and a third category (**brain–gut peptides**) contains neuropeptides that were first discovered in the gut. The fourth category (**opioid peptides**) contains neuropeptides that are similar in structure to the active ingredients of opium, and the fifth (**miscellaneous peptides**) is a catch-all category that contains all of the neuropeptide transmitters that do not fit into one of the other four categories.

Figure 4.16 summarizes all the neurotransmitters that were introduced in this module. If it has not already occurred to you, this table should be very useful for reviewing the material in this module.

Pharmacology of Synaptic Transmission and Behavior

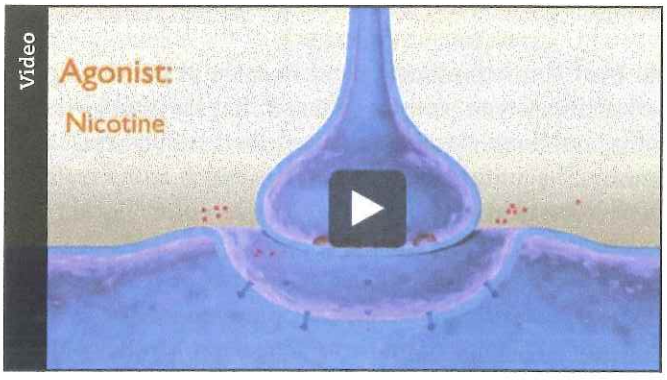
In case you have forgotten, the reason we have asked you to invest so much effort in learning about the neurotransmitters is that they play a key role in how the brain works. This chapter began on a behavioral note by considering the pathological behavior of Roberto Garcia d'Orta, which resulted from a Parkinson's disease–related disruption of his dopamine function. Now, let's return to behavior.

Most of the methods that biopsychologists use to study the behavioral effects of neurotransmitters are *pharmacological* (involving drugs). To study neurotransmitters and behavior, researchers administer to human or nonhuman subjects drugs that have particular effects on particular neurotransmitters and then assess the effects of the drugs on behavior.

Drugs have two fundamentally different kinds of effects on synaptic transmission: They facilitate it or they inhibit it. Drugs that facilitate the effects of a particular neurotransmitter are said to be **agonists** of that neurotransmitter. Drugs that inhibit the effects of a particular neurotransmitter are said to be its **antagonists**.

Watch this video on MyPsychLab

AGONIST AND ANTAGONIST



How Drugs Influence Synaptic Transmission

LO 4.17 Provide a general overview of how drugs influence synaptic transmission.

Although synthesis, release, and action vary from neurotransmitter to neurotransmitter, the following seven general steps are common to most neurotransmitters: (1) synthesis of the neurotransmitter, (2) storage in vesicles, (3) breakdown in the cytoplasm of any neurotransmitter that leaks from the vesicles, (4) exocytosis, (5) inhibitory feedback via autoreceptors, (6) activation of postsynaptic receptors, and (7) deactivation. Figure 4.17 illustrates these seven steps, and Figure 4.18 illustrates some ways that agonistic and antagonistic drugs influence them. For example, some agonists of a particular neurotransmitter bind to postsynaptic receptors and activate them, whereas some antagonistic drugs, called **receptor blockers**, bind to postsynaptic receptors without activating them and, in so doing, block the access of the usual neurotransmitter.

Behavioral Pharmacology: Three Influential Lines of Research

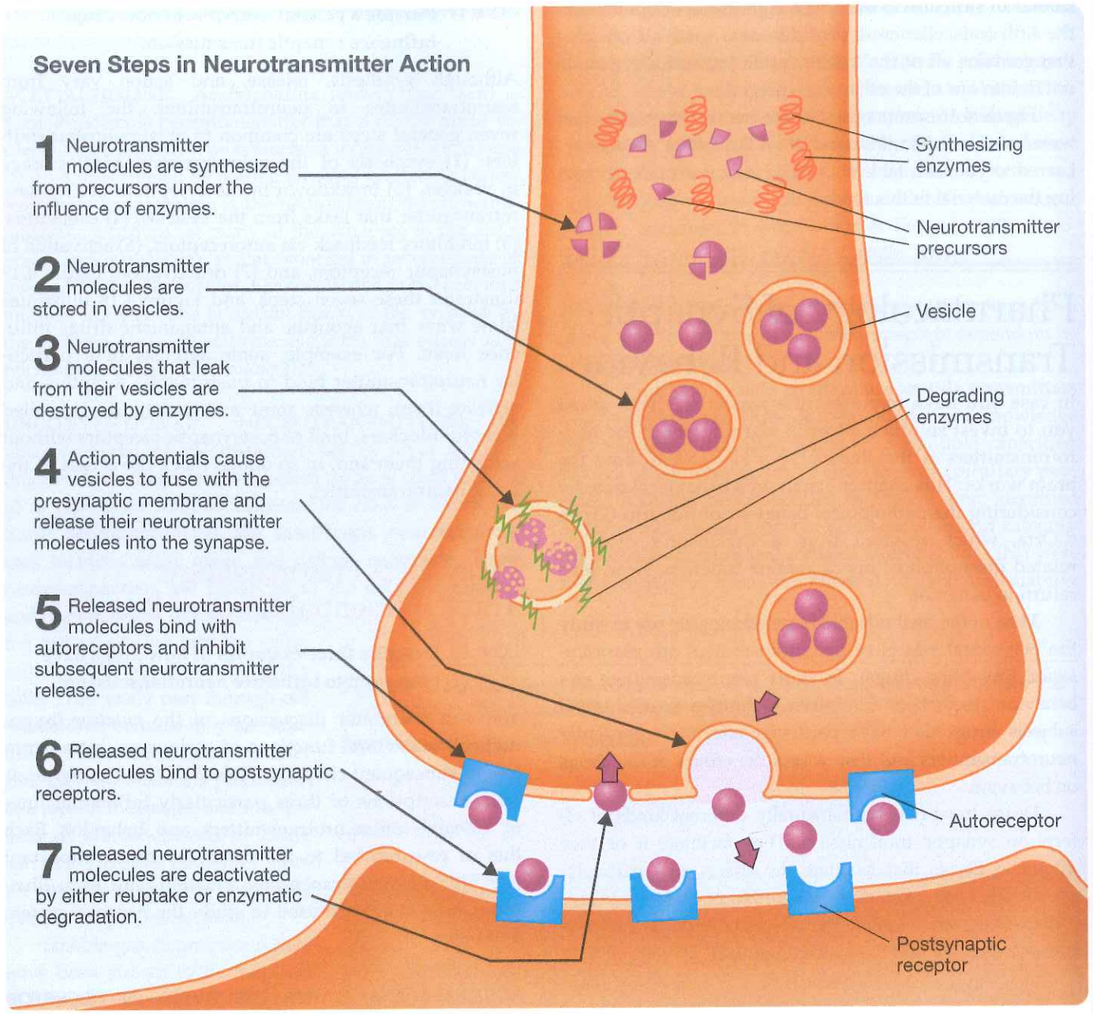
LO 4.18 Describe three examples of how drugs have been used to influence neurotransmission.

You will encounter discussions of the *putative* (hypothetical) behavioral functions of various neurotransmitters in subsequent chapters. However, this chapter ends with descriptions of three particularly influential lines of research on neurotransmitters and behavior. Each line of research led to the discovery of an important principle of neurotransmitter function, and each illustrates how drugs are used to study the nervous system and behavior.

WRINKLES AND DARTS: DISCOVERY OF RECEPTOR SUBTYPES. It was originally assumed that there was one kind of receptor for each neurotransmitter, but this notion was dispelled by research on acetylcholine receptors (see Changeux, 2013; Papke, 2014). Some acetylcholine receptors bind to *nicotine* (a CNS stimulant and the major psychoactive ingredient of tobacco), whereas other acetylcholine receptors bind to *muscarine* (a poisonous substance found in some mushrooms). These two kinds of acetylcholine receptors thus became known as *nicotinic receptors* and *muscarinic receptors*.

Next, it was discovered that nicotinic and muscarinic receptors are distributed differently in the nervous system, have different modes of action, and consequently have different behavioral effects. Both nicotinic and muscarinic

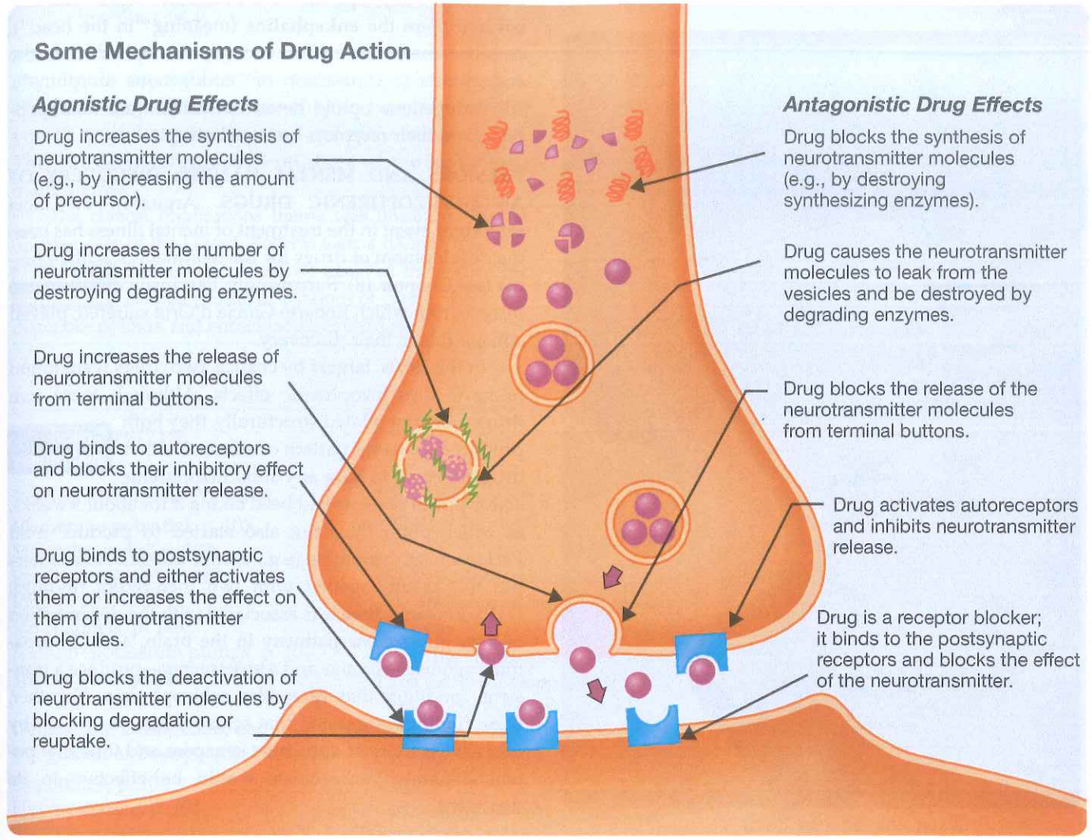
Figure 4.17 Seven steps in neurotransmitter action: (1) synthesis, (2) storage in vesicles, (3) breakdown of any neurotransmitter leaking from the vesicles, (4) exocytosis, (5) inhibitory feedback via autoreceptors, (6) activation of postsynaptic receptors, and (7) deactivation.



receptors are found in the CNS and the PNS. In the PNS, many nicotinic receptors occur at the junctions between motor neurons and muscle fibers, whereas many muscarinic receptors are located in the autonomic nervous system (ANS). Nicotinic and muscarinic receptors are ionotropic and metabotropic, respectively.

Many of the drugs used in research and medicine are extracts of plants that have long been used for medicinal and recreational purposes. The cholinergic agonists and antagonists illustrate this point well. For example, the ancient Greeks consumed extracts of the belladonna plant to treat stomach ailments and to make themselves more attractive. Greek women believed that the pupil-dilating effects of these extracts enhanced their beauty (*belladonna* means "beautiful lady"). **Atropine**, which is the main active ingredient of belladonna, is a receptor blocker that exerts its antagonist effect by binding to muscarinic receptors, thereby blocking the effects of acetylcholine on them. The pupil-dilating effects of atropine are mediated by its antagonist actions on muscarinic receptors in the ANS. In

Figure 4.18 Some mechanisms of agonistic and antagonistic drug effects.



contrast, the disruptive effects of large doses of atropine on memory are mediated by its antagonistic effect on muscarinic receptors in the CNS. The disruptive effect of high doses of atropine on memory was one of the earliest clues that cholinergic mechanisms may play a role in memory (see Chapter 11).

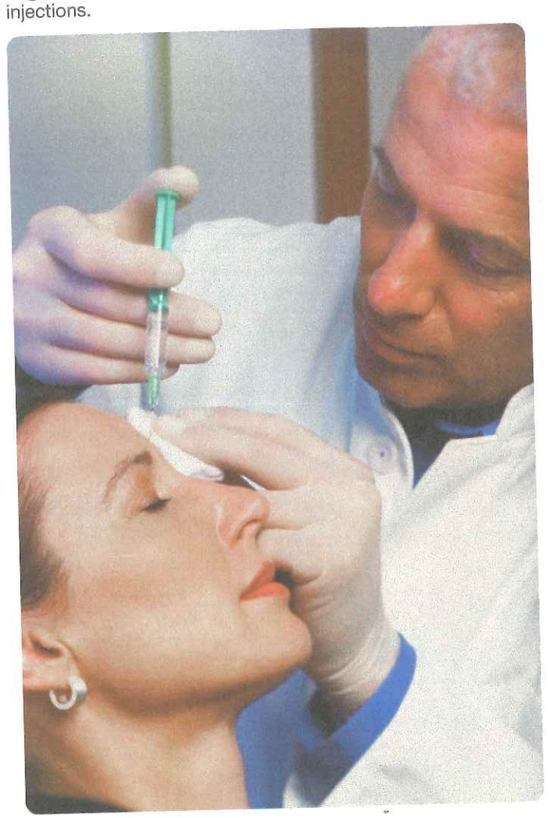
South American natives have long used *curare*—an extract of a certain class of woody vines—on the tips of darts they use to kill their game. Like atropine, curare is a receptor blocker at cholinergic synapses, but it acts at nicotinic receptors. By binding to nicotinic receptors, curare blocks transmission at neuromuscular junctions, thus paralyzing its recipients and killing them by blocking their respiration. You may be surprised, then, to learn that the active ingredient of curare is sometimes administered to human patients during surgery to ensure that their muscles do not contract during an incision. When curare is used for this purpose, the patient's breathing must be artificially maintained by a respirator.

Clinical Implications

Botox (short for *Botulinium toxin*), a neurotoxin released by a bacterium often found in spoiled food, is another nicotinic antagonist, but its mechanism of action is different: It blocks the release of acetylcholine at neuromuscular junctions and is thus a deadly poison. However, injected in minute doses at specific sites, it has applications in medicine (e.g., reduction of tremors) and cosmetics (e.g., reduction of wrinkles; see Figure 4.19).

PLEASURE AND PAIN: DISCOVERY OF ENDOGENOUS OPIOIDS. Opium, the sticky resin obtained from the seed pods of the opium poppy, has been used by humans since prehistoric times for its pleasurable effects. Morphine, its major psychoactive ingredient, is addictive. But morphine also has its good side: It is an effective *analgesic* (painkiller)—see Chapters 7 and 15.

Figure 4.19 A woman receiving cosmetic Botox injections.



In the 1970s, it was discovered that opioid drugs such as morphine bind effectively to receptors in the brain. These receptors were generally found in the hypothalamus and other limbic areas, but they were most concentrated in the area of the brain stem around the cerebral aqueduct, which connects the third and fourth ventricles; this part of the brain stem is called the **periaqueductal gray (PAG)**. Microinjection of morphine into the PAG, or even electrical stimulation of the PAG, produces strong analgesia.

Clinical Implications

The existence of selective opioid receptors in the brain raised an interesting question: Why are they there? They are certainly not there so that once humans discovered opium, opioids would have a place to bind. The existence of opioid receptors suggested that *opioid* chemicals occur naturally in the brain, and that possibility triggered an intensive search for them.

Several families of **endogenous** (occurring naturally within the body) opioids have been discovered. First discovered were the **enkephalins** (meaning "in the head"). Another major family of endogenous opioids are the **endorphins** (a contraction of "endogenous morphine"). All endogenous opioid neurotransmitters are neuropeptides, and their receptors are metabotropic.

TREMORS AND MENTAL ILLNESS: DISCOVERY OF ANTISCHIZOPHRENIC DRUGS. Arguably, the most important event in the treatment of mental illness has been the development of drugs for the treatment of schizophrenia (see Chapter 18). Surprisingly, Parkinson's disease, the disease from which Roberto Garcia d'Orta suffered, played a major role in their discovery.

In the 1950s, largely by chance, two drugs were found to have antischizophrenic effects. Although these two drugs were not related structurally, they both produced a curious pattern of effects: Neither drug appeared to have any antischizophrenic activity until patients had been taking it for about 3 weeks, at which point the drug also started to produce mild Parkinsonian symptoms (e.g., tremor-at-rest). Researchers put this result together with two then-recent findings: (1) Parkinson's disease is associated with the degeneration of a main *dopamine* pathway in the brain, and (2) dopamine agonists—*cocaine* and *amphetamines*—produce a transient condition that resembles schizophrenia. Together, these findings suggested that schizophrenia is caused by excessive activity at dopamine synapses and thus that potent dopamine antagonists would be effective in its treatment.

Clinical Implications

Why is it important for biopsychologists to understand neural conduction and synaptic transmission? Is it important for all psychologists to have such knowledge? Discuss.

It was ultimately discovered that one particular dopamine receptor, the D_2 receptor, plays a key role in schizophrenia and that drugs that most effectively block it are the most effective antischizophrenic drugs.

It would be a mistake to think that antischizophrenic drugs cure schizophrenia or that they help in every case. However, they help many patients, and the help is sometimes enough to allow them to live at home. You will learn much more about this important line of research in Chapter 18.

Themes Revisited

The function of the nervous system, like the function of any circuit, depends on how signals travel through it. The primary purpose of this chapter was to introduce you to neural conduction and synaptic transmission. This introduction touched on three of the text's four main themes.

The clinical implications theme was illustrated by the opening case of the Lizard, Roberto Garcia d'Orta. Then this theme was picked up again at the end of the chapter during discussions of curare, Botox, endogenous opioids, and antischizophrenic drugs.

Clinical Implications

The evolutionary perspective theme was implicit throughout the entire chapter because almost all neurophysiological research is conducted on the neurons and synapses of nonhuman subjects.

Evolutionary Perspective

The thinking creatively theme arose in two metaphors: the firing-gun metaphor of action potentials and the mouse-traps-on-a-wobbly-shelf metaphor of axonal conduction. Metaphors are useful in teaching, and scientists find them useful for thinking about the phenomena they study.

Thinking Creatively

Key Terms

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Microelectrodes, p. 103
Resting potential, p. 103
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Sodium–potassium pumps, p. 104
Transporters, p. 104

Generation, Conduction, and Integration of Postsynaptic Potentials
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