Academic year 2020-2021

3rd year S 6

Chemical Disturbances of Brain Function

Session:7

Lecture: 1

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Objectives:

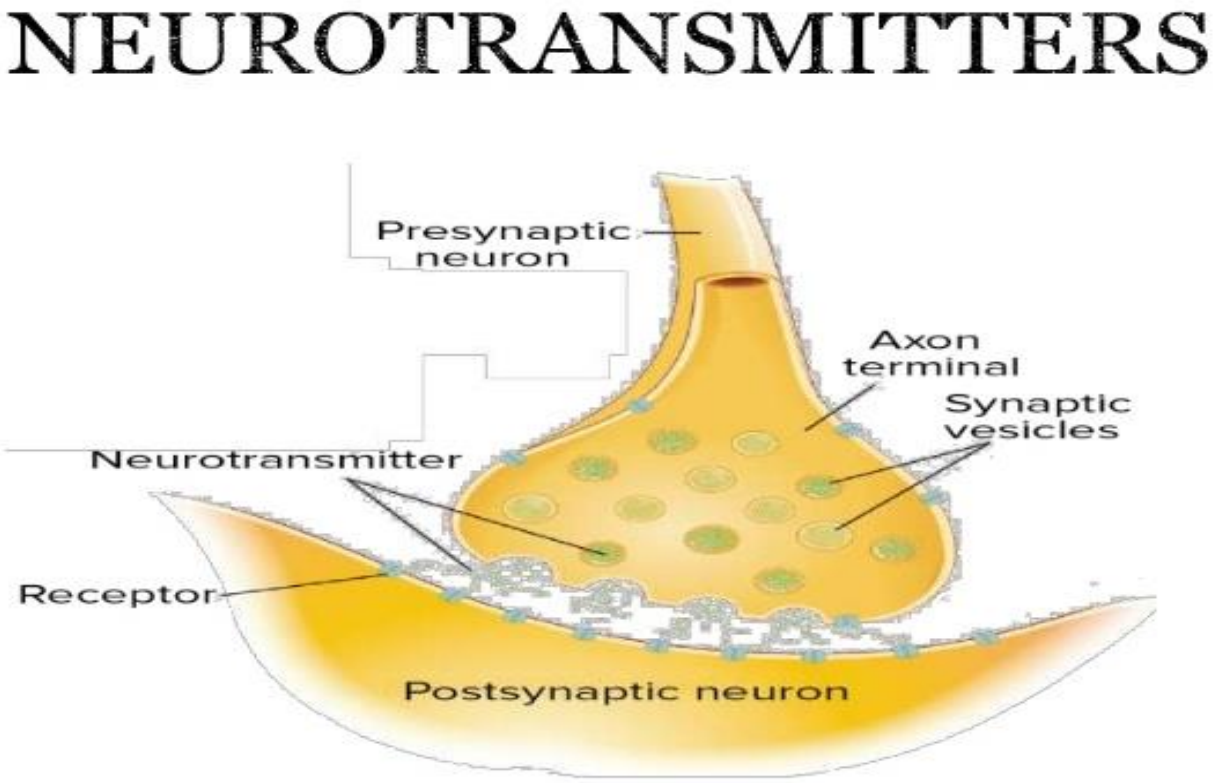
After this lecture and with appropriate reading you should be able to:

1. **Identify the major neurotransmitter system of the brain.**
2. **Outline the major classes and origins of chemicals disruptions of brain function.**
3. **Understand the consequences of disruptions of the normal chemistry of the brain.**

LO 1

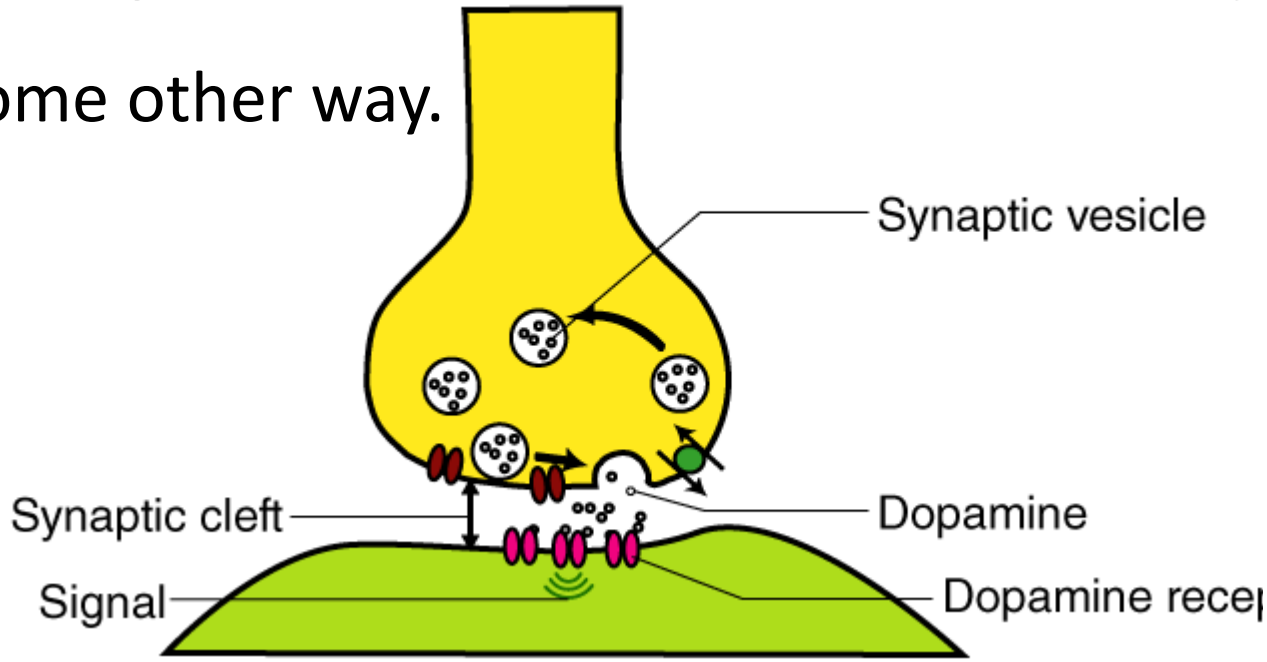
Neurotransmitters (chemical messengers)

are molecules used by the nervous system to transmit messages between neurons, or from neurons to muscles.



LO 1

- Neurotransmitters are synthetized in and released from nerve endings into the synaptic cleft.
- It binds to receptor proteins in the cellular membrane of the target tissue.
- The target tissue gets excited, inhibited, or functionally modified in some other way.



Neurotransmitters can be classified according to : LO 1

1. chemical structure

a. Amino acids: GABA, glutamate, glycine, aspartate

b. Amines:

1. - Catecholamine (dopamine, norepinephrine, epinephrine) .
   - Acetylcholine
2. Indolamines- serotonin, melatonin

2. functional

a. excitatory (Ach, glutamate, histamine)

b. inhibitory (GABA)

LO 1

A. Amino Acids

α-Ketoglutarate —GABA-T→ Glutamate

Glutamine —Glutaminase→ Glutamate

Glutamate —GAD→ GABA

B. Acetylcholine

Acetyl-CoA + Choline

Choline acetyltransferase

Acetylcholine

C. Serotonin

Tryptophan

Tryptophan hydroxylase

5-Hydroxytryptophan

5-Hydroxytryptophan decarboxylase

5-Hydroxytryptamine

D. Catecholamines

Tyrosine

Tyrosine hydroxylase

Dihydroxyphenylalanine (DOPA)

Amino acid decarboxylase

Dopamine

Dopamine-β-hydroxylase

Norepinephrine

Phenylethanolamine-N-methyltransferase

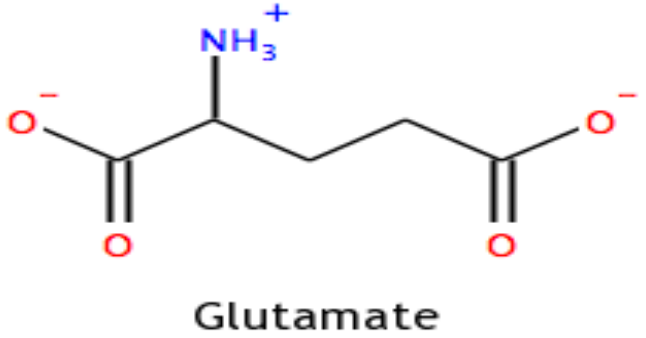
Epinephrine

Major classes of Neurotransmitters:

LO 2

Glutamate (Glu):

1. **Excitatory** neurotransmitter
2. Released from **sensory neurons and cerebral cortex**
3. Does not cross the blood brain barrier (BBB)
4. Precursor for GABA
5. Most abundant neurotransmitter in CNS about 30% of neurons use glutamate
3. Regulates

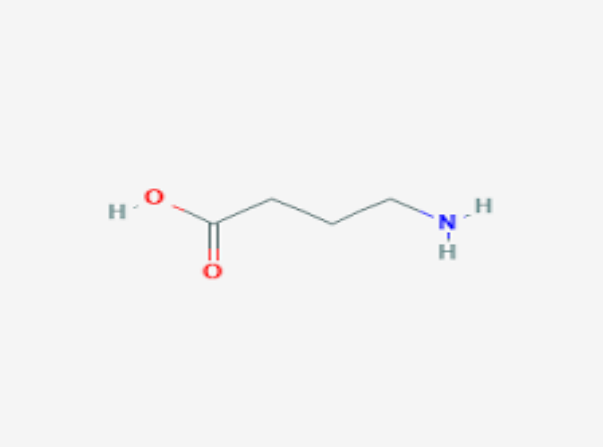


Glutamate

CNS excitability, learning process and memory

LO 2

Gamma-aminobutyric acid(GABA):

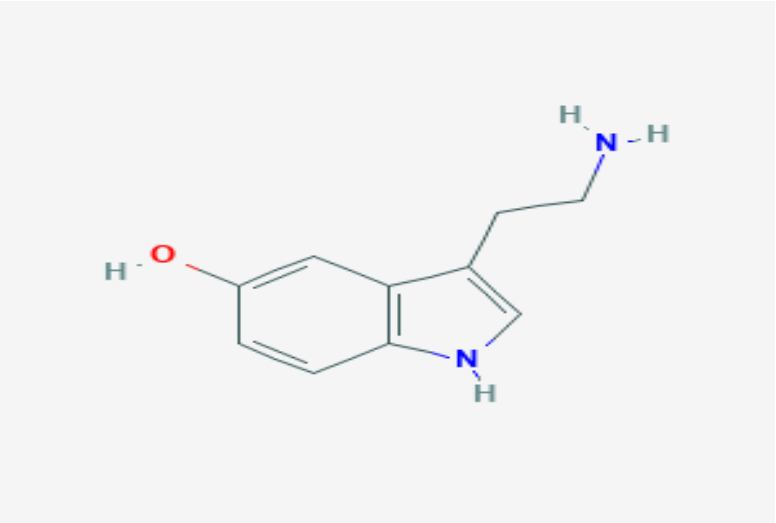


1. **Inhibitory** neurotransmitter.
2. Synthesized from glutamate
3. Released from neurons of the **spinal cord, cerebellum, basal ganglia and many areas of the cerebral cortex**.
4. Reduces neuronal excitability throughout the nervous system.

LO 2

Serotonin (5-HT):

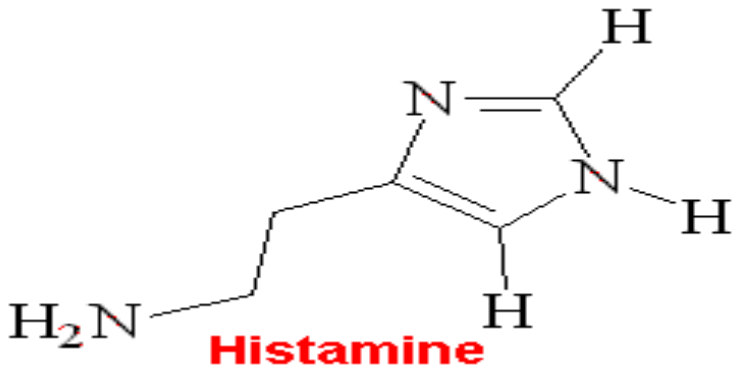
1. **Inhibitory** neurotransmitter.
2. Released from **neurons of the brainstem and GIT, thrombocytes.**
3. Regulates body temp., perception of pain, emotions and sleep cycle.



LO 2

Histamine:

1. **Excitatory** neurotransmitter.
2. Released from **hypothalamus, cells of the stomach mucosa, mast cells and basophils in the blood.**
3. Regulates blood pressure, pain and sexual behavior, increase the acidity of stomach, mediates inflammatory reactions.



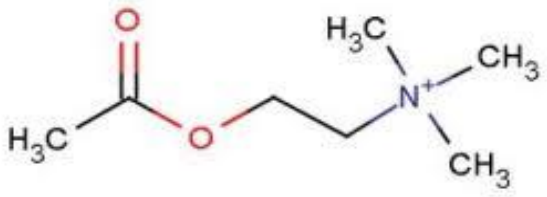
Histamine

Acetylcholine (ACh):

LO 2

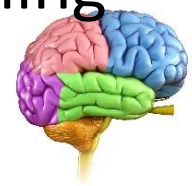
1. **Excitatory** neurotransmitter except in the heart (inhibitory).

2. Released from
   a. **Motor neurons,**
   b. **basal ganglia,**
   c. **preganglionic neurons of the autonomic nervous system**
   d. **postganglionic neurons of the parasympathetic and sympathetic nervous system that innervate the sweat glands.**



Acetylcholine

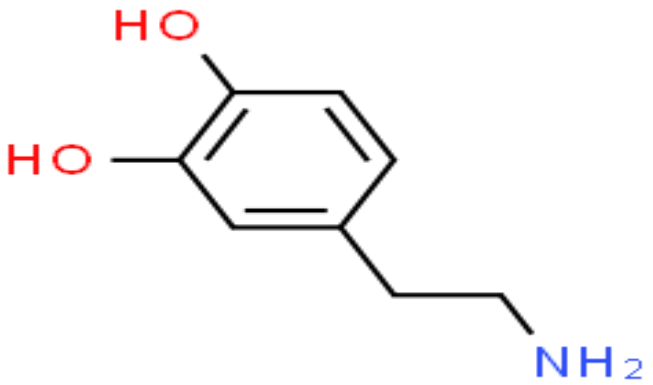
3. Regulates the sleep cycle, essential for muscle functioning



LO 2

Dopamine:

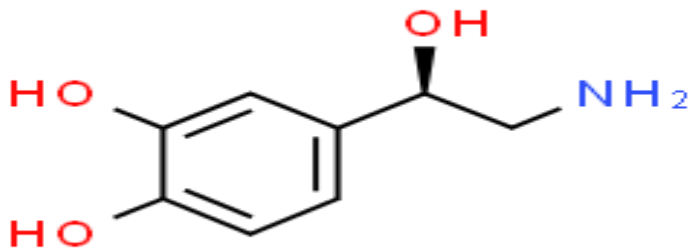
1. Both **excitatory** and **inhibitory.**
2. Released from **Substantia nigra.**
3. Inhibits unnecessary movements, inhibits the release of prolactin, and stimulates the secretion of growth hormone.



LO 2

Norepinephrine (NE):

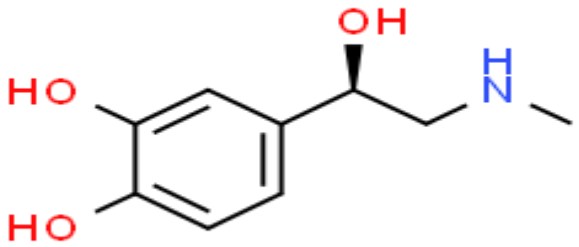
1. **Excitatory** neurotransmitters.
2. Released from **Brainstem, hypothalamus, and adrenal glands.**
3. Increases the level of alertness and wakefulness, stimulates various processes of the body



LO 2

Epinephrine (Epi):

1. **Excitatory** neurotransmitters.
2. Released from **Chromaffin cells of the medulla of adrenal gland.**
3. The fight-or-flight response (increased heart rate, blood pressure, and glucose production)



Causes of Neurotransmitter Imbalances

LO 3

1. Stress

- is considered one of the primary sources of neurotransmitter imbalance.
- It can lead to increased neurotransmitter activity and/or turnover.
- Chronic stress taxes the nervous system over time and may lead to a depletion of neurotransmitter stores.

2. Diet

High carbohydrate or high fat diets may not provide sufficient levels of essential amino acids to act as precursors for some neurotransmitters.

3. Environmental toxins

LO 3

- Many neurotoxins are lipid soluble and able to cross the blood-brain barrier.
- Storage within the brain may lead to cell damage or death and may influence neurotransmission.

4. Genetics

Genetic variation may influence neurotransmitter packaging, transport or removal from synapses.

LO 3

Neurotransmitter	Abbreviation	Behaviors or Diseases Related to These Neurotransmitter
Acetylcholine	ACh	Learning and memory; Alzheimer's disease' muscle movement in the peripheral nervous system
Dopamine	DA	Reward circuits; Motor circuits involved in Parkinson's disease; Schizophrenia
Norepinephrine	NE	Arousal; Depression
Serotonin	5HT	Depression; Aggression; Schizophrenia
Glutamate	GLU	Learning; Major excitatory neurotransmitter in the brain
GABA	GABA	Anxiety disorders; Epilepsy; Major inhibitory neurotransmitter in the brain

The consequences of disruptions of the normal chemistry of the brain

LO 3

Alzheimer's disease:

- Is a neurodegenerative disorder characterized by learning and memory impairments.
- It is associated with a **lack of acetylcholine** in certain regions of the brain.

The consequences of disruptions of the normal chemistry of the brain

LO 3

Depression:

- It's believed to be caused by a depletion of **norepinephrine, serotonin, and dopamine** in the central nervous system.
- pharmacological treatment of depression aims at increasing the concentrations of these neurotransmitters in the central nervous system.

The consequences of disruptions of the normal chemistry of the brain LO 3

Schizophrenia

- It's a severe mental illness, has been shown to involve excessive amounts of **dopamine** in the frontal lobes,
- leads to psychotic episodes in these patients.
- The drugs that block dopamine are used to help schizophrenic conditions.

The consequences of disruptions of the normal chemistry of the brain LO 3

Parkinson's disease:

- The destruction of the substantia nigra leads to the destruction of the only central nervous system source of dopamine.
- **Dopamine** depletion leads to uncontrollable muscle tremors seen in patients suffering from Parkinson's disease.

The consequences of disruptions of the normal chemistry of the brain LO 3

Epilepsy:

- Are caused by the lack of inhibitory neurotransmitters, such as **GABA**, or by the increase of excitatory neurotransmitters, such is **glutamate**.
- Depending on the cause of the seizures, the treatment is aimed to either increase GABA or decrease glutamate.

The consequences of disruptions of the normal chemistry of the brain LO 3

Huntington's disease:

- Is a chronic reduction of **GABA** in the brain.
- It is an autosomal dominant inherited disease related to abnormality in DNA, one of the products of such disordered DNA is the reduced ability of the neurons to take up **GABA**.
- There is no cure for Huntington's disease, but we still can treat symptoms by pharmacologically increasing the amount of inhibitory neurotransmitters.

The consequences of disruptions of the normal chemistry of the brain LO 3

Myasthenia gravis:

- It's a rare chronic autoimmune disease.
- characterized by the impairment of synaptic transmission of **acetylcholine** at neuromuscular junctions, leading to fatigue and muscular weakness without atrophy.

LO 3

Is there a test to identify a chemical imbalance in the brain?

- There are **no reliable** tests available to help diagnose a chemical imbalance in the brain. **LO 3**
- Tests that use urine, saliva, or blood to measure neurotransmitters in the brain are unlikely to be accurate.
- Not all neurotransmitters are produced in the brain.
- The tests that are currently marketed don't distinguish between neurotransmitter levels in the brain and in the rest of the body.
- In addition, neurotransmitters levels in the body and brain are constantly and rapidly changing. This makes such tests unreliable.

LO 3

How can you diagnose mental illness ???

LO 3

1. Blood tests to rule out other conditions, such as a thyroid disorder or vitamin deficiency. Both conditions can trigger symptoms of a mental health condition.

2. Other investigation

a) **Electromyography** (**EMG**).

measures muscle response or electrical activity in response to a nerve's stimulation of the muscle.

b) **Computerized Tomography (CT) scan**.

Neurological CT scans are used to view the brain and spine.

LO 3

c) **Magnetic resonance imaging (MRI)**

- uses a large magnet and radio waves.
- MRIs are very useful for examining the brain and spinal cord.

3. Mental health professional, such as a psychiatrist or psychologist. They'll perform a psychological evaluation.

Includes :

- Thoughts
- feelings
- eating and sleeping habits
- daily activities

LO 3

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