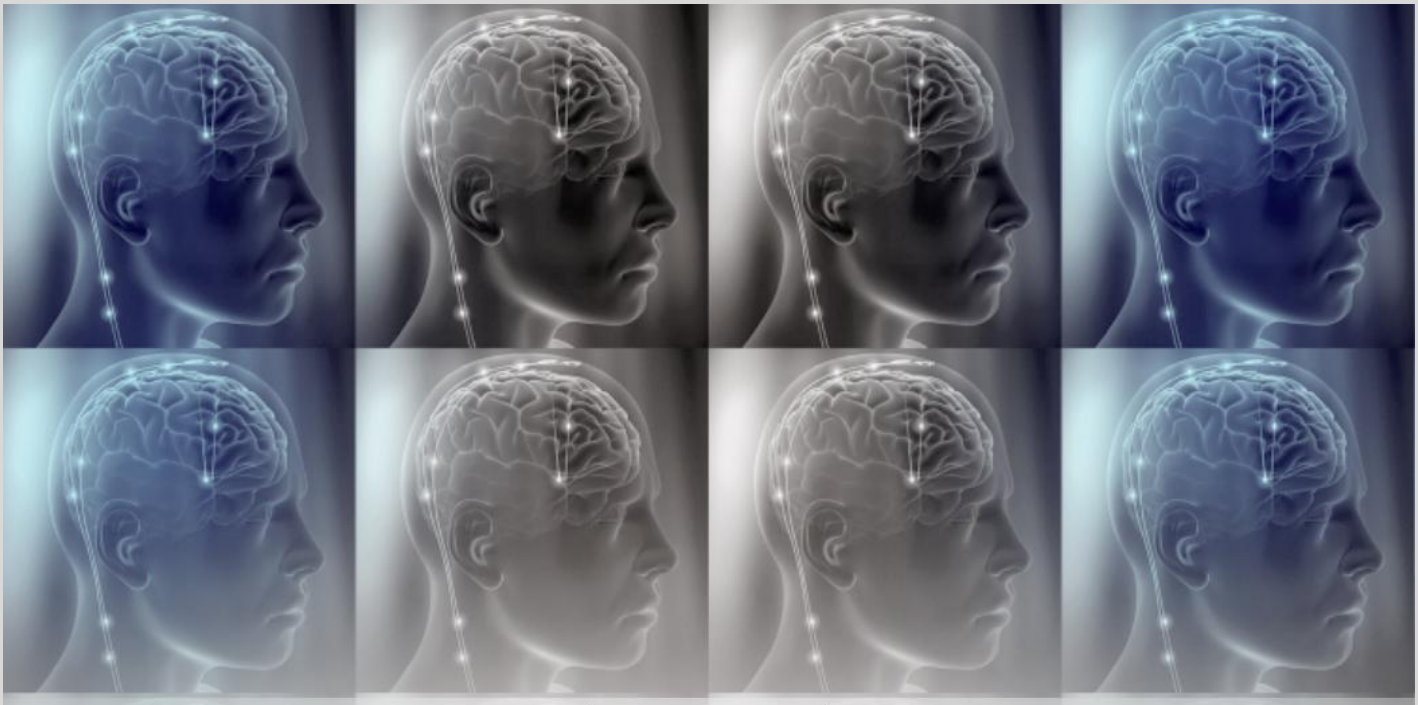


431

CNS Central Nervous System

Block

Physiology Team

	Female Side	Male side
Done By:	Rand AL-haweal	Abdulrahman Al-jadoa
Revised By:	Nour Al-Khawajah	Mohammed Asiri

CNS System Nervous central

Block

Slide No.(1)

NEUROTRANSMITTERS

Team Notes :

CNS Central Nervous System

Block

Slide No.(2)

NEUROTRANSMITTERS

DEFINITION:

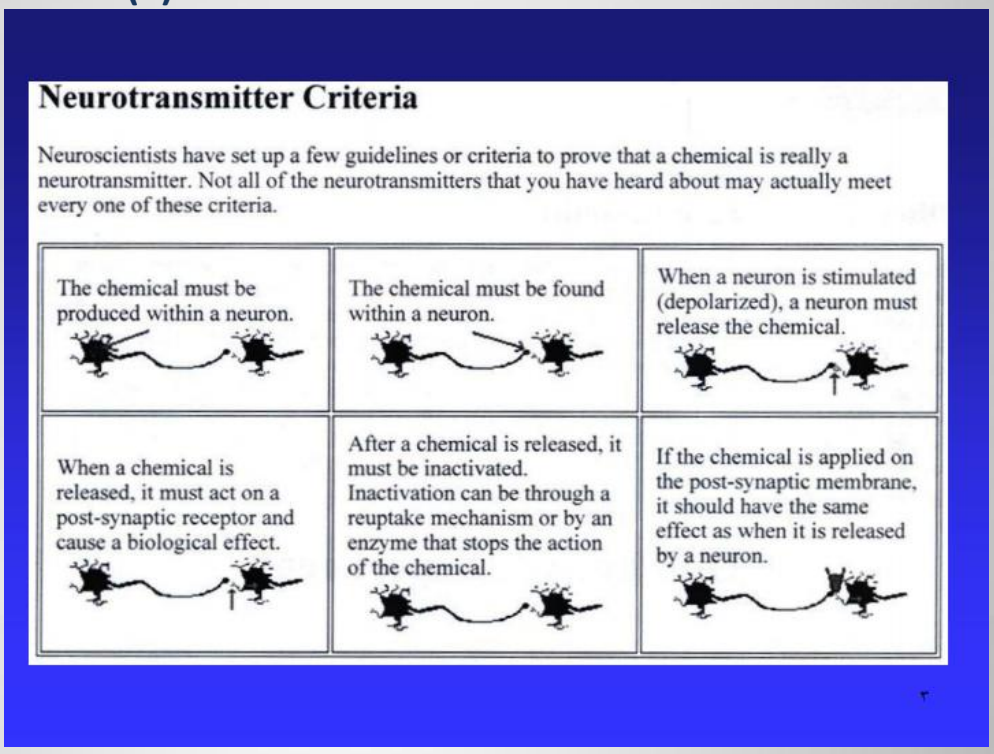
Are chemical substances released by electrical impulses into the synaptic cleft from synaptic vesicles of presynaptic membrane . It then diffuses to the postsynaptic membrane, binds to and activates the receptors present leading to initiation of new electrical signals or inhibition of the post-synaptic neuron.

Team Notes :

CNS Central Nervous System

Block

Slide No.(3)



Team Notes :

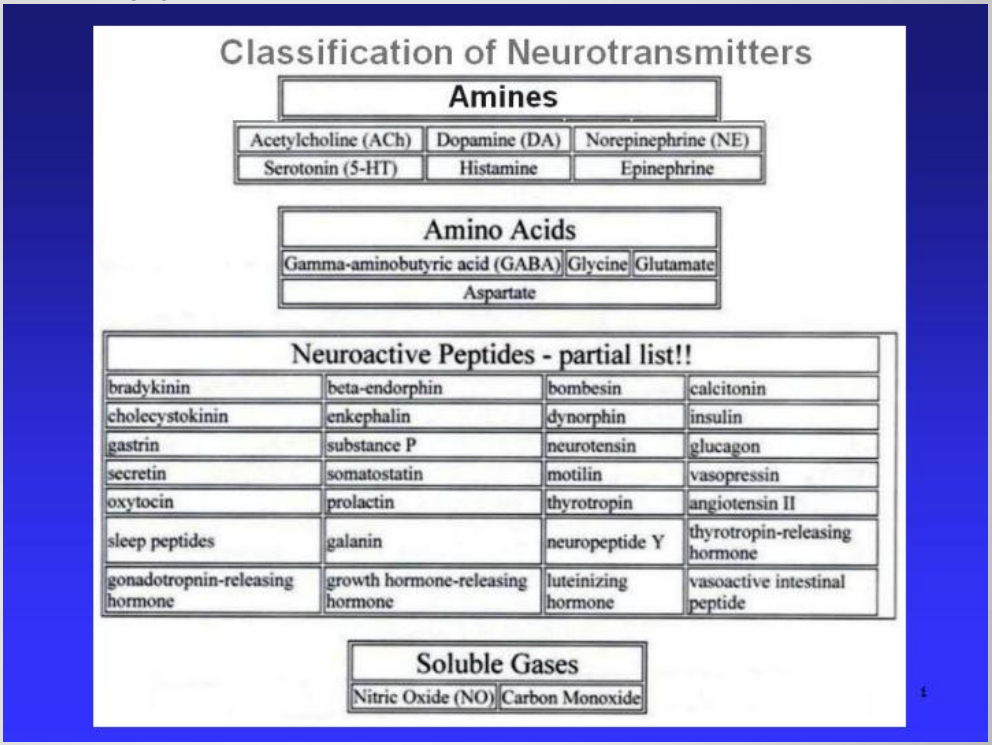
Neurotransmitter criteria:

1. Has to be produced within the neuron.
2. Found in the neuron.
3. Released when the neuron is stimulated (depolarized).
4. Act on the post-synaptic neuron (must work on a receptor not a channel.
5. After the neurotransmitter does its job, it is either goes throw degradation mechanism by enzyme or reuptake mechanism.

CNS Central Nervous System

Block

Slide No.(4)



Team Notes :

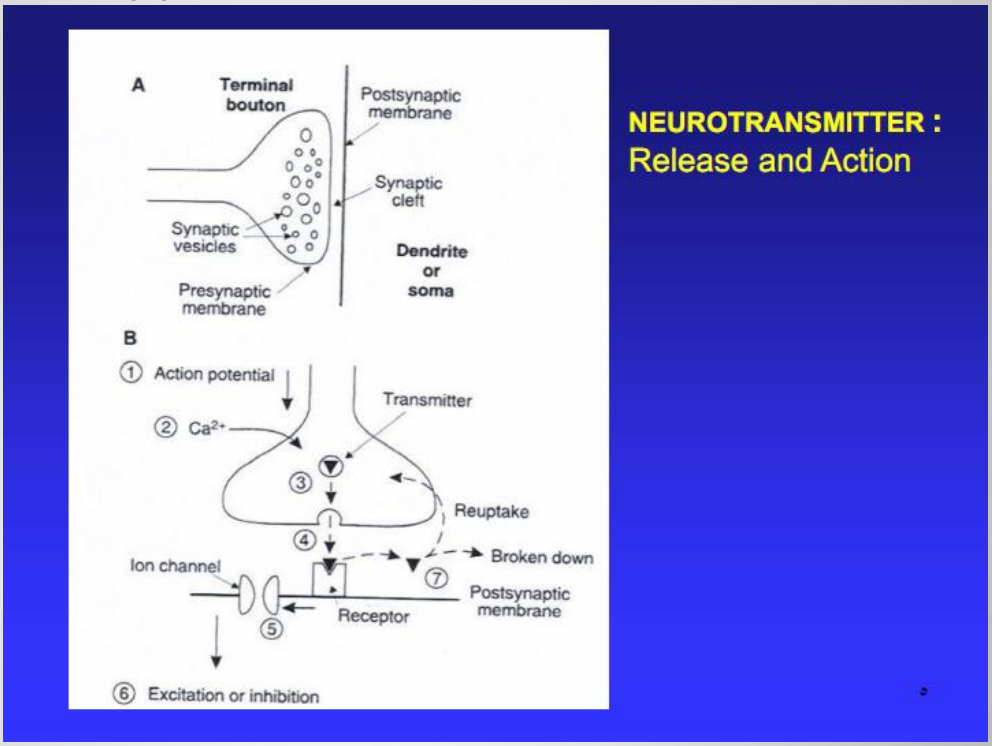
Main classification of neurotransmitter _based on chemical structure_:

- Amines → Acetylcholine, Dopamine, Noepinephrine, Epinephrine, Histamine and Serotonin.
- Amino acids → GABA, Glycine and Glutamate.
- Neuro-active peptides → it acts as neurotransmitters other than its main action. E.g. Prolactine is a hormone, Substance P is mediator but they work as neurotransmitters.
- Gases → Nitric Oxide and Carbone Monoxide(depress neurone).

CNS Central Nervous System

Block

Slide No.(5)



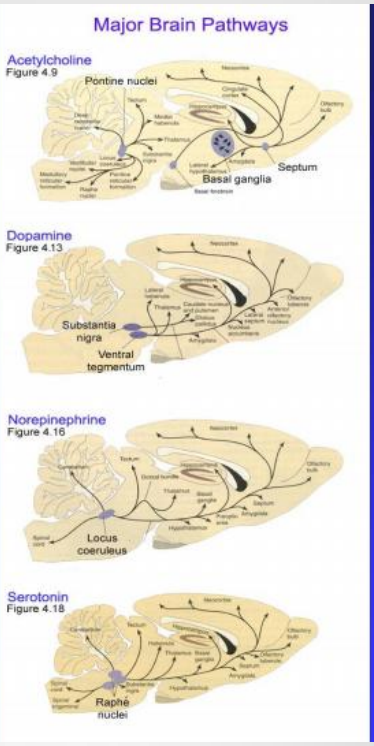
Team Notes :

When the signal comes, the neurotransmitter is released to the postsynaptic membrane and binds to its receptors and produces effect.

CNS Central Nervous System

Block

Slide No.(6)



Team Notes :

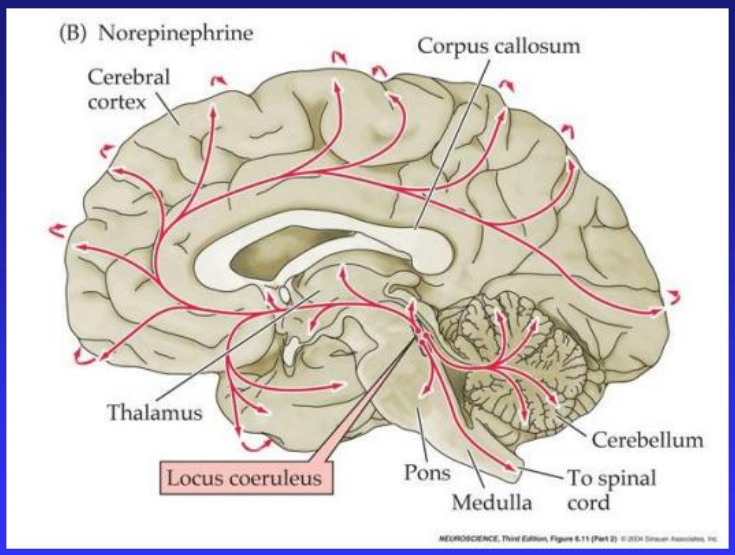
Major brain pathways (it is important in neuropsychiatry, to know which receptors to block or stimulate in psychiatry patients.):

- Cholinergic system. → Acetylcholine __ in the basal ganglia (cholinergic nuclei) excitatory system. → caudate nucleus.
- Dopaminergic system. → Dopamine __ in the basal ganglia (Dopaminergic nuclei) counteract the cholinergic system. → Substentia nigra.
- Adrenergic system. → Noepinephrine
- Serotonergic system. → serotonin

CNS central Nervous System

Block

Slide No.(7)



Team Notes :

Connectionof locus coeruleus is wide spread.

It secretes norepinephrine.

Activated in stress and fear conditions.

Make you more aroused and ready to act and move (like in fire alarm)

CNS central Nervous System

Block

Slide No.(8)

The Locus Coeruleus/Norepinephrine System

- Very wide-spread projection system
- LC is activated by stress and co-ordinates responses via projections to thalamus, cortex, hippocampus, amygdala, hypothalamus, autonomic brainstem centers, and the spinal cord
- Sleep: LC activity predicts changes in sleep/wake cycle.
- Attention/Vigilance: LC activated by novel stimuli, and LC activates EEG

Team Notes :

LC: Locus Coeruleus.

Vigilance: awake

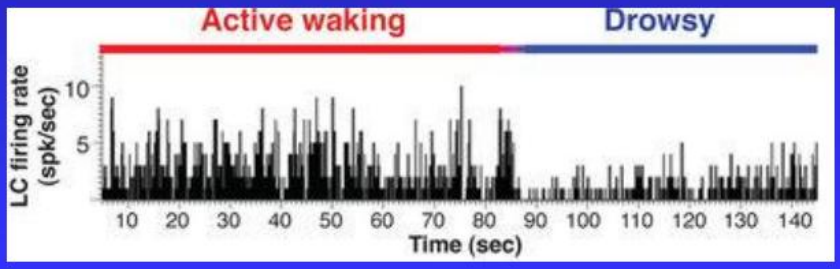
LC is decreased when sleeping, it is active when awaken and its stimulation is more in fear or stress.

CNS central Nervous System

Block

Slide No.(9)

Locus coeruleus neurons fire as a function of vigilance and arousal. They display a slow irregular firing during quiet wakefulness and a sustained activation if the subject is stressed or excited. Their firing decreases markedly during slow-wave sleep and virtually disappears during REM sleep



Team Notes :

CNS Central Nervous System

Block

Slide No.(10)

Norepinephrine (NE) Implicated in Stress-Related Disorders

- **Depression**
- **Withdrawal from some drugs of abuse:**

When opioid consumption is stopped, the increased activity of the locus coeruleus contributes to the symptoms of opiate withdrawal. The alpha2 adrenoceptor agonist " Clonidine" is used to counteract this withdrawal effect by decreasing adrenergic neurotransmission from the locus coeruleus

- **Other stress-related disorders such as panic disorder.**

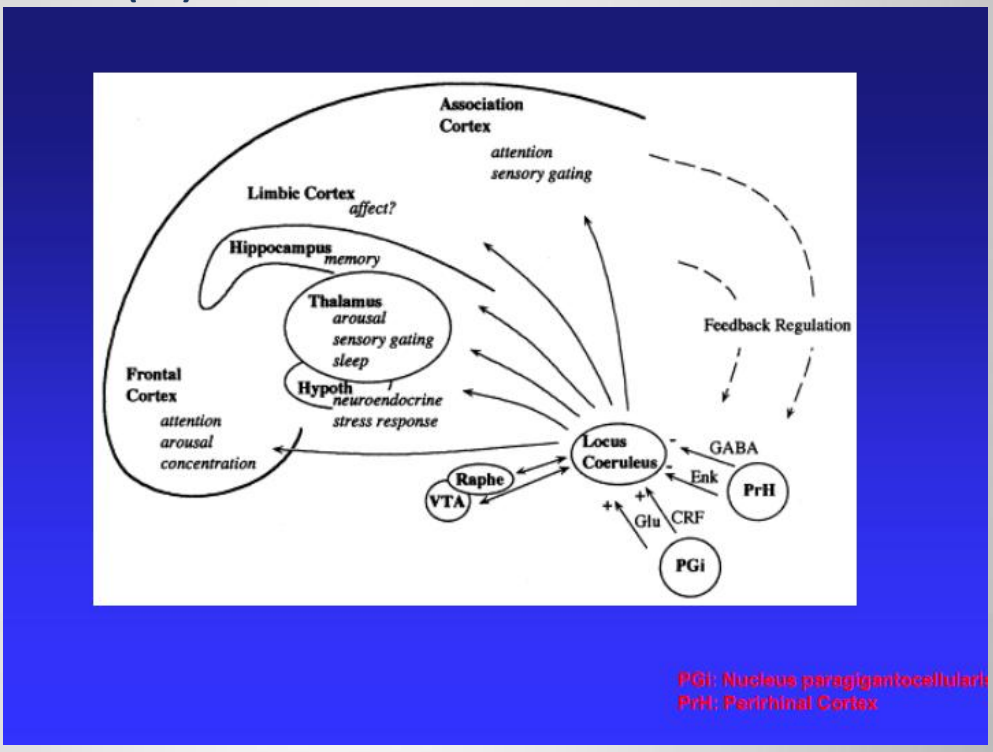
Team Notes :

Disorders in LC function

CNS central Nervous System

Block

Slide No.(11)



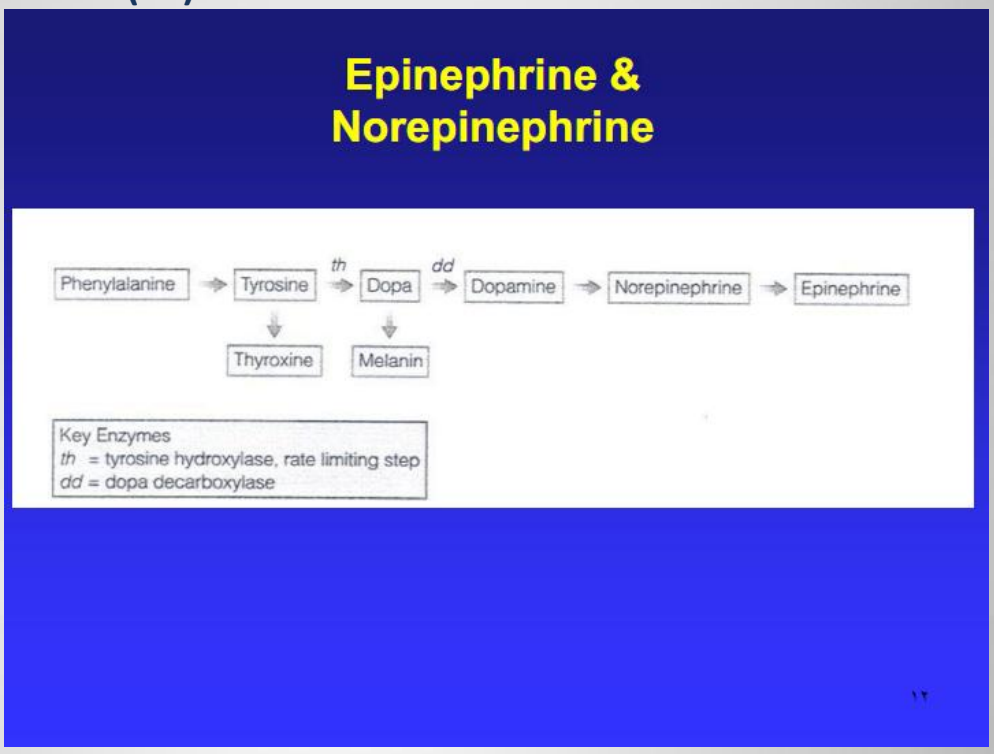
Team Notes :

LC connection + function

CNS Central Nervous System

Block

Slide No.(12)



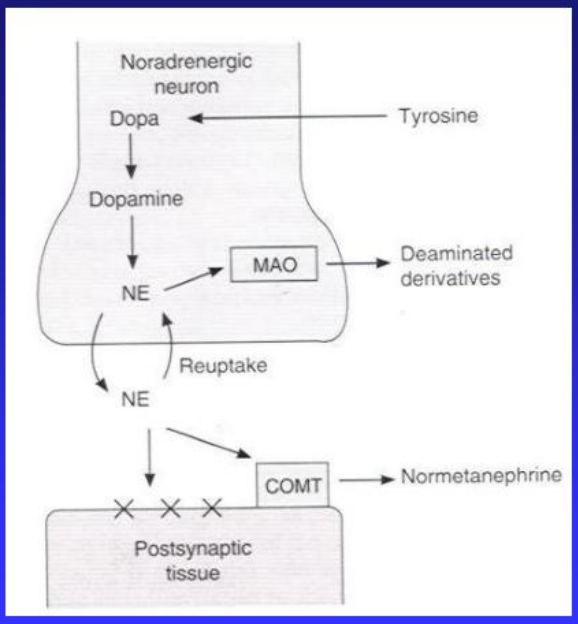
Team Notes :

Tyrosine is an important precursor for an important substances and neurotransmitters.

CNS central Nervous System

Block

Slide No.(13)



Norepinephrine synthesis and fate at synapses

Team Notes :

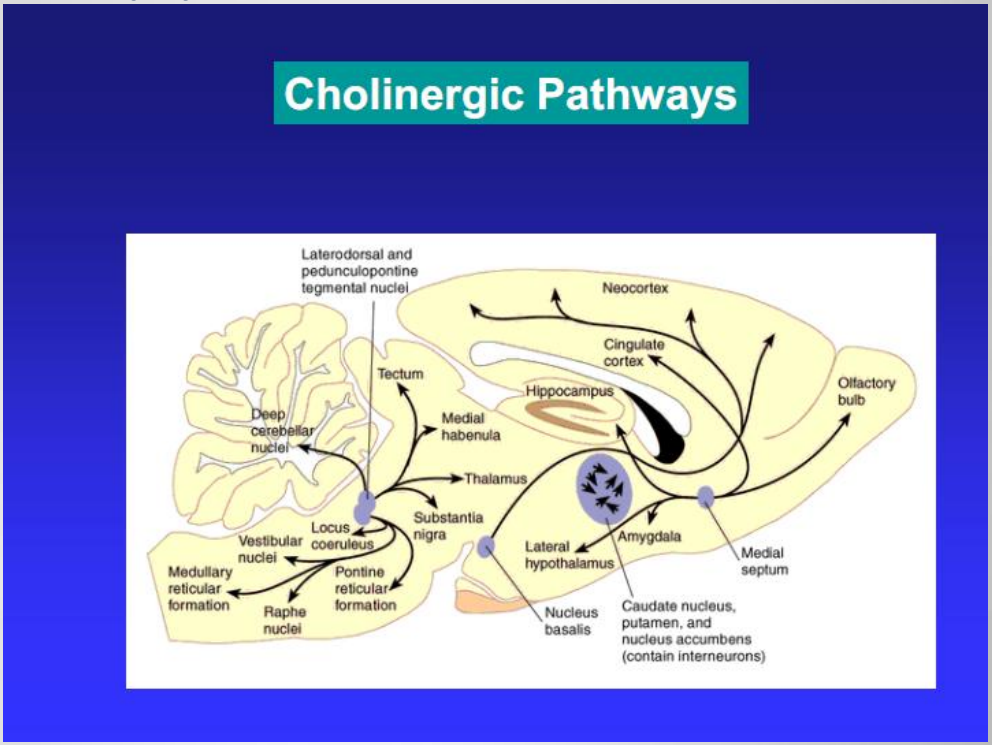
Mono Amino oxidase (MAO) is important because there are some drugs (e.g. hypertension drugs) that inhibit it there for they cause depression.

You should know the transmitter and the enzymes mentioned.

CNS Central Nervous System

Block

Slide No.(14)



Team Notes :

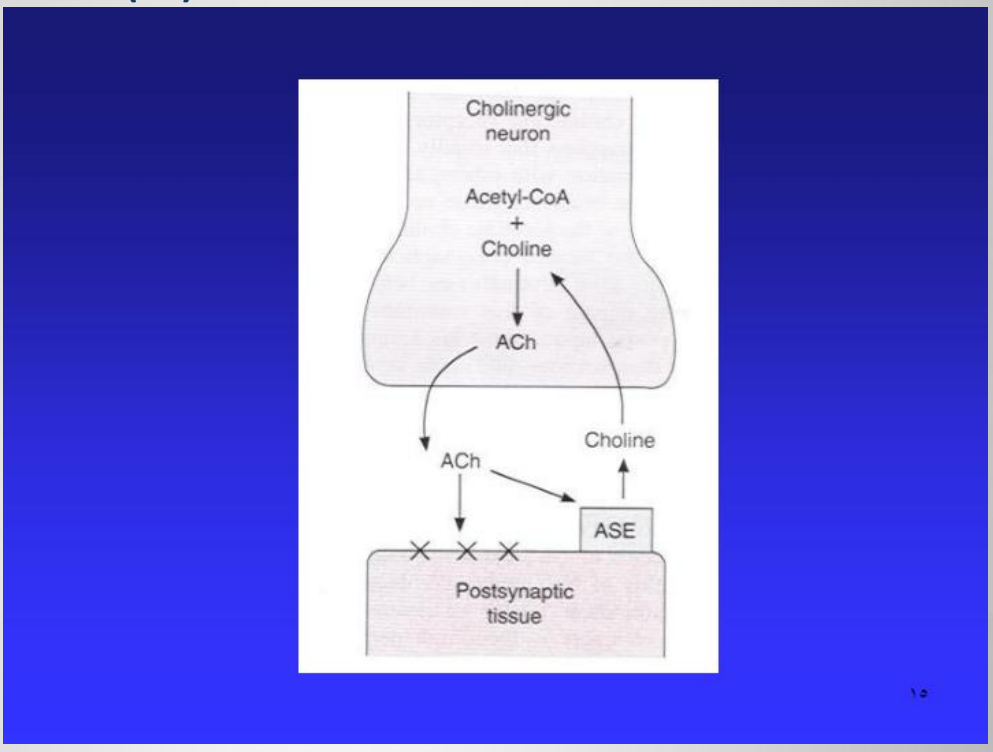
Caudate + putamen and nucleus accumbens are the heart of this bathway because they have cholinergic neurons (they secrete acetylcholine).

Goes to cortex, olfactory, hippocampus_ mostly for memory_ and other parts of the brain.

CNS Central Nervous System

Block

Slide No.(15)



Team Notes :

You should know the basics in this figure: neurotransmitter (ACh) and the enzymes (ASE= acetylcholinestrase)

CNS Central Nervous System

Block

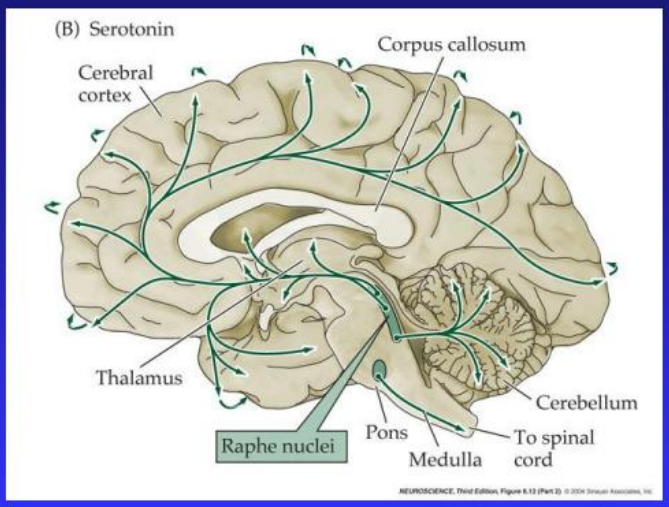
Slide No.(16)

Team Notes :

CNS central Nervous System

Block

Slide No.(17)



Team Notes :

Secreted from raphe nucleus.

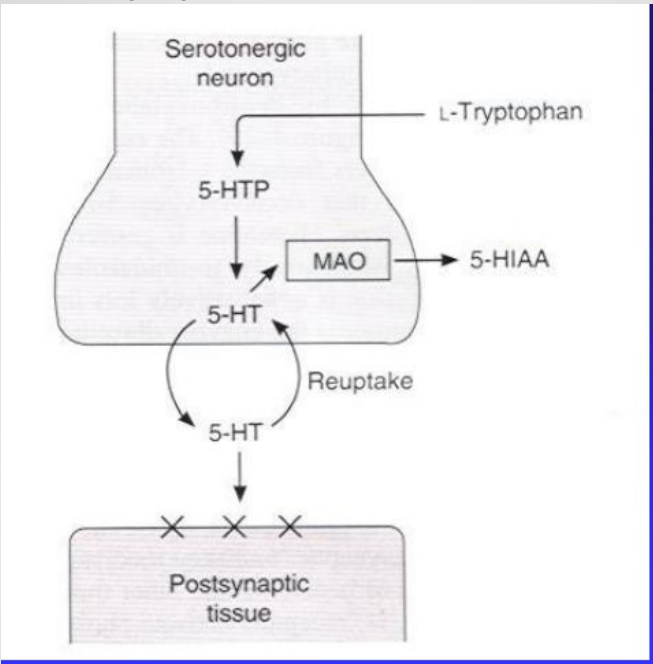
Most important functions of serotonin are: mood and sleep

If there is disorder in it, the patient will suffer from insomnia and depression.

CNS Central Nervous System

Block

Slide No.(18)



Formation of serotonin =5-HT
Hydroxy tryptamine
HIAA=hydroxyindoleacetic acid

Team Notes :

CNS Central Nervous System

Block

Slide No.(19)

Serotonin (5-HT) Disorders

- Depression
- Anxiety

Team Notes :

CNS central Nervous System

Block

Slide No.(20)

Dopaminergic Pathways

Dopamine is transmitted via three major pathways:

1- The first extends from the substantia nigra to the caudate nucleus-putamen (neostriatum) and is concerned with sensory stimuli and movement.

2- The second pathway projects from the ventral tegmentum to the mesolimbic forebrain and is thought to be associated with cognitive, reward and emotional behavior.

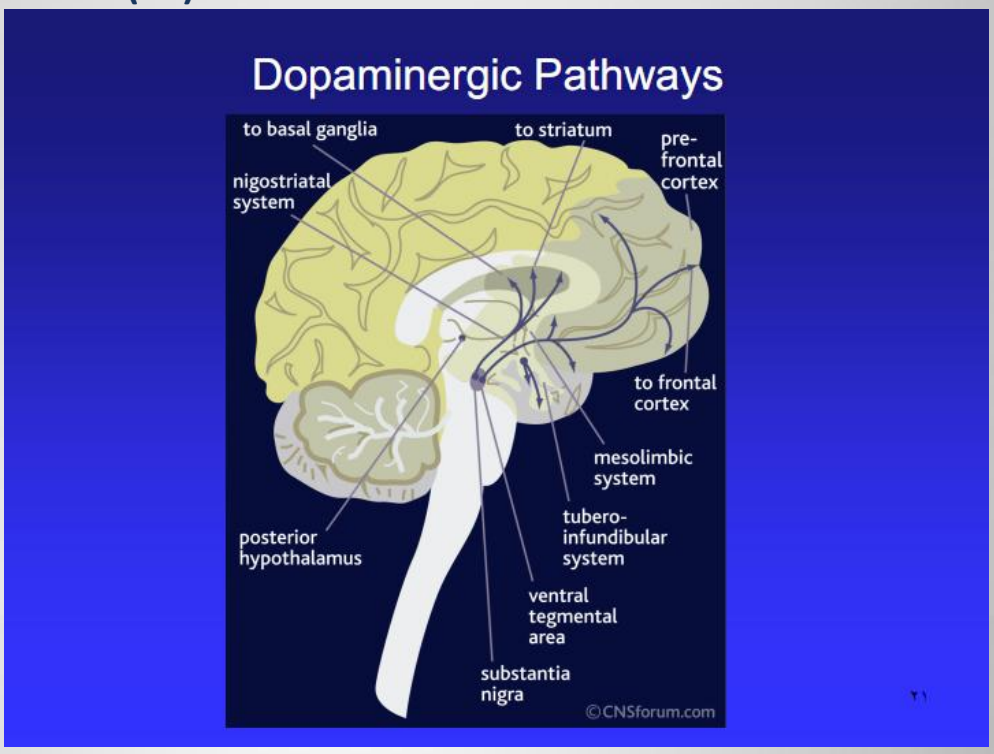
3- The third pathway, known as the tubero-infundibular system, is concerned with neuronal control of the hypothalmic-pituatory endocrine system.

Team Notes :

CNS central Nervous System

Block

Slide No.(21)



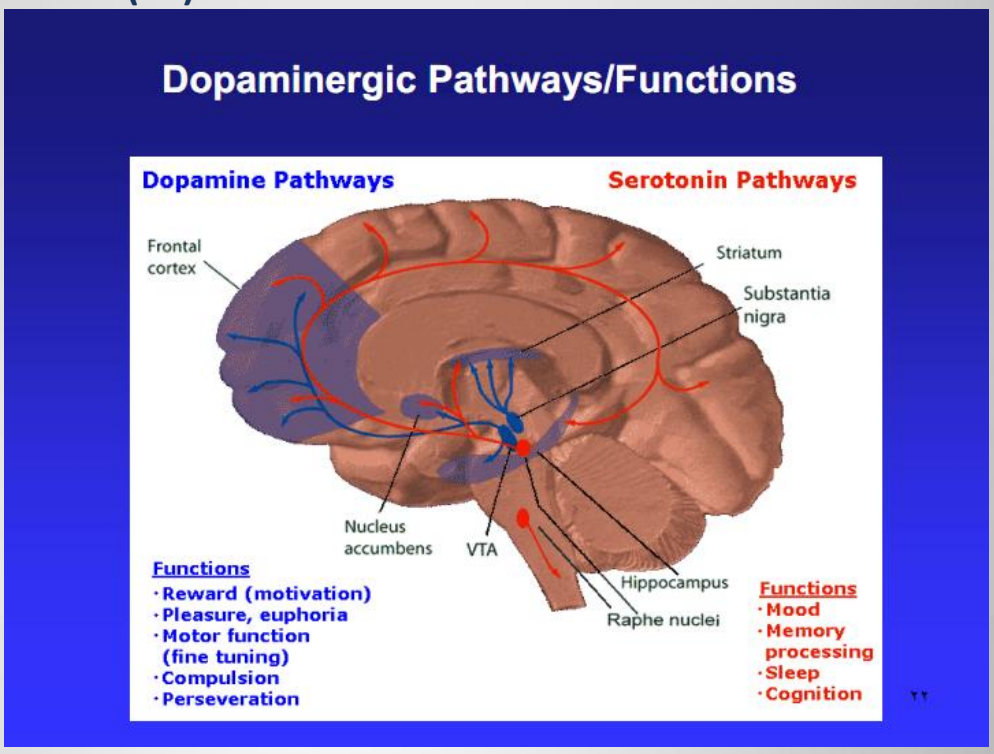
Team Notes :

Connection to prefrontal lobe, hypothalamus, straiatum and others.

CNS Central Nervous System

Block

Slide No.(22)

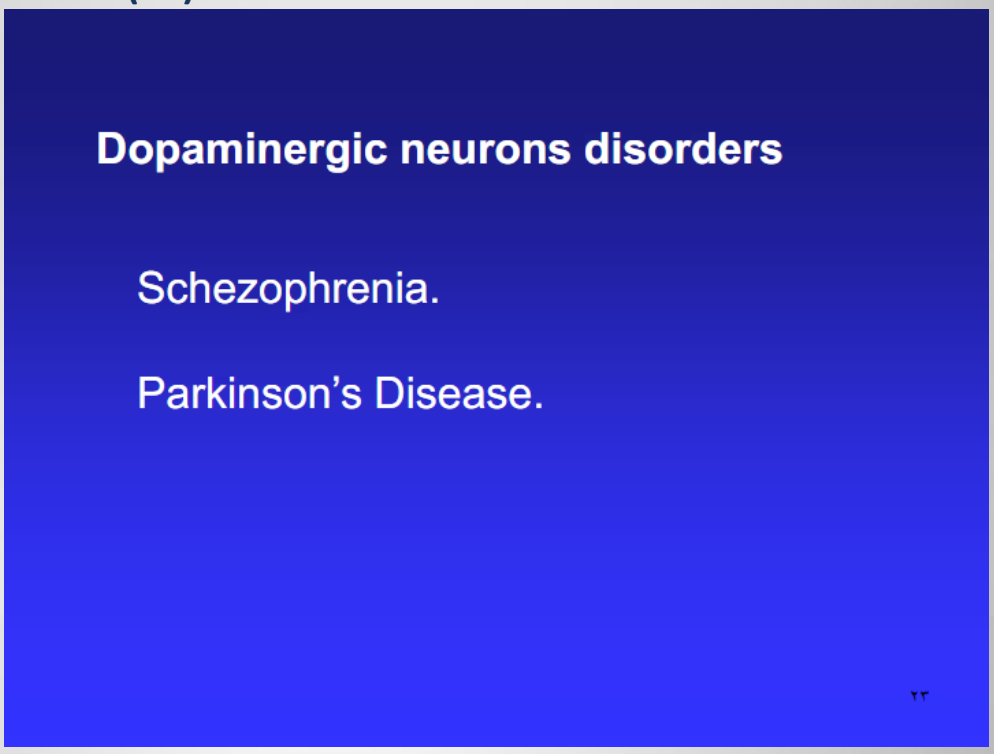


Team Notes :

CNS Central Nervous System

Block

Slide No.(23)



Team Notes :

CNS Central Nervous System

Block

Slide No.(24)

Histamine

- Histamine forming cells are in posterior hypothalamus also found in gastric mucosa and in mast cells.
- Formed by decarboxylation of amino acid histidine with the help of enzyme histaminase.
- Three known types of histamine receptors in found e.g. H_1, H_2, H_3.
- H_3 receptors are presynaptic. Its function in brain is not very certain. Its main function is that it is excitatory.

٢٤

Team Notes :

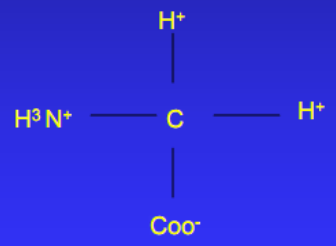
CNS Central Nervous System

Block

Slide No.(25)

Glycine

- It is simplest of all aminoacids, consisting of amino group and a carboxyl group attached to a carbon atom



٢٥

Team Notes :

CNS Central Nervous System

Block

Slide No.(26)

Glycine……..

- Its an inhibitory neurotransmitter.
- It binds to a receptor which makes the post synaptic membrane more permeable to Cl^- Ion and cause hyperpolarization (inhibition).
- The glycine receptor is primarily found in the ventral part of the spinal cord.
- Strychnine is glycine antagonist.

Team Notes :

Participate in pain transmetion___ refer to pain gait theories lec. No. 29_

CNS Central Nervous System

Block

Slide No.(27)

Glutamic acid

- It is the most commonly found neurotransmitter in the brain.
- It is always excitatory.
- Glutamate is formed during Kreb's cycle for α – ketoglutarate.
- Glutamate is carried into astrocytes where it is converted to glutamine and passed on to glutaminergic neurones.
- Glutamate is neurotoxic while glutamine is not.
- There are two types of receptors e.g. metabotropic and iontropic receptors.

٢٧

Team Notes :

Most commonly found excitatory neurotransmitter

It is excitatory so it could cause convulsions if it is not regulated well.

CNS Central Nervous System

Block

Slide No.(28)

Gamma Aminobutyric acid (GABA)

- Inhibitory neurotransmitter of CNS and is also found in retina.
- Formed by decarboxylation of glutamate.
- The enzyme that catalyzes this reaction is glutamate decarboxylase(GAD)
- Three types of GABA receptors e.g. $GABA_{A\ B\ \&\ C}$.
- $GABA_{A\ \&\ B}$ receptors are widely distributed in CNS.
- $GABA_C$ are found in retina only.
- $GABA_B$ are metabotropic (G-protein) in function.

Team Notes :

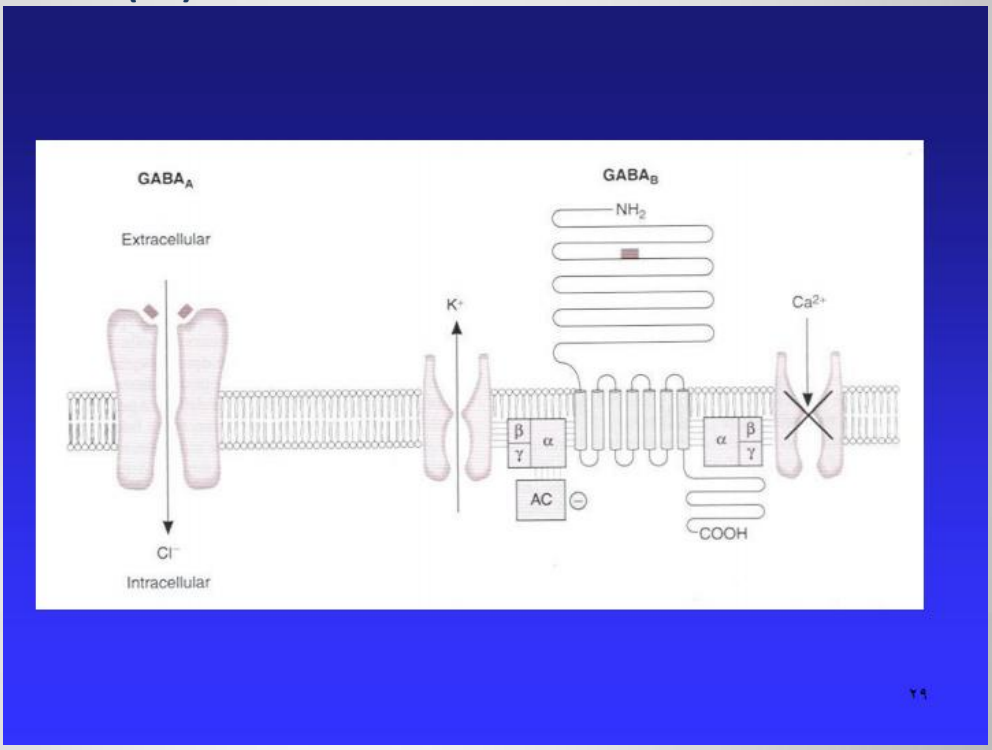
Inhibition in tow levels:

Central nervous system→ GABA
spinal cord level → Glycin

CNS System Nervous central

Block

Slide No.(29)



Team Notes :

CNS Central Nervous System

Block

Slide No.(30)

Neurotransmitter	Postsynaptic effect	Derived from	Site of synthesis	Postsynaptic receptor	Fate	Functions
1.Acetyl choline (Ach)	Excitatory	Acetyl co-A + Choline	Cholinergic nerve endings Cholinergic pathways of brainstem	1.Nicotinic 2.Muscarinic	Broken by acetyl cholinesterase	Cognitive functions e.g. memory Peripheral action e.g. cardiovascular system
2. Catecholamines i. Epinephrine (adrenaline)	Excitatory in some but inhibitory in other	Tyrosine produced in liver from phenylalanine	Adrenal medulla and some CNS cells	Excites both alpha α & beta β receptors	1.Catabolized to inactive product through COMT & MAO in liver 2.Reuptake into adrenergic nerve endings 3.Diffusion away from nerve endings to body fluid	For details refer ANS. e.g. fight or flight, on heart, BP, gastrointestinal activity etc. Norepinehrine controls attention & arousal, sleep/wake cycle.
ii.Norepinephrine	Excitatory	Tyrosine, found in pons. Reticular formation, locus coerules, thalamus, mid-brain	Begins inside axoplasm of adrenergic nerve ending is completed inside the secretary vesicles	α_1 α_2 β_1 β_2		
iii. Dopamine	Excitatory	Tyrosine	CNS, concentrated in basal ganglia and dopamine pathways e.g. nigrostriatal, mesocorticolimbic and tubero-hypophyseal pathway	D_1 to D_5 receptor	Same as above	Sensory motor Cognetive/emotional behavior Endocrine Hypothalamic Decreased dopamine in parkinson's disease. Increased dopamine concentration causes schizophrenia.

Team Notes :

Study this table.

The doctor asked "what happen if there is defect in one of the neurotransmitters" and the answer was to reverse the function. E.g. decrease in dopamine will cause parkinsonism.

CNS System Nervous central

Block

Slide No.(31)

Neurotransmitter	Postsynaptic effect	Derived from	Site of synthesis	Postsynaptic receptor	Fate	Functions
3. serotonin (5HT)	Excitatory	Tryptophan	CNS, Gut (chromaffin cells) Platelets & retina	5-HT_1 to 5-HT 7, 5-HT_2A receptor mediate platelet aggregation & smooth muscle contraction	Inactivated by MAO to form 5-hydroxyindoleacetic acid(5-HIAA) in pineal body it is converted to melatonin	Mood control, sleep, pain feeling, temperature, BP, & hormonal activity
4. Histamine	Excitatory	Histidine	Hypothalamus	Three types H_1, H_2, H_3 receptors found in peripheral tissues & the brain	Enzyme diamine oxidase (histaminase) cause breakdown	Arousal, pain threshold, blood pressure, blood flow control, gut secretion, allergic reaction (involved in sensation of itch)
5. Glutamate	Excitatory 75% of excitatory transmission in the brain	By reductive amination of Kreb's cycle intermediate α –ketoglutarate.	Brain & spinal cord e.g. hippocampus	Ionotropic and metabotropic receptors. Three types of ionotropic receptors e.g. NMDA, AMPA and kainate receptors.	It is cleared from the brain ECF by Na^+ dependent uptake system in neurons and neuroglia.	Long term potentiation involved in memory and learning by causing Ca^{++} influx.

٣١

Team Notes :

CNS Central Nervous System

Block

Slide No.(32)

Neurotransmitter	Postsynaptic effect	Derived from	Site of synthesis	Postsynaptic receptor	Fate	Functions
6. Aspartate	Excitatory	Acidic amines	Spinal cord	Spinal cord	Aspartate & Glycine form an excitatory / inhibitory pair in the ventral spinal cord	
7. Gama amino butyric acid(GABA)	Major inhibitory mediator	Decarboxylation of glutamate by glutamate decarboxylase (GAD) by GABAergic neuron.	CNS	GABA – A increases the Cl^- conductance, GABA – B is metabotropic works with G – protein GABA transaminase catalyzes. GABA – C found exclusively in the retina.	Metabolized by transamination to succinate in the citric acid cycle.	GABA – A causes hyperpolarization (inhibition) Anxiolytic drugs like benzodiazepine cause increase in Cl^- entry into the cell & cause soothing effects. GABA – B cause increase conductance of K^+ into the cell.
8. Glycine	Inhibitory	Is simple amino acid having amino group and a carboxyl group attached to a carbon atom	Spinal cord	Glycine receptor makes postsynaptic membrane more permeable to Cl^- ion.	Deactivated in the synapse by simple process of reabsorbtion by active transport back into the presynaptic membrane	Glycine is inhibitory transmitted found in the ventral spinal cord. It is inhibitory transmitter to Renshaw cells.

Team Notes :

CNS central Nervous System

Block

Slide No.(33)

Neurotransmitter Disorders

Neuro-transmitters	Precursor, enzymes	Receptors	Areas of concentration	Related disorders
Acetylcholine (Ach)	Choline, Choline-*O*-acetyltransferase	Nicotinic Muscarinic	Basal nucleus of Meynert, Limbic system, NM junctions, Parasympathetic neurons, Autonomic ganglia	Alzheimer disease, Myasthenia gravis, Botulism
Dopamine	Phenylalanine, Tyrosine hydroxylase DOPA decarboxylase	D1 D2 (main receptors) D3, D4, D5	Nigrostriatal pathway, Hypothalamus	Parkinson disease, Prolactinoma, Schizophrenia
Norepinephrine (NE)	Phenylalanine, Tyrosine hydroxylase Dopamine-β-hydroxylase	α-receptor β-receptor	Locus coeruleus, Lateral tegmental nuclei, Sympathetic ganglia	Sleep-wake cycle
Glutamate	α-Ketoglutarate, Glutamate dehydrogenase	NMDA, Kainate, AMPA	Cerebral cortex, Brainstem, Spinal cord, Hippocampus	Epilepsy, Migraine, Stroke
Gamma-aminobutyric acid (GABA)	Glutamate, Glutamic acid decarboxylase (GAD)	$GABA_A$ $GABA_B$	Striatonigral system, Cerebellum, Hippocampus, Cerebral cortex	Sleep, Epilepsy Anxiety
Glycine	Serine		Spinal cord, Brainstem	Tetanus, Strychnine poisoning
Serotonin	Tryptophan, Tryptophan hydroxylase		Raphe nuclei	Levels of arousal, Pain modulation, Migraine, Depression

Team Notes :

IMPORTANT TABLE

CNS Central Nervous System

Block

Slide No.(34)

RECEPTORS DYSFUNCTION

1. Presynaptic effect

i) Botulinum toxin: Its an exotoxin that binds to the presynaptic membrane and prevents the release of Ach resulting in weakness and reduction of tone. It is used to control dystonia in which body shows overactive muscular activity.

٣٤

Team Notes :

CNS Central Nervous System

Block

Slide No.(35)

2. Effects at Postsynaptic level:

i) Curare binds to the acetylcholine receptor (AchR) and prevents Ach from acting on it and so that it induces paralysis.

ii) Myasthenia gravis: is caused by an antibody against the Ach receptors and Ach receptors are reduced hence the Ach released has few Ach receptor available to work and patients complain of weakness that increases with exercise.

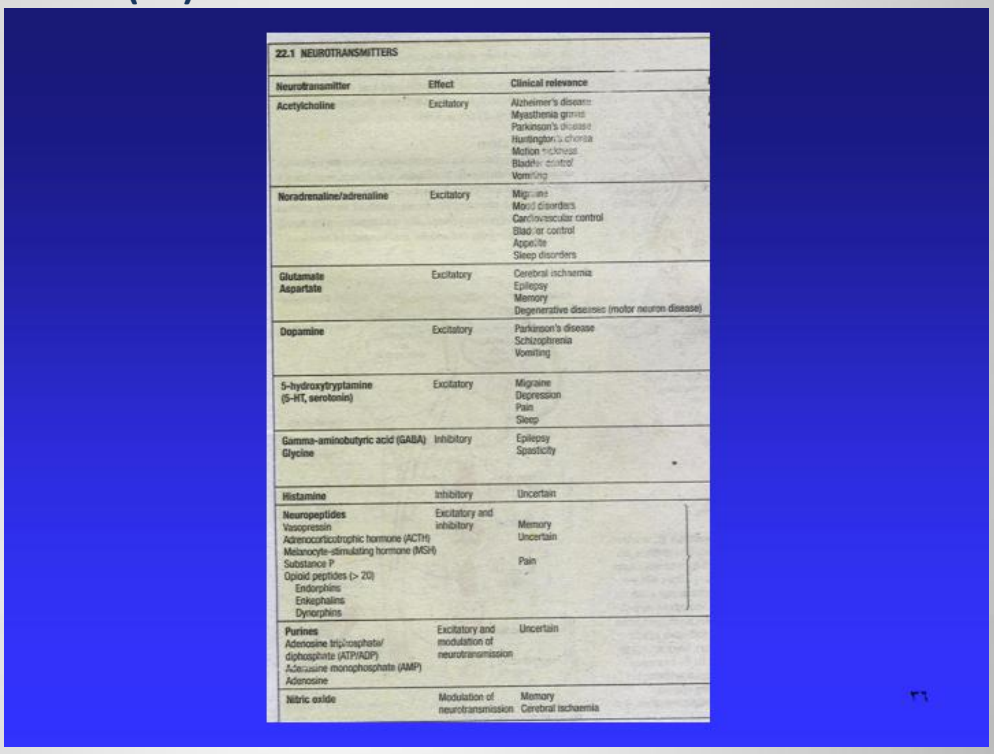
٣٥

Team Notes :

CNS Central Nervous System

Block

Slide No.(36)



22.1 NEUROTRANSMITTERS

Neurotransmitter	Effect	Clinical relevance
Acetylcholine	Excitatory	Alzheimer's disease Myasthenia gravis Parkinson's disease Huntington's chorea Motion sickness Bladder control Vomiting
Noradrenaline/adrenaline	Excitatory	Migraine Mood disorders Cardiovascular control Bladder control Appetite Sleep disorders
Glutamate Aspartate	Excitatory	Cerebral ischaemia Epilepsy Memory Degenerative diseases (motor neuron disease)
Dopamine	Excitatory	Parkinson's disease Schizophrenia Vomiting
5-hydroxytryptamine (5-HT, serotonin)	Excitatory	Migraine Depression Pain Sleep
Gamma-aminobutyric acid (GABA) Glycine	Inhibitory	Epilepsy Spasticity
Histamine	Inhibitory	Uncertain
Neuropeptides Vasopressin Adrenocorticotrophic hormone (ACTH) Melanocyte-stimulating hormone (MSH) Substance P Opioid peptides (> 20) Endorphins Enkephalins Dynorphins	Excitatory and inhibitory	Memory Uncertain Pain
Purines Adenosine triphosphate/ diphosphate (ATP/ADP) Adenosine monophosphate (AMP) Adenosine	Excitatory and modulation of neurotransmission	Uncertain
Nitric oxide	Modulation of neurotransmission	Memory Cerebral ischaemia

Team Notes :

CNS Central Nervous System

Block

1) GABA is a neurotransmitter, which is:

a. Inhibitory at spinal cord level.
b. Excitatory at spinal cord level.
c. Inhibitory at brain level.
d. Excitatory at brain level.

2) the most common excitatory neurotransmitter is:

a. Glycine.
b. Glutamate.
c. Serotonin
d. Histamine.

3) In Parkinson's disease there is decreased level in:

a. Serotonin.
b. Glycine.
c. Dopamine.
d. Acetylcholine

4) Which of the following areas is considered the major source of brain norepinephrine:

a. Locus cereuleus
b. Basal forebrain
c. Walls of the lateral ventricles
d. Ventral tegmental erea

C, B, C, A

CNS central Nervous System

Block

5) Damage of central cholinergic neurons occurs in which of the following diseases:

a. Anxiety
b. Hypertension
c. Alzheimer
d. Discriminated sclerosis

6) Decrease brain serotonin level is found in association with which of the following condition:

a. Hullocination
b. Depression
c. Involuntary movement of facial muscles
d. Feeling of unexplained excessive confidence and well-being

7) Which of the following is NOT a major class of neurotransmitters?

a. Pituitary hormones
b. Amino acids
c. Neuropeptides
d. Biogenic amines

8) which of the following transmitters is involved in the awakening action of reticular activating system(RAS):

a. GABA
b. Histamine
c. Endorphin
d. Norepinephrine

C, B, A, D