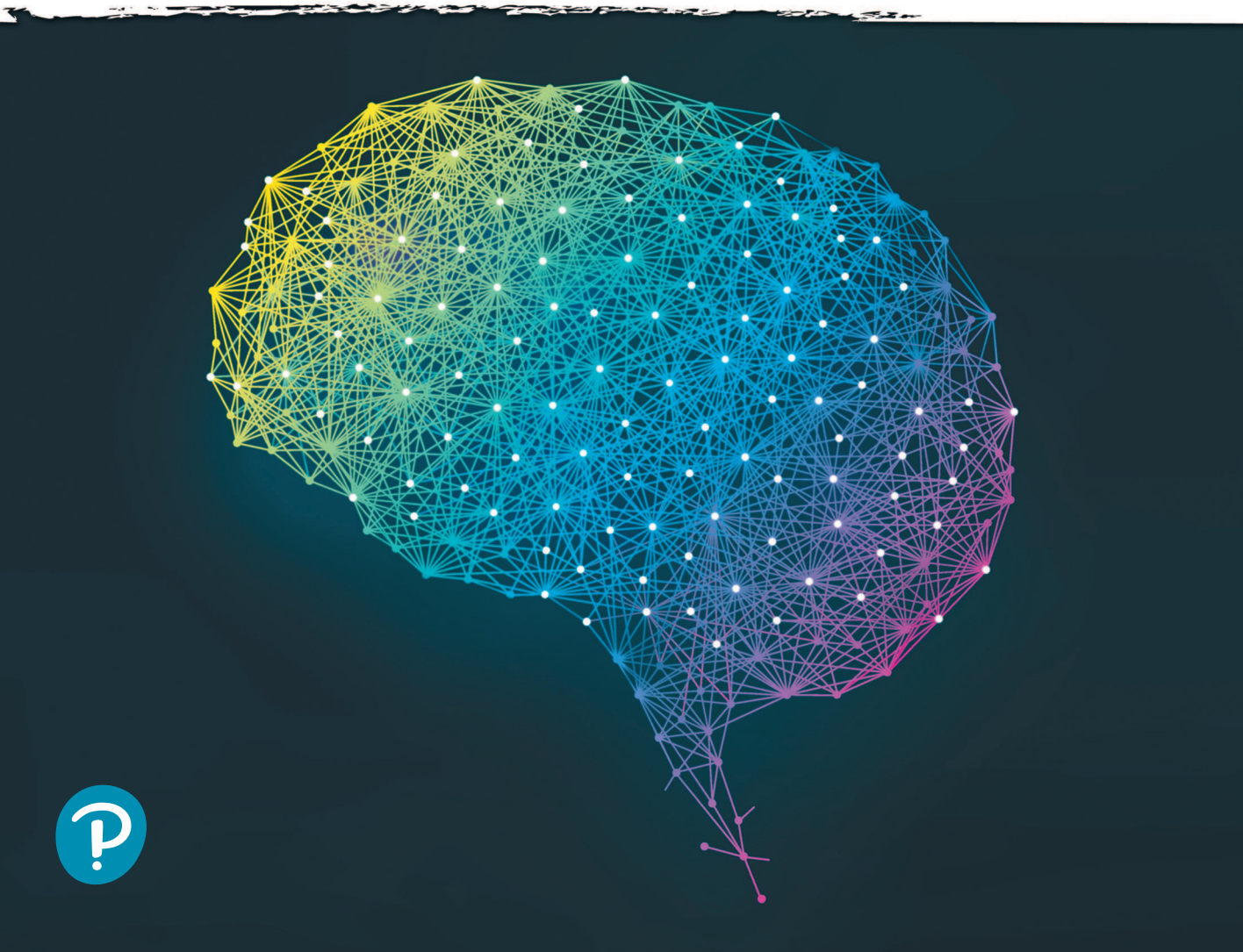
The Merrill Counseling Series

3RD EDITION

BASIC PSYCHOPHARMACOLOGY FOR MENTAL HEALTH PROFESSIONALS

RICHARD S. SINACOLA TIMOTHY PETERS-STRICKLAND JOSHUA D. WYNER



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Third Edition

Basic Psychopharmacology for Mental Health Professionals

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To my students, past and present, who always inspire me to do better.

R. S. Sinacola

To my loving family who help me grow and thrive: Howard, Alexia, and Alyssa.

T. Peters-Strickland

To my loving parents, Garret and Peggy, who taught me to be good, and to my amazing girls, Erin, Eliana, and Kayla, who push me to be better.

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PREFACE

Welcome to the third edition of *Basic Psychopharmacology for Mental Health Professionals (formally Basic Psychopharmacology for Counselors and Psychotherapists).* With more psychotherapy patients taking psychotropic medications than ever before, counselors, psychologists, social workers, and family therapists need quick and accurate information. Finding this information is not easy because most textbooks on psychotropic medications are written by physicians for physicians. In the few cases that nonphysicians, usually biologically oriented Ph.D.'s, have attempted this endeavor, they have produced works that are more like physiological psychology texts, which are beyond the basic questions and interests of the student, counselor, or psychotherapist.

The third edition of *Basic Psychopharmacology for Mental Health Professionals,* like the first and second editions, is designed to provide basic yet comprehensive information for the typical graduate student in a mental health training program, as well as the practicing clinician in the field. Most graduate students have not taken undergraduate courses in physiological psychology, and their knowledge of the brain and neuronal functions is minimal. This textbook presents these and other topics in easy-to-understand language. In fact, the entire text continues to be written in a familiar style that invites the otherwise intimidated professional to learn more. The text is even written so the interested layperson can obtain a basic understanding of how these medications work. Medical jargon is kept to a minimum, and voluminous information on psychopathology is also omitted because we assume that clinicians and graduate students are familiar with the *Diagnostic and Statistical Manual of Mental Disorders,* 5th edition (DSM-5) and the criteria used in diagnostic determinations.

In addition to offering up-to-date information on the latest medications currently available for treating mental illness and other related conditions, this book will assist clinicians in working more effectively with their patients on medication and with the professionals prescribing them. The book is organized to address the most commonly presented types of pathology first.

What's New in the Third Edition

- Updated throughout to reflect DSM-5 criteria for diagnoses and appropriate considerations for psychopharmacology agents for those diagnoses
- Updated information on the latest medications used to treat a variety of mental health concerns
- Updated research on the newest medications, including novel applications of some of the older, well-known medications
- Updated tables in each treatment-related chapter that reflect the latest medications and their properties
- An updated comprehensive table of all psychopharmacology agents, located in the appendix
- An additional clinical case example providing the reader with two typical case examples in each treatment-related chapter
- The addition of new diagnostic considerations and medications in Chapter 14, Treatment of Comorbidity and Other Disorders

Chapter Outlines for the Third Edition

- Chapter 1 gives students and their professors and practicing clinicians reasons why the study of psychopharmacology is so important for the mental health professional. Some ethical and spiritual considerations are also explored.
- Chapter 2 provides a basic explanation of the functions of the brain and neurological system, including the anatomy and function of neurons, the role of neurotransmitters and other neurochemicals involved in emotions and behavior, and the electrical and chemical communications between cells.
- Chapter 3 addresses issues related to psychopharmacology and pharmacokinetics, including methods of administering drugs; absorption, distribution, and elimination of drugs; therapeutic dose and therapeutic index; tolerance, withdrawal, and discontinuance of drugs; synergism and potentiation; placebo effects; and prescription and pharmaceutical terms.
- Chapter 4 provides the therapist with tools and techniques for taking a thorough history of the patient, including a patient history outline, a mental status outline, assessment and testing instruments, and an outline for an initial patient interview. Suggestions for additional assessment tools are available online.
- Chapters 5 through 12 address trade and generic medications and herbals used to treat common mental health conditions: unipolar depression, bipolar illness, anxiety and psychotic disorders, ADHD and attention disorders, and cognitive, sleep, and personality disorders.
- Chapter 11 concentrates solely on sleep disorders. It was included because many clinicians who deal with patients presenting with these concerns are unfamiliar with the medications used to treat insomnia.
- Chapter 13 addresses chemical dependency, co-occurring conditions, and the special medications used to treat this population. This topic is not addressed in most other texts.
- Chapter 14 provides typical medication regimens used to treat patients with comorbid conditions, including patients with chronic pain, eating disorders and obesity, impulse control problems, sexual compulsivity, gambling, and other intrusive behaviors.
- Chapters 15 through 19 present cases across the developmental continuum, including children and adolescents and early, middle, and older adults. Many of the cases are based on actual patients. The cases are used to demonstrate both the diagnostic process and the rationale for choosing one medication over another.
- Complete, easy-to-read tables of medications appear throughout the text and are combined into a master table in the Appendix.

This text serves as a basic introduction to psychopharmacology for the nonmedical provider. Although information on dosage and use was accurate at the time of writing, the clinician should not use this information as a guide for prescribing medications. All clinicians should consult their respective codes of ethics and their home state's scope of practice to ensure that discussing medications and their effects with patients is within the scope of their license to practice.

This text was developed to be a brief yet comprehensive overview of clinical psychopharmacology. It can be read easily in a weekend and will serve as a handy reference guide for mental health professionals from all disciplines. Combined, we authors have more than 62 years of clinical experience—one of us as a psychologist with a private practice and a professor teaching psychopharmacology in a graduate setting, one as a psychiatrist treating patients from all walks of life and conducting research in the application of pharmaceutical agents, and one as an educator of marriage and family therapy who also practices as a marriage and family therapist. We hope that the readers find this book informative as well as interesting.

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BRIEF CONTENTS

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CHAPTER 1

Why Study Psychopharmacology

REASONS FOR THE NONMEDICAL THERAPIST TO READ THIS BOOK

Over the years, various counseling and psychotherapy models have emerged, flourished, continued, or faded from use. Many of these theories or models offered the clinician options for maximizing the therapeutic progress of his/her clients. Many of them emphasized humanistic, psychoanalytic, existential, or behavioral techniques that downplayed the role of medication in the treatment of many conditions. In fact, except for those patients with serious psychopathology requiring inpatient hospitalization, most patients were not placed on medications. This did not concern most psychologists, social workers, counselors, and other psychotherapists, as their work with the nonpsychiatric population was stable and secure. Many clinicians were quite happy providing nonmedical care, leaving the medications to psychiatrists and primary care physicians.

Today, a vast majority of the patients seen in private practice settings and in community mental health agencies have been, are, or will be on psychotropic medications. Most therapists, however, have not received adequate education to keep pace with a changing treatment arena. In fact, most nonmedical therapists—namely, psychologists, social workers, professional counselors, marriage and family therapists, and even clergy—have never taken a course in psychopharmacology, or they have taken only a brief survey course and feel ill prepared to handle patients and clients on psychotropic medications (Barlow & Herbert, 1995; Sinacola, 1997). Even if they have taken a formal course in psychopharmacology, the course typically does not cover the rather complex approaches to psychopharmacology, such as dealing with treatment, medication-resistant depression, or the need for polypharmacy to fully address a condition.

Some therapists choose not to seek this information. They offer the argument that they work with cancer patients and do not need to know the etiology or how to treat the disease. This argument has some truth in it; however, it might not be a valid premise for choosing to be naïve on the topic. For example, it has been well documented that all therapists need to be aware of the role physical illness plays in mental illness. If any ethical or professional therapist or counselor feels that a physical condition might be a cause for a patient's mental condition, the therapist should immediately refer the patient to a physician for an evaluation. Amazingly, many do not. Although a physical condition may resolve quickly when it is physically treated, a mental illness often requires a combination of psychotherapy and medication. As a mental health *expert*, the clinician is expected to diagnose and treat various conditions and be aware of the best treatment for them. To limit treatment options by excluding medications, which represent a large part of the available protocol, is a disservice to the patient. Therapists who claim that medication would interfere with their approach are often lulled into a false sense of inclusiveness. They believe the only way to treat a patient is with nonmedical therapy, and if the patient is not responding, they believe he or she is resisting treatment. Many never even consider the possibility that the patient may need something more than the clinician can provide. Some pastoral or Christian counselors have taken the position along with some of their clients that taking medication is unnatural and not in God's plan of treatment for them (Sinacola, 2017). They fail to understand that most major religions in the Eastern and Judeo-Christian philosophies, with the exception of some Christian

Science congregations, utilize modern medicine. It is important to work closely with clients from religious backgrounds to help them formulate a healthy approach to medication while maintaining their spiritual beliefs and practices.

For years, nonmedical therapists have accused psychiatrists of being "pill pushers." Indeed, changes in coverage on certain mental health insurance plans have reduced the amount of time psychiatrists can spend with patients. Nonmedical therapists often cite the refusal of psychiatrists to spend any real therapeutic time with patients as evidence that psychiatrists either lack therapeutic skills or view everything as a medical issue. The reduction in time often leads to less social and medical history being taken from the patient, leading to hasty diagnostic conclusions. The sad truth here is also that many nonmedical practitioners feel uncomfortable talking to psychiatrists and other prescribers about medications. Many nonmedical practitioners choose to reduce every psychological concern to purely behavioral manifestations and are reluctant to even consider the role of biology or neurology. This choice is not new, even among medical therapists. When advising clients, some social workers and nurses have minimized the need for psychological testing because they do not perform these services. Many were reluctant to refer clients to psychologists for psychological testing because they feared that the psychologist might steal their client, even when information like IQ is critical in determining the cause of behavior or the need for placement or custody. Historically, psychologists and psychiatrists have waged turf wars over the issue of who is really in charge. In many states, both the physician and the psychologist share hospital privileges. In addition, some states and jurisdictions, such as Louisiana, New Mexico, Illinois, Iowa, and Guam, allow properly trained psychologists to prescribe psychotropic medications. For years, clinical nurse specialists and physician assistants have been prescribing medications.

Many nonmedical therapists agree that knowledge of psychotropic medications is necessary and attempt to gain this knowledge, yet they still feel that their knowledge is inadequate. They shy away from discussing medications with clients and defer to the case physician. These therapists may claim that they do not wish to practice medicine without a license. Many therapists, such as licensed psychologists, are aware that their scope of practice in many states allows them to discuss medication options with patients, but they are not necessarily the person who may ultimately prescribe them. Still, these therapists claim ignorance and defer any decisions to the physician, nurse practitioner, or physician's assistant. They may be unclear as to what role they should take with patients regarding their medications.

An analogy may apply here. Your washing machine (patient) is not working properly. You need to repair (treat) it. In most cases, you would call a repair technician who comes to your home, listens to the machine (therapy), and makes a recommendation. The technician has a basic understanding of how the machine works and the function of each part, but not a deep understanding of why the part works or how to design or correct design flaws. The technician cannot usually explain why a part failed—only that it did and that it must be replaced. The mechanical engineer (the physician), who knows what the part was designed to do and why it physically failed, may be able to offer an explanation here and also may be able to fix the part if it is taken to the factory (hospital). If the machine has to be redesigned, the engineer, not the mechanic, would attempt to do it. A therapist who has no knowledge of psychotropic medications is like the repair technician who listens to the machine and says, "Yep, you have a problem all right, and I think it's in the rinse agitator. Maybe you want to see an engineer."

In reality, most good repair facilities and retailers employ mechanical engineers, electrical engineers, and technicians who work together to repair machines (provide treatment). In the same way, therapists and physicians need to work together in the best interests of the patient.

Today, the model of the *medical home* calls upon primary care doctors and providers to work collaboratively with mental health therapists in the service of the patient. It is imperative to have open channels of communication with other providers in the patient's case, especially the primary care physician.

How do nonmedical therapists or counselors determine just what they need to know? Consider the following quiz:

1. What is an SSRI?
   If you answered "an antidepressant," you get one point. But do you know that SSRI stands for selective serotonin reuptake inhibitors? Do you know the primary neurotransmitter involved in their action? Do you know the major side effects? Can you name the six major drugs in this class by brand name? Would you recognize the chemical or generic names if you saw them in a medical record? If a client told you a doctor placed him on meds and he was having side effects A, B, and C, would you know that the side effects came from the SSRI?
2. What is a neuroleptic?
   If you answered "a medication for treating schizophrenia," you get another point. But do you know the primary neurotransmitter that is involved in their action? Do you know the side effects? Do you know which medications are major tranquilizers and which are minor ones? Do you know which medications are better for the negative symptoms of psychoticism?
3. What is a SPARI?
   If you answered an "SSRI on steroids," you would be half right. How are these new-generation serotonin medications different, and how does partial agonism affect the drug's effectiveness?
4. What is a benzodiazepine?
   If you answered "They are used to treat anxiety," you once again get a point. But do you know where they interact in the brain? Do you know what neurotransmitter or amino acid is involved? Are they habit forming? Can someone overdose on them?

If you were able to answer all of the preceding questions correctly, you do not need to read this book and could probably teach others about psychopharmacology. If you knew a few answers, consider reading further and you will not be disappointed. If you knew none of the answers, definitely read on.

This book will help the nonmedical therapist to increase his or her knowledge of medications and their proper use. Without complicating the picture with excessive biological terms and neurochemistry, it will give the counselor or psychotherapist the necessary information to work safely with a patient currently taking or considering medications. It will also offer helpful suggestions to therapists working directly with psychiatrists and other prescribers, allowing them to feel confident using language both can understand in the optimum treatment of the patient.

CHAPTER 2

Basic Neurobiology

This chapter will provide basic information on the purpose and function of the brain's neurological system with regard to mental health functioning.

Topics to be addressed include the following:

- Neurons
- Neural communication
- Electrical and chemical properties of neural transmission
- Neurotransmitters of emotion and behavior

As a counselor or psychotherapist, you need to understand how the brain works to control thinking, behavior, and overall health. Further knowledge in this area should assist you in comprehending your client's symptoms and disease process. The field of psychopharmacology is evolving rapidly and will continue to change with advances in medical research. New interventions to treat psychiatric illnesses should enhance the quality of life for your mental health clients.

This chapter provides some basic information on which to build an understanding of various medications, their mechanisms of action, and how they might be used in day-to-day practice. This chapter describes the anatomy of nerve cells or neurons, how they fit together, and the ways they communicate.

NEURONS

Because the brain is the most complex organ in the body, the discussion here will be limited to neurons in the central nervous system and the effect of drugs on them. Within the central nervous system, neurons transmit messages or communicate with each other, and as will be explored later, drugs can affect this transmission. In order to understand how the messages are transmitted, you must first understand how a neuron is structured.

A neuron has four basic parts: the soma, dendrites, axon, and terminal buttons (see Figure 2.1).

- The *soma*, or cell body, contains the vital parts of the cell, including the nucleus, mitochondria, and other substances in the cytoplasm (the space inside the neuron). A membrane defines the boundary of the cell.
- *Dendrites* are large and small branches of the neuron, similar to branches of a tree, which receive messages from other neurons through multiple molecular receptors.
- The *axon* is a long, slender tube that carries messages from the soma to its terminal buttons.
- *Terminal buttons* are found at the ends of the axon. They contain small sacs, or vesicles, that hold chemical messengers, or *neurotransmitters*. Terminal buttons deliver neurotransmitters to other neurons across a physical gap called a *synapse*. The neurotransmitters can cross the synapse between a terminal button of one neuron and a dendrite of another neuron or between a terminal button of one neuron and the soma of another neuron.

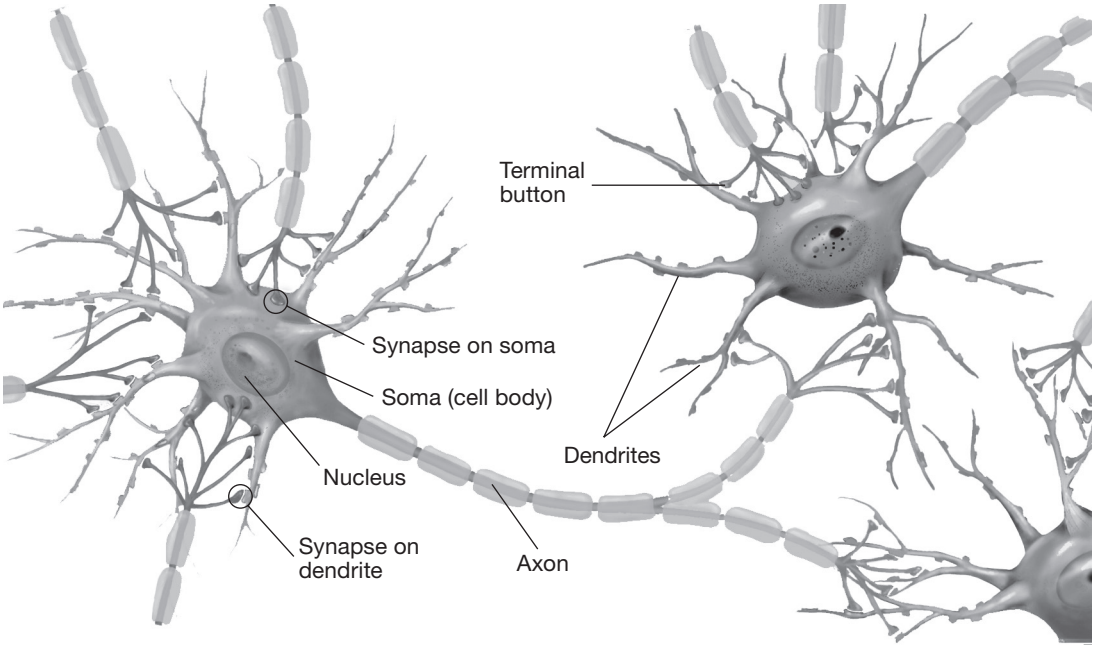


FIGURE 2.1 The Structure of a Neuron

NEURAL COMMUNICATION

Within the central nervous system, neuron communication is facilitated either electrically or chemically. This communication is facilitated electrically within the neuron and chemically between neurons.

All drugs and substances that can activate neurons in the brain or central nervous system and thus affect communication among neurons are classified as either endogenous or exogenous. *Endogenous* substances, such as endorphins, insulin, and adrenaline (also known as ephinephrine), come from within the body. *Exogenous* substances, such as caffeine, vitamins, herbs, and medications, are produced outside the body and introduced into the body in some manner.

Receptor sites on the postsynaptic membranes of dendrites are the most common targets of medications that can activate their respective cells. That action begins when a receptor is stimulated by a neurotransmitter. If enough receptors are stimulated at once, an electrical impulse (called an *action potential*) travels along the axon toward the terminal button. Because an electrical signal or impulse is unable to cross the synapse, the transmission of the signal across the synapse depends on chemical messengers, or neurotransmitters. After the electrical impulse reaches the terminal button, a neurotransmitter is released. It travels from the presynaptic membrane of the terminal button across the synapse to the postsynaptic membrane of another neuron's dendrites, where it might interact. The postsynaptic membrane of the dendrite contains numerous receptors that receive the chemical signal and, in turn, activate the postsynaptic cell, allowing it to transmit again (see Figure 2.2).

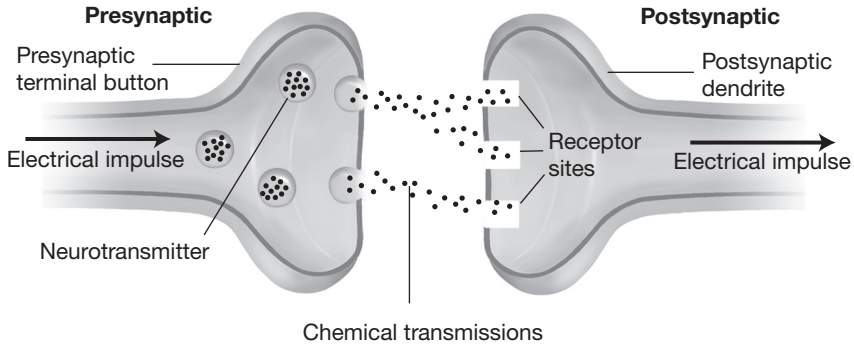


FIGURE 2.2 Electrical and Chemical Communication Between Cells

ELECTRICAL AND CHEMICAL PROPERTIES OF NEURAL TRANSMISSION

The electrical properties of a neuron are mediated by electrically charged particles called ions. In their resting state, most neurons are slightly negatively charged when compared to their surroundings, with the difference between intracellular (inside the cell) ion concentrations and extracellular (outside the cell) ion concentrations, known as the *resting potential*, typically averaging –70 millivolts (mV) (the outside is more negative than the inside). In this resting state, the extracellular spaces are populated primarily by sodium (Na^+) and chloride (Cl^-) ions, while the intracellular spaces are populated primarily by potassium (K^+). The *resting potential* of a neuron is the unexcited or relaxed state in which the average electrical difference between the inside and outside of the cell is about 70 millivolts (mV). Some drugs can directly affect various phases of the action potential, and it is therefore important to understand the process in more detail. This process can be broken down into four key phases: stimulation, rising phase, falling phase, and the refractory period.

Phase 1: Stimulation

For an action potential to occur, the membrane potential (the potential difference between the inside and outside of the cell) must be significantly reduced, usually to around –55mV (known as the *threshold potential*). Each time a receptor is activated by a neurotransmitter, it has the potential to either increase or decrease the membrane potential. Excitatory messages *depolarize* the cell, usually by allowing sodium (Na^+) to flow in; this reduces the membrane potential and increases the chance of reaching that threshold potential. Inhibitory messages *hyperpolarize* the cell, usually by allowing chloride (Cl^-) to flow in; this increases the membrane potential and decreases the chance of reaching the threshold potential. Neurons are constantly receiving both excitatory and inhibitory signals. Whether a message is or is not transmitted depends on the relative number of excitatory and inhibitory signals a neuron receives. For example, if the excitatory messengers outnumber the inhibitory messengers, an action potential (message) will be initiated along the axon.

All action potentials are the same size when they are generated, but not all behavioral responses are equal in magnitude. More significant, or stronger, environmental stimuli produce a higher number of action potentials (a higher rate of firing of action potentials). The higher the

rate of firings of action potentials, the stronger we would expect the behavioral response. For example, a loud sound may generate 10 action potentials in a time period, whereas a soft sound may generate only 2 action potentials during the same period. Thus, the behavioral response to the loud sound is usually greater than the response to the soft sound. In short, the magnitude of an effect is typically related to the number of action potentials that occur in sequence rather than to any change in action potential strength.

Phase 2: Rising Phase

Once an action potential is triggered by reaching the threshold potential, *voltage-gated* sodium channels open and a positive feedback condition occurs known as *runaway*: As the cell lets in more sodium, more of these sodium channels open, and even more sodium enters the cell. The result is a rapid depolarization that typically continues until the cell reaches around +40mV (known as the *peak*). Certain drugs and toxins, such as the tetrodotoxin found in the puffer fish, can block these voltage-gated sodium channels and thus stop this rising phase and resultant action potential, leading to paralysis in severe cases.

As the depolarization continues, the cell begins to compensate by opening potassium (K^+) channels that allow potassium to flow *out* of the cell in order to hyperpolarize it (imagine a boat flooding with water [Na^+] while the crew begins dumping buckets of water back out [K^+]). Because these potassium channels open more slowly, they typically are unable to match the speed of the sodium channels right away.

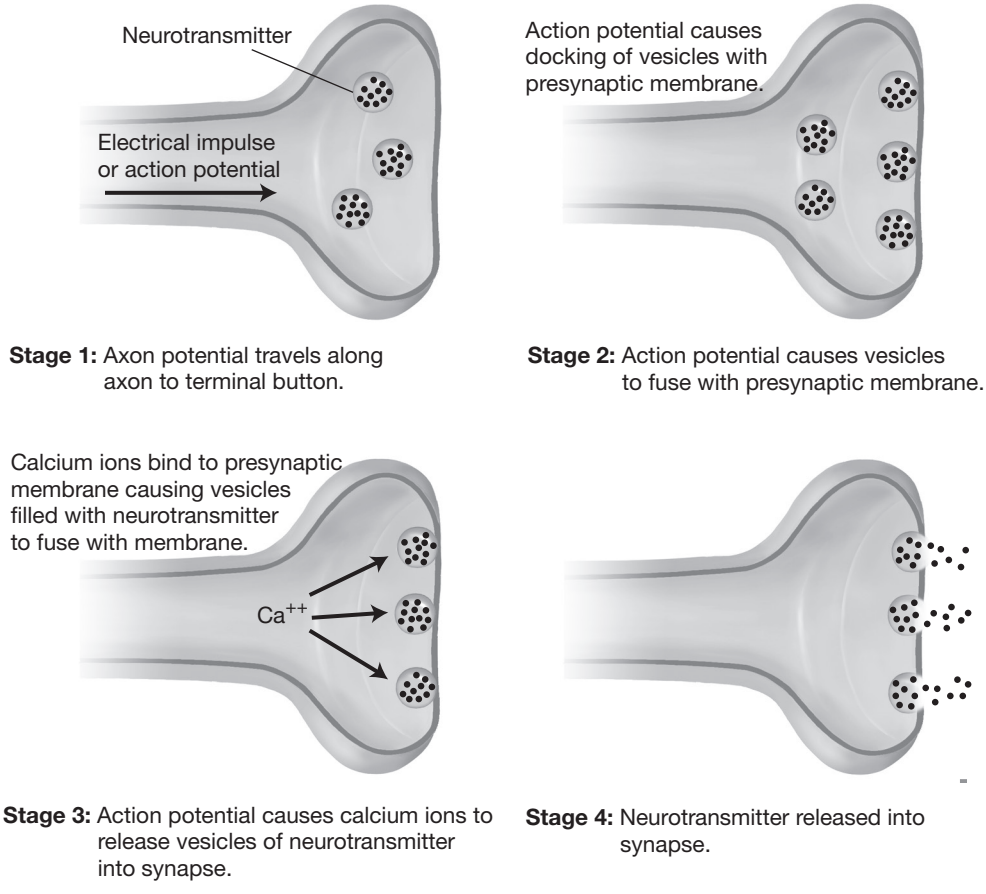
Phase 3: Peak and Falling Phase

Once the potassium channels fully open, they match the speed of the sodium channels such that the voltage no longer changes. In other words, for every sodium ion that enters the cell, a potassium ion leaves. This is called the *peak* of the action potential, and it usually occurs at around +40mV. At this point, the voltage-gated sodium channels do something special: They *inactivate.* This is a process unique to voltage-gated sodium channels and involves a small protein block that stops them from letting more sodium through even though they're still open (imagine a cork blocking the open channel). Once this inactivation occurs, the outgoing potassium flow is much greater than the incoming sodium, and the voltage rapidly drops. Certain drugs and toxins, such as the alpha toxins from a scorpion sting, can block this sodium inactivation, resulting in prolonged action potentials that do not have this traditional falling phase and in severe cases lead to ataxia (involuntary limb movement) and even muscle lock.

Phase 4: Undershoot and Refractory Period

Once this hyperpolarization is complete, the cell is typically at an even lower voltage than the –70mV resting potential discussed earlier. At this point, the cell has entered a *refractory period* during which it is nearly impossible to get another action potential started. This is because the cell is now almost entirely filled with sodium and has released most of its potassium stores into the extracellular space. During this time, *ion exchangers* move potassium back into the cell and sodium back out. This process can last nearly as long as the action potential itself and must be completed before another action potential can be stimulated. Once the cell has fully reset, the action potential is complete.

When the action potential reaches the nerve terminal, neurotransmitters are released by a process called *exocytosis*, the secretion of a substance by a cell (see Figure 2.3). At the end of the



Stage 1: Axon potential travels along axon to terminal button.

Stage 2: Action potential causes vesicles to fuse with presynaptic membrane.

Stage 3: Action potential causes calcium ions to release vesicles of neurotransmitter into synapse.

Stage 4: Neurotransmitter released into synapse.

FIGURE 2.3 The Four Stages of Exocytosis

axon, the action potential causes calcium ions (Ca^{++}) in the terminal button to release the neurotransmitter into the synapse, which in turn causes *vesicles* (small packets of neurotransmitter) to bind to the cell wall. As these vesicles fuse, the neurotransmitter they contain diffuses across the synapse to interact with receptors on the postsynaptic membrane of the dendrites or soma. When receptors are activated, ion channels, or little gateways, open on the postsynaptic membrane, causing either depolarization or hyperpolarization. An excitatory signal leads to the process occurring again; an inhibitory effect decreases further signals. Remember that depolarization excites and hyperpolarization inhibits. The signaling is technically over only when the neurotransmitter is no longer present in the synapse. The primary method for removing neurotransmitter when some of the neurotransmitter is taken back into the terminal button in a process called *reuptake* (see Figure 2.4).

A neurotransmitter and its individual receptor site together act like a key fitting into a lock (see Figure 2.5). Receptors, located on the extracellular membrane, are specific types of protein structures made of amino acids. The structures make each receptor unique. By a process known as *signal transduction*, the first messenger or neurotransmitter binds to a receptor that transmits the message by changing the electrical characteristics of the cell, by starting a biochemical action

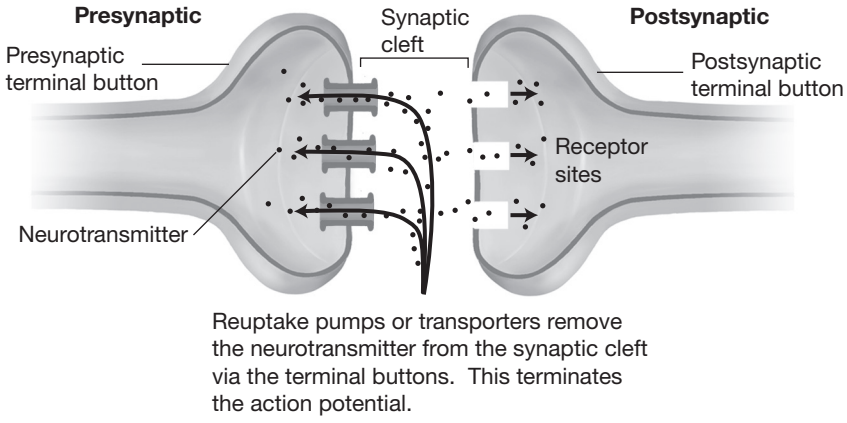


FIGURE 2.4 The Process of Reuptake

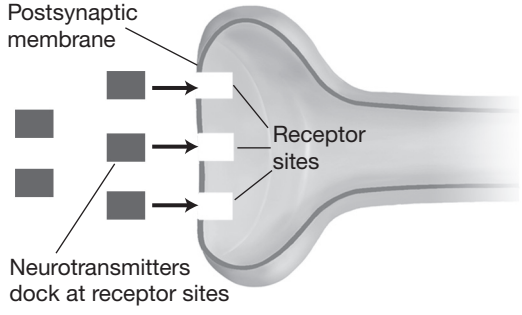


FIGURE 2.5 Receptor Sites

within the cell, or by both. (The second messenger will be explained later.) In general, a neurotransmitter may open an ion channel in either of two major ways. One direct way is through ligand-gated ion channel receptors (neurotransmitter and drugs are generally referred to as ligands). An ion channel opens when a ligand binds to the receptor site (see Figure 2.6). In turn, the influx of particular ions leads to either depolarization or hyperpolarization. For example, the acetylcholine receptor works in this manner. When two acetylcholine molecules occupy the two acetylcholine sites on a single receptor, a sodium channel is opened, resulting in an influx of sodium (Na^+) ions that causes depolarization.

The second way a neurotransmitter opens an ion channel is by inducing chemical changes within the cell. The majority of receptors that produce these effects are called G protein–linked receptors because they bind guanine nucleotides. For example, dopamine, glutamate, gamma-aminobutyric acid (GABA), and serotonin all facilitate neurotransmission by utilizing G protein–linked receptors.

After the first messenger or neurotransmitter interacts with the extracellular receptor, the chemical effects of the G proteins activate a second messenger within the cell. The best-known second messenger is cyclic adenosine monophosphate, or cyclic AMP. Thus, the neurotransmitter or first messenger binding to the receptor causes a cascade of chemical reactions in the postsynaptic neuron involving a second messenger. Cyclic AMP usually activates other molecules or

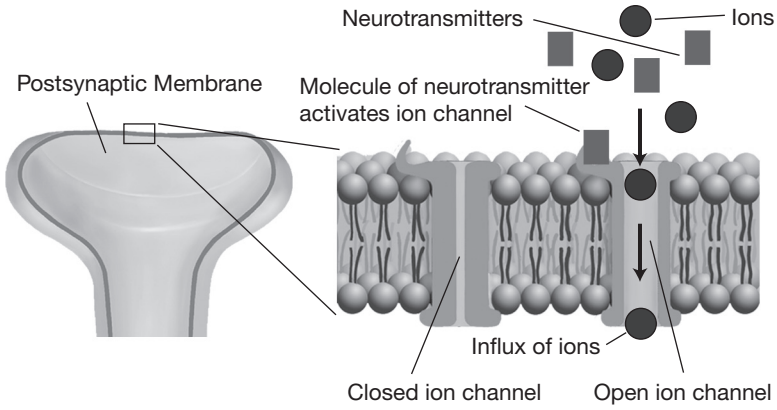


FIGURE 2.6 Ion Channel Activation

enzymes that in turn activate or inhibit other chemicals. The resulting substances are known as protein kinases. The protein kinases facilitate a change in the physical shape of other proteins that control the opening of an ion channel. The alteration in the physical shape of the protein permits the channel to open, allowing an influx of ions into the postsynaptic neuron. This ion influx causes either depolarization or hyperpolarization. The final results of this process vary but may include making other neurotransmitters, up- or down-regulating the number of receptors, sending further electrical charges, and so on. An increasingly complex cascade of effects occurs that alters cellular function.

NEUROTRANSMITTERS OF EMOTION AND BEHAVIOR

Three main neurotransmitters involved in emotion and behavior are the monoamines, comprised of two catecholamines (dopamine and norepinephrine) and one indolamine (serotonin). The category designation catecholamine or monoamine is based upon chemical structure. Other neurotransmitters that might be considered include three important amino acids: GABA, glycine, and glutamate. In addition, certain chains of amino acids known as neuropeptides, including substance P and endorphins, may play a role in emotion and behavior.

Dopamine and norepinephrine are closely related and synthesized from the same precursor substance known as tyrosine (see Figure 2.7). Tyrosine is an amino acid that comes from diet. Synthesized tyrosine can be purchased in a health food store; however, some believe tyrosine is not effective unless it is obtained from food. Dietary sources of tyrosine include meat, poultry, seafood, beans, tofu, and lentils. Tyrosine enters dopaminergic neurons by diffusion, where the cytoplasmic enzyme tyrosine hydroxylase converts it to L-DOPA. The L-DOPA is then converted by DOPA decarboxylase into dopamine. Some of the dopamine may be further converted by dopamine β-hydroxylase into norepinephrine.

The noradrenergic (or norepinephrine) pathways in the brain seem to be involved in the regulation of sleep–wake cycles, sustained attention, alertness, and biological responses to new stimuli. Noradrenaline is also thought to mediate anxiety, fear, and stress responses. Thus, noradrenergic abnormalities or drops in norepinephrine levels are thought to play a large role in mood and anxiety disorders.

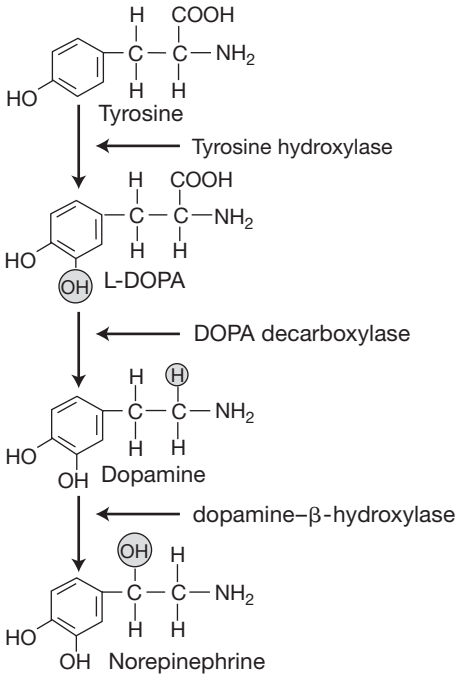


FIGURE 2.7 Synthesis of Catecholamines

Serotonin or 5-hydroxytryptamine (5-HTP) is synthesized from tryptophan in the diet (see Figure 2.8). Once again, synthesized tryptophan supplements have not been shown to be an effective way of obtaining serotonin. Dietary sources of tryptophan include bananas, sunflower seeds, and milk. Tryptophan is converted into 5-hydroxytryptophan by an enzyme called tryptophan hydroxylase. Then 5-hydroxytryptophan decarboxylase acts on 5-hydroxytryptophan to produce serotonin or 5-HTP.

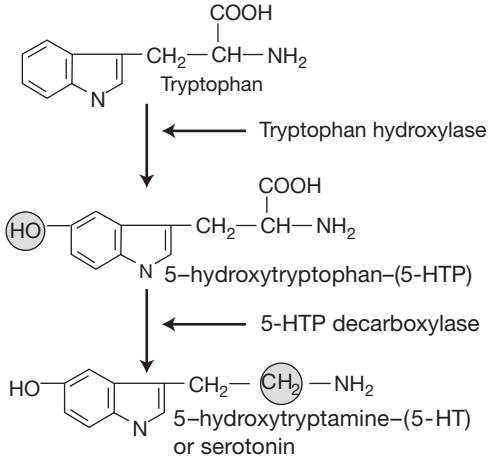


FIGURE 2.8 Synthesis of Indolamines

Scientists believe that serotonin plays a large role in brain functioning, including mood, anxiety, arousal, irritability, tranquility, cognition, appetite, sleep–wake cycles, and obsessions. Serotonergic abnormalities or drops in serotonin levels are associated with anxiety disorders, mood disorders, and even psychotic disorders. Explanations of neural activity might seem quite concrete and straightforward, but the systems are much more complex. Neurons have an extraordinary number of diverse interconnections. Because behavior is complicated, no one neurotransmitter should be considered in isolation; for example, an individual's depression might be caused by insufficient levels of serotonin, norepinephrine, dopamine, or, in some cases, all three. Most brain functions result from multiple influences of several different neurotransmitters trying to find their own delicate balance.

Drugs may alter behavior by interfering with or interrupting any of the processes that occur during neural communication. A drug that increases the availability or action of a neurotransmitter is called an *agonist*. Agonists are agents that bind to receptors and act. For example, fluoxetine (Prozac) increases the action of serotonin on the postsynaptic membrane. Conversely, a drug that decreases the availability or action of a neurotransmitter is called an *antagonist*. They bind to receptors and block. For example, risperidone (Risperdal) blocks dopamine at the postsynaptic membrane. Keep these concepts in mind. They will be revisited in later chapters with respect to specific diseases and medications.

In summary, a few neurotransmitters are particularly important for those in the mental health field. The following gives you a general foundation for each one.

- ***Acetylcholine.*** In the central nervous system, acetylcholine is widely distributed and thought to play a role in memory, learning, behavioral arousal, attention, mood, and rapid eye movement that occurs during sleep. In the peripheral nervous system, acetylcholine is found at synapses where the nerve terminals meet skeletal muscles, causing excitation leading to muscle contractions.
- ***Epinephrine or adrenaline.*** This neurotransmitter is probably more active in the peripheral nervous system than in the central nervous system. Epinephrine is secreted by the adrenal glands, small endocrine glands above the kidneys. In the peripheral nervous system, epinephrine regulates our fight-or-flight response. Its role is described in more detail in Chapter 7.
- ***Norepinephrine.*** Primarily, norepinephrine is an excitatory neurotransmitter in the central nervous system. Norepinephrine cell bodies in the brainstem have axons projecting into the limbic system (brain structures involved in emotions) and the frontal lobes. Wakefulness and alertness are the two major functions of norepinephrine. The role of norepinephrine is discussed later in Chapter 7 and Chapter 9.
- ***Dopamine.*** Another major neurotransmitter, dopamine is involved with behavioral regulation, movement, learning, mood, and attention. Dopamine may have both excitatory and inhibitory effects in the brain. It is believed that overactivity of dopamine or oversensitivity of dopamine receptors is responsible for the major symptoms in schizophrenia. Amphetamines, cocaine, and other drugs of abuse directly activate dopamine receptors. The resulting excitation helps account for the psychotic symptoms commonly seen when these drugs are abused.
- ***Serotonin.*** Another major neurotransmitter in the central nervous system is serotonin, which involves the inhibition of activity and behavior, and it also is a key neurotransmitter involved in maintaining *homeostasis* in the brain (the brain's equilibrium or "resting" state). Other areas where serotonin plays a significant role include mood regulation, control of appetite, sleep and arousal, and pain regulation. Serotonin and norepinephrine axons project into almost the same areas of the brain and are thought to have opposing actions.

• ***Other neurotransmitters.*** By virtue of its inhibitory nature, GABA makes the brain more stable by decreasing the neural transmission that prevents overexcitation. Benzodiazepines and barbiturates are two good examples that act to increase GABA. (See Chapter 7 for more about GABA.) Glycine is another inhibitory amino acid neurotransmitter that is present mostly in the spinal cord. When glycine receptors are activated, the cell becomes hyperpolarized and less likely to transmit a signal. Strychnine, a toxin that causes convulsions, acts by blocking these glycine receptors, leading to overexcitation and possibly death. Glutamate, another amino acid neurotransmitter, is definitely excitatory. More neurotransmission occurs because glutamate lowers the threshold for neural excitation. Glutamate is often found in Asian food in the form of monosodium glutamate (MSG), which excites the taste buds on the tongue (for further reading see Carlson, 2004).

CHAPTER 3

Psychopharmacology and Pharmacokinetics

This chapter will address issues related to psychopharmacology and pharmacokinetics, how drugs work and bring about chemical and behavioral changes in the body, and how drugs are dispensed and prescribed. It will provide some basic information that is helpful in understanding the patient.

Topics to be addressed include the following:

- Routes of drug administration
- Drug absorption, distribution, and metabolism
- Other pharmacokinetic principles
- Prescription and pharmacy terms

When we talk about pharmacology and more specifically, psychopharmacology, we need to start with some basic concepts. In Chapter 2 we described *pharmacodynamics*, which may be defined as the study of how drugs affect receptor sites, send signals, and cause some neurochemical changes. On the other hand, *pharmacokinetics* refers to the administration, absorption, distribution, metabolism, and elimination of a drug inside the body.

ROUTES OF DRUG ADMINISTRATION

Medications may be introduced into the body by various methods, including orally (by mouth), subcutaneously (deep tissue injection), intramuscularly or IM (muscle injection), intradermally (dermal injection), intranasally (nasal spray), inhalational (respiratory infusion), sublingually (dissolution under the tongue), transdermally (skin absorption), and intravenously or IV (venous injection). The most common way that a drug is administered is orally. In recent times, a few medications have been delivered orally in the form of a "soltab" or orally dissolving tablet. Many psychiatric drugs are introduced into the body in this way. Examples of medications available as soltabs include olanzepine (Zyprexa Zydis), mirtazapine (Remeron Soltabs), risperidone (Risperdal M-tabs), and clonazepam (Klonopin Wafers).

In more acute settings such as a hospital or clinic, intramuscular injections are commonly used to control behavior. Long-acting intramuscular injections such as haloperidol (Haldol Decanoate), fluphenazine (Prolixin Decanoate), or risperidone (Risperdal Consta) are used for more chronically mentally ill patients.

DRUG ABSORPTION, DISTRIBUTION, AND METABOLISM

Drug Absorption

When a drug is introduced orally, the rate of absorption is determined by the form of the drug. For example, liquids are absorbed faster than capsules or tablets. Over the last few years, many slow- or extended-release forms of medications have become available. They allow for fewer doses per day and cause fewer side effects because of the slower rate of absorption. Oral

administration has the slowest rate of absorption when compared to intramuscular, intravenous, and other available forms. Absorption usually occurs in the stomach and duodenum (the first segment of the small intestines). Some medications need to be given with food for better absorption (e.g., ziprasidone); some need to be given without food, which might interfere with absorption. Some gastrointestinal diseases and their treatments may also interfere with drug absorption; for example, antacids interfere with certain antibiotics.

Drug Distribution

After administration and absorption into the venous system, drugs are delivered throughout the body by the circulatory system. The liver is the first organ encountered by orally absorbed drugs. It will break down some of the drug into active metabolites that the body can more readily absorb, as well as nonactive metabolites that the body can expel. This process in the liver is known as *first-pass metabolism*. After leaving the liver, the active metabolites are delivered to their target organs via the bloodstream. The central nervous system is the target for psychotropic drugs. Other factors that affect drug absorption include protein binding, drug half-life, and lipid solubility.

PROTEIN BINDING Some drugs bind tightly to plasma proteins such as albumin in the bloodstream. This *protein-binding* phenomenon determines how much drug is available to act on the brain. Drug protein binding also hinders a drug's metabolism and excretion, which causes it to remain in the circulatory system longer.

DRUG HALF-LIFE The *half-life* of a drug is the average time required to eliminate one-half of the drug's concentration. For example, alprazolam (Xanax) has a half-life of 11 hours. Thus, the concentration of alprazolam will be reduced by about 50% after 11 hours, by 75% after 22 hours, and so on. In general, it takes approximately five half-lives for any drug to be eliminated completely from the body.

LIPID SOLUBILITY The *lipid* or fat *solubility* of a drug determines how easily it crosses a cell membrane, which is important for absorption and effectiveness at its target site. Drugs that are more lipid soluble (lipophilic) cross membranes easily and are more likely to cross over the blood–brain barrier. Some drugs do not cross this barrier and do not exert their effects on the central nervous system.

Drug Metabolism

In ways that can get very complex, drugs are metabolized or broken down primarily in the liver by the *P450* family of *enzymes*. These enzymes are important because of the potential for drug interactions when multiple drugs compete for the same pathways. The liver breaks down the drug into other forms or metabolites that are later excreted in the urine. Geriatric patients have decreased liver enzyme activity that requires drug dosages to be reduced to avoid toxicity. Other medical conditions, such as viral hepatitis or liver cirrhosis, might also decrease a drug's metabolism. A few of the psychiatric medications, such as lithium (Lithobid), are not metabolized by the liver and are excreted unchanged by the kidneys in urine. A patient with kidney dysfunction may not excrete the drug normally, and the concentration may become elevated or toxic.

OTHER PHARMACOKINETIC PRINCIPLES

Therapeutic Index and Dose

The concept of *therapeutic index* is a pharmacokinetic principle that must be addressed. When a certain drug concentration gives a desired response, it is referred to as a *therapeutic dose*. When a drug concentration causes mild or severe side effects, it is referred to as a *toxic dose*. The *therapeutic index* then is the ratio of the *toxic dose* to the *therapeutic dose*. Desirable drugs have a high therapeutic index because the risk of toxicity at therapeutic doses is minimal. On the other hand, drugs that have a low therapeutic index carry more risk because the therapeutic concentration is relatively close to its toxic level. For example, lithium is difficult to use because the toxic level is only slightly higher than the typical therapeutic level (see Chapter 6 for further details).

When determining a drug's therapeutic dose, it might be helpful to consider a dose-response curve (see Figure 3.1). When a drug is introduced into the body, a slow titration upward of the dose usually corresponds to an increasing response. This effect is true up to a certain point, at which the response of the drug levels off despite significant increases in the drug dose. As you might expect, increasing the drug's dose at this point only increases the risk of side effects and toxicity. Although most medications are introduced slowly into the body, some drugs may be initiated at high doses to obtain a certain desired response. We call this a *loading dose* of the medication. After *loading* the patient, further dosage adjustments are seldom needed because we have introduced the therapeutic dose into the body all at once.

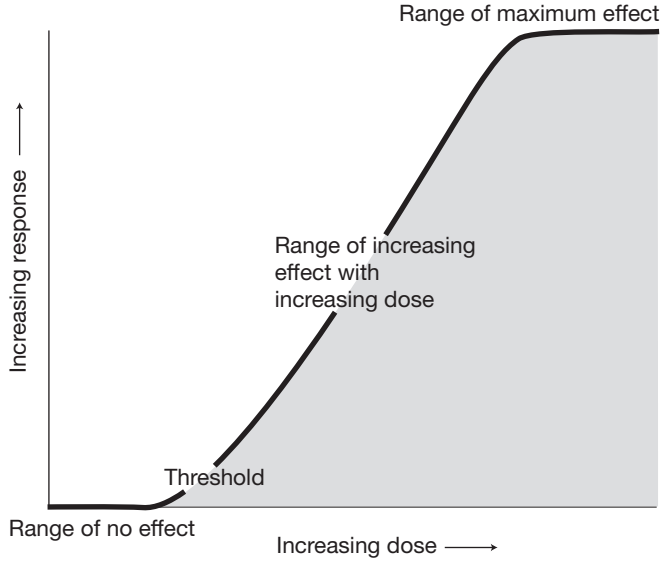


FIGURE 3.1 Dose-Response Curve

Tolerance and Withdrawal

Two important concepts that need to be defined are tolerance and withdrawal. If a patient develops *tolerance* for a drug, he or she needs greater amounts of the drug over time to produce the

desired effect. *Withdrawal* from a drug is defined as a set of characteristic symptoms that emerge when a drug is abruptly discontinued after heavy and prolonged use. Depending on the substance, withdrawal symptoms can be medically dangerous and require inpatient treatment. Tolerance and withdrawal are relatively easy to understand when considering alcohol. Tolerance to alcohol develops over time, causing a person to increase the amount consumed to obtain the desired effect. Withdrawal from alcohol develops when an alcoholic suddenly stops drinking, thus throwing his or her body into a state of shock. This withdrawal causes an expected array of symptoms, such as tremors, agitation, insomnia, hallucinations, and even seizures. *Tolerance* and *withdrawal* are terms commonly used when working in the field of chemical dependency or addictions. In the *Diagnostic and Statistical Manual of Mental Disorders,* Fifth Edition (DSM-5), addiction is more specifically defined as *substance abuse and dependence*. Addiction is discussed in more detail in Chapter 13.

Discontinuation Syndrome

A related concept in the field of psychopharmacology is *discontinuation syndrome*. This syndrome is distinct from withdrawal because it is not medically dangerous, although some people claim that they are going through withdrawal. For example, patients who take paroxetine (Paxil) or venlafaxine (Effexor XR) often report that when they miss a dose or stop taking the medication, they feel malaise and other flulike symptoms.

Potentiation and Synergism

A therapist must understand the concepts of potentiation and synergism. *Potentiation* means that one drug may enhance the effect of a second drug. For example, drug X added to drug Y may potentially cause drug Y to be more sedating. One drug that potentiates another drug may increase the sedation effect only twofold or so. *Synergism* refers to the fact that one drug may enhance the effect of a second drug significantly more than expected. For example, drug X added to drug Y may increase the sedation effect of drug Y sixfold. Because of synergism, a patient should not mix alcohol with benzodiazepines.

Placebo Response

A discussion about psychopharmacology and pharmacokinetics would not be complete without mentioning the *placebo response*. During any patient interaction, a complex series of events and communications occurs in addition to any prescribed drug effects. Some patients respond regardless of the specific therapeutic intervention just because of a helper's "therapeutic interaction" with them. Many patients have shown actual chemical changes in their brain when they receive a placebo even when an actual drug is not present. The brain acts "as if" the drug were present even though it is not. When this effect is negative, the term *nocebo* is used. The power of the placebo response should never be underestimated.

PRESCRIPTION AND PHARMACY TERMS

Therapists will encounter numerous Latin abbreviations when reviewing records, dealing with prescriptions, and discussing issues with their prescribing professional (see Table 3.1). Although these abbreviations seem quite foreign at first, they become familiar with use over time.

Table 3.1 Latin Abbreviations

Abbreviation	Meaning	Latin
a.c.	before food	ante cibum
b.i.d.	twice a day	bis in die
cap.	capsule	capula
c with bar on top (c)	with	cum
h.	hour	hora
hs	at bedtime	hora somni
p.c.	after food	post cibum
p.o.	by mouth	per os
p.r.n.	as occasion requires	pro re nata
q4h	every 4 hours	quaque 4 hora
q6h	every 6 hours	quaque 6 hora
qd*	every day	quaque 1 die
q.i.d.	four times a day	quater in die
q.o.d.*	every other day	quaque altera die
Rx	prescription	recipere
stat.	immediately	statim
tab.	tablet	tabella
t.i.d.	three times a day	ter in die

* These abbreviations are on the Joint Commission's DO NOT USE LIST as of June 2017. The Joint Commission is a not-for-profit organization that accredits healthcare organizations, with the goal of improving healthcare quality and safety. www.jointcommission.org

It is always good practice to record a patient's medication regimen in his or her chart. This information might be necessary when consulting with other professionals involved in the patient's care. Chapter 4 describes history taking and assessment techniques in further detail.

CHAPTER 4

History Taking and Assessment Techniques

This chapter reminds the clinician that good history taking is essential to a good diagnosis, and a good diagnosis is essential before any referral or recommendation for medication.

Topics to be addressed include the following:

- Obtaining patient history
- Mental status examination
- Patient questionnaires and assessment instruments
- Structuring the initial interview

OBTAINING PATIENT HISTORY

No mental health professional should underestimate the importance of good history taking. It is always important to inquire about a patient's physical and spiritual health before starting any counseling relationship, especially when a patient presents with issues of depression, anxiety, psychoticism, or other highly intrusive behavior. By getting all of the facts surrounding a presenting issue, a therapist is assured that all relevant contributing factors have been considered.

It is critical to take a thorough history from a patient and to use assessment instruments that address the issue the patient presents. Depending on the setting where the history is taken, a few simple questions on the presenting problem, nature of concern, history of the problem, relevant family history, physical findings, and history of treatment might be sufficient. If time allows, however, a more detailed assessment may be in order. The following outline provides a detailed history and assessment of the patient.

Patient's History Format

I. Identifying Information
Name, age, identified gender, biological gender, race, grade, religion or spiritual beliefs, marital status, occupation, and diagnosis (if applicable)

II. Presenting Problem
- **a.** Chief complaint
- **b.** How the person was referred to you
- **c.** Dates of treatment or assessment including any medications taken
- **d.** How the person defines the problem
- **e.** Duration, intensity of concern (history of presenting problem)
- **f.** Any history of counseling or therapy

III. Personal/Family History
- **a.** Grandparents, parents, or other relatives, and the quality of the relationships
- **b.** Spouse, significant other, or lover, and the quality of the relationship
- **c.** Children, stepchildren, and the quality of the relationships
- **d.** Siblings and the quality of the relationships
- **e.** Friends and the quality of the relationships

- **f.** Religion or other spiritual beliefs
- **g.** Complete school history (elementary, high school, military, college)
- **h.** Present career status and beliefs about work
- **i.** Physical health or chronic illnesses
- **j.** Sexual history or concerns
- **k.** Any cultural or environmental issues

IV. Summary of Psychometric Information
- **a.** Summarize the results of any test instruments used. Be sure to mention the type of test, norms, and all scores collected.
- **b.** If you are interpreting test results administered by another professional, be sure to state all observations as quotes and compare with your findings.
- **c.** Accurately summarize reports from other sources such as family and friends. Give reasons for using this source of information.

V. Diagnostic Assessment
- **a.** Present a developed, logical summary of the status of the patient. This summary should include a mental status exam, the clinician's observations, and conclusions about the patient's level of functioning. Be sure to comment on the patient's intellect and maturity level.
- **b.** Assess the patient's coping abilities and comment on ego strengths and defense mechanisms.
- **c.** Give an example of the patient's insight level and his/her strengths and weaknesses.
- **d.** Make a complete diagnostic statement, including an appropriate DSM-5 diagnosis.
- **e.** Be sure not to diagnose family members or others who have not been seen or evaluated personally.

VI. Proposed Treatment Goals and Methods
- **a.** Be sure that all goals and methods relate to the diagnostic assessment.
- **b.** Define the goals and the objectives leading to them.
- **c.** Differentiate between short- and long-term goals.
- **d.** Describe the length and frequency of planned sessions.
- **e.** Describe the theoretical approach chosen.
- **f.** Describe any special issues anticipated during treatment—for example, transference, countertransference, financial limitations, or other ethical issues.
- **g.** List other resources or professionals to contact (psychiatrist, nurse, psychologist, clergy, social services, etc.).
- **h.** List referrals to make to other professionals or agencies.
- **i.** Set a time to reevaluate the treatment approach.
- **j.** Describe the complete prognosis.

VII. Other Information
- **a.** Describe special circumstances encountered—for example, the sudden death of a loved one.
- **b.** List releases needed for consults.

MENTAL STATUS EXAMINATION

It is wise to obtain a baseline measure of mental status from all patients. This information not only gives a snapshot of how the patient is doing, but it gives a general sense of the patient in several different realms, including cognitive capacity, intelligence, memory impairment, abstract

reasoning, and judgment. If done properly, a good mental status exam (MSE) can help to predict a patient's behavior and provide valuable information for making a diagnosis. A full MSE should include information from the following sources:

Mental Status Information

Attitude and Behavior

- Describe appearance, including hygiene, makeup, and dress.
- Describe mannerisms: lethargic, hyperactive, echopraxia, posture, etc.
- Describe attitude toward self and others.
- Describe affect: sad, flat, labile, etc.

Stream of Mental Activity

- Describe flow of speech: tangential, rapid, spontaneous, blocked, etc.
- Describe language deviations: clang associations or echolalia.

Emotional Reactions

- Describe displays: tearful, anxious, flat. Congruent with stated mood?

Mental Trend and Thought Content

- Describe major themes of conversation: anger, regret, revenge, etc.
- Describe evidence of auditory, visual, gustatory, tactile, olfactory, or visceral hallucinations.
- Describe delusions, ideas of reference, paranoia, or grandiosity.
- Describe somatizations, suicidal or homicidal ideation: Is there a means, intent, or plan?
- Describe history of substance abuse and list current medications and prescriber.

Sensorium, Mental Grasp, and Capacity

Ask questions to determine the following:

- Oriented × 3 (person, place, and time)
- Memory: Immediate (recall of three items after five minutes); recent (events of last evening); remote (name last nine presidents). *Note:* If from another culture or country, ask patient who their last four leaders were, and you can verify the answers later.
- Calculations: Serial 7s and 3s; digits forward and backward
- General intelligence and similarities: Abstract reasoning and proverbs

General Fund of Knowledge

- Ask questions of common knowledge and current events and of items that assess past academic achievements—for example, how many stars and stripes are present in the U.S. flag and why.

Judgment and Insight

- Ask questions to assess the patient's common sense (ego strengths) and ability to live independently—for example, what to do if their home is flooded or what they would do with $10,000.

A typical narrative description for the findings of the mental status exam would be worded in the following fashion, depending on the particular questions asked of the patient and his or her level of cooperation:

> Mrs. Jane Doe is a 30-year-old, African American female of average height and weight. Her hygiene and dress were appropriate for the evaluation. She was oriented X3, and while her speech appeared normal, she began to stutter when she became nervous. She denied hallucinations or other psychotic manifestations. Memory

appeared intact with good immediate, recent, and remote memory. She appeared to have no educational or learning deficits. The patient appeared to have an above-average level of intelligence. She denied suicidal/homicidal ideation and chemical dependency. Judgment and insight appeared sound and within normal limits.

PATIENT QUESTIONNAIRES AND ASSESSMENT INSTRUMENTS

For therapists, including those who are not psychologists, several patient checklists and questionnaires are available that can be used for patients who present with depression and/or anxiety. These instruments are designed to be easy to use by both the clinician and the patient. While some psychometric knowledge is helpful, most of these self-report format instruments are designed to be administered by mental health professionals with at least a master's degree and some relevant clinical experience. Some assume that the clinician has special training in their use, and some may require the practitioner to be a licensed psychologist. A test's publisher may require professional credentials before selling the instrument. The following list is by no means exhaustive, but it represents some popular tools used in the field today. To learn more about them, type in the name of the test as a keyword on the Internet for publisher and research information.

Assessments for Depression

- The Beck Depression Inventory II: 21 items, easy to score
- The Hamilton Depression Inventory: available in a 17- or 21-item format; better for assessing somatic, less cognitive-related depression
- The Geriatric Depression Inventory: helpful to use with an older population
- The PHQ-9 Patient Health Questionnaire: simple 11-question instrument; available online; helps to determine if the patient is experiencing depression

Assessments for Anxiety

- The Beck Anxiety Inventory: brief, easy to score, and helpful in differentiating between generalized anxiety and panic disorder
- The State-Trait Anxiety Inventory: helpful in determining if the anxiety is one of an emotional reaction "state" versus more of a personality "trait"
- The GAD-7: 7-question instrument; helps clinician to determine if generalized anxiety disorder may be present; also available online

General Assessment of Personality Including Depression, Anxiety, and Other Manifestations

- The Minnesota Multiphasic Personality Inventory (MMPI-2): consists of 567 true/false questions over 10 clinical scales including depression, somatization, anxiety, antisocial tendencies, paranoia, mania, and psychoticism; also available in an adolescent version (MMPI-A)
- The Millon Clinical Multiaxial Inventory-IV (MCMI-IV): a shorter test with 195 items; better for assessing the presence of a personality disorder; maps well on the DSM-5
- The Personality Assessment Inventory (PAI): consists of 344 items; shorter version, called the PAS or Personality Assessment Screener, contains only 22 items and takes less than six minutes to administer

STRUCTURING THE INITIAL INTERVIEW

When a patient presents for counseling services and the therapist is aware that the patient may need medication to treat a serious affective, anxiety, or thought disorder, it is very important to gather as much information as possible. The following are information-gathering suggestions to keep in mind.

1. Document the name of the patient's primary care physician or provider (PCP) and the date of his or her last history and physical. Be sure to include any information on known diseases such as hypertension, diabetes, cancer, stroke, thyroid conditions, and so on. If the patient does not have a PCP, then he or she should be referred to one for a workup as soon as possible. Be sure to ask the physician to assess for thyroid function, glucose tolerance, and electrolyte imbalances. Typical tests would include complete blood count (CBC), thyroid function tests, a basic metabolic panel, and urine toxicology.

2. Take a complete history of any treatment for the presenting problem. This history should include the types of symptoms—that is, depression, panic, anxiety, and so on. Be sure to include all professionals the patient has seen and any medications he or she has taken. Ask the patient if the medications were helpful, effective, or intolerable. What side effects, if any, did the patient experience, and did they lead to noncompliance?

3. Prepare a complete mental status using other assessment instruments as appropriate to confirm initial impressions. It would be appropriate for the therapist to formulate some initial short-term goals for proceeding with this patient.

Good treatment starts with a good history and assessment. Taking a few extra moments with the patient to address the issues mentioned above will assure both the patient and the therapist that no stone was left unturned. Be sure to review the treatment plan with the patient to confirm that he or she is also in agreement. By knowing the patient's history, the therapist can save time later by not reexposing the patient to medication regimes that did not work or that interacted with other medications the patient was taking for a medical condition. Pleading ignorance or claiming not to be a physician is no protection from a malpractice claim. Always remember that you are treating the whole patient.

CHAPTER 5

Treatment of Unipolar Depression

In this chapter, we examine the medications and other treatment considerations for patients with unipolar depression. Depression is the most common presenting concern in all treatment settings. Assessing the nature and type of depression is key to suggesting proper medication.

Topics to be addressed include the following:

- Biological versus environmental depression
- Causes of biological depression
- Counseling and psychotherapy
- Medications for depression
- Herbal and holistic substances
- Light therapy for major depressive disorder (MDD) and seasonal affective disorders (SAD)
- Importance of exercise
- Electroconvulsive therapy (ECT) and other treatments
- Procedural steps for patient treatment
- Case vignettes

BIOLOGICAL VERSUS ENVIRONMENTAL DEPRESSION

Depression is probably the most frequently presented issue in any mental health setting. Researchers have estimated that at least 3% of the population suffers from chronic depression at any one time. More than 17% have had at least one episode in their lifetime, and another 10% reported an episode in the last 12 months (Sutherland, Sutherland, & Hoehns, 2003). It is interesting and sad that despite the recent advances in both psychotherapy and medications for depression, only 30% of those with depression seek treatment for the condition (Rakel, 1999). In addition, less than 20% of those who seek treatment take antidepressants (McIntyre, Muller, Mancini, & Silver, 2003). The lifetime prevalence of major depressive disorder (MDD) in the United States is about 16% in a given year, with about 7% of the population experiencing an episode of MDD, half of which will be moderate in severity. In patients with chronic medical illness, the annual prevalence rate for MDD is up to 25%. Risk factors are multifactorial and include genetic, medical, social, and environmental factors (Bentley, Pagalilauan, & Simpson, 2014). According to Pratt and Brody (2014), recent information indicates that depression is more prevalent among females and people ages 40 to 59. As we might expect, people living below the poverty level were nearly 2.5 times more likely to have depression than those at or above the poverty level. In addition, almost 43% of people with severe depressive symptoms reported serious difficulties in work, home, and social activities. Finally, when looking at those with severe depressive symptoms, only 35% reported having contact with a mental health professional in the past year (Pratt & Brody, 2014). Thus, there is a huge unmet medical need that we must address.

Therapists have many issues to consider when treating depression. First, they must determine the nature of the depression. Some forms of depression are biological or *endogenous*: It is believed they stem from *within* the person. This form of depression is likely to have a biological

link or perhaps a family link to others who also have depression. In fact, Rakel (1999) mentions that monozygotic twins have a 65% concordance rate, and dizygotic twins have a 14% rate. According to Lohoff (2010), twin studies suggest a heritability of 40% to 50%, and family studies indicate a twofold to threefold increase in lifetime risk of developing MDD among first-degree relatives. Some forms of depression are more reactive or *exogenous* and are typically caused from forces *outside* of the body. In these cases, stress or grief may be the cause. Therapists often find that both internal and external factors play a role in many patients' depression (Barlow & Durand, 2005).

It is important for the therapist to determine the nature and source of a patient's depression. At times it may be rather clinical or endogenous in nature. Typically, major depression and the depressive phases of bipolar conditions meet these criteria, but therapists are also aware that dysthymia, cyclothymia, and grief reactions have some biological components. Further, the clinician must determine the role of other complicating factors, such as substance use, psychotic features, physical diseases, and medications that may cause depression.

CAUSES OF BIOLOGICAL DEPRESSION

For many patients presenting with depression, the cause can be related to another physical disorder that they may have. The following is a list of diseases and disorders that can cause or exacerbate depression:

Addison's disease
Alzheimer's disease
Anemia
Asthma
Brain tumor
Cancer
Cardiovascular conditions
Chronic fatigue syndrome
Chronic infections
Chronic pain syndrome
Colitis
Congestive heart failure
Cushing's disease
Diabetes mellitus
Fibromyalgia
Hepatitis
HIV/AIDS
Huntington's disease
Hyperthyroidism
Hypothyroidism
Influenza
Lupus
Malnutrition
Menopause
Mental retardation
Metabolic abnormalities
Mononucleosis
Multiple sclerosis
Myocardial infarction
Pancreatitis
Parkinson's disease
Porphyria
Postpartum hormonal changes
Premenstrual dysphoric disorder
Rheumatoid arthritis
Stroke
Syphilis
Tuberculosis
Uremia

In addition to these diseases and disorders, many medications and other substances have been known to cause or worsen a patient's depression. The following is a list of these medications and substances:

- Alcohol
- Antianxiety medications: diazepam, chlordiazepoxide, alprazolam, lorazepam, clonazepam, phenobarbital

- Antihypertensive medications: reserpine, propranolol, methyldopa, guanethidine sulfate, clonidine, hydralazine, metoprolol, prazosin
- Anti-inflammatory medications: indomethacin, butazolidin, rofecoxib (withdrawn from U.S. market in 2004), celecoxib
- Antiparkinsonian medications: levodopa/carbidopa, amantadine
- Cold remedies: antihistamines, others containing alcohol
- Corticosteroids and other hormones: estrogen, progesterone, cortisone acetate, most oral contraceptives, etc.
- Drugs of abuse: marijuana, codeine, morphine, PCP, crystal methamphetamine, psychedelics, opium derivatives, synthetic pain killers
- Sedative–hypnotic medications: zolpidem, zaleplon, triazolam, flurazepam, temazepam, meprobamate

If after careful history and assessment the therapist determines that the patient's depression appears to have little or no physical cause, a treatment plan is proposed to address the concern. While it is a well-known fact that psychotherapy and counseling alone are very effective treatments for depression, psychotherapy and medication together are most efficacious (Segal, Kennedy, Cohen, & CANMAT Depression Work Group, 2000); combining the two increases response rates, with estimates of the increase ranging from 6% to 33% (Hollon et al., 2014). In cases of dysthymia (chronic-mild depression), psychotherapy alone may be attempted. If little response is noticed, an antidepressant may be added. In cases of a grief reaction with sleep disturbances, medications to improve sleep may be used without an antidepressant. Only when the grief is prolonged, severe, and accompanied by suicidal ideation should antidepressants be considered. Suicide assessment is very important to keep in mind, as up to 80% of depressed patients also have suicidal ideation (Sonawalla & Fava, 2001). Those suffering from depression are at 25 times greater risk for suicide than is the general population (American Association of Suicidology, 2014).

The following is a list of treatment options for the patient with moderate to severe depression:

- Counseling and psychotherapy
- Medication, including pharmaceuticals and herbal remedies
- Light therapy for those with seasonally influenced depression
- Exercise
- Electroconvulsive therapy (ECT) and other treatments

COUNSELING AND PSYCHOTHERAPY

Psychotherapists often underestimate the effective nature of therapy. However, psychotherapy as a medical treatment has been found to be more effective than bypass surgery, drug treatments for arthritis, and even aspirin for heart attack (Lipsey & Wilson, 1993). Further, research on the percentage of improved patients at selected sessions has demonstrated that patients typically show the greatest gains in the first 16 to 20 sessions (Howard, Kopta, Krause, & Orlinsky, 1986). While nearly every form or approach of counseling or psychotherapy is helpful, some therapists believe that solution-focused therapy or briefer forms of therapy offer quicker solutions. Still others believe that cognitive-behavioral approaches work better than other forms (Rakel, 1999). To further support this position, a recent randomized controlled trial in Finland showed the effectiveness of three treatment regimens (interpersonal psychotherapy, psychoeducational group therapy, and treatment as usual) with marked improvement over one year

(Saloheimo el al., 2016). Current guidelines from the Anxiety and Depression Association of America (2017) support the use of multiple psychotherapies over waitlists or other minimal contact treatments. Meta-analyses that compare the effectiveness of cognitive-behavioral therapy, interpersonal psychotherapy, and problem-solving therapy indicate no large differences in effectiveness between these treatments.

MEDICATIONS FOR DEPRESSION

For the most part, antidepressants can be divided into five main categories: tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and atypicals or "others."

The oldest antidepressants are the TCAs. Tricyclic antidepressants have been around for more than 60 years. They prevent the reuptake of neurotransmitter substance back into the presynaptic cell. Although effective, TCAs are not "clean" medications, and, therefore, they affect many nontarget organs and systems in the body. They have troublesome anticholinergic side effects that include sedation, weight gain, difficulty urinating, dizziness, dry mouth, sexual dysfunction, orthostatic hypotension, and blurred vision. Typically, these medications are not safe for children or the elderly. Due to their toxic cardiovascular nature, TCAs pose a serious risk of overdose for patients with significant suicidal ideation.

As was mentioned in Chapter 2, a patient's depression may be caused by depletions in the neurotransmitters serotonin (5-HT), norepinephrine (NE), dopamine (D), or all three. Table 5.1 lists TCAs with their trade and generic names, typical daily doses, neurotransmitter action, and level of sedation.

Table 5.1 Tricyclic Antidepressants (TCAs)

Trade Name	Generic Name	Typical Dose (mg/day)	Neurotransmitter 5-HT	Neurotransmitter NE	Level of Sedation
Anafranil	clomipramine	100–250	***	*	Heavy
Ascendin	amoxapine	150–400	*	***	Moderate-heavy
Elavil	amitriptyline	150–300	***	*	Heavy
Ludiomil	maprotiline	150–225	***	0	Moderate
Norpramin	desipramine	150–300	0	***	Light
Pamelor, Aventyl	nortriptyline	75–125	**	***	Moderate-heavy
Sinequan, Adapin, Silenor	doxepin	150–300	**	***	Heavy
Surmontil	trimipramine	100–300	**	**	Moderate
Tofranil	imipramine	150–300	***	**	Light-moderate
Vivactil	protriptyline	15–60	*	***	Light

* Minimal neurotransmission

** Moderate neurotransmission

*** Significant neurotransmission

The second major classification of antidepressants is known as monoamine oxidase inhibitors or MAOIs. These drugs work a bit differently than the others. They inhibit monoamine oxidase (MAO), the enzyme that breaks down neurotransmitters and renders them ineffective. MAOIs exert most of their influence in the presynaptic cell. While the side effects of MAOIs closely resemble those of TCAs, MAOIs are usually well tolerated. Patients taking MAOIs must adhere to strict dietary restrictions, as ingestion of any food containing tyramine may cause a hypertensive crisis. MAOIs have fallen out of use in the United States but are still widely used in Europe. Many prescribers use them as a last-resort drug for patients who do not respond well to other medications (see Table 5.2).

In the early 1980s, another drug was introduced with the trade name Desyrel and the generic name trazodone. This medication primarily affects serotonin but acts more as a 5-HT2 receptor antagonist. Trazodone is less likely to cause sexual side effects but may cause priapism, a condition resulting in a prolonged, painful erection in men. Overall, it has fewer side effects than older TCAs and is less of a suicidal risk, but the typical side effects of sedation and dry mouth remain. Trazodone is often used as a general sedating medication without the risk of addiction to sedative hypnotics for those who have trouble sleeping. Less expensive generic TCAs are available, making this class of medication more affordable for many patients.

In the late 1980s, a new generation of drugs was born. Selective serotonin reuptake inhibitors (SSRIs) block the reuptake of serotonin back into the presynaptic cell. This blocking action allows more serotonin to exert its influence on the postsynaptic cell. Research has found no statistical differences between the various SSRIs with relation to effectiveness, but some research maintains that escitalopram (Lexapro) and sertraline (Zoloft) may be better tolerated, and are, therefore, more likely to be continued than others (Cipriani et al., 2009; Hansen et al., 2008). Table 5.3 lists SSRIs, their trade and generic names, typical daily dose, and level of sedation.

The side effects for SSRIs are considerably less severe than those for older TCAs. Typical side effects include headache, nausea, diarrhea, dry mouth, anorexia, weight gain, restlessness, insomnia, tremor, sweating, yawning, dizziness, inhibited sexual desire, and inhibited orgasm for some (Hansen et al., 2008). As mentioned, SSRIs are "cleaner" and interact with few other medications the patient may be taking. They are considered safer medications for children, seniors, and

Table 5.2 Monoamine Oxidase Inhibitors (MAOIs)

Trade Name	Generic Name	Typical Dose (mg/day)	Neuro-transmitter 5-HT	Neuro-transmitter NE	Neuro-transmitter DA	Level of Sedation
EMSAM	selegiline transdermal system	3 mg/24 hrs–12 mg/24 hrs	**	**	**	None
Marplan	isocarboxazid	10–40	**	**	**	Light
Nardil	phenelzine	30–90	**	**	**	Light
Parnate	tranylcypromine	20–60	**	**	**	Light

* Minimal neurotransmission

** Moderate neurotransmission

*** Significant neurotransmission

Table 5.3 Selective Serotonin Reuptake Inhibitors (SSRIs) Antidepressants

Trade Name	Generic Name	Typical Dose (mg/day)	Level of Sedation
Celexa	citalopram	10–60	Light
Lexapro	escitalopram	5–20	None
Luvox	fluvoxamine	50–300	Light
Paxil, Paxil CR, Pexeva	paroxetine	20–50/25–50	Moderate-heavy
Prozac, Sarafem	fluoxetine	20–80	None
Prozac Weekly	fluoxetine	90 (weekly)	None
Zoloft	sertraline	50–200	None

patients who may be at risk for a suicide overdose; however, FDA warnings suggest that 4% on drugs versus 2% on placebo of children and adolescents demonstrate an increase in suicidal thinking and behavior (see the FDA website, https://www.fda.gov/drugs/drugsafety/postmarketdrugsafetyinformationforpatientsandproviders/ucm161679.htm). Many clinicians believe that the benefits of SSRIs outweigh their risks because severely depressed children and teenagers without treatment are at serious risk of suicide. Although research has found that SSRIs and medications like them (e.g., venlafaxine) increase the risk of gastrointestinal bleeding, newer research has found that this may be to a lesser degree than once thought due to alcohol abuse among subjects (Opatrny, Delaney, & Suissa, 2008).

If serotonin levels inside the central nervous system become too elevated from using SSRIs or other medications, some patients may experience *serotonin syndrome*. Symptoms may include agitation, confusion, insomnia, flushing, fever, shivering, muscle rigidity, hyperreflexia, incoordination, diarrhea, and hypotension. Many of these symptoms can be life-threatening; therefore, any patient started on medication for the first time should be closely monitored.

In the 1990s, a new class of antidepressants were developed known as serotonin-norepinephrine reuptake inhibitors (SNRIs). Venlafaxine (Effexor/Effexor XR) is usually well tolerated and has been shown to be helpful in general depression, generalized anxiety, and postpartum depression (Cohen, 1997). It has been known to increase blood pressure at higher doses. Desvenlafaxine succinate (Pristiq) is the succinate salt of the isolated major active metabolite of venlafaxine, O-desmethylvenlafaxine. This drug was approved by the FDA in 2008. Its potential advantages over other SNRIs include a narrow dose range, requiring less adjustment and more effectiveness at lower dosing. Since the drug is mainly excreted in urine, it has minimal effect on the CYP450 pathway in the liver, and, therefore, it may be a preference for medically ill patients without renal impairment who may be taking multiple medications (Lourenco & Kennedy, 2009). Duloxetine (Cymbalta), released in 2004, is similar to venlafaxine and desvenlafaxine in that it has a dual mechanism of action. Duloxetine has the advantage of equally stimulating both serotonin and norepinephrine at all doses. Venlafaxine is more serotonergic at lower doses.

The latest SNRI is levomilnacipran (Fetzima) which was approved in 2009. It is unique among other SNRIs in that it predominantly potentiates norepinephrine over serotonin; it has more than a 15-fold higher selectivity for norepinephrine versus serotonin reuptake inhibition compared with duloxetine, desvenlafaxine, or venlafaxine (Asnis & Henderson, 2015). See Table 5.4 for more details.

Table 5.4 Serotonin-Norepinephrine Reuptake Inhibitor Antidepressants (SNRIs)

Trade Name	Generic Name	Typical Dose (mg/day)	Neuro-transmitter 5-HT	Neuro-transmitter NE	Neuro-transmitter DA	Level of Sedation
Cymbalta	duloxetine	20–60	***	***	0	None
Effexor	venlafaxine	50–300	***	***	*?	None
Effexor XR	venlafaxine XR	75–300	***	***	*?	None
Fetzima	levomilnacipran	40–120	**	****	0	None
Pristiq	desvenlafaxine	50–400	***	***	*?	None

* Minimal neurotransmission
** Moderate neurotransmission
*** Significant neurotransmission
**** Major neurotransmission

Table 5.5 Atypical or Other Antidepressants

Trade Name	Generic Name	Typical Dose (mg/day)	Neuro-transmitter 5-HT	Neuro-transmitter NE	Neuro-transmitter DA	Level of Sedation
Aplenzin	bupropion hydrobromide	174–522	0	**	**	None
Desyrel, Oleptro	trazodone	50–400	***	0	0	Heavy
Remeron, Remeron Soltab	mirtazapine	15–45	***	***	0	Heavy
Serzone[1]	nefazodone	100–500	***	*	0	Moderate
Trintellix	vortioxetine	5–20	***	0	0	None
Viibryd	vilazodone	20–40	***	0	0	None
Wellbutrin	bupropion	75–450	0	**	**	None
Wellbutrin SR	bupropion SR	100–400	0	**	**	None
Wellbutrin XL	bupropion XL	150–450	0	**	**	None

[1] Serzone is no longer available by prescription; the generic, nefazodone, is available by prescription.
* Minimal neurotransmission
** Moderate neurotransmission
*** Significant neurotransmission

In the last few years, atypical or other antidepressant medications have been introduced. These medications offer many possibilities as noted in Table 5.5. Atypical antidepressants have side effects similar to SSRIs, but they have less possibility of sexual dysfunction. Mirtazapine (Remeron) is helpful in restoring normal sleep patterns. It has also been found to increase

appetite, which is an undesirable side effect for overweight, depressed patients. However, because of this side effect, mirtazapine may work wonders in depressed HIV or cancer patients who are having trouble with weight loss. Like mirtazapine, nefazodone (Serzone) may help restore sleep patterns and cause sedation for many. Unfortunately, the medication has an FDA "black-box" warning due to its increased risk of liver failure and must be used only with caution, especially for patients taking other medications that also use the CYP450 3A4 pathway for drug elimination in the liver. Patients who begin nefazodone therapy should have a baseline liver function test and periodic tests for at least the first six months (Stewart, 2002). Bupropion (Wellbutrin) is well tolerated but is rather uplifting and agitating for some. While bupropion has not been associated with sexual dysfunction, it is not appropriate for patients with seizure or eating disorders, as it lowers the seizure threshold and reduces appetite. Vilazodone (Viibryd) was approved in 2011 for MDD and is both a serotonin transport inhibitor and a 5-HT1A receptor partial agonist (Caraci, Leggio, Salomone, & Drago, 2017). It has been referred to as a serotonin partial agonist-reuptake inhibitor (SPARI) (Wang et al., 2016). Finally, Trintellix (vortioxetine) was approved in 2013 for MDD. The mechanism of action of Trintellix is selective blockade of serotonin reuptake (by inhibiting the serotonin transporter [SERT]) and direct modulation of 5-HT receptors activity (such as 5-HT3, 5-HT7, 5-HT1D, and 5-HT1B). Trintellix is considered an SSRI and a serotonin modulator given the other effects as already noted (Sowa-Kucma et al., 2017).

To be comprehensive, lithium must be mentioned as a possible treatment option for unipolar depression, as well as for bipolar depression. This strategy is usually reserved for more difficult and treatment-resistant cases. Lithium will be explored further in Chapter 6.

HERBAL AND HOLISTIC SUBSTANCES

St. John's wort is a plant that is said to have medicinal properties. Research, primarily conducted in Europe, claims that St. John's wort helps to control mild to moderate levels of depression with virtually no side effects (Bloomfield, Nordfors, & McWilliams, 1996). Most practicing clinicians believe that few patients are helped by St. John's wort, and they are now learning that it may interfere with or react to other medications that patients may be taking. For example, St. John's wort potentiates blood thinners such as warfarin (Coumadin) and lessens the effectiveness of other heart medications such as digoxin (Lanoxin). It may also interfere with protease inhibitors taken by HIV/AIDS patients. The active ingredient in St. John's wort is *hypericin*. The Latin name of the plant is *hypericum perforatum*. Patients who are allergic to plant derivatives should not take St. John's wort because they might break out in a rash or become seriously photophobic to it and experience severe burn when exposed to the sun. Patients who take hypericum perforatum should take it in its liquid form, which ensures that they get a true dose. Health food stores sell brands that may contain more inactive plant parts and less hypericum. St. John's wort should not be taken with other antidepressants because it may potentiate their effects and cause serotonin syndrome. Recent information indicates that St. John's wort demonstrates comparable response and remission rates, and a significantly lower discontinuation rate compared to SSRIs, which are first-line drugs recommended for depression in most countries worldwide (Ng, Venkatanarayanan, & Ho, 2017).

Ginkgo biloba is a tree of Chinese origin. An extract from it is said to relieve mild depression and increase memory and concentration. While 60 mg/day of ginkgo biloba is typical for depression and mild memory concerns, as much as 240 mg/day has been used with Alzheimer's patients (Trebatická1 & Duracková, 2015). Since it is said to have blood-thinning properties,

ginkgo biloba should be used with caution by those taking blood-thinning medications. In our experience, it has not been as effective as antidepressants in the treatment of moderate to severe depression.

The hormone *dehydroepiandrosterone* or *DHEA* is normally secreted by the adrenal gland and is a precursor to testosterone and estrogen. Typically, adolescents have high levels of this substance, but the levels decrease with age. Some clinicians believe that when DHEA is taken orally (90–450 mg daily), it reduces mild to moderate depression, causes weight loss, increases large muscle mass, and may increase sexual appetite. While these claims have yet to be fully proven, many practicing endocrinologists believe DHEA may increase the risk of certain types of cancer. Side effects are usually mild but may include oily skin, acne, irritability, and even psychosis (Qureshi & Al-Bedah, 2013).

S-adenosyl-L-*methionine* (SAM-e) is a substance that is endogenous to the body. It is essential to many biological processes, such as cell methylation. The body converts SAM-e into the amino acid homocysteine, which accumulates and can cause depression, joint problems, and cancer. Homocysteine can be converted back into SAM-e by utilizing vitamins B_6, B_{12}, and folic acid. Research conducted in Italy has shown that depressed patients have much lower levels of SAM-e than nondepressed patients. Patients with poor diet typically make less SAM-e. It is now available as a synthesized substance and has been shown to be as effective at 1600 mg daily as many prescription antidepressants for relieving depression. It is available as a prescription in many European countries. SAM-e may also be helpful in relieving joint pain and for cleansing the liver of other toxins. Researchers believe that SAM-e may increase the synthesis of serotonin and dopamine and aid chemical communication between cells by potentiating the postsynaptic membrane (Martínez-Cengotitabengoa & González-Pinto, 2017).

Animal research has also demonstrated that zinc and magnesium may possess antidepressant properties and may serve as valuable agents in enhancing the activity of conventional antidepressants (Szewczyk et al., 2008). Other substances have been studied, including *Rhodiola rosea*, saffron, lavender, other herbs, omega-3 fatty acids, and Ayurvedic medicines with mixed results (Qureshi & Al-Bedah, 2013).

In addition to the substances mentioned, research into the use of ketamine demonstrates that it may reduce depressive symptoms, and especially reduce suicidal ideation, but the potential for abuse, the potential cardiovascular and respiratory issues, and the cost of administration still warrant further research and investigation to determine if this will prove to be a viable option for treatment (Sanacora et al., 2017). NAC or N-acetylcysteine, an antioxidant that is often used in the treatment of acetaminophen overdose and pulmonary conditions, may prove to be helpful in the treatment of depression, especially bipolar depression at 2,400 mg daily. Side effects are minimal, but results of research suggest it is worth considering along with more conventional medications (Berk et al., 2008; Muskin, Gerbard, & Brown, 2013).

LIGHT THERAPY FOR MAJOR DEPRESSIVE DISORDER (MDD) AND SEASONAL AFFECTIVE DISORDER (SAD)

Antidepressants have been shown to be helpful for patients with MDD and seasonal affective disorder; however, the use of light boxes is also effective. Therapists who treat patients living in colder, darker climates and suffering from seasonal depression might consider suggesting the use of a light box first unless the patient's depression worsens and he or she becomes suicidal. Several commercially produced lamps or boxes are available for $50 to $300. The light source should produce at least 10,000 lux of full-spectrum light. Patients need to be directly exposed to the light

for 30 to 60 minutes per day and sit approximately 10 to 12 inches from most light sources. Bulbs sold in hardware stores for use in overhead fixtures and in doorways may be esthetically pleasing, but they offer little in the form of treatment. Most good-quality lamps can be found by searching the Internet under *seasonal affective disorders* or *full-spectrum lamps*. In some cases, a letter from a physician or psychologist is required for the patient to purchase such lamps. In a randomized controlled trial, Lam et al. (2016) demonstrated that bright-light treatment, both as monotherapy and in combination with fluoxetine, was efficacious and well tolerated in the treatment of adults with nonseasonal MDD.

IMPORTANCE OF EXERCISE

Therapists should always encourage depressed patients to exercise. Not only does exercise lead to weight loss and increased levels of motivation, but it also helps to release important endorphins and neuromodulators such as phenylethylamine (PEA). The presence of PEA is associated with increased levels of endorphins and improvement in motivation, energy, and mood. A meta-analysis of the literature by Josefsson, Lindwall, and Archer (2014) showed a significant and large overall effect favoring exercise interventions. Exercise may be recommended for people with mild and moderate depression who are willing, motivated, and physically healthy enough to engage in such a program.

ELECTROCONVULSIVE THERAPY (ECT) AND OTHER TREATMENTS

In some cases, patients with severe depression do not respond to antidepressants. If their depression worsens and includes suicidal ideation, they may be referred for ECT. Electroconvulsive therapy is given when the patient is anesthetized and paralyzed. Electrodes are placed on the scalp, usually on the nonspeech-dominant hemisphere to avoid later damage to verbal memories. Electricity is then administered, resulting in a seizure. No movement is noted because the patient is paralyzed or immobilized. Most patients receive three sessions per week for up to four weeks, or until improvement is noted. While excessive use of ECT may cause brain damage and memory loss, some researchers have noted that naloxone (Narcan), a drug that blocks opioid receptors, may reduce some of the adverse cognitive side effects of ECT (Prudic, Fitzsimons, Nobler, & Sackeim, 1999). Some clinicians, especially those who treat elderly and medically ill patients, believe that the risks associated with ECT are equivalent or even preferable to those associated with many medications used to treat depression (Kelly & Zisselman, 2000).

For patients who may not be good candidates for ECT, new research into the use of repetitive transcranial magnetic stimulation or rTMS to the prefrontal cortex, stimulation of the vagus nerve, and stimulation of other areas of the brain through deep brain stimulation may offer some relief (Klein et al., 1999; Triggs et al., 1999). In addition, a meta-analysis and systematic review of ECT and rTMS by Chen, Zhao, Liu, Fan, and Xie (2017) showed that ECT was the most efficacious treatment for MDD but not well tolerated, whereas rTMS was the best tolerated. Bilateral rTMS appears to have the most favorable balance between efficacy and acceptability.

PROCEDURAL STEPS FOR PATIENT TREATMENT

When a decision is made to use medication to treat a patient's depression, the therapist should follow a *treatment protocol* or procedural steps to decide on the appropriate medications and how to use them.

Step 1 Most prescribing professionals start with the easier medications first. These include the SSRIs such as fluoxetine (Prozac), sertraline (Zoloft), escitalopram (Lexapro), and so on. These medications have fewer side effects and interact with fewer other medications. In many cases, the patient is started on a low dose and titrated up. The patient must end up on a therapeutic dose of the medication to truly determine if the medication is helpful. Research suggests that too many patients are maintained on too small a dose of antidepressants, which are no better than no dose at all (Leon et al., 2003). (This is a common problem when primary care physicians write prescriptions.) If the patient has a satisfactory response and all symptoms appear to remit, the therapist should continue with psychotherapy and not increase the medication. The clinician may need to wait at least four to five weeks to determine the level of response.

Step 2 In some cases the patient has only a partial response to SSRIs, even when the dose is increased to maximum dose. Since SSRIs affect only the neurotransmitter serotonin, the patient's depression may be related to norepinephrine and/or dopamine. In such cases, additional medications aimed at the other neurotransmitters might need to be added or substituted. It is not unusual for such patients to be taking an SSRI like fluoxetine or an SNRI like venlafaxine (Effexor) with bupropion (Wellbutrin). Polypharmacy is more complicated and should not be attempted by the patient's primary care physician. In addition, antidepressants can be augmented or boosted by adding a low dose of lithium, or by adding a stimulant such as methylphenidate (Ritalin). Buspirone (Buspar), a nonbenzodiazepine anxiety medication with antidepressant qualities, and folic acid may also boost the antidepressant response.

Step 3 If the patient appears to have psychotic features in addition to his or her depression, an appropriate neuroleptic or antipsychotic medication might need to be added to the regimen. In rare cases, the patient may also have racing thoughts that interfere with his or her ability to relax. In these cases, neuroleptics may also be added to calm the thoughts and allow the patient to sleep better (Baune, 2008; Nelson, Pikalov, & Berman, 2008). Refer to Chapter 8 for further information on these medications.

Step 4 If the therapist and the prescriber have tried several drugs with no response, they should check with the patient to determine if he or she is using alcohol or other substances, taking the medication as directed, not taking the medication at all, and/or taking an unreported dietary supplement. Adherence to the medication regimen is crucial to achieve the desired outcome.

Step 5 The therapist should keep in mind that certain medications are contraindicated for certain types of patients. For patients with poor appetite or eating disorders, do not use bupropion as it may decrease appetite. For overweight patients, use mirtazapine (Remeron) and TCAs with caution, as they have been shown to cause an increase in weight and appetite. Patients with a history of seizure should not take bupropion because it lowers the seizure threshold. Nefazodone (Serzone) must be used with extra caution because it may cause liver failure in some patients. It is important to remember that MAOIs do not mix with other antidepressants and can cause a hypertensive crisis. It is imperative to wait at least two weeks after using an MAOI before starting another antidepressant because of potential drug interactions; the prescriber must wait two weeks after stopping another medication before trying MAOIs. There is one exception: The prescriber should wait five weeks after discontinuing fluoxetine before MAOIs are used. This is called the "washout period."