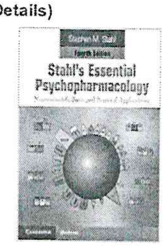
chapter 1

Stahl's Essential Psychopharmacology

Drug Interactions (/drug_interaction.jsf?page=drugDetails)

4th Edition - 9781107686465

This fully revised edition returns to the essential roots of what it means to become a neurobiologically empowered psychopharmacologist. This remains the essential text for all students and professionals in mental health seeking to understand and utilize current therapeutics.



Chemical neurotransmission

Modern psychopharmacology is largely the story of chemical neurotransmission. To understand the actions of drugs on the brain, to grasp the impact of diseases upon the central nervous system, and to interpret the behavioral consequences of psychiatric medicines, one must be fluent in the language and principles of chemical neurotransmission. The importance of this fact cannot be overstated for the student of psychopharmacology. This chapter forms the foundation for the entire book, and the roadmap for one's journey through one of the most exciting topics in science today, namely the neuroscience of how disorders and drugs act upon the central nervous system.

Anatomical versus chemical basis of neurotransmission

What is neurotransmission? Neurotransmission can be described in many ways: anatomically, chemically, electrically. The *anatomical* basis of neurotransmission is neurons (Figures 1-1 through 1-3) and the connections between them, called synapses (Figure 1-4), sometimes also called the *anatomically addressed* nervous system, a complex of "hard-wired" synaptic connections between neurons, not unlike millions of telephone wires within thousands upon thousands of cables. The anatomically addressed brain is thus a complex wiring diagram, ferrying electrical impulses to wherever the "wire" is plugged in (i.e., at a synapse). Synapses can form on many parts of a neuron, not just the dendrites as axodendritic synapses, but also on the soma as axosomatic synapses, and even at the beginning and at the end of axons (axoaxonic synapses) (Figure 1-2). Such synapses are said to be "asymmetric" since communication is structurally designed to be in one direction; that is, anterograde from the axon of the first neuron to the dendrite, soma, or axon of the second neuron (Figures 1-2 and 1-3). This means that there are presynaptic elements that differ from postsynaptic elements (Figure 1-4). Specifically, neurotransmitter is packaged in the presynaptic nerve terminal like ammunition in a loaded gun, and then fired at the postsynaptic neuron to target its receptors.

Neurons are the cells of chemical communication in the brain. Human brains are comprised of tens of billions of neurons, and each is linked to thousands of other neurons. Thus, the brain has trillions of specialized connections known as synapses. Neurons

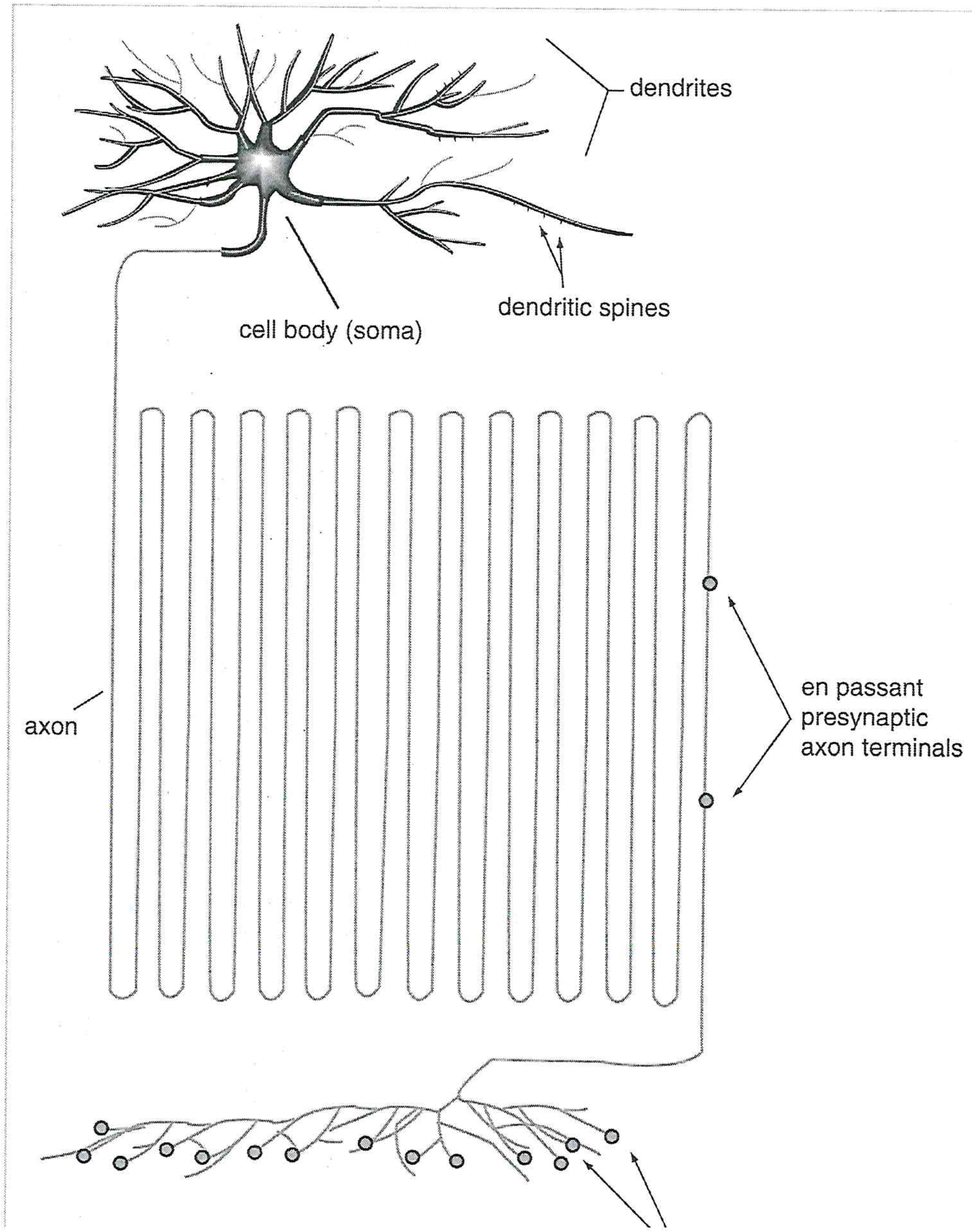


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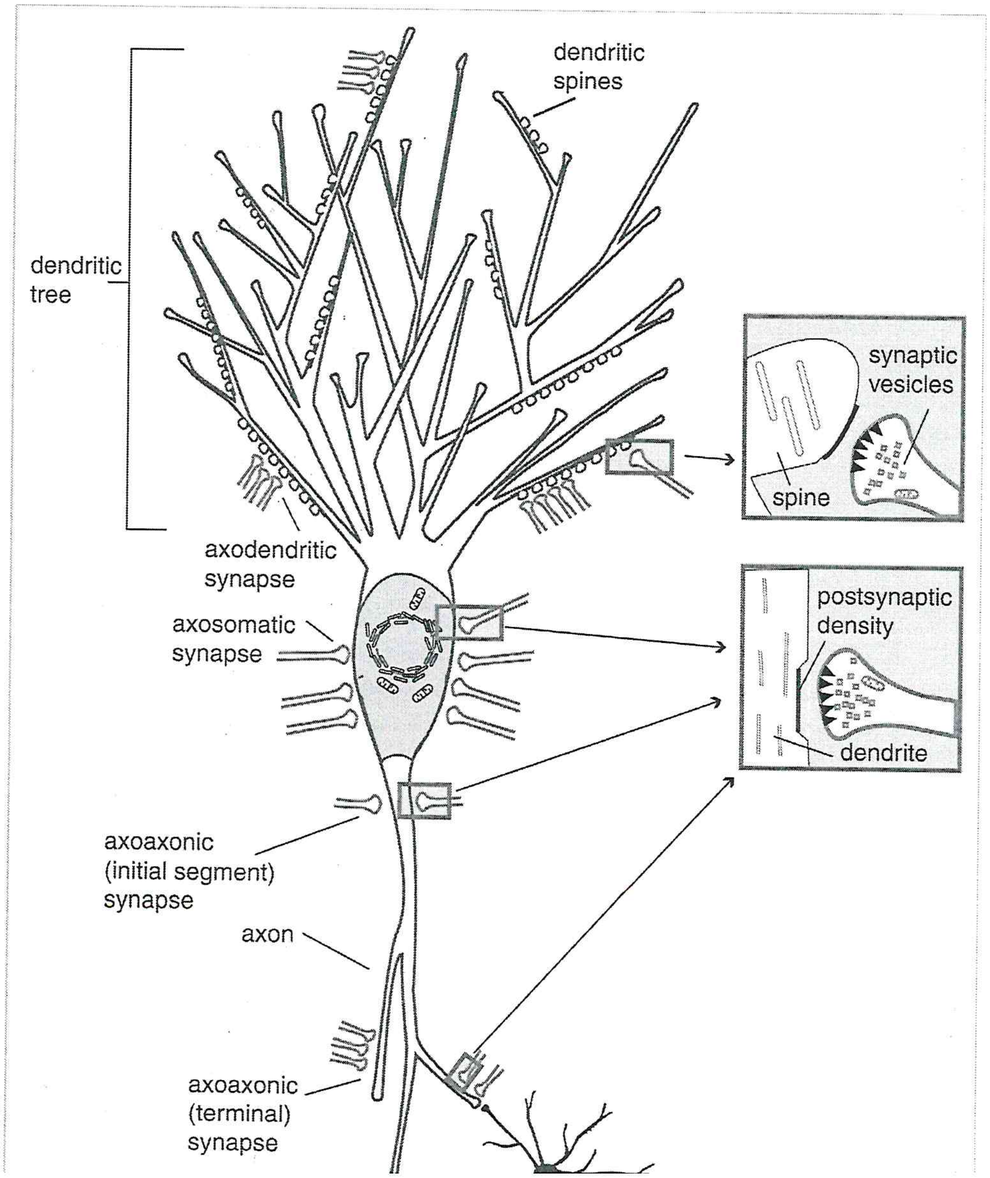
Figure 1-1. General structure of a neuron. This is an artist's conception of the generic structure of a neuron. All neurons have a cell body known as the soma, which is the command center of the nerve and contains the nucleus of the cell. All neurons are also set up structurally to both send and receive information. Neurons send information via an axon that forms presynaptic terminals as the axon passes by (en passant) or as the axon ends.

have many sizes, lengths, and shapes that determine their functions. Localization within the brain also determines function. When neurons malfunction, behavioral symptoms may occur. When drugs alter neuronal function, behavioral symptoms may be relieved, worsened, or produced.

General structure of a neuron. Although this textbook will often portray neurons with a generic structure (such as that shown in Figures 1-1 through 1-3), the truth is that many neurons have unique structures depending upon where in the brain they are located and what their function is. All neurons have a cell body known as the soma, and are set up structurally to receive information from other neurons through dendrites, sometimes via spines on the dendrites and often through an elaborately branching "tree" of dendrites (Figure 1-2). Neurons are also set up structurally to send information to other neurons via an axon that forms presynaptic terminals as the axon passes by (en passant, Figure 1-1) or as the axon ends (presynaptic axon terminals, Figures 1-1 through 1-4).

Neurotransmission has an *anatomical* infrastructure, but it is fundamentally a very elegant *chemical* operation. Complementary to the anatomically addressed nervous system is the *chemically addressed* nervous system, which forms the *chemical* basis of neurotransmission: namely, how chemical signals



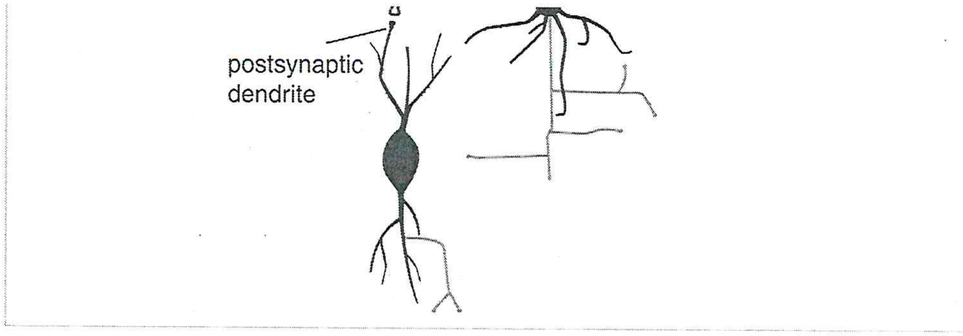


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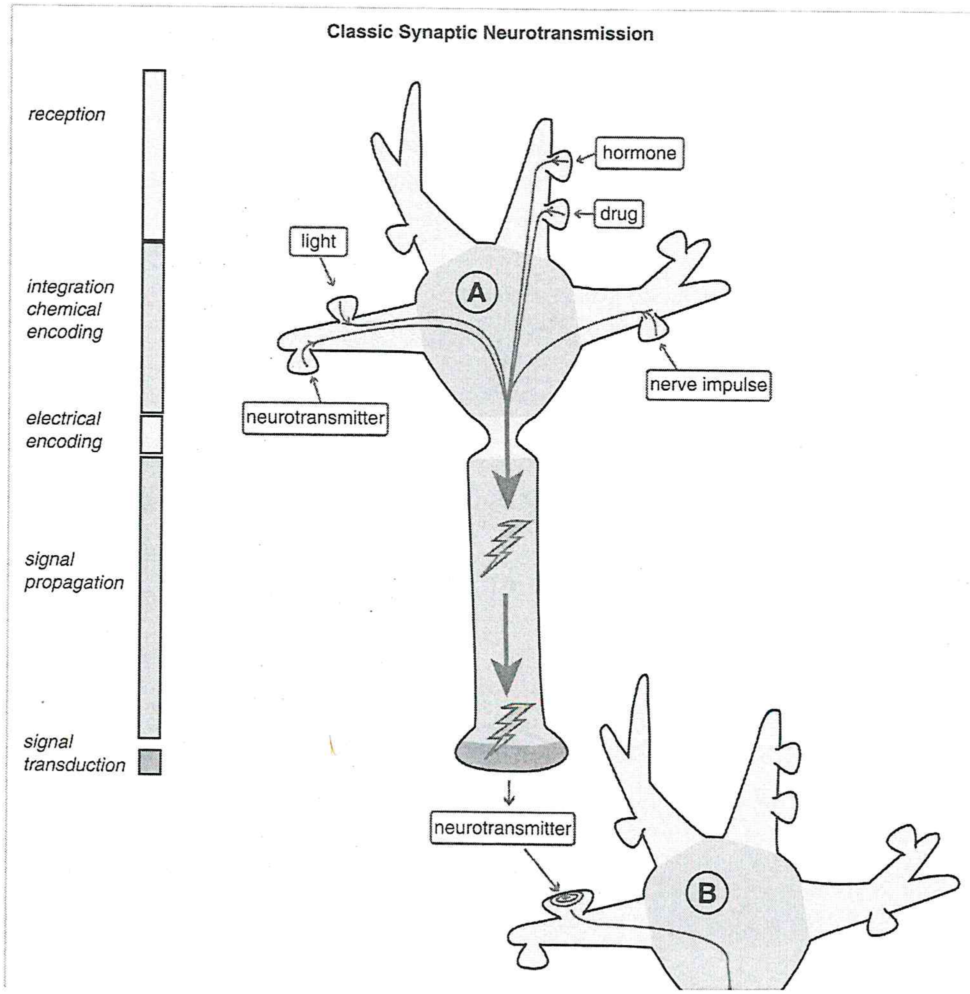
Figure 1-2. Axodendritic, axosomatic, and axoaxonic connections. After neurons migrate, they form synapses. As shown in this figure, synaptic connections can form not just between the axon and dendrites of two neurons (axodendritic) but also between the axon and the soma (axosomatic) or the axons of the two neurons (axoaxonic). Communication is anterograde from the axon of the first neuron to the dendrite, soma, or axon of the second neuron.

are coded, decoded, transduced, and sent along the way. Understanding the principles of chemical neurotransmission is a fundamental requirement for grasping how psychopharmacologic agents work, because they target key molecules involved in neurotransmission. Drug targeting of specific chemical sites that influence neurotransmission is discussed in Chapters 2 (essential_4th_chapter.jsf?page=chapter2_introduction.htm&name=Chapter 2&title=Neurotransmitter transporters as targets of drug action#c02598-2-1) and 3 (essential_4th_chapter.jsf?page=chapter3_introduction.htm&name=Chapter 3&title=Ligand-gated ion channels as targets of psychopharmacological drug action#c02598-3-1).

Understanding the chemically addressed nervous system is also a prerequisite for becoming a "neurobiologically informed" clinician: that is, being able to translate exciting new findings on brain circuitry, functional neuroimaging, and genetics into clinical practice, and potentially improving the manner in which psychiatric disorders and their symptoms are diagnosed and treated. The chemistry of neurotransmission in specific



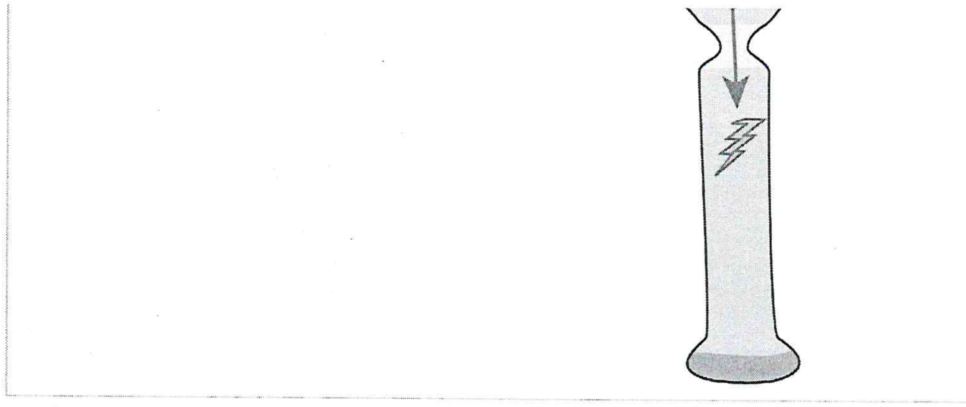


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Figure 1-3. Classic synaptic neurotransmission. In classic synaptic neurotransmission, stimulation of a presynaptic neuron (e.g., by neurotransmitters, light, drugs, hormones, nerve impulses) causes electrical impulses to be sent to its axon terminal. These electrical impulses are then converted into chemical messengers and released to stimulate the receptors of a postsynaptic neuron. Thus, although communication *within* a neuron can be electrical, communication *between* neurons is chemical.

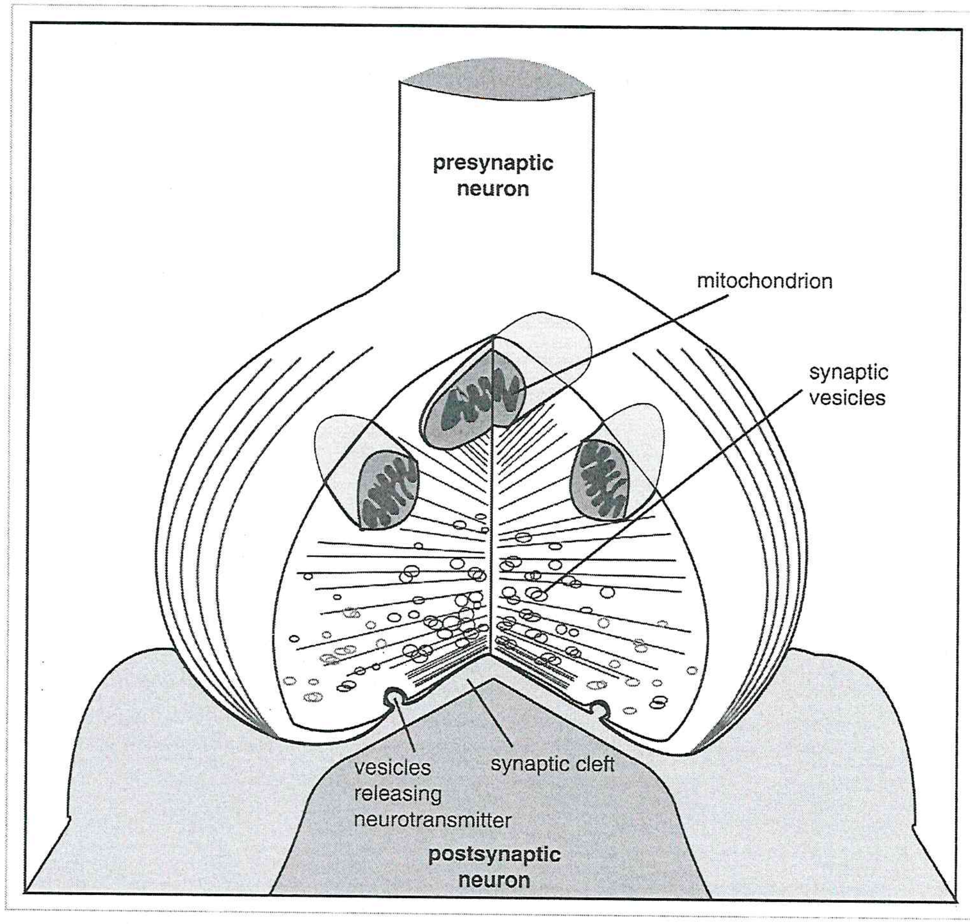

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Figure 1-4. Enlarged synapse. The synapse is enlarged conceptually here to show the specialized structures that enable chemical neurotransmission to occur. Specifically, a presynaptic neuron sends its axon terminal to form a synapse with a postsynaptic neuron. Energy for neurotransmission from the presynaptic neuron is provided by mitochondria there. Chemical neurotransmitters are stored in small vesicles, ready for release upon firing of the presynaptic neuron. The synaptic cleft is the gap between the presynaptic neuron and the postsynaptic neuron; it contains proteins and scaffolding and molecular forms of "synaptic glue" to reinforce the connection between the neurons. Receptors are present on both sides of this cleft and are key elements of chemical neurotransmission.

brain regions and how these principles are applied to various specific psychiatric disorders and treated with various specific psychotropic drugs are discussed throughout the rest of the book.