

CHAPTER 12

LECTURE OUTLINE

I. OVERVIEW OF THE NERVOUS SYSTEM

1. The nervous system, along with the endocrine system, helps to keep controlled conditions within limits that maintain health and helps to maintain homeostasis.
2. The nervous system is responsible for all our behaviors, memories, and movements.
3. The branch of medical science that deals with the normal functioning and disorders of the nervous system is called neurology.

A. Central Nervous System

1. The central nervous system (CNS) consists of the brain and spinal cord (Figure 12.1a).

B. Peripheral Nervous System

1. The peripheral nervous system (PNS) consists of cranial and spinal nerves with sensory (efferent) and motor (afferent) components, ganglia, and sensory receptors.
 - a. The sensory system consists of a variety of different receptors as well as sensory neurons.
 - b. The motor system conducts nerve impulses from the CNS to muscles and glands.
2. The PNS is also subdivided into somatic (voluntary), autonomic (involuntary), and enteric nervous systems (Figure 12.1a)
3. The somatic nervous system (SNS) consists of neurons that conduct impulses from cutaneous and special sense receptors to the CNS, and motor neurons that conduct impulses from the CNS to skeletal muscle tissue.
4. The autonomic nervous system (ANS) contains sensory neurons from visceral organs and motor neurons that convey impulses from the CNS to smooth muscle tissue, cardiac muscle tissue, and glands.
 - a. The motor part of the ANS consists of the sympathetic division and the parasympathetic division.
 - b. The enteric nervous system (ENS) consists of neurons in enteric plexuses that extend the length of the GI tract.
 - 1) Many neurons of the enteric plexuses function independently of the ANS and CNS.
 - 2) Sensory neurons of the ENS monitor chemical changes within the GI tract and stretching of its walls, whereas enteric motor neurons govern contraction of GI tract organs, and activity of the GI tract endocrine cells.

C. Functions of the Nervous Systems

1. The sensory function of the nervous system is to sense changes in the internal and external environment through sensory receptors. Sensory neurons serve this function.
2. The integrative function is to analyze the sensory information, store some aspects, and make decisions regarding appropriate behaviors. Association or interneurons serve this function.
3. The motor function is to respond to stimuli by initiating action. Motor neurons serve this function.

II. HISTOLOGY OF THE NERVOUS SYSTEM

A. Neurons

1. Neurons have the property of electrical excitability.
2. Most neurons, or nerve cells, consist of a cell body (soma), many dendrites, and usually a single axon (Figure 12.2).
3. The cell body contains a nucleus, lysosomes, mitochondria, a Golgi complex, cytoplasmic inclusions such as lipofuscin, chromatophilic substances, and neurofibrils.
4. Chromatophilic substances (Nissl bodies) are an orderly arrangement of rough ER
5. Neurofibrils form the cytoskeleton.
6. The dendrites are the receiving or input portions of a neuron.
7. The axon conducts nerve impulses from the neuron to the dendrites or cell body of another neuron or to an effector organ of the body (muscle or gland).
8. The site of functional contact between two neurons or between a neuron and an effector cell is called a synapse
9. Axonal transport, a natural mechanism of intracellular transport in neurons, is exploited by certain microorganisms to reach other parts of the nervous system.

B. Structural diversity in Neurons

1. Both structural and functional features are used to classify the various neurons in the body.
2. On the basis of the number of processes extending from the cell body (structure), neurons are classified as multipolar, bipolar, and unipolar (Figure 12.3a,b,c).
3. Most neurons in the body are interneurons and are often named for the histologist who first described them (Purkinje cells) or named for the shape or appearance (pyramidal cells) (Figure 12.5)
4. On the basis of function, neurons are classified as sensory (Figure 12.10), association, and motor (Figure 12.10)

C. Neuroglia

1. Neuroglia (or glia) are specialized tissue cells that support neurons, attach neurons to blood vessels, produce the myelin sheath around axons, and carry out phagocytosis.
2. The types of neuroglia include those in the CNS (astrocytes, oligodendrocytes, microglia, ependymal cell, Figure 12.6) and those of the PNS, (neurolemmocytes or Schwann cells, and satellite cells, Figure12.7)
 - a. Astrocytes functions include:
 - 1) Microfilaments for strength
 - 2) Blood brain barrier
 - 3) Regulate growth
 - 4) Maintain chemical environments
 - 5) Learning and memory
 - b. Oligodendroctye functions
 - 1) Myelin sheath
 - c. Microglial cells
 - 1) Phagocytes
 - d. Ependymal cells:
 - 1) Circulate cerebral spinal fluid
3. Neuroglia of the PNS
 - a. Schwann cells
 - 1) Myelin sheath
 - b. Satellite cells
 - 1) Exchange material between neuronal cell bodies and interstitial fluid

III. MYELINATION

- A. A multilayered lipid and protein covering called the myelin sheath and produced by Schwann cells and oligodendrocytes surrounds the axons of most neurons (Figure 12.8a,b).
 1. The sheath electrically insulates the axon and increases the speed of nerve impulse conduction.
 2. Schwann cells produce the myelin sheath in the PNS.
- B. The outer nucleated cytoplasmic layer of the Schwann cell, which encloses the myelin sheath, is called the neurolemma (sheath of Schwann) and is found only around axons in the PNS.
 1. The neurolemma aids in regeneration in an injured axon by forming a regeneration tube that guides and stimulates regrowth of the axon.

- C. The myelin sheath has gaps called neurofibril nodes or nodes of Ranvier along the axon.
- D. Oligodendrocytes form myelin sheaths for CNS axons.
 - 1. No neurolemma is formed.
 - 2. No regrowth after injury occurs.
- E. Collections of nervous tissue include several structures Clusters of cell bodies include:
 - 1. Ganglia in the PNS
 - 2. Nuclei in the CNS
 - 3. Nerves and tracts are groups of axons in the PNS and CNS, respectively.
 - 4. Gray and White Matter
 - a. White matter is composed of aggregations of myelinated processes whereas gray matter contains nerve cell bodies, dendrites, and axon terminals or bundles of unmyelinated axons and neuroglia (Figure 12.9).
 - b. In the spinal cord, gray matter forms an H-shaped inner core, surrounded by white matter; in the brain a thin outer shell of gray matter covers the cerebral hemispheres.

IV. ELECTRICAL SIGNALS IN NEURONS

- A. Excitable cells communicate with each other by action potentials or graded potentials.
- B. Action potentials allow communication over short and long distances whereas graded potentials allow communication over short distances only.
 - 1. Production of both types of potentials depend upon the existence of a resting membrane potential and the presence of certain types of ion channels.
 - 2. The membrane potential is an electrical voltage across the membrane.
 - 3. Graded and action potentials occur because of ion channels in the membrane that allow ion movement across the membrane that can change the membrane potential.
 - a. Figure 12.10 depicts nervous system functions provided by the different signals acting through and on various cells in the pathway.
- C. **Ion Channels**
 - 1. The two basic types of ion channels are leakage (nongated) and gated.
 - a. Leakage (nongated) channels are always open (Figure 12.11)
 - b. Gated channels open and close in response to some sort of stimulus.
 - 1) Gated ion channels respond to voltage changes, ligands (chemicals), and mechanical pressure.

- 2) Voltage-gated channels respond to a direct change in the membrane potential (Figure 12.11d).
- 3) Ligand-gated channels respond to a specific chemical stimulus (Figure 12.11b).
- 4) Mechanically gated ion channels respond to mechanical vibration or pressure (Figure 12.11c)
- 5) Table 12.1 provides descriptions and locations of the different ion channels.

V. RESTING MEMBRANE POTENTIAL

- A. The membrane of a nonconducting neuron is positive outside and negative inside owing to the distribution of different ions across the membrane and the relative permeability of the membrane toward Na^+ and K^+ (Figure 12.12a).
 1. A typical value for the resting membrane potential is -70mV , and the membrane is said to be polarized (Figure 12.12b)
 2. The resting membrane potential is determined by several factors (Figure 12.13).
 - a. the unequal distribution of ions across the plasma membrane and the selective permeability of the membrane to Na^+ and K^+
 - b. Most anions cannot leave the interior of the cell.
 - c. The sodium-potassium pumps compensate for slow leakage of Na^+ into the cell by pumping it back out.

VI. GRADED POTENTIALS

- A. A graded potential is a small deviation from the resting membrane potential that makes the membrane either more polarized (hyperpolarization) or less polarized (depolarization) (Figure 12.14).
 1. Graded potentials occur most often in the dendrites and cell body of a neuron.
 2. Graded potentials occur as the result of opening of ligand-gated or mechanically gated channels (Figure 12.15)
 3. The signals are graded, meaning they vary in amplitude (size), depending on the strength of the stimulus and localized (Figure 12.16)
 4. Graded potentials can be summed to create larger membrane voltage values (Figure 12.17)

VII. GENERATION OF AN ACTION POTENTIAL (Figure 12.18)

- A. An action potential (AP) or impulse is a sequence of rapidly occurring events that decrease and eventually reverse the membrane potential (depolarization) and then restore it to the resting state (repolarization).
1. During an action potential, voltage-gated Na⁺ and K⁺ channels open in sequence (Figure 12.18).
 2. Rapid opening of voltage-gated Na⁺ channels causes depolarization. If the depolarization is to threshold, the membrane potential reverses. Depolarization occurs due to the interaction of the two voltage-gated Na⁺ channel gates: an activation gate and an inactivation gate (Figure 12.18).
 3. The slower opening of voltage-gated K⁺ channels and closing of previously open Na⁺ channels leads to repolarization, the recovery of the resting membrane potential.
 4. Different stimulus strength will affect action potential generation (Figure 12.19)
 - a. A subthreshold stimulus does not generate an action potential
 - b. A threshold stimulus generates an action potential
 - c. A suprathreshold stimulus generates an action potential and often more than one action potential.
 5. Figure 12.20 depicts a review of ion flow during depolarization and repolarization phases.
 6. During the refractory period (Figure 12.20), another impulse cannot be generated at all (absolute refractory period) or can be triggered only by a suprathreshold stimulus (relative refractory period).

B. Propagation of action potentials

1. An action potential conducts or propagates (travels) from point to point along the membrane; the traveling action potential is a nerve impulse.
2. **Clinical Connection:** Local anesthetics and certain neurotoxins prevent opening of voltage-gated Na⁺ channels so nerve impulses cannot pass the obstructed region
3. The step-by-step depolarization of each adjacent area of the plasma membrane is called continuous conduction (Figure 12.21a). Nerve impulse conduction in which the impulse jumps from neurofibril node to node is called saltatory conduction (Figure 12.21).
4. The propagation speed of a nerve impulse is not related to stimulus strength.
 - a. Larger-diameter fibers conduct impulses faster than those with smaller diameters.
 - 1) A fibers are the largest-diameter axons (5–20 μm) and are myelinated.

- i. conduct nerve impulses (action potentials) at speeds of 12 to 130 m/sec (27–290 mi/hr)
- 2) B fibers are axons with diameters of 2–3 m.
- 3) C fibers are the smallest-diameter axons (0.5–1.5 m) and all are unmyelinated
- b. Myelinated fibers conduct impulses faster than unmyelinated fibers.
 - c. Nerve fibers conduct impulses faster when warmed and slower when cooled.
 - d. Neurons are classified by diameter and myelination, and therefore conduction speed.
5. Encoding of stimulus intensity-The intensity of a stimulus is coded in the rate of impulse production, i.e., the frequency of action potentials.

C. Comparison of electrical signals produced by excitable cells.

1. Nerve and muscle action potentials differ in size of the resting membrane potential, duration of the impulses, and velocity of conduction of the impulse.
2. Graded and action potentials differ in amplitude, duration, types of channels used, location, polarity, propagation, and refractory period.
3. The various differences between graded potentials and action potentials are summarized in Table 12.2.

VIII. SIGNAL TRANSMISSION AT SYNAPSES

- A. A synapse is the functional junction between one neuron and another or between a neuron and an effector such as a muscle or gland.

B. Electrical Synapses

1. At an electrical synapse, ionic current spreads directly from one cell to another through gap junctions.
2. Electrical synapses allow faster communication and can synchronize the activity of a group of neurons or muscle fibers.

C. Chemical Synapses

1. At a chemical synapse, there is only one-way information transfer from a presynaptic neuron to a postsynaptic neuron (Figure 12.23).

D. Excitatory and Inhibitory Postsynaptic Potentials

1. The postsynaptic neuron is an integrator, receiving and integrating signals, then responding.

- a. If the excitatory effect is greater than the inhibitory effect but less than the threshold level of stimulation, the result is a subthreshold EPSP, making it easier to generate a nerve impulse.
- b. If the excitatory effect is greater than the inhibitory effect and reaches or surpasses the threshold level of stimulation, the result is a threshold or suprathreshold EPSP and a nerve impulse.
- c. If the inhibitory effect is greater than the excitatory effect, the membrane hyperpolarizes (IPSP) with failure to produce a nerve impulse.

E. Structure of Neurotransmitter Receptors

- 1. Neurotransmitters at chemical synapses cause either an excitatory or inhibitory graded potential.
- 2. Neurotransmitter receptors have two structures (Figure 12.24)
 - a. Ionotropic receptors are ion channels that directly bind to the neurotransmitter.
 - b. Metabotropic receptors are proteins (G proteins) that bind to the neurotransmitter but are not the ion channel. Instead, the binding protein initiates ion flow through another protein.
 - c. An excitatory neurotransmitter is one that can depolarize or make less negative the postsynaptic neuron's membrane, bringing the membrane potential closer to threshold (Figure 12.24a).
 - d. An inhibitory neurotransmitter hyperpolarizes the membrane of the postsynaptic neuron, making the inside more negative and generation of a nerve impulse more difficult. A hyperpolarizing PSP is inhibitory and is termed an inhibitory postsynaptic potential (IPSP) (Figure 12.24b).

F. Removal of Neurotransmitter

- 1. Neurotransmitter is removed from the synaptic cleft in three ways: diffusion, enzymatic degradation, and uptake into cells (neurons and glia).

G. Spatial and Temporal Summation

- 1. If several presynaptic end bulbs release their neurotransmitter at about the same time, the combined effect may generate a nerve impulse due to summation; summation may be spatial or temporal (Figure 12.25a,b and Figure 12.26).
- 2. **Clinical Connection:** Strychnine poisoning demonstrates the importance of inhibitory neurons.

IX. NEUROTRANSMITTERS

- A. Both excitatory and inhibitory neurotransmitters are present in the CNS and PNS; the same neurotransmitter may be excitatory in some locations and inhibitory in others.
 - 1. Many neurotransmitters are also hormones released by endocrine glands.
 - 2. Some brain neurotransmitters are released by neurosecretory cells.
- B. Important small-molecule neurotransmitters include acetylcholine, amino glutamate, aspartate, gamma aminobutyric acid, glycine, norepinephrine, epinephrine, and dopamine (Figure 12.27)
 - 1. Acetylcholine
 - 2. Amino Acids
 - a. Glutamate
 - b. Aspartate
 - c. GABA aminobutyric acid
 - d. Glycine
 - 3. Biogenic amines
 - a. Norepinephrine
 - b. Dopamine
 - c. Serotonin
 - 4. ATP and other Purines
 - 5. Nitric Oxide
 - 6. Carbon Monoxide
 - 7. Neuropeptides
 - a. Enkephalines
 - b. Endorphins
 - c. Dynorphins
 - d. Substance P
 - 8. Neuropeptides are also widely distributed and have many different roles in the body (Table 12. 4)
 - 9. Neurotransmitters can be modified by stimulating or inhibiting neurotransmitter synthesis, blocking or enhancing neurotransmitter release, stimulating or inhibiting neurotransmitter removal, and/or blocking or activating the receptor site.
 - 10. **Clinical Connection:** modifying the effects of neurotransmitters

X. NEURONAL CIRCUITS

- A. Neurons in the CNS are organized into definite patterns called neuronal pools; each pool differs from all others and has its own role in regulating homeostasis. A neuronal pool may contain thousands or even millions of neurons.
- B. Neuronal pools are organized into circuits. These include simple series, diverging, converging, reverberating, and parallel after-discharge circuits (Figure 12.28).

XI. REGENERATION AND REPAIR OF NERVOUS TISSUE

- A. Throughout life, the nervous system exhibits plasticity, the capability for change with learning.
- B. Despite plasticity, neurons have a limited capacity to repair or replicate themselves.
- C. In the PNS, damage to dendrites and myelinated axons may be repaired if the cell body remains intact and if Schwann cells are active
- D. In the CNS, there is little or no repair of damage to neurons.
- E. Current research is going on to find ways to promote neurogenesis and to find ways to encourage and promote regrowth in the CNS.
 - 1. Epidermal growth factor
- F. Damage and Repair in the Peripheral Nervous System (figure 12.29)
 - 1. When there is damage to an axon, usually there are changes, called chromatolysis, which occur in the cell body of the affected cell; this causes swelling of the cell body and peaks between 10 and 20 days after injury. (Figure 12.29)
 - 2. By the third to fifth day, degeneration of the distal portion of the neuronal process and myelin sheath (Wallerian degeneration) occurs; afterward, macrophages phagocytize the remains. Retrograde degeneration of the proximal portion of the fiber extends only to the first neurofibril node.
 - 3. Regeneration follows chromatolysis; synthesis of RNA and protein accelerates, favoring rebuilding of the axon and often taking several months.

XII. DISORDERS: HOMEOSTATIC IMBALANCES

- A. Multiple Sclerosis (MS)
 - 1. Multiple sclerosis is an autoimmune disease that results in the progressive destruction of myelin sheaths in neurons in the CNS.
 - 2. Myelin sheaths deteriorate to scleroses, which are hardened scars or plaques, in multiple regions.
 - 3. This is a progressive debilitating disease.
- B. Epilepsy

1. The second most common neurological disorder after stroke is epilepsy, which affects 1% of the population. It is characterized by short, recurrent, periodic attacks of motor, sensory, or psychological malfunction called epileptic seizures.
2. These seizures are initiated by abnormal synchronous electrical discharges from millions of neurons in the brain, perhaps resulting from abnormal reverberating circuits.
3. Epilepsy has many causes, including brain damage at birth, the most common cause; metabolic disturbances, infections, toxins, vascular disturbances, head injuries, and tumors and abscesses of the brain. Most epileptic seizures, however, are idiopathic (i.e., they have no demonstrable cause).
4. Epileptic seizures can be eliminated or alleviated by drugs that depress neuronal excitability.

C. Excitotoxicity

1. High levels of glutamate causes destruction of neurons caused by oxygen deprivation

D. Depression

1. People who are depressed feel sad and helpless
 - a. Major depression – symptoms last more than two weeks
 - b. Dysthymia – alternate between depression and periods of normal
 - c. Bipolar disorder – manic depressive illness with extreme elation (mania)
 - d. Seasonal affective disorder (SAD) – depression during winter months