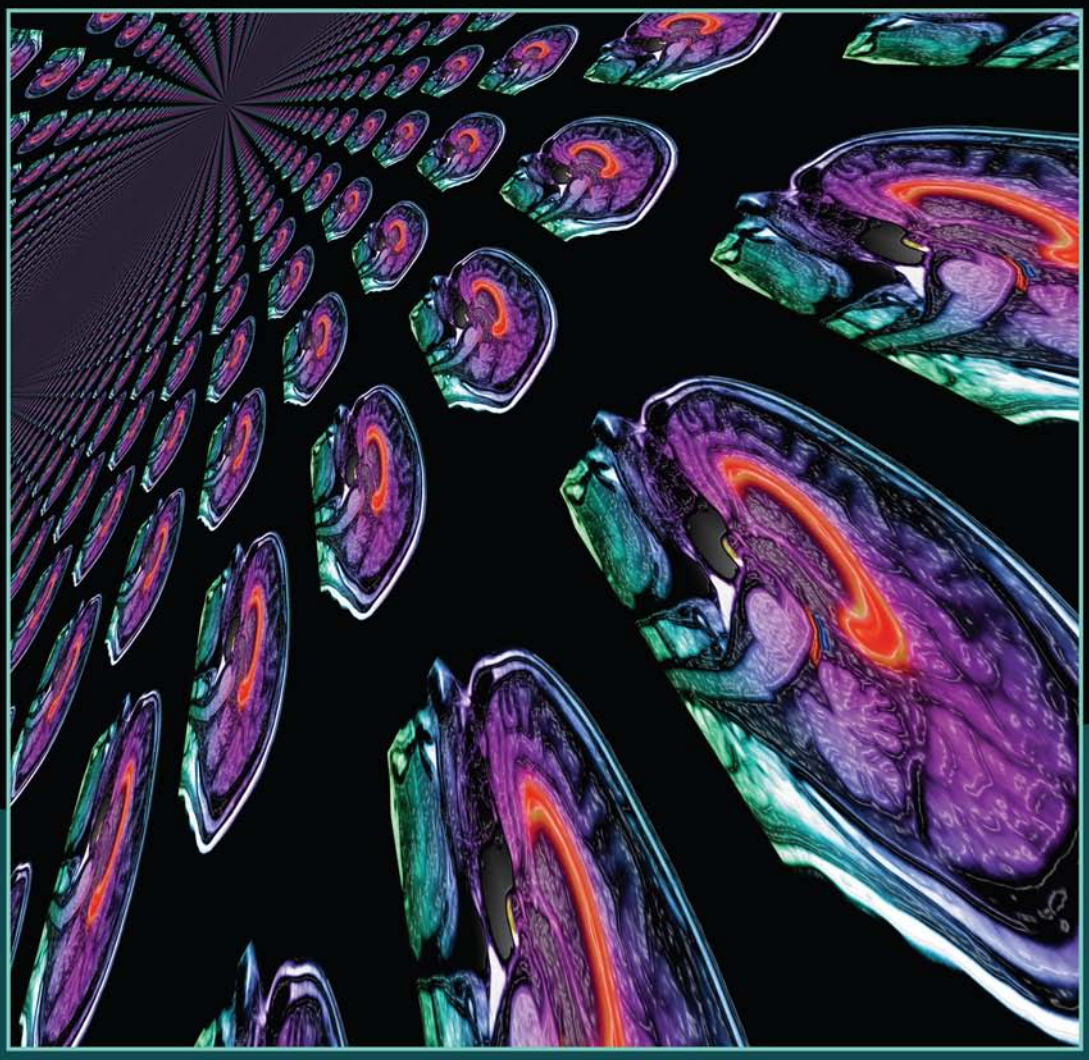
Elliott Ingersoll | Carl Rak

Psychopharmacology

FOR MENTAL HEALTH PROFESSIONALS

AN INTEGRATIVE APPROACH



Second Edition

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AN INTEGRATIVE APPROACH

2nd Edition

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Psychopharmacology for Mental Health Professionals: An Integrative Approach, **Second Edition**
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To my students from the Clinical Counseling, School Counseling, Clinical Psychology and School Psychology programs at Cleveland State University. You've all kept me believing in and improving this work as we used early drafts in our classes—thank you so much! Also to my co-author Carl. This would not have happened without your extensive clinical experience and friendship.

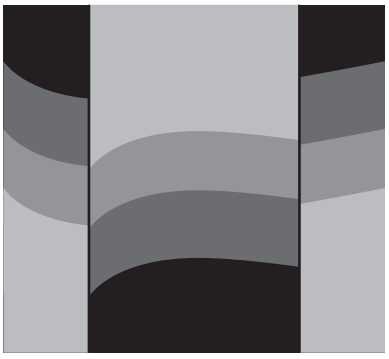
—R.E.I.

This edition is dedicated to Timothy Dugan MD, greatest of friends, mentor, and counselor on this endeavor. Tim is a passionate child and adult psychoanalyst and psychiatrist practicing in the Boston area.

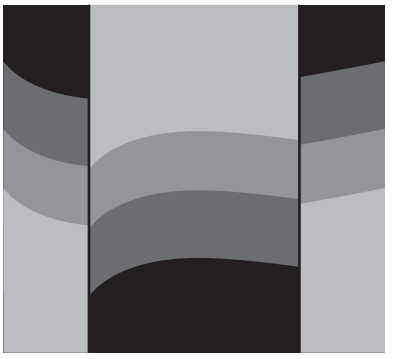
To Elliott Ingersoll, my lead author, this is your dream endeavor and this second edition is so much better because of you. Thanks!

—C.F.R.

Contents



Preface



These early years of the 21st century are a time of great opportunity for nonmedical mental health professionals. For the first time since the inception of the mental health fields we have excellent research on how to treat many mental health symptoms like depression and anxiety. Perhaps more importantly, the lay public is learning what many of us in mental health fields have known for years: we don't know what causes mental disorders and when medications work; we don't fully understand why medications work. There is no support for the overused cliché that mental disorders are caused by chemical imbalances in the brain. We know this now. Just because we can intervene chemically (in some but not all cases) in no way means the chemicals affected by the intervention were "unbalanced" to begin with. The truth is we still don't know what balanced brain chemistry is, let alone unbalanced brain chemistry. So why is this a great time of opportunity for nonmedical mental health professionals? Because the public is learning that there are no psychotropic medications that act as "magic bullets" that will "cure" mental disorders. Now that that misconception is dispelled we have a chance to teach laypeople which symptoms may respond to talk therapy, which seem to require medications and which will likely respond to a combination of medications and therapy. This sort of education and advocacy is critical in all mental health professions to inform clients and their families about what we know and what we do not know. An informed client can then make informed choices. The medications discussed in this book are like any tool. They can be used wisely or mendaciously misused. We have tried to present both the benefits and risks of these medications as well as their implications for our society. We hope dear reader that you find what you are seeking in the following pages.

ACKNOWLEDGMENTS

I (Ingersoll) want to thank my research assistants over these years, Kevin Blake, Laura McIntyre and Doreen George Thomas. Thanks to Carlene Ortiz for her selfless support when I was losing faith in my ability and my sense of vocation. Finally thanks to Cleveland State University for giving me sabbatical time to finish this project. CSU has been an excellent place for me to work and I appreciate the support I have gotten there.

I (Rak) also wish to thank Drs. Patrick Enders, Zinovi Goubar, Kay McKenzie, and Luis Ramirez. They are all careful and thoughtful psychiatrists working in the Cleveland area. They always took time to answer my questions and speak with me about the dilemmas of medicating children and adults. Thank you!

Finally, we both are so grateful to Julie Martinez who believed enough in this project to give us a much needed extension when our lives were "off the rails" and we needed more time.

PART ONE

An Overview of the New Edition

This book is an introductory level text on psychopharmacology for students preparing for careers in psychology, counseling, and social work. Like other texts, we cover pharmacodynamics and pharmacokinetics for each class of psychotropic medications. We also discuss psychosocial treatments that are recommended concurrent with medications. In addition, we discuss the psychological, cultural, and social issues around psychopharmacology. In the United States, the pharmaceutical industry is an enormous economic force with at least two lobbyists for every Senate and Congressional representative (Petersen, 2009). The industry's power (like any other) can be used constructively or destructively but it forms much of the cultural and social discourse. Given this, it is unrealistic and irresponsible to omit discussion of the relevant issues, which include influence on diagnosis, the creation of *DSM-5* (American Psychiatric Association, 2013), and the increasing medicating of children and adolescents despite scant evidence supporting the practice.

Although this book is a revised edition of *Psychopharmacology for Helping Professionals: An Integral Exploration*, it is a different book. Our aim is that this text meets your needs. Having used the first edition for six years, our students have taught us a great deal about how we can help them organize and learn this material. We have presented the basic information (updated) in a more traditional manner and deleted much of the historical discussion. This allowed us to add sections on psychosocial treatments, expand the discussion of medication and children, and add chapters on psychotropic medications and the elderly as well as drug replacement therapy for addictions. Rather than simply listing study questions at the end of each chapter, we have added learning objectives for each main heading in the chapters and then review questions *at the end* of each section that should tell the student whether or not they met the objectives. Our students have said that because much of this information is new, this style helps them "digest material" in "small bites." This makes sense to us as we want the journey to be nourishing for all readers.

WHAT IS AN INTEGRATIVE APPROACH?

Integrative approaches have been around in psychology and psychotherapy for decades and are making their way into psychiatry and thinking about psychopharmacology. In the 21st century, with a new diagnostic manual (*DSM-5*), the truth is we still do not know definitively why people develop mental and emotional disorders and, when medications work, precisely how they work. An integrative approach is one that takes multiple perspectives on the topic being discussed. In this book, we will examine psychotropic medications from four perspectives.

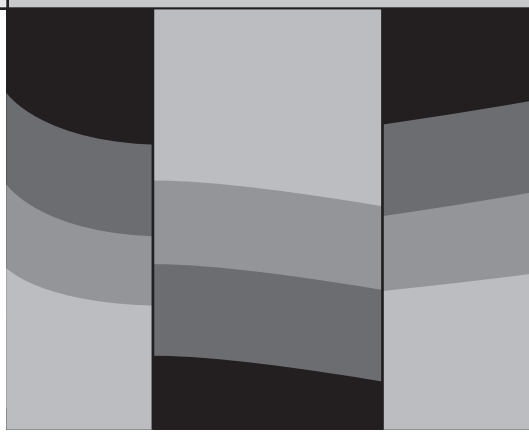
The first perspective is from a biological or physiological point of view. Because this model is frequently called the *medical model*, we will use that phrase when writing about this perspective. This perspective examines what seems to be happening in the nervous system when people are suffering mental illness and what medications seem to do in the nervous system that correlates with a decrease or remission of symptoms. The second perspective is a psychological one. This is not usually part of psychopharmacology books but if you are a clinician you know it is important. What does the client think/feel about taking medication? How might medications change the subjective, phenomenological experience of the client? The psychological perspective is more concerned with the client's "mind" than their brain.

The other two perspectives are cultural and social. The cultural perspective reflects the subjective shared experience of particular groups. It reflects shared beliefs of groups whether they be groups of people identified with an ethnic label (e.g., Orthodox Jews) or the shared worldview of a client's family of origin (e.g., "we don't believe in mental illness or taking medication"). The social perspective reflects that more objective aspects of our society. Things like laws governing psychotropic medications, power to prescribe medications, and the economic power of the pharmaceutical industry would all be views from the social perspective.

These four perspectives derive from Integral Theory (Wilber, 2000) and, although the theory is far more complex than these four perspectives, it emphasizes that the more perspectives you account for, the more complete your understanding of the topic in question. For example, because this book is aimed at nonmedical mental health professionals or students training to enter those professions, it would not make sense to omit the psychological perspective that offers ideas on how to work with clients around medication issues that are more psychological than physiological. Equally, no discussion of pharmaceuticals can omit the power of the industry without becoming two-dimensional and unrealistic. Given that, as we progress we will be very clear which perspectives we are using at different points in the book. Although a majority of the material is focused on the biological perspective (that we will call the "medical model") these other points of view will give a fuller picture of psychopharmacology and help clinicians advocate for their clients across cultures.

CHAPTER ONE

Introduction



Learning Objectives

- Be able to conceptualize the "information explosion" and how it relates to the brain sciences.
- Be able to describe pharmacodynamics and pharmacokinetics.
- Be able to articulate the benefits of an integrative approach to psychopharmacology.

ENCOURAGEMENT TO THE READER

Some of you may begin this book with some anxiety because this is a new area for you. You may imagine that psychopharmacology is exclusively a "hard science," and perhaps you don't think of yourself as a "hard science" kind of person. You may even feel uncertain about your ability to master basic psychopharmacological concepts. First, let us assure you one more time that our goal is to make this topic accessible to readers who are practicing as or studying to be mental health professionals, many of whom may not have a background in the physical or organic sciences. Second, we recommend to those teaching a course in psychopharmacology that, because of the rapid nature of change in the field, teaching styles that rely on memorization are of limited use in this area. We recommend helping students master basic concepts and then applying these concepts to cases. To facilitate that process, we supply cases and objectives/review questions for main sections of the book. Finally, we invite you students to join us in an incredible journey centering on the most complex organ known to humanity—the human mind and brain. We hope you can revel in the complexity of the brain and the sheer magnitude of its power. We hope you can resist the temptation to want simple and concrete answers to many of the questions this journey will raise. We also hope you learn to appreciate the ambiguous nature of "mind" and its relationship to the brain. As authors and researchers who have traveled this path before us will attest, there are no simple or even known answers to many of the questions that arise (Grilly & Salmone, 2011; Schatzberg & Nemeroff, 1998). We encourage a mixture of trying to comprehend the information while dwelling in the mystery that is the context for the information. Before moving on, we offer a mantra to help you implement this recommendation.

A MANTRA

Even though psychopharmacology is in its embryonic stage, it is a vast and complex topic. Several years ago I (Ingersoll) engaged in some multicultural counseling training with Paul Pederson. In that training, Dr. Pederson commented, "Culture is complex, and complexity is our friend." We offer a paraphrase as a mantra for psychopharmacology students: "Reality is complex, and complexity is our friend." We remind the reader of this mantra throughout the book. You might try saying it aloud right now: "Reality is complex, and complexity is our friend." If you reach a passage in this book that is challenging for you or that arouses anxiety, stop, take a deep breath, and practice the mantra.

The primary audience for this book is mental health clinicians who may not have had much training in biology, neurology, and psychopharmacology. This includes counselors, psychologists, clinical social workers, marriage and family therapists, and substance abuse counselors. We will refer specifically to these different mental health professionals throughout the book as well as including all of them in the phrase "mental health professionals." Although there are significant differences in the training models of these different professionals, they all draw on the same knowledge base when treating clients in school or clinical settings. We also want to add that there are several labels used to describe the therapeutic relationships clients have with mental health professionals. These labels include "counseling," "therapy," "talk therapy," "psychosocial interventions," and "psychotherapy." There is great debate across the mental health professions about whether and how these labels differ, but in this book we use them synonymously for the sake of simplicity. While reading this book, you will notice technical terms highlighted with bold print the first time they appear. These terms are defined in the Glossary at the end of the book. Although not all key terms are highlighted, those that nonmedical mental health professionals are less likely to have been exposed to are defined in the Glossary. We encourage you to keep a dictionary handy for other terms that may be new to you. If you come across a word you do not understand, stop reading and check the definition in the glossary or a dictionary. Many readers skip over unfamiliar words assuming the meaning will become clear in a later sentence. Clarifying unfamiliar words when they occur adds to the enjoyment of reading the book and facilitates a better understanding of the topic.

SCIENTIFIC TRUTH AND THE ACCELERATION OF KNOWLEDGE

It is no secret that knowledge accumulation is accelerating. We are familiar with the label "information explosion" to describe this phenomenon. In the early 1970s, the French economist Georges Anderla (1973, 1974) prepared a statistical estimate of how quickly knowledge has been growing, based on a variety of indicators. According to Anderla, if you begin in the year 1 C.E. (which stands for Current or Common, Era) it took 1500 years for knowledge to double. The second doubling took only 250 years (1750). The third doubling took only 150 years (1900), the fourth 50 years (1950), and the fifth doubling only 10 years (1960). If there is any accuracy in Anderla's model, knowledge began doubling almost monthly in the late 20th century (Wilson, 1992). Increase in knowledge about the human brain is particularly pronounced.

The final decades of the 20th century unearthed more knowledge about the human brain than all prior centuries combined. One of the most exciting fields benefiting from these developments is psychopharmacology. *Pharmacology* is the science of the preparation, uses, and effects of drugs. *Psychopharmacology* is the branch of pharmacology related to the psychological effects of drugs and the use of drugs to treat symptoms of mental and emotional disorders. These drugs are called *psychotropic medications*. "Psyche" colloquially refers to "mind," and "tropic" means "acting on" or "moving toward" but many in the field would say these medications act on the brain and this affects the mind.

Developing neuroscience technologies have helped accelerate brain research and change in the field of psychopharmacology by letting scientists peer more deeply into the brain and nervous system. The latest technological advances include positron emission tomography (PET) scans, magnetic resonance imaging (MRI), Diffusion Tensor Imaging (DTI), Voxel-Based Morphometry, and magneto-encephalography. PET scans for brain functions work thus: The technician injects a radioactive form of oxygen into a person and then asks the person to perform a particular task under a PET scanner. Because the brain area most active during the task requires more oxygen, the PET scanner can trace the radioactive oxygen to those sites in the brain used in the task. The computer scanner then generates a picture that maps the brain activity. MRI scans generate images by magnetizing hemoglobin (the iron-containing colored

matter in red blood corpuscles that carry oxygen to tissues) and by tracing changes in blood oxygen levels in the brain. Like the PET scan, MRI images of the brain can be used for diagnostic or research purposes. DTI is a type of MRI that can highlight microstructural changes in the white matter of the brain or glial cells (Emsell & McDonald, 2009). This is becoming more important because we discovered that, far from being only glue or insulation for neuronal axons (*glia* comes from the Greek word for *glue*), glial cells actually send neurotransmission and communicate with other cells (Fields, 2009, 2010; Sasaki, Matuski, & Ikegaya, 2011).

Magnetoencephalography measures the magnetic field associated with electrical currents in the brain to trace activity levels across brain structures when subjects are engaged in a particular task (Bloom, Nelson, & Lazerson, 2001).

There are also multiple techniques for extracting information from MRI scans. The most common quantitative techniques are "region of interest" (ROI) and computational morphometry studies. In ROI analysis, a trained rater manually traces a brain region of interest using "boundary rules" to compare sizes between different brains scanned. *Computational morphometry* is an automated method of comparing brain structures between different populations in a study. The most common variation is called voxel-based morphometry (VBM), which allows viewing of gray matter, white matter, and cerebrospinal fluid (Emsell & McDonald, 2009).[1] Voxel-based morphometry is neuroimaging analysis technique that uses a type of mapping (statistical parametric mapping) to identify regions of interest in the brain and calculate their volume. Finally, there are also deformation-based morphometry (DBM) and tensor-based morphometry (TBM). Both techniques are used to compare brain structures, but they rest upon different theoretical assumptions.

[1]As with any approach, VBM has received criticism because of the assumptions on which it is based. See Ashburner and Friston (2001) and Bookstein (2001).

Computer technology has also enabled pharmaceutical researchers to generate three-dimensional models of brain cell receptors and the drug molecules that bind to them. Brain-scanning technologies have allowed us to see how the drugs act on the nervous system (**pharmacodynamics** covered in Chapter Two) and how the body metabolizes and eliminates drugs (**pharmacokinetics** covered more extensively in Chapter Three). These are only some of the advances that have contributed to the exponential increase in the number of drugs developed annually.

Despite the explosion of advances in psychopharmacology in the last 30 years, the field can still be thought of as in an embryonic stage (Advokat, Comaty, & Julien, 2014). Although scientists know a lot about the physiological mechanisms of many psychotropic medications, we know little about how they actually change mood. Researchers are just now beginning to explore how the effects of psychotropic medication differ depending on the age, sex, and race of the person taking them (Heinrich & Gibbons, 2001). Although Western society is emerging from a postmodern era where multiculturalism was heavily emphasized, little research has been done on differing cultural worldviews regarding psychotropic agents, let alone how such agents differentially affect people of various racial and ethnic backgrounds. In addition, people are now rethinking whether current diagnostic categories for mental and emotional disorders apply to younger children (Ingersoll & Marquis, 2014; McClure, Kubiszyn, & Kaslow, 2002a) and how medications affect the dozens of developmental variables in this age group. Although the Human Genome Project has initiated efforts to understand human DNA, in the late 20th century scientists were still unclear about the role of over 90% of human DNA (Suurkula, 1996). In 2012, teams of scientists agreed that much of the DNA previously thought to be "junk" are actually "switches" that regulate how genes work or turn "off" and "on" (Doolittle, 2013). Efforts to describe the human genetic code and mechanisms of gene expression hold great promise for drug development, but there is still a great deal to be learned.

As recently as 30 years ago, psychopharmacology was a medical subspecialty for psychiatrists in particular. At that time, nonmedical mental health providers could ethically practice with little knowledge of psychotropic medications. As long as they had a medical professional to whom they could refer clients, their knowledge of psychotropic medications could be minimal. This is no longer the case. Most (if not all) mental health professionals work with clients taking psychotropic medications and need to be knowledgeable about the drugs their clients are taking. The integrative perspective we emphasize in this book provides a template that, when applied properly, suggests that understanding the physiological properties of psychotropic medications is merely the beginning of the journey. We use the integrative Model to address many pressing issues rarely discussed in books on psychopharmacology. For example, most psychopharmacology books simply discuss what medications are used for particular symptoms but do not address how to deal with cultural issues that may influence a client's resistance to taking a prescribed medication. Another example is the place of **direct-to-consumer advertising.** Although mental health professionals may know that changes in federal law in the 1980s allowed pharmaceutical companies to advertise directly to consumers via television ads and other media, they may not know that there is a fierce debate over whether such advertising for psychotropic medications is ethical.

Pharmacologists working in controlled conditions in laboratories may have the luxury of limiting their focus to interactions between drug molecules and neurotransmitters. But mental health professionals in the field must understand clients' perceptions and subjective experiences of taking medications, cultural views of psychotropic medications, group differences in response to the medications (according to sex, age, race, etc.), developmental considerations, socioeconomic institutions that mediate access to medications, and competing worldviews and theories on what causes mental health symptoms. The four perspectives of our integrative framework requires consideration of these topics and sets this book apart from other books on psychopharmacology. Although this consideration requires more effort, it contributes to a well-rounded knowledge of psychopharmacology that translates into better clinical practice.

Review Questions

- What is meant by "information explosion" and how is it reflected in psychopharmacology?
- Describe pharmacodynamics and pharmacokinetics.
- What are the benefits of an integrative approach to psychopharmacology?

CHAPTER ONE: SECTION TWO

Learning Objectives

- Be able to describe why therapists need more than just a physiological or medical understanding of psychotropic medications.
- Discuss the differences between what is commonly thought of as "mind" and what is thought of as "brain."

Everybody Is Right (About Something): The Many Faces of Truth

History shows that extremists, despite the strength of their convictions, are rarely correct (Radin, 1997, p. 205).

In this book, we consider multiple dimensions of and perspectives on psychopharmacology. Although it would be convenient to state that all mental and emotional symptoms derive from some malfunction of brain chemistry, there is no evidence to support this statement. Many people are surprised to hear this, so it is important to restate: There is no evidence that all mental and emotional symptoms derive from some *malfunction or imbalance* of brain chemistry. Today pharmaceutical companies advertise directly to consumers and often give the impression that

psychological disorders are really "medical disorders" that can be alleviated with a particular medication, much as antibiotics can alleviate a bacterial infection. If psychological disorders were like medical disorders, then studying the brain, brain chemistry, and scientific method would suffice. Even the *International Classification of Diseases, tenth edition* (*ICD-10*) has a separate volume for mental and behavioral disorders (WHO, 1992). So although the medical model provides an important perspective, we also need to study the mind, the sociocultural contexts in which mind and brain function, and the consciousness underlying mind and brain.

The entire truth of psychopharmacology cannot be explored solely through scientific method. Like a diamond, truth has many facets, which are complementary (but not necessarily competing). As philosopher Ken Wilber (2003) notes, no mind is capable of 100% error, so everyone is right about something but not everyone is equally right about everything. Given that insight, exploring the different perspectives of psychopharmacology need not produce warring factions championing mutually exclusive theories of **etiology** and treatment. Taking different perspectives in exploring psychopharmacology reveals different truths about it.

Lest you think we are lapsing into some type of **radical constructivism** or **relativism** (we are not), consider these questions: What sort of blood test would you use to determine your political philosophy? How might exploring your feelings about your mother help diagnose a streptococcus infection? How can a firsthand understanding of a person's religion be used to tell you how much money he or she earns? How could data about your yearly income be used as an indicator of your sexual orientation? These questions are meaningless, because each proposes an incorrect tool for finding the answer. Because different perspectives reveal different faces of truth, they require tools matched to the task. There are different forms of truth and knowledge and different tools are employed in exploring them. We emphasize this point because many people believe that medical science (or science in general) is the only tool and that it can solve any problem.

The Medical Model Perspective

The perspective of medical science (and science in general) clearly reflects one type of truth, and we draw amply from it in this book. Whereas a relativist would say that one perspective or type of truth is just as good as another for any job, we maintain that some perspectives and tools are better than others for particular tasks. Everyone knows that no blood test can determine a person's political philosophy. Does this mean one's preference for a political philosophy does not exist? No. It simply means a blood test is not a good tool to use to explore the issue. In this case, dialogue is far better than a blood test. To find out a person's political philosophy, you talk with the person to learn what his or her political philosophy is. Regarding the diagnosis of streptococcus infection, a throat culture is a far better test than discussing feelings about one's mother.

Scientific truth is objective truth that can be verified by some observable measurement. This is the type of truth emphasized by the tools of scientific method, the medical model, and most psychopharmacology books. The perspective of scientific truth is an important cornerstone of psychopharmacology. This is what we are referring to as the **medical model perspective**. It is characterized by its focus on objective, measurable data related to individuals. Although labeled "medical model" for the purposes of this book, this perspective also includes schools of psychology that rely heavily on objective measurement (such as behaviorism). In psychopharmacology, the medical model perspective helps us understand parts of the brain that seem correlated with symptoms of mental or emotional disorders and things such as the molecular structure of drugs. But mental health professionals are concerned with more than the correlations of symptoms with brain functions or the molecular structures of drugs. As professionals, we are also concerned with *how clients feel* about taking medications, how and whether psychotropic medications alter their consciousness, relevant cultural issues that may affect their attitudes or increase their preference for alternatives to psychotropic medications, aspects of group membership (race, sex) that may predict differential responses to psychotropic

medications, as well as how our clients' place in society affects their ability to get the drugs they may need.

The Psychological Perspective

Other perspectives complement the medical model and help mental health professionals build a well-rounded understanding of psychopharmacology. These other perspectives reveal other faces of truth that the medical model is not equipped to explore but that are equally important for mental health professionals. As Wilber (1997) noted, the techniques of the medical model perspective can trace the electrical currents in a subject's brain but can only give scientific verification about the electrical activity in that brain—they cannot tell whether the person is thinking about opening a homeless shelter or robbing a liquor store. Further, there is no evidence that the experience of consciousness is caused solely by electrical activity in our brains (Chalmers, 1995).

Information about what other people (including our clients) are thinking can only be obtained through truthful dialogue with them. This introduces the second perspective we use in this book, the **psychological perspective**. Psychology's name is derived from the goal of studying the mind or soul. Despite that origin, it has evolved into the scientific study of mind and behavior and has come to greatly resemble the medical model. Schwartz and Begley (2002) assert that psychologists have become overly attached to a version of the medical model that dismisses conscious experience and focuses only on what is observable or measurable. They conclude, "Surely there is something deeply wrong, both morally and scientifically, with a school of psychology whose central tenet is that people's conscious life experience … is irrelevant" (p. 6). It is that conscious experience that we are referring to when we use the phrase "psychological perspective" or what consciousness feels like from the inside. We include the psychological perspective because clients' **phenomenological** experiences of the world cannot be dismissed as irrelevant and are often a key ingredient in their growth.

Our psychological perspective deals with consciousness. Although one of the most ambitious pursuits of scientific knowledge is the Human Genome Project, there exists an equally ambitious (even if less well known) human consciousness project. The psychological perspective as revealed by the consciousness project is summarizing millennia of knowledge about the human mind, the subjective human experience, consciousness, the domain of the unconscious, and the farther reaches of human nature (be they existential or spiritual). For more on the human consciousness project go to http://www.nourfoundation.com/events/Beyond-the-Mind-Body-Problem/The-Human-Consciousness-Project.html. This knowledge is different from knowledge generated by the medical model perspective, but is no less important for mental health professionals who deal with the whole person. The subjective knowledge about oneself that counseling, psychotherapy, or meditation explore is different from the type of knowledge that science produces to tell us about how nerve cells fire in our brain. It is truly odd that although psychotropic medications are actually supposed to modify experienced consciousness, very few books on the topic actually address that and instead prefer just to discuss how drug molecules bind to neuronal receptors.

Suppose, for example, that you experience an insight about yourself that leads to more effective ways of living. For the sake of the example, assume the insight is that you fear emotionally depending on others, so you tend to push them away and isolate yourself. When you experience this insight, certainly nerve cells will fire in your brain, but no one can prove the cells are "causing" the insight—in some cases they accompany it and in others they fire slightly before your conscious knowledge of the insight. Further, others cannot learn about the insight by reading a PET scan of your brain taken when you had the insight. You must truthfully share the insight in order for others to learn about it—no physical measurement of any type (brain cells firing, heart rate, blood pressure, and so forth) will reveal the insight—you must share it. This is an important type of knowledge of the sort commonly shared and explored in counseling sessions.

The psychological perspective also includes people's unconscious life experience. The many tools we use to explore the psychological perspective include introspection, dialogue about that introspection, interpreting dialogue, and sharing our interpretation to assess its accuracy. Although we can only be aware of those things that are conscious, by definition, the tools of the psychological perspective can help clients bring to awareness things that were previously unconscious. As Wilber (2003) noted, psychotherapy is always about increasing awareness and this increase in awareness is experienced through the psychological perspective. These tools are familiar to anyone trained in the mental health professions, but it is amazing how easily we forget their importance.

The Cultural Perspective

A third perspective or type of truth concerns how people should treat one another as well as the beliefs and worldviews people may share. These shared beliefs constitute aspects of culture. Culture, ways of living that groups of humans transmit from one generation to another, includes the shared beliefs and worldviews that different groups develop to understand the world and their place in it. Because shared worldviews are so important to culture, we refer to this third perspective as the **cultural perspective**. The word *culture* may refer to a subgroup of people who share similar genetic and social histories, as in "African-American culture" or a subgroup that comes about for other reasons, such as a business or industry, as in the culture of a pharmaceutical company. Again, no number of PET or MRI scans of brains can show what worldview a person holds, which ways of relating or worldviews are better than others, or whether a person prefers to be "in time" or "on time." As Wilber (1995) puts it, scientific knowledge can never tell us why compassion is better than murder, why social service is better than genocide. Michael Polanyi (1958) also articulated this insight. Polanyi was a Nobel Prize–winning chemist who realized during the communist revolutions in Europe that the revolutionaries were trying to build a culture and a society on scientific principles (the Lenin-Trotsky five-year plan) and that those principles were the wrong tools for the task. Polanyi understood that the tools of science could never help these revolutionaries build a culture or a society worth living in. History has validated his judgment. Although the design of the Soviet Union tried to account for and control all the measurable aspects of society, it severely underestimated the cultural/ethnic differences that, since its dissolution, have erupted between former member nations. Scientific truth can tell us which psychotropic medication has the greatest probability of easing a client's suffering. But the scientific truth and the medication cannot erase nonbiological sources of suffering nor address what this suffering means to the client. For example, if the client shares a worldview that is highly suspicious of taking psychotropic medication, the client is unlikely to comply with the prescription.

The Social Perspective

A fourth type of truth, which concerns the structure and impact of social institutions, we call the **social perspective**. Social institutions are based in shared beliefs, policies, and laws that affect people in observable, measurable ways. Whereas the medical model perspective deals with measurable, observable data about individuals, the social perspective deals with measurable, observable data about groups and particularly institutions. One good example in psychopharmacology is the ongoing debate about whether a person can and should be medicated against his or her will (Gelman, 1999). Although the legal system is ideally based on the public's shared understanding of how we need to be regulated with laws, laws prohibiting or permitting forced pharmacological treatment have profound impact on individuals. Besides the legal institutions of our society, other institutions relevant to psychopharmacology include the government (e.g., the Food and Drug Administration, the Drug Enforcement Agency) and the pharmaceutical industry in general. Issues such as whether people in the United States should be able to import medications from Canada are the domain of the social perspective. (Again, imagine the absurdity of trying to resolve this import question through the medical model perspective.)

Most books on psychopharmacology focus on scientific or medical model perspectives of what medications seem to do, how they correlate with symptom relief, how much of the medication is needed, and so on. Although we cover these issues in detail, we also discuss the other perspectives that are pertinent to mental health professionals. For example, what does it mean to a client to take a psychotropic medication (psychological perspective)? What does it mean that a significant number of children in this society are referred for medication instead of for counseling (social perspective)? How should we interpret and interact with a family that believes psychotropic medication is spiritually damaging (cultural perspective)? It is time for humanity to integrate the various types of knowledge people have access to, and a study of psychopharmacology can benefit by such integration.

We have mentioned the power of the pharmaceutical industry particularly in the United States. Like all power it can be used well or misused. One of the most striking things since the publication of the first edition of this book is the increase in lawsuits prosecuting pharmaceutical companies for illegal practices related to psychotropic medication. Some examples:

- In 2011, Massachusetts filed a lawsuit against Janssen for "deceptive" marketing of the antipsychotic resperidone (Mental Health Weekly, 2011) and settled for $158 million.
- Since 2004, the United States has collected nearly $8 billion from fraud enforcement actions against pharmaceutical companies for illegally promoting drugs for off-label uses (Avorn & Kesselheim, 2011).
- In 2009, Eli Lilly Company pled guilty to illegal marketing of the antipsychotic olanzapine and paid a $1.42 billion fine (Associated Press, 2009).
- In 2010, AstraZeneca was fined $520 million for illegal marketing of the antipsychotic quetiapine (Wilson, 2010).

What seems to be happening is that the culture of the pharmaceutical industry is being more closely monitored by government agencies due to a history of ethically questionable actions. This definitely affects clinicians and clients. For example, what if one of your clients was taking a drug that is not FDA approved for a serious disorder like Bipolar I Disorder and that has no documented efficacy? Certainly the client's welfare is at stake and this is where clinicians advocating for clients and maintaining healthy relationships with prescribing professionals is important.

PSYCHOPHARMACOLOGY AND MAGICAL THINKING

R. Stivers, in his book *Technology as Magic* (2001) suggests that as different technologies "disenchant" our sense of the world, people may respond with magical thinking by endowing those technologies with magical attributes. "Today our expectations for technology are magical" (p. 7). You can see this change particularly in psychopharmacology. We have had clients who thought that if they took antidepressant medication prescribed for their symptoms it would (almost magically) erase all suffering from their lives. We agree with Stivers that this society has almost magical expectations of pharmaceutical companies, their products, and the medical professionals who prescribe those products. One practice tied to this expectation is what we call "word magic."

"Word magic" is the use of words in such a way so as to create the illusion of certainty where certainty does not exist. Word magic is used to increase one's control over the world (and other people), to artificially reduce the complexity of reality, and to help one deal with the insecurity experienced in the face of complexity. Particularly in the service of control, word magic can be used to trigger strong emotions in a reader or listener for the purpose of increasing the speaker's own power. Former U.S. Attorney General A. Mitchell Palmer and Senator Joseph McCarthy engaged in word magic, wielding the key term "communist" to increase their political power during "red scares" in the early- and mid-20th century. The same type of word magic was used in the witch hunts, in the Inquisition, and is still being used in the

current "war on drugs" (which is really a war on drug users) in the United States (revisited in Chapter Ten).

How does this relate to psychopharmacology? When various professionals, groups, or companies use words to convey pharmacological certainty where little certainty exists, they are engaging in word magic and in some cases trying to increase their own power. An example of this is the flawed idea that mental illness is caused by a chemical imbalance in the brain. As noted this "hypothesis" has been falsified multiple times. This can result in what Charles Tart (1997) refers to as scientism: "a dogmatic, psychological hardening of materialistic belief systems with emotional attachments, rather than authentic science" (p. 22). Frequently this hardening of belief systems with emotional attachments takes the form of proclaiming something to be much simpler than it is in reality. An example is when pharmaceutical companies, in ads for antidepressants, state, "Depression is a serious medical disease." The payoff for pharmaceutical companies in framing depression this way is that if the general public thinks of depression first and foremost as a medical disease, their first response if feeling depressed will be to go to a medical doctor for a prescription rather than to a mental health professional for counseling. As we will show, depression is an overdetermined set of symptoms that may be biological, psychological, or spiritual in etiology. Just because depression is described in the *ICD-10* (the diagnostic manual for physicians) does not mean it is a medical disease in the same sense that influenza is a disease. Tart goes on to explain that we are conditioned to assume people in lab coats are dealing with certainty and that sometimes people in lab coats perpetuate that misunderstanding.

MOVING ON: WHAT WE KNOW, WHAT WE DO NOT KNOW

To avoid falling into word magic, people must be willing to admit what they do not know. Studying the mind and brain moves us all to the knowledge frontier of the 21st century. Consider this: Despite considerable success in developing medications that ease the symptoms of mental and emotional disorders, scientists have little understanding of how most of these medications work. Researchers are learning more about how psychotropic agents act on the brain and body (pharmacodynamics) and how the body disposes of them (pharmacokinetics), but scientists still know very little about why certain drugs decrease certain symptoms and contribute to emotional and behavioral changes. Even more interesting (although less publicized) is that in a great number of studies (and with particular symptoms like depression), as many participants respond to placebos as respond to the actual medications being investigated (Fisher & Greenberg, 1997; Khan, Leventhal, Khan, & Brown, 2002). There are many unanswered questions about the brain, the mind, and the relationship between the two. All together now: "Reality is complex, and complexity is our friend."

An example of this complexity is the case of Louise. Throughout the book, we provide cases that illustrate good responses to medications, treatment-resistant symptoms, side effects, client psychological issues related to medications, and cultural and social considerations. The cases illustrate the complementary types of truths we have summarized as the medical model, psychological, cultural, and social. Although it would be much simpler only to use cases where clients have symptoms, take medications, then get better, this has seldom been our experience. Lawrence's case illustrates many of the perspectives we have introduced in this chapter. It does not lend itself to a single interpretation that relies solely on one perspective. Read the case, and consider the questions following it.

The Case of Lawrence

Lawrence is a 35-year-old lawyer who anguishes with a very poor self-image, terrible anxiety, depression, and lability of mood. He is the oldest of three and his mother left the family permanently when he was five. At that time, his father expected him to be the little man of the house and take care of his younger sisters. Lawrence remembers that he always complained to his father that he didn't feel

right, not like the other boys. His father would always reply with the same phrase, "Just move on, son." Lawrence always believed that no one got him, not even his new stepmom. Both at home and in school he was a loner. He was very bright and got more than acceptable grades. He grew very anxious whenever he had to interact with others. His father had no patience for his isolation. Lawrence gradually developed what seemed to be a social phobia.

From an intrapsychic perspective, this client suffered a serious loss of the mothering one at a critical time in development. Just as he began to enter the latency age of child development, he loses his primary relationship with whom he can share insights and changes that he is experiencing. This aspect of his development was delayed or foreclosed while his father expected him to accelerate his development to an advanced stage of caretaker of his sisters. In both roles he became very passive. By the time he reached high school he was in a suicidal depression and had to be hospitalized for attempting suicide. Each day of his life was a burden. The attending physicians at the hospital tried to get him to take an antidepressant. He refused.

Lawrence graduated from college, served in the army, and married. Eventually, he attended law school with very little alteration of his mood or self-efficacy. He failed the law boards and his wife threatened to divorce him if he did not pass them the second time. He was distraught and angry. He felt betrayed by his wife who had almost forced him to attend law school. He sought out therapy and consultation with a psychiatrist. The therapist recommended twice-a-week psychotherapy and the psychiatrist put him on 100 mg of sertraline (brand name Zoloft). Lawrence tried the sertraline for three months and indicated that he felt no improvement. The psychiatrist added 250 mg of bupropion (brand name Wellbutrin) to be taken along with the sertraline. Lawrence expressed his concern about being over medicated, but the psychiatrist encouraged him to try both medications.

After four months, Lawrence spoke to both his therapist and psychiatrist that he believed the medications were not really helping him. After much consultation and discussion with Lawrence, the psychiatrist decided to titrate him off the buproprion and to add 2 mg of aripiprazole (brand name Abilify a newer antipsychotic used at very low doses in the treatment of depression). Within a week, Lawrence was unable to sleep, was very agitated, and could not focus on his work. The psychiatrist, although puzzled, was not totally baffled by this development in Lawrence. He expanded his clinical interview, consulted in-depth with the therapist, and concluded that Lawrence had been masking a bipolar presentation with some moderate drinking. He started Lawrence on a course of lithobid (Lithium) after discontinuing his other medications. This course of treatment served Lawrence well for several years and he periodically had his blood levels checked for lithium poisoning. The course of pharmacological treatment that Lawrence received is far more the norm for the patient of 2013.

THE MIND–BRAIN PROBLEM

If you were on a game show and the host asked you (for $1000) to clearly define mind, brain, and the difference between the two, how would you answer? How you answer is basically how you conceptualize the mind–brain problem. The mind–brain problem is an old philosophical issue that addresses whether or not the mind and brain are distinct entities and what their relationship is. Scientific knowledge of both the mind and the brain is incomplete. No one knows what the mind is, where it comes from, or how it interacts with the brain (Dossey, 2001). However, numerous scholars have noted that even if there were complete knowledge of the mind and brain, the problem might still be unsolvable (Koch, 2012). Consider being asked to define "the mind." At first glance this might seem a simple task for a mental health counselor or a student training in one of the mental health professions. In fact, it is a rather vexing question with a multitude of answers depending on your theoretical orientation. As much as many hate to admit it, to "define" what "mind" means first requires a leap of faith in the theory or theories you believe most accurately reflect the reality of

what the mind is. To say you adhere to a particular theory of the mind–brain problem is fine; to claim a particular theory is ultimately true at this point in history is scientism, not science. Generally, the mind–brain problem has been explored through two hypotheses, the epiphenomenon hypothesis and the dual-substance hypothesis, discussed as follows.

The Epiphenomenon Hypothesis

The first hypothesis is called the **epiphenomenon** hypothesis (sometimes called the "side effect" hypothesis—the mind is a side effect of the brain). The theory underlying this is what might be called *radical materialism*. The basis of radical materialism is that all things, including the mind, derive from other things that can be objectively observed and measured. This hypothesis states that the mind derives from the brain. In other words, the mind is an epiphenomenon of the brain. In a sense, this theory claims that your mind, including your sense of self, is a "side effect" of having a developed brain. The 19th-century biologist Thomas Huxley (known as "Darwin's Bulldog" for his fervent support of Darwin's theory of evolution) popularized this hypothesis. More recently Damasio (2000), Dennett (1991), and Churchland (1995, 1999) have set forth varieties of the theory. Sometimes the theory is not stated outright but implied, as if this were the only acceptable theory on mind and brain. Richard Thompson (2000) gave one example when he wrote, "What is consciousness and how does it arise from the brain?" (p. 481). His implication that it does arise from the brain is a theoretical assumption, not an indisputable fact even though he presents it as such. This is another example of word magic—using words to create an illusion of certainty where there is none.

Advocates of the epiphenomenon hypothesis support it by first noting a brain structure responsible for a particular function (such as the relationship of Broca's area to speech, for example). Next they point out that, for example, if Broca's area is damaged, speech is impaired. The reasoning is that one's sense of self (one's mind) is a consequence of brain functioning and if those parts of the brain responsible for the sense of self are damaged, the sense of self is either impaired or vanishes, just as speech becomes impaired if Broca's area is damaged.

Perhaps the most time-worn example used to support the epiphenomenon hypothesis is the 19th-century case of Phineas Gage. Gage was a railroad construction worker who had a tamping iron driven through his skull as the result of an explosion. Although he miraculously survived the accident, the story used to be that his personality became so altered that those who knew him say Gage was a different person after the accident. Damasio (1995) hypothesized that from a materialist perspective Gage, the person, had changed because the areas of his brain that maintained and expressed personality had changed when damaged in the accident. Of course, as in most things, there is now a difference of opinion on Gage. Kean (2014) wrote that descriptions of Gage's personality change are greatly exaggerated. In fact, he noted that historical documents show that Gage went to South America and worked as a stage coach driver. Even if the stories about his drinking and aggression after the accident are true, how much of that may have been related to pain or depression (the psychological perspective)?

Our sense of self is somewhat more complicated than other functions that are traced to specific brain areas, so researchers do not yet know exactly which areas, and the relationships between them, result in the sense of self. Damasio (2010) and others have begun to tackle this problem, but science is far from an explanation. Thus to accept the radical materialist position is a statement of faith that neuroscientists will be able to completely map out the brain and its functions (and that they are correct in thinking such knowledge would resolve the mind–brain problem).

As you can imagine, those who adhere to the medical model of mental and emotional disorders often support the epiphenomenon hypothesis. This model is the basis of allopathic medicine. Allopathic medicine (as opposed to homeopathic or osteopathic) is the branch of medicine that adheres to the philosophy that to treat or cure a disease

process, you introduce an agent (such as a drug) that acts in a manner opposite to the disease process you are trying to treat or cure. Although it is often assumed that if scientists know a disease process they also know its etiology (cause), this is far from true. Thus, there is no foundation for the allopathic assumption that identifying a disease process (depressive symptoms for example) and decreasing or stopping that process means that the process had a physical origin. Strict adherence to the medical model leads to unfounded assumptions that all mental or emotional disorders derive from faulty functioning in the brain or nervous system. Many follow this strict adherence despite strong evidence that the mind (at least the thought processes and emotions of the mind) influences the body as much as any organ like the brain and particularly disorders like depression and anxiety. Although we would agree that severe mental disorders like Schizophrenia will almost certainly turn out to be primarily physiological in their etiology, others like depression are overdetermined (meaning there are many ways one may develop depression).

The Dual-Substance Hypothesis

The dual-substance hypothesis is often dated back to the philosopher René Descartes who lived in the early 17th century, although it certainly predates Descartes, because it exists to some extent in both Hindu and Buddhist philosophy. Descartes proposed both that a divine being exists and that this divine being created thinking things (*res cogitans*) and material things (such as bodies) that extend into the material realm (*res extensa*). He thought thinking things do not actually exist in time and space and cannot be externally observed. The extended beings do exist in time and space and can be externally observed. Although Gabbard (2001) believes that substance dualism has fallen out of favor, there is still ample support for variations on the hypothesis. Most variations equate "mind" with "consciousness."

Those holding a spiritual worldview often accept the dual-substance argument (in various formulations). Such a worldview may endorse a belief in a God or Divinity of some sort and possibly some notion of an eternal soul. This is not necessary, however, because the Buddhist view, for example, refers to different types of consciousness. One such type is a nonmaterial, ever-present "subtle consciousness" that we are thought to be most in touch with in deep sleep, advanced meditation, sneezing, and orgasms (think about that next time you sneeze!). From the Tibetan Buddhist perspective, epiphenomenalism and radical materialism fall into the trap of reifying physical phenomena (Descartes's *res extensa*) and denying the existence of mental phenomena (Descartes's *res cogitans*) (Wallace, 1999). From this perspective, to say that consciousness depends on the brain for existence is akin to saying that food depends on a stomach for existence. Psychologist Dean Radin (1997) wrote, "The average neuron consists of about 80 percent water and about 100,000 molecules. The brain contains about 10 billion cells, hence about 10^{15} molecules. Each nerve cell in the brain receives an average of 10,000 connections from other brain cells, and the molecules within each cell are renewed about 10,000 times in a lifetime" (p. 259). Radin then asked why, despite this continuous change, the patterns of our sense of self remain stable even though the physical material supporting that sense of self is in constant flux. The body you have while reading this (including your brain) is not at all the same body you had three years ago, but your sense of self is.

In addition to these two perspectives on the mind–brain problem, there are also variations such as interactionism (mind and brain are different but mutually causal) and parallelism (mind and brain are totally separate and do not communicate).

The mind–brain problem is an important context for the study of psychopharmacology. If this context is ignored, it is far easier to ignore things, such as the placebo effect, that hold important truths, as yet untapped, that may contribute to our knowledge of healing the symptoms of mental/emotional disorders. Ignoring the mind–brain problem also makes it easier to commit category errors and support them

with word magic (such as asserting that all depression is caused by a "chemical imbalance").

THE LAYOUT OF THIS BOOK

Part One

The first part of this book covers introductory material on the basic principles of psychopharmacology derived from the medical model as well as material representing the different truths or perspectives that complement the medical model. The information in Chapter Two focuses on pharmacokinetics: how the body acts on drugs. Chapter Three focuses on pharmacodynamics: how drugs act on the body. Chapter Four is an overview of the nervous system and tells the story of neurotransmission. The story of neurotransmission is the story of how brain cells (neurons) communicate both electrically and chemically. If you know this story, you have a general understanding of how psychotropic medications are designed and what they are supposed to do. The story of neurotransmission gives you a sense of the complexity of neurotransmission and a sense of how much people have yet to learn about it. By understanding the story of neurotransmission you will also be able to conceptualize what we currently know about mechanisms of action of psychotropic medications and about strategies pharmaceutical companies use to develop newer drugs.

Chapter Five gives an overview of relevant issues from the psychological perspective—the subjective sense of our experience of life. Psychological issues also include interpersonal issues relevant to mental health practitioners working with clients and other professionals. These issues include how to talk with clients about medication and compliance, how to approach collaboration with prescribing professionals, and how to process particular issues in supervision. In Chapter Six, the last chapter in Part One, we cover important social and cultural issues. We give an overview of cultural, racial, and gender differences regarding responses to psychotropic medication and then discuss the relevance of powerful institutions such as the pharmaceutical industry and the Food and Drug Administration.

Part Two

The second part of the book contains four chapters covering classes of commonly prescribed psychotropic drugs used to treat depression, anxiety, psychosis, mood instability, and a host of other conditions. Each chapter includes some history on the discovery and use of each category of drugs. This history provides the context that informs the four perspectives we comment on in each chapter. In addition to the history, we present medical model theories of how the drugs work and cover common drugs in each category including their side effects. Then, in each chapter, we include relevant material from the psychological, cultural, and social perspectives. Note that a medication approved by the FDA for some use has both a generic name and a brand name (or brand names). For example, Prozac is a brand name for a drug, the generic name for which is *fluoxetine*. Throughout the book when we refer to a drug in an example we try to provide the reader with both generic and brand names. The *PDR*, the *Physicians' Desk Reference*, is the standard reference book on drug names, both generic names and brands. It is available both at the reference desk of most public libraries and online.

Part Three

Part Three of the book, titled "Newer Issues," addresses psychotropic medications for children (including stimulant medications), the elderly and psychotropic medication, an update on herbaceuticals, a chapter on drug replacement therapy and the conclusion. The chapters in this part differ from those in Part Two in that these are newer areas and often have been the subject of fewer research studies. Many of the agents discussed in Part Two and used with adults are still being investigated for efficacy with children. Although scientists have done a great deal of research on the medical model of how stimulants affect children, they have only just begun to deal with which children

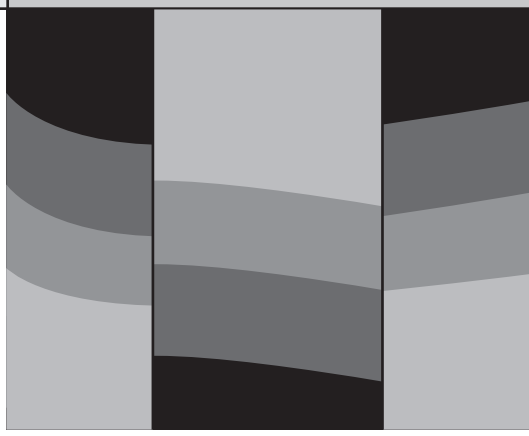
are really good candidates for stimulant therapy and what the medicating of young children means for this society. Note that each chapter contains study questions and exercises for the reader.

STUDY QUESTIONS AND EXERCISES

1. Describe the four perspectives derived from the Integral Model introduced in this chapter.
2. Outline some of the differences between a medical disorder that can be treated allopathically, such as a bacterial infection, and a mental/emotional disorder, such as depression.
3. Discuss with your classmates the mind–brain problem and your beliefs about the role of the mind and brain. In the context of your beliefs, discuss why you chose to enter a mental health profession.

CHAPTER TWO

Introduction to the Nervous System, Neurons, and Pharmacodynamics



INTRODUCTION

This chapter has six sections. The first introduces the central and peripheral nervous systems. The second takes a closer look at the central nervous system. The third section introduces glial cells and neurons. The fourth section introduces neurotransmitters. The fifth tells the story of neurotransmission and the sixth discusses pharmacodynamics or how drugs act on the brain.

SECTION ONE: AN OVERVIEW OF PHYSIOLOGY RELEVANT TO PSYCHOPHARMACOLOGY

Learning Objectives

- Know the basic parts of the central nervous system.
- Know the divisions of the peripheral nervous system.
- Understand that side effects can impact the central and peripheral nervous systems.

In this chapter, we provide an overview of the central nervous system, the brain, the brain's individual cells (called *neurons*) and **pharmacodynamics** (how drugs act on your body). This material has been the focus of most psychopharmacology texts, but remember, it is only part of the story—an important part that discloses truth—but not the whole truth.

In studying this material, some students become anxious, thinking, "I don't really have any background in biology or physiology." Relax. If "hard science" doesn't come naturally to you, think of the brain and the nervous systems as miraculous works of art that you can experience even if you cannot fully understand them. Set aside quiet study time to read this material. If it is new to you, don't expect to grasp it reading in 20-minute intervals or in a distracting environment. Approach this chapter as a "brain appreciation" tour. Remembering our mantra and the fact that the best "hard science" minds in the world are really just starting to understand the brain, sit back with a warm drink and join us for this tour through the most complex organ known to human beings.

A FEW BASICS

We start with a sketch of the **central** and **peripheral nervous systems**. Figure 2.1 illustrates key parts in both systems. Although we focus on central nervous system effects from various medications, it is important to understand some basics of the peripheral nervous system, because many drugs have **side effects** on this system. Much of the information in this section is drawn from Advokat, Comaty and Julien (2014), Bloom, Nelson, and Lazerson (2005), Carlson (2012), and Thompson (2000). Readers interested in full expositions of the brain and central nervous system are referred to their work.

The central nervous system includes the brain and spinal cord. The peripheral nervous system (the nervous system outside the brain and spinal cord) is divided into the **somatic** and **autonomic** (or visceral) **nervous systems**. The somatic nervous

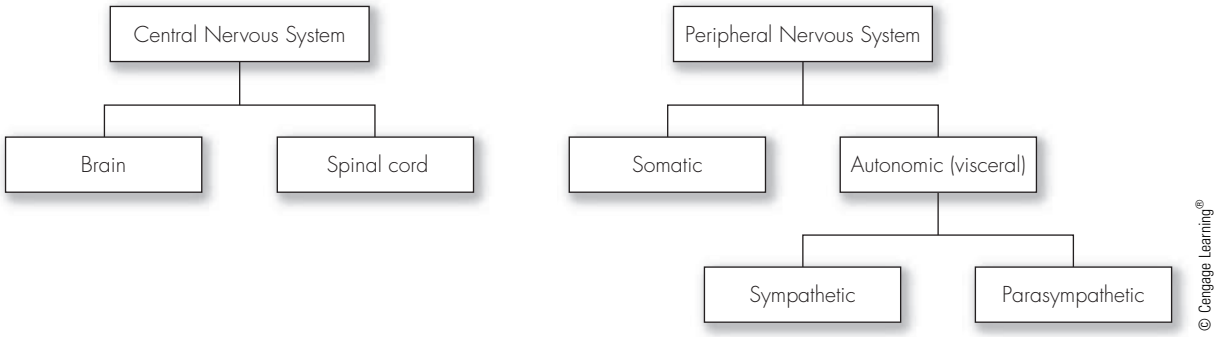


FIGURE 2.1 Basic Overview of Human Nervous Systems

system connects with sense receptors and skeletal muscles while the autonomic nervous system controls involuntary functions related to the glands, smooth muscles, heart, and viscera. This is important, because the goal for **psychotropic** drug compounds is to get them into the central nervous system. Remember that "psychotropic" means acting on or moving toward the mind, but because we lack a clear understanding of the relationship between mind and brain (as discussed in Chapter One) the medical model perspective assumes most psychotropic medications have to reach the brain. Note that there is also ample evidence that what we call "mind" may have correlates in other parts of the body, such as the bacterial signature we each carry in the gut which may also affect mental disorders (Bested, Logan, & Selhub, 2013; Forsythe, Kunze, & Bienenstock, 2012; Rodriguez, 2013; Stafford, 2012).

The nerves in your body and head that send information to and from the central nervous system are peripheral nerves. As you can see in Figure 2.1, the peripheral nervous system consists of the somatic and autonomic nervous systems. The somatic nervous system consists of peripheral nerves (nerves outside the central nervous system) that connect with sense receptors (receptors for vision, taste, and so on) and with skeletal muscles. The somatic nervous system regulates voluntary activity and relays information from the sensory organs to the central nervous system and from the central nervous system to the skeletal muscles. Thus, when you see a pint of Haagen-Dazs ice cream, the somatic nervous system relays the visual stimulus to the central nervous system where you decide to reach for the pint (and a spoon). Next the signal for reaching for the ice cream is relayed back to the skeletal muscles, and that signal brings a creamy delight within your reach.

The autonomic (visceral) nervous system regulates activities that are primarily involuntary. For example, once you have enjoyed your ice cream, the autonomic nervous system is correlated with activities such as digesting, so you can just bask in the afterglow of a good "sugar high." The autonomic nervous system is further subdivided into the sympathetic nervous system (active during arousal such as fight, flight, or freeze responses) and the parasympathetic nervous system (active during conservation of energy). Activation of the sympathetic nervous system mobilizes your bodily resources and prepares you to expend energy. For example, if you left the Haagen-Dazs on the counter and your dog spied it just before you reached for it, your sympathetic nervous system would help you spring into action, thwarting Fido and capturing your prize. The activation of the parasympathetic nervous system deactivates organs that the sympathetic nervous system activated. Once the ice cream is safe in your grasp, your parasympathetic nervous system returns your body to **homeostasis** so you can settle down.

A ready example of how a drug affects the peripheral nervous system is the popular antidepressant fluoxetine/Prozac (when referencing drugs in a chapter we will use the generic name, a forward

slash ("/") and then the brand name). Physicians often recommend that patients take fluoxetine/Prozac with food. This is because a common side effect of fluoxetine/Prozac (and most similar antidepressants) is nausea. This nausea occurs because the fluoxetine/Prozac affects serotonin receptors, and the peripheral nervous system in our digestive tracts is rich in these receptors. Because the drug must pass through these peripheral nervous system structures to get into the bloodstream and eventually the central nervous system, along the way any receptors to which the drug binds are affected. This also returns us to the interesting point about the "mind" being linked with the "gut." Could antidepressants acting on these gut receptors be causing more than just "side effects"? Even if the mind did turn out to be totally generated by the brain (the epiphenomenon hypothesis in Chapter One), what if the "brain" we are referring to includes the entire nervous system? Until researchers can secure funding to think beyond the limits of the current models, such questions remain unexplored.

Review Questions

- What are the two general parts of the central nervous system?
- What are the functions of the somatic and autonomic nervous systems?
- Why can drugs cause side effects in areas like the gut?

SECTION TWO: EXPLORING THE CENTRAL NERVOUS SYSTEM

Learning Objectives

- Be able to generally describe functions related to the brain stem, midbrain, and neocortex.
- Know what sorts of mental health symptoms may be directly related to the functioning of the limbic system.
- Understand the structural relationship between different parts of the brain.

As noted, the central nervous system consists of the brain and the spinal cord. The brain has three general "layers" that developed through evolution, commonly called the **brain stem** or **reptilian brain**, the midbrain or **mammalian brain** (which is technically part of the brain stem), and the **neocortex**. There is also the cerebellum (Latin for "little brain") that controls motor functions and posture. The brain has structures in and across these layers that we have correlated with particular functions. There are several ways to classify brain structures. We have followed the systems used by Advokat et al. (2014) and Carlson (2012), because these authors are highly respected in the field. Note that although some names of the brain structures may seem unfamiliar, they are usually Latin or Greek words for rather mundane objects and we will translate them as we go.

Exploring the Brain Stem

The brain stem includes structures that function to keep us alive. Figure 2.2 illustrates the structures of the brain stem and midbrain. When drugs interfere with the function of these structures, the results can be life threatening. For example, when a person drinks so much alcohol that it inhibits the neurons in these structures, the result can be coma and death.

The medulla oblongata is described as "the continuation of the spinal cord in the brain" (Thompson, 2000, p. 14) and controls breathing, heart rate, blood pressure, skeletal muscle tone, and digestion. This small, complex structure forms many connecting links between brain and spinal cord. Shaped like a pyramid, it is about an inch long and less than an inch across at its widest area. Its name comes from the Latin for "long marrow." The structure is so dense in neurons that the tissue looks dark, like bone marrow. Sometimes it is simply called the "medulla."

There is an important cluster of neurons in the brain stem called the **locus coeruleus** (pronounced *sa **roo** lee us*), from the Latin for "blue disc"; the cluster of neurons has a blue appearance. This structure consists of neurons that release norepinephrine and appear to help the person set priorities on

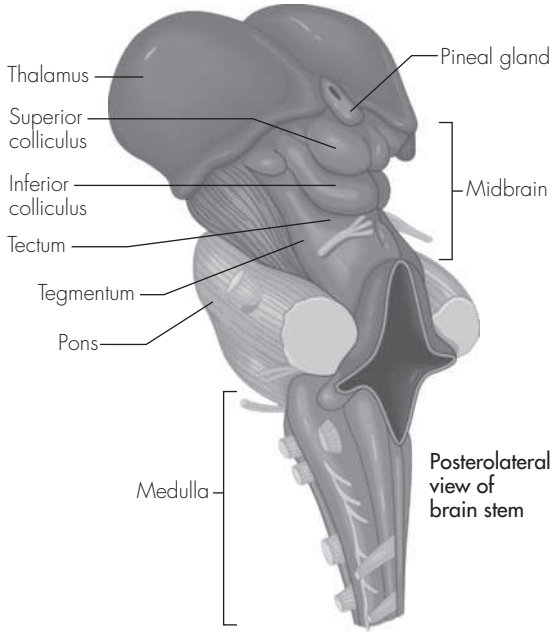


FIGURE 2.2 The Brain Stem and Midbrain

Source: From *Biological Psychology*, 7th ed., by J. W. Kalat.

incoming signals and decide where to place attention. Because of this link with attention, the role of the locus coeruleus is being investigated for links to the symptoms of attention deficit hyperactivity disorder (ADHD).

The pons (from the Latin for "bridge") connects the medulla oblongata and the midbrain. It also connects the two halves of the cerebellum. The pons extends into the reticular formation (part of the midbrain) and governs alertness, waking, sleeping, muscle tone, and some reflexes. The reticular formation has a netlike appearance (from the Latin *reticular*, "netlike"). The brain stem also includes the raphe nuclei (meaning "nerve cells forming a seam"). The raphe nuclei contain serotonin neurons and are thought to trigger slow-wave sleep. You can imagine the importance of understanding this if a client is going to take a drug that radically increases levels of serotonin in the brain. By increasing serotonin in this area, the drug is also going to cause sleepiness and possibly disrupt the sleep cycle, because serotonin is involved in sleep functions in the brain.

Exploring the Midbrain

The midbrain is also labeled **mesencephalon** (Greek for "midbrain") and is a continuation of the brain stem (see Figure 2.2). It merges into the thalamus and hypothalamus and encompasses what Advokat et al. (2014) call the "subthalamus." The subthalamus, combined with the basal ganglia, constitutes one of our motor systems called the **extrapyramidal motor system**. All information that passes between the brain and the spinal cord travels through the midbrain. As mentioned, the reticular formation is an interconnected network of neurons that extends from the spinal cord into the midbrain. These neurons are implicated in sleep, arousal, and a number of vital functions. The medulla, pons, and midbrain are thought to have developed early in human evolution (thus the common name "reptilian brain").

The Cerebellum

The cerebellum (from the Latin, meaning "little brain") looks like a little brain attached onto the larger cerebrum (illustrated in Figure 2.3). The cerebellum lies over the pons and is crucial to things such as balance and smooth, coordinated movement. It has connections with the vestibular system (the balance system located in the inner ear), the auditory, and the visual systems. The cerebellum, the subthalamus, and the basal ganglia make up the **extrapyramidal system**, which helps coordinate movement, including initiation, smoothness, and termination of movement. If people take a medication that interferes with the functioning of the extrapyramidal system, they will likely suffer from involuntary movements called **extrapyramidal side effects**. We discuss these in detail in our treatment of antipsychotic medications.

Exploring the Diencephalon

"**Encephalon**" is a Greek word that simply means "brain." "Di" means "between," so the diencephalon

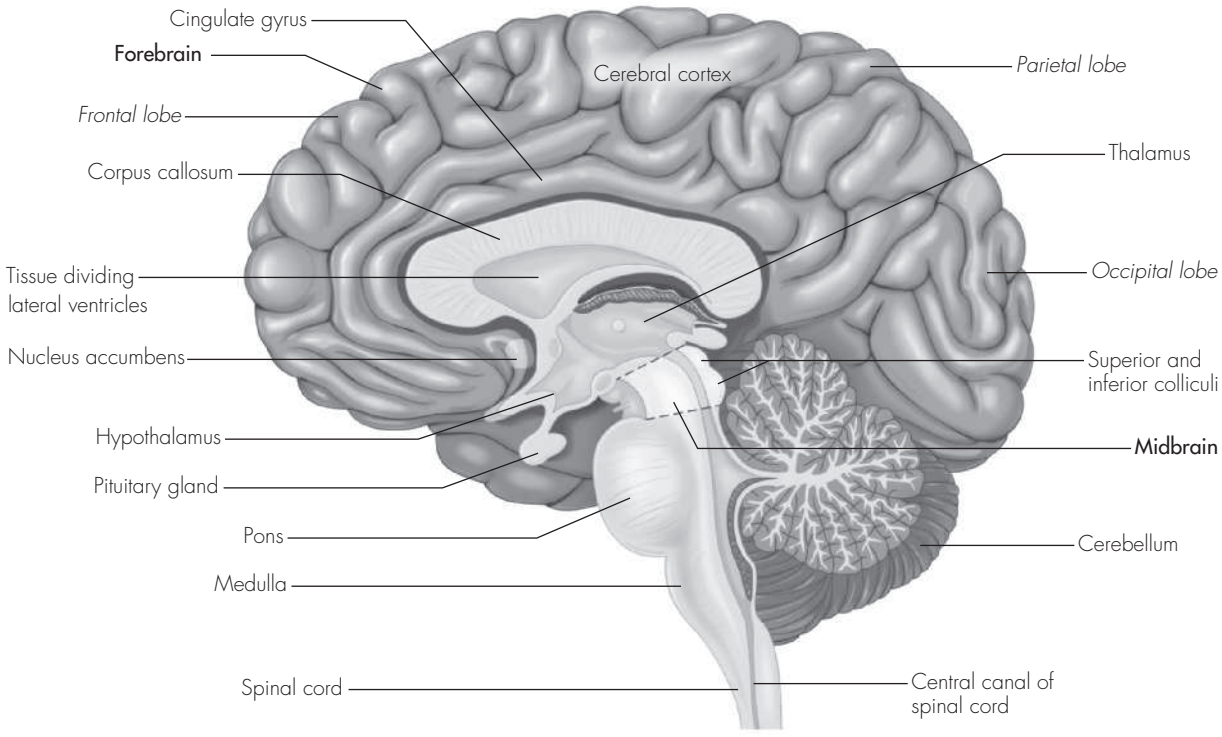


FIGURE 2.3 A Sagittal Section Through the Human Brain

Source: From *Biological Psychology*, 7th ed., by J. W. Kalat.

is between the telencephalon and the brain stem. There are several important structures in this brain area. The thalamus, a large group of nerve cells, acts as the final relay area for the major sensory systems that project to the cerebral cortex: the visual, auditory, and somatic sensory systems (Thompson, 2000). Oddly enough, the translation of the Latin word *thalamus* is "bedroom" or "receptacle." Although "receptacle" means basically "final relay area," we have yet to figure out how "bedroom" fit in for the ancient translators, but feel free to use your imagination.

The hypothalamus ("below the thalamus") is a collection of cells that lie above the pituitary gland and immediately in front of the midbrain. The hypothalamus controls the autonomic nervous system and endocrine system and maintains the body's homeostasis (internal state). It also regulates temperature, fluids, metabolism, appetite for specific nutrients, as well as what are called the "four Fs" (Fighting, Feeding, Fleeing, and Mating—again, use your imagination). Hormones secreted by the hypothalamus control the pituitary gland. Part of the wide-ranging influence of the hypothalamus is related to its control over the pituitary gland. Together, they act as a "master control system." "The hormones they release act on the other **endocrine glands** such as the thyroid, adrenal, and pituitary glands that secrete certain substances, particularly hormones, directly into the blood. The hormones released by the endocrine glands then act back on the pituitary gland and hypothalamus to regulate their activity, an example of feedback control" (Thompson, 2000, p. 17). The hypothalamus is also located near and has influence over what Olds and Milner (1954) dubbed the brain's **pleasure centers**.

Exploring the Limbic System

The limbic system is a series of brain structures that help us attach emotional meaning to sensory stimulation. In some systems of classification the limbic system is associated with the diencephalon, and in others it is associated with the telencephalon. The limbic system includes the amygdala (Latin for "almond," which it resembles), the septum (Latin for "dividing wall" or "enclosure"), the hippocampus (Latin for "seahorse" and based on resemblance), and portions of the thalamus. Bear in mind that many of the structures we are discussing are actually two—one on each side of the brain so technically you have two "amygdalae" but for sake of ease we refer to these in the singular. The amygdala integrates and directs emotional behavior, attaches emotional significance to what the senses signal, and mediates defensive aggressive behavior. Damage here can produce **Kluver-Bucy syndrome**, which is characterized by diminished fear and aggression as well as amnesia and hyper sexuality. The septum inhibits emotionality, as evidenced by the fact that lesions in the septum produce septal rage syndrome. In this syndrome, damage to the septum leads to uninhibited emotional expression, particularly the expression of anger and aggression. The septum is also part of the pleasure centers of the brain. The hippocampus is a curved ridge in the limbic system, involved in moving signals from short-term memory to long-term memory.

Exploring the Telencephalon

The **telencephalon** consists of the right and left halves of the cerebrum (*tel* is a variation of the Greek *tele*, meaning "end" or "complete," so the translation is "end of the brain" or "completion of the brain"). The outer portion of the cerebrum is the cerebral cortex. This is the brain's outermost layer, the image you are probably familiar with from pictures of the human brain. This cortex is divided into four lobes (roundish projections) by sulci (deep grooves in the surface). The four lobes are named for the bones of the skull covering them (see Figure 2.3) (Carlson, 2012). This part of the brain is correlated with the functions related to self-awareness or sentience that make humans unique in the animal kingdom. The tissue in the lobes can generally be mapped according to function, although in many cases, if an area is damaged another part of the brain may pick up that function. For most functions, their expression is contralateral ("opposite-sided"), meaning that an area on the right side of the brain controls something on the left side of the body. Next we summarize the four main lobes and some of their general functions.

The frontal lobes of the cerebral cortex are generally involved in motor behavior, expressive language, concentration, orientation (time, place, and person) thinking, and reasoning. These lobes contain the pyramidal system that is involved in fine, intricate movements. The left frontal lobe contains **Broca's area**, which is involved in speech production, and damage to this area can produce the experience of *expressive* aphasia (a self-conscious deficit in the ability to articulate or express language). The temporal lobes (located near the areas of your head called the "temples") are related to receptive language, memory, and emotion. These lobes contain **Wernicke's area**, which is involved in comprehending language. Damage to this area can produce *receptive* aphasia. The parietal lobes are located under the skull on the top of your head and contain the primary **somatosensory cortex**. This area receives and identifies sensory information from tactile receptors and processes visual and auditory sensations. Damage to the parietal lobes can produce Gertsmann's syndrome, which includes agraphia (inability to write), acalculia (difficulty with mathematical calculation), and right–left confusion. As you can imagine, researchers are trying to link what *DSM-5* calls Specific Learning Disorders to these areas of the brain (e.g., impairment in mathematics is related to problems in the parietal lobe). Finally, the occipital lobes (at the back of your head at the base of the skull) are largely associated with the **visual cortex**. Damage to the occipital lobes produces visual agnosia (the inability to recognize familiar objects on sight).

Under the cortex lie the smaller areas of the telencephalon (Bloom et al., 2005). The basal ganglia

lie at the central regions of the cerebral hemispheres and are systems of cell **nuclei** that effect voluntary movement. They form the primary part of the extrapyramidal motor system (described earlier). Next we focus on the nerve cells in these structures and their function, so that we can begin to explain the mechanisms of action in psychotropic medications.

Review Questions

- How would you generally describe the functions of the brain stem, midbrain, and neocortex?
- What part of the midbrain is likely indicated in anxiety symptoms?
- What is the relationship of the cerebral cortex to the cerebrum?

SECTION THREE: AN OVERVIEW OF NEURONS AND GLIAL CELLS

"Neurons do not define the essence of people, nor do deficiencies in neurotransmitters explain mental disorders" (Kay, 2009, p. 288).

Learning Objectives

- Be able to discuss how neurons differ from other cells in the body.
- Be able to draw a simplistic picture of a neuron and label the soma, nucleus, axon, terminal button, synaptic vesicles, dendrites, and receptors.
- Know why the blood–brain barrier is important to designers of psychotropic medications.
- Understand our revised science of what glial cells do.

The brain weighs about 3 pounds and has a volume of about 3 pints. It contains a lot of **neurons**. Accounts vary on to how many neurons the brain contains: for example, Churchland (1995) and Cozolino (2010) estimate about 100 billion while Barlow and Durand (2002) estimated about 140 billion. Most recently Advokat et al. (2014) estimated 90 billion. Perhaps we are best off estimating "many billions of neurons in every human brain" (Thompson, 2000, p. 29) (or as Carl Sagan might have put it, "billions and billions"). As cells, neurons are unique in that they are created before we are born and have the capacity to live as long as we do. Up until the beginning of the 21st century, scientists commonly believed that at birth human beings had all the neurons they were ever going to have. This view is changing, as researchers now confirm that neurogenesis (the growth of new neurons) occurs in adult mammals (Martino, Butti, & Bacigaluppi, 2014; Shors et al., 2001; Van Praag, Christie, Sejnowski, & Gage, 1999) and correlates with the learning of new tasks (Gould, Beylin, Panapat, Reeves, & Shors, 1999).

Although all human cells renew themselves, not all cells divide regularly. One reason that neurons may not divide as regularly as other types of cells is that they form essential functional units in brains. As Thompson (2000) pointed out, everything people are or do has correlates in the sequencing of neurons and their interconnections. If neurons had to keep dividing to replace themselves, valuable sequences and interconnections might not form.

Although neurogenesis research continues to explore questions about how new neurons form, most knowledge about the correlation of neuronal function concerns the growth of axons and dendrites from existing neurons. This growth (called **arborization**) is prolific in the first few years of life. Moreover, you may have heard the saying "Size doesn't matter," and this is particularly true of the brain. Whales and dolphins have larger brains than humans, and although these mammals are no slouches intellectually, they do not match the human brain capacity for representational power. Nor do the *number* of neurons matter; it is the number of connections between the neurons that is important.

The neurons of the human brain have an enormous representational capacity. By way of analogy, Churchland (1995) compares this capacity to a standard 17-inch television screen. Such a screen has a representational capacity of about 200,000 pixels (a pixel is the smallest element of an image that can be

processed). To get enough pixels to match the representational power of your brain, you would have had to cover all four sides of the Sears Tower in Chicago with such screens—and you have it all between your ears, as the saying goes. Such is the representational power of the brain.

THE BASIC ANATOMY OF A NEURON

Figure 2.4 is a simplistic rendering of a neuron. Actual neurons vary in length from a few millimeters up to about a meter and may have several thousand synaptic connections with other neurons (Julien, Advokate, & Comaty, 2014). Neurons come in many different types and shapes, but they all have structures similar to the ones in the figure. It is important to learn a simplistic version of a neuron first so that you can learn the story of neurotransmission. Then you can learn how medications interfere with the sequence of events in that story (or in other words how medications change the story of neurotransmission). Once you've learned that, you have a basic sense of the mechanisms of drug action. The importance of learning the basic parts of the neuron will become clear as we discuss the mechanisms of action of psychotropic medications. Using Figure 2.4 as your guide, let us begin by discussing the soma or cell body of the neuron. The dark spot on the figure of the soma is the cell nucleus, which contains the genetic material of the cell. The soma contains the **mitochondria**, which are structures that provide energy for the neuron. Extending from the soma in one direction are **dendrites**, which are structures that receive inputs or messages from other cells through receptors. The receptors are typically pictured as located on the ends of the dendrites but can occur anywhere on the neuron. Receptors are basically chains of proteins that act as communication devices, allowing neurotransmitters (chemical messengers) to bind to them.

In our illustration, extending in the other direction from the soma is the axon. Many elements made in the soma (such as enzymes and receptors), as well as the "raw materials" for these elements, are transported up and down the axon. The axon also transmits electrical signals that can cause the cell to "fire." When a cell "fires," it releases neurotransmitter molecules from its terminal button. In our illustration at the far end of the axon are the terminal buttons. The terminal buttons contain sacks (called *synaptic vesicles*) of neurotransmitter molecules. When the electrical signal causes the cell to "fire," these sacks merge with the **permeable** membrane of the terminal button and the neurotransmitters are released into the synaptic cleft or synapse (the space between the terminal button and the neighboring receptors to which the neurotransmitter will bind). Although there is a universe of activity in each cell, this glance at the general

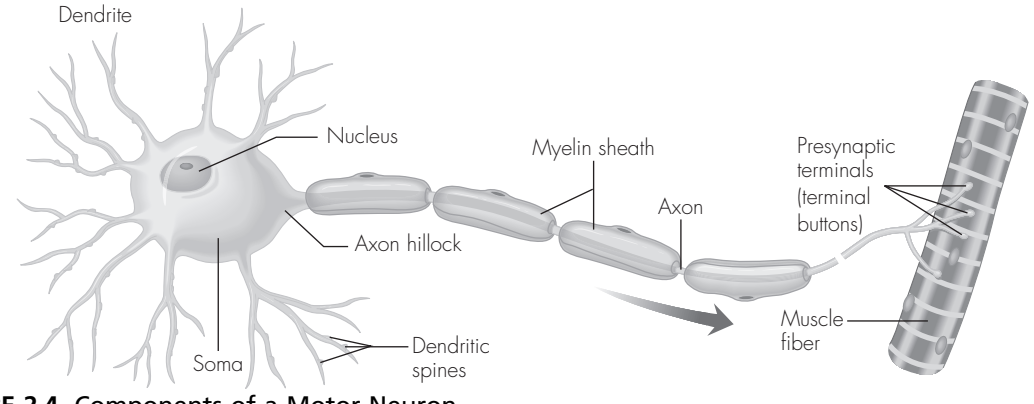


FIGURE 2.4 Components of a Motor Neuron

Source: From *Biological Psychology*, 7th ed., p. 32, by J. W. Kalat.

components will suffice until later in the chapter, when we discuss neurotransmission in more detail.

Now, we say that chemical neurotransmission occurs at the **synapses**, which Stahl (2000) defines as "specialized sites that connect two neurons" (p. 1). Neurons send synaptic information through firing and releasing neurotransmitter molecules. They receive synaptic information through their receptors. The number of synapses (points of connection between a neuron and neighboring neurons) on each neuron varies from around 5000 on a mammalian motor neuron to some 90,000 on a single Purkinje cell in the cerebral cortex. (This type of cell, named after the Czech physiologist who first charted its function, is related to the contraction of the heart.)

When the body is resting, the brain, which accounts for only about 2% of the body's mass, consumes about 20% of the body's oxygen. This is a lavish consumption of energy! The brain needs all this energy to maintain ionic gradient essential to receiving and sending information via the synapses. An ionic gradient is a form of potential energy that keeps the chemistry inside a cell different than the chemistry outside the cell so it can be thought of as a charged signal (an electrical charge). You can think of this charge as a rate of change in relation to the distance of the axon. There is a structure on the axon called the axon hillock. It is the last site in the soma or cell body where incoming signaling is summed and if it surpasses a particular threshold, the action potential (charge) is initiated down the axon toward the terminal button. As the electrical charge travels down the axon it may be facilitated by the influx of positively charged ions (e.g., sodium) or inhibited by an influx of negatively charged ions (e.g., chloride). When the action potential is facilitated all the way across the axon to the terminal button the cell fires, or releases, its neurotransmitter. As noted, to carry an electrical charge down an axon, positive ions must flow into the axon. Once the charge is carried down the axon, these positive ions are pumped back out of the cell (this is sometimes referred to as the *sodium potassium pump*). As you will see, these ionic gradients play the key role in determining whether or not neurons fire. Imagine: A single neuron handles a thousand signals in the space of a second, and it may fire several hundred times a second, so its energy consumption must be lavish.

GLIAL CELLS

Once thought to be an energy-saving device, glial cells have turned out to be much more. Myelin (pictured in Figure 2.4) is peculiar to vertebrates, although not all neurons in vertebrates are myelinated. For example, phylogenetically older fibers such as the C-fibers that innervate the skin and carry information about pain are less myelinated. If you have ever been pounding a nail and the hammer slipped, smashing your finger, you may recall having that split-second knowledge that it is going to hurt in a few milliseconds. With more myelin, you wouldn't have those milliseconds to anticipate the coming pain. Myelin is made of glial cells (particularly Schwann cells and oligodendroglia) but as you proceed up the evolutionary ladder, a particular type of glial cell called astrocytes increase in size and number.[1] In the 20th century, it was believed that myelin acted like the insulation on electrical wiring. This is one function of myelin. The more myelinated an axon is, the better insulated it is and the faster it can conduct a signal. When you see a person with a disease that degrades the myelin (such as multiple sclerosis), you see that he or she has difficulty moving, because the nerves coordinating the signals for the movement cannot send the electrical signals efficiently.

The conduction velocity depends on the diameter and myelination of the axon. A well-myelinated axon in a human motor neuron can conduct an impulse as fast as 130 meters per second (equivalent to approximately 300 miles per hour), whereas an unmyelinated fiber conducts at about 0.5 meters per second (a little over 1 mph). Events in the world of silicon chips happen in the nanosecond (a one-billionth of a second), whereas events in the

[1]There are three types of glial cells: astrocytes, Schwann cells, and oligodendroglia. Astrocytes move neurotransmitters, food, and waste. Schwann cells and oligodendroglia wrap around neurons like sheaths.

world of neurons happen in the millisecond (a one-thousandth of a second). Brain events are quite slow in comparison to computer events, but in complex tasks such as recognition, brains leave computers "in the dust," because brains accomplish recognition more quickly. In addition, all computers must put information through a central processing unit (CPU) whereas brains have enormous redundancy in the system so that if a signal does not get from point A to point B, the same signal can be sent from point C to point D or from point E to point F. Neurons are plastic and dynamic. Their information-relevant parts grow and shrink. The axons and dendrites are constantly changing, establishing new connections and removing old connections. This "arborization" is an important concept in psychopharmacology, because many drugs exert an influence to change the information-relevant parts of the neurons. Neurogenesis research findings are so new that speculations on the implications for pharmacology have just begun.

Myelin is made from a type of cell called a "glial cell." "Glial" means "glue," and glial cells form different types of protective barriers (sheaths) around neurons (of which myelin is one). In the late 19th century, when Ramon Santiago Cajal was doing work with neurons, his brother Pedro set forth a theory that glial cells were simply "support cells" for neurons. Cajal accepted his brother's theory and this led to the "neuron doctrine," which posited that neurons alone were responsible for our thought and mental processes. Glial cells usually outnumber neurons by a ratio of 10:1 making up 85–90% of the brain. Under the influence of the neuron doctrine, 20th century laypeople came to believe that we only used 10–15% of our brain power (because of course 85–90% of the cells were glial cells).

In different parts of the body, glial cells have different names that reflect the person who discovered them or their function. In the peripheral nervous system, Schwann cells perform the myelinating function; in the central nervous system, oligodendrocytes perform the same function. A third glial cell type, astrocytes, function as fences and filters for the blood–brain barrier and more importantly move neurotransmitters, food, and waste around the brain. A fourth type, microglia, function as scavengers cleaning up dead neurons and other disintegrated material (Fields, 2008, 2011). We'll take another look at the blood–brain barrier shortly.

Another important finding about astrocytes is that we learned that they can communicate to themselves with calcium waves. Astrocytes have hundreds of "endfeet" that spread out from their body toward blood vessels, other astrocytes, and neuronal synapses. Calcium released from internal stores can spread from astrocytes to areas hundreds of times larger than the original astrocyte. These calcium waves can also cause neurons to fire (Koob, 2009). This could radically alter our understanding of the electro-chemical processes in the brain. The implications are huge as we add the impact from 85% of the brain's cells, which previously have been more or less ignored in our efforts to understand the brain. This might be akin to thinking you know football as a game where a team must move the ball 100 yards to score a touchdown. Then you learn that actually it is 350 yards and the ball moves not just because of the teams but also in response to the volume of the crowd and how their cheers bounce off cars in the parking lot. It looks as if taking glial cells into the equation is literally a "whole new ball game."

THE BLOOD–BRAIN BARRIER

Over 100 years ago, Paul Ehrlich discovered that if blue dye is injected into an animal's bloodstream, all the tissues are tinted blue *except* the brain. You must inject the dye into the brain ventricles to get that tissue to turn blue. Although Ehrlich was working for a dye company on a different project, he thus unwittingly discovered the blood–brain barrier. In most of the body, the cells that form the capillaries are not spaced tightly together, so substances can move from blood plasma to the tissue.

In the central nervous system, the capillary cells do not have the same gaps, because they are filled

by the astrocytes that make up the blood–brain barrier. This barrier blocks many substances from entering the central nervous system. In some areas, the barrier is weaker than others, to allow specific functions that have developed through evolution. One example of such an area is the *area postrema*, which signals vomiting. The barrier is weak here, so toxins in the blood can be detected. Once it detects toxins, the brain triggers the vomiting response to preserve the organism.

The blood–brain barrier serves an important survival function by keeping foreign elements such as toxins out of the brain. But what about things such as nutrients? Nutrients such as glucose must be transported through the capillary walls by special proteins. This is very important, because to exert their effects all current psychotropic medications must reach the central nervous system. To do so, they must pass through the blood–brain barrier. The glial cells that make up the blood–brain barrier have a high fat content. The myelination of the brain in infancy is one reason babies need a lot of fat in their diet. We refer to fatty cells as fat soluble (the technical term for this is **lipophilicitous**—another great cocktail party word). Thus, to pass through the blood–brain barrier, a molecule also must be highly fat soluble. Almost all psychotropic medication molecules are fat soluble, with perhaps the sole exception of lithium, which must be carried across the blood–brain barrier by other means.

Review Questions

- How do neurons differ from other cells in the body?
- Draw a simplistic picture of a neuron and label the soma, nucleus, axon, terminal button, synaptic vesicles, dendrites, and receptors. Explain why it is "simplistic."
- What is the function of the blood–brain barrier and why is it important to designers of psychotropic medications?
- How has our understanding of glial cells progressed in the 21st century?

SECTION FOUR: TYPES OF NEUROTRANSMITTERS

Learning Objectives

- Generally understand what makes a ligand a neurotransmitter.
- Be able to identify both excitatory and inhibitory neurotransmitters.
- Be able to describe the difference between polypharmacy and co-treatment.

The brain has literally dozens of known or suspected neurotransmitters. Scientists may discover many more. To be considered a neurotransmitter, a substance must (1) be synthesized in the **presynaptic** neuron, (2) be released from the presynaptic terminal, (3) cause excitatory or inhibitory signals, and (4) have some mechanism for removing it from the site of action (Churchland, 1995). Despite the number of existing neurotransmitters, only a fraction of those we know of are affected directly by the psychotropic medications we discuss in this book. Table 2.1 lists neurotransmitters commonly involved in the actions of psychotropic medications.

Neurotransmitters are made from **precursor compounds** in the neuron. You can think of precursors as the "raw materials" with which

TABLE 2.1 Neurotransmitters Involved in Psychotropic Medications and Their Abbreviations

Glutamate	Glu
Gamma-aminobutyric acid	GABA
Acetylcholine	Ach
Dopamine	DA
Norepinephrine	NE
Epinephrine	Epi
Serotonin	5-HT

neurotransmitters are made. These compounds include amino acids, glucose, and certain amines such as choline. You take many of these precursors into your body through the foods you eat. Think of neurotransmitters as chemical messengers in the nervous system. As we explain later, when a cell fires and releases neurotransmitters, these same transmitters bind to receptors on other neurons, conveying information and further exciting or inhibiting neighboring neurons.

Now we provide an overview of the primary neurotransmitters. Become generally acquainted with them, so that when we discuss mechanisms of action in drugs you can recognize the primary neurotransmitters involved. Although scientists generally think that typically neurons only produce one type of neurotransmitter, each neuron may be outfitted with receptors for multiple neurotransmitters. Thus, although typically a neuron that produces only dopamine releases only dopamine (there are always exceptions though), it can be affected by changes in available serotonin, norepinephrine, acetylcholine, and so on. This multiple sensitivity produces a "ripple effect": Using a drug to affect the levels of only one neurotransmitter may end up affecting the levels of many neurotransmitters.

GLUTAMATE (GLU)

Glutamate (also called *glutamic acid*) is one of the nonessential amino acids, meaning it is synthesized in the body and you do not have to acquire it in your diet. One of the main sources of glutamate in the body is the breakdown of **glucose**. Most neurons have glutamate receptors. Glutamate generally serves an excitatory function, encouraging neurons to fire, and plays a key role in sensory functions and in some brain structures we have discussed in this chapter, including the pyramidal and extrapyramidal nervous systems, the hippocampus, and the cerebellum. Glutamate may be the dominant excitatory neurotransmitter in our brains. Julien et al. (2014) noted that a newer drug for narcolepsy actually works by augmenting glutamate neurotransmission (as opposed to drugs such as amphetamines that augment dopamine neurotransmission). Researchers hope that a drug augmenting glutamate transmission will not show the dependence-inducing properties that amphetamines have. In addition, drugs that modulate glutamate have been recently targeted as a possible intervention for Schizophrenia (Hasimoto, Malchow, Falkai, & Schmitt, 2013). This is difficult because too much glutamate can trigger seizures or kill brain cells while too little can cause comas (Locke, 2008).

GAMMA-AMINOBUTYRIC ACID (GABA)

Gamma-aminobutyric acid (GABA) is one of the amino acid neurotransmitters and occurs almost exclusively in the brain. GABA reduces the firing of neurons and may be the predominant inhibitory neurotransmitter of the brain. Paradoxically, glutamate is a precursor for GABA, but whereas glutamate is excitatory, GABA is inhibitory. GABA is so common in the central nervous system that neurologists believe a full one-third of synapses are receptive to it (Zillman, Spiers, & Culbertson, 2007). Although GABA is inhibitory, it is important not to oversimplify this into the erroneous belief that all GABA transmission "mellows you out." For example, some areas of your brain (such as your sleep centers), when stimulated, calm you down. If GABA molecules inhibit these areas, then the end result is the *opposite* of calming you down. GABA-ergic areas of the brain also help people control motor behavior. People with **Huntington's chorea** have difficulty controlling their motor behaviors, and physiologists believe this is caused by losing GABA-ergic neurons (Zillman et al., 2007).

ACETYLCHOLINE (ACH)

Acetylcholine was the first major neurotransmitter to be identified in the 1920s. (Epinephrine was discovered in 1904 but is less important in psychopharmacology.) Acetylcholine is prominent in the peripheral and central nervous systems. It is present peripherally at the muscle–nerve connection for all voluntary muscles and at many involuntary nervous system synapses. The exact role of acetylcholine neurons is becoming clearer with research. Generally, they are believed to be involved in alertness, attention,