6.2: Review of the Central Nervous System

To understand how psychotropic medications work, it is important to understand the anatomy and physiology of the central nervous system. The nervous system is divided into the central and peripheral nervous systems. The central nervous system (CNS) is the brain and spinal cord, and the peripheral nervous system includes everything else in the nervous system. See Figure 6.1 for an illustration of the central and peripheral nervous systems.

![Central and Peripheral Nervous Systems Diagram]

Figure 6.1 The Central and Peripheral Nervous Systems

The peripheral nervous system consists of sensory neurons and motor neurons. Sensory neurons sense the environment and conduct signals to the brain that become a person’s conscious perception of that stimulus. This
conscious perception may lead to a motor response that is conducted from the brain to the peripheral nervous system via motor neurons. Motor neurons are part of the somatic nervous system that stimulates voluntary movement of muscles and the autonomic nervous system that controls involuntary responses.

**Sympathetic and Parasympathetic Nervous System**

The autonomic nervous system is divided into the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS). Homeostatic mechanisms are regulated by the body through a balance of SNS and PNS stimulation. For example, stimulation of SNS receptors increases the heart rate, increases blood pressure via the constriction of blood vessels, and causes bronchodilation, whereas stimulation of the PNS slows the heart, lowers blood pressure due to vasodilation, and causes bronchoconstriction. Due to these effects, the SNS is associated with the “fight-or-flight” response, and the PNS is often referred to as the “rest and digest” system. See Figure 6.2 to compare the effects of PNS and SNS stimulation on target organs.

![Figure 6.2 Effects of SNS and PNS Stimulation](image)

**SNS Receptors**

SNS receptors include Alpha-1, Alpha-2, Beta-1, and Beta-2 receptors that are stimulated by epinephrine and norepinephrine. Medications that stimulate these receptors are referred to as adrenergic agonists because they mimic the effects of the body’s natural SNS stimulation. For example, stimulants like methylphenidate are adrenergic agonists used to treat attention deficit hyperactivity disorder (ADHD). Conversely, adrenergic antagonists block SNS receptors. For example, propranolol is a Beta-2 antagonist used to treat the physical symptoms of severe anxiety (e.g., trembling, rapid heartbeat, and sweating).

**PNS Receptors**

PNS receptors include nicotinic and muscarinic receptors that are stimulated by acetylcholine (ACh). Drugs that stimulate nicotinic and muscarinic receptors are called cholinergics. For example, nicotine in tobacco products stimulates nicotinic receptors. Stimulation of muscarinic receptors primarily causes smooth muscle contraction. An
example of a muscarinic agonist is bethanechol used to treat urinary retention by increasing the tone of the detrusor muscle to increase bladder emptying.[3] Drugs that block the effects of PNS receptors are called **anticholinergics.** For example, benztropine is an anticholinergic used to treat muscle spasms associated with extrapyramidal symptoms from antipsychotic medications.[4] Many psychotropic medications cause anticholinergic adverse effects that can be especially hazardous for older adults. **SLUDGE** is a mnemonic for anticholinergic side effects: Salivation decreased, Lacrimation decreased, Urinary retention, Drowsiness/dizziness, GI upset, and Eyes (blurred vision/dry eyes). See Figure 6.3[5] for an illustration of the “SLUDGE” effects caused by anticholinergics.

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**Figure 6.3 SLUDGE Effects of Anticholinergics**

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## Opioid System

The opioid system in the brain controls pain, reward, and addictive behaviors. There are three types of opioid receptors called mu, delta, and kappa receptors. Opioid receptors are stimulated by endogenous peptides released by neurons (such as endorphins) and exogenous opiates. **Opiates** include powerful analgesics (such as morphine and oxycodone) prescribed to treat moderate to severe pain. Opiates also include illicit drugs (such as heroin). Chronic use of prescribed and illicit opiates can be highly addictive because of their actions on the reward system of the brain.[6] Read more about the addictive cycle in the “Substance Use Disorders” chapter.

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## Neurotransmitters

**Neurotransmitters** are chemical substances released at the end of a neuron by the arrival of an electrical impulse. They diffuse across the synapse and cause the transfer of the impulse to another nerve fiber, a muscle fiber, or other structure. Neurotransmitters interact with specific receptors like a key and a lock. See Figure 6.4[7] for an illustration of neuron communication with neurotransmitters and receptors.

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There are several types of neurotransmitters associated with mental health disorders and psychoactive medications, including acetylcholine, glutamate, GABA, glycine, dopamine, serotonin, norepinephrine, and histamine:

- **Acetylcholine**: Acetylcholine stimulates nicotinic and muscarinic receptors in the parasympathetic nervous system. Other substances also bind to these receptors. For instance, nicotine (in tobacco products) binds to nicotinic receptors, and muscarine (products of specific mushrooms used as a hallucinogenic) binds to muscarinic receptors.

- **Glutamate**: Glutamate is an excitatory neurotransmitter. Elevated levels of glutamate are associated with psychosis symptoms that can occur with schizophrenia, as well as with illicit drug use such as methamphetamines. Conversely, lamotrigine, a medication used to treat bipolar disorder, inhibits glutamate.

- **Gamma-Aminobutyric Acid and Glycine**: Gamma-aminobutyric acid (GABA) and glycine are inhibitory neurotransmitters that act like brakes in a car by slowing down overexcited nerve cells. Low levels of GABA are associated with seizures, anxiety, mania, and impulse control. Pregabalin is an anticonvulsant that mimics the effects of GABA and is used to treat generalized anxiety disorder.

- **Dopamine**: Dopamine plays an essential role in several brain functions, including learning, motor control, reward, emotion, and executive functions. It is associated with several mental health disorders and is targeted by many psychotropic medications. For example, bupropion is an antidepressant that inhibits dopamine reuptake, leading to increased dopamine levels in the synapse and relieving the symptoms of depression. Conversely, chlorpromazine blocks dopamine receptors and is used to treat psychosis, but this blockade can cause extrapyramidal side effects (involuntary and uncontrolled muscle movements).

- **Serotonin**: Serotonin modulates multiple neuropsychological processes such as mood, sleep, libido, and temperature regulation. Abnormal levels of serotonin have been linked to many mental health disorders such as depression, bipolar disorder, and anxiety. Many psychotropic medications target serotonin. For example, fluoxetine belongs to a class of antidepressants called selective serotonin reuptake inhibitors (SSRIs). SSRIs prevent the
reuptake of serotonin at the synapse, making more of the chemical available in the brain and relieving depression.

- **Norepinephrine and Epinephrine:** Norepinephrine and epinephrine stimulate alpha- and beta-receptors in the sympathetic nervous system. Their release exerts effects on a variety of body processes, including stress, sleep, attention, and focus. Many psychotropic medications target these neurotransmitters. For example, venlafaxine belongs to a class of antidepressants called norepinephrine reuptake inhibitors (NRIs). NRIs are prescribed to treat depression by preventing the reuptake of norepinephrine at the synapse and boosting levels of norepinephrine in the brain.

- **Histamine:** Histamine mediates homeostatic functions in the body, promotes wakefulness, modulates feeding behavior, and controls motivational behavior. For example, diphenhydramine, a histamine antagonist, causes drowsiness and is also used to treat extrapyramidal symptoms.

View a YouTube video called the Receptor Debate that compares the effects of neurotransmitters.

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