Synapses and synaptic transmission

MSTN121 - Neurophysiology
Session 2

Department of Myotherapy
Session objectives

• Identify and describe the components of a synapse.
• Describe the events at the synapse resulting in synaptic communication.
• Define excitatory postsynaptic potential (EPSP) and inhibitory postsynaptic potential (IPSP).
• Describe presynaptic facilitation and inhibition.
• Contrast the effects of activating ligand-gated channels with the effects of activating G-protein second-messenger systems.
• Describe how drugs can enhance or diminish neuromessenger function.
• Compare and contrast neurotransmitters and neuromodulators.
Structure of a synapse

A presynaptic terminal
- Projection specialized for the release of chemicals

A postsynaptic terminal
- Membrane region of the receiving cell

A synaptic cleft
- Space between the two terminals

(Lundy-Ekman, 2018, p. 122)
Events at the Synapse

Synaptic communication

- Action potential arrives at the presynaptic terminal.
- Membrane of the presynaptic terminal depolarizes, opening $\text{Ca}^{2+}$ channels.
- Influx of $\text{Ca}^{2+}$ into the neuron terminal, combined with the liberation of $\text{Ca}^{2+}$ from intracellular stores, triggers the movement of synaptic vesicles toward a release site in the membrane.
- Synaptic vesicles fuse with the membrane and release neurotransmitter into the cleft.
- Neurotransmitter diffuses across the synaptic cleft.
- Neurotransmitter that contacts a receptor on the postsynaptic membrane binds to that receptor.
- Receptor changes shape. The changed configuration of the receptor either:
  - Opens an ion channel associated with the membrane receptor
  - Activates intracellular messengers associated with the membrane receptor

Image (Lundy-Ekman, 2018, p. 124)
Electrical Potentials at Synapses

- Chemical stimulation of post synaptic receptors can result in the opening of membrane ion channels. Ion channels that open when a neurotransmitter bonds are known as ligand-gated ion channels.
- If the synapse is neuromuscular, axosomatic, or axodendritic, the flux of ions in the postsynaptic membrane generates a local postsynaptic potential.
- A xoaxonic activity produces presynaptic effects.
At the postsynaptic membrane, changes in the membrane potential are either excitatory or inhibitory to the neuron.

- **Local depolarization is an EPSP** - are common particularly at the neuromuscular junction, in this case acetylcholine (Ach) causes an opening at the ligand gated channels to allow Na⁺ into the muscle cell, which results in contraction of that muscle cell.

- **Local hyperpolarization is an IPSP** - respond to a neurotransmitter binding to the post synaptic membrane by releasing Cl⁻ and/or K⁺ this decreases the likelihood of an action potential occurring

**Summation** – determines if an action potential will occur when both EPSP and IPSP’s coincide

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Image (Lundy-Ekman, 2018, pp.125-6)
Neuromessengers - Neurotransmitters and Neuromodulators

Neuromessengers are chemical used to convey information among neurons. Two types;

- **Neurotransmitters** are released by a presynaptic neuron and acts directly on postsynaptic ion channels or activates proteins inside the postsynaptic neuron. May be excitatory or inhibitory
  - Fast-acting: those that act directly
  - Transmission requires less than 1/1000 of a second.
  - Slow-acting: those that act indirectly
  - Transmission requires 1/10 of a second to minutes

- **Neuromodulators** are released into extracellular fluid and adjust the activity of many neurons. Neuromodulators alter neural function by acting at a distance away from the synaptic cleft. Effects manifest more slowly and usually last longer than those of neurotransmitters, which happen in seconds; the effects last from minutes to days.
  - The same molecule may act as a neurotransmitter or a neuromodulator depending on where it is released.
  - Often neuron will contain more than one type of neuromessenger simultaneously

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Synaptic Receptors

• Receptors are typically named for the transmitter/modulator to which they bind.
• Produce either direct or indirect actions
  – Act directly: when the receptor and ion channel make up a single functional unit
  – Act indirectly: using a cascade of intracellular molecules to activate ion channels or cause other changes within the postsynaptic neuron
• Postsynaptic receptors use two mechanisms to transduce signals. When activated, receptors produce fast or slow responses by:
  – Ligand-gated ion channels (fast responses)
  – G-protein activation of ion channels (slow responses).

(Lundy-Ekman, 2018, p. 127)
Extrasynaptic Receptors

• Extrasynaptic receptor binding activates a cascade of events via the G-protein second-messenger

• G-proteins activate intracellular second messages, initiating a cascade of intracellular events
  – Activation of genes (causing cell to manufacture different neurotransmitters, or other specific cellular products)
  – Opening of membrane ion channels
  – Release of internal stores of Ca$^{2+}$ to regulate metabolism and other cellular processes

(Lundy-Ekman, 2018, p. 128)
Specific Neurotransmitters and Neuromodulators: Acetylcholine

- Ach is the major conveyer of information in the peripheral nervous system (PNS)
- Has slow-acting effects in the PNS that regulate heart rate and other autonomic functions
- Receptors that bind Ach fall into two categories: nicotinic and muscarinic

<table>
<thead>
<tr>
<th>Site of action</th>
<th>Effect</th>
<th>Disorder</th>
<th>Agonist / antagonist</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skeletal muscle</td>
<td>Initiates skeletal muscle contraction</td>
<td>Myasthenia gravis destroys Ach receptors</td>
<td>- Botulinum toxin</td>
</tr>
<tr>
<td>Autonomic Nervous system</td>
<td>Slows heart rate, constricts pupil, increases digestive secretions and smooth muscle contraction</td>
<td></td>
<td>- Atrpine</td>
</tr>
<tr>
<td>Brain</td>
<td>Arousal, pleasure, feelings of reward Cognitive function</td>
<td>Tabaco smoking Alzheimer's</td>
<td>+Nicotine</td>
</tr>
</tbody>
</table>
# Amino acids

- **Glutamate**
  - Principal fast excitatory transmitter of CN
  - Over activity of NMDA receptors may cause epileptic seizures
- **Glycine**
  - Inhibits postsynaptic membranes, primarily in brainstem and spinal cord
- **GABA**
  - Activates slow-acting responses, Linked to ion channels via second-messenger systems

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<td>Glutamate: brain</td>
<td>Excitation learning and memory</td>
<td>Excess: epileptic seizures, excitotoxicity, chronic pain, Parkinsons disease, schizophrenia</td>
<td>-Phencyclidine</td>
</tr>
<tr>
<td>Glycine: Spinal cord</td>
<td>Inhibition</td>
<td>Low: unwanted skeletal muscle contraction</td>
<td>-Strychnine: convulsions, respiratory, paralysis</td>
</tr>
<tr>
<td>GABA: CNS</td>
<td>Inhibition; sedation, antianxiety, antiseizure, and sleep inducing</td>
<td>Low: seizures, unwanted skeletal muscle contraction, anxiety</td>
<td>+Alcohol +Benzodiazapines +Barbituates +Epilepsy drugs +Baclofen</td>
</tr>
</tbody>
</table>
Amines

- DA - Affects motor activity, cognition, and behavior
- Norepinephrine (NE) - role in active surveillance by increasing attention to sensory information
- Serotonin - Affects sleep, general arousal level, cognition, perception, motor activity, and mood
- Histamine - Concentrated in the hypothalamus

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<tr>
<td>Dopamine: Emotional system</td>
<td>Feeling of wanting a reward</td>
<td>Low: depression Drug: addiction</td>
<td>+amphetamines</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+cocaine</td>
</tr>
<tr>
<td>Dopamine: Basal ganglia</td>
<td>Control of movements, attentions, decision making</td>
<td>Low: Parkinson’s disease ADHD</td>
<td>+L-dopa</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+amphetamines (Adderall)</td>
</tr>
<tr>
<td>Dopamine: frontal lobe</td>
<td>Thinking, planning</td>
<td>Excess: schizophrenia</td>
<td>-antipsychotic drugs</td>
</tr>
<tr>
<td>NE: adrenal glands and sympathetic NS</td>
<td>Increased heart rate and force of contraction: dilation of bronchioles, inhibition of peristalsis</td>
<td>Excess: feeling fearful, panic disorder, PTSD</td>
<td>+amphetamines</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+cocaine</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+tricyclic antidepressants</td>
</tr>
<tr>
<td>NE: emotional system and some areas of the cerebral cortex</td>
<td>Control of mood, increased attention to sensory information</td>
<td>Excess: feeling fearful, panic disorder, PTSD</td>
<td>+amphetamines</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+cocaine</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+tricyclic antidepressants</td>
</tr>
<tr>
<td>Serotonin: CNS</td>
<td>Regulates sleep, appetite, arousal and mode</td>
<td>Low: depressions, anxiety</td>
<td>+ Serotonin reuptake inhibitors (prozac)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Excess: obsessive compulsive disorder, schizophrenia</td>
<td></td>
</tr>
<tr>
<td>Histamine: brain</td>
<td>Regulates wakefulness and attention</td>
<td></td>
<td>-antihistamines</td>
</tr>
</tbody>
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(Lundy-Ekman, 2018, p. 131)
## Peptides

- **Opioid peptides**
  - Endorphins, enkephalins, and dynorphins
  - Opioids inhibit neurons in the CNS that are involved in the perception of pain.
- **Substance P**
  - Stimulates nerve endings at the site of injury
- **Calcitonin gene-related peptide**
  - Acts as a neuromodulator

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</thead>
<tbody>
<tr>
<td>Opioid peptides: peripheral sensory neurons and CNS</td>
<td>Inhibit nociceptive signals</td>
<td>Excess; anxiety</td>
<td>+opiates -naloxone</td>
</tr>
<tr>
<td>Substance P: nerve endings in skin, muscle, or joints</td>
<td>Signals tissue damage or potential damage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Substance P: brain</td>
<td>Respiratory and cardiovascular control; mood regulation; signals interpreted as pain</td>
<td>Excess; some pathological pain conditions</td>
<td></td>
</tr>
<tr>
<td>Calcitonin gene-related peptide: brain</td>
<td>Vasodilation; long term neural changes in migraine</td>
<td>Excess; migraine</td>
<td></td>
</tr>
</tbody>
</table>
Receptor Regulation

- Cells regulate receptor activity in several ways.
- In response to frequent stimulation by a ligand, the cell will decrease receptor activity by:
  - receptor internalization - Activated receptors are internalized when part of the postsynaptic membrane folds into the cell
  - receptor inactivation - Inactivation leaves the total number of receptors at the membrane constant but switches some off

(Lundy-Ekman, 2018, pp. 133-4)
Disorders of Synaptic Function: Diseases Affecting Neuromuscular Junction

Diseases that affect the NMJ generally impede signal transmission by either decreasing the volume of neurotransmitters released or its ability to activate the receptors.

- **Lambert-Eaton syndrome**
  - Antibodies destroy voltage-gated Ca\(^{2+}\) in presynaptic terminal.
  - Typically occurs in people with small cell cancers of the lung.

- **Myasthenia gravis**
  - Autoimmune disease
  - Antibodies attack and destroy nicotinic receptors on muscle cells.
Disorders of Synaptic Function: Channelopathy

• Disease that involves dysfunction of ion channels
• Common in inherited neurologic disorders that disrupt skeletal muscle contraction, in this case both volted-gated and ligand-gated ion channels are affected.
• Cause some cases of epilepsy and migraines
• Channelopathies affecting skeletal muscles cause paralysis or slow relaxation following muscle contraction

(Lundy-Ekman, 2018, p.135)
Blog Posts

• The platforms of marketing and health writing are continuing to develop in the manual therapies world. It is becoming more common that we as practitioners, are required to write a blog post to help educate our clients.

• When writing these, it should be considered who you are writing for, to avoid confusion.

In this subject you are required to write a **500 word blog post** for your clients.
Blog Posts

When writing a blog post there are several steps to consider. Listed below are some of the main steps (but you are not limited to these):

- Choose your topic
- Come up with a title
- Write a captivating opening
- Create the main content of the article
- Summarise and add in a call to action
- You should reference throughout the article
Blog Post Assignment Overview

This assessment will require you to create a 500 word blog post on one (1) of the following concepts:

1. Nociceptive pain
2. Neuropathic pain
3. Pain matrix dysfunction

Regardless of which of these topics you choose, you must make reference to the involvement of neuroplasticity in your answer.

This assignment is due Week 6, Sunday 11.59pm.
Blog Post Assignment: Activity

In last week's session, we discussed the peripheral and central nervous system.

From the key concepts learnt on these topics, as a class, discuss these in terms that a patient would understand.

Ensure you are explaining all main concepts in a clear concise manner.
Blog Post Assignment:
Activity

In last week’s session, we discussed the central nervous system demyelination.

From the key concepts learnt on these topics, as a class discuss these in terms that a patient would understand.

Ensure you are explaining all main concepts in a clear concise manner.
Blog Post Assignment:

Activity

In groups of 3 read the following section:

After reading the following, in your groups interpret this information and write an overview in language that a patient will understand.

Once completed please read to the class.
Blog Post Assignment: Activity

In groups of 3 read the following section:

After reading the following, in your groups interpret this information and write an overview in language that a patient will understand.

Once completed please read to the class.
Revision Questions

• Describe the three components of a synapse.
• List the seven events at the synapse resulting in synaptic communication.
• Define excitatory postsynaptic potential (EPSP) and inhibitory postsynaptic potential (IPSP). Explain the effects of EPSPs and IPSPs.
• Describe presynaptic facilitation and inhibition.
• Contrast the effects of activating ligand-gated channels with the effects of activating G-protein second-messenger systems.
• Describe how drugs can enhance or diminish neuromessenger function.
• Explain the differences between neurotransmitters and neuromodulators.
• Associate the following neuromessengers with their agonists and antagonists, associated disorders, and common actions on postsynaptic membranes: acetylcholine (ACh), NE, dopamine (DA), serotonin, γ-aminobutyric acid (GABA), glutamate, and glycine.
• Botulinum toxin (BTX) and myasthenia gravis both affect communication at the neuromuscular junction. Explain the differences between therapeutic use of BTX and the disease myasthenia gravis.
Image references

References

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