Communication within the Nervous System

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Communication Within the Nervous System: The Exchange of Information

• Types of information exchange:
  – axodendritic—from the axon of one neuron to the dendrite of another
  – axosomatic—from axon to cell body
  – axoaxonic—from axon to axon
  – dendrodendritic—from dendrite to dendrite
The Resting Membrane Potential

- Factors involved in the resting membrane potential:
  - Channel proteins — provide channels for the passage of substances from one side of the membrane to the other
  - Receptor proteins — recognize and bind to neurotransmitters or other chemicals
  - Pump proteins — exchange one type of substance for another

- Polarity — The cell membrane is polarized and the resulting difference between the outside and inside of the membrane is -70mv. This difference in polarity is called the resting membrane potential.
  - There is a greater concentration of positive ions (charged particles) on the outside of membrane as compared to the inside.
Recording the Resting Membrane Potential of a Neuron

The Resting Membrane Potential

- Forces affecting the membrane potential
  - Diffusion
  - Electrostatic pressure
  - Sodium-potassium pump
Resting Membrane Potential: Diffusion

- Diffusion—refers to the movement of molecules from an area of higher concentration to an area of lower concentration (difference in concentration produces a concentration gradient which causes the diffusion)
  - There is a higher concentration of sodium ions (Na⁺) outside the cell membrane and a higher concentration of potassium ions (K⁺) and chloride (Cl⁻) inside the cell.
Resting Membrane Potential: Electrostatic Pressure

- **Electrostatic pressure**—attraction of opposite-polarity molecules and repulsion of same-polarity molecules
- The K⁺ and Cl⁻ counteract each other because of two passive forces (diffusion and electrostatic).
- However, Na⁺ has a higher concentration gradient outside and an electrostatic pressure (a more negative charge inside) to move the Na⁺ ions into the cell.

Influence of Diffusion and Electrostatic Pressure on the Movement of Ions into and out of the Neuron
Resting Membrane Potential: Sodium-Potassium Pump

- Sodium-potassium pump—an active mechanism which excludes 3 Na\(^+\) ions for every 2 K\(^+\) ions taken into the cell
- Requires energy supplied by adenosine triphosphate (ATP), which is converted to ADP.

Resting Membrane Potential: Forces Acting While at Rest

A. K\(^+\) ion concentration is higher inside the cell, so diffusion tends to push K\(^+\) out. But because the inside of the cell is more negative than the outside, electrostatic pressure tends to pull K\(^+\) in. So K\(^+\) ions leaves the cell and is returned by the sodium-potassium pump.

B. Cl\(^-\) ion concentration is higher outside the cell, so diffusion tends to pull Cl\(^-\) in. But because the inside of the cell is more negative than the outside, electrostatic pressure tends to push Cl\(^-\) out.

C. Negatively charged protein molecules cannot leave the cell, so they create a negative charge inside the cell.
The Action Potential

- The action potential is also called the spike potential or firing of the neuron.
- The action potential only refers to depolarization of axon, not to dendrites or cell bodies.
- Excitatory stimulus—A stimulus which causes depolarization in the axon when the inside becomes more positively charged due to the influx of Na⁺ ions.

The Action Potential

- Threshold—The level of stimulation required for the neuron to fire (about -55 mV).
- Voltage-gated ion channels—Channels sensitive to changes in cell membrane potential.
- These ion channels open to Na⁺ ions when threshold is reached, followed by the opening of K⁺ channels. The K⁺ ions are expelled by the electrostatic charge from the Na⁺ ions which have entered the cell.
Action Potential: Repolarization and the Refractory Period

- **Absolute refractory period**—The time during which the neuron is insensitive to further stimulation.
- **Relative refractory period**—The time following the absolute refractory period during which a neuron can generate another action potential but only by a stronger than normal stimulus.

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Action Potential: Repolarization and the Refractory Period

- **Hyperpolarized**—A cell is hyperpolarized when it’s negative potential becomes larger than normal (e.g., -80 mv instead of -70 mv).
- **Repolarization**—The process of recovery of the resting membrane potential.
Changes in Membrane Potential During the Action Potential

Action Potential: The Intensity of a Stimulus

- All-or-none law—the strength of the action potential is independent of the intensity of the stimulus that elicits it.
- Coding of intensity is by the firing rate (rate law) of a neuron and by the number of neurons firing.
Illustration of the Rate Law

The Neural Impulse

- **Neural impulse**—The propagation of an action potential along an axon.
- The axon depolarizes in a sequential fashion from the axon hillock to the presynaptic terminal.
- A graded depolarization is a depolarization which has not reached threshold.
- The neural impulse occurs only one way because of the absolute refractory period.
- Speed of transmission varies due to thickness of the axon, presence or absence of myelination, and number of synapses.
The Neural Impulse: Saltatory Conduction

- **Saltatory Conduction**—from the Latin saltare (“to jump”)
  - Occurs on myelinated neurons at the nodes of Ranvier.
  - Faster than unmyelinated neurons (a neuron of 1.5 mm conducts about 1 m/sec whereas a myelinated neuron of the same size conducts about 100 m/sec).
  - Requires less energy than unmyelinated neurons since depolarization only occurs at the nodes of Ranvier.
Propagation of the Action Potential Along a Myelinated Axon

Synaptic Transmission: Neurotransmitter Release

- Action potentials arriving at the presynaptic terminal cause calcium ion channels to open and Ca^{2+} ions to enter the cell.
- Calcium entry causes the synaptic vesicles to move to the release site on the presynaptic membrane where they release neurotransmitter molecules into the synaptic cleft.
- Synaptic transmission occurs when neurotransmitter molecules pass across the synaptic cleft and depolarize or hyperpolarize the postsynaptic membrane.
- Neurotransmitter molecules are carried across the synaptic cleft by diffusion.
Overview of Synaptic Transmission

Synaptic Transmission: Neurotransmitter Release

- **Transmitter-gated ion channels**—sensitive to a specific neurotransmitter
  - A neurotransmitter will have an excitatory (EPSP) or inhibitory effect (IPSP).
  - EPSP—results from depolarization produced by neurotransmitter molecules on a postsynaptic membrane
  - IPSP—results from hyperpolarization produced by neurotransmitter molecules on a postsynaptic membrane
Ionic Changes Caused by Neurotransmitters Interacting with the Postsynaptic Membrane

Synaptic Transmission: Summation Effects

- Summation effects—the result of multiple inputs (excitatory and inhibitory) on neurons
  - Spatial summation—the combined effects of neurotransmitters binding to different locations on the postsynaptic membrane at a particular moment in time
  - Temporal summation—the combined effects of neurotransmitters binding over time
Spatial Summation and Temporal Summation

(a) Spatial summation

- 1 Stimulus
- A only
- B only
- A + B

(b) Temporal summation

- A once
- A twice

Synaptic Transmission: Presynaptic Effects

- Release of neurotransmitters is not automatic and can be influenced by several processes:
  - Presynaptic inhibition
  - Presynaptic facilitation
  - Autoreceptors (inhibition)
Synaptic Transmission: Presynaptic Effects

- **Presynaptic inhibition**
  - A decrease in the release of neurotransmitters from the presynaptic membrane (despite the occurrence of an action potential) caused by the action of another neuron.

- **Presynaptic facilitation**
  - The enhanced release of neurotransmitters from the presynaptic membrane caused by the action of another neuron.

Axoaxonic Synapse and Presynaptic Inhibition and Facilitation
Synaptic Transmission: Presynaptic Effects

- Autoreceptors—stimulation of autoreceptors by a released neurotransmitter causes a decrease in subsequent neurotransmitter release.

Synaptic Transmission: Postsynaptic Receptors

- Types of postsynaptic receptors:
  - Ionotropic—These receptors’ ion channels are opened quickly by the direct action of a neurotransmitter.
  - Metabotropic—These receptors’ ion channels are opened indirectly by a second messenger.
  - Second messenger—A chemical that causes changes inside the cell in response to a neurotransmitter that leads to ion channel changes.
Ionotropic and Metabotropic Receptors

(a) Ionotropic receptor  
(b) Metabotropic receptor

Table 4.1
Differences Between Ionotropic and Metabotropic Receptors

<table>
<thead>
<tr>
<th>Ionotropic Receptors</th>
<th>Metabotropic Receptors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ion channels open directly</td>
<td>Ion channels open indirectly</td>
</tr>
<tr>
<td>Effect begins and ends rapidly</td>
<td>Effect begins and ends relatively slowly</td>
</tr>
<tr>
<td>Only first messenger (neurotransmitter) is involved</td>
<td>Both neurotransmitter and a second messenger (another chemical) are involved</td>
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Synaptic Transmission: Termination of Neurotransmitter Effects

- Termination of synaptic transmission
  - Diffusion—transmitter substance floats away from the synapse
  - Enzymatic degradation—The transmitter action is deactivated by an enzyme (e.g., acetylcholinesterase deactivates acetylcholine).
  - Reuptake—The transmitter substance is returned to the presynaptic neuron (e.g., norepinephrine).

- See Scientific American Spotlight “The ‘Magic’ of Lithium”

Agents of Synaptic Transmission: Small-Molecule Neurotransmitters

- Amino acids
  - glutamate
  - gamma-amino butyric acid (GABA)
  - aspartate
  - glycine

- Monoamines
  - catecholamines
    - epinephrine (adrenalin)
    - norepinephrine (noradrenalin)
    - dopamine
  - indoleamines
    - serotonin
    - melatonin
Agents of Synaptic Transmission: Small-Molecule Neurotransmitters

• Soluble gases
  – nitric oxide
  – carbon monoxide
• Acetylcholine

Agents of Synaptic Transmission: Large-Molecule Neurotransmitters

• endogenous opioids
• substance P
• oxytocin
• antidiuretic hormone (ADH)
• cholecystokinin (CCK)
Small-Molecule Neurotransmitters: Amino Acids

- Glutamate is the most common excitatory neurotransmitter in the CNS. Synapses that use glutamate are called glutamatergic. Termination of action is by reuptake.
- Gamma-aminobutric acid (GABA) is the most common inhibitory transmitter in the brain. It is produced from glutamate by the enzyme glutamate decarboxylase. Its synapses are called GABAergic and it is terminated by reuptake.
- Both these transmitters are implicated in Huntington’s disease. Extreme anxiety, linked to below normal GABA levels, may be treated with Valium. Both transmitters appear to be involved with memory storage and retrieval.
Small-Molecule Neurotransmitters: Monoamines

- The **monoamines** are classified into two subclasses: the **catecholamines** and **indoleamines**
  - **Catecholamines**—norepinephrine (NE) and dopamine (DA)
    - NE transmission is called **adrenergic**.
    - NE is terminated by reuptake and degradation of NE within the cytoplasm, not in synaptic vesicles, by **monoamine oxidase** (MAO).
    - NE is the transmitter in the sympathetic nervous system and is involved in regulating attention, concentration, arousal, sleep and depression.

A Noradrenergic Synapse
Small-Molecule Neurotransmitters: Monoamines

- **Catecholamines (cont.)**
  - Dopamine
    - A precursor to NE.
    - Found in the substantia nigra and basal ganglia
    - Involved in voluntary movements, schizophrenia, Parkinson's disease, and addictions including nicotine, alcohol and others

**A Dopaminergic Synapse**
Small-Molecule Neurotransmitters: Monoamines

• **Indoleamines**
  – Serotonin (5-HT)
    • Synthesized from tryptophan
    • Synapses called serotonergic
    • Terminated by reuptake and MAO breakdown
    • Involved in regulation of sleep, depression, and mood disorders
    • Prozac is a drug which is an agonist for 5-HT

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**A Serotonergic Synapse**

- Tryptophan hydroxylase
- Aromatic L-amino acid decarboxylase
- 5-HTP
- MAO
- Postsynaptic membrane
- 5-HT receptor
Small-Molecule Neurotransmitters: Soluble Gases

• **Nitric oxide** may be involved in dilation of blood vessels in metabolically active brain regions, penile erection, and learning.
• **Carbon Monoxide**—not widely studied

Small-Molecule Neurotransmitters: Acetylcholine

• **Acetylcholine** (ACh)
  – Synapses are called **cholinergic**
  – Types of receptors are **nicotinic** and **muscarinic**
  – Terminated by the enzyme **acetylcholinesterase (AChE)** in the synapse
  – ACh is the transmitter in the parasympathetic nervous system and at the neuromuscular junction.
  – Poisons often disrupt the actions of AChE.
Agents of Synaptic Transmission:
Large-Molecule Neurotransmitters

• **Neuropeptides**—peptides that function as neurotransmitters and they include:
  – *Endogenous opioids*—involved in runner’s high
  – Substance P—involved in pain perception
  – Oxytocin—involved in sexual functioning
  – ADH (antidiuretic hormone, vasopressin)—involved in fluid regulation
  – CCK (cholecystokinin)—involved in hunger
  – Neuropeptide Y (NPY)—involved in hunger

Agents of Synaptic Transmission:
Large-Molecule Neurotransmitters

• **Neuromodulators**
  – A type of chemical that modifies the sensitivity of groups of cells to neurotransmitters or the amount of neurotransmitter released is called a neuromodulator.
  – *Endogenous opioid*—One of a class of neurotransmitters that have opiate-like characteristics.
Hormones and the Endocrine System

- **Endocrine system**—The system of glands that releases hormones into the bloodstream, where they are carried to distant target areas.
- **Hormone**—A chemical produced by the endocrine glands that is circulated widely throughout the body via the bloodstream.
- **Positive feedback loop**—The release of a substance that acts to promote its further release.
- **Negative feedback loop**—The release of a substance that acts to inhibit its subsequent release.

Hormones and the Endocrine System

- **Pheromone**—A chemical released into the air, rather than into the bloodstream, that affects other members of a species (e.g., a female dog in heat releases pheromones).
- Although hormones have similar actions to neurotransmitters, they are distinguished from neurotransmitters because they are released into the general circulation and not directly onto a target organ.
Electrical Synaptic Transmission

- **Anaxonic neuron**—a neuron without an axon.
  - Transmission is dendrodendritic (dendrite to dendrite)
  - The synapse is called *electrical synapse*.
  - Gap junction is the name for the space between the dendrites of two neurons (another name for an electrical synapse)
  - Connexon—A specialized protein channel through which ions move across gap junctions.

Electrical Synaptic Transmission: Gap Junctions
The Blood-Brain Barrier

- **Blood-brain barrier**—prevents free flow of substances from the bloodstream to the brain
- Uncharged small molecules and lipid-soluble substances can pass into the brain.
- Multiple sclerosis may be caused by damage to the blood-brain barrier.