

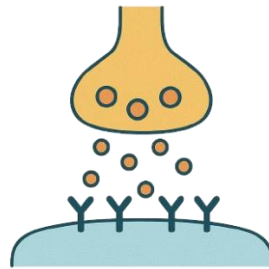
Cholinergic Neurotransmitter

Cholinergic Neurotransmitters

Definition

- Cholinergic neurotransmitters refer specifically to **acetylcholine (ACh)**, a key chemical messenger used by certain neurons to communicate with each other or with muscle cells.
- These neurons are called **cholinergic neurons** because they release acetylcholine as their primary neurotransmitter.

CHOLINERGIC NEUROTRANSMITTERS



Function and Importance

Acetylcholine is involved in various physiological functions depending on where in the body it's acting:

- In the Central Nervous System (CNS):** It's important for learning, memory, attention, and arousal.
- In the Peripheral Nervous System (PNS):**
 - In the somatic nervous system, it stimulates skeletal muscle contraction.
 - In the autonomic nervous system, it:
 - Acts on all preganglionic neurons (both sympathetic and parasympathetic).
 - Acts on postganglionic parasympathetic neurons.
 - In a few cases, it acts on postganglionic sympathetic neurons (like sweat glands).

Acetylcholine

Biosynthesis of acetylcholine

Location

- Synthesized in the cytoplasm of cholinergic neurons, particularly at nerve terminals.

Precursors

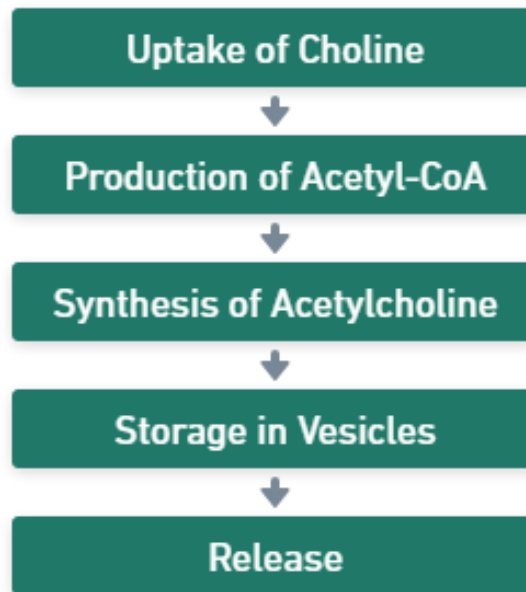
- **Choline:** Obtained from diet and recycled ACh.

- **Acetyl-CoA:** Formed in mitochondria from **pyruvate** (product of glucose metabolism).

Enzyme Involved

- **Choline acetyltransferase (ChAT):** Exclusively present in cholinergic neurons.

Step-by-Step Process



1. Uptake of Choline

- Choline enters the presynaptic neuron via high-affinity choline transporters (CHT1).
- This is an active, sodium-dependent process.
- Choline can be derived from:
 - Diet (e.g., eggs, meat)
 - Breakdown of previously released acetylcholine

2. Production of Acetyl-CoA

- Produced by the pyruvate dehydrogenase complex in mitochondria.
- Acetyl-CoA provides the acetyl group for ACh synthesis.

3. Synthesis of Acetylcholine

- Catalyzed by **choline acetyltransferase (ChAT)** in the cytoplasm.
- Reaction:



4. Storage in Vesicles

- Acetylcholine is actively transported into synaptic vesicles by vesicular acetylcholine transporter (VACHT).
- Stored until released upon nerve stimulation.

5. Release

- Triggered by **influx of calcium ions** following an action potential.
- Vesicles fuse with the presynaptic membrane and release ACh via **exocytosis**.

Catabolism of acetylcholine

Enzyme Involved

- Acetylcholinesterase (AChE): Present in the synaptic cleft and on postsynaptic membranes.

Reaction



- **Choline:** Taken back up by **presynaptic choline transporters** and reused.
- **Acetate:** Diffuses away and is metabolized.

Importance

- Prevents **continuous stimulation** of the postsynaptic cell.
- Ensures **precise, short-lived** synaptic signaling.
- Rapid breakdown (within milliseconds) is crucial, especially at **neuromuscular junctions**.

Cholinergic receptors

Acetylcholine acts on two types of receptors:

- **Nicotinic receptors** (ionotropic)
- **Muscarinic receptors** (metabotropic)

Muscarinic receptors

Type

- G-protein-coupled receptors (GPCRs)

Subtypes and Signal Pathways

Subtype	G-protein	Pathway	Effect
M1	Gq	Activates phospholipase C → IP ₃ & DAG → ↑Ca ²⁺	CNS excitation, gastric acid secretion
M2	Gi	Inhibits adenylate cyclase → ↓cAMP, opens K ⁺ channels	Slows heart rate (SA node), decreases atrial contraction
M3	Gq	Same as M1	Smooth muscle contraction, glandular secretion



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