Chapter 12

Nervous Tissue

INTRODUCTION

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

Nervous System

- Three basic functions:
  - sensing changes with sensory receptors
    - fullness of stomach or sun on your face
  - interpreting and remembering those changes
  - reacting to those changes with effectors
    - muscular contractions
    - glandular secretions

Major Structures of the Nervous System
Structures of the Nervous System - Overview

- Twelve pairs of cranial nerves emerge from the base of the brain through foramina of the skull.
  - A nerve is a bundle of hundreds or thousands of axons, each serving a specific region of the body.
- The spinal cord connects to the brain through the foramen magnum of the skull and is encircled by the bones of the vertebral column.
  - Thirty-one pairs of spinal nerves emerge from the spinal cord.
- Ganglia, located outside the brain and spinal cord, are small masses of nervous tissue, containing primarily cell bodies of neurons.
- Sensory receptors are either parts of neurons or specialized cells that monitor changes in the internal or external environment.

Functions of the Nervous Systems

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

Nervous System Divisions

- Central nervous system (CNS)
  - consists of the brain and spinal cord
- Peripheral nervous system (PNS)
  - consists of cranial and spinal nerves that contain both sensory and motor fibers
  - connects CNS to muscles, glands & all sensory receptors

Subdivisions of the PNS

- Somatic (voluntary) nervous system (SNS)
  - neurons from cutaneous and special sensory receptors to the CNS
  - motor neurons to skeletal muscle tissue
- Autonomic (involuntary) nervous systems (ANS)
  - sensory neurons from visceral organs to CNS
  - motor neurons to smooth & cardiac muscle and glands
  - sympathetic division (speeds up heart rate)
  - parasympathetic division (slow down heart rate)
- Enteric nervous system (ENS)
  - involuntary sensory & motor neurons control GI tract
  - neurons function independently of ANS & CNS
**Organization of the Nervous System**

- CNS is brain and spinal cord
- PNS is everything else

**Enteric NS**

- The *enteric nervous system* (ENS) consists of neurons that extend the length of the GI tract.
  - Many neurons of the enteric plexuses function independently of the CNS.
  - Sensory neurons of the ENS monitor chemical changes within the GI tract and stretching of its walls
  - Motor neurons of the ENS govern contraction of GI tract organs, and activity of the GI tract endocrine cells.

**Neuronal Structure & Function**

**Neurons**

- Functional unit of nervous system
- Have capacity to produce action potentials
  - electrical excitability
- Cell body
  - single nucleus with prominent nucleolus
  - Nissl bodies (chromatophilic substance)
    - rough ER & free ribosomes for protein synthesis
    - neurofilaments give cell shape and support
- Cell processes = dendrites & axons
Parts of a Neuron

- **Nucleus with Nucleolus**
- **Neuroglial cells**
- **Axons or Dendrites**
- **Cell body**

**Dendrites**
- Conducts impulses towards the cell body
- Typically short, highly branched & unmyelinated
- Surfaces specialized for contact with other neurons

**Axons**
- Conduct impulses away from cell body
- To another neuron or to an effector (muscle or gland)
- Long, thin cylindrical process of cell
- Arises at axon hillock
- Impulses arise from initial segment (trigger zone)
- Swollen tips called synaptic end bulbs contain vesicles filled with neurotransmitters

**Axonal Transport**
- Cell body is location for most protein synthesis
  - neurotransmitters & repair proteins
- Axonal transport system moves substances
  - slow axonal flow
    - movement in one direction only -- away from cell body
    - movement at 1-5 mm per day
  - fast axonal flow
    - moves organelles & materials along surface of microtubules
    - at 200-400 mm per day
    - transports in either direction
- Fast axonal transport route by which toxins or pathogens reach neuron cell bodies
  - tetanus (Clostridium tetani bacteria)
  - disrupts motor neurons causing painful muscle spasms
**Structural Classification of Neurons**

- Based on number of processes found on cell body
  - multipolar = several dendrites & one axon
    - most common cell type
  - bipolar neurons = one main dendrite & one axon
    - found in retina, inner ear & olfactory
  - unipolar neurons = one process only
    - are always sensory neurons

**Functional Classification of Neurons**

- Sensory (afferent) neurons
  - transport sensory information from skin, muscles, joints, sense organs & viscera to CNS
- Motor (efferent) neurons
  - send motor nerve impulses to muscles & glands
- Interneurons (association) neurons
  - connect sensory to motor neurons
  - 90% of neurons in the body

**Neuroglial Cells**

- Half of the volume of the CNS
- Smaller cells than neurons
- 50X more numerous
- Cells can divide
  - rapid mitosis in tumor formation (gliomas)
- 4 cell types in CNS:
  - astrocytes, oligodendrocytes, microglia & ependymal
- 2 cell types in PNS:
  - schwann and satellite cells

**Astrocytes**

- Star-shaped cells
- Form blood-brain barrier by covering blood capillaries
- Metabolize neurotransmitters
- Regulate K+ balance
- Provide structural support
Microglia

- Small cells found near blood vessels
- Phagocytic role -- clear away dead cells
- Derived from cells that also gave rise to macrophages & monocytes

Ependymal cells

- Form epithelial membrane lining cerebral cavities & central canal
- Produce cerebrospinal fluid (CSF)

Satellite Cells

- Flat cells surrounding neuronal cell bodies in peripheral ganglia
- Support neurons in the PNS ganglia

Oligodendrocytes

- Most common glial cell type
- Each forms myelin sheath around multiple axons in CNS
- Analogous to Schwann cells of PNS
Myelination

- A multilayered lipid and protein covering called the *myelin sheath* and produced by Schwann cells and oligodendrocytes surrounds the axons of most neurons
- The sheath electrically insulates the axon and increases the speed of nerve impulse conduction.

Axon Coverings in PNS

- Neurolemma is cytoplasm & nucleus of Schwann cell
  - gaps called nodes of Ranvier
- Tube guides growing axons that are repairing themselves
- Myelinated fibers appear white
  - jelly-roll like wrappings made of lipoprotein = myelin
  - acts as electrical insulator
  - speeds conduction of nerve impulses
- Unmyelinated fibers
  - slow, small diameter fibers
  - only surrounded by neurilemma but no myelin sheath wrapping

Schwann Cell

- Cells encircling PNS axons
- Each cell produces part of the myelin sheath surrounding an axon in the PNS

Myelination in the CNS

- Oligodendrocytes myelinate axons in the CNS
- Broad, flat cell processes wrap about CNS axons, but the cell bodies do not surround the axons
- No neurilemma is formed
- Little regrowth after injury is possible due to the lack of a distinct tube or neurilemma
**Gray and White Matter**

- White matter = myelinated axons (white in color)
- Gray matter = nerve cell bodies, dendrites, axon terminals, bundles of unmyelinated axons and neuroglia (gray color)
  - 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 surface & is found in clusters called nuclei inside the CNS
- A nucleus is a mass of nerve cell bodies and dendrites inside the CNS.

**Electrical Signals in Neurons**

- Neurons are electrically excitable due to the voltage difference across their membrane
- Communicate with 2 types of electric signals
  - action potentials that can travel long distances
  - graded potentials that are local membrane changes only

**Ion Channels**

- In living cells, a flow of ions occurs through ion channels in the cell membrane
- Gated channels open and close in response to a stimulus
  - results in neuron excitability

**Ion Channels**

- **Gated ion channels**:
  - Voltage-gated channels respond to a direct change in the membrane potential
  - Ligand-gated channels respond to a specific chemical stimulus
  - Mechanically gated ion channels respond to mechanical vibration or pressure
Gated Ion Channels

- Negative ions along inside of cell membrane &
  positive ions along outside
  - potential energy difference at rest is -70 mV
  - cell is “polarized”

- Resting potential exists because
  - concentration of ions different inside & outside
    - extracellular fluid rich in Na+ and Cl
    - cytosol full of K+, organic phosphate & amino acids

Graded Potentials

- Small deviations from resting potential of -70mV
  - hyperpolarization = membrane has become more negative
  - depolarization = membrane has become more positive

- The signals are graded, meaning they vary in amplitude (size), depending on the strength of the stimulus and are localized.

- Graded potentials occur most often in the dendrites and cell body of a neuron.

How do Graded Potentials Arise?

- Source of stimuli
  - mechanical stimulation of membranes with mechanical gated ion channels (pressure)
  - chemical stimulation of membranes with ligand gated ion channels (neurotransmitter)

- Graded/postsynaptic/receptor or generator potential
  - ions flow through ion channels and change membrane potential locally
  - amount of change varies with strength of stimuli

- Flow of current (ions) is local change only
Generation of an Action Potential

- 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).
  - During an action potential, voltage-gated Na$^+$ and K$^+$ channels open in sequence.
- According to the all-or-none principle, if a stimulus reaches threshold, the action potential is always the same.
  - A stronger stimulus will not cause a larger impulse.

Depolarizing Phase of Action Potential

- Chemical or mechanical stimulus caused a graded potential to reach at least (-55mV or threshold)
- Voltage-gated Na$^+$ channels open & Na$^+$ rushes into cell
  - in resting membrane, inactivation gate of sodium channel is open & activation gate is closed (Na$^+$ can not get in)
  - when threshold (-55mV) is reached, both open & Na$^+$ enters
  - inactivation gate closes again in few ten-thousandths of second
  - only a total of 20,000 Na$^+$ actually enter the cell, but they change the membrane potential considerably (up to +30mV)
- Positive feedback process

Repolarizing Phase of Action Potential

- When threshold potential of -55mV is reached, voltage-gated K$^+$ channels open
- K$^+$ channel opening is much slower than Na$^+$ channel opening which caused depolarization
- When K$^+$ channels finally do open, the Na$^+$ channels have already closed (Na$^+$ inflow stops)
- K$^+$ outflow returns membrane potential to -70mV
- If enough K$^+$ leaves the cell, it will reach a -90mV membrane potential and enter the after-hyperpolarizing phase
- K$^+$ channels close and the membrane potential returns to the resting potential of -70mV
Refractory Period of Action Potential

- Period of time during which neuron can not generate another action potential
- Absolute refractory period
  - even very strong stimulus will not begin another AP
  - inactivated Na+ channels must return to the resting state before they can be reopened
  - large fibers have absolute refractory period of 0.4 msec and up to 1000 impulses per second are possible
- Relative refractory period
  - a suprathreshold stimulus will be able to start an AP
  - K+ channels are still open, but Na+ channels have closed

Local Anesthetics

- Local anesthetics and certain neurotoxins
  - Prevent opening of voltage-gated Na+ channels
  - Nerve impulses cannot pass the anesthetized region

Examples:
  - Novocaine and lidocaine

Propagation of Action Potential

- An action potential spreads (propagates) over the surface of the axon membrane
  - as Na+ flows into the cell during depolarization, the voltage of adjacent areas is affected and their voltage-gated Na+ channels open
  - self-propagating along the membrane
- The traveling action potential is called a nerve impulse

The Action Potential: Summarized

- Resting membrane potential is -70mV
- Depolarization is the change from -70mV to +30 mV
- Repolarization is the reversal from +30 mV back to -70 mV
Continuous vs. Saltatory Conduction

- Continuous conduction (unmyelinated fibers)
  - step-by-step depolarization of each portion of the length of the axolemma
- Saltatory conduction (myelinated fibers)
  - depolarization only at nodes of Ranvier where there is a high density of voltage-gated ion channels
  - current carried by ions flows through extracellular fluid from node to node

Speed of Impulse Propagation

- The propagation speed of a nerve impulse is not related to stimulus strength.
  - larger, myelinated fibers conduct impulses faster due to size & saltatory conduction
- Fiber types
  - A fibers largest (5-20 microns & 130 m/sec)
    - myelinated somatic sensory & motor to skeletal muscle
  - B fibers medium (2-3 microns & 15 m/sec)
    - myelinated visceral sensory & autonomic preganglionic
  - C fibers smallest (.5-1.5 microns & 2 m/sec)
    - unmyelinated sensory & autonomic motor

Encoding of Stimulus Intensity

- How do we differentiate a light touch from a firmer touch?
  - frequency of impulses
    - firm pressure generates impulses at a higher frequency
  - number of sensory neurons activated
    - firm pressure stimulates more neurons than does a light touch
**SIGNAL TRANSMISSION AT SYNAPSES**

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

**Signal Transmission at Synapses**

- 2 Types of synapses
  - **electrical**
    - ionic current spreads to next cell through gap junctions
    - faster, two-way transmission & capable of synchronizing groups of neurons
  - **chemical**
    - one-way information transfer from a presynaptic neuron to a postsynaptic neuron
      - axodendritic -- from axon to dendrite
      - axosomatic -- from axon to cell body
      - axoaxonic -- from axon to axon

**Chemical Synapses**

- Action potential reaches end bulb and voltage-gated Ca\(^{2+}\) channels open
- Ca\(^{2+}\) flows inward triggering release of neurotransmitter
- Neurotransmitter crosses synaptic cleft & binding to ligand-gated receptors
  - the more neurotransmitter released the greater the change in potential of the postsynaptic cell
- Synaptic delay is 0.5 msec
- One-way information transfer
Excitatory & Inhibitory Potentials

- The effect of a neurotransmitter can be either excitatory or inhibitory
  - A depolarizing postsynaptic potential is called an EPSP
    - It results from the opening of ligand-gated Na+ channels
    - The postsynaptic cell is more likely to reach threshold
  - An inhibitory postsynaptic potential is called an IPSP
    - It results from the opening of ligand-gated Cl- or K+ channels
    - It causes the postsynaptic cell to become more negative or hyperpolarized
    - The postsynaptic cell is less likely to reach threshold

Removal of Neurotransmitter

- Diffusion
  - Away from synaptic cleft
- Enzymatic degradation
  - Acetylcholinesterase
- Uptake by neurons or glia cells
  - Neurotransmitter transporters
  - Prozac = serotonin reuptake inhibitor

Comparison of Graded & Action Potentials

- Origin
  - GPs arise on dendrites and cell bodies
  - APs arise only at trigger zone on axon hillock
- Types of Channels
  - GP is produced by ligand or mechanically-gated channels
  - AP is produced by voltage-gated ion channels
- Conduction
  - GPs are localized (not propagated)
  - APs conduct over the surface of the axon

Comparison of Graded & Action Potentials

- Amplitude
  - GPs vary depending upon stimulus
  - Amplitude of the AP is constant (all-or-none)
- Duration
  - The duration of the GP is as long as the stimulus lasts
- Refractory period
  - The AP has a refractory period and the GP has none
Summation

- 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*

Spatial Summation

- Summation of effects of neurotransmitters released from several end bulbs onto one neuron

Temporal Summation

- Summation of effect of neurotransmitters released from 2 or more firings of the same end bulb in rapid succession onto a second neuron

Neurotransmitters

- 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.
- Important neurotransmitters include acetylcholine, glutamate, aspartate, gamma aminobutyric acid, glycine, norepinephrine, epinephrine, serotonin and dopamine.
Neurotransmitter Effects

• Neurotransmitter effects can be modified
  – synthesis can be stimulated or inhibited
  – release can be blocked or enhanced
  – removal can be stimulated or blocked
  – receptor site can be blocked or activated

• Agonist
  – anything that enhances a transmitter's effects

• Antagonist
  – anything that blocks the action of a neurotransmitter

Small-Molecule Neurotransmitters

• Acetylcholine (ACh)
  – released by many PNS neurons & some CNS
  – excitatory on NMJ but inhibitory at others
  – inactivated by acetylcholinesterase

• Amino Acids
  – glutamate released by nearly all excitatory neurons in the brain
  – GABA is inhibitory neurotransmitter for 1/3 of all brain synapses (Valium is a GABA agonist -- enhancing its inhibitory effect)

• Biogenic Amines
  – modified amino acids (tyrosine)
    • norepinephrine -- regulates mood, dreaming, awakening from deep sleep
    • dopamine -- regulating skeletal muscle tone
    • serotonin -- control of mood, temperature regulation & induction of sleep

• ATP and other purines (ADP, AMP & adenosine)
  – excitatory in both CNS & PNS

• Gases (nitric oxide or NO)
  – formed from amino acid arginine by an enzyme
  – formed on demand and acts immediately
    • diffuses out of cell that produced it to affect neighboring cells
    • may play a role in memory & learning
  – first recognized as vasodilator that helps lower blood pressure
Neuropeptides

- 3-40 amino acids linked by peptide bonds
- Substance P - enhances our perception of pain
- Pain relief
  - enkephalins - pain-relieving effect by blocking the release of substance P
  - acupuncture may produce loss of pain sensation because of release of opioid-like substances such as endorphins or dynorphins

Strychnine Poisoning

- In spinal cord, an inhibitory neurotransmitter (glycine) is normally released onto motor neurons preventing excessive muscle contraction
- Strychnine binds to and blocks glycine receptors in the spinal cord
- Massive tetanic contractions of all skeletal muscles are produced
  - when the diaphragm contracts & remains contracted, breathing can not occur

Regeneration & Repair

- Plasticity maintained throughout life
  - sprouting of new dendrites
  - synthesis of new proteins
  - changes in synaptic contacts with other neurons
- Limited ability for regeneration (repair)
  - PNS can repair damaged axons
  - CNS no repairs are possible

Repair within the PNS

- Axons may be repaired if:
  - neuron cell body remains intact
  - Schwann cells remain active and form a tube
  - scar tissue does not form too rapidly
- Within several months, regeneration occurs
  - Schwann cells on each side of injury repair tube
  - axonal buds grow down the tube to reconnect (1.5 mm per day)
Neurogenesis in the CNS

• Formation of new neurons from stem cells was not thought to occur in humans
  – 1992 -- a growth factor was found that stimulates adult mice brain cells to multiply
  – 1998 -- new neurons found to form within adult human hippocampus (area important for learning)
• There is a lack of neurogenesis in other regions of the brain and spinal cord

Multiple Sclerosis (MS)

• Autoimmune disorder causing destruction of myelin sheaths in CNS
  – sheaths becomes scars or plaques
  – 1/2 million people in the United States
  – appears between ages 20 and 40
  – females twice as often as males
• Symptoms include muscular weakness, abnormal sensations or double vision
• Remissions & relapses result in progressive, cumulative loss of function

Epilepsy

• The second most common neurological disorder
  – affects 1% of population
• Characterized by short, recurrent attacks initiated by electrical discharges in the brain
  – lights, noise, or smells may be sensed
  – skeletal muscles may contract involuntarily
  – loss of consciousness
• Epilepsy has many causes, including;
  – brain damage at birth, metabolic disturbances, infections, toxins, vascular disturbances, head injuries, and tumors