

Brain Neurotransmitters

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● Objectives

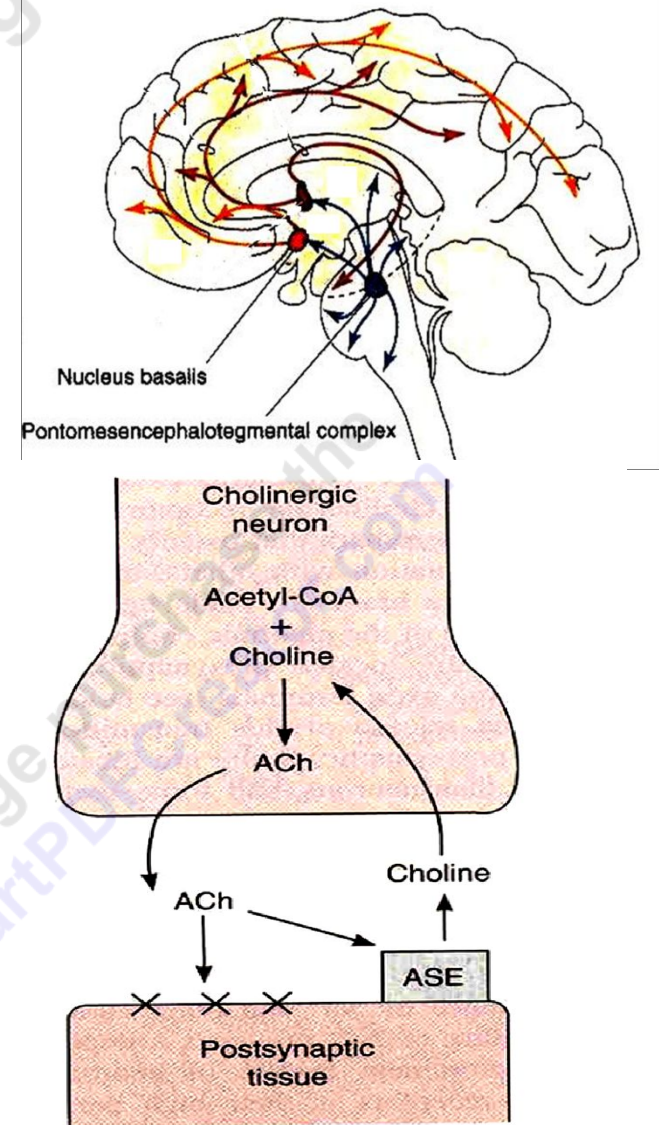
- At the end of this lecture the student should be able to describe the following brain neurotransmitter systems and their functions :
- Acetylcholine (Ach) .
- Norepinephrine (NE) .
- Dopamine (DA)
- Glutamate .
- GABA .
- Serotonin .

Reference Book

- Ganong's Review of Medical Physiology , 23rd edition . Barrett KE, Barman SM, Boitano S, Brooks HL , editors . McGraw Hill, Boston 2010 .
- Pages 129 - 147

Acetylcholine (Ach)

- In the brain , ACh is found in →
- (1) the Basal Forebrain (mainly Nucleus Basalis) , and
- (2) Ponto-Mesencephalic Cholinergic Complex
- Synthesis of ACh involves the reaction between Choline & Acetyl-CoA .
- After being released , ACh is rapidly hydrolyzed into Choline and Acetate by the action of the enzyme Acetylcholinesterase .
- ACh receptors of both types (i.e., nicotinic & muscarinic) are present in large numbers in the brain



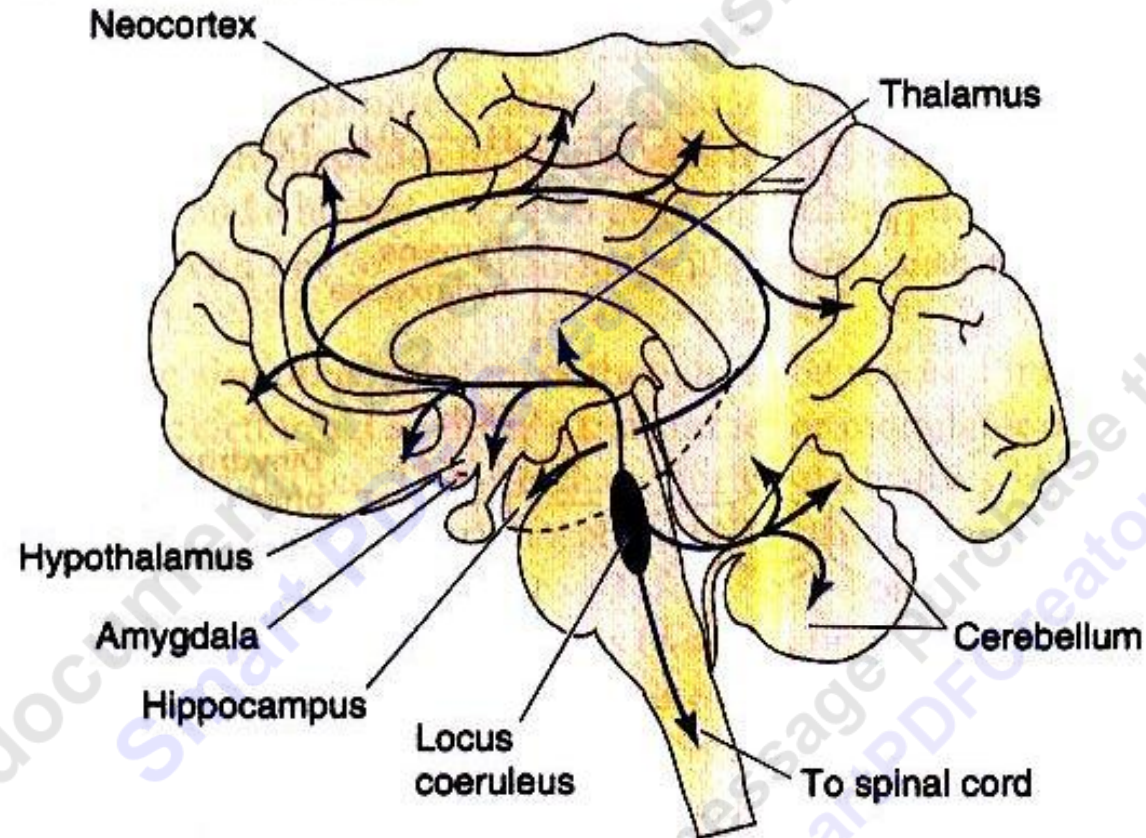
- Functions : The brain Cholinergic (Ach) system is concerned with
 - (1) Consciousness ,wakefulness/sleep states
 - (2) Learning & Memory
- Defects in the brain cholinergic system are associated with loss of memory (dementia) , such as occurs in Alzheimer's disease

Norepinephrine & Epinephrine

(Noradrenaline & Adrenaline)

Formation of Catecholamines

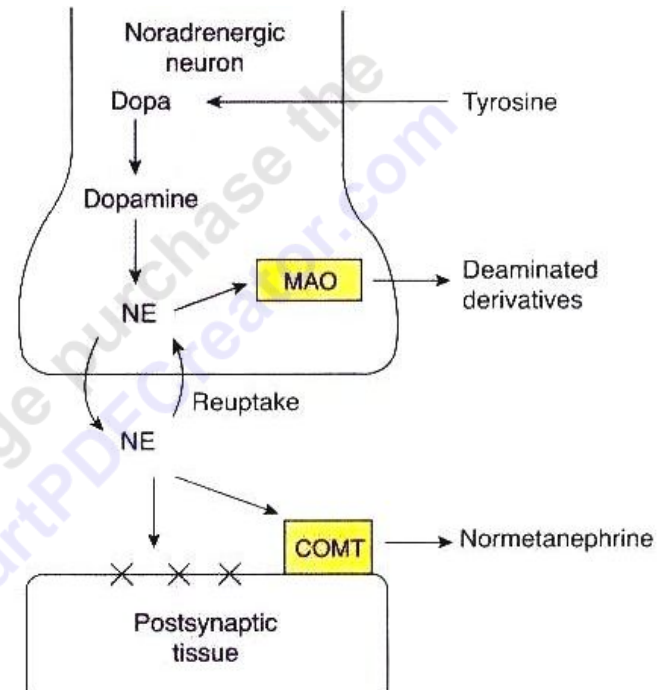
A NOREPINEPHRINE



- The three Catecholamines (Norepinephrine , epinephrine and dopamine) are formed from the amino acid Tyrosine .
- The cell-bodies of Noradrenergic neurons are located in mainly in the Locus Cereulus.
- From the Locus Cereulus the axons of noradrenergic neurons arborize widely , constituting the Locus Cereulus System .

Catabolism of Catecholamines

- After binding to receptors , NE is either
- 1/ re-uptaken into the presynaptic neuron
→ then intracellularly degraded by the enzyme **Monoamine Oxidase (MAO)** (which s located in the cytoplasm of the presynaptic neuron)
- or
- 2/ extracellular inactivaation by the enzyme **Catechol-O-Methyl Transferase (COMT)** (which is bound/ attached to postsynaptic membrane
- (COMT is not present inside the prsynaptic neuron)
- The first mechanism (re-uptake & intracellular degradation by MAO) is the major mechanism of inactivation of NE .

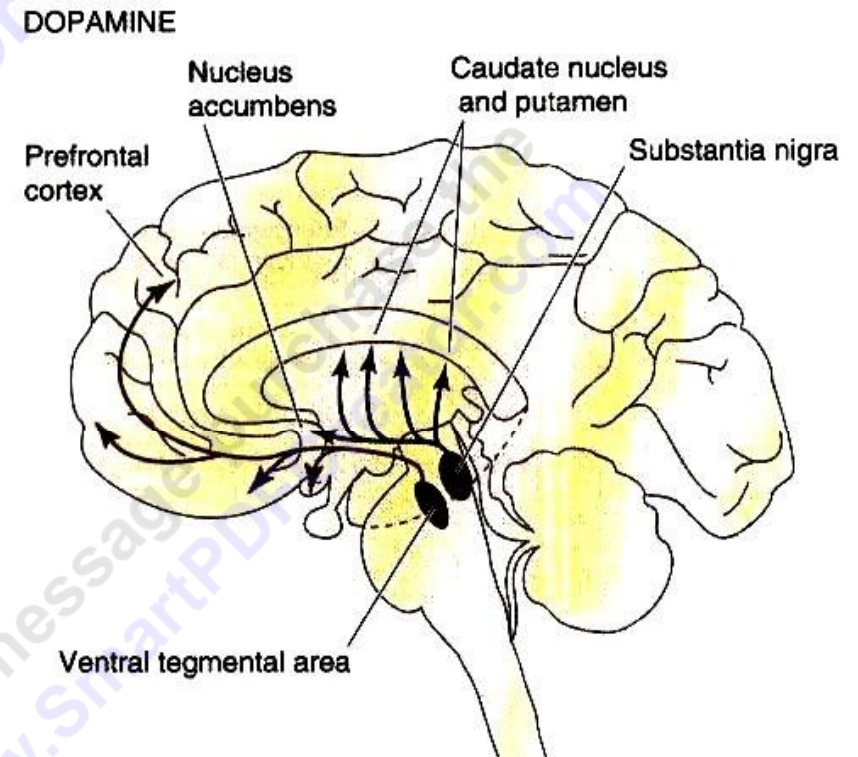


- Functions : of the Brain NE System

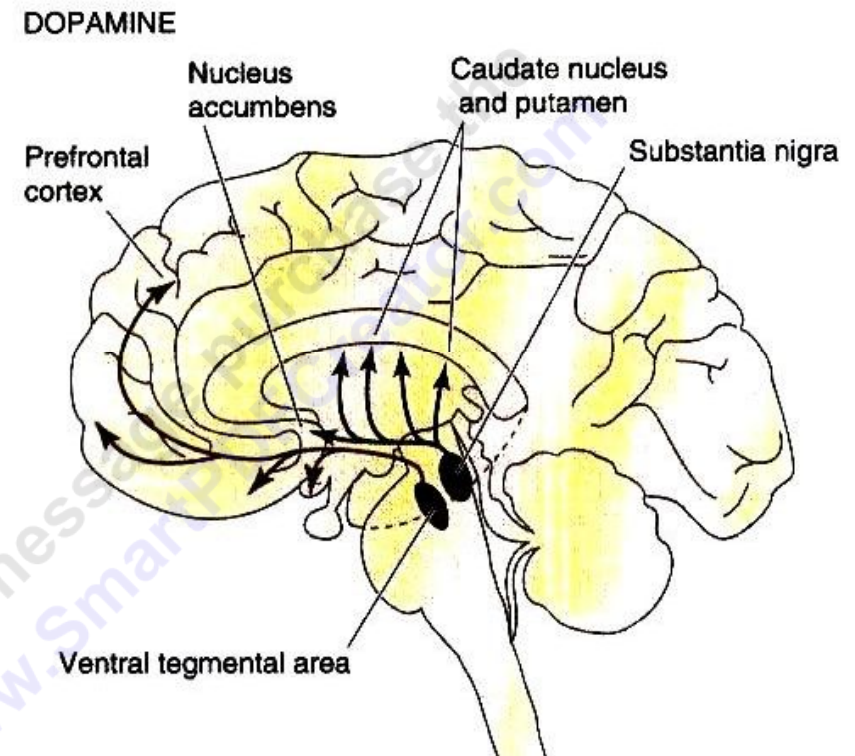
- (1) It constitutes part of the RAS (alertness)
+ plays role in →
- (2) fight-flight situations , including competitive athletic behavior , and aggressive behavior .
- (3) Norepinephrine and Serotonin deficiencies are implicated in pathogenesis of depression

Dopamine (DA)

- Similar to NE , DA is metabolized by MAO and COMT .
- In the brain , dopaminergic neurons comprise →
- (A) Nigrostriatal System :
- Dopaminergic fibers originate in Substantia Nigra and project to the Striatum (part of Basal Ganglia) .
- This system is involved in motor control .
- Dopamine deficiency in the Basal Ganglia is associated with Parkinsonism



- (B) Mesocortical System :
- Here dopaminergic fibers arise from the Ventral Tegmental Area (VTA) , and projects to Nucleus Accumbens and Limbic System
- The Mesocortical System is involved in behaviors of Pleasure , Reward , and Addiction .
- Overstimulation of Dopaminergic receptors leads to Schizophrenia-like psychotic symptoms .



Glutamate

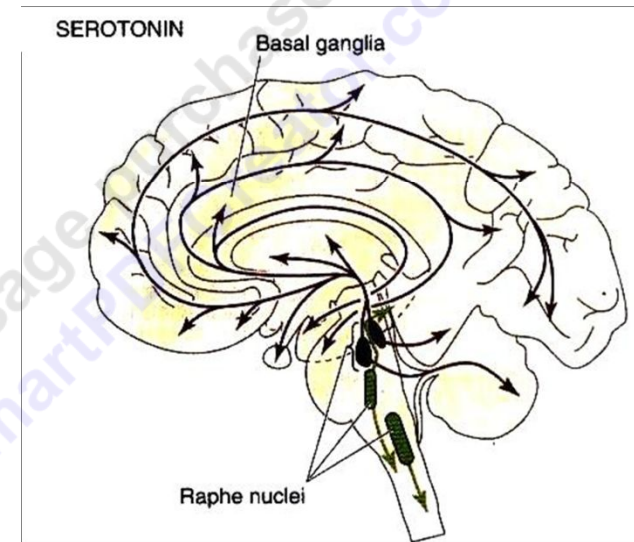
- Glutamic acid , beside being the major excitatory amino acid in the brain , is also involved in Long-Term Potentiation (LTP) & memory storage .
- Role in Disease :
- Excessive glutamate activity is implicated in epilepsy , stroke , multiple sclerosis and Alzheimer's disease.

GABA

- GABA is a major inhibitory amino acid transmitter in the brain .
- Drugs such as Diazepam (Valium) potentiate the inhibitory action of GABA on its receptors .
- Hence Diazepam is used in medicine as →
 - (1) anxiolytic (anti-anxiety) /sedative drug .
 - (2) muscle relaxant drug , and
 - (3) Anticonvulsants drug .

Serotonin

- Serotonin is formed in the brainstem **Raphe Nuclei** , and from there fibers spread to different brain areas .
- One of its important physiological functions is induction of sleep during the normal everyday Wake-Sleep cycle .
- Decreased serotonin activity causes depression .
- Increased serotonin activity can induce hallucinations .



- Thanks .

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