Lecture 4

Pharmacology of central Neurotransmitters

Objectives

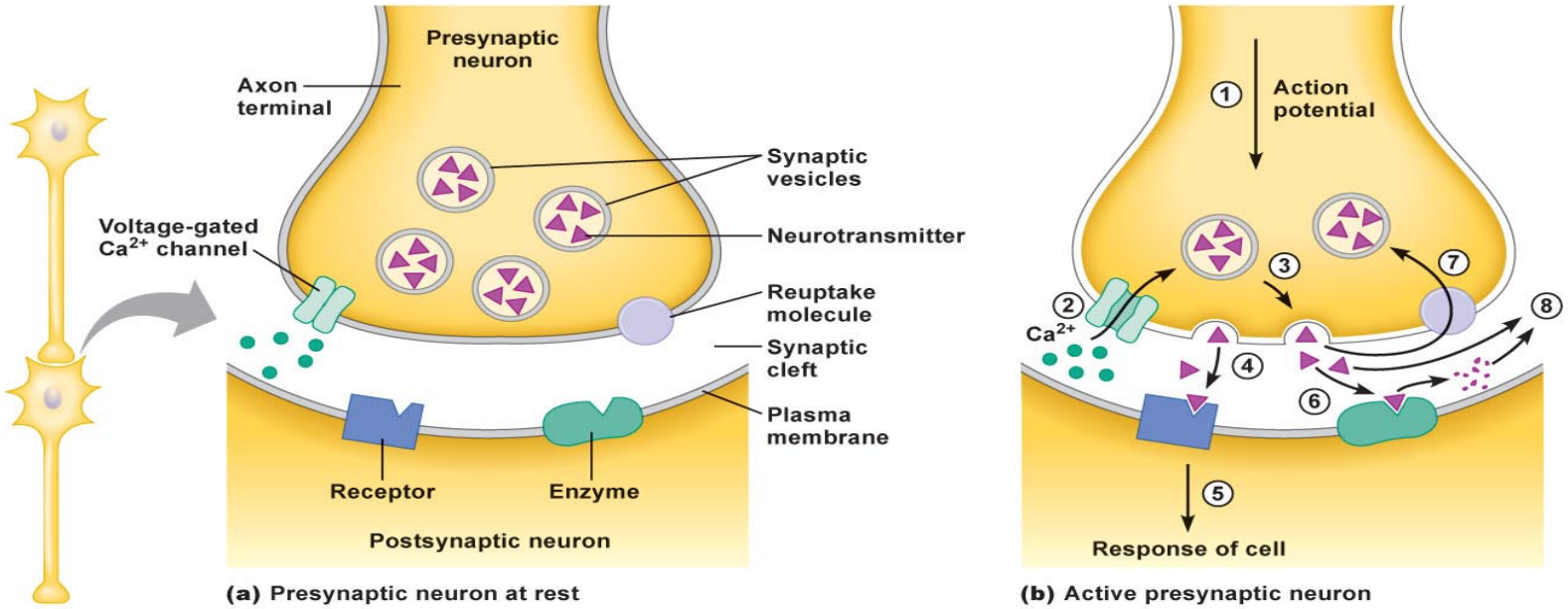
The main objective of this lecture is to understand the role of neurotransmitters in the etiology and treatment of CNS diseases.

- Additional Notes
- Important
- Explanation –Extra-

Neurotransmitters:

- Endogenous chemicals that transmit signals from a neuron to a target cell across a synapse.
- They're packed into synaptic vesicles under the membrane in the axon terminal, on the presynaptic side.
- They are released into & diffuse across the synaptic cleft to bind to a specific receptors on the post synaptic side.

A membrane action potential arriving at the terminal opens axonal Ca channels; Ca inflow releases neurotransmitter molecules from many vesicles by fusing the vesicle membranes to the nerve terminal membrane. Membrane fusion generates an opening through which the molecules are expelled into the synaptic cleft via exocytosis



Axon terminal , transporter, voltage gated Ca++ channel , The neurotransmitter-receptor interaction must be terminated quickly to allow rapid, repeated activation of receptors. One of the following can happen to neurotransmitters that have interacted with receptors:

- They can be quickly pumped back into the presynaptic nerve terminals by active, ATP-dependent processes (reuptake).
- They can be destroyed by enzymes near the receptors.
- They can diffuse into the surrounding area and be removed.

Neurotransmitters taken up by the nerve terminals are repackaged in vesicles for reuse.

Neuropsychopharmacological science seeks to :

- Understand how drugs can affect the CNS selectively to relieve pain, improve attention, induce sleep, reduce appetite, suppress disordered movements ….ect.
- 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.

Examples of neurotransmitters:

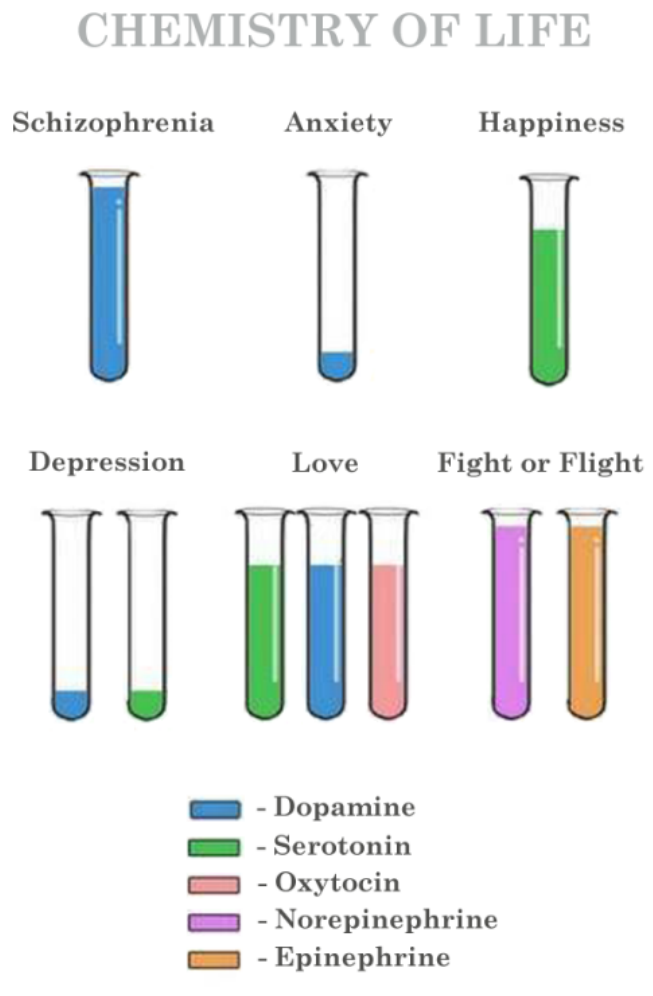
- Amino acids:

  Glutamate (Glu), gamma aminobutryic acid (GABA)
- Monoamines & other biogenic amines:

  Dopamine (DA), Norepinephrine (NE), Serotonin (5-HT)
- Peptides:

  Somatostatin
- Others:

  Acetylcholine (Ach)



	Norepinephrine (NE)	Serotonin (5-HT)	Dopamine
disorders	**↑NE:** Mania. - Rx: Drugs that decrease NE. **↓NE:** Depression. -Rx: Drugs that increase NE.	– Depression – Social phobia – Obsessive Compulsive Disorders – Generalized Anxiety – Schizophrenia Vomiting	– Parkinson's disease – attention deficit hyperactivity disorder(ADHD) – Schizophrenia – Depression – drug addiction
notes		Primarily found in the CNS , GIT, platelets, ….. It is a popular thought that serotonin is responsible for feeling of well-being & happiness. Serotonin plays an important role : in regulation of: Mood ,sleep, appetite and pain perception.	Blockade of postsynaptic dopamine R: 1- In **CTZ:** antiemetic effect. 2- In **Mesolimbic system**: schizophrenia. 3- In **Nigrostriatal system**: parkinsonism. 4- In **Tuberoinfundibular**: hyperprolactinemia.

	Acetylcholine	Glutamic acid	GABA
disorders	– Damage to cholinergic receptors (muscarinic) is associated with memory deficits as in Alzheimer's disease. – Muscarinic antagonists as hyoscine cause amnesia. – Increased brain level of Ach predispose to Parkinson's disease. – Schizophrenia may be due to imbalance between Ach & dopamine brain levels. – Depression may be a manifestation of a central cholinergic predominance.	An increase in its level predispose to epilepsy	Decrease GABA brain content is associated with : – Epilepsy – Anxiety – Convulsions – Insomnia
notes	– Acetylcholine, the first neurotransmitter discovered – Inside the brain Ach functions as a neuro-modulator—a chemical that alters the way other brain structures process information rather than a chemical used to transmit information from point to point – Ach is excitatory. **Role:** cognitive functions such as : Memory, Arousal, Attention	- is an excitatory neurotransmitte -therapeutic effect of glutamate antagonists: – Reduction of brain damage following strokes & head injury – **Treatment of epilepsy** – Drug dependence – Schizophrenia	– is the main inhibitory transmitter in the brain – Present throughout the brain; there is very little in peripheral tissues

Norepinephrine (NE)

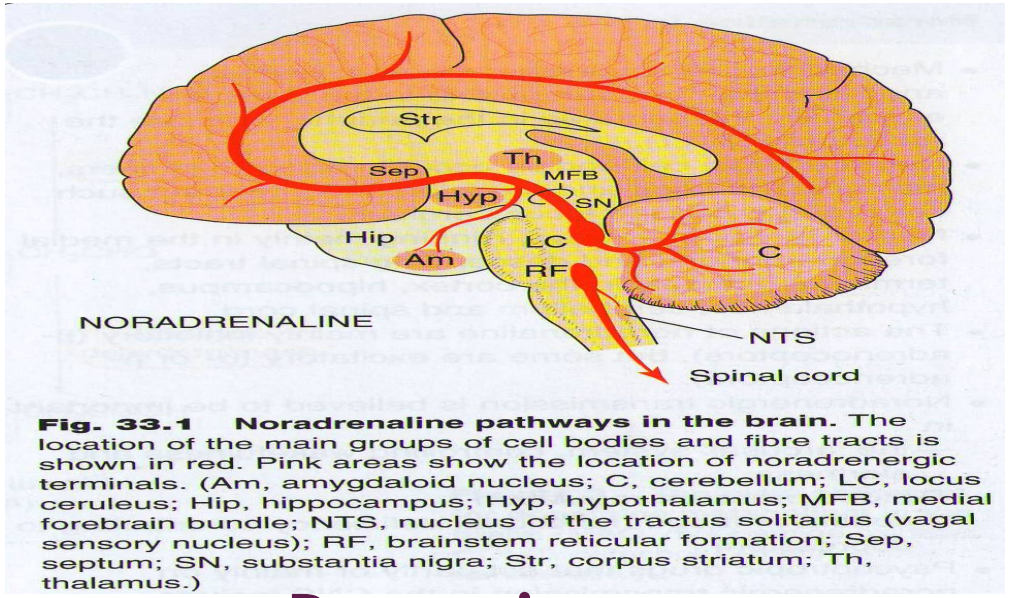


Fig. 33.1 Noradrenaline pathways in the brain. The location of the main groups of cell bodies and fibre tracts is shown in red. Pink areas show the location of noradrenergic terminals. (Am, amygdaloid nucleus; C, cerebellum; LC, locus ceruleus; Hip, hippocampus; Hyp, hypothalamus; MFB, medial forebrain bundle; NTS, nucleus of the tractus solitarius (vagal sensory nucleus); RF, brainstem reticular formation; Sep, septum; SN, substantia nigra; Str, corpus striatum; Th, thalamus.)

Serotonin (5-HT)

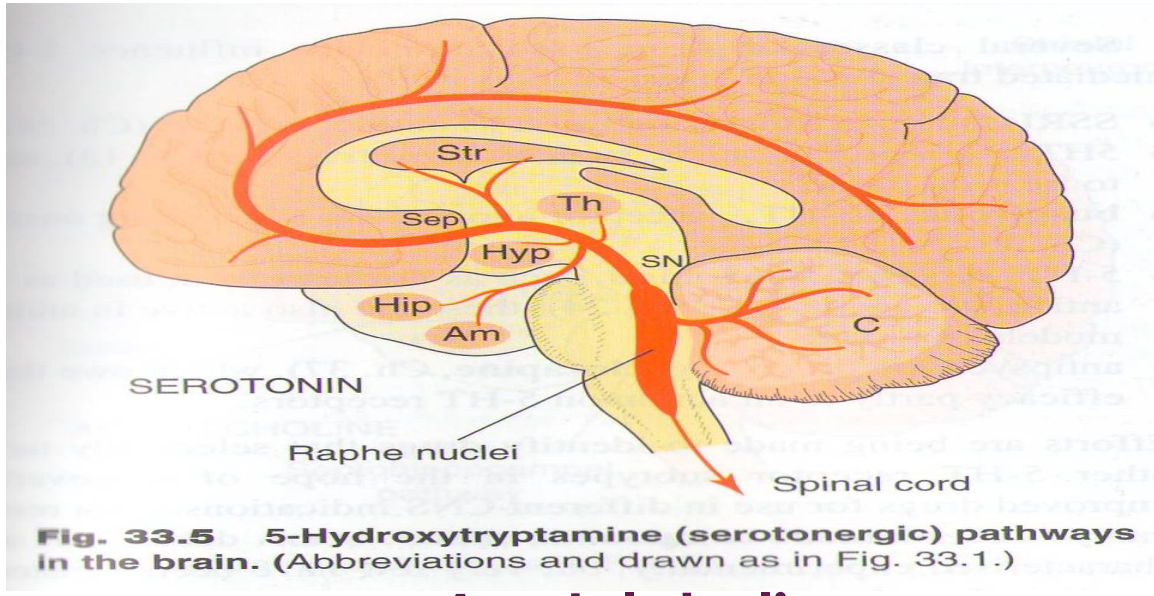


Fig. 33.5 5-Hydroxytryptamine (serotonergic) pathways in the brain. (Abbreviations and drawn as in Fig. 33.1.)

Dopamine

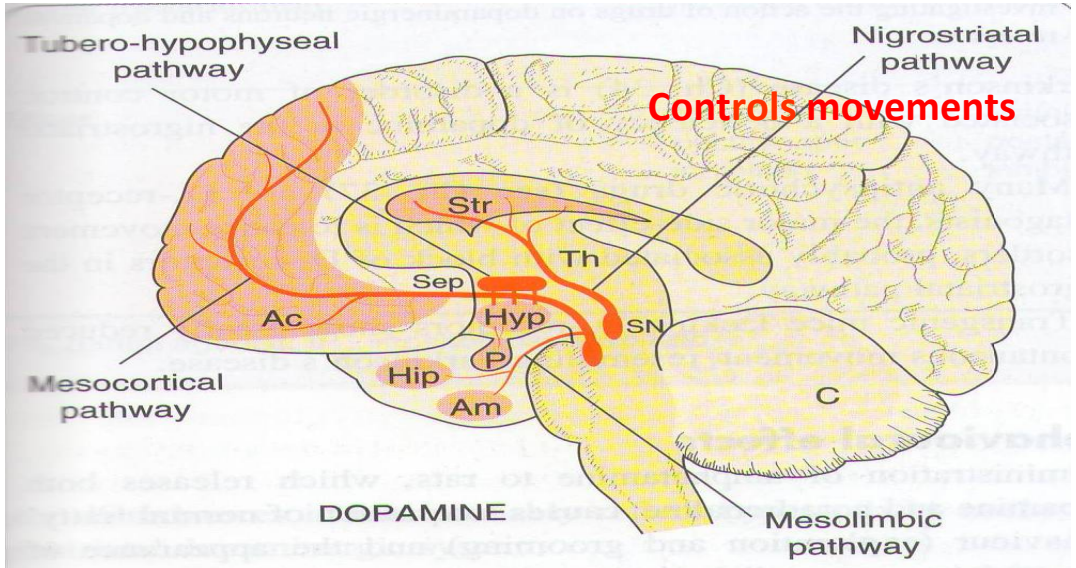


Fig. 33.3 Dopamine pathways in the brain (drawn as in Fig. 33.1). The pituitary gland (P) is shown, innervated with dopaminergic fibres from the hypothalamus. (Ac, nucleus accumbens; other abbreviations as in Fig. 33.1.)

Acetylcholine

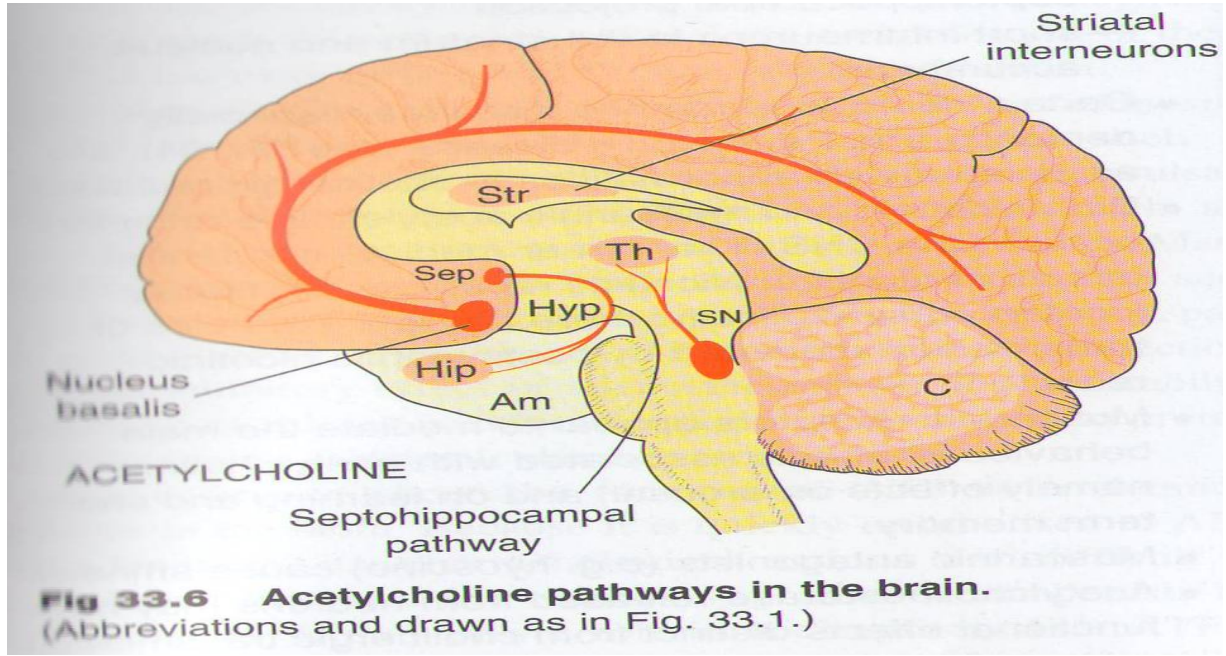
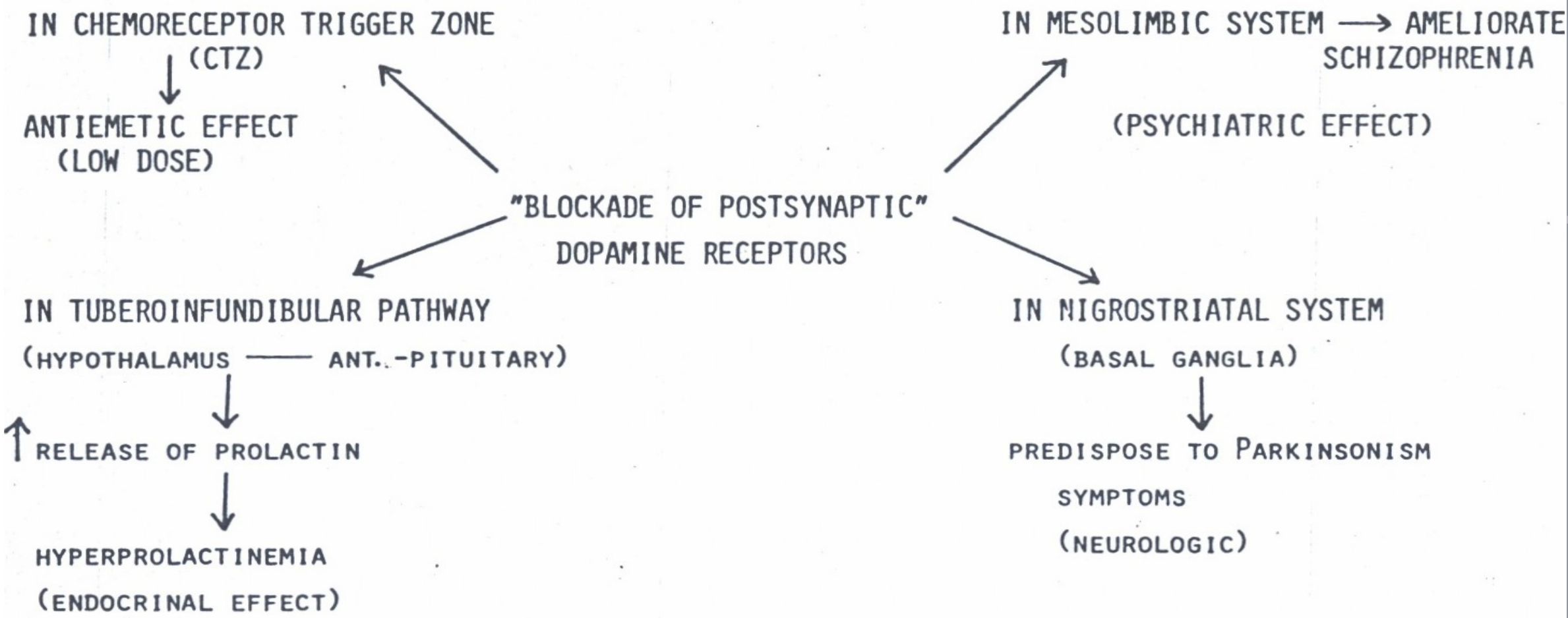


Fig 33.6 Acetylcholine pathways in the brain. (Abbreviations and drawn as in Fig. 33.1.)

EFFECTS ON DOPAMINERGIC SYNAPSES



THE SAME PHARMACODYNAMIC ACTION MAY HAVE DISTINCT PSYCHIATRIC "NEUROLOGIC" AND ENDOCRINE EFFECTS.

Good luck!

Done by Pharmacology team 434

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For any correction, suggestion or any useful information do not hesitate to contact us: Pharmacology434@gmail.com