pharmacology
Team 438

MED438

Reviewed by Razan AlRabah & Ibrahim AlDakhil

Neuropsychiatry Block

Pharmacology Team 438

Pharmacology of Central Neurotransmitter

Objectives

By the end of the lecture , you should know:

- The main objective of this lecture is to understand the role of neurotransmitters in etiology and treatment of CNS diseases.

Color index:

Black : Main content
Red : Important
Blue: Males' slides only

Pink : Females' slides only
Grey: Extra info or explanation
Green : Dr. notes

Editing File

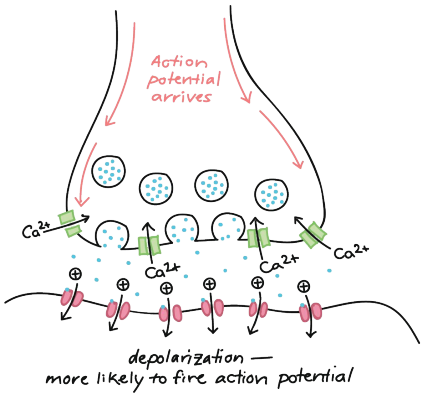
Neurotransmitters

Definition: **Endogenous**[1] **chemicals** or chemical messengers that transmit signals from a neuron to a target cell across a synapse.

Overview:

1 They are packed into synaptic vesicles under the membrane in the axon terminal, on the presynaptic side.

2 They are released into & diffuse across the synaptic cleft to bind to a specific receptors on the postsynaptic side. [2]



Fate of Neurotransmitters:

Female slides only

The neurotransmitter-receptor interaction must be terminated **quickly** to allow rapid, repeated activation of receptors. So:

1 They can be re-uptaken by active, ATP-dependent [3] processes to be repackaged in vesicles for reuse.

2 They can be destroyed by enzymes [4] near the receptors.

3 They can diffuse into the surrounding area and be removed.

Neuropsychopharmacological science seeks to:

- Understand how drugs can affect the CNS selectively to relieve pain, improve attention, induce sleep, reduce appetite, suppress disordered movements...etc.
- To provide the means to develop appropriate drugs to correct pathophysiological events in the abnormal CNS.

What is the importance of understanding neurotransmitters?

- To understand the etiology of diseases
- To suggest the best drugs to be used
- To understand the other clinical uses of any particular drug [5]

1- Made in the body
2-Release is triggered by diffusion of calcium ions into the presynaptic terminal, by opening of voltage gated calcium channels driven by the action potential that reached the nerve endings.
3- Some antidepressant drugs will act here
4- MAO inhibitors and some antidepressant will act on the enzyme
5- antidepressant can treat sexual dysfunction

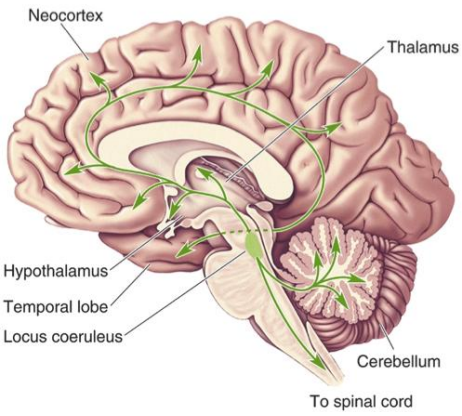
Examples of Neurotransmitters

Monoamines & Other biogenic amines	Amino acids	Peptides	Others
• Dopamine • Norepinephrine • Serotonin	• Glutamate • GABA	• Somatostatin [1]	• Acetylcholine

Norepinephrine

Female slides only

- also called noradrenaline , belongs to catecholamines, the direct precursor of NE is dopamine
- ★ **Function:** alertness, arousal , and readiness for action.[2]
- A variety of medically important drugs work by altering the actions of NE
  e.g. for treatment of CV problems and some of psychiatric conditions.



Diseases that are influenced by changes in NE level :

Mania

- **Treated by:** Drugs that decrease NE

↑NE level

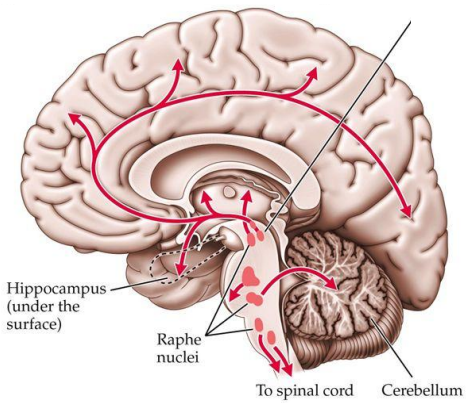
↓NE level

Depression

- **Treated by:** Drugs that Increase NE

Serotonin (5-HT)

- 5-hydroxytryptamine (5-HT) is a monoamine primarily found in the CNS , GIT, platelets.
- A contributor for feeling of well-being & happiness.
- ★ **Function:** regulation of Mood, sleep, appetite and pain perception. [3]
- Modulation of serotonin at synapses is a major action of several classes of **antidepressants**
  e.g selective serotonin re-uptake inhibitors (SSRIs).



Diseases that are influenced by changes in 5-HT level:

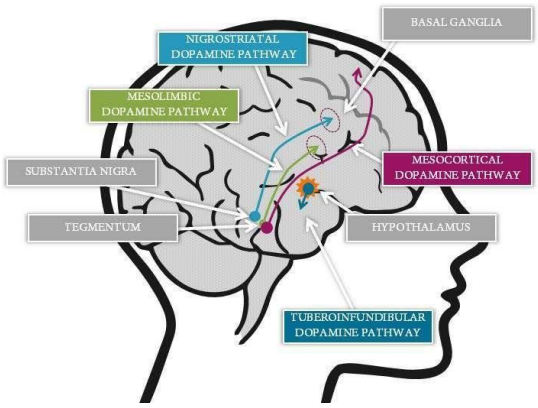
Depression, Social phobia, Obsessive Compulsive Disorders, Generalized Anxiety, Schizophrenia, Vomiting.

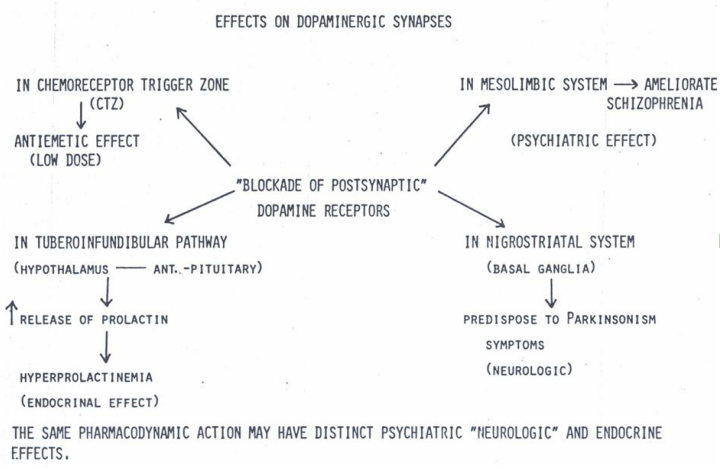
1- related to endocrine system
2- in case of depression all of those functions are decreased
3- determine development of depression

Dopamine

Dopamine have **3 main pathways** in the brain, each has specific function.

- Nigrostriatal: control movement
- Mesolimbic & mesocortical: related to cognitive and emotional reward. Over activity lead to delusions & schizophrenia
- Tuberoinfundibular: related to endocrine system





Blockade of postsynaptic Dopamine receptors in any of the 3 pathways will lead to:

1-Neurologic effect:

in the **Nigrostriatal system** will lead to **Parkinsonism symptoms**

2-Endocrinal effect:

in the **Tuberoinfundibular pathways** will increase the release of prolactin and cause **Hyperprolactinemia** and as a result of that if the patient is:

Female → amenorrhea -missed menstrual periods- and Galactorrhea -milky breast discharge in non lactating female- can occur.

If male → Gynecomastia.

3-Psychiatric effect:

-in the **Mesolimbic and Mesocortical system** will treat **Schizophrenia**

4-Antiemetic:

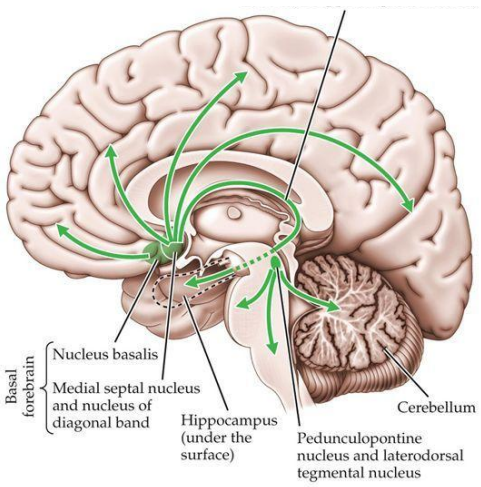
- Blocking of Dopamine receptors in CTZ using a low dose will give us an antiemetic effect.

Diseases that influenced by dopamine level:

Parkinson's disease, attention deficit hyperactivity disorder, schizophrenia, depression and drug addiction.[2]

Acetylcholine

- Acetylcholine, the first neurotransmitter discovered
- Inside the brain Ach functions as a neuromodulator (A chemical that alters the way other brain structures process information rather than a chemical used to transmit information from point to point).
- ★ **Function:** Memory , Arousal, Attention.
- Is ACh an inhibitory or excitatory neurotransmitter?
  Ans : both, plz refer to the table in pg 6



Diseases that are influenced by changes in Ach:

Damage to cholinergic receptors (muscarinic) is associated with memory deficits.

- **Treated by:** **Cholinomimetics**

Alzheimer's disease.[1]

Parkinson's disease

Increased brain level of ACh

- **Treated by:** **Anticholinergic** [3]

Other diseases:

- Muscarinic antagonists as hyoscine cause **amnesia**
- **Depression** may be a manifestation of a central cholinergic predominance.
- **Schizophrenia** may be due to imbalance between ACh & dopamine brain levels.

1- treating a Alzheimer's disease can cause Parkinson symptoms due to increased levels of Ach
2- like Cocaine
3- in case of Parkinson , dopamine decreases so effect of ach will be predominant so we give anticholinergic drugs
4- what is the difference between neuromodulator and neurotransmitter?
a - Neurotransmitters are chemical transmitter which allow transmission of impulse from one neuron to One or Two neurons only , have short and rapid effect .
b - Neuromodulator : transmit impulse from one neuron to a group of neurons , could be target organ or gland , have slow and long effect .
Examples of neuromodulator : Ach and serotonin

Glutamic Acid

- An **excitatory** neurotransmitter.
- **Potential therapeutic effect of glutamate antagonists:**
  - Reduction of brain damage following strokes & head injury.
  - Treatment of epilepsy- Drug dependence.
  - Schizophrenia.

Diseases that are influenced by changes in Glutamate level:

An increase in its level predispose to **epilepsy**

Gamma-Aminobutyric Acid (GABA)

- GABA is the main **inhibitory** neurotransmitter in the brain.
- Present throughout the brain; there is very little in peripheral tissues.

Diseases that are influenced by ↓ in GABA level:

★ Benzodiazepine (diazepam) enhances GABA function and used in treatment of above diseases.

This table may come as MCQ* !

Transmitter	Receptor subtypes	Receptor Mechanisms
Ach	Muscarinic **M1**: blocked by pirenzepine & atropine	Excitatory:↓K+ ↑IP3 & DAG
	M2: blocked by atropine	Inhibitory: ↑K+ ↓cAMP
	Nicotinic **N**	Excitatory: ↑ cation conductance
Dopamine	D1: blocked by phenothiazines	Inhibitory:↑ cAMP
	D2: blocked by phenothiazines & haloperidol	Inhibitory (presynaptic): ↓Ca2+ Inhibitory (postsynaptic): ↑K+ ↓cAMP
NE	**α1:** blocked by prazosin	Excitatory:↓K+ ↑IP3 & DAG
	α2: blocked by clonidine	Inhibitory (presynaptic): ↓Ca2+ Inhibitory (postsynaptic): ↑K+ ↓cAMP
	β1: blocked by propranolol	Excitatory:↓K+ ↑ cAMP
	β2: blocked by propranolol	Inhibitory: ↑ Na+ pump ↑ cAMP
5-HT	$5HT_{1A}$: buspirone is a partial agonist	Inhibitory:↑K+ ↓cAMP
	$5HT_{2A}$: blocked by clozapine, risperidone and olanzapine	Excitatory:↓K+ ↑IP3 & DAG
	$5HT_3$: blocked by ondansetron	Excitatory: ↑ cation conductance
	$5HT_4$	Excitatory:↓K+
GABA	$GABA_A$: facilitated by benzodiazepines and zolpidem	Inhibitory:↑Cl-
	$GABA_B$: activated by baclofen	Inhibitory (presynaptic): ↓Ca2+ Inhibitory (postsynaptic):↑K+
Glutamate	Four subtypes: NMDA blocked by phencyclidine	Excitatory:↑Ca2+
	Metabotropic subtypes	Inhibitory (presynaptic): ↓Ca2+ ↓cAMP Excitatory: ↓K+ ↑IP3 & DAG

* The doctor if I will write the questions I will choose the drugs, receptors and their action. Though the Female doctor didn't give it importance

Quiz

MCQ

1. A 72-year-old man is brought to his physician by his son. The son complains that this patient has been becoming forgetful, confused, moody, and aggressive over the past few months. One drug that may be used to treat this patient's symptoms is donepezil. Which of the following describes an effect of donepezil?
   (A) Decreases synaptic acetylcholine (B) Decreases synaptic dopamine
   (C) Decreases synaptic norepinephrine (D) Increases synaptic acetylcholine

2. A 48-year-old man with schizophrenia on thioridazine for 20 years develops bilateral facial and jaw movements and rhythmic motions of his tongue. Physical examination of the heart, lungs, and abdomen are unremarkable. What is the most likely aberration on a neurotransmitter level?
   (A) Acetylcholine (B) Dopamine
   (C) Serotonin (D) Norepinephrine

3. In patients with Parkinson's disease, histologic studies suggest an imbalance in brain neurotransmitters. In contrast to normal individuals, the patients with Parkinson's disease have an abundance of which of the following neurons and associated neurotransmitters?
   (A) Acetylcholine (B) Dopamine
   (C) Epinephrine (D) Norepinephrine

4. A 43-year-old man with depression who has been in and out of the psychiatric unit because of noncompliance with medications decides to take intranasal cocaine on a regular basis. He notes that he feels better and thinks that this helps his depression. Through which of the following mediators does this effect likely occur?
   (A) Dopamine (B) Epinephrine
   (C) Glutamine (D) Norepinephrine

5. Stimulation of inhibitory neurons causes which of the following effects at the postsynaptic membrane?
   (A) Binding of GABA at the postsynaptic membrane (B) Depolarization
   (C) Stimulation of epinephrine (D) Transient decrease in permeability of chloride

6. Five patients present to their primary care physician with various complaints and problems. Which of the following patients would have the most limited response to their symptoms if given a prescription for diazepam?
   (A) A 24-year-old woman with chronic pelvic pain
   (B) A 36-year-old man with chronic anxiety
   (C) A 42-year-old man with seizure disorder
   (D) A 45-year-old woman with seizure disorder
   (E) A 52-year-old man with spinal cord pain from an accident

Answers:

MCQ

Q1	D
Q2	B
Q3	A
Q4	A
Q5	A
Q6	A

Explanation please click here

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Good Luck , Future Doctors!

Team Leaders:

May Babaeer Zyad Aldosari

This Stunning Work Was Done By:

Nayef Alsaber
Hameed M. Humaid
Njoud Alabdullatif

Note takers:

Nouf Alshammari
Njoud Almutairi

Share with us your ideas !

"Your secret lecture-reviewer said that this is a magnificent lecture 10/10 best lecture ever I love the pharmacology team lol" - very secret lecture reviewer