

Biomedical
Science

Molecular
Genetics



BMS 23110B | Fall 2026-2027

Inherited Neurological Disorders

**Review of neurotransmitters, Neural circuits,
Neuroplasticity and**



Free Session

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What are Neurotransmitters?

DEFINITION

Neurotransmitters are **chemical messengers** that allow nerve cells (neurons) to communicate with each other and with their target tissues through a process called **synaptic transmission (neurotransmission)**.

A neurotransmitter signal travels **from a neuron, across the synapse**, to the next neuron / nerve, muscle or gland cell.

WHY THEY MATTER

- Neurotransmitters play a role in **nearly every function in the body.**
- They are important in **boosting and balancing signals** in the brain and for keeping the brain functioning.
- They are **essential** for normal physiological and neurological functioning.
- Too high or too low levels of specific neurotransmitters result in **specific health problems.**
- Medications work by **increasing or decreasing** the levels or actions of neurotransmitters.



What Body Functions Do They Control?

Neurotransmitters help manage **automatic responses** such as breathing and heart rate, and they also play a role in **psychological functions** such as learning, managing mood, fear, pleasure and happiness.

Autonomic

- Heartbeat
- Blood Pressure
- Breathing
- Digestion
- Hormone regulation

Somatic

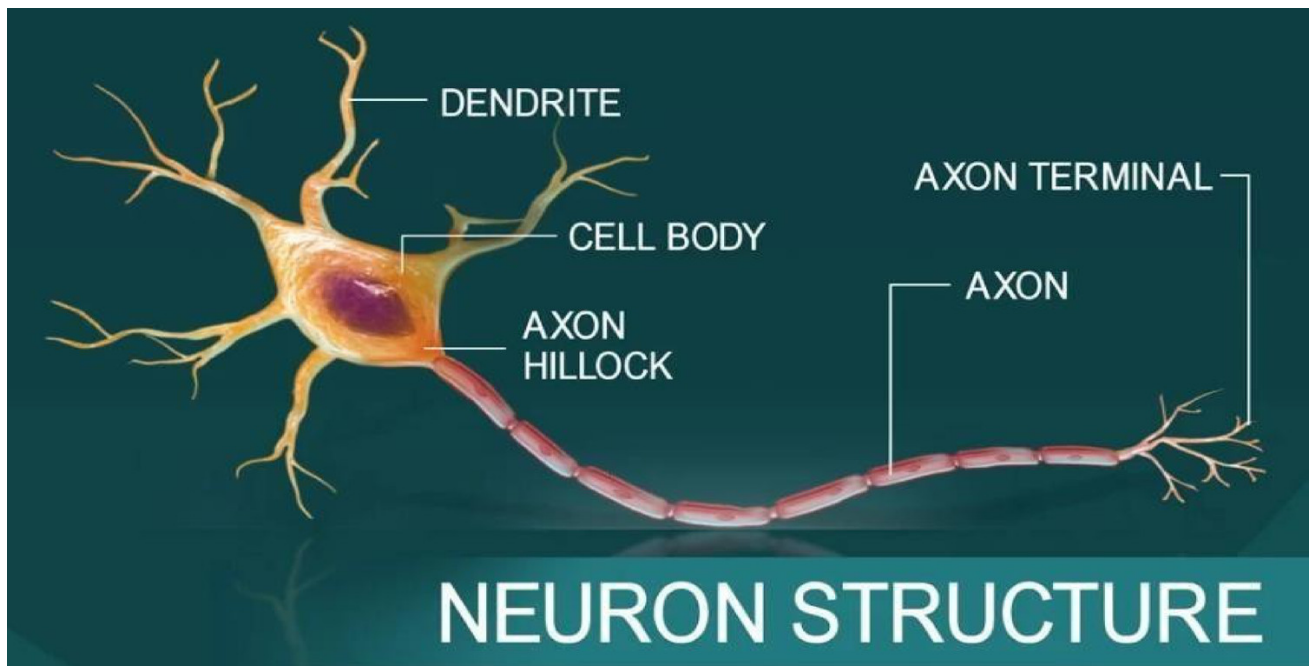
- Muscle Movements

Cognitive / Emotional

- Thoughts
- Memory
- Learning
- Mood
- Stress Response
- Pleasure
- Sleep
- Healing
- Aging



Neurotransmission · A Look at the Neuron



1 Cell body

Contains the nucleus and essential organelles for synthesizing neurotransmitters and supporting neuronal function.

2 Dendrite

Branched cytoplasmic projections of the cell body that receive signals from the axons of other neurons.

3 Axon

Carries the electrical signals along the nerve cell to the axon terminal.

4 Axon terminal

Where the electrical signal is converted into a chemical message via the release of neurotransmitters into the synaptic cleft.



Electrical Signals in a Neuron

A **synapse** is the **functional junction** between one neuron and another, or between a neuron and an effector such as a muscle or a gland.

Presynaptic neuron

Carries the impulse **toward the synapse** and releases neurotransmitters. Neurotransmitters are stored within thin-walled sacs called **synaptic vesicles**.

Postsynaptic cell

Receives the signal, either as a neuron **propagating the signal** or as an **effector** (e.g. muscle, gland).



Synaptic Connections

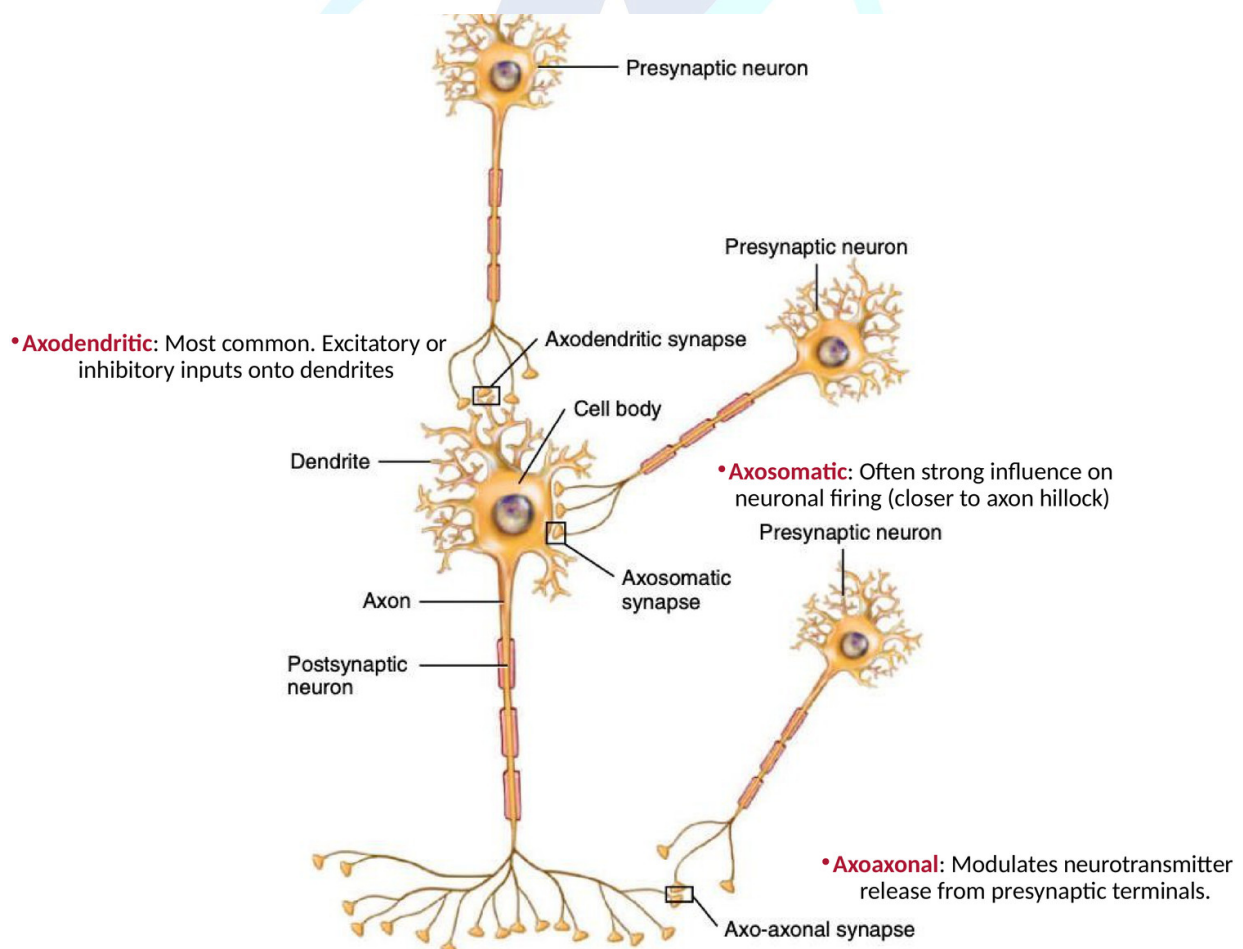


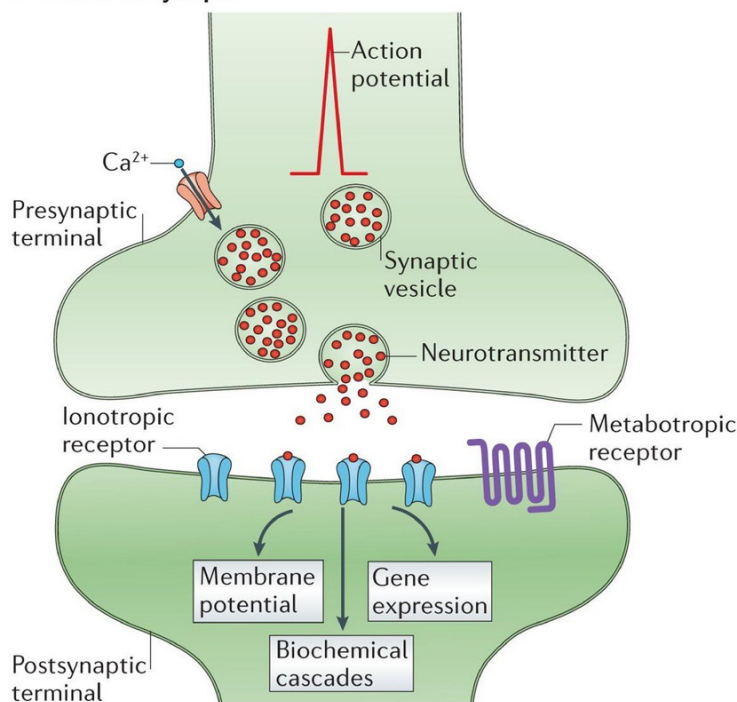
Fig 12.22, Examples of Synapses. *Principles of Anatomy and Physiology*, 16th edition, Gerard J. Tortora & Bryan H. Derrickson; Wiley, Nov 2020.



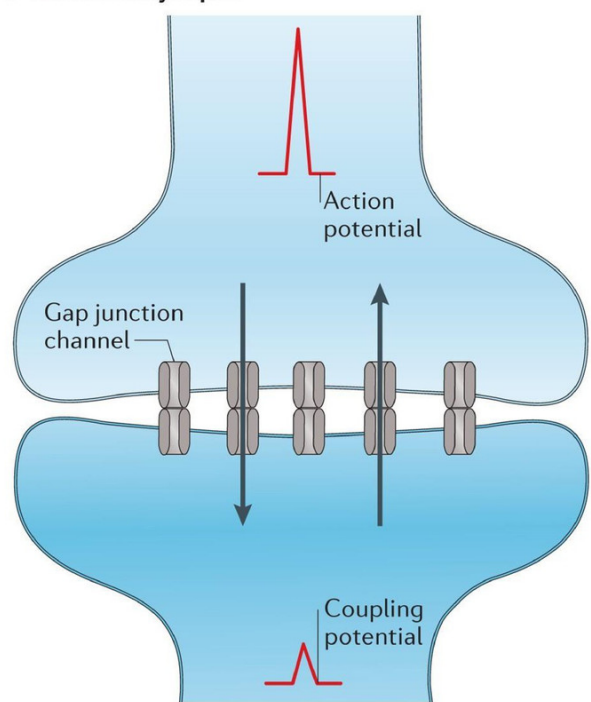
Signal Transmission at a Chemical Synapse

- In a chemical synapse, the presynaptic and postsynaptic membranes are close but **do not touch**.
- They are separated by the **synaptic cleft**; a narrow space filled with interstitial fluid.
- Nerve impulses **cannot directly cross this gap**.
- Instead, the presynaptic neuron **releases neurotransmitters** in response to a nerve impulse.
- These neurotransmitters **diffuse across the synaptic cleft**.
- They then **bind to specific receptors** on the postsynaptic membrane.
- This binding generates a **postsynaptic potential**, which is a type of graded potential.

a Chemical synapse



b Electrical synapse



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a Chemical synapse · **b** Electrical synapse

Neurotransmitters are stored within thin-walled sacs called **synaptic vesicles**. Each vesicle can contain **thousands of neurotransmitter molecules**.



The Neurotransmission Cycle

Released

- Nerve impulse reaches pre-synaptic terminal
- Voltage-gated Ca^{2+} channels open
- Increased Ca^{2+} influx causes synaptic vesicles to **fuse with the presynaptic membrane**
- Neurotransmitters are released into the **synaptic cleft**

Binding

- Neurotransmitters bind to **receptors** on the post-synaptic membrane
- Ion channels open — inflow of Na^{+} and K^{+} ions
- **Depolarization** occurs, triggering the formation of a new action potential

Deactivate

- Neurotransmitter is **cleared from the synaptic cleft**

AFTER THEY DELIVER THEIR MESSAGE

The molecules must be **removed or inactivated** from the synaptic cleft. They do this in one of three ways:

Diffusion

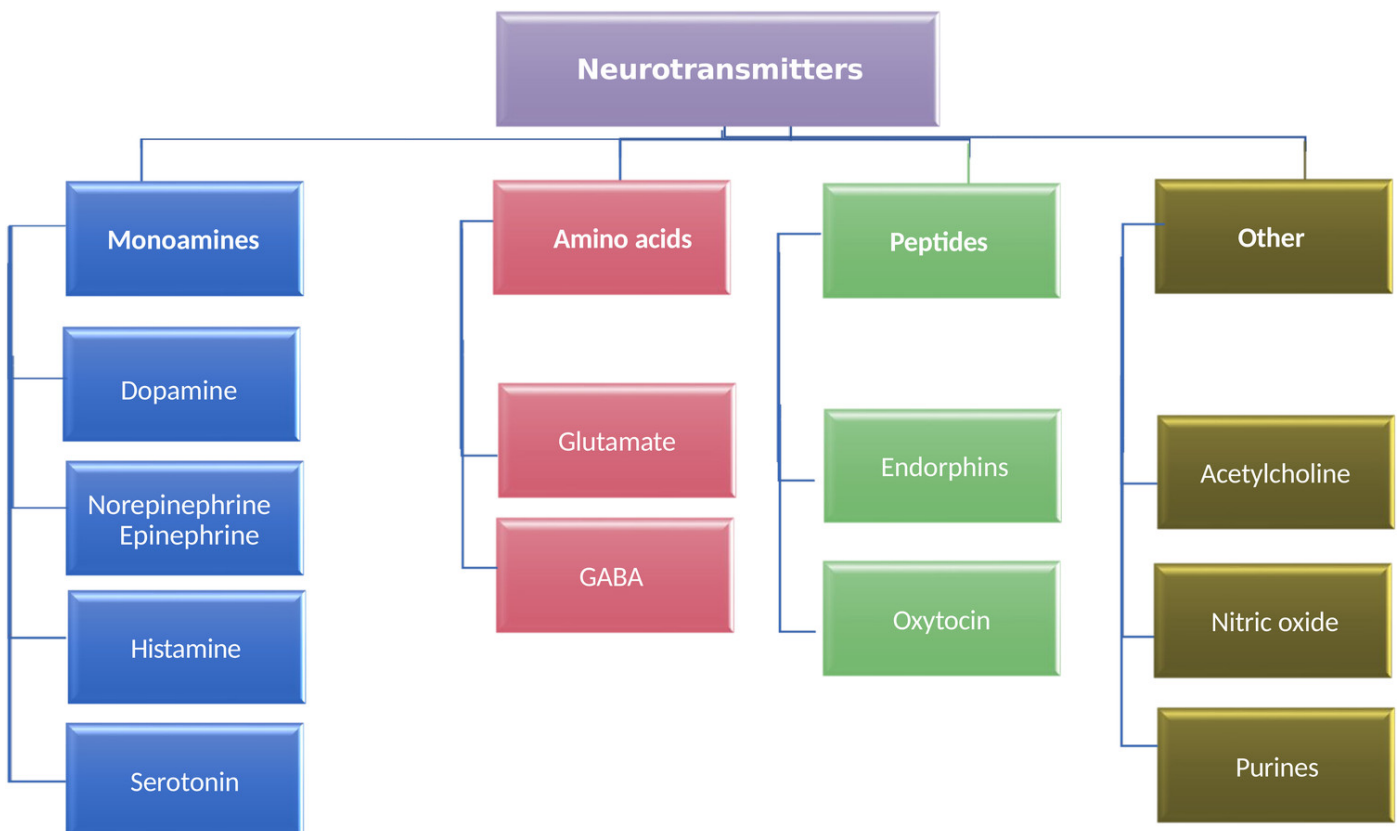
Reuptake or uptake by cells

Enzymatic degradation



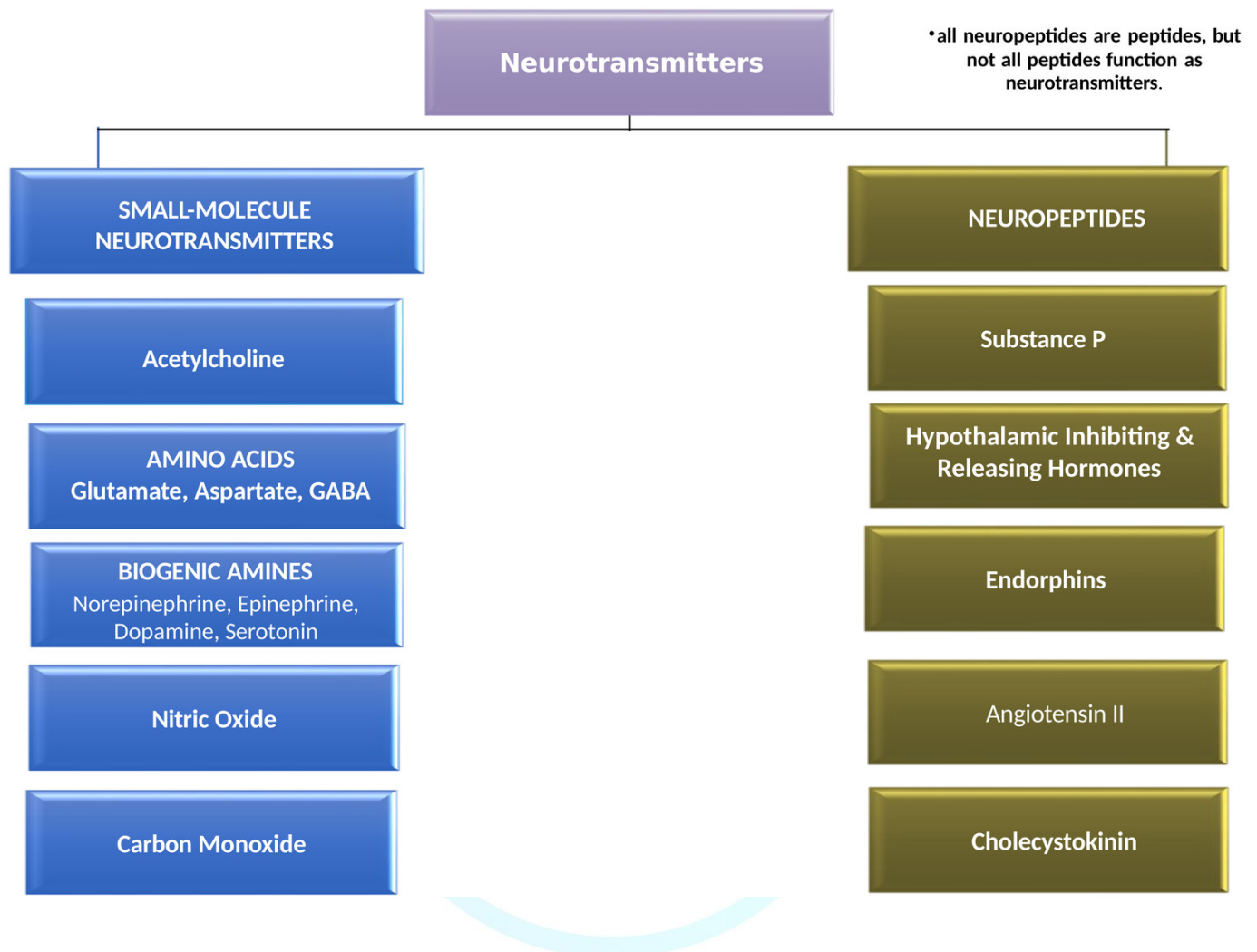
Classification by Chemical Nature

Scientists have identified **more than 100 neurotransmitters** and suspect there are many others yet to be discovered. They can be grouped into types based on their **chemical nature** and based on their **size**.





Classification by Size

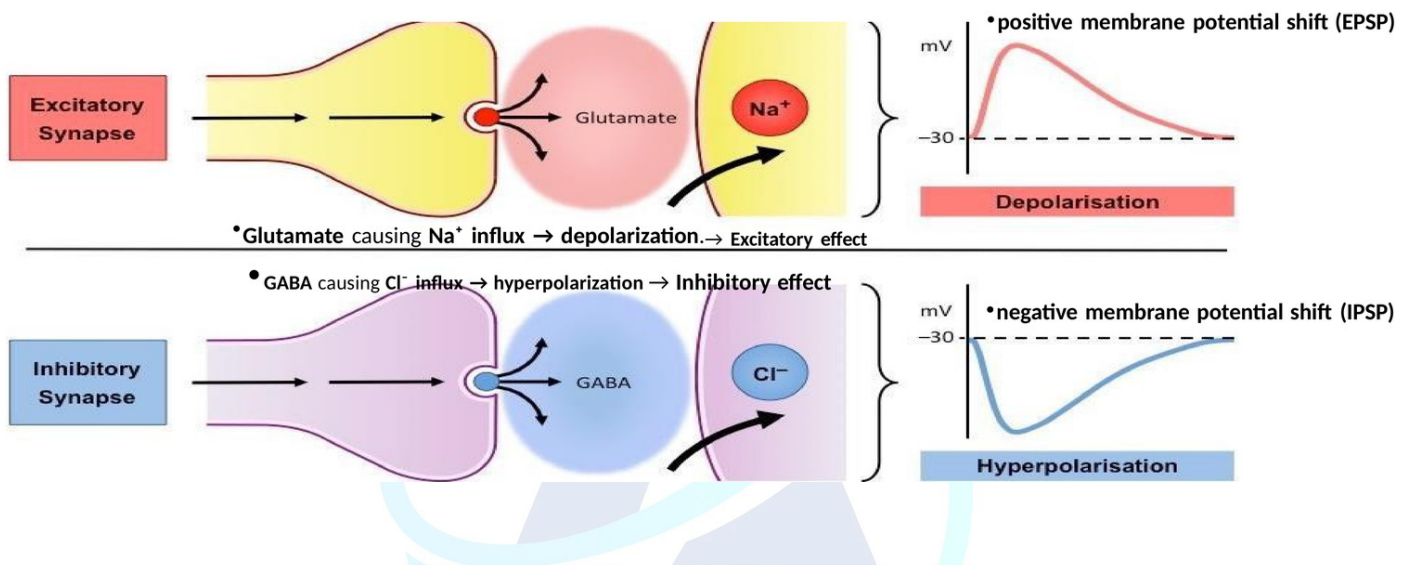


All **neuropeptides** are peptides, but **not all peptides function as neurotransmitters.**



What Action Do They Transmit to the Target Cell?

- The neurotransmitters **bind to receptor proteins** in the cellular membrane of the target tissue.
- The target tissue gets **excited**, **inhibited**, or **functionally modified** in some other way, depending on the specific neurotransmitter.



Excitatory synapse · EPSP

Glutamate causing Na^+ influx → **depolarization** → excitatory effect — a **positive membrane potential shift (EPSP)**.

Inhibitory synapse · IPSP

GABA causing Cl^- influx → **hyperpolarization** → inhibitory effect — a **negative membrane potential shift (IPSP)**.



Excitatory, Inhibitory and Modulatory

Excitatory

Excitatory neurotransmitters

increase the likelihood

that a neuron will fire an action potential by stimulating it.

Inhibitory

Inhibitory neurotransmitters

decrease the likelihood

of firing by blocking or suppressing the signal.

Modulatory

Neuromodulators **adjust how other neurotransmitters**

work. They can affect many neurons at once and may activate different receptor types. Their effect depends on the receptor they bind to.

EXAMPLES OF NEUROTRANSMITTERS

EXCITATORY	INHIBITORY	NEUROMODULATORS
Glutamate (Glu) Acetylcholine (ACh) Dopamine (DA) Norepinephrine (NE) Epinephrine (Epi) Histamine	gamma-Aminobutyric acid (GABA) Serotonin (5-HT) Dopamine (DA)	Dopamine (DA) Serotonin (5-HT) Acetylcholine (ACh) Norepinephrine (NE) Histamine

Remember — excitatory doesn't always mean 'good', and inhibitory doesn't mean 'bad'. It's all about regulating neural signals: **balance is key.** The effect depends on receptor subtype and location, as some neurotransmitters are neither purely excitatory nor inhibitory.



Why Might Neurotransmitters Fail to Work?

Imbalance in neurotransmitter levels

Too much or too little of one or more neurotransmitters may be produced or released.

Defective receptors

The receptors on the postsynaptic cell (nerve, muscle or gland) may be damaged or non-functional.

Synaptic cleft damage

Inflammation or injury at the synapse may prevent neurotransmitters from binding effectively to receptors.

Premature reuptake

Neurotransmitters may be reabsorbed too quickly into the presynaptic neuron before they can act.

Enzymatic breakdown

Enzymes such as monoamine oxidase (MAO) or acetylcholinesterase (AChE) may degrade neurotransmitters before they reach the receptor.

Underlying diseases or medications

Certain neurological disorders or drugs can interfere with neurotransmitter production, release or action.



Diseases Associated with Neurotransmitters

When neurotransmitters **do not function well**, disease can occur.

Acetylcholine

Alzheimer

Serotonin

Autism

Dopamine

High — Schizophrenia

Low — Parkinsonism

Glutamate

Huntington

GABA

Epileptic seizures



How Do Medications Affect Neurotransmitters?

1 · Block enzymes that break down neurotransmitters

- This **increases neurotransmitter availability** in the synapse.
- **Example:** Donepezil and Galantamine inhibit acetylcholinesterase, which breaks down **acetylcholine (ACh)**.
- Used to stabilize memory and cognition in Alzheimer's disease (early to moderate stages).
- These medications **do not cure** the disease but help manage symptoms.

Mechanism 2: Blocking reuptake

- **Medications can increase neurotransmitter levels in the synapse.**
- **This prevents reabsorption (reuptake) of neurotransmitters into the presynaptic cell.**

Example:

- Selective serotonin reuptake inhibitors (SSRIs) prevent serotonin reabsorption by the presynaptic cell.
- Increases serotonin levels in the synapse.
- Used to treat depression, anxiety, and other mental health disorders.

3 · Block the release of neurotransmitters

- This reduces the amount released into the synaptic cleft.
- **Example:** Lithium inhibits the release of **norepinephrine (NE)**.
- Used in the treatment of **bipolar disorder** to manage mood swings.



Modifying the Effects of Neurotransmitters

Substances naturally present in the body, as well as **drugs and toxins**, can modify the effects of neurotransmitters in several ways.

1 Synthesis can be stimulated or inhibited

Many patients with Parkinson's disease benefit from **L-dopa** because it is a precursor of dopamine. For a limited period, taking L-dopa boosts dopamine production in affected brain areas.

2 Release can be enhanced or blocked

Amphetamines promote release of dopamine and norepinephrine. **Botulinum toxin** causes paralysis by blocking release of acetylcholine from somatic motor neurons.

3 Receptors can be activated or blocked

An **agonist** binds to receptors and enhances or mimics the effect of a natural neurotransmitter — Isoproterenol is a powerful agonist of epinephrine and norepinephrine, used to dilate the airways during an asthma attack. An **antagonist** binds to and blocks receptors — Zyprexa, prescribed for schizophrenia, is an antagonist of serotonin and dopamine.

4 Removal can be stimulated or inhibited

Cocaine produces euphoria by blocking transporters for dopamine reuptake. This allows dopamine to linger longer in synaptic clefts, producing excessive stimulation of certain brain regions.



Neural Circuits

A circuit typically refers to a set of **interconnected components** that together subserve a specific function.

A cluster of neurons

A neural circuit in the brain may be a cluster of neurons that receives **electrochemical information** which the circuit modifies and transmits to other circuits for further modification.

A network of brain regions

Alternatively, a neural circuit may comprise a network of interconnected brain regions that together **integrate vast amounts of information** and perform more complicated cognitive and regulatory functions.

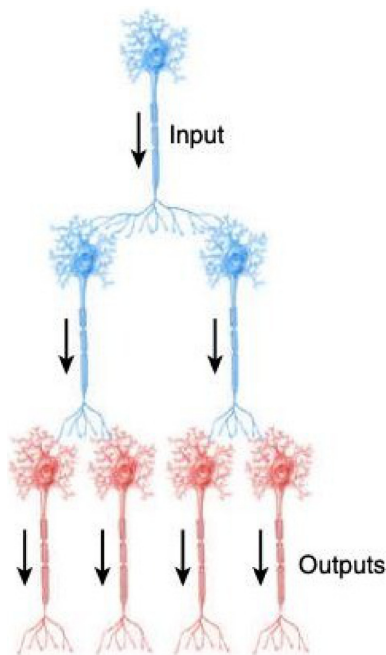
- The CNS contains **billions of neurons** organized into complicated networks called neural circuits — functional groups of neurons that process specific types of information.
- In a **simple series circuit**, a presynaptic neuron stimulates a single postsynaptic neuron. The second neuron then stimulates another, and so on.
- Most neural circuits are **more complex**.
- Neural circuits **process sensory information, generate motor output** and create spontaneous activity.



Diverging & Converging Circuits

Diverging circuit

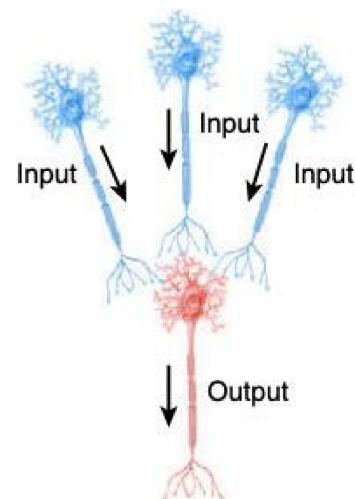
- A single presynaptic neuron may synapse with **several postsynaptic neurons**, permitting one neuron to influence several at the same time.
- The nerve impulse causes stimulation of **increasing numbers of cells** along the circuit.
- A small number of neurons in the brain that govern a particular body movement stimulate a much larger number in the spinal cord.
- This arrangement **amplifies the signal**.



(a) Diverging circuit

Converging circuit

- Several presynaptic neurons synapse with a **single postsynaptic neuron**.
- This permits **more effective stimulation or inhibition** of the postsynaptic neuron.
- The postsynaptic neuron receives nerve impulses from **several different sources**.
- A single motor neuron synapsing with skeletal muscle fibers receives input from several pathways originating in different brain regions.



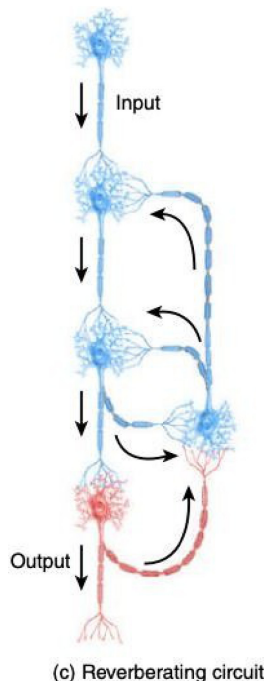
(b) Converging circuit



Reverberating & Parallel After-Discharge Circuits

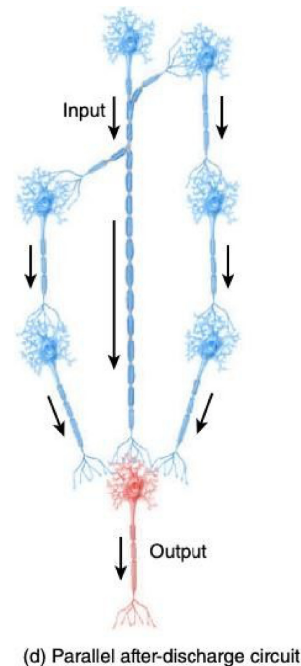
Reverberating circuit

- Stimulation of the presynaptic cell causes the postsynaptic cell to transmit a **series of nerve impulses**.
- The incoming impulse stimulates the first neuron, which stimulates the second, and so on. **Branches from later neurons synapse with earlier ones.**
- This sends impulses **back through the circuit again and again.**
- The output may last from a few seconds to many hours. **Inhibitory neurons** may turn the circuit off.
- Responses thought to result from these circuits: breathing, coordinated muscular activities, waking up and short-term memory.



Parallel after-discharge circuit

- A single presynaptic cell stimulates a group of neurons, each of which synapses with a **common postsynaptic cell**.
- A differing number of synapses imposes **varying synaptic delays**, so the last neuron exhibits multiple EPSPs or IPSPs.
- If the input is excitatory, the postsynaptic neuron can send out a **stream of impulses in quick succession.**
- These circuits may be involved in precise activities such as **mathematical calculations.**





Neural Circuits Involved in Movement Control

The neural circuits responsible for movement control are organized into **four distinct but highly interactive subsystems.**

- 1 Local circuitry in the spinal cord and brainstem**
These circuits reside within the grey matter and are responsible for reflexes and basic movement patterns such as walking.
- 2 Upper motor neurons in the brainstem or cerebral cortex**
These neurons initiate and control voluntary movements by influencing lower motor circuits.
- 3 The cerebellum**
Critical for the coordination, timing and precision of movement. It constantly compares intended movement with actual performance.
- 4 Basal ganglia** (embedded deep in the forebrain)
Important for the initiation and smooth execution of voluntary movements.

CLINICAL CORRELATION

Disorders such as **Parkinson's disease** and **Huntington's disease** highlight the role of the basal ganglia in movement regulation.



Neuroplasticity

DEFINITION

The ability of the nervous system to **change its activity** in response to intrinsic or extrinsic stimuli by **reorganizing its structure, functions or connections**.

Beneficial

restoration of function
after injury

Neutral

no change

Negative

can have pathological
consequences

Temporal (functional) change

Divided into **short-term** and **long-term** change, and takes place at **individual neurons**.

Spatial (structural) change

Takes place either at **synapses**, within **neurons** or within **glial cells**.

- Neuroplasticity aids **brain recovery** after damage produced by events like stroke or traumatic injury.
- This ability to manipulate specific neuronal pathways and synapses has important implications for **physiotherapeutic clinical interventions**.
- A better understanding of the mechanisms governing neuroplasticity after brain damage or nerve lesion will help improve the **patient's quality of life**.



Neurogenesis

Neurogenesis — the birth of new neurons from undifferentiated stem cells — occurs regularly in some animals.

HOW THE VIEW CHANGED

- Until recently, the dogma in humans and other primates was **"no new neurons"** in the adult brain.
- 1992** Researchers published the unexpected finding that the hormone-like protein **epidermal growth factor (EGF)** stimulated cells taken from the brains of adult mice to proliferate into both neurons and astrocytes. Previously, EGF was known to trigger mitosis in non-neuronal cells and to promote wound healing and tissue regeneration.
- 1998** Scientists discovered that significant numbers of new neurons do arise in the adult human **hippocampus**, an area of the brain crucial for learning.

WHY NEUROGENESIS IS NEARLY ABSENT ELSEWHERE

Inhibitory influences from neuroglia

Particularly **oligodendrocytes**. Axons in the CNS are myelinated by oligodendrocytes rather than Schwann cells, and this CNS myelin is one of the factors inhibiting regeneration of neurons.

Absence of growth-stimulating cues

Cues that were present during **fetal development** are missing. Perhaps this same mechanism stops axonal growth once a target region has been reached.

After axonal damage, nearby **astrocytes proliferate rapidly**, forming a type of scar tissue that acts as a **physical barrier to regeneration**. Thus, injury of the brain or spinal cord usually is **permanent**.

ONGOING RESEARCH

Improving the environment for existing spinal cord axons to bridge the injury gap; stimulating **dormant stem cells** to replace neurons lost through damage or disease; and developing **tissue-cultured neurons** for transplantation.



Genetics and Neurological Disorders

- Neurological disorders consist of a broad array of conditions that impact the **brain, spinal cord and nerves.**
- Ranging from **Alzheimer's disease** and **Parkinson's** to **epilepsy** and **multiple sclerosis**, the variety is extensive.
- These conditions can result from a mix of **genetic, environmental and lifestyle** elements.
- Some exhibit a recognized **genetic inclination**, stemming from gene mutations or a blend of genetic factors that heighten susceptibility.



Single Gene Mutations

Some neurological conditions are caused by mutations in a **single gene**. These disorders often follow **Mendelian inheritance** patterns, such as autosomal dominant, autosomal recessive or X-linked.

Huntington's disease

Autosomal dominant mutation in the **HTT** gene.

Friedreich's ataxia

Autosomal recessive mutation in the **FXN** gene.

Duchenne muscular dystrophy

X-linked mutation in the **DMD** gene.



Primary Genetic Causes of Neurological Disorders

Multiple gene (polygenic) involvement

- Some disorders arise from the **combined effects of mutations in multiple genes**, often in conjunction with environmental factors. These are termed polygenic or complex disorders.
- **Alzheimer's disease**, for instance, has several genetic risk factors, with the **APOE ε4 allele** being the most prominent.

Copy number variations (CNVs)

- CNVs are alterations in the DNA that result in the cell having an **abnormal number of copies** of one or more sections of the DNA.
- They can be associated with various neurological disorders, including some forms of **epilepsy** and **autism spectrum disorders**.

Mitochondrial DNA mutations

- The mitochondria have **their own DNA**, separate from the nuclear DNA.
- Mutations can lead to neurological disorders since the brain is **highly dependent on the energy produced by mitochondria**.
- Examples include **Leber's hereditary optic neuropathy** and some forms of **mitochondrial myopathy**.



Primary Genetic Causes of Neurological Disorders

Repeat expansion disorders

- Caused by the **abnormal repetition of short sequences of DNA**. Over time these repeats can expand, leading to disease.

Huntington's disease · CAG repeat

Fragile X syndrome · CGG repeat

Spinocerebellar ataxias · various repeats

Epigenetic changes

- Epigenetics refers to changes in gene activity that **don't involve alterations to the underlying DNA sequence**.
- These changes can affect gene expression and are implicated in some neurological conditions.
- Rett syndrome**, for instance, involves mutations in the **MECP2** gene, which plays a role in epigenetic regulation.

Prion diseases

- Caused by **misfolded proteins called prions**.
- While most prion diseases are sporadic, some — like **familial Creutzfeldt-Jakob disease** — have a genetic component.



To Summarise...

MESSENGERS

100+

Neurotransmitters

- **Chemical messengers** of synaptic transmission
- Grouped by **chemical nature** and by **size**
- Removed by diffusion, reuptake or enzymatic degradation

EFFECT

3

Types of effect

- **Excitatory** — increases firing
- **Inhibitory** — decreases firing
- **Modulatory** — adjusts other transmitters

SYNAPSE

3

Synaptic connections

- **Axodendritic** — most common
- **Axosomatic** — strong influence on firing
- **Axoaxonal** — modulates release

CIRCUITS

4

Neural circuit types

- **Diverging** — amplifies the signal
- **Converging** — input from many sources
- **Reverberating** and **parallel after-discharge**

CHANGE

2

Neuroplasticity & neurogenesis

- Plasticity change is **temporal** or **spatial**
- New neurons arise in the adult **hippocampus**
- CNS myelin and astrocyte scarring inhibit regeneration

GENETICS

7

Genetic causes

- Single gene · polygenic · CNVs
- Mitochondrial DNA · repeat expansion
- Epigenetic changes · prion diseases

NEUROTRANSMITTERS AND DISEASE

Acetylcholine · Alzheimer

Serotonin · Autism

Dopamine · Schizophrenia / Parkinsonism

Glutamate · Huntington

GABA · Epileptic seizures