

Neurotransmitters: The Body's Chemical Messengers

Neurotransmitters are specialized chemical messengers used by the nervous system to transmit signals across synapses from one neuron to another or from neurons to effector organs such as muscles and glands. They play a central role in coordinating sensory input, motor output, mood regulation, cognition, and autonomic functions.

Neuronal communication typically occurs across a **synaptic cleft**, where an **electrical signal (action potential)** in the presynaptic neuron is converted into a **chemical signal (neurotransmitter release)** that binds to receptors on the postsynaptic neuron to elicit a response.

Classification of Neurotransmitters

Neurotransmitters can be categorized based on:

1. Functional Effect

- **Excitatory neurotransmitters:** Promote depolarization of the postsynaptic membrane (e.g., glutamate, acetylcholine)
- **Inhibitory neurotransmitters:** Induce hyperpolarization and suppress action potentials (e.g., GABA, glycine)
- **Modulatory neurotransmitters (Neuromodulators):** Modulate the strength, duration, or spread of neural signaling (e.g., dopamine, serotonin, histamine)

2. Chemical Structure

- **Amino acids:** Glutamate, GABA, glycine
- **Amines (monoamines):** Dopamine, norepinephrine, epinephrine, serotonin, histamine
- **Peptides:** Substance P, endorphins, enkephalins
- **Others:** Acetylcholine, purines (e.g., ATP)

Major Neurotransmitters

1. Acetylcholine (ACh)

- **Type:** Excitatory (mostly)
- **Sites of action:**
 - Neuromuscular junctions (somatic nervous system)
 - Autonomic nervous system (preganglionic sympathetic and both pre- and postganglionic parasympathetic neurons)
 - Basal forebrain and brainstem (cognitive and memory functions)

Clinical relevance:

- **Alzheimer's disease** is associated with degeneration of cholinergic neurons in the CNS.
- **Botulinum toxin** blocks ACh release, leading to flaccid paralysis.
- **Myasthenia gravis** is an autoimmune condition that targets ACh receptors at the neuromuscular junction.

2. Norepinephrine (Noradrenaline)

- **Type:** Primarily excitatory
- **Sites of action:**
 - Postganglionic sympathetic neurons
 - Locus coeruleus in the brainstem (regulates alertness, mood, arousal)

Clinical relevance:

- Increased levels are linked to **anxiety**, **hypertension**, and **stress response**.
- Decreased levels are associated with **depression** and **attention deficits**.
- Key target in **SNRIs and tricyclic antidepressants**.

3. Epinephrine (Adrenaline)

- **Type:** Excitatory
- **Source:** Primarily secreted by the **adrenal medulla** (acts as both hormone and neurotransmitter)
- **Function:** Activates **fight-or-flight** response ? HR, BP, blood glucose

Clinical relevance:

- Used pharmacologically in **anaphylaxis** and **cardiac arrest**.
- Overactivity may cause **panic symptoms** or **pheochromocytoma** signs.

4. Dopamine

- **Type:** Both excitatory and inhibitory (modulatory)
- **Pathways in CNS:**
 - **Mesolimbic/mesocortical:** reward, mood, motivation
 - **Nigrostriatal:** motor control
 - **Tuberoinfundibular:** inhibits prolactin secretion

Clinical relevance:

- **Parkinson's disease:** degeneration of dopaminergic neurons in the substantia nigra
- **Schizophrenia:** associated with excess dopamine in mesolimbic pathway
- **Addiction and reward** involve increased dopamine activity

5. Gamma-Aminobutyric Acid (GABA)

- **Type:** Inhibitory
- **Main inhibitory neurotransmitter in the CNS**

- **Action:** Opens Cl⁻ channels, causing hyperpolarization and reducing excitability

Clinical relevance:

- Low GABA activity is linked to **anxiety** , **epilepsy** , and **insomnia**
- **Benzodiazepines** and **barbiturates** enhance GABAergic activity

6. Glutamate

- **Type:** Excitatory
- **Main excitatory neurotransmitter in the CNS**
- Acts on NMDA, AMPA, and kainate receptors

Clinical relevance:

- Plays a role in **learning and memory** via long-term potentiation (LTP)
- Excess glutamate causes **excitotoxicity** , seen in **stroke** and **ALS**
- **NMDA antagonists** used in Alzheimer's disease (e.g., memantine)

7. Glycine

- **Type:** Inhibitory
- **Main inhibitory neurotransmitter in the spinal cord and brainstem**

Clinical relevance:

- Inhibitory action enhanced by **strychnine antagonism** , leading to convulsions
- Works synergistically with GABA

8. Serotonin (5-HT)

- **Type:** Mostly inhibitory (modulatory)
- **Produced in:** Raphe nuclei (brainstem)
- Regulates **mood** , **sleep** , **appetite** , **pain perception** , **GI motility**

Clinical relevance:

- Low serotonin levels linked to **depression** , **OCD** , and **anxiety**
- Target of **SSRIs** and **SNRIs**
- Involved in **migraine pathophysiology** and **GI disorders**

9. Histamine

- **Type:** Excitatory (modulatory)
- **Produced by:** Hypothalamus (tuberomammillary nucleus) and mast cells
- Regulates **wakefulness** , **arousal** , and **immune response**

Clinical relevance:

- Antihistamines cause **sedation** by blocking central histamine receptors
- Contributes to symptoms of **allergic reactions** (itching, swelling)

Neuromodulators vs Neurotransmitters

- **Neurotransmitters** act locally and quickly, typically within milliseconds, and are confined to the synaptic cleft.
- **Neuromodulators** (e.g., dopamine, serotonin, neuropeptides):
 - Influence broader areas of the CNS
 - Operate over longer timescales
 - Modify sensitivity or response of neurons to other neurotransmitters