Chapter 10
Lecture Outline

10.1: Overview of the Nervous System

Nervous system:
- Detects changes, makes decisions, stimulates muscles and glands to respond, and maintains homeostasis

Neural tissue contains 2 cell types:

**Neurons:**
- React to changes
- Send nerve impulses for communication

**Neuroglia:**
- Surround and support neurons
- Nourish neurons
- Send & receive messages
- Help maintain blood-brain barrier

Divisions of the Nervous System

**Central Nervous System (CNS):**
- Brain
- Spinal cord

**Peripheral Nervous System (PNS):**
Connects CNS to other body parts
- Cranial nerves
- Spinal nerves

Clinical Application 10.1

Migraine
- Signs: pounding head, nausea, aura (shimmering images in visual field), light or sound sensitivity
- Environmental triggers: bright light, certain foods, lack of sleep, stress, high altitude, stormy weather, excess caffeine or alcohol
- Hormonal triggers in women; migraine occurs just prior to menstruation
- Lasts 4 – 72 hours
- Period of excitation followed by unresponsiveness in particular neurons stimulates production of pain sensations in areas at base of brain
- Treated with drugs that block neurotransmitter release from certain neurons
- Newer treatment: Transcranial Magnetic Stimulation
- Certain antidepressants, anticonvulsants, blood pressure medications are helpful in treating migraines

10.2: General Functions of the Nervous System

**Sensory Function:**
- Nervous system receives information
- Sensory receptors gather information by detecting changes
- Information is carried to the CNS

**Integrative Function:**
- Nervous system coordinates sensory information to create sensations, memory, thoughts
- Nervous system makes decisions on body’s response to sensory information

**Motor Function:**
- Decisions are acted upon
- Impulses are carried to effectors (muscles or glands)
- Divisions of motor portion of PNS:
  - **Somatic Nervous System:** transmits voluntary instructions to skeletal muscles
  - **Autonomic Nervous System:** transmits involuntary instructions from the CNS to smooth muscles, cardiac muscle, and glands
10.3: Description of Cells of the Nervous System

- Neurons vary in size and shape.
- They may differ in length and size of their axons and dendrites.
- Neurons share certain features:
  - **Cell body (soma):** contains nucleus, cytoplasm, organelles, neurofilaments, chromatophilic substance (Nissl bodies).
  - **Dendrites:** branched receptive surfaces; a neuron may have many.
  - **Axon:** transmits impulses and releases neurotransmitters to another neuron or effector (another neuron, a muscle cell or a gland cell); a neuron may have only 1 axon.

**Neuron Structure**

- **Cell body:**
  - Neurofilaments
  - Chromatophilic substance
- **Dendrites:**
  - Axon hillock
  - Collaterals
  - Axon terminal
  - Synaptic knob
- **Schwann cells:**
  - Myelin
  - Myelin sheath

10.4: Classification of Cells of the Nervous System

**Classification of neurons by structure:**

- **Multipolar neurons:**
  - 99% of neurons
  - Many processes
  - Most neurons of CNS
- **Bipolar neurons:**
  - Two processes
  - Eyes, ears, nose
- **Unipolar neurons:**
  - One process
  - Cell bodies are in ganglia
  - Sensory

**Myelination of Axons**

- Schwann Cells:
  - PNS neuroglia that encase axons in a sheath.
  - Schwann cells wrap tightly around axon in layers composed of myelin, a lipoprotein mixture.
  - Coating is called the Myelin Sheath.
  - Nodes of Ranvier: Gaps in myelin sheath between Schwann cells.

- Myelination of Axons:
  - Not all axons are myelinated.
  - Myelinated axons in the PNS have a series of Schwann cells lined up along the axon, each having a wrapped coating of myelin insulating the axon.
  - Unmyelinated axons are encased by Schwann cell cytoplasm, but there is no wrapped coating of myelin surrounding the axons.

**Clinical Application 10.2**

**Multiple Sclerosis**

- Destruction of myelin sheaths in CNS by an immune response.
- Myelin is attacked by a person’s own antibodies.
- Scars (sclerosis) are left behind, which stop neurons from conducting impulses.
- Without input from motor neurons, muscles stop contracting and atrophy.
- Other symptoms: fatigue, mood problems, blurred vision, and weak, numb limbs.
- Treatments involve drugs that suppress immune activity.

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**Classification of Neurons**

**Sensory Neurons:**
- Afferent neurons
- Carry impulse to CNS
- Most are unipolar
- Some are bipolar

**Interneurons:**
- Association neurons
- Link neurons
- Multipolar
- Located in CNS

**Motor Neurons:**
- Multipolar, efferent
- Carry impulses away from CNS
- Carry impulses to effectors

**Classification of Neuroglia**

**General Functions of Neuroglia:**
- Provide structural support for neurons
- In embryo, guide neurons into position, may stimulate specialization
- Produce growth factors to nourish neurons and remove excess ions and neurotransmitters
- Aid in formation of synapses

**Neuroglia of the CNS**

**Astrocytes:**
- Connect neurons to blood vessels; exchange nutrients and growth factors
- Form scar tissue
- Aid metabolism of certain substances
- Regulate ion concentrations, such as K⁺
- Part of Blood Brain Barrier

**Oligodendrocytes:**
- Myelinate CNS axons; also provide structural support

**Microglia:**
- Phagocytic cell; also provides structural support

**Ependyma or ependymal cells:**
- Line central canal of spinal cord & ventricles of brain, cover choroid plexuses
- Help regulate composition of cerebrospinal fluid
- Cuboidal or columnar cells; ciliated

**Neuroglia of the PNS**

**Schwann Cells:**
- Produce myelin sheath found on some peripheral axons
- Speed up speed of nerve impulse transmission

**Satellite Cells:**
- Support clusters of neuron cell bodies (ganglia)

**Neuroglia and Axonal Regeneration**

- Mature neurons do not divide
- If cell body is injured, the neuron usually dies

**Neuron Regeneration in the PNS:**
- If a peripheral axon is injured, it may regenerate
- Axon separated from cell body and its myelin sheath will degenerate
- Schwann cells and neurilemma remain
- Remaining Schwann cells provide guiding sheath for growing axon
- If growing axon establishes former connection, function will return; if not, function may be lost

**Neuron Regeneration in the CNS:**
- CNS axons lack neurilemma to act as guiding sheath
- Oligodendrocytes do not proliferate after injury
- Regeneration is unlikely
Neuron Regeneration in the PNS

10.5: The Synapse

- Neurons communicate with each other at **Synapse**.
  - A synapse is a site at which a neuron transmits a nerve impulse to another neuron.
  - **Presynaptic neuron** sends impulse.
  - **Postsynaptic neuron** receives impulse.
  - Synaptic cleft separates the 2 neurons.

Synaptic Transmission:

- One-way transfer of information.
- Impulse travels down axon of presynaptic neuron to axon terminal.
- When impulse reaches synaptic knob, causes influx of Ca^{2+} ions.
- This leads to release of neurotransmitters from synaptic vesicles by exocytosis.
- Neurotransmitter will exert either excitatory or inhibitory effect on postsynaptic neuron.

10.6: Cell Membrane Potential

- A cell membrane is usually electrically charged, or polarized, so that the inside of the membrane is negatively charged with respect to the outside of the membrane.
  - This is a result of unequal distribution of ions on the inside and the outside of the membrane.
  - Important in conduction of impulses in neurons and muscle fibers.

Distribution of Ions

- **Potassium (K^+) ions**: major intracellular positive ions (cations).
- **Sodium (Na^+) ions**: major extracellular positive ions (cations).
- This distribution is largely created by the Sodium/Potassium Pump (Na^+/K^+ pump) but also by ion channels in the cell membrane.
- **Na^+/K^+ Pump**: transports Na^+ ions out of cell and K^+ ions into cell.
- **Ion channels**, formed by membrane proteins, help regulate passage of specific ions into or out of the cell.
- Many chemical & electrical factors affect opening & closing of gated channels.

Resting Potential

**Resting Membrane Potential (RMP):**

- Resting neuron is one that is not being stimulated.
- Na^+ and K^+ ions follow rules of diffusion, and move from area of high concentration to area of low concentration.
- 70 mV potential difference from inside to outside of cell.
- Membrane of the neuron is a polarized membrane, with more K^+ ions inside the cell, more Na^+ ions outside the cell, and more negatively charged ions & proteins inside.
- Inside of cell is negative relative to the outside of the cell.
- RMP = -70 mV, due to unequal charge distribution.
- If resting potential changes, Na^+/K^+ pump restores it.
Resting Potential

- Neurons are excitable cells
- Detect stimuli, and respond by changing their resting potential
- Common response is the opening of a gated ion channel
  - If membrane potential becomes more negative, the membrane is hyperpolarized
  - If membrane potential becomes less negative (more positive), the membrane is depolarized
- Local potential changes are graded—the greater the stimulus intensity, the greater the potential change
- If degree of depolarization reaches threshold potential of -55 mV, an action potential results
- If degree of depolarization does not reach threshold potential, an action potential will not occur

Local Potential Changes

- At rest, the membrane is polarized (RMP = -70)
  - Threshold stimulus reached (-55 mV)
  - Sodium channels open and membrane depolarizes (toward 0)
  - Potassium leaves cytoplasm and membrane repolarizes (+30 mV)
  - Brief period of hyperpolarization (-90)
  - Return to RMP (-70 mV)

Ion Movements During Action Potentials

- Axon hillock / initial segment / trigger zone at first part of axon contains many voltage-gated sodium channels
- Voltage-gated Na⁺ channels remain closed at resting potential
- Voltage-gated Na⁺ channels open when threshold is reached
- As Na⁺ ions diffuse into the cell, the membrane depolarizes until it reaches +30 mV (beginning the action potential)
- Na⁺ channels close and K⁺ channels open
- K⁺ diffuses out, and membrane repolarizes
- As membrane potential then drops below -70 mV, the membrane is temporarily hyperpolarized
- K⁺ channels then close
- Active transport re-establishes the resting potential of -70 mV as Na⁺ and K⁺ concentrations are restored by the Na⁺/K⁺ pump
- Concentration gradients are maintained while the neuron is at rest
Action potentials are propagated down the length of the axon as nerve impulses:

Events Leading to Impulse Conduction

| 1. Nerve cell membrane maintains resting potential by diffusion of Na+ and K+ down their concentration gradients at the cell pumps them up the gradients. |
| 2. Neuron receives stimulus, causing local potentials, which may sum to reach threshold. |
| 3. Sodium channels in the trigger zone of the axon open. |
| 4. Sodium ions diffuse inward, depolarizing the membrane. |
| 5. Potassium channels in the membrane open. |
| 6. Potassium ions diffuse outward, repolarizing the membrane. |
| 7. The resulting action potential causes an electric current that stimulates adjacent portions of the membrane. |
| 8. Action potentials occur sequentially along the length of the axon. |

All-or-None Response

- An action potential is an all-or-none response
- If a neuron axon responds at all, it responds completely with an action potential (which propagates down the axon as a nerve impulse)
- A nerve impulse is conducted whenever a stimulus of threshold intensity or above is applied to an axon
- All impulses carried on an axon are the same strength
- Stimulus of greater intensity produces higher frequency of action potentials (impulses/sec), not stronger impulses

Refractory Period

During an impulse, the portion of the axon actively conducting the action potential is not able to respond to another threshold stimulus of normal strength. This is called the refractory period, and has 2 parts:

Absolute Refractory Period:
- Time when threshold stimulus cannot generate another action potential
- Voltage-gated Na+ channels are briefly unresponsive

Relative Refractory Period:
- Time when only high-intensity stimulus can generate another action potential
- Repolarization is not complete, and membrane is re-establishing resting potential

Refractory period limits number of action potentials generated per second

Impulse Conduction

- The speed of impulse conduction varies with myelination
- Myelin is rich in lipids, and prevents water and water-soluble substances (such as ions) from crossing membrane; acts as electrical insulator
- Ions can cross membrane only through gaps in myelin sheath, the Nodes of Ranvier
- Myelinated axons transmit impulses through saltatory conduction, in which action potentials “jump” from node to node down the axon
- Saltatory conduction is much faster than impulse conduction in unmyelinated axons
- Axon diameter also affects conduction speed; thick axons transmit faster than thin axons
- Thick, myelinated axons: 120 m/sec
- Thin, unmyelinated axons: 0.5 m/sec

Saltatory Conduction

The transmission of a nerve impulse down a myelinated axon in saltatory conduction:
Factors Affecting Impulse Conduction

Changes in permeability of axons to certain ions affects impulse conduction:

- **Increase in concentration of K⁺ in extracellular fluid**:
  - Reduces gradient for K⁺ to leave cell; threshold potential reached with stimulus of lower intensity; leads to excitable neurons, perhaps convulsions

- **Decrease in concentration of K⁺ in extracellular fluid**:
  - Neurons can become hyperpolarized; action potentials are not generated; lack of impulses leads to muscle paralysis

- **Decrease in permeability to Na⁺ ions**:
  - Can be caused by some anesthetic drugs; stops impulses from passing through tissue fluid around axon; impulses do not reach brain, and there is no perception of touch and pain

### Clinical Application 10.3

#### 10.7: Synaptic Transmission

**Synaptic transmission**:
Transmission of a nerve impulse from one neuron to another

- Released neurotransmitters cross the synaptic cleft and react with specific receptors in the membrane of postsynaptic neuron
- Effects of neurotransmitters vary; some open ion channels and others close ion channels.
- Chemically gated ion channels respond to neurotransmitters
- Local potentials resulting from changes in chemically gated ion channels are called **synaptic potentials**
  - **Excitatory neurotransmitters** increase permeability to Na⁺ ions, bringing membrane closer to threshold; increase likelihood of generating impulses
  - **Inhibitory neurotransmitters** move membrane farther from threshold, decrease likelihood of generating impulses

**Synaptic Potentials**

**Excitatory postsynaptic potential (EPSP)**:
- Membrane change in which neurotransmitter opens Na⁺ channels
- Depolarizes membrane of postsynaptic neuron, as Na⁺ enters axon
- Action potential in postsynaptic neuron becomes more likely

**Inhibitory postsynaptic potential (IPSP)**:
- Membrane change in which neurotransmitter opens K⁺ channels (or Cl⁻ channels)
- Hyperpolarizes membrane of postsynaptic neuron, as K⁺ leaves axon
- Action potential of postsynaptic neuron becomes less likely

**Summation of EPSPs and IPSPs**

- EPSPs and IPSPs are added together in a process called **summation**
- Net excitatory effect leads to greater probability of an action potential
- Net inhibitory effect does not generate action potentials
- Summation of all inputs usually occurs at the trigger zone (axon hillock)

**Neurotransmitters and Actions**

- There are at least 100 neurotransmitters
- Acetylcholine stimulates skeletal muscle contraction
- Neurotransmitters may be monoamines, amino acids, peptides
- Neurotransmitters are produced in the rough ER or cytoplasm
- When impulse reaches synaptic knob of an axon, neurotransmitters are released by exocytosis

**Disorders Associated with Neurotransmitter Imbalances**

- Acetylcholine stimulates skeletal muscle contraction
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- Neurotransmitters are produced in the rough ER or cytoplasm
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Drugs That Alter Neurotransmitter Levels

<table>
<thead>
<tr>
<th>Drug</th>
<th>Neurotransmitter Affected</th>
<th>Mechanism of Action</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine</td>
<td>Dopamine</td>
<td>Inhibits dopamine receptors</td>
<td>Depression</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>Norepinephrine</td>
<td>Stimulates release of norepinephrine</td>
<td>Increased heart rate</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Serotonin</td>
<td>Inhibits reuptake of serotonin</td>
<td>Hallucinations</td>
</tr>
<tr>
<td>LSD</td>
<td>Serotonin</td>
<td>Acts as a serotonin agonist</td>
<td>Hallucinations</td>
</tr>
<tr>
<td>Ketamine</td>
<td>GABA</td>
<td>Inhibits reuptake of GABA</td>
<td>Sedation</td>
</tr>
</tbody>
</table>

Vesicle trafficking:
- Process of membrane recycling
- Synaptic vesicle becomes part of cell membrane as it releases neurotransmitter
- Endocytosis returns membrane to cytoplasm; forms new vesicles

Events Leading to Neurotransmitter Release

- Neurons in the brain or spinal cord synthesize neuropeptides
- Some neuropeptides act as neurotransmitters
- Other neuropeptides act as neuromodulators: substances which alter a neuron’s response to a neurotransmitter or block the release of a neurotransmitter
- Examples:
  - Enkephalins: relieve pain sensations
  - Beta endorphin: relieves pain sensations; potent, long-lasting
  - Substance P: found in neurons that conduct pain impulses; enkaphalins & endorphins inhibit release of Substance P

10.8: Impulse Processing

The way the nervous system processes nerve impulses and acts upon them reflects the organization of neurons and axons in the brain and spinal cord.

Neuropeptides

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Clinical Application 10.4

Opiates in the Human Body

- Opiate drugs (morphine, heroin, codeine, opium) are potent painkillers; derived from poppy plant
- Human body produces opiates called endorphins
- Endogenous opiates relieve pain in acupuncture, analgesia during childbirth, feeling of well-being during exercise
- Opiate drugs are very useful in relief from severe pain
- Opiates are also very addictive
- Withdrawal symptoms (specifically pain) experienced by addict that stops taking the drug are due to the fact that taking repeated doses of opiate drug causes body to stop producing its own endorphins; when drug is stopped, person is short of endogenous endorphins, and feels pain

Neuronal Pools

- Groups of interneurons that make synaptic connections with each other, and are located completely within the CNS
- Interneurons work together to perform a common function
- Each pool receives input from other neurons
- Each pool generates output to other neurons
- Pools may affect other pools or peripheral effectors
- Facilitation:
  - Increased neurotransmitter release, resulting from repeated impulses on excitatory presynaptic neurons
  - Increases likelihood that postsynaptic cell will reach threshold
Convergence:
- One neuron receives input from several neurons
- Incoming impulses often represent information from different types of sensory receptors
- Allows nervous system to collect, process, and respond to information
- Makes it possible for a neuron to sum impulses from different sources

Divergence:
- One neuron sends impulses to several neurons, via branching of its axon
- Can amplify an impulse
- Impulse from a single neuron in CNS may activate several motor units in a skeletal muscle
- Impulse from a sensory receptor may reach different regions of the CNS for processing

Clinical Application 10.5

Drug Addiction
- Drugs alter activity of a neurotransmitter on a postsynaptic neuron; either stop or enhance synaptic transmission
- **Antagonist**: A drug that binds to receptor, and blocks neurotransmitter binding
- **Agonist**: A drug that activates receptor, causing action potential or aiding in binding of neurotransmitter
- Repeated use of addictive drug causes a decrease in its receptors, so person must take more of drug to have same effects
- Amphetamines enhance norepinephrine activity, elevating alertness and mood
- Nicotine binds to nicotinic acetylcholine receptors; channels for positive ions open, allowing influx; this leads to dopamine release, which leads to pleasurable feeling from smoking