Objective:

• Central Nervous System Glial cells & neuronal activity Satellite cells of Ganglia
• Central Nervous System Cerebral and cerebellar cortex layers Autonomic and peripheral ganglia
• Central & peripheral Nervous System tissue

Nervous System

The human nervous system is the body's most intricate system, consisting of billions of **neurons** supported by **glial cells.** Each neuron connects with hundreds of others, creating a highly complex network for processing **information and generating responses**. Nervous tissue forms an integrated communication network throughout the body. Anatomically, the nervous system is organized into two main divisions.

The nervous system is divided into:

- **Central nervous system (CNS)**: brain and spinal cord.
- **Peripheral nervous system (PNS):** cranial, spinal, and peripheral nerves that carry impulses to and from the CNS, along with ganglia, which are clusters of nerve cells outside the CNS.

Both CNS and PNS contain neurons (cells with long processes that transmit signals) and glial cells (cells with short processes that support, protect, and nourish neurons).

Neurons are excitable cells that respond to stimuli by altering their membrane potential. This change, called depolarization, spreads along the neuron as an action potential (nerve impulse), allowing communication with other neurons, muscles, and glands.

Through collecting and processing these signals, the nervous system regulates body conditions (blood pressure, gas levels, pH, glucose, hormones) and controls behavior (feeding, reproduction, defense, social interaction).

Neurons

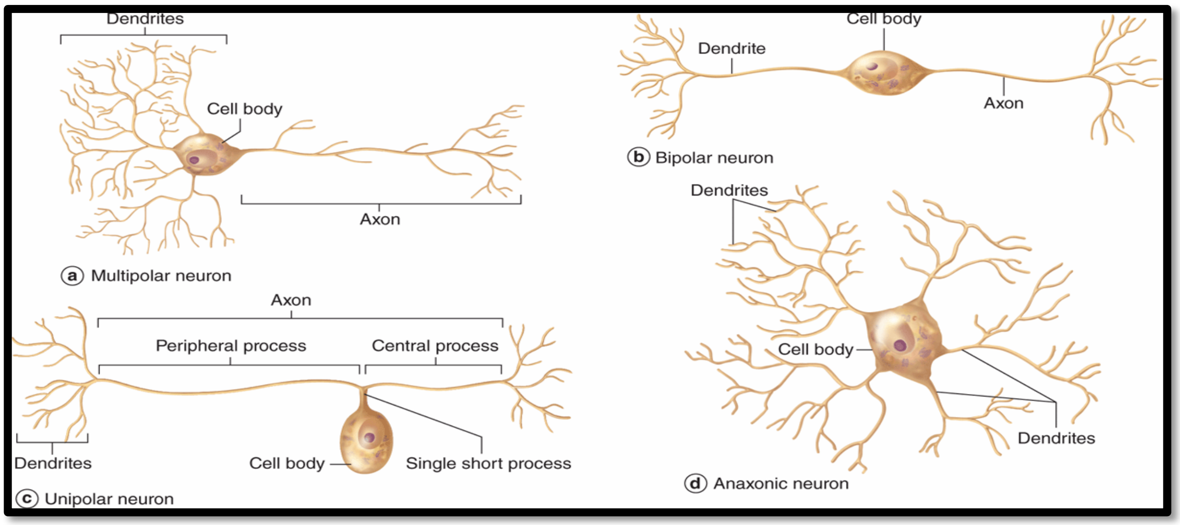
Functional Units of the Nervous System

- **Functional unit:** The neuron (in both CNS and PNS).
- **Main parts of a neuron:**
  1. **Cell body (soma/perikaryon):** Contains the nucleus and organelles; acts as the metabolic and synthetic center.
  2. **Dendrites:** Multiple extensions receiving stimuli from other neurons at **synapses**.
  3. **Axon:** Single long process conducting impulses to neurons, muscles, or glands; can also receive modifying signals.
- **Neuron classification by processes:**
  1. **Multipolar:** One axon, multiple dendrites (most common).
  2. **Bipolar:** One axon, one dendrite (sensory neurons of retina, inner ear, olfactory epithelium).
  3. **Unipolar/Pseudounipolar:** Single process that bifurcates (most other sensory neurons).
  4. **Anaxonic:** Many dendrites, no true axon; regulate electrical activity of nearby CNS neurons
- **Neuron function types:**
  1. **Sensory (afferent):** Carry stimuli from receptors to CNS.
  2. **Motor (efferent):** Send impulses to effectors (muscles, glands).
     - **Somatic motor nerves:** Voluntary, control skeletal muscle.
     - **Autonomic motor nerves:** Involuntary, control glands, cardiac, smooth muscle.
  3. **Interneurons:** Connect neurons in CNS, forming circuits; 99% of neurons; mostly multipolar or anaxonic.
- **Anatomical notes:**
  1. CNS: Cell bodies mainly in **gray matter**, axons in **white matter**.

2. PNS: Cell bodies in **ganglia** and sensory regions; axons bundled in nerves.

Cell Body (Perikaryon or Soma)

The neuronal cell body contains the nucleus and surrounding cytoplasm, exclusive of the cell processes . It acts as a trophic center, producing most cytoplasm for the processes. Most cell bodies are in contact with a great number of nerve endings conveying excitatory or inhibitory stimuli generated in other neurons



Dendrites

Dendrites are typically short, small processes emerging and branching off the soma . Usually covered with many synapses, dendrites are the principal signal reception and processing sites on neurons. The large number and extensive arborization of dendrites allow a single neuron to receive and integrate signals from many other nerve cells. For example, up to 200,000 axonal endings can make functional contact with the dendrites of a single large Purkinje cell of the cerebellum.

Axons

Most neurons have a single axon, usually longer than the dendrites, with size varying by neuron type. The axon arises from the axon hillock, where ion channels initiate the action potential after integrating excitatory and inhibitory signals. Axons branch less than dendrites and end in terminal arborization.

Glial cells

Glial cells support neuronal survival and function and are about ten times more numerous than neurons in the mammalian brain. Like neurons, most glial cells develop from progenitor cells of the embryonic neural plate. In the CNS, glial cells surround neuronal cell bodies, axons, and dendrites, filling the spaces between neurons. Because connective tissue and collagen are scarce in the CNS, glial cells provide structural and supportive roles similar to connective tissue.

Glial cells create microenvironments that optimize neuronal activity. The fibrous intercellular network in CNS tissue, called the **neuropil**, consists of fine processes from neurons and glial cells and superficially resembles collagen under light microscopy. There are six main types of glial cells: four in the CNS and two in the PNS.

Table 1. Glial Cell Types by Location and Basic Function

CNS glia	PNS glia	Basic function
Astrocyte	Satellite cell	Support
Oligodendrocyte	Schwann cell	Insulation, myelination

Microglia	–	Immune surveillance and phagocy
Ependymal cell	–	Creating CSF

Oligodendrocytes

are glial cells in the CNS that extend multiple processes, each wrapping around a segment of a nearby axon to form the **myelin sheath**. Most cytoplasm is displaced during wrapping, leaving compact layers of membrane. Multiple oligodendrocytes cover the full length of an axon. The myelin electrically insulates the axon and speeds nerve impulse conduction. Oligodendrocytes are the main glial cells in CNS white matter, which appears white due to the lipid-rich myelin. These processes and sheaths are not visible under a routine light microscope.

Astrocytes

Astrocytes are CNS-specific glial cells with numerous long, branching processes. The proximal parts contain bundles of intermediate filaments made of **GFAP**, a marker for these cells, while the distal processes lack GFAP and form an extensive network contacting synapses and other structures. Each astrocyte can interact with over a million synaptic sites. Originating from embryonic neural tube progenitors, astrocytes are the most abundant and structurally/functionally diverse glial cells in the brain. **Fibrous astrocytes** with long processes are common in white matter, while **protoplasmic astrocytes** with shorter processes predominate in gray matter. Their dynamic processes support most of their many functions.

Functions attributed to astrocytes of various CNS regions include the following:

1- Extending processes that associate with or cover synapses, affecting the formation, function, and plasticity of these structures

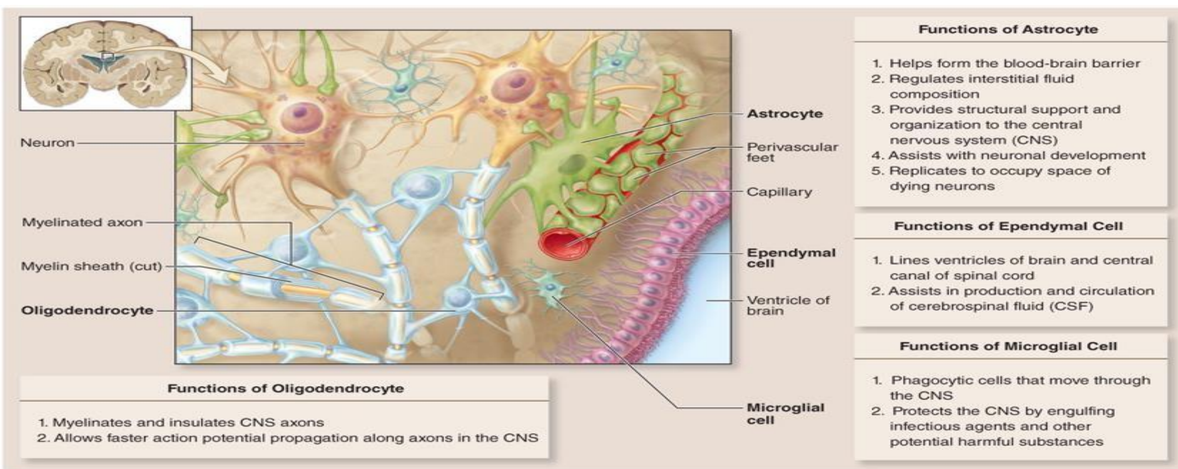
2- Regulating the extracellular ionic concentrations around neurons, with particular importance in buffering extracellular K+ levels

3- Guiding and physically supporting movements and locations of differentiating neurons during CNS development

4- Extending fibrous processes with expanded perivascular feet that cover capillary endothelial cells and modulate blood flow and help move nutrients, wastes, and other metabolites between neurons and capillaries

5- Forming a barrier layer of expanded protoplasmic processes, called the glial limiting membrane, which lines the meninges at the external CNS surface

6- Filling tissue defects after CNS injury by proliferation to form an astrocytic scar.



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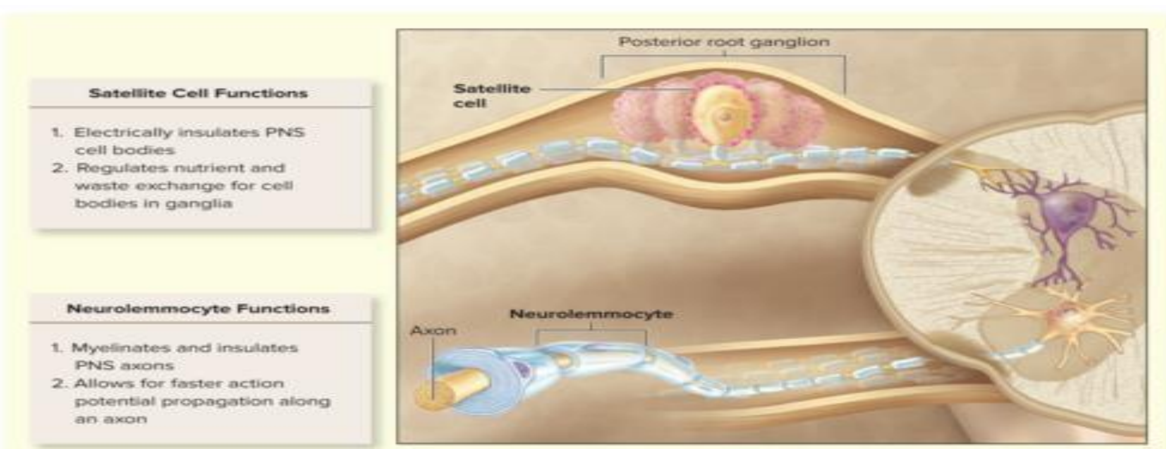
Source: Anthony L. Mescher: Junqueira's Basic Histology, 14th Edition.
www.accessmedicine.com



Ependymal cells are columnar or cuboidal cells lining the brain ventricles and the spinal cord's central canal. Their apical ends have **cilia** to move cerebrospinal fluid (CSF) and **microvilli** likely involved in absorption.

Microglia are small, mobile glial cells distributed throughout gray and white matter. They actively migrate, monitor the neuropil, remove damaged synapses or fibrous components, and serve as the CNS's main immune defense by eliminating microbial invaders and releasing immunoregulatory cytokines.

In **multiple sclerosis (MS)**, autoimmune damage to myelin sheaths impairs neuronal function, causing neurological problems. T lymphocytes and microglia phagocytose myelin debris, but their destructive activity often surpasses oligodendrocytes' ability to repair myelin, driving disease progression.

- **Schwann cells**: Found only in the PNS, each wraps myelin around a single axon segment, supporting axonal function.
- **Satellite cells**: Surround neuronal cell bodies in ganglia, providing support, insulation, and regulation of their microenvironment.

CNS Structures:

- Major CNS components: cerebrum, cerebellum, spinal cord.
- CNS is covered by **meninges** but contains little collagen, making it soft and susceptible to injury.
- **White matter**: Myelinated axons (tracts), oligodendrocytes, astrocytes, and microglia; few neuronal bodies.

- **Gray matter**: Neuronal cell bodies, dendrites, astrocytes, microglia; main site of synapses. Includes cerebral cortex, cerebellar cortex, and cerebral nuclei.

Cerebral Cortex:

- Six neuronal layers; most notable are pyramidal neurons.
- Function: Integration of sensory input and initiation of voluntary motor responses.

Cerebellar Cortex:

- Three layers:
  1. **Molecular layer**: Neuropil, scattered neurons.
  2. **Purkinje cell layer**: Large neurons with dendritic trees extending into molecular layer.
  3. **Granular layer**: Densely packed small neurons (granule cells).
- Function: Coordinates body movements.

Spinal Cord:

- White matter is peripheral; gray matter forms H-shaped central region.
- **Anterior horns**: Motor neuron cell bodies → ventral roots.
- **Posterior horns**: Interneurons receiving sensory fibers from dorsal root ganglia.
- Central canal: Lined by ependymal cells, continuous with brain ventricles, contains CSF.

Meninges:

- Three layers: **Dura mater**, **arachnoid**, **pia mater**.

1. **Dura mater**: Thick, dense connective tissue; outer periosteal layer, inner meningeal layer; forms dural venous sinuses. Epidural space contains veins and loose connective tissue.
2. **Arachnoid**: Connective tissue sheet in contact with dura, plus loose trabeculae connecting to pia mater. Subarachnoid space contains CSF for cushioning. Arachnoid villi absorb CSF into venous sinuses.
3. **Pia mater**: Closely follows CNS surface; together with arachnoid often called pia-arachnoid.

Pia mater is the innermost meningeal layer, composed of flattened mesenchymal cells closely applied to the CNS surface. It does not directly contact neurons or fibers; a thin layer of astrocytic processes, called the **glial limiting membrane (glia limitans)**, separates the neural tissue from the pia. Together, the pia and astrocytic end feet form a barrier between CNS tissue and cerebrospinal fluid (CSF) in the subarachnoid space. Blood vessels enter the CNS through perivascular spaces covered by pia mater, and although the pia disappears at capillary branches, these small vessels remain covered by astrocytic processes.

Blood-Brain Barrier (BBB):

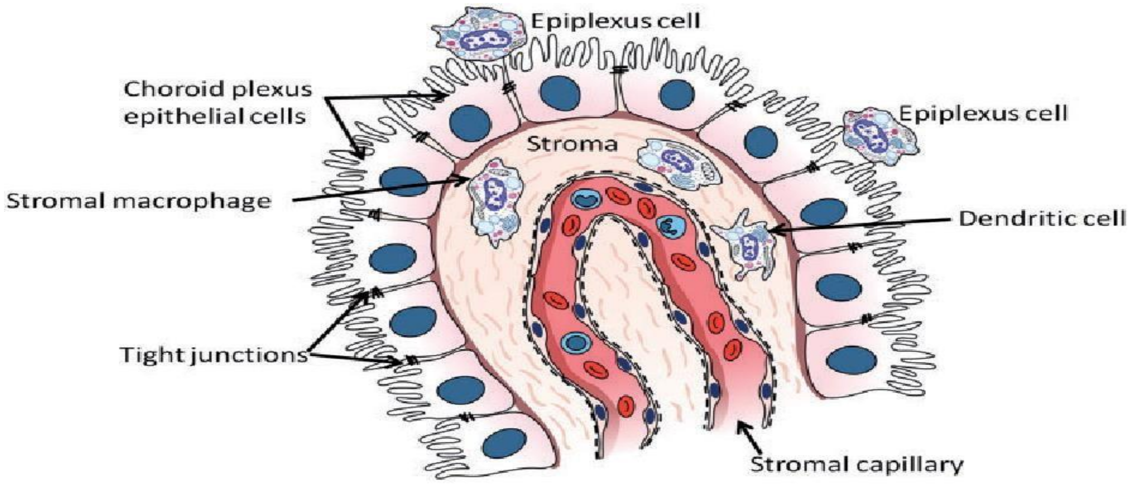
- The BBB tightly controls the passage of substances from blood into CNS tissue.
- Its main structural component is the **capillary endothelium**, with tight junctions, minimal transcytosis, and a surrounding basement membrane.
- **Perivascular astrocytic end feet** envelop capillaries and further regulate molecular and ionic passage.

- Functions: Protects neurons and glia from toxins, pathogens, and exogenous substances; maintains stable ion composition in interstitial fluid for normal neuronal activity.
- BBB is absent in regions like the hypothalamus (plasma monitoring), posterior pituitary (hormone release), and choroid plexus (CSF production).

Choroid Plexus:

- A vascularized cell plexus in the brain ventricles (third, fourth, and lateral ventricles) that produces most CSF.
- Each villus contains a vascularized pia mater layer covered by cuboidal ependymal cells.
- Function: Extracts water from blood to produce CSF, which is clear, contains Na^+, K^+, and Cl^- ions, very little protein, and sparse lymphocytes.
- CSF fills ventricles, the spinal cord's central canal, subarachnoid, and perivascular spaces, providing ions for neuronal activity and cushioning the CNS.
- **Arachnoid villi** are the main sites for CSF absorption back into venous circulation.

- CNS has very few lymphatic vessels.



Cerebellum:

- The cerebellum ("little brain") lies beneath the occipital and temporal lobes, making up ~10% of brain volume but containing over 50% of its neurons.
- Historically considered a motor structure, it **modifies motor commands** to improve accuracy and coordination; it does not initiate movement.

Cerebellar Cortex Layers:

1. **Molecular Layer (outer):**
   - Synaptic layer with few neurons, containing axons of granule cells and dendrites of Purkinje cells.
   - Stellate cells (short dendrites, contact few Purkinje dendrites) and basket cells (extensive dendrites, contact many Purkinje cells) are present.
   - Receives excitatory input from parallel fibers and provides inhibitory regulation to Purkinje cells.
2. **Purkinje Cell Layer (middle):**
   - Single layer of large, pear-shaped Purkinje cells.
   - Dendrites extend into the molecular layer; axons project through the granular layer to synapse in deep cerebellar nuclei.

3. **Granular Layer (inner):**
    - Densely packed **granule cells** (~5 µm diameter) and scattered Golgi type II cells.
    - Granule cells receive mossy fiber input, extend axons into molecular layer, branch as parallel fibers, and synapse with Purkinje, basket, and stellate cell dendrites.
    - Golgi cells have dendrites in molecular layer and axons synapsing with granule cells.
    - Nuclei of granule cells stain dark, giving the layer a darker appearance than the molecular layer and white matter.

Function:

- Coordination of muscular activity throughout the body.
- Integration of excitatory and inhibitory inputs in the three cortical layers allows precise motor control.

Key facts about the histology of the cerebellum

Structure	Inner white matter (medulla) coated by an outer grey matter (cerebellar cortex). In cross sections, the cerebellum consists of lobulations and folia (gyri)
Cortex	Molecular layer (outer) - granule cells axons, Purkinje cells dendrites, stellate cells, basket cells Purkinje layer (middle) - Purkinje cell bodies Granular layer (inner) - granule cell bodies, Golgi cells, Purkinje cell axons
Medulla	Contains nerve fibers and small blood vessels Supports neuroglial cells

Function of the Cerebellum:

- Receives input from the **cerebrum, brainstem, and spinal cord**.
- Regulates and coordinates **voluntary movements** (e.g., walking, throwing).

Additional Roles:

- **Balance and posture:** Integrates sensory input from eyes and ears to maintain stability.
- **Motor learning:** Fine-tunes movements for tasks like writing or riding a bicycle.
- **Speech:** Coordinates movements required for speaking.
- **Cognitive functions (under investigation):** Language, emotion processing, attention, reward/pleasure, and fear responses.

Medical Relevance (Disorders):

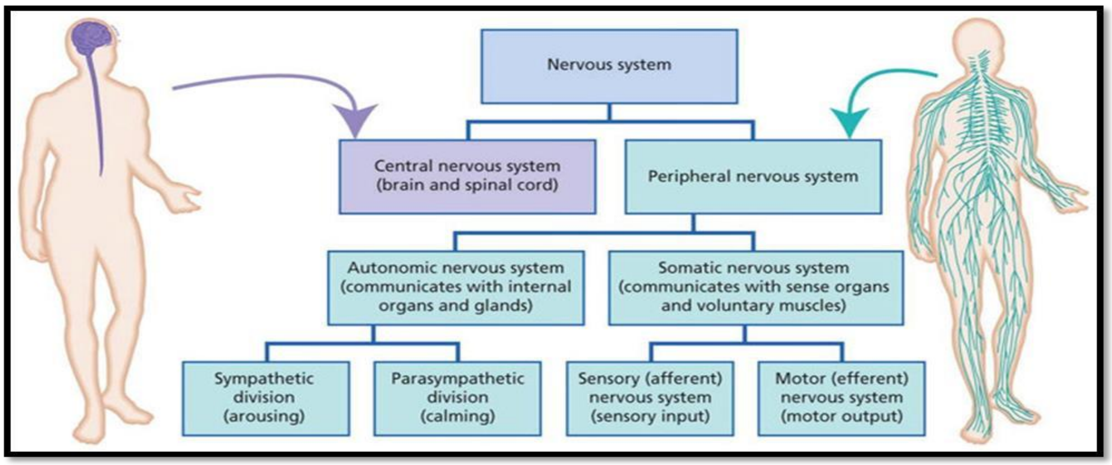
- Cerebellar dysfunction leads to **impaired muscle control** and coordination.
- Symptoms may include:
  1. Lack of coordination
  2. Difficulty walking or mobility problems
  3. Slurred speech
  4. Abnormal eye movements
  5. Headaches
  6. Ataxia (loss of voluntary movement control)

The Peripheral Nervous System (PNS):

- The **PNS** includes cranial, spinal, somatic, and autonomic nerves along with their ganglia and connective tissue coverings.

- Peripheral nerves contain bundles of axons, which are surrounded by Schwann cells that may form myelin depending on axon diameter.

- Nerve fibers are organized into fascicles that vary in size and number depending on the nerve and its location.



Myelinated and Unmyelinated Axons

- Nerve fibers (axons) transmit nerve impulses in response to environmental signals. They include **sensory neurons**, **interneurons**, and **motor neurons**.
- Based on the presence of a myelin sheath, axons are classified into:
  - **Myelinated axons** – covered by myelin, conduct impulses rapidly, and are better protected.
  - **Unmyelinated axons** – lack myelin, are thinner (usually <1 µm), and conduct impulses more slowly.
- The **axon** is a long projection of a neuron responsible for transmitting impulses from one neuron to another. Axon length varies; for example, some (like in long peripheral nerves) can reach about 1 meter.
- **Myelin** is a lipid-rich insulating layer around axons that increases conduction

speed and protects the fiber.

- Gaps in the myelin sheath are called **nodes of Ranvier**, which enable rapid impulse transmission through **saltatory conduction** (impulses jump from node to node).
- In the **CNS**, myelin is produced by **oligodendrocytes**; in the **PNS**, it is produced by **Schwann cells**.

Autonomic nervous system

Autonomic nervous system is an involuntary system that primarily controls and modulates the functions of the visceral organs.

Autonomic nerves effect the activity of smooth muscle, the secretion of some glands, heart rate, and many other involuntary activity by which the body maintains a constant internal environment (**homeostasis**).

- **Autonomic ganglia** are small swellings along autonomic nerves that contain mainly multipolar neurons.
- Some are located within organs (especially in the digestive tract), where they form intramural ganglia.
- Their connective tissue capsule may be poorly defined, and neurons are surrounded by satellite cells, which may be less visible in intramural ganglia.
- **The autonomic nervous system functions through a two-neuron pathway:**
    - The first neuron (preganglionic neuron) is located in the CNS.
    - Its axon synapses with a second neuron (postganglionic neuron) in a peripheral autonomic ganglion.
    - The neurotransmitter released by all preganglionic fibers is acetylcholine.

Sympathetic	Parasympathetic

Involved in the fight or flight response.	Involved in maintaining homeostasis and also, permits the rest and digest response.
The sympathetic system prepares the body for any potential danger.	The parasympathetic system aims to bring the body to a state of calm.
Sympathetic system has shorter neuron pathways, hence a faster response time.	Has comparatively longer neuron pathways, hence a slower response time.
Increases heartbeat, muscles tense up.	Reduces heartbeat, muscles relaxes.
The pupil dilates to let in more light.	The pupil contracts.
Saliva secretion is inhibited.	Saliva secretion increases, digestion increases.
On "fight and flight" situations, Adrenaline is released by the adrenal glands; more glycogen is converted to glucose.	No such functions exist in "fight or flight" situations.

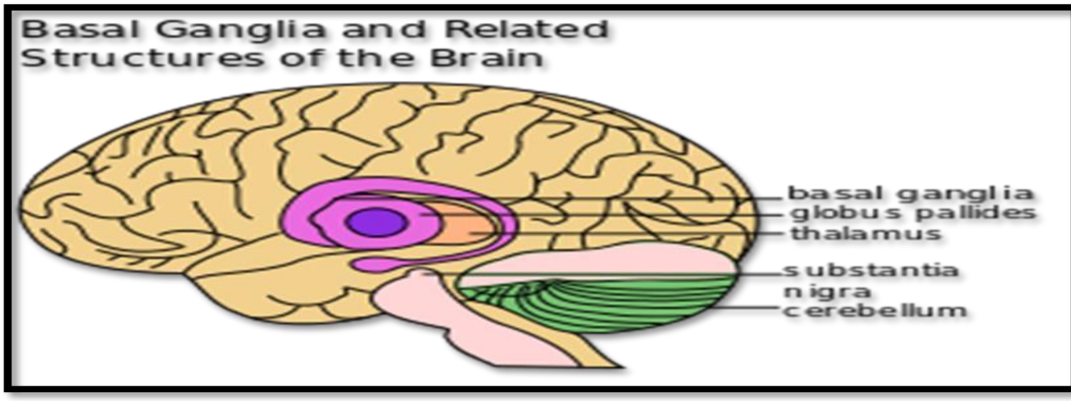
Basal Ganglia

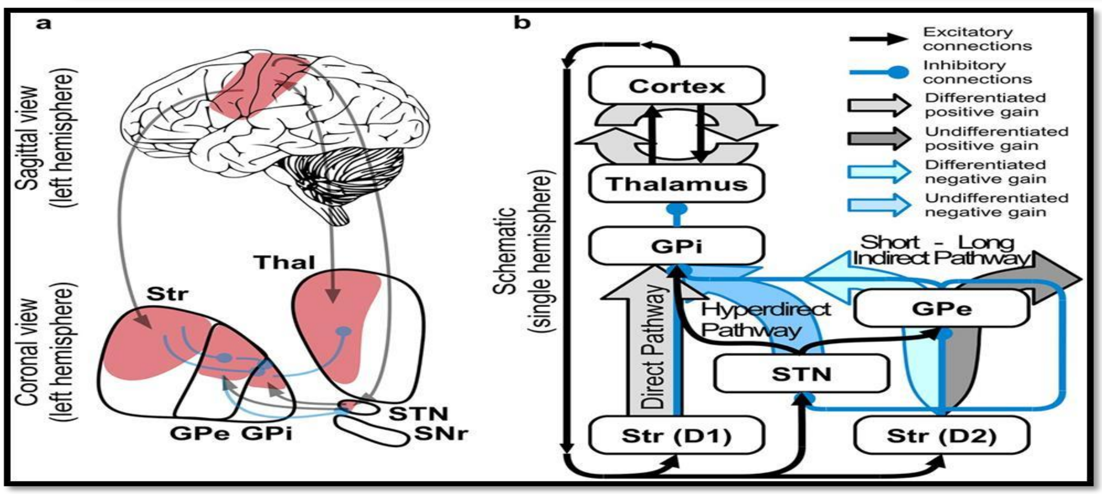
- The **basal ganglia** are a group of subcortical nuclei located at the base of the forebrain.

  They are primarily responsible for **motor control**, and also play roles in motor learning, executive functions, emotional behavior, reward, reinforcement, addiction, and habit formation.

  Dysfunction of the basal ganglia leads to movement disorders such as **Parkinson's disease** and **Huntington's disease**.

The classical model of the basal ganglia describes two opposing pathways that regulate the flow of information back to the cortex to ensure proper movement execution.





The classical basal ganglia model has been updated with new research findings.

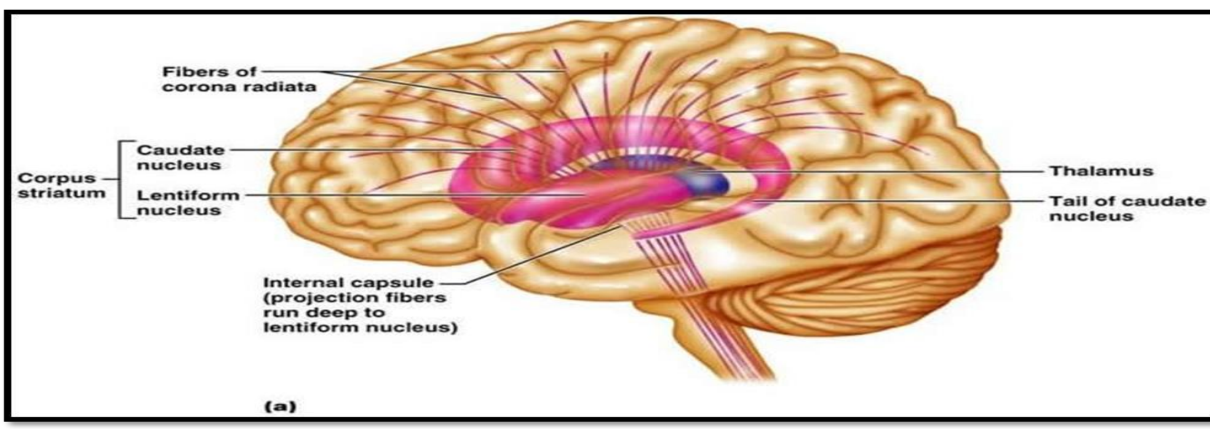
The basal ganglia are now understood as **multiple parallel and re-entering circuits**, rather than just two simple pathways.

These circuits involve **motor, associative, and limbic areas**.

They contribute not only to movement control, but also to behavior, cognition, and emotional regulation.

Structure

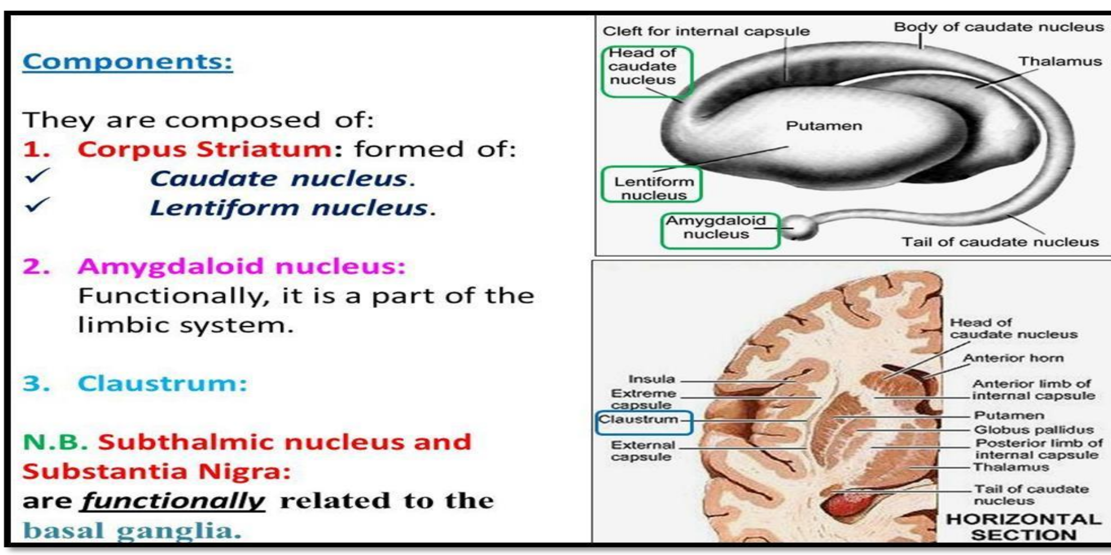
- The **basal ganglia** are four main subcortical nuclei involved in voluntary movement. Unlike most motor system components, they do not directly connect with the spinal cord.
- They receive input mainly from the **cerebral cortex** and send output to the **brainstem** and back to the cortex (prefrontal, premotor, and motor areas) via the **thalamus**. Thus, their motor effects are mediated largely through the frontal motor cortex.
- The largest part of the basal ganglia is the **corpus striatum**, which includes:
    - **Caudate nucleus**
    - **Lentiform nucleus** (putamen + globus pallidus externus and internus)
    - **Subthalamic nucleus (STN)**
    - **Substantia nigra (SN)**
- These structures are interconnected and work together to either facilitate or inhibit movement.
- The **striatum** is the largest subcortical structure of the basal ganglia and receives input from multiple cortical and subcortical areas, projecting to other basal ganglia nuclei. It has two main divisions.



A-**Dorsal striatum (DS):-** Primarily involved in control over conscious motor movements and executive functions. The dorsal striatum consists of the caudate nucleus and the putamen. A white matter, nerve tract (the internal capsule) in the dorsal striatum separates the caudate nucleus and the putamen.

B-**Ventral striatum (VS)**:- responsible for limbic functions of reward and aversion. Consists of nucleus accumbens and the olfactory tubercle.

1- **Internal and External segments of Globus Pallidus** (until the first half of the 19th century the globus pallidus and putamen were considered one structure, collectively referred to as the lentiform or lenticular nucleus.
2- **Subthalamic Nucleus (STN)** a lens-shaped cell group that makes up the largest part of the subthalamus
3- **Substantia Nigra (SN**) ("black substance" in Latin) is a long nucleus located in the midbrain but considered functionally a part of the basal ganglia because of its reciprocal connections with other brainstem nuclei. It consists of two components, the pars compacta and the pars reticulata, which have different connections and use different neurotransmitters.



Basal Ganglia - Current Concepts

- Originally, the basal ganglia were described as a **single motor loop**, where cortical input is processed and sent back to the cortex to either facilitate or inhibit movement.

- They were considered a simple "relay station" in motor control.
- Current understanding shows that the basal ganglia consist of **multiple interconnected loops**, including cortical and subcortical projections with internal re-entry circuits.
- This complex network allows for **simultaneous selection and inhibition of movements**, as well as regulation of behavior and other functions.

Pons and Medulla Oblongata

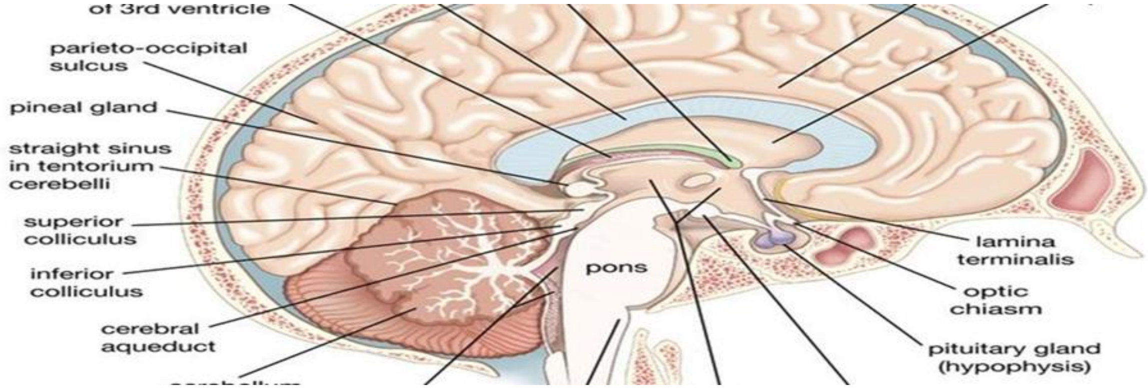
Medulla Oblongata

- The **medulla oblongata** is the lowest part of the brainstem.
- It connects the **pons** above and continues inferiorly as the spinal cord at the **foramen magnum**.
- It plays a vital role in:
  - Transmission of signals between the spinal cord and brain
  - Control of vital autonomic functions such as **heartbeat and respiration**

Structure of the Medulla

- Divided into:
  - **Ventral (anterior) medulla**
  - **Dorsal (posterior) medulla (tegmentum)**
- The ventral medulla contains:
  - **Pyramids** → contain corticospinal and corticobulbar tracts
  - **Pyramidal decussation** → where 80–90% of corticospinal fibers cross to the opposite side
  - **Olivary bodies** → located laterally to the pyramids

These structures are essential for motor pathway transmission and coordination.



Spinal Cord

- The spinal cord is a long, thin tubular structure of nervous tissue that extends from the medulla oblongata to the level between the first and second lumbar vertebrae (L1–L2).
- It passes through the foramen magnum and lies within the vertebral canal.
- It contains a central canal filled with cerebrospinal fluid (CSF).
- Together with the brain, it forms the central nervous system (CNS).

Size

- Length: about 45 cm in adult males and 43 cm in adult females.
- Diameter:
  - ~13 mm in the cervical and lumbar enlargements
  - ~6.4 mm in the thoracic region

Functions

- Transmits motor signals from the motor cortex to the body.
- Transmits sensory information from peripheral receptors to the sensory cortex.
- Acts as a reflex center, containing reflex arcs that function independently of the brain.
- Contains central pattern generators (CPGs) responsible for rhythmic

movements such as walking.

- Gives rise to 31 pairs of spinal nerves that exit the vertebral column.

Regions of the Spinal Cord

The spinal cord is divided into five regions:

1. Cervical region – the uppermost part, continuous with the medulla oblongata.
2. Thoracic region – located below the cervical region.
3. Lumbar region – a shorter segment.
4. Sacral region
5. Coccygeal region – the most inferior “tip” of the spinal cord.