University of Al-Mustaqbal
College of Science
Department of Medical Physics

Neurophysics

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The Connection Between Neurons

Fifth Licture

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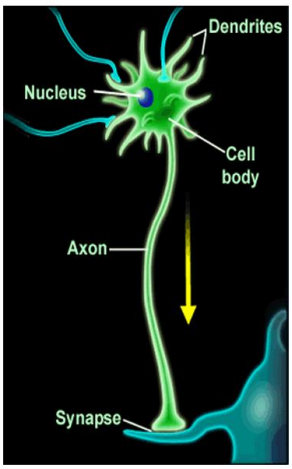
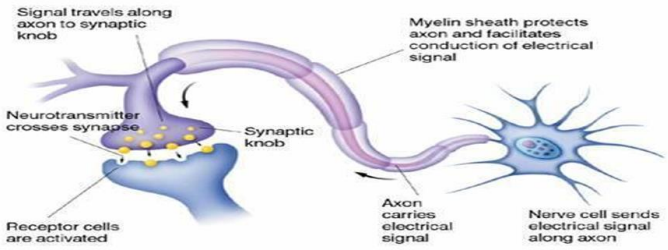
2025

How does the brain work?





Connections between neurons

Dendrites = *Take in information*
Axon = *Send out information*

How neurons communicate?

Communication within neurons is :-
1-Electrical.
2-Chemical.

Neurotransmitters

Neurotransmitters are the molecules that act as chemical signals between nerve cells. The diverse chemical substances that carry information between neurons are called neurotransmitters.
Otto Loewi discovered the first neurotransmitter in 1926
• Neurotransmitter and neurotransmission chemical substances which transmit impulses from one neuron to another neuron or from neuron to effector organ is called neurotransmitter and the process is known as neurotransmission.
There are dozens of different neurotransmitters (NT) in the neurons of the body.
• NTs can be either excitatory or inhibitory
• Each neuron generally synthesizes and releases a single type of neurotransmitter

Criteria for Neurotransmitters

1. Synthesis of molecule occur within the neurons.
2. Storage of molecule occurs within the nerve ending prior to release. E.g. in Synaptic vesicles.
3. Release of molecule from presynaptic ending occurs in response to an appropriate stimulus such as action potential.
4. There is binding and recognition of the putative neurotransmitter molecule on the postsynaptic target cell.
5. Mechanism exists for the inactivation and termination of the biological activity of the neurotransmitter.

Properties of Neurotransmitters

1. Precursor(s)
2. Synthesizing enzymes
3. Storage vesicles
4. Release by neural stimulation
5. Postsynaptic receptors
6. Specific antagonists
7. Degrading enzymes.

Types of Neurotransmitters

Now more than one hundred substances and a far larger number of receptors have been implicated in synaptic transmission such as:-
1. Acetylcholine (ACH) is involved in both learning and memory and muscle movement.
2. Dopmaine impacts our arousal and mood states, thought processes, and physical movement
3. Serotonin and norepinephrine are neurotransmitters involved in levels of arousal and mood, and play a major role in mood disorders such as depression
4. GABA is the main inhibitory neurotransmitter in the nervous system;
5.Glutamate is the main excitatory neurotransmitter
6. Endorphins are a group of neurotransmitters that are involved in pain perception and relief.

1-Acetylcholine (ACH)

Type	Excitatory in all cases except in the heart (inhibitory)
Released from	Motor neurons, basal ganglia, preganglionic neurons of the autonomic nervous system, postganglionic neurons of the parasympathetic nervous system, and postganglionic neurons of the sympathetic nervous system that innervate the sweat glands
Functions	Regulates the sleep cycle, essential for muscle functioning

2-Dopamine

Type	Inhibitory Neurons of the spinal cord, cerebellum, basal ganglia, and areas of the cerebral cortex Reduces neuronal excitability throughout the nervous system
Released from	Substantia nigra
Functions	Inhibits unnecessary movements, inhibits the release of prolactin, and stimulates the secretion of growth hormone

3-Epinephrine (Epi)

Type	Excitatory
Released from	Chromaff in cells of the medulla of adrenal gland
Functions	The fight-or-flight response (increased heart rate, blood pressure, and glucose production)

4-Gamma-Amino Butyric Acid (GABA)

Type	Inhibitory
Released from	Neurons of the spinal cord, cerebellum, basal ganglia, and areas of the cerebral cortex
Functions	Reduces neuronal excitability throughout the nervous system

5-Glutamate (Glu)

Type	Excitatory
Released from	Sensory neurons and cerebral cortex
Functions	Regulates central nervous system excitability, learning process, memory

6-Histamine

Type	Excitatory
Released from	Hypothalamus, cells of the stomach mucosa, mast cells, and basophils in the blood
Functions	Regulates wakefulness, blood pressure, pain, and sexual behaviour , increases the acidity of the stomach; mediates inflammatory reactions

Regulation of neurotransmitters

Concentration of neurotransmitters may be manipulated by:

1. Changing the rate of synthesis
2. Altering the rate of release at the synapse
3. Blocking reuptake
4. Blocking degradation

Neurotransmitters function in your body

1-Glutamate excites neurons to fire, involved in memory
2- GABA - inhibits (stops) other neurons from firing
3-Serotonin - affects mood
4-Dopamine - involved with feeling reward, learning, & emotion
5-Acetylcholine - involved with memory & attention &muscle action
6-Norepinephrine - involved with alertness.

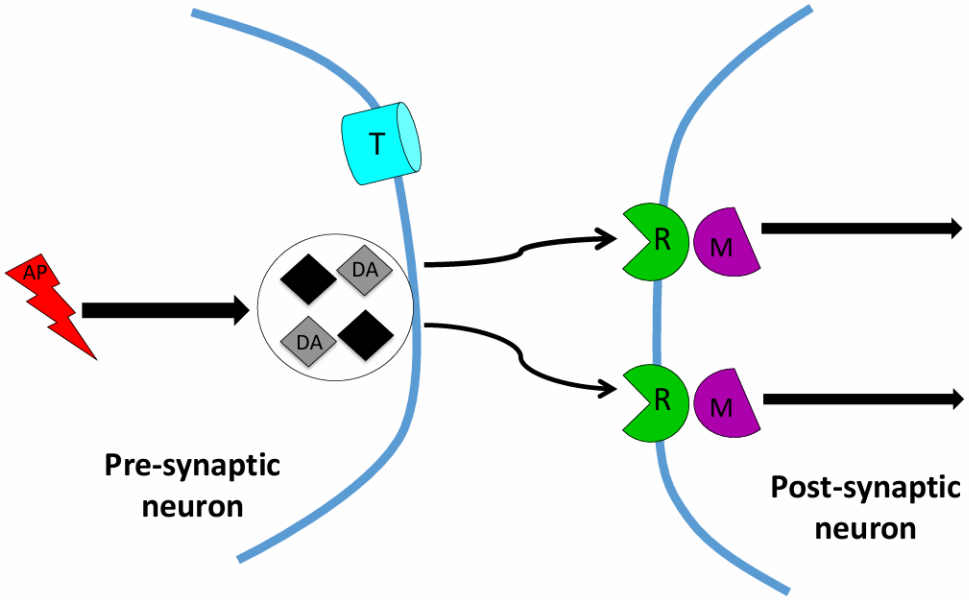
Role of neurotransmitters in some diseases :-

All the NTs combine with their concern receptors and in normal cases, produce the (physiological) desired effects. Deficiency or excess of activity of these NTs may occur in many diseases, e.g.

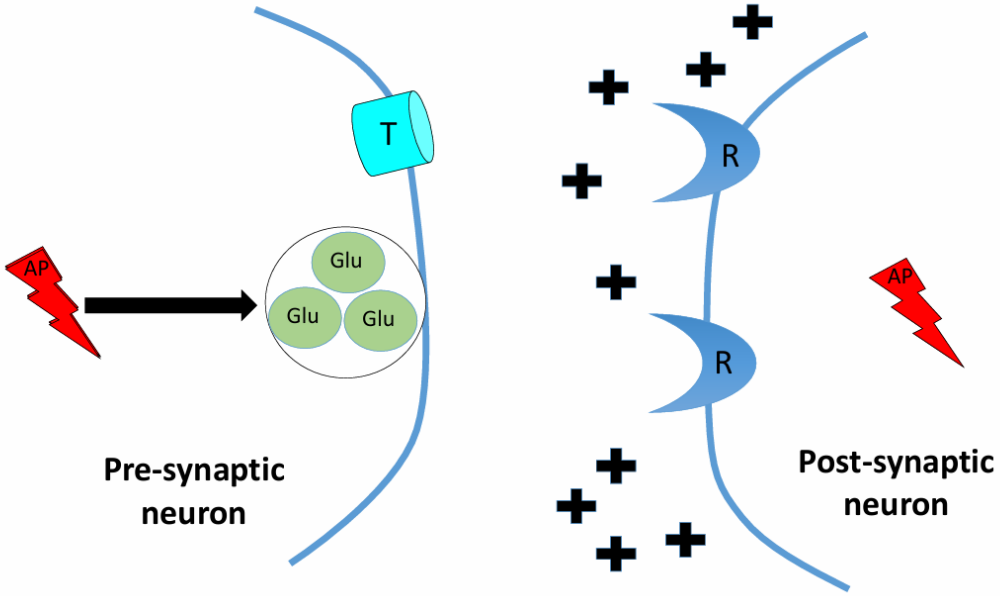
1. Overactivity of dopamine is seen in schizophrenia.
2. Either cholinergic overactivity or dopaminergic deficiency occur in parkinsonism.
3. In depression, there is deficiency of serotonin and/or noradrenaline.
4. In epilepsy, NMDA mediated over activity or GABA under activity is seen.
5. Loss of cholinergic neuron may be the cause of Alzheimer's diseases.

Normal **Neurotransmission**

(Dopamine signals)



An example – Glutamate & Epilepsy



Three Drugs [of many]which Affect Neurotransmissions

Methamphetamine

Nicotine

Alcohol

Methamphetamine alters Dopamine transmission in two ways:

1. Enters dopamine vesicles in axon terminal causing release of NT
2. Blocks dopamine transporters from pumping dopamine back into the transmitting neuron

Result: More dopamine in the Synaptic Cleft ,This causes neurons to fire more often than normal resulting in a euphoric feeling.

After the drug wears off, dopamine levels drop, and the user "crashes". The euphoric feeling will not return until the user takes more methamphetamine

Long-term use of methamphetamine causes dopamine axons to wither and die. Note that cocaine also blocks dopamine transporters, thus it works in a similar manner.

What about Nicotine?

Similar to methamphetamine and cocaine, nicotine increases dopamine release in a synapse.

1- However, the mechanism is slightly different.

2- Nicotine binds to receptors on the presynaptic neuron.

3-Nicotine binds to the presynaptic receptors exciting the neuron to fire more action potentials causing an increase in dopamine release.

4-Nicotine also affects neurons by increasing the number of synaptic vesicles released.

How does alcohol affect synapses?

• Alcohol has multiple effects on neurons. It change neuron membranes, ion channels, enzymes, and receptors.

• It binds directly to receptors for acetylcholine, serotonin, and gamma aminobutyric acid (GABA), and glutamate.

• We will focus on GABA and its receptor

• GABA and the GABA Receptor

• GABA is a neurotransmitter that has an inhibitory effect on neurons. When GABA attaches to its receptor on the postsynaptic membrane, it allows Cl- ions to pass into the neuron.

• This hyperpolarizes the postsynaptic neuron to inhibit transmission of an impulse.

Drugs Interfere with Neurotransmission

Drugs can affect synapses at a variety of sites and in a variety of ways, including:

1. Increasing number of impulses

2.Release NT from vesicles with or without impulses

3. Block reuptake or block receptors

4.Produce more or less NT

5.Prevent vesicles from releasing NT

Drug That Influence Neurotransmitters

Change in Neurotransmission	Effect on Neurotransmitter release or availability	Drug that acts this way
increase the number of impulses	increased neurotransmitter release	nicotine, alcohol, opiates
release neurotransmitter from vesicles with or without impulses	increased neurotransmitter release	amphetamines methamphetamines
release more neurotransmitter in response to an impulse	increased neurotransmitter release	nicotine
block reuptake	more neurotransmitter present in synaptic cleft	cocaine amphetamine
produce less neurotransmitter	less neurotransmitter in synaptic cleft	probably does not work this way
prevent vesicles from releasing neurotransmitter	less neurotransmitter released	No drug example
block receptor with another molecule	no change in the amount of neurotransmitter released, or neurotransmitter cannot bind to its receptor on postsynaptic neuron	LSD caffeine

What do you predict happen when neurotransmitters are out of balance ?

Neurotransmitter	Normal Function	Imbalance
Glutamate	Excites neurons, memory	**TOO MUCH** leads to migraines or seizures
GABA	Inhibits (stops) neurons	**TOO LITTLE** leads to seizures, tremors, & insomnia
Serotonin	Affects mood, hunger, & sleep	**TOO LITTLE** leads to depression
Dopamine	Involved in reward, learning, emotion	**TOO MUCH** leads to schizophrenia. TOO LITTLE leads to tremors and decreased mobility in Parkinson's & ADHD
Acetylcholine	Enables muscles, learning, & memory	Alzheimer's decreases the amount of this
Norepinephrine	Helps control alertness	**TOO LITTLE** can cause depressed mood and cause attention deficit problems

Also the Pathologic changes include:

1- Mitochondrial dysfunction
2-Increased deposits of amyloid ß peptide in the cerebral cortex
3-Formation of extracellular plaques and cerebral vascular lesions, and intraneuronal fibrillary tangles consisting of the tau protein This interferes with synaptic signaling