. • Fritsch and Hitzig identify localization of motor function in the cerebral cortex.
1900–Present	• Ramón y Cajal declares that the nervous system is composed of separate cells; he shares the 1906 Nobel Prize with Camillo Golgi. • John Hughlings Jackson explains brain functions as a hierarchy, with more complicated functions carried out by higher levels of the brain. • Otto Loewi demonstrates chemical signaling at the synapse. • Charles Sherrington coins the term *synapse*; he wins the Nobel Prize in 1932. • Sir John Eccles, Andrew Huxley, and Alan Hodgkin share the 1963 Nobel Prize for their work in advancing our understanding of the way neurons communicate. • Bernard Katz receives the 1970 Nobel Prize for his work on chemical transmission at the synapse. • Society for Neuroscience counts more than 42,000 members in 2012.

Summary Points

1. Neuroscience is the field that explores the structures, functions, and development of the nervous system in illness and in health. Behavioral neuroscience is

the branch of the neurosciences that studies the correlations between the nervous system and behavior. **(L01)**

2. Although some periods of enlightenment regarding the relationship between the nervous system and behavior emerged among the Egyptians and Greeks, the major advances in biological psychology have been relatively modern and recent. **(L02)**
3. Highlights in the neuroscience timeline include discoveries regarding the electrical and chemical nature of neural communication, the control of sensation and motor functions by separate nerves, the role of single cells as building blocks for the nervous system, and the localization of functions in the brain. **(L02)**

Review Questions

1. How would you describe the goals and methods of the interdisciplinary field of neuroscience?
2. What historical discoveries contributed to our modern understanding of the brain and behavior? Which concepts actually led us in the wrong direction?

Behavioral Neuroscience Research Methods

The methods described in this section have helped neuroscientists discover the structure, connections, and functions of the nervous system and its components. From the level of single nerve cells to the operation of large parts of the nervous system, we now have the ability to make detailed observations that would likely astonish the early pioneers of neuroscience.

Histology

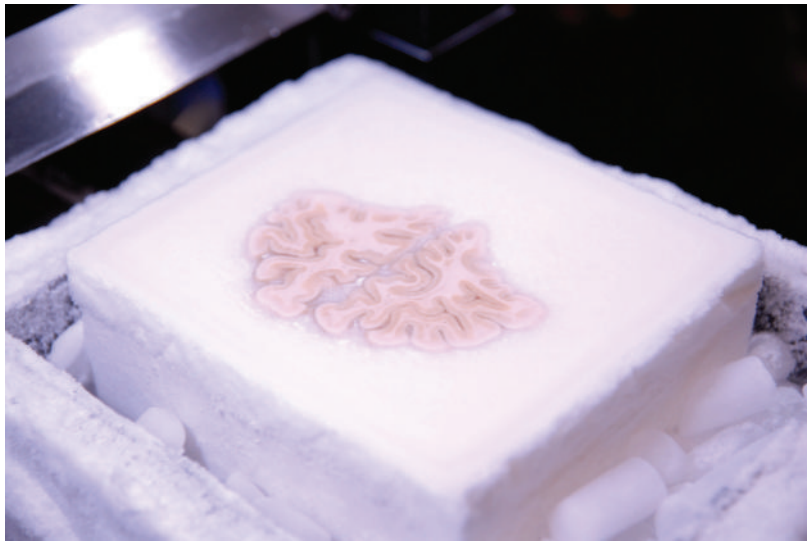
Histology refers to the study of microscopic structures and tissues. Histological methods provide means for observing the structure, organization, and connections of individual cells. As mentioned earlier, the first investigation of nerve tissue under a microscope was conducted by Anton van Leeuwenhoek in 1674. However, due to the technical challenges of viewing structures as small and complex as those found in the nervous system, most of the advances in microscopy occurred following the development of stronger, clearer lenses during the 1800s.

Tissue to be studied under the microscope must be prepared for viewing in a series of steps. Tissue must be made thin enough to allow light to pass through it. Brain tissue is fragile and somewhat watery, which makes the production of thin enough slices impossible without further treatment. To solve this problem, the first step in the histological process is to "fix" the tissue, either by freezing it or by treating it with formalin, a liquid containing the gas formaldehyde. Formalin not only hardens the tissue, making it possible to produce thin slices, but it also preserves the tissue from breakdown by enzymes or bacteria. Freezing the tissue accomplishes these objectives as well.

Once tissue is fixed, it is sliced by a special machine known as a **microtome**. A microtome typically looks and works like a miniature version of the meat slicers found in most delicatessens. The tissue is pushed forward while a sliding blade moves back and forth across the tissue, producing slices. For viewing tissue under the light microscope, tissue slices between 10 and 80 μm (micrometers) thick are prepared. A micrometer is one one-millionth of a meter or one one-thousandth of a millimeter. Electron microscopes require slices of less than 1 μm. The fragile slices are mounted on slides for viewing. Sectioning a single rat brain produces several thousand slides.

Even when fixed and mounted on slides, nerve tissue would appear nearly transparent under the microscope if it were not for a variety of specialized stains. Researchers select particular stains depending on the features they wish to examine. For example,

histology The study of cells and tissues at the microscopic level.
microtome A device used to make very thin slices of tissue for histology.



● **Figure 1.5 Using a Microtome to Section Patient H.M.'s Brain** Researchers at UC San Diego broadcast the careful sectioning of the brain of the late Henry Molaison, otherwise known as the famous amnesic patient H.M., via streaming video on the Internet. Molaison's temporal lobe surgery and the resulting memory deficits he experienced are familiar to all students of psychology.

to make a detailed structural analysis of a small number of single cells, the best choice is a **Golgi silver stain**, named after its discoverer, Camillo Golgi. On the other hand, you might be more interested in identifying clusters of cell bodies, the major bulk of the nerve cell, within a sample of tissue. In this case, you would select a **Nissl stain**. A **myelin stain** would allow you to follow pathways carrying information from one part of the brain to another by staining the insulating material that covers many nerve fibers. If you know where a pathway ends but would like to discover its point of origin, you should use **horseradish peroxidase**. When this enzyme is injected into the end of a nerve fiber, it travels backward toward the cell body. Antibodies, proteins normally produced by the immune system to identify invading organisms, can be combined with a variety of dyes to highlight particular proteins found in cells in a process known as immunohistochemistry (IHC). In particular, antibodies are helpful in identifying the activity of the c-Fos gene in the brain, which in turn is a reliable indicator of brain activity in response to a wide variety of stimuli such as administration of methamphetamine (Cornish, Hunt, Robins, & McGregor, 2012).

Once tissue is appropriately prepared, it can be viewed under either a light or electron microscope. Electron microscopes, first developed in Germany in the 1930s, use short, highly concentrated electron beams rather than light to form images. Modern electron microscopes produce magnifications of up to one million times. Using an electron microscope, Sanford Palay and George Palade (1955) provided the first clear images of the synapse (see Chapter 3).

Autopsy

Researchers have frequently relied on observations made during an **autopsy**, or examination of the body following death. The word *autopsy* means "to view for oneself." Although autopsy for research purposes has been largely replaced by modern imaging methods, it remains a useful technique. Simon LeVay (1991) used autopsy to examine an area of the brain known as INAH-3 (see Chapter 10). LeVay believed that the size of INAH-3 might be used to differentiate between homosexual and heterosexual males. Because this structure was too small to see well with existing imaging techniques, LeVay studied the brains of deceased individuals. Autopsies, like other correlational methods, must be interpreted carefully and precisely. Although LeVay's data indicate that differences in brain structure are correlated with sexual orientation, we cannot conclude on the basis of these correlational data that brain structure either causes or is caused by sexual orientation.

Golgi silver stain A stain developed by Camillo Golgi used to observe single neurons.
Nissl stain A stain used to view populations of cell bodies.
myelin stain A stain used to trace neural pathways.
horseradish peroxidase A stain used to trace axon pathways from their terminals to points of origin.
autopsy The examination of body tissues following death.

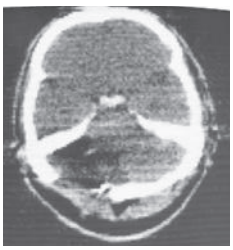
Imaging

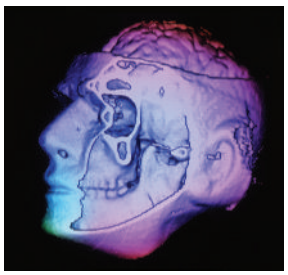
New imaging techniques provide significant advantages over autopsy. With current imaging technologies, we can watch the living brain as it engages in processes such as reading (Chapter 13) or emotional response (Chapter 14). We can identify differences in the ways the brains of serial murderers function compared with the brains of typical people (Chapter 16).

COMPUTERIZED TOMOGRAPHY (CT) The groundwork for brain imaging was laid by German physicist Wilhelm Röntgen, who discovered X-rays in 1896. Röntgen was astonished to learn that X-rays could move through the human body and that they would produce a negative photographic image of the body's major structures. The first X-ray ever taken was an image of Röntgen's wife's hand.

Normal X-rays do not do a very good job of imaging soft tissue. If you have ever seen an X-ray of your head taken by your dentist or orthodontist, you probably saw bones and teeth, but not much brain. However, with adaptations made possible by more modern computers, X-rays can be used to image previously unseen anatomical structures. **Computerized tomography (CT)** was invented in 1972 by Godfrey Hounsfield and Allan Cormack. "Tomography" comes from the Greek words *tomos,* or slice, and *graphia,* to write or describe. CT technology provided the first high-resolution look at a living brain. More modern CT technology allows for the construction of highly detailed three-dimensional images.

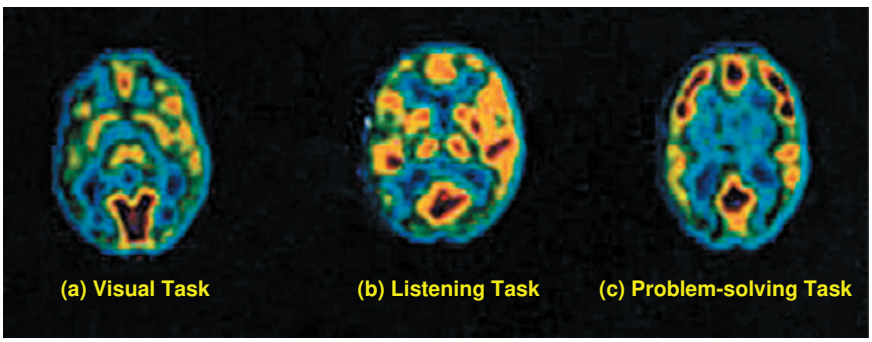
However useful CT scanning may be for medical imaging, the technology does have drawbacks for research purposes. Although it provides excellent structural information, a CT scan cannot distinguish between a living brain and a dead one. In other words, the CT scan provides no information regarding activity levels in the brain. This limits the usefulness of CT in helping us answer questions about behavior.


Courtesy of Siemens Healthcare


GJLP, CNRI/Science Source

● **Figure 1.6 CT Scans** Hounsfield's original machine took several hours to obtain data for a single slice (above). Modern scanning equipment is much faster, and can produce detailed 3-D images (bottom).

POSITRON EMISSION TOMOGRAPHY (PET) The next major breakthrough in imaging technology was the development of the **positron emission tomography**, or **PET**, scan, which allowed researchers to observe brain activity for the first time. PET scans were made possible by the invention of the gamma camera, which is used to detect radiation released by radioactive atoms that are decaying or breaking up. Beginning in the mid-1970s, Michael Phelps and Edward Hoffman of Washington University began to apply this basic technique to the study of brain function (Hoffman, Phelps, Mullani, Higgins, & Ter-Pogossian, 1976; Phelps, Hoffman, Mullani, Higgins, & Ter-Pogossian, 1976).



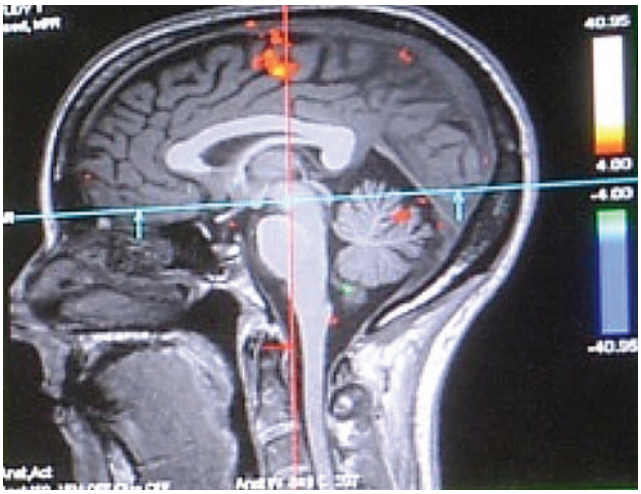
Courtesy Dept. of Energy Office of Public Affairs

● **Figure 1.7 PET Scans Show Patterns of Brain Activation** PET scans do not provide much structural detail, but they do offer a clear picture of brain activity. Red and yellow areas are most active, whereas blue and black areas are least active. These three images show different patterns of brain activity during a visual task, a listening task, and a problem-solving task.

computerized tomography (CT) An imaging technology in which computers are used to enhance X-ray images.
positron emission tomography (PET) An imaging technique that provides information regarding the localization of brain activity.

PET brain studies combine radioactive tracers with a wide variety of molecules, including oxygen, water, and drugs. Each gamma ray resulting from the breakdown of the tracer is recorded by detectors and fed to a computer, by which the data are reconstructed into images. Typically, programmers have assigned red and yellow to areas of high activity and green, blue, and black to areas of low activity. Newer PET machines can take images of adjacent slices at the same time, which allows for three-dimensional reconstruction of brain activity. A closely related procedure, single photon emission computed tomography (SPECT), is less expensive than PET but provides less visual detail.

MAGNETIC RESONANCE IMAGING (MRI) **Magnetic resonance imaging**, or **MRI**, has become a standard medical diagnostic tool and a valuable research asset. Raymond Damadian, Larry Minkoff, and Michael Goldsmith produced the first MRI image in 1977. This imaging technology uses powerful magnets to align hydrogen atoms within a magnetic field. Next, radio frequency (RF) pulses are directed at the part of the body to be imaged, producing "resonance," or spinning, of the hydrogen atoms. When the RF pulses cease, the hydrogen atoms return to their natural alignment within the magnetic field. As the atoms "relax," each becomes a miniature radio transmitter, emitting a characteristic pulse that is detected by the scanner. To construct the image, each small area of tissue is assigned a **voxel**, which is a three-dimensional version of a pixel. The darkness or coloration of each voxel represents the level of pulse activity in an area.



Courtesy of Laura Freberg

● **Figure 1.8 Functional Magnetic Resonance Imaging (fMRI) Tracks Cerebral Blood Flow** This image demonstrates the use of fMRI to identify parts of the brain (the red and yellow areas) that became selectively active when the author engaged in a "finger tap" exercise (touching each digit of her right hand one by one with her thumb).

Functional MRI (fMRI) is used to assess brain activity. The first fMRI of the brain was conducted by Belliveau et al. (1991). Functional MRI takes advantage of the fact that active neurons require more oxygen than less active neurons, and that variations in blood flow to a particular area will reflect this need.

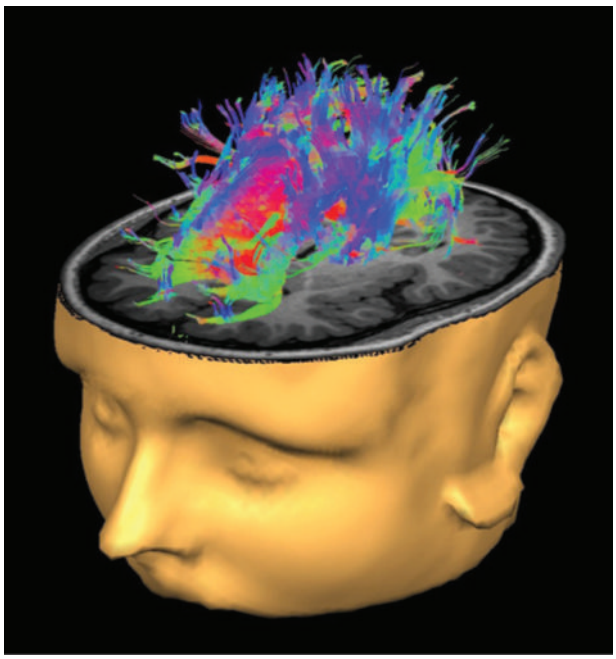
The use of fMRI to track blood flow in the brain was previewed in the 19th century by America's first official psychologist, William James, who was impressed by the observations of Italian physiologist Angelo Mosso on patients with head injuries. Due to the nature of these injuries, in which some of the patients' skull bones were missing or damaged, Mosso was able to measure and correlate blood flow with the patients' mental activity (Mosso, 1881). James's reflections on Mosso's work sound very contemporary: "Blood very likely may rush to each region of the cortex according as it is most active, but of this we know nothing" (James, 1890, vol. 1, p. 99). Mosso's observations were confirmed by Roy and Sherrington (1890), who reported the existence of "an automatic mechanism by which the blood supply of any part of the cerebral tissue is varied in accordance with the activity of the chemical changes which underlie the functional action of that part" (p. 105).

How does fMRI track cerebral blood flow? Hemoglobin, the protein molecule that carries oxygen within the blood, has different magnetic properties when combined with oxygen or not (Ogawa, Lee, Kay, & Tank, 1990). Consequently, signals from a voxel will change depending on the oxygenation of the blood in that area, known as the Blood Oxygenation Level Dependent (BOLD) effect. Let's look at an example of the author's own results of a standard demonstration conducted at the Brain Imaging Laboratory at the University of California, Santa Barbara. Scans were taken as the author alternated 20 second intervals of remaining very still with 20 second intervals of touching her right thumb to each of the other digits of her right hand one at a time. The image highlights the voxels that showed changes in activity correlated with movement and stimulation.

magnetic resonance imaging (MRI) An imaging technique that provides very high resolution structural images.
voxel Short for "volume pixel." A pixel is the smallest distinguishable square part of a two-dimensional image. A voxel is the smallest distinguishable box-shaped part of a three-dimensional image.
functional MRI (fMRI) A technology using a series of MRI images taken one to four seconds apart in order to assess the activity of the brain.
diffusion tensor imaging (DTI) Use of MRI technology to trace fiber pathways in the brain by tracking the flow of water.

MRI technology has significant advantages over both CT and PET. It can provide images taken at any angle without any movement of the individual. In tracking brain activity, fMRI is considered superior in both spatial and temporal resolution to PET scans (Cohen & Bookheimer, 1994).

The same machinery used for MRI and fMRI can also produce images using **diffusion tensor imaging (DTI)**. This technique allows researchers to track the movement of water in the fiber pathways of the nervous system (Le Bihan & Breton, 1985; Moseley et al., 1990). Using this technique, the negative effects of occasional binge drinking episodes on brain fiber integrity in adolescents becomes all too apparent (McQueeny et al., 2009).



Parkinson Research Foundation

● **Figure 1.9 Diffusion Tensor Imaging (DTI)** Using MRI technology, the flow of water down the length of nerve fibers can be imaged to construct maps of the fiber pathways of the brain.

Recording

Although perhaps less dramatic than the imaging techniques, methods that allow researchers to record the electrical and magnetic output from the brain continue to be useful. As we will see in greater detail in Chapter 3, nerve cells are capable of generating small electrical charges across their membranes, much like miniature batteries. Although small in scale, this electrical activity can be recorded using electrodes either on the surface of the skull or brain or imbedded within the brain tissue itself.

●●● Connecting to **Research**

SOCIAL PAIN AND THE BRAIN

Nobel Laureate Konrad Lorenz wrote that "It is a good morning exercise for a research scientist to discard a pet hypothesis every day before breakfast. It keeps him young." This is often easier said than done, but with the rapid changes we experience in the world of neuroscience, being able to update your thinking is an essential skill.

One of the most "fun" results that many instructors of behavioral neuroscience have shared with students is the work of Naomi Eisenberger and her colleagues (2003), in which a Cyberball game was used to initiate feelings of social isolation. Brain imaging of the 13 participants indicated that the brain's "pain matrix," which included a structure known as the anterior cingulate cortex (ACC), was activated by this experience of social pain. In other words, the brain had appeared to co-opt the system responsible for responding to physical pain for use in responding to social pain. Publication by Eisenberger et al. (2003) was followed by a long string of positive replications.

One of the challenges of using fMRI is the statistical analyses involved. Brains come in rather different sizes and shapes, and to make any conclusions, the researcher must demonstrate that activity in a voxel in one brain is analogous to activity in a voxel in a completely different brain. The methods used to conduct these analyses have continued to evolve along with the technology. So 10 years after Eisenberger et al. (2003) published their original report, Stephanie Cacioppo and her colleagues (2013) used multilevel kernel density analysis (MKDA) to conduct a meta-analysis of Cyberball imaging studies featuring 244 participants. This analysis failed to support the attractive notion that social and physical pain activate the same network. Instead, Cacioppo et al. (2013) argue that the "neural correlates of social pain are more complex than previously thought" (p. 1).

One of the common themes of study in the neurosciences is that things always seem to become "more complex than previously thought" as technologies improve. While this can be occasionally frustrating, as we all tend to prefer straightforward answers instead of "it depends," good science requires that we continue to modify our thinking to be as accurate as possible.

THINKING *Ethically*

CAN WE READ MINDS WITH BRAIN IMAGING?

In the 2002 film *Minority Report*, Tom Cruise plays a police officer who arrests people for crimes they have not yet committed. How close are we to knowing what people are planning to do before they actually do it? Perhaps closer than you think.

Current imaging technologies, such as fMRI, do not exactly allow us to "read" the human mind, but we are getting ever closer to that ability (Tong & Pratte, 2012). For example, researchers were able to use fMRI recordings taken while a participant watched Steve Martin playing Inspector Clouseau in the movie *The Pink Panther* to reconstruct the image (Nishimoto et al., 2011).

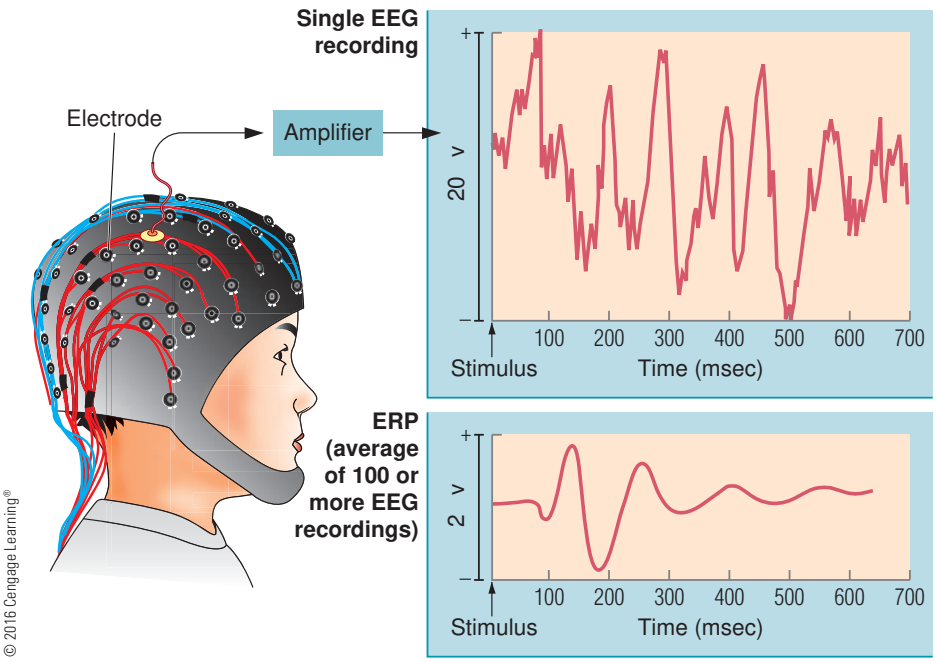
Of even greater importance for society is the fact that researchers are closing in on the ability to use fMRI to detect deception (Langleben, Willard, & Moriarty, 2012). As we will see in our discussion of emotion in Chapter 14, typical lie detection technologies, which rely on indirect measures of arousal, are so poor that they are not admissible as court evidence in the United States. The ability to detect deception directly through brain imaging promises enormous benefits to criminal justice and national security, but raises equally substantial concerns about ethics. Not only can we envision the legislative need to expand our constitutional right to privacy to include "mental privacy," but legislators will also have to consider that the new technology may acquire information from brain scans that is irrelevant to the purpose of the investigation in the first place.

THE ELECTROENCEPHALOGRAM (EEG) The first recordings of the human brain's electrical activity, measured through electrodes placed on the scalp, were made by a German psychiatrist, Hans Berger, in 1924. Berger noted that the recordings varied during wakefulness, sleep, anesthesia, and epilepsy. Chapter 11 investigates the relationship between the EEG and these states of consciousness in greater detail.

For many years, EEG technology did not change much. Although it was useful in the study of sleep and the diagnosis of epilepsy, EEG did not offer anything further to our understanding of brain function. With the advent of more powerful computers, however, new quantitative methods for analyzing EEG recordings became possible. Computerized EEG brain tomography can be used to generate maps of activity, making it possible to pinpoint the source of abnormal activity. EEG brain tomography can be used to follow a patient through withdrawal from psychoactive drugs or during a coma. The technique can aid in diagnoses of many disorders, including schizophrenia, dementias, epilepsy, and attention deficit hyperactivity disorder (see Chapters 5, 15, and 16). Computerized analysis of EEG recordings can be used to generate animations of activity over time and for the construction of three-dimensional maps of brain activity. These analysis tools have breathed new life into EEG technology.

EVENT-RELATED POTENTIALS (ERPS) An application of basic EEG technology used to assess sensation is the recording of **event-related potentials (ERPs)**. This technique allows researchers to correlate the activity of cortical sensory neurons recorded through scalp electrodes with stimuli presented to the participant. The brain's electrical activity in response to a stimulus, such as a tone, is quite small compared to the activity normally recorded in an EEG, so responses to many presentations of a stimulus are averaged. This type of analysis can be helpful in cases in which a person's behavior does not provide a clear indication of whether a particular stimulus has been perceived. For example, young children with autism spectrum disorder (see Chapter 16) often behave as though their hearing were impaired. When spoken to by parents or others, a child with autism spectrum disorder often shows no reaction at all. Through observations of event-related potentials to sound, we can determine whether the child can actually hear.

electroencephalogram (EEG) The recording of the brain's electrical activity through electrodes placed on the scalp.
event-related potential (ERP) An alteration in the EEG recording produced in response to the application of a particular stimulus.



● **Figure 1.10 Event-Related Potentials (ERPs)** The analysis of event-related potentials allows researchers to map the brain's EEG response to environmental stimuli. In this example, a characteristic waveform emerges when responses to the presentation of a tone are averaged over 100 trials.

MAGNETOENCEPHALOGRAPHY (MEG) **Magnetoencephalography (MEG)** allows researchers to record the brain's magnetic activity (Cohen, 1972). Active neurons put out tiny magnetic fields. By "tiny," we mean that the fields generated by neural activity are about one billion times smaller than Earth's magnetic field and about 10,000 times smaller than the field surrounding a typical household electric wire. The major advantage of recording magnetism rather than electrical activity from the brain relates to the interference of the skull bones and other tissues separating the brain from the electrodes, which prevents a large amount of the brain's electrical activity from being recorded using EEG. In contrast, the skull bones and tissues allow magnetism to pass through without any reduction. In addition, recordings of the magnetic fields produced by the brain can be taken much faster than either fMRI or PET scans, providing a moment-by-moment picture of brain activity. MEG has the added advantage of being silent, as opposed to the loud hammering sound produced by the magnets used in MRI. Consequently, MEG provides researchers with an important technique for studying brain responses to sound.

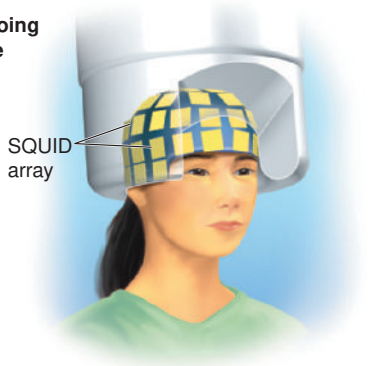
MEG utilizes sensors known as superconducting quantum interference devices, or SQUIDs, that convert magnetic energy into electrical impulses that can be recorded and analyzed. Because MEG does not provide any anatomical data, researchers superimpose MEG recordings on three-dimensional images obtained with MRI. This combination provides simultaneous information about brain activity and anatomy. Not only does MEG allow researchers to localize cognitive functions such as language, but it also provides precise localization of the source of the abnormal electrical activity that characterizes a seizure (see Chapter 15).

SINGLE-CELL RECORDINGS The activity of single neurons can be assessed using tiny microelectrodes surgically implanted in the area of interest. Electrodes can be permanently implanted, allowing animals free range of movement during stimulation.

The use of single-cell recordings was pioneered by Vernon Mountcastle, David Hubel, and Torsten Wiesel for use in their investigations of the visual system. More recently, this technique was used to identify mirror neurons, or neurons that fire in response to an action, like reaching for a banana, whether the reaching is done by a monkey or an experimenter (Caggiano et al., 2011; Pellegrino, Fadiga, Fogassi, Gallese, & Rizzolatti, 1992).

magnetoencephalography (MEG) A technology for recording the magnetic output of the brain.
single-cell recording The recording of the activity of single neurons through microelectrodes surgically implanted in the area of interest.

● **Figure 1.11 Magnetoencephalography (MEG)** (a) To record the tiny magnetic fields generated by the brain, a series of supercooled sensors known as superconducting quantum interference devices (SQUIDs) are arrayed around the participant's head. (b) This sequence illustrates the process of using MEG to record a participant's response to a tone.



Brain Stimulation

One of the important questions raised in behavioral neuroscience relates to the localization of functions within the brain and nervous system. Although this question can be approached with a number of techniques, we can begin by artificially stimulating the area in question and watching for resulting behavior. Interpretation of the results of stimulation research must be done with great caution. Because brain structures are richly connected with other areas of the brain, stimulating one area will also affect other areas to which it is connected.

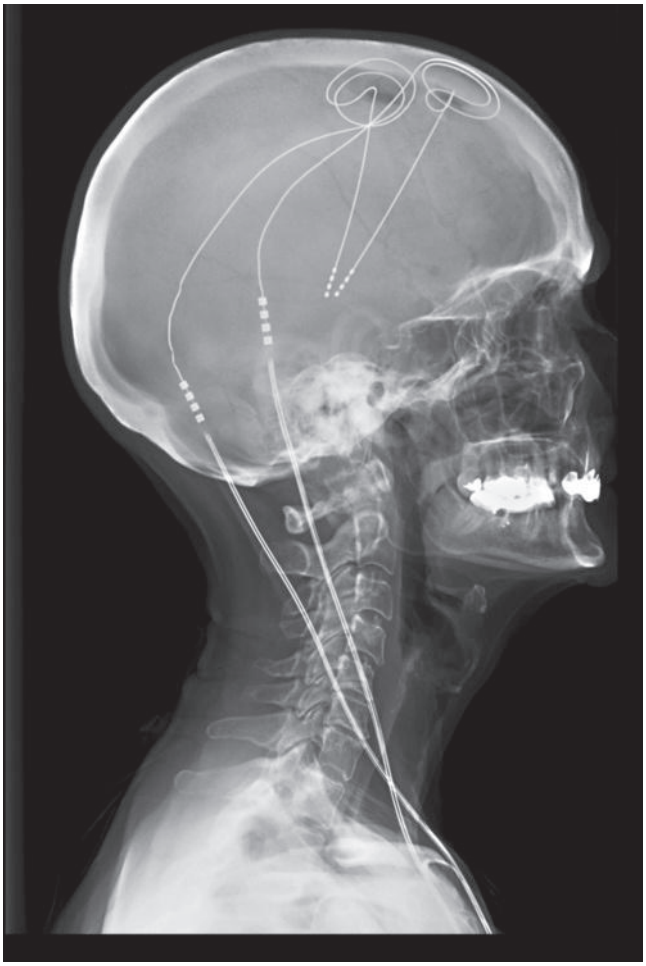
Electrical stimulation of the brain can be applied during neurosurgery. As unpleasant as it may sound to you, most neurosurgery is conducted under local, as opposed to general, anesthesia. The tissues of the brain itself lack receptors for pain. Once the bone and the tissues covering the brain are anesthetized, the surgeon can work on the brain of the conscious patient without causing pain. Why would we put people through such an unpleasant experience? Although brains are similar in many ways from person to person, individual differences frequently do occur. By stimulating an area with a small amount of electricity and assessing any changes in behavior,

the surgeon can identify whether the area participates in a particular type of behavior.

Considerable knowledge regarding the mapping of the functions of the cortex has been derived from this technique. Neurosurgeon Wilder Penfield investigated the brains of more than a thousand patients undergoing surgery for the treatment of epilepsy (see Chapter 15). Penfield's work contributed significantly to our understanding of the mapping of movement, memory, and language (Penfield, 1958). Penfield's stimulation was restricted to the surface of the cortex. Others have investigated stimulation of deeper structures through implanted electrodes. Robert Heath (1963) implanted electrodes in a patient who suffered from the sleep disorder narcolepsy (see Chapter 11) and allowed the patient to push a button that administered a brief electrical stimulus. The patient was able to describe his reactions to stimulation of each of the 14 electrodes implanted in his brain. One of the electrodes, which the patient activated most frequently, elicited sexual arousal.

Encouraged by the improvements provided by brain stimulation in patients with the movement disorder Parkinson's disease, discussed in Chapter 8, physicians have begun to surgically implant electrodes in areas of the brain believed to participate in feelings of reward to treat individuals with depression (Bewernick et al., 2010).

Repeated transcranial magnetic stimulation (rTMS) consists of magnetic pulses delivered through a single coil of wire encased in plastic that is placed on the scalp. Low frequency rTMS (about one pulse per second) provides an interesting technique for temporarily changing brain activity immediately below the stimulation site (Hoffman et al., 2003). This technique has shown promise in the treatment of auditory hallucinations associated with schizophrenia and of depression (Slotema, Blom, Koek, & Sommer, 2010). Repeated TMS has also been shown to temporarily produce unusual calculation skills, like those occasionally found in people with autism spectrum disorder, in healthy participants (Snyder, 2006).



Living Art Enterprises/Science Source

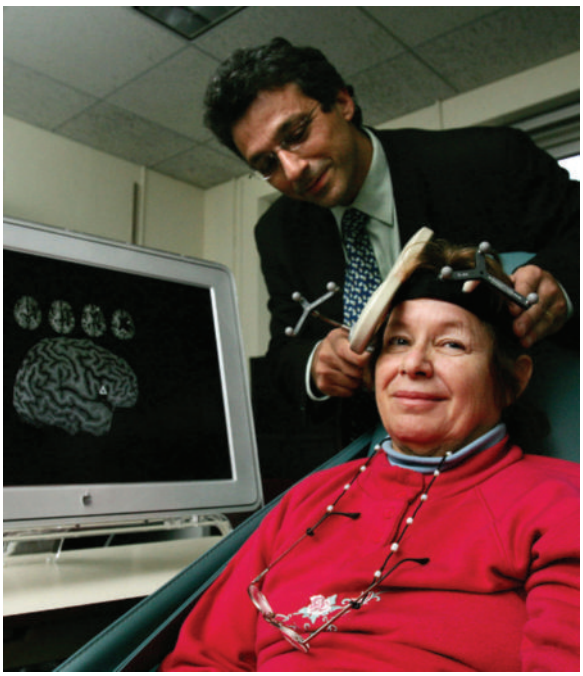
● **Figure 1.12 Deep Brain Stimulation** In research, brain stimulation is typically used to identify the possible functions of a part of the brain. Recently, brain stimulation has been used to treat Parkinson's disease and, less frequently, major depressive disorder.

Optogenetics (Boyden, 2011) involves the use of molecules genetically inserted in specific neurons in the brain, which then allows neural function to be modified by light. In other words, light can be used to turn living neurons on and off. Stimulation is provided through optical fibers attached to the skull or surgically implanted. In one study, optogenetics was used to confirm a role for the chemical messenger glutamate (see Chapter 4) in pathways involved with reward and addiction (Tecuapetla et al., 2010).

repeated transcranial magnetic stimulation (rTMS) A technique for stimulating the cortex at regular intervals by applying a magnetic pulse through a wire coil encased in plastic and placed on the scalp.
optogenetics The genetic insertion of molecules into specific neurons that allows the activity of the neurons to be controlled by light.
lesion Pathological or traumatic damage to tissue.

Lesion

A **lesion** is an injury to neural tissue and can be either naturally occurring or deliberately produced. As was the case with stimulation, the primary purpose of lesion analysis is to assess the probable function of an area. Behavior observed prior to the lesion can be compared with behavior occurring after the lesion, with changes



AP Images/Charles Krupa, File

● **Figure 1.13 Repeated Transcranial Magnetic Stimulation (rTMS)** Repeated TMS changes the activity of the cortex underlying the stimulator. The technique is used for research purposes and potentially could be used for treating hallucination, depression, and migraine headaches.

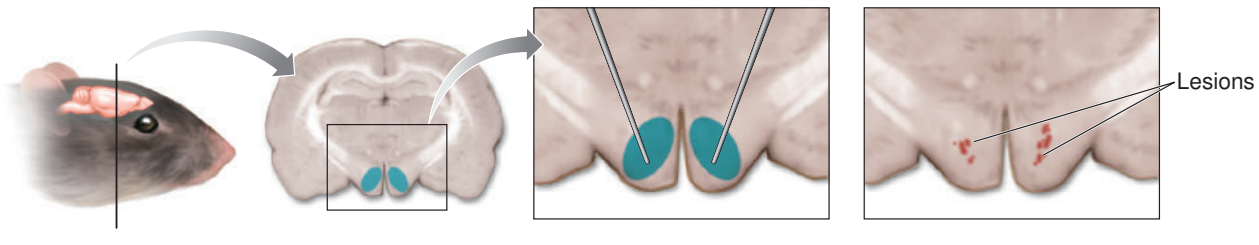
attributed to the area that was damaged. Once again, interpretation must be done very carefully. Lesions not only damage a particular area of the brain but also damage any nerve fibers passing through that area.

Neuropsychologists (see Chapter 15) evaluate naturally occurring lesions that result from injury or disease, gaining a great deal of information about the function of the brain. Many examples of this type of analysis will be discussed in the remainder of the text. The ability to perform an autopsy allowed Paul Broca to make the previously mentioned correlations between the damage he observed and the clinical observations he made during the patient's lifetime.

Deliberate lesions are generally performed in research using laboratory animals, as opposed to human participants. However, as we will see in Chapter 15, lesions are occasionally used to treat cases of epilepsy that do not respond to medication. The technique of producing deliberate lesions in research animals originated with Pierre Flourens in the 1800s. A classic example of lesion work using animals identified a role for the ventromedial hypothalamus (VMH) in satiety (Hoebel & Teitelbaum, 1966). When this area is electrically stimulated, an animal will stop eating. When this area is lesioned, the animal eats so much that its body weight can double or even triple (see Chapter 9).

Deliberate lesions are performed in a number of ways. In some studies, large areas of brain tissue are surgically removed. In this case, we might refer to the procedure as **ablation** rather than lesion. Lesions are experimentally produced when an electrode is surgically inserted into the area of interest. The electrode is insulated except at the very tip, to prevent damage to cells lining the entire pathway of the electrode. Heat is generated at the tip of the electrode, effectively killing a small population of cells surrounding the tip. Small lesions can also be produced by applying neurotoxins, chemicals that specifically kill neurons, into the area of interest through a surgically implanted micropipette. Chemically produced lesions have the advantage of harming only the cell bodies of neurons while leaving the nerve fibers traveling through the area intact. Conversely, fiber pathways can be chemically lesioned while sparing adjacent cell bodies. Obviously, both heat-produced and chemically produced lesions result in permanent damage to the brain. A reversible type of lesion can be produced by cooling

ablation The surgical removal of tissue.



● **Figure 1.14 Lesion** To investigate the function of a particular part of the brain (a), radio frequency current is passed through the tips of insulated electrodes that have been surgically implanted (b). Resulting changes in behavior are correlated with the lesions produced (c).

an area using a probe. When the area is chilled, the neurons are unable to function. However, when the area returns to normal temperatures, normal behavioral function is restored.

Biochemical Methods

As we will see in Chapters 3 and 4, the brain and nervous system are unusually well protected, compared with other organs in the body, from circulating toxins. As a result, if a researcher wishes to investigate the effects of chemical stimulation in the brain, these normal protective mechanisms often must be bypassed. Obviously, some chemicals naturally gain access to the brain, resulting in psychoactive effects. Many other chemicals are blocked from exiting the blood supply into neural tissue. For example, most agents used for cancer chemotherapy simply circulate through the brain without leaving the blood supply, adding to the challenges of treating brain tumors (see Chapter 15).

Different methods used to administer drugs to a subject include eating, inhaling, chewing, and injecting the drug (see Chapter 4). These methods result in the delivery of very different concentrations of a drug into the blood supply within a given period. For research purposes, chemicals can be directly administered to the brain through the surgical implantation of micropipettes. This technique allows researchers to observe the effects of chemicals administered in an awake, freely moving animal.

On occasion, it is desirable to be able to identify the chemicals that naturally exist in a particular location. Using implanted micropipettes, small amounts of extracellular fluid are filtered from the area of the brain surrounding the tip of the pipette for analysis. This technique is known as **microdialysis**. Microdialysis allows researchers to identify which neurochemicals are active in a precise location, as well as the approximate quantity of these chemicals.

Genetic Methods

Many researchers strive to identify the interactions between hereditary and environmental variables on a particular behavior. In general, we wish to avoid either—or thinking in these analyses. Heredity and environment always work together to produce the ultimate outcome.

TWIN STUDIES The natural comparison between monozygotic (identical) and dizygotic (fraternal) twins provides some insight into the relative contributions of heredity and environment. Monozygotic twins share an identical set of genes, whereas fraternal twins average about 50 percent of their genes in common, just like any other pair of non-identical siblings.

As is discussed in Chapter 16, some psychological disorders, such as bipolar disorder and schizophrenia, seem to be influenced more by heredity than others, like major depressive disorder. The contribution of heredity to these conditions is often stated in the form of a **concordance rate**, a type of statistical probability. Given the existence of a trait in one twin, the concordance rate for the remaining twin estimates the probability of the other twin having the trait. For example, in the case of bipolar disorder, we see concordance rates as high as 71–77 percent (Edvardsen et al., 2008). If one identical twin has the disorder, the other has a 71–77 percent likelihood of also being diagnosed with the disorder. Note that this is not 100 percent. In contrast, the concordance rate for identical twins in regard to major depressive disorder is usually reported to be about 40 percent (Shi et al., 2011). This indicates that environmental variables play a more significant role in depression than in bipolar disorder. However, it is important to remember that "environmental variables" might still include biological components such as prenatal environment and exposure to infection.

microdialysis A technique for assessing the chemical composition of a very small area of the brain.

concordance rate The statistical probability that two cases will agree; usually used to predict the risk of an identical twin for developing a condition already diagnosed in his or her twin.

ADOPTION STUDIES Another approach to investigating the influences of heredity and environment is to compare the similarities of an adopted individual to his or her biological and adoptive parents. Similarities to the biological parents suggest a stronger role for heredity, whereas similarities to the adoptive parents suggest a stronger role for the environment. Adoption studies have been used to assess the relative contributions of heredity and environment to such characteristics as intelligence and criminality. Interpretation of such studies remains controversial, because adoptive families are often quite similar to one another, which in turn magnifies genetic influences. **Heritability**, or the amount that a trait varies in a population due to genetics, is still influenced by the environment. For example, if you planted seeds under ideal conditions (good soil, lots of sunlight, regular watering), the differences you observe among your mature plants are largely due to genetics. In contrast, if you planted seeds under more variable conditions, the resulting plants would reflect contributions of both genetic and environmental factors. Like the ideal conditions for our plants, genetic influences may be magnified by the similar environments provided by adoptive parents.

STUDIES OF GENETICALLY MODIFIED ANIMALS We review a number of studies in this text that use a relatively new genetic technique in which specially engineered, defective versions of genes are inserted into the chromosomes of animals, usually mice. The normal version of these knockout genes encodes for a specific protein. The **knockout genes** take the place of the normal genes but fail to produce the specific protein. By using this method, researchers can assess the roles of particular genes and the proteins they encode.

One example of this method is found in the work of H. W. Matthes and his colleagues (1996). As we will see in Chapter 4, many drugs have effects on behavior because they are chemically similar to normally occurring chemicals found in the nervous system. Opoids, such as morphine and heroin, activate receptors for naturally occurring substances known as endorphins. Matthes et al. (1996) bred mice that lacked the genes for producing some of the endorphin receptors. Their general behavior seemed unaffected, but they did not experience any pain relief when given morphine. They were incapable of becoming addicted to morphine, and they showed no withdrawal symptoms when morphine administration was discontinued. We can therefore conclude that certain aspects of an animal's normal reaction to morphine are dependent on the existence of endorphin receptors. Without these receptors, pain reduction, addiction, and withdrawal related to opioids do not occur.

EPIGENETICS The production of proteins by a particular gene can be influenced by a whole host of external factors, including diet, whether or not a person smokes, or stress. **Epigenetics** describes the development of traits by factors that influence the performance of genes without changing the underlying genes themselves (see Chapter 5). For example, baby rats that were licked frequently by their mothers (the rat version of a hug from mom) were calmer in the face of stress later in life than rats that received less nurture (Champagne, Francis, Mar, & Meaney, 2003). This type of interaction helps to explain why identical twins become less and less similar to each other over the course of their lifetimes. Their different choices in lifestyle and accumulated experience can change the way their genes behave (Fraga, 2005).

heritability The amount that a trait varies in a population due to genetics.
knockout gene A gene used to replace a normal gene that does not produce the protein product of the normal gene.
epigenetics The development of traits by factors that influence the performance of genes without changing the underlying genes themselves.
stem cell A cell that can divide and differentiate into other types of cells.

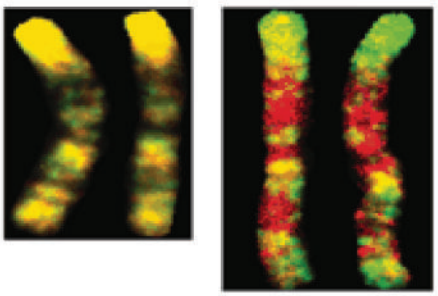
Stem Cells

One of the most promising approaches to understanding neural development, regeneration, and disease is the use of stem cells (Vunjak-Novakovic & Scadden, 2011). A **stem cell** is a cell that can divide and differentiate into other types of cells (see Chapter 5). If provided with the appropriate laboratory environment, a stem cell line,

or culture, can replicate indefinitely. Currently, researchers can derive stem cell lines from a number of sources, including adult stem cells, stem cells from umbilical cord blood, and embryonic stem cells.

The various types of stem cells offer different sets of advantages and disadvantages. Embryonic stem cells are usually obtained from embryos in the blastocyst stage, or about five days after conception in humans. These cells are pluripotent, meaning that they can differentiate into any type of tissue. In addition, embryonic cells are virtually immortal, as they can divide endlessly in the laboratory. On the other hand, these cells will provoke an immune reaction in a recipient, just like any other transplanted tissue. Adult stem cells have been retrieved from blood, nerve cells, muscle, the cornea and retina of the eye, some internal organs, and skin. Typically, these cells are less flexible than the embryonic cells and can only differentiate into cells similar to their source. They lack the immortality of the embryonic cells, but they are less likely to cause rejection by a tissue recipient.

Researchers are very excited about the potential of using stem cells to repair damage to the nervous system. For example, stem cells derived from human tooth pulp reestablished the ability to move in mice whose spinal cords had been completely severed (Sakai et al., 2012).



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● **Figure 1.15 Epigenetics** Epigenetics, or changes in the performance of genes without any underlying changes in the genes themselves, explains why identical twins become "less identical" as they age. The twins' individual experiences, including diet, stress, smoking, and so on, produce epigenetic change. Compared with 3-year-old identical twins on the left, the 50-year-old twins on the right show much greater amounts of red and green, which indicate areas of less and more methylation respectively. The yellow areas indicate equal levels of methylation. Methylation, or the addition of a methyl group to a molecule like DNA, is one of several mechanisms capable of epigenetic change that are discussed further in Chapter 5.

INTERIM SUMMARY 1.2

Methods in Behavioral Neuroscience

Method	Function
Histology	Studying the microscopic structure of the nervous system
Autopsy	Studying the structure of the nervous system following death
Computerized tomography (CT)	Studying structure and diagnosing structural damage
Positron emission tomography (PET)	Studying the relative activity of nervous system structures
Magnetic resonance imaging (MRI)	Studying structure in very fine detail
Functional MRI (fMRI)	Studying the activity of nervous system structures
Diffusion Tensor Imaging (DTI)	Studying fiber pathways in the nervous system
Electroencephalogram (EEG)	Studying brain activity, primarily during sleep and waking or seizures
Event-related potential (ERP) recording	Studying the brain's response to specific stimuli using an adapted EEG
Magnetoencephalography (MEG)	Studying brain activity

(*continued*)

Method	Function
Single-cell recordings	Identifying the stimulus responsible for activating an individual neuron
Electrical stimulation and lesion	Identifying behavior linked to a particular location in the nervous system
Optogenetics	Using light to initiate neural activity
Repeated transcranial magnetic stimulation (rTMS)	Producing long-lasting changes in cortical activity; linking behavior to a particular location in the cortex
Microdialysis	Identifying particular chemicals in a very small location
Twin and adoption studies	Studying contributions of genetic and nongenetic factors to behavior
Genetically modified animals (knockout genes)	Studying the role of particular genes and the proteins they produce
Epigenetics	Studying changes in the performance of genes
Stem cells	Growing replacement tissue for repairing damaged organs, including the brain and spinal cord

Summary Points

1. Improvements in histology provided the means for examining the nervous system at the microscopic level. **(L04)**
2. Imaging technologies, including CT scans, PET scans, MRI, fMRI, and DTI have built on knowledge gained through autopsy regarding the structure and function of the brain. **(L03)**
3. Recording techniques include measurements of the brain's overall electrical and magnetic outputs. In addition, recordings can also be made of the activity of single cells. **(L03)**
4. Stimulation and lesion techniques can be used to assess the function of particular areas of the brain. Magnetic stimulation can enhance or reduce the activity of the brain. **(L03)**
5. Biochemical methods allow for the artificial stimulation of the nervous system with chemicals as well as the assessment of the biochemical environment in an area of particular interest within the nervous system. **(L03)**
6. Genetic methods, including twin studies, adoption studies, and the analysis of epigenetics, allow researchers to assess the role of our genetic inheritance in the relationship between the nervous system and behavior. **(L05)**

Review Questions

1. What are the relative strengths and weaknesses of the major imaging methods?
2. What are the challenges involved with the interpretation of data from stimulation and lesion research?

Research Ethics in Behavioral Neuroscience

The Greek physician and scholar Hippocrates set a standard for ethical behavior in the sciences that has certainly stood the test of time. Hippocrates wrote in the *Epidemics*: "As to diseases, make a habit of two things—to help, or at least do no harm." As you have seen in this chapter, we have developed a wealth of technology in the neurosciences that has moved our understanding forward quite rapidly. In our rush for knowledge, what controls are in place to ensure that Hippocrates' rule of "do no harm" is respected by those entrusted with the lives and welfare of research participants?

Protection for research participants in the United States begins with the federal government and the Common Rule, a set of standards shared by seventeen federal agencies (Center for Science, Technology, and Congress, 2001). These standards apply to any researcher obtaining federal funds or conducting research at an institution that receives federal funds, which includes most universities. In addition, guidance is provided by professional societies, such as the American Psychological Association (APA) and the Society for Neuroscience (SfN). To evaluate compliance with ethical standards, each university maintains institutional review boards (IRBs) for human research and institutional animal care and use committees (IACUCs) for animal research. These committees are composed of faculty members with expertise in the appropriate areas, plus at least one faculty member from a nonscience discipline. In addition, the boards include a community member, so that the university is not simply policing itself behind closed doors.

Human Participant Guidelines

Thinking about the protection of human participants has changed dramatically over the past 30 years. Today's scientific community is far more protective of the safety and well-being of research participants. As an undergraduate student in introductory psychology, I was compelled to serve as a research participant in a fixed number of experiments to pass the course. I found myself acting as the confederate in a Milgram-type obedience experiment in which the real participant was supposed to administer a punishment to me in the form of increasingly potent electrical shocks. As in Milgram's original experiment (1963), I received no shocks, but the real participant (a girl from my floor in the dorm) believed that I was being shocked. After she "administered" the maximum levels of shock to me, I never quite trusted her again, and she avoided me for the remainder of our undergraduate days.

Today, coercing people into serving as research participants, either for course credit or any other incentive, is unacceptable. Although we recognize as psychologists that people who volunteer for research are probably quite different from people who don't volunteer, the resulting limitations on our abilities to generalize are a reasonable price to pay for ethical practice. Benefits for participation, including money, should not be "excessive or inappropriate" (American Psychological Association, 1992). Participants must be informed at the outset that they can leave the experiment at any point in time without penalty. In this text, you will read about research conducted with human participants who are not able to volunteer freely to participate. For example, individuals may not be capable of fully understanding the nature of the experiment or of their participation due to conditions such as schizophrenia or Alzheimer's disease. In these situations, legal permission must be obtained from a third party. The university-level review boards play an essential role in deciding these gray areas on a case-by-case basis.

To freely volunteer, a participant must be told enough about the experiment to make an informed decision about participating. This disclosure is accomplished through a carefully worded informed consent form prepared by the researchers and reviewed by the campus IRB. The form provides information about the general purpose of the experiment and any risks that may be involved. Participants are provided with contact

Centers for Disease Control and Prevention

● **Figure 1.16 Human Research Ethics** One of the studies that provoked today's concerns with the safety of human research participants was the Tuskegee Syphilis Study, in which men infected with syphilis were not made aware that effective treatments were available, among other ethical lapses.

information in case they have further questions regarding the study. Participants are assured that their data will be confidential and that they can choose to receive information about the outcomes and conclusions of the experiment.

Animal Subjects Guidelines

According to the American Psychological Association (APA, 2005), 90 percent of animals used in research are rodents and birds, and monkeys and other primates are used in 5 percent or less of all studies. The use of dogs and cats in behavioral neuroscience is exceedingly rare.

Building Better HEALTH

WHEN IS IT APPROPRIATE TO USE PLACEBOS?

A placebo is an inert substance or procedure often used as a control condition in clinical trials for new therapeutic drugs (see Chapter 4). The "gold standard" for drug efficacy studies is the double-blind placebo-controlled study. The "double-blind" refers to the fact that neither the participant nor the researcher evaluating the participant's responses knows whether the participant received the active or placebo treatment. This research design controls for the powerful cognitive expectations that often accompany use of a drug. I know for a fact that it takes about 45 minutes for caffeine to have its peak effect in my brain, but that does not stop me from feeling more alert as I begin to sip my morning coffee.

Miller et al. (2010) identify two ethical issues with placebo use. First, placebo research is inherently deceptive to some degree. Participants are commonly misled about the purpose of the study and are not aware of the deception until they are debriefed at the end. In only a few cases, "authorized deception" is used, in which the participants are told in advance that the study involves deception that will be revealed to them at the conclusion of the study. Second, placebo use in clinical practice is not uncommon. Although "only" 5 percent of a random sample of 1,200 US physicians prescribed true placebos (sugar pills or saline injections), close to a majority used some "alternative" approaches such as vitamins specifically to boost "patient expectations."

The fact that placebos might result in true physical changes, such as the release of our body's natural opiates or endorphins, further complicates the situation. These are topics for which accurate research is vital, yet are truly complicated when it comes to ethical constraints.

The first provision for the protection of animal subjects relates to necessity. The American Psychological Association (2008) stipulates that animal research should have a clear scientific purpose, such as increasing our knowledge of behavior or improving the health and welfare of humans or other animals. In other words, the research needs to do more than build a scientist's résumé for tenure and promotion. The knowledge gained should balance and justify the use of animals. The species used should be appropriate to the task. If the same questions can be asked without using animals, the alternate method should be used.

A second provision relates to basic care and housing of the animals. Animal research is expensive, but there are no alternatives to excellent care. When I was a graduate student in the 1970s, a furnished apartment near UCLA cost about $165 per month. In that same period, housing a single rhesus monkey for research purposes cost approximately $650 per month. Regular checkups by veterinarians and inspections occurred. We were extensively trained regarding the typical behavior of the animals (more for our own safety, in this case, as adult rhesus can be quite dangerous to humans).

Finally, experimental procedures should cause as little pain and distress as possible. Consider, however, that animals are generally used when procedures are not acceptable for human participants. The American Psychological Association guidelines include provisions related to the use of pain, surgery, stress, and deprivation with animal subjects, as well as to the termination of the animal's life. Some individuals and groups object to the notion that research that is considered unethical with humans is acceptable when animal subjects are used. Nonetheless, this is the primary rationale for the use of animal subjects, and we can expect a continued lively debate on the topic.

INTERIM SUMMARY 1.3

Ethical Principles

Participants	Ethical Principles
Human participants	No coercion Informed consent Confidentiality
Animal subjects	Necessity Excellent food, housing, vet care Avoidance of pain and distress

Summary Points

1. Research ethics agreed upon by government agencies, universities, and individual researchers are designed to protect both human participants and animal subjects from harm. **(LO6)**
2. In addition to being protected from physical and psychological harm, human participants must not be coerced into participation, and their confidentiality must be strictly maintained. **(LO6)**
3. Animal subjects must be protected from unnecessary pain and suffering. Researchers must establish the necessity of using animal subjects and are obligated to provide excellent housing, food, and veterinary care. **(LO6)**

Review Question

1. What are the major considerations for the protection of human participants and animal research subjects?

Chapter Review

Thought Questions

1. How have societal factors influenced scientific discovery in the past? What aspects of our current environment act to enhance or hinder scientific understanding in behavioral neuroscience?
2. Which of the methods outlined in this chapter have the greatest potential for producing further advancements in our understanding of brain and behavior?

Key Terms

autopsy (p. 8)
behavioral neuroscience/biological psychology (p. 2)
computerized tomography (CT) (p. 9)
concordance rate (p. 17)
diffusion tensor imaging (DTI) (p. 11)
electroencephalogram (EEG) (p. 12)
epigenetics (p. 18)
event-related potential (ERP) (p. 12)
functional MRI (fMRI) (p. 10)
heritability (p. 18)
histology (p. 7)
lesion (p. 15)
magnetic resonance imaging (MRI) (p. 10)
magnetoencephalography (MEG) (p. 13)
mind-body dualism (p. 4)
neuroscience (p. 2)
optogenetics (p. 15)
positron emission tomography (PET) (p. 9)
repeated transcranial magnetic stimulation (rTMS) (p. 15)
single-cell recording (p. 13)
stem cell (p. 18)