

ANATOMY, PHYSIOLOGY & PATHOLOGY NOTES OF THE NERVOUS SYSTEM AND SPECIAL SENSES

FOURTH EDITION

**PRE-SUMMARIZED
READY-TO-STUDY
HIGH-YIELD NOTES**

**FOR THE TIME-POOR
MEDICAL, PRE-MED,
USMLE OR PA STUDENT**



297 PAGES

A Message From Our Team

Studying medicine or any health-related degree can be stressful; believe us, we know from experience! The human body is an incredibly complex organism, and finding a way to streamline your learning is crucial to succeeding in your exams and future profession. Our goal from the outset has been to create the greatest educational resource for the next generation of medical students, and to make them as affordable as possible.

In this fourth edition of our notes we have made a number of text corrections, formatting updates, and figure updates which we feel will enhance your study experience. We have also endeavoured to use only open-source images and/or provide attribution where possible.

If you are new to us, here are a few things to help get the most out of your notes:

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- BLOOD SUPPLY OF THE BRAIN
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- MYASTHENIA GRAVIS
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- BRAIN TUMOURS
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EMBRYONIC DEVELOPMENT OF THE NERVOUS SYSTEM

EMBRYONIC DEVELOPMENT OF THE NERVOUS SYSTEM

General Embryonic Development is Described as Either:

- **Trimesters** (3x 3-Month Periods):
 - **First:** - *Foundations* of Major Organs
 - **Second:** - *Development* of Organs
 - **Third:** - *Rapid Growth & Fully Functional Organs.*
- **OR... Anatomical Stages: ****(These are more relevant)
 - **Pre-Embryonic Period: 0-2 Weeks**
 - Fertilisation
 - Blastocyst Formation & Implantation
 - Gastrulation
 - **Embryonic Period: 3-8 Weeks**
 - Development & Differentiation of 3 Germ Layers into foundations of Organs.
 - **Foetal Period: 9 Weeks → Birth.**
 - Period of *Growth*, NOT Differentiation.

	PRE-EMBRYONIC PERIOD	EMBRYONIC PERIOD	FETAL PERIOD
Developmental stage	 <p style="text-align: center;">Blastocyst</p>	 <p style="text-align: center;">Embryo</p>	 <p style="text-align: center;">Fetus</p>
Events	Weeks 1 and 2: <ul style="list-style-type: none"> • Zygote divides mitotically many times to produce a multicellular blastocyst that implants in the uterus. 	Weeks 3 through 8: <ul style="list-style-type: none"> • Blastocyst grows, folds, and forms rudimentary organ systems. • It is now called an embryo. 	Weeks 9 through 38 (until birth): <ul style="list-style-type: none"> • Embryo is now called a fetus. • It grows larger and develops until its organ systems can function without assistance from the mother.

Source: Unattributable

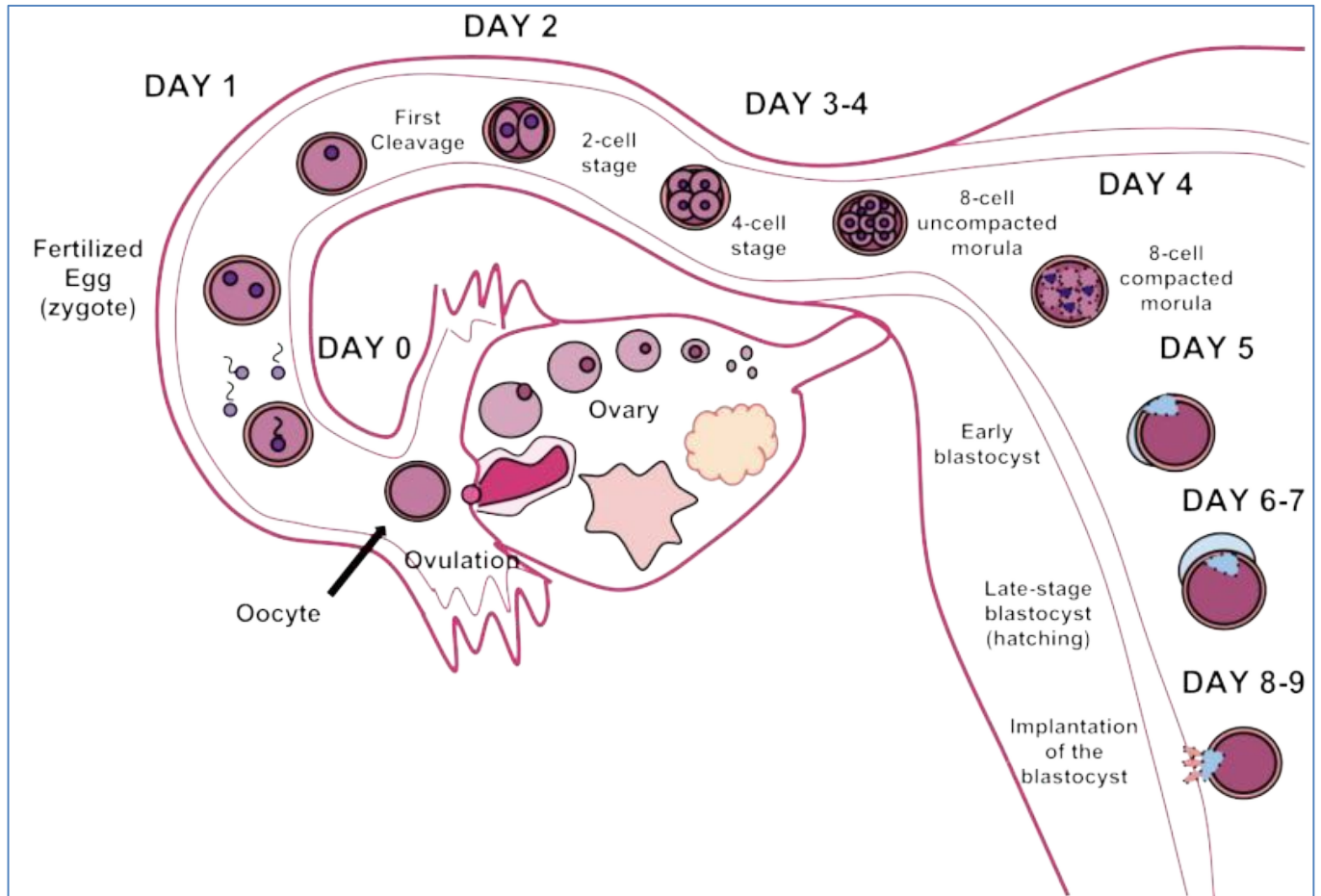
Some Useful Terminology:

- "Rostral" = Head
- "Caudal" = Tail
- "Dorsal" = Back
- "Ventral" = Front
- "Ganglia" = Groups of Nerve-Cell Bodies
- "Gyrus" = Elevations (Crests) of the folds on the Cerebral Cortex.
- "Sulcus" = Grooves / Furrows between the Gyri on the Cerebral Cortex.

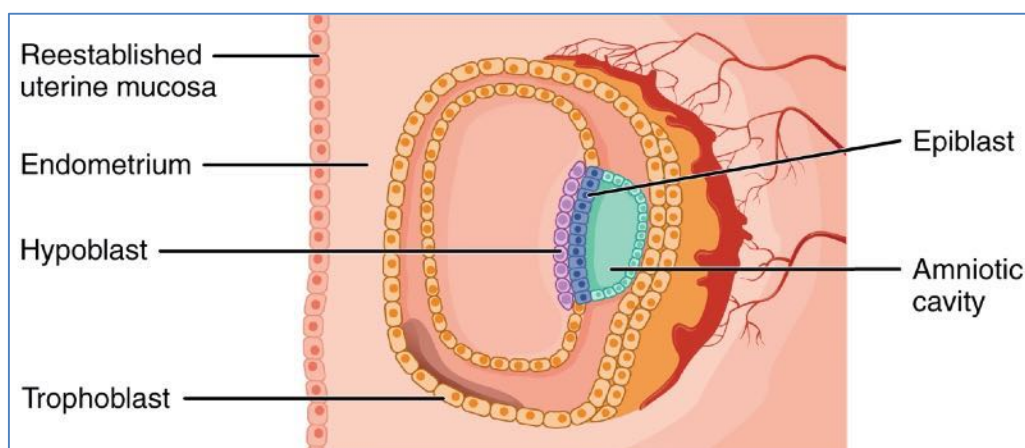
Embryonic Development of the Nervous System:

1. Blastocyst: (Pre-Embryonic Period)

- A fertilised egg reaches the **Morula** stage (Day 3), differentiates into a **Blastocyst** (Day 7) and then implants in the endometrium.
- The implanted **Blastocyst** consists of an 'Inner-Cell Mass' surrounded by Trophoblasts.
- This 'Inner-Cell Mass' differentiates to form the '**Bilaminar Disc**' (2 layers of cells)
 - Epiblast Layer:** The *top* layer of *Columnar Cells*.
 - Hypoblast Layer:** The *bottom* layer of *Cuboidal Cells*.



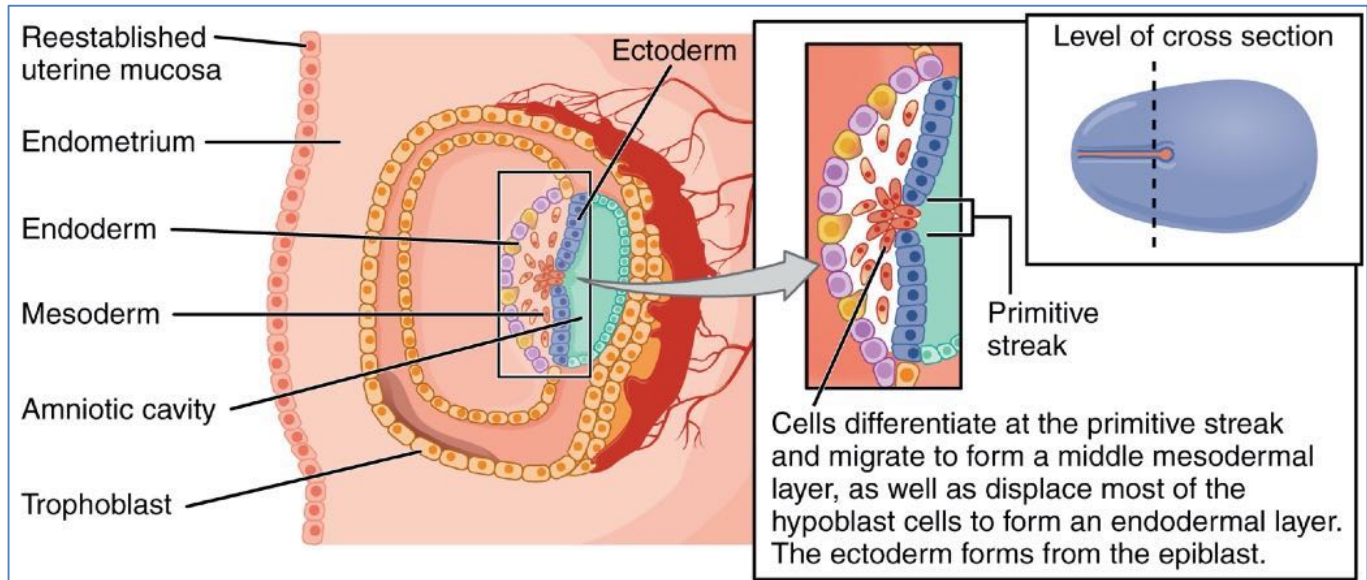
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2. Gastrulation: (Embryonic Period [wk 3+])

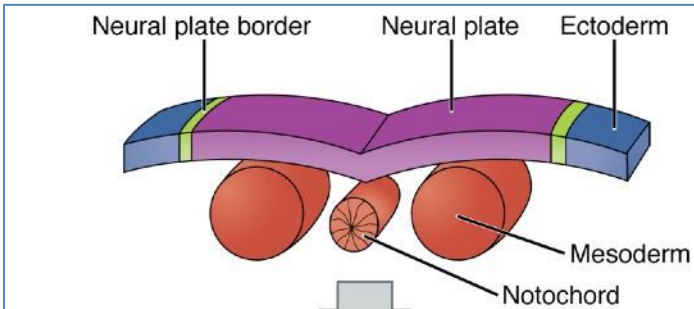
- Gastrulation = the process that establishes the **3 Primary Germ Layers** in the Embryo.
- Begins with formation of the **Primitive Streak** (a shallow midline groove) along the caudal/tail half of bilaminar disc.
- At the cephalic/head end of the Primitive Streak is the **Primitive Node** which surrounds the small **Primitive Pit**. Cells of the **Epiblast** proliferate & migrate *through* the **Primitive pit** into the gap between the Epiblast & the Hypoblast. This is known as **Invagination**
- The **Epiblast** then becomes the **Ectoderm**, the invaginated cells become the **Mesoderm** and the **Hypoblast** becomes the **Endoderm**.



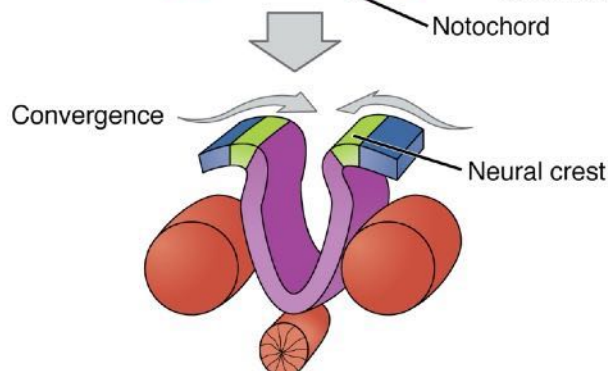
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3. Neurulation:

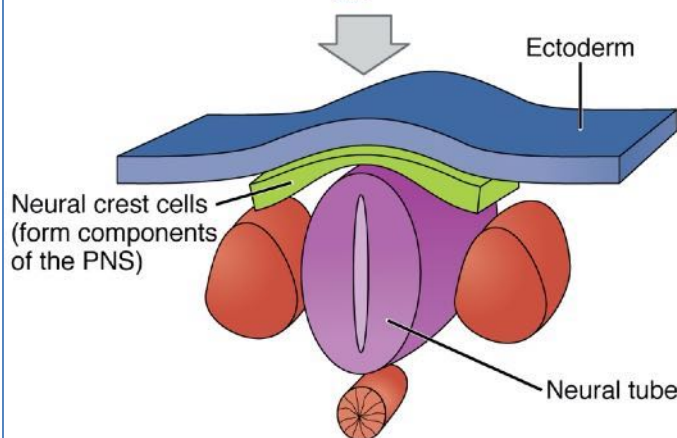
- Neurulation = Where the ectoderm around the midline thickens to form an elevated **Neural Plate**.
- This **Neural Plate** invaginates to form a **Neural Groove** down the midline, flanked by 2 **Neural Folds**. The **Notochord**, a flexible rod of mesoderm-derived cells, defines the primitive axis of the embryo.
- The outer edges of the 2 **Neural Folds** continue folding towards the midline where they fuse together to form the **Neural Tube**. (Note: Initially this happens around the centre of the embryo, leaving open Neural Grooves at both the Cephalic & Caudal ends. However, these Neural Grooves, aka **Neuropores**, close off by around wk 6 of development. Failure of a **Neuropore** to close can result in Neural Tube Defects such as Spina-Bifida)
- The hollow part inside the **Neural Tube** is called the **Neurocoele**
- The **Neural Tube** then separates from the **Ectoderm** and sinks down to the level of the Mesoderm.
 - The Mesoderm that flanks the sunken Neural Tube develops into **The Somites**, which eventually become the Skin, Skeletal Muscle & Vertebrae+Skull.
- Next, some cells on the top of the **Neural Tube** differentiate and separate to form the **Neural Crest**. Cells of the **Neural Crest** eventually migrate & give rise to **Peripheral Sensory Neurons, Autonomic Neurons & Sensory Ganglia** of the spinal nerves.



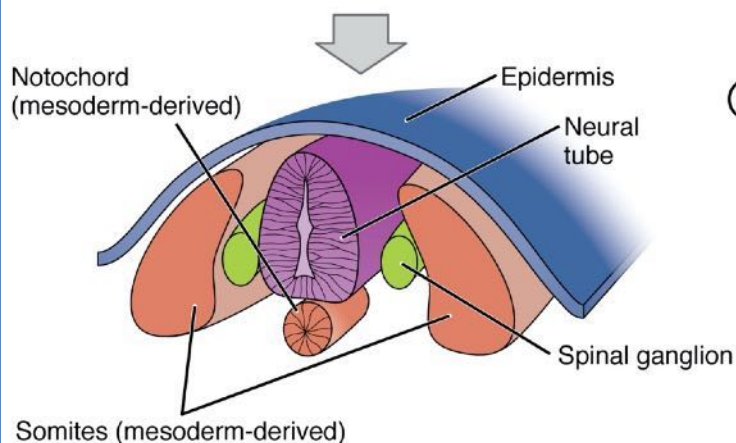
- ① Neuroectodermal tissues differentiate from the ectoderm and thicken into the neural plate. The neural plate border separates the ectoderm from the neural plate.



- ② The neural plate bends dorsally, with the two ends eventually joining at the neural plate borders, which are now referred to as the neural crest.



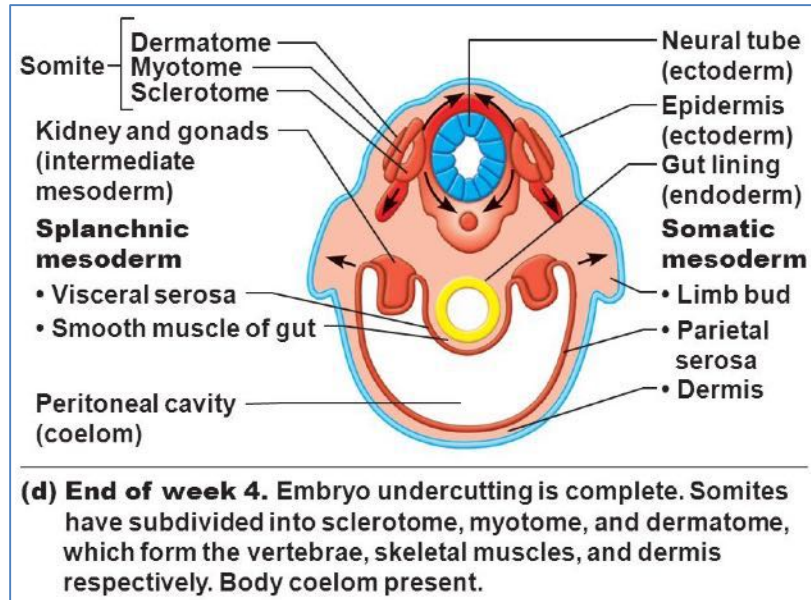
- ③ The closure of the neural tube disconnects the neural crest from the epidermis. Neural crest cells differentiate to form most of the peripheral nervous system.



- ④ The notochord degenerates and only persists as the nucleus pulposus of the intervertebral discs. Other mesoderm cells differentiate into the somites, the precursors of the axial skeleton and skeletal muscle.

The Somites:

- **Somites** = The Mesoderm Tissue directly adjacent to Neural Tube.
 - The Mesoderm that flanks the sunken Neural Tube develops into **The Somites**, which eventually become the Skin, Skeletal Muscle & Vertebrae+Skull.
- Somites grow in association with the developing nervous system → establish early connections.
- **Somites** differentiate into **3 regions**:
 - **Sclerotome**: Becomes the **Vertebral Column & Skull**
 - **Myotome**: Becomes **Skeletal Muscle**
 - **Dermatome**: Becomes **Skin**
- Hence, the **Somites** determine the distribution of *Nervous Supply* to all Mesoderm-Derived Tissue.

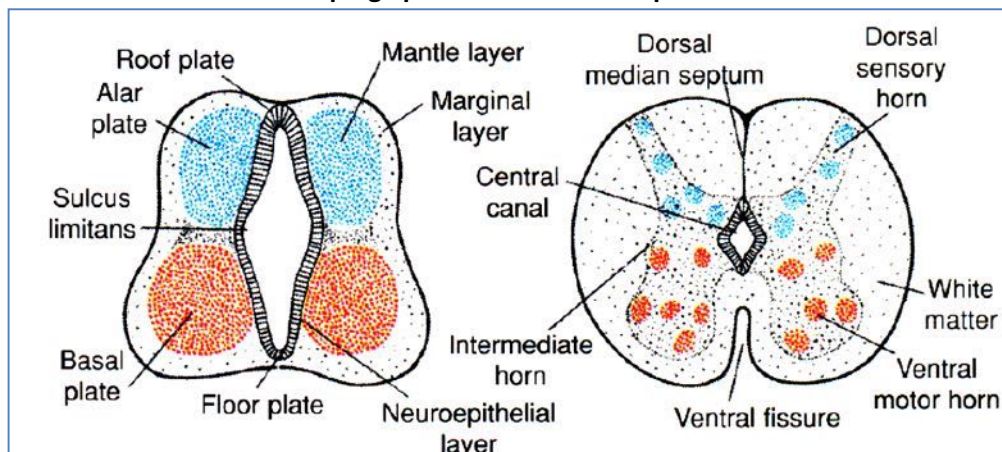


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Development of the Neural Tube Into the Spinal Cord:

1. Once the **Neural Tube** closes, the cells differentiate into **Neuroblasts**
 2. These **Neuroblasts** give rise to 2 concentric layers, **The Mantle Layer** (Inner) and **The Marginal Layer** (Outer).
 - a. **Mantle Layer**: Later forms the *Grey-Matter* of the Spinal Cord. (Ventral & Dorsal 'Horns')
 - b. **Marginal Layer**: Later forms the *White-Matter* of the Spinal Cord.
 3. The Dorsal & Ventral regions of the **Mantle Layer** thicken forming 2x**Basal Plates**, and 2x**Alar Plates**.
 - a. **Basal Plates**: (Motor Plates) Develop into *Motor Neurons* innervating skeletal muscles.
 - i. Become the **Ventral Horns**
 - b. **Alar Plates**: (Sensory Plates) Develop into *Sensory Neurons*.
 - i. Become the **Dorsal Horns**
- Note: The **Lateral Horns** in the Thoracic & Lumbar Regions of the Spinal Cord are **Autonomic Motor Neurons** and their Axons exit via the Ventral Roots.

Developing Spinal Cord vs Adult Spinal Cord

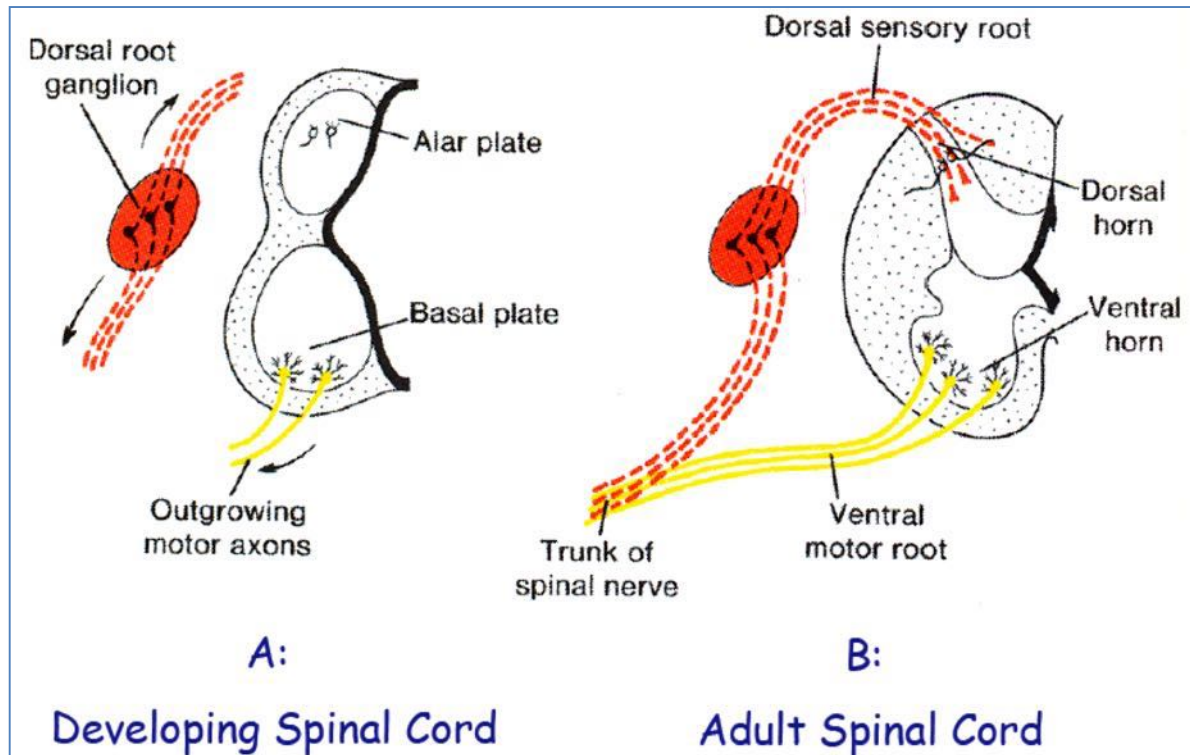


Source: Unattributable

Development of the Neural Crest cells Into the Sensory ('Dorsal-Root') Ganglia of PNS:

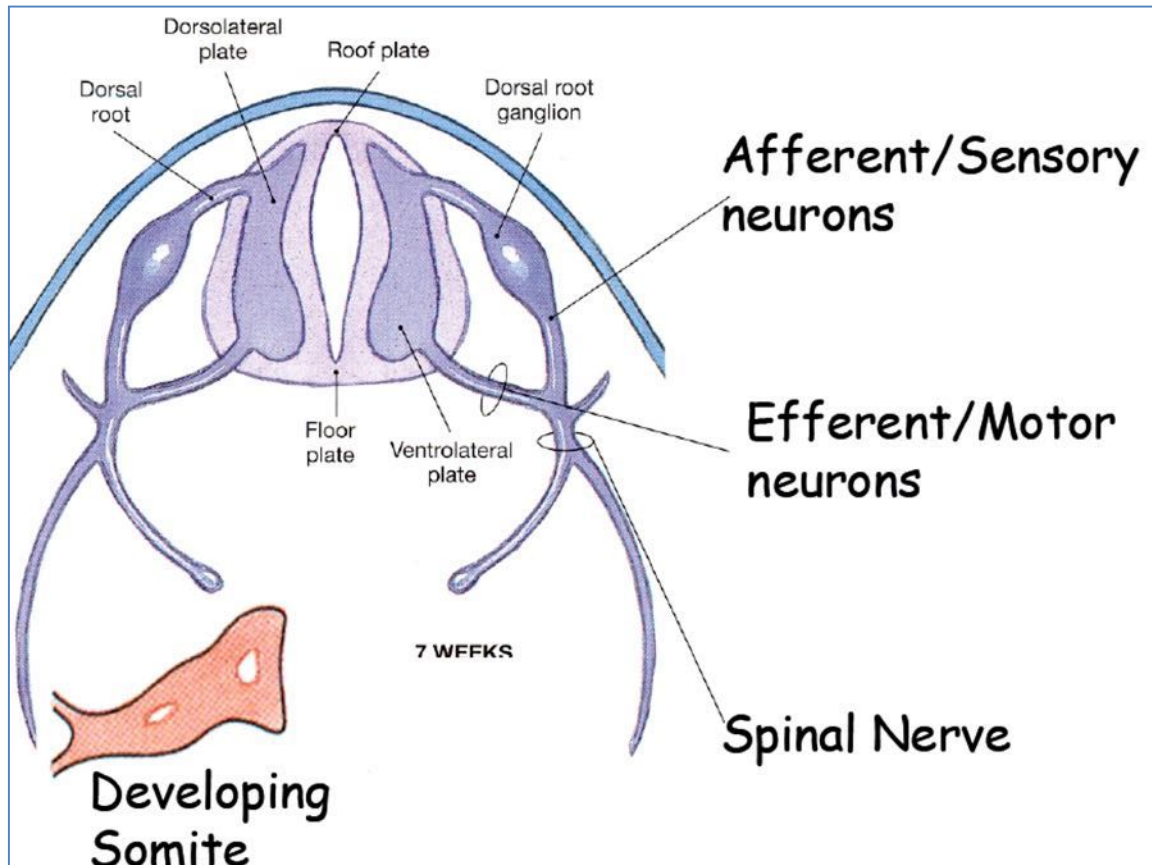
1. **Neural Crest** Cells also differentiate into **Neuroblasts** which become the **Sensory ('Dorsal-Root') Ganglia**.
2. The **Neuroblasts** of the Dorsal-Root Ganglia develop 2 processes:
 - a. Penetrates into the **Alar Plate** of the Neural Tube AND/OR into the **Marginal Layer** & up to brain.
 - b. Grows distally (outwards) and integrates with the Ventral Motor Root, forming the **Trunk** of the **Spinal Nerve**. These neurons eventually terminate in the sensory receptors in skin/muscle/tendons.

Note: These Dorsal-Root Ganglia Processes form the '**Sensory PseudoUnipolar**' Nerve-Type.



Source: Unattributable

Note: By Wk 7 we have a *Nearly-Functional* Nervous System very similar in Organisation to Adult Anatomy.



Source: Unattributable

Development of the Head & Brain:

1. Neural-Tube Enlargement (Cephalic End):

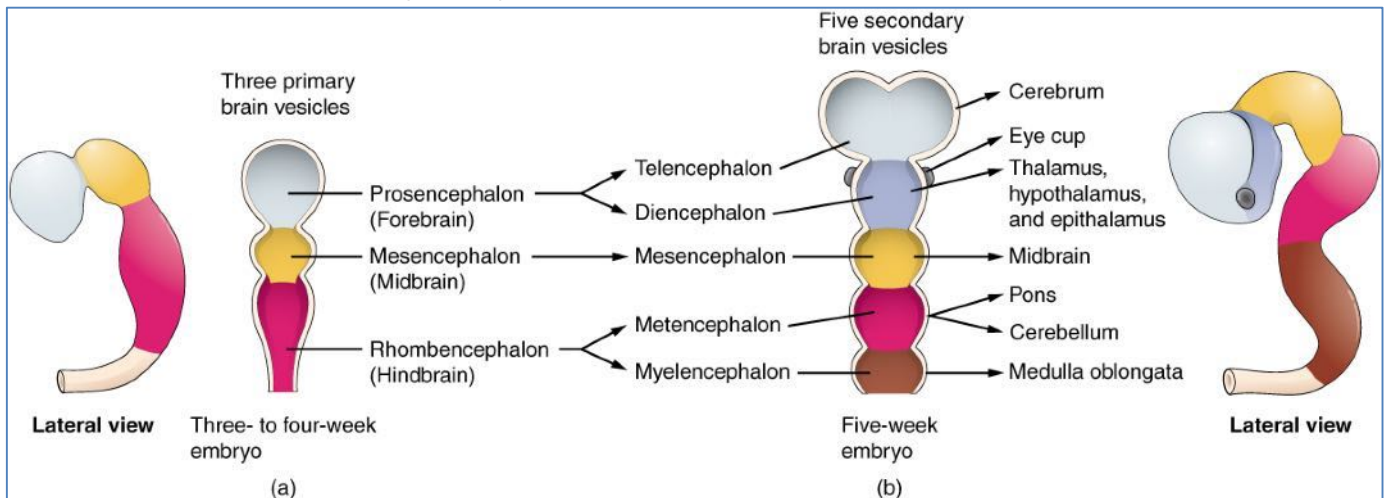
- a. **At around 3-4wks**, the Cephalic portion of the **Neural Tube** enlarges to form 3 regions; the **Primary Brain Vesicles**:

- i. **Prosencephalon** (Fore Brain)
- ii. **Mesencephalon** (Mid Brain)
- iii. **Rhombencephalon** (Hind Brain)

Note: The **Cephalic Flexure** between the Prosencephalon & Mesencephalon – important in humans for **Bipedalism** (Brain @ 90° to Spinal Cord).

- b. **By around 4-5wks**, the **Primary Brain Vesicles** develop further:

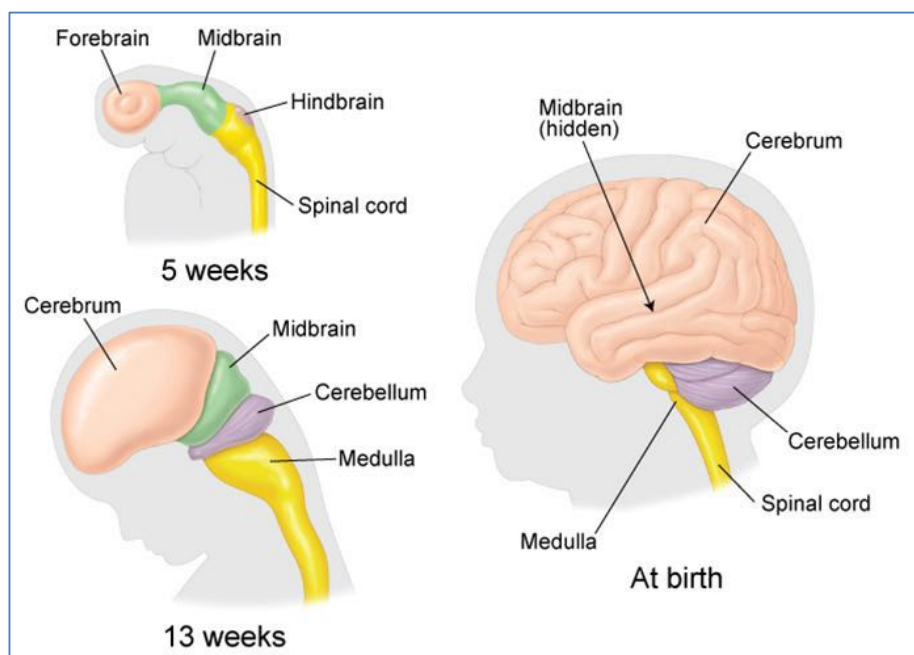
- i. **Prosencephalon** (Fore Brain) develops into:
 1. **Telencephalon** (Future Cerebral Hemispheres)
 2. **Diencephalon** (Future Thalamus & Hypothalamus)
- ii. **Mesencephalon** (Mid Brain)
- iii. **Rhombencephalon** (Hind Brain) develops into:
 1. **Metencephalon** (Future Pons & Cerebellum)
 2. **Myelencephalon** (Future Medulla)



<https://open.oregonstate.edu/aandp/chapter/14-1-embryonic-development/>

2. Brain Formation:

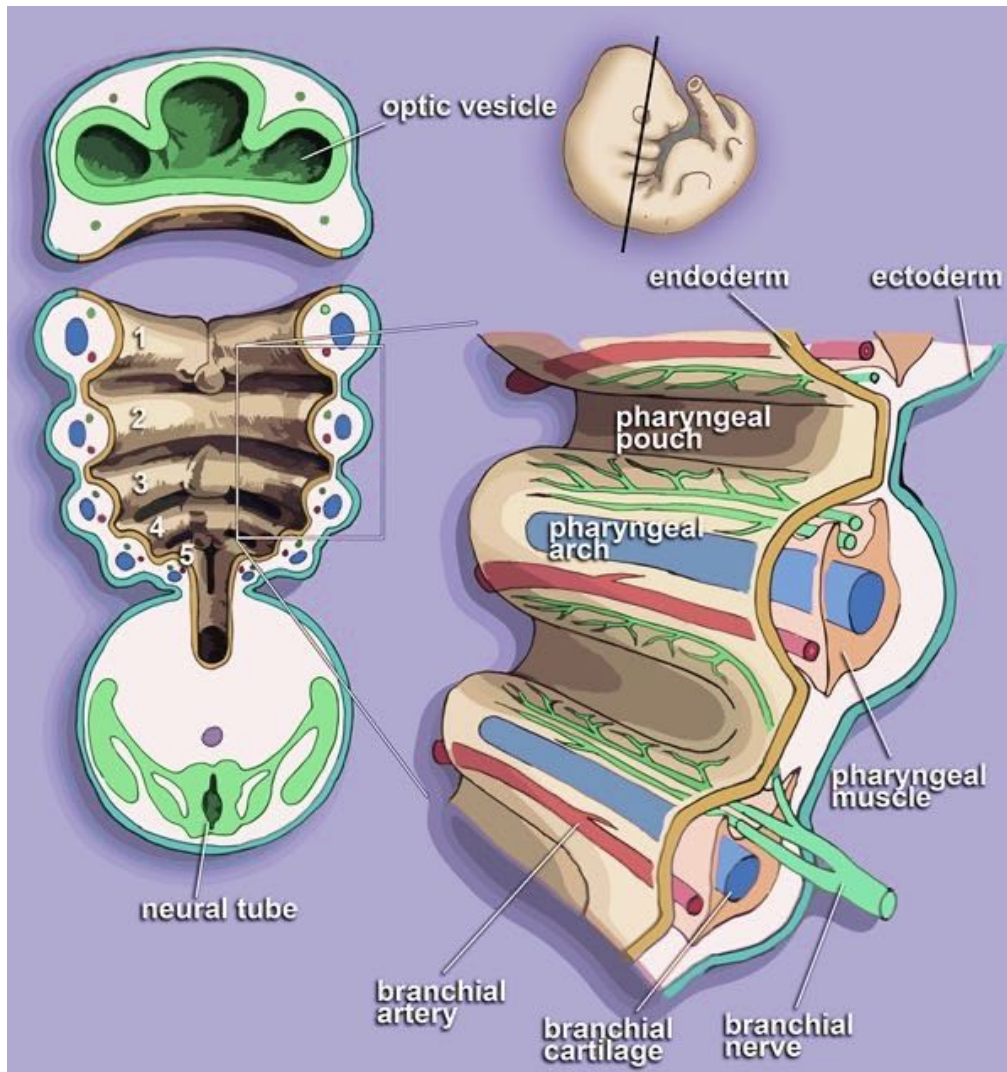
- a. **At around 11-13wks**, there is massive **Proliferation of Neuroblasts** in Cephalic Neural Tube, causing folding due to lack of space within the cranium.



Source: Jonathan Dimes for BabyCenter; https://www.babycenter.com/pregnancy/your-baby/fetal-development-your-babys-brain_20004924

3. Pharyngeal Arches & Cranial Nerves:

- a. **Pharyngeal Arches** = Similar to the **Somites** in lower parts of embryo. Each Pharyngeal Arch consists of:
 - i. **Ectoderm Tissue** → Cranial Nerves & Skin of Face.
 - ii. **Mesenchyme (Mesoderm) Tissue** → Musculature of Face & Neck
 - iii. **Endoderm Tissue** → Pharyngeal Epithelium.
- b. Note: Essentially, this results in *Segmental Development* of the Head & Neck, similar to Somites.



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4. Formation of Ventricles:

a. The **Neurocoele** of the Neural Tube becomes the **Ventricles** of the Adult Brain.

i. **Lateral Ventricles (Vent. 1 & 2):**

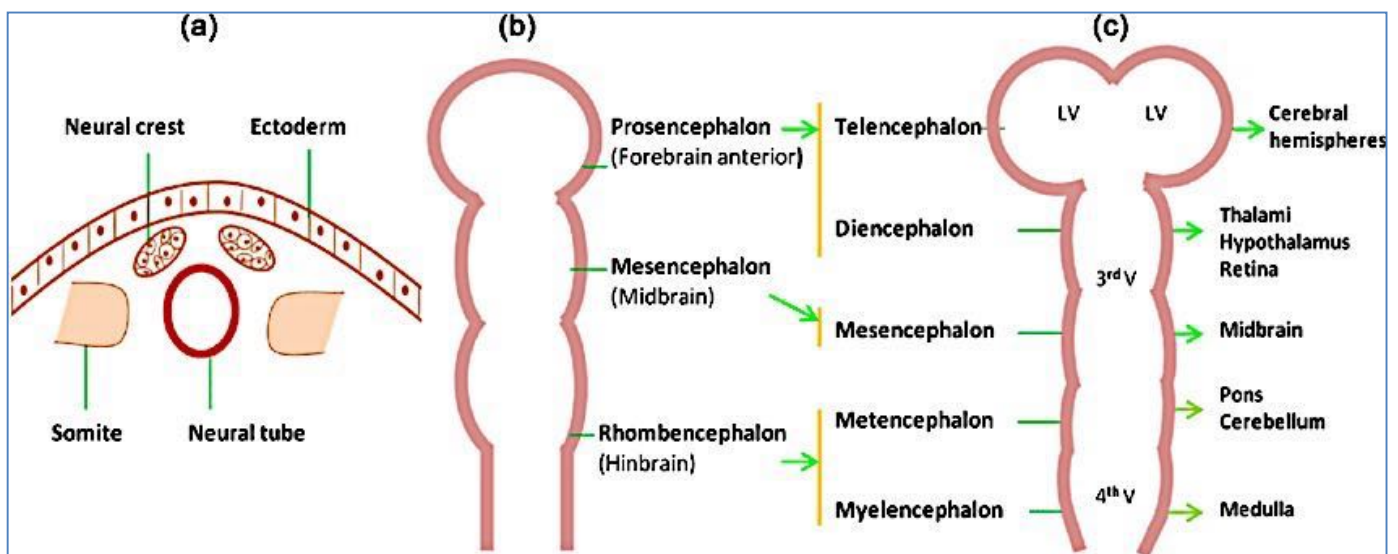
1. Sits in the Cerebral Hemispheres (Telencephalon)
2. Are shaped due to folding of brain during development.
3. Each Consists of:
 - a. An Frontal (Anterior) Horn
 - b. A 'Body'
 - c. An Occipital (Posterior) Horn
 - d. A Temporal (Inferior) Horn

ii. **Third Ventricle:**

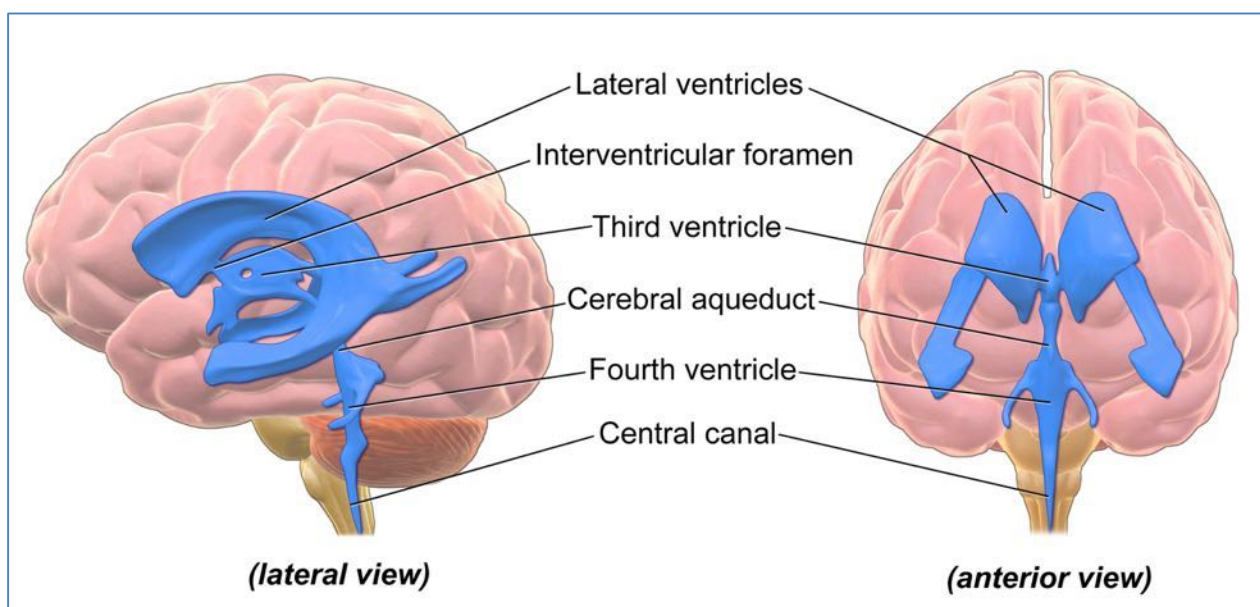
1. Sits in the Diencephalon
2. Lateral Walls formed by Thalamus & Hypothalamus
3. Connects with the 4th Ventricle via the **Cerebral Aqueduct**.

iii. **Fourth Ventricle:**

1. Sits in the Brainstem
2. Is Continuous with the **Spinal Canal (Central Canal)**.



Creative Commons: https://www.researchgate.net/figure/Neurulation-and-formation-of-the-cerebral-vesicles-a-neural-tube-at-the-end-of-the-3_fig2_335125768



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OVERVIEW & ORGANISATION OF THE NERVOUS SYSTEM

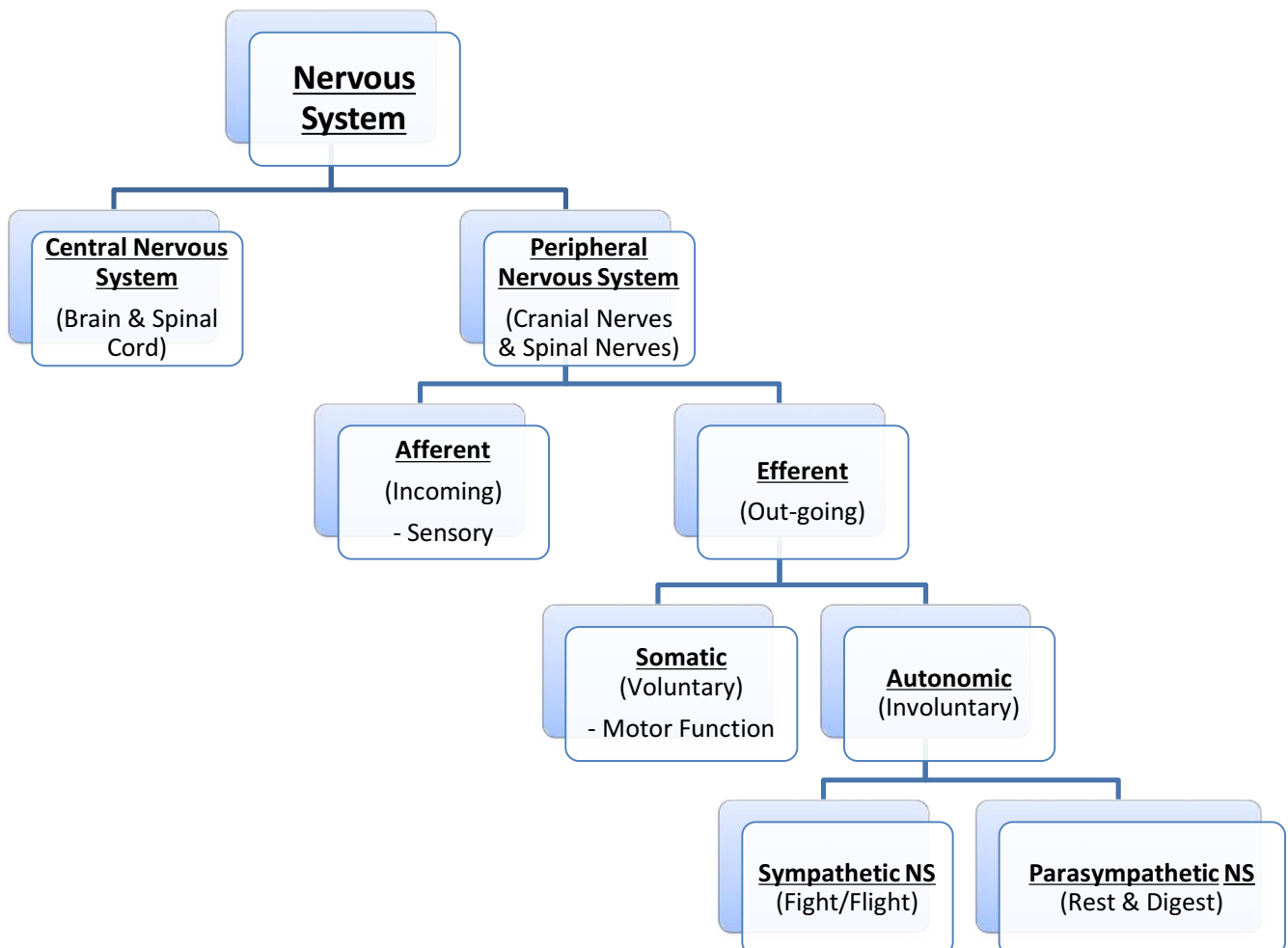
OVERVIEW & ORGANISATION OF THE NERVOUS SYSTEM

The Nervous System - Overview:

- **Macro Structures:**
 - Brain
 - Spinal Chord
 - Peripheral Nerves
 - Sense Organs
 - Eyes
 - Ears
 - Tongue
 - Olfactory bulbs
 - Skin
- **Functions:**
 - Detection of stimuli (external/internal)
 - Response to stimuli
 - Coordinates activity of other organs & systems

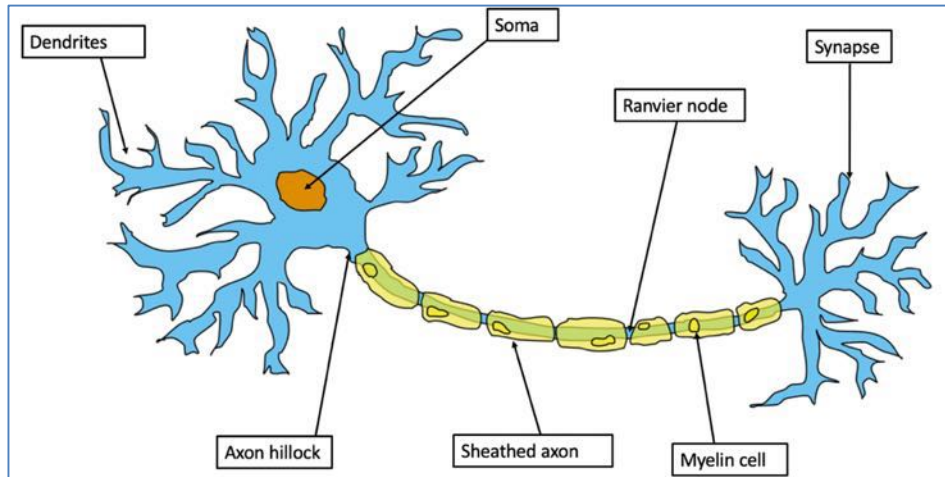
Organisation of the Nervous System:

- **Central Nervous System (the “CPU” & “Motherboard”)**
 - Brain
 - Spinal Cord
- **Peripheral Nervous System (the “Cables”)**
 - Cranial Nerves & Spinal Nerves
 - Communication between CNS & rest of body



The Neuron - Structural Features:

- a) **Receptive Field: Dendrites**
 - Stimulated by inputs
- b) **Cell Body: Soma**
 - Responds to graded inputs
- c) **Efferent Projection: Axon (and Axon Hillock)**
 - Conducts nerve impulses to target
 - Myelinated and unmyelinated
- d) **Efferent Projection: Myelin Sheath**
- e) **Efferent Projection: "Nodes of Ranvier"**
- f) **Output: Synaptic Terminals (Axon Terminals)**

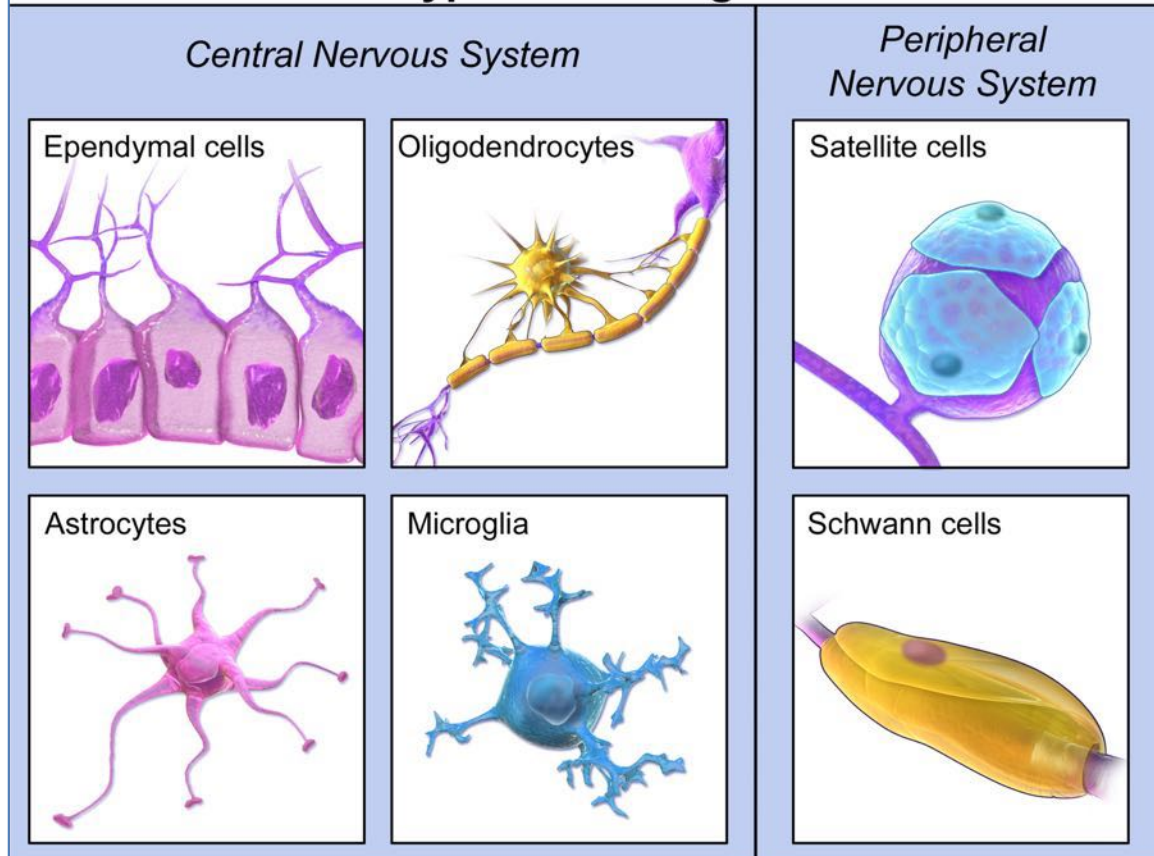


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Supporting Cells: "Neuroglia" (Glia)

- Smaller **support cells** of NS
- Outnumber neurons 10:1
- Structural & mechanical support
- Roles in maintaining homeostasis & Myelination
- Immune responses via phagocytosis.
- **Neuroglia of the Central Nervous System (CNS):**
 - **Astrocytes**
 - Nutrient bridge between neuron & capillaries
 - Guide migrating young neurons
 - Synapse formation
 - Mop up excess K^+ ions + neurotransmitters
 - **Microglia**
 - Long thorny processes
 - Monitors neuron health
 - Senses damaged neurons
 - Migrates to damaged neuron
 - Phagocytoses microbes & debris (immune cells are denied access to CNS)
 - **Oligodendrocytes**
 - Myelin formation in CNS
 - **Ependymal Cells**
 - Lines central cavities of brain + spinal chord
 - Blood-brain barrier
 - Beating cilia circulates cerebrospinal fluid
- **Neuroglia of the Peripheral Nervous System (PNS):**
 - **Schwann Cells**
 - Myelin Formation – wrap around axon
 - Regeneration of damaged neurons
 - **Satellite cells**
 - Surround neuron bodies
 - Structure, nutritional support & protection.

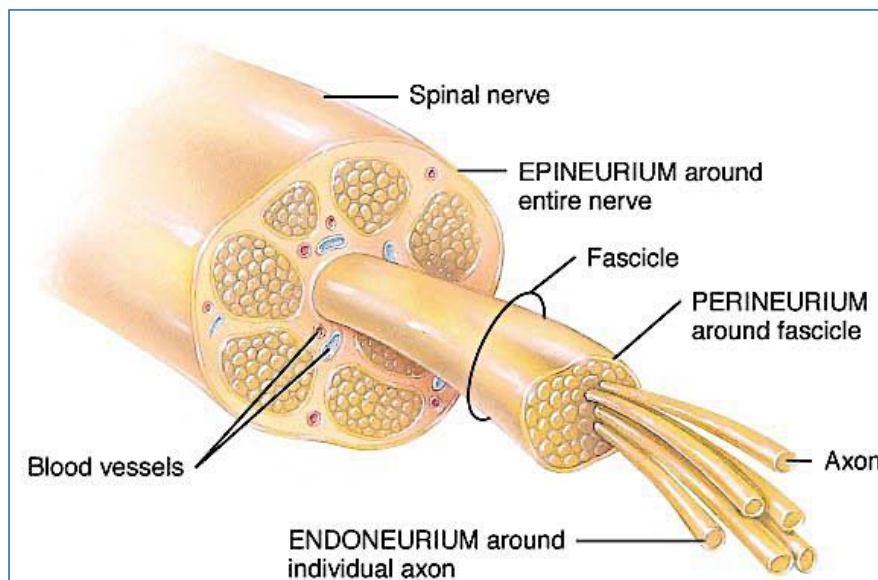
Types of Neuroglia



Blausen.com staff (2014). "Medical gallery of Blausen Medical 2014". WikiJournal of Medicine 1 (2). CC BY 3.0
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Connective Tissue Sheaths on Peripheral Nerves:

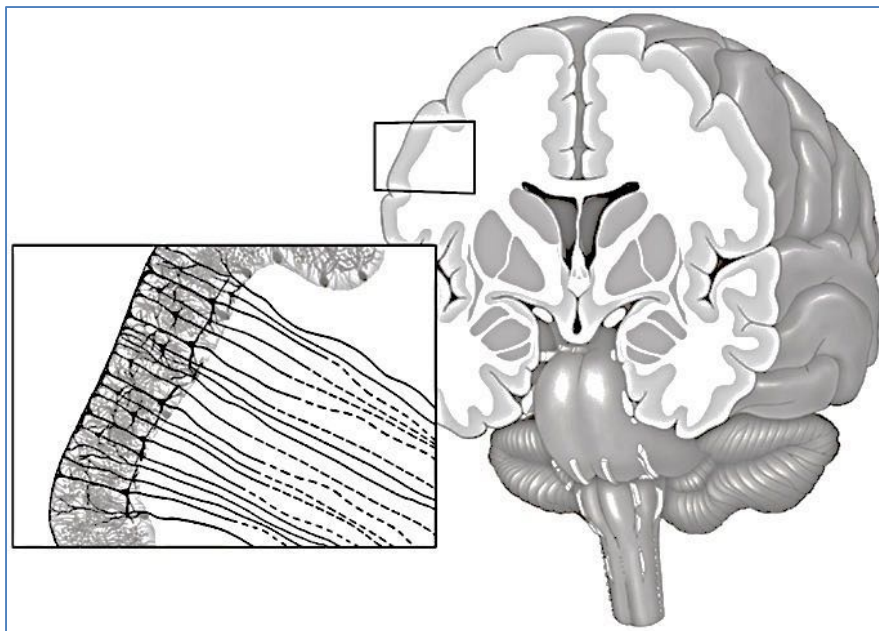
- **Endoneurium**
 - Delicate connective tissue layer
 - Surrounds each axon
- **Perineurium**
 - Coarser connective tissue layer
 - Bundles groups of fibers into **fascicles**
- **Epineurium**
 - Tight, fibrous sheath
 - Bundles fascicles into a **single nerve**.
 - Houses blood vessels



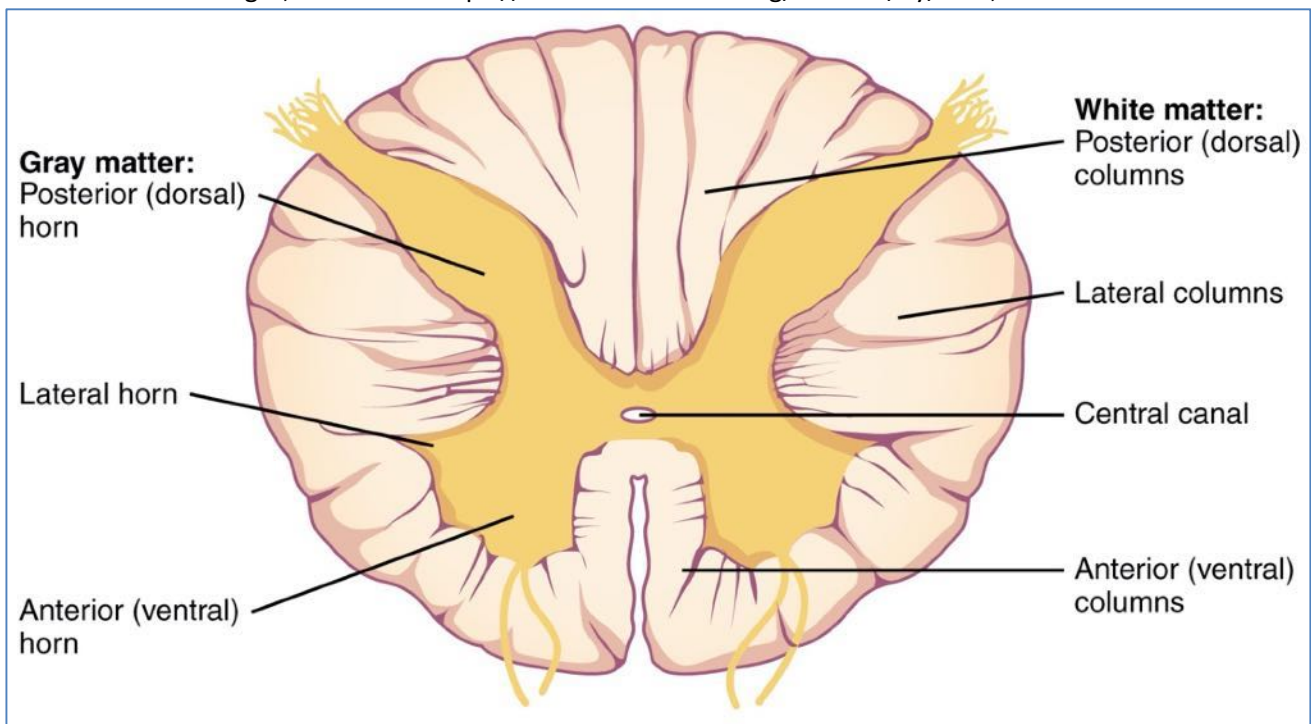
<https://www.tamiaplant.com/blog/2018/8/7/fascial-layers-part-2-anatomy-of-a-nerve>

Gray Matter & White Matter:

- **Gray Matter**
 - Made up of Neuron bodies (Soma)
 - Imbedded in Neuroglial cells
 - Eg:
 - Cortex of Brain
 - Centre of Spinal Chord
 - Ganglia/nuclei
- **White Matter**
 - Neuron fibers (axons & dendrites)
 - White due to myelin
 - Eg:
 - Peripheral Nerves & Plexuses
 - Central fiber tracts



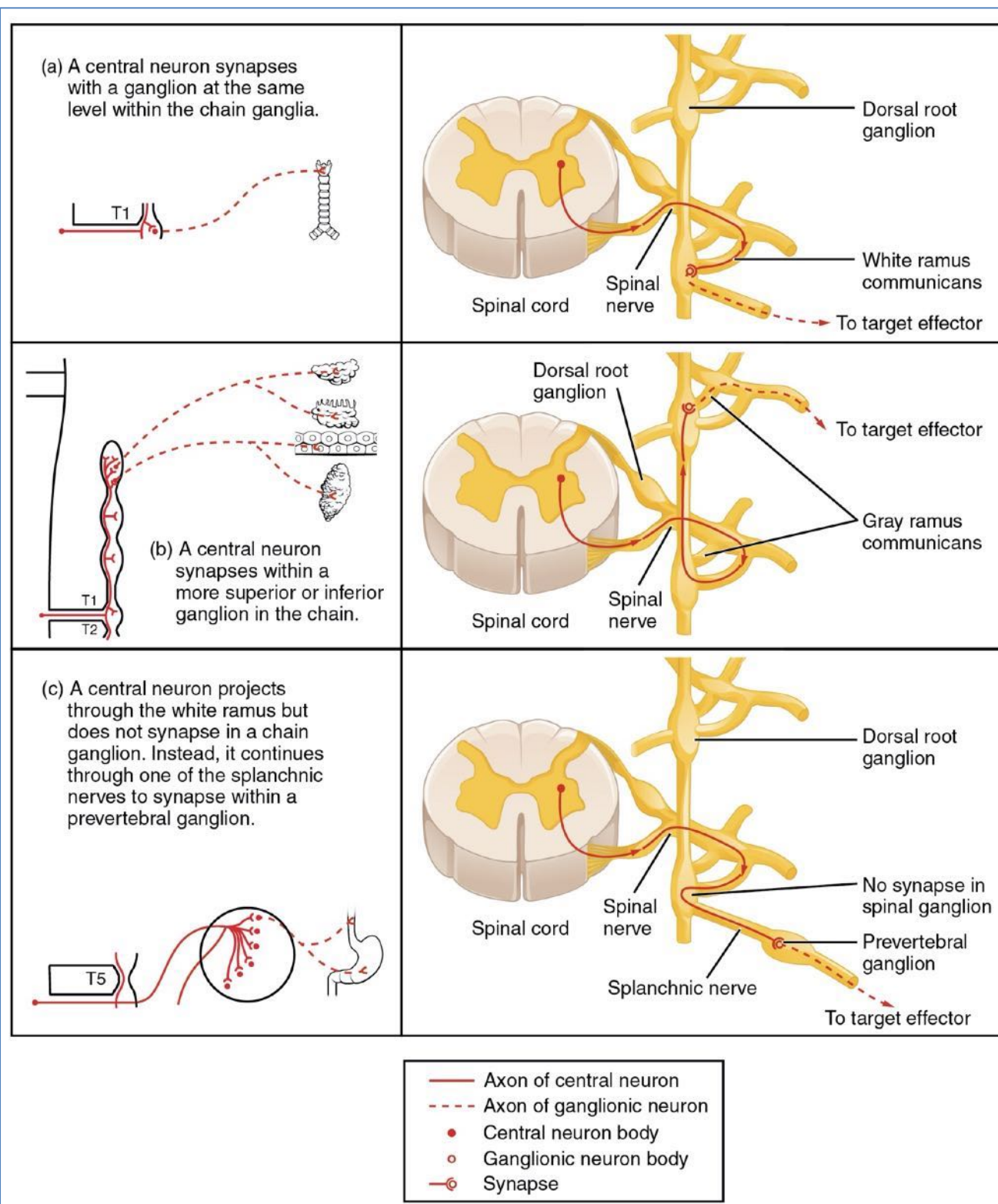
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Ganglia

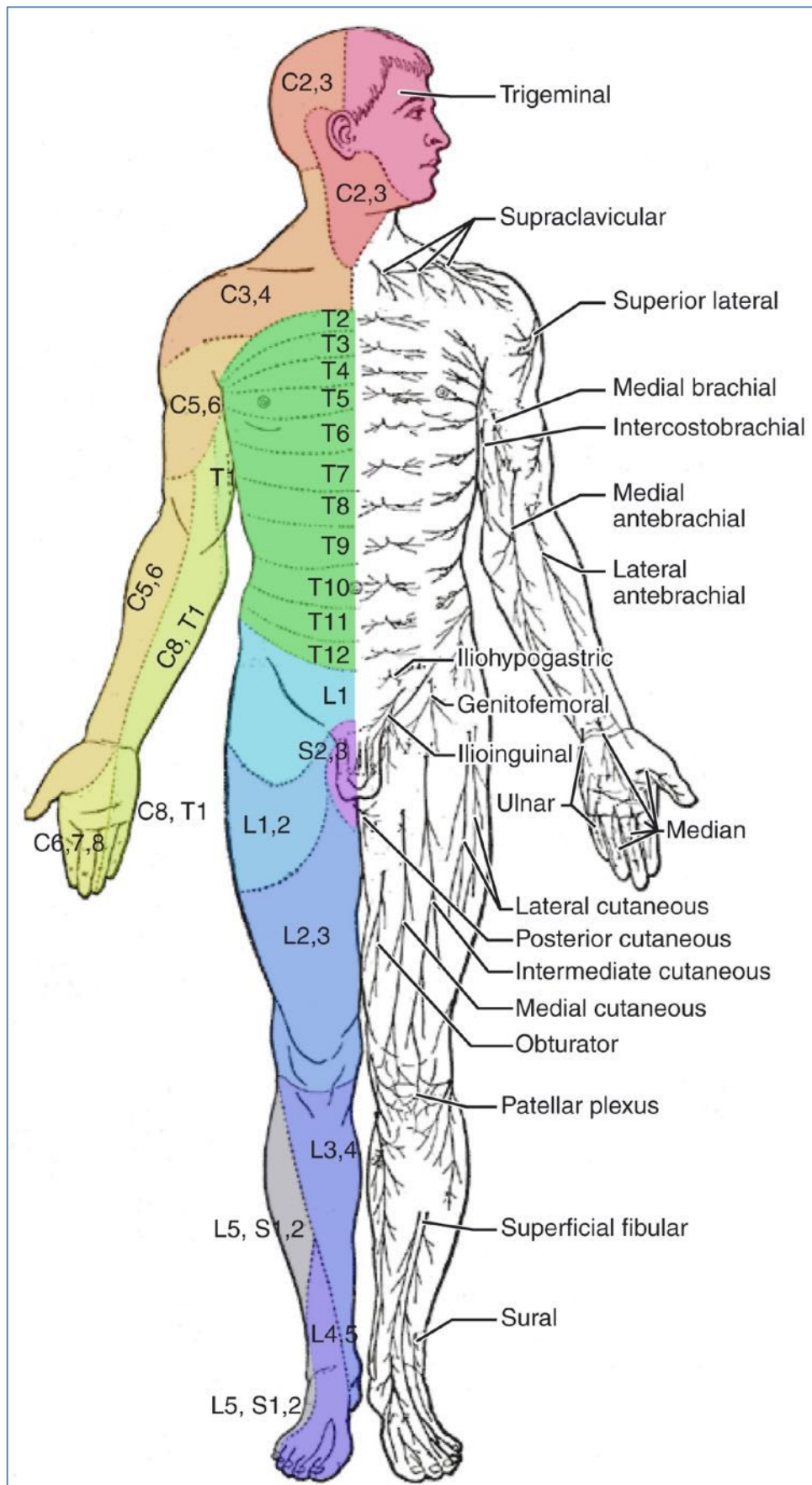
- = Collections of neuron **cell bodies** in **PNS**
 - Afferent Spinal Nerves:**
 - Cell bodies of sensory neurons
 - 'Dorsal root ganglion'
 - Efferent Spinal Nerves:**
 - Cell bodies of autonomic nerve fibers
 - 'Sympathetic trunk ganglion'
 - In Central Nervous System:**
 - Called: **Basal Nuclei / Nuclei**
 - Important for BOTH Motor & Autonomic Nervous Systems**



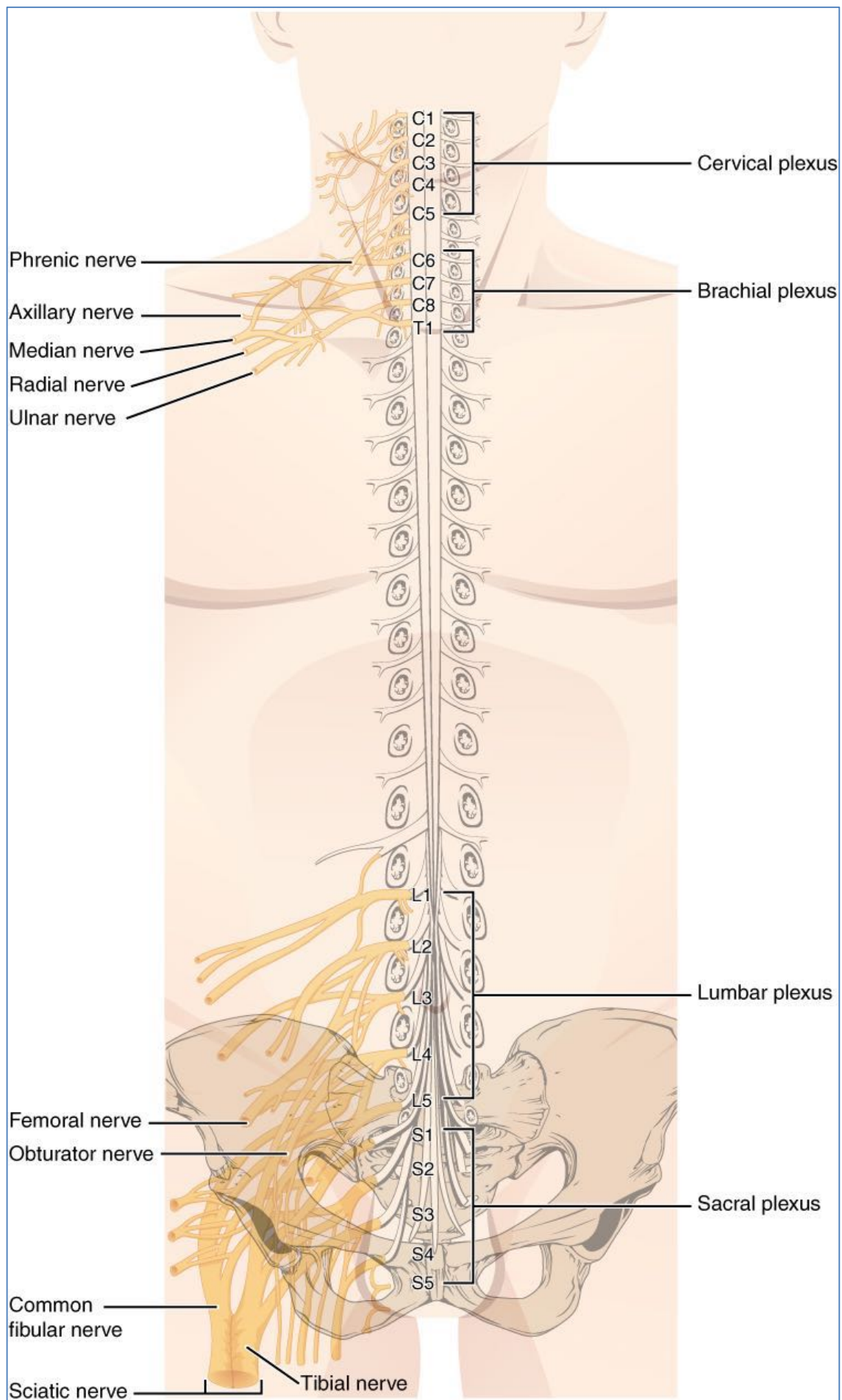
Spinal Nerves:

- **Dermatomes - Innervation of the Skin:**

- A portion of the mesoderm (skin, sensory receptors, sebaceous glands, blood vessels) innervated by the cutaneous branches of a single spinal nerve.



https://commons.wikimedia.org/wiki/File:Dermatomes_and_cutaneous_nerves_-_posterior.png

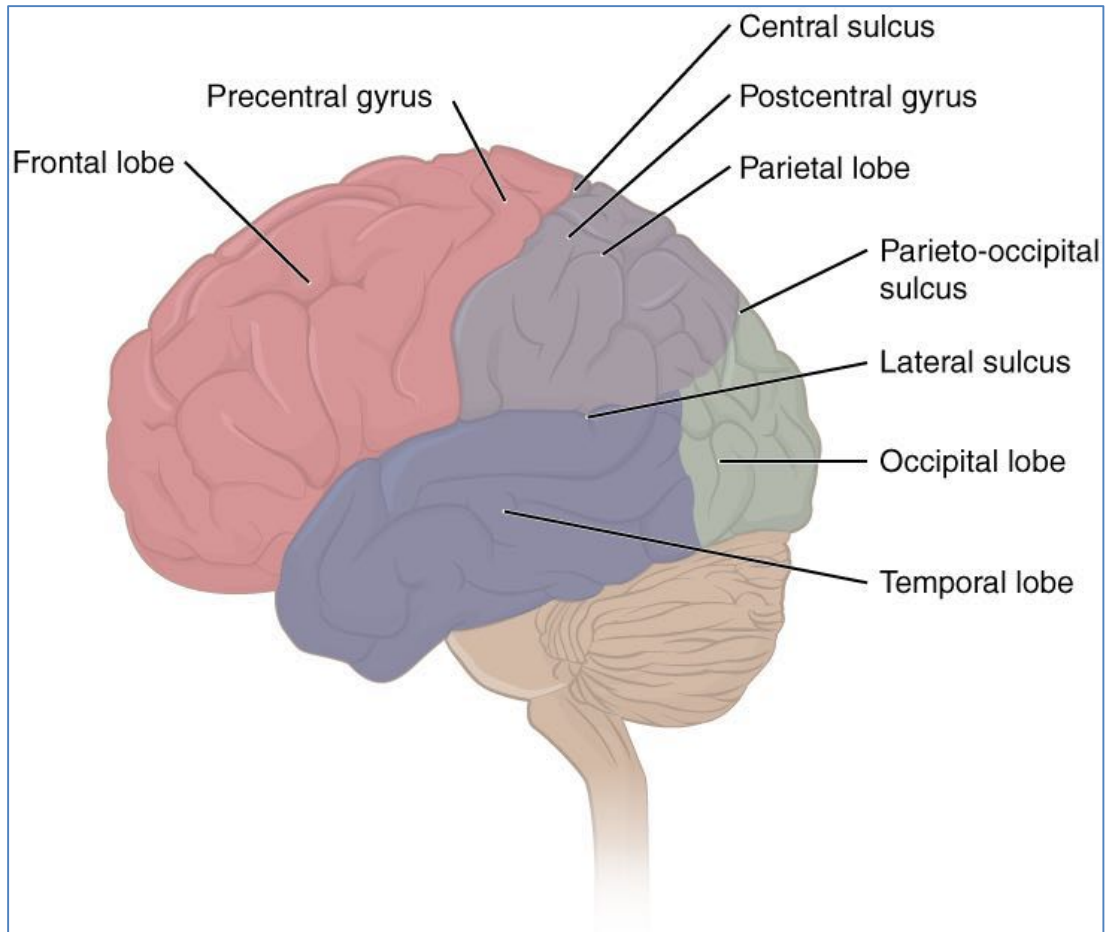


SURFACE ANATOMY OF THE BRAIN

Surface Anatomy of the Brain:

- Dorsal Landmarks:

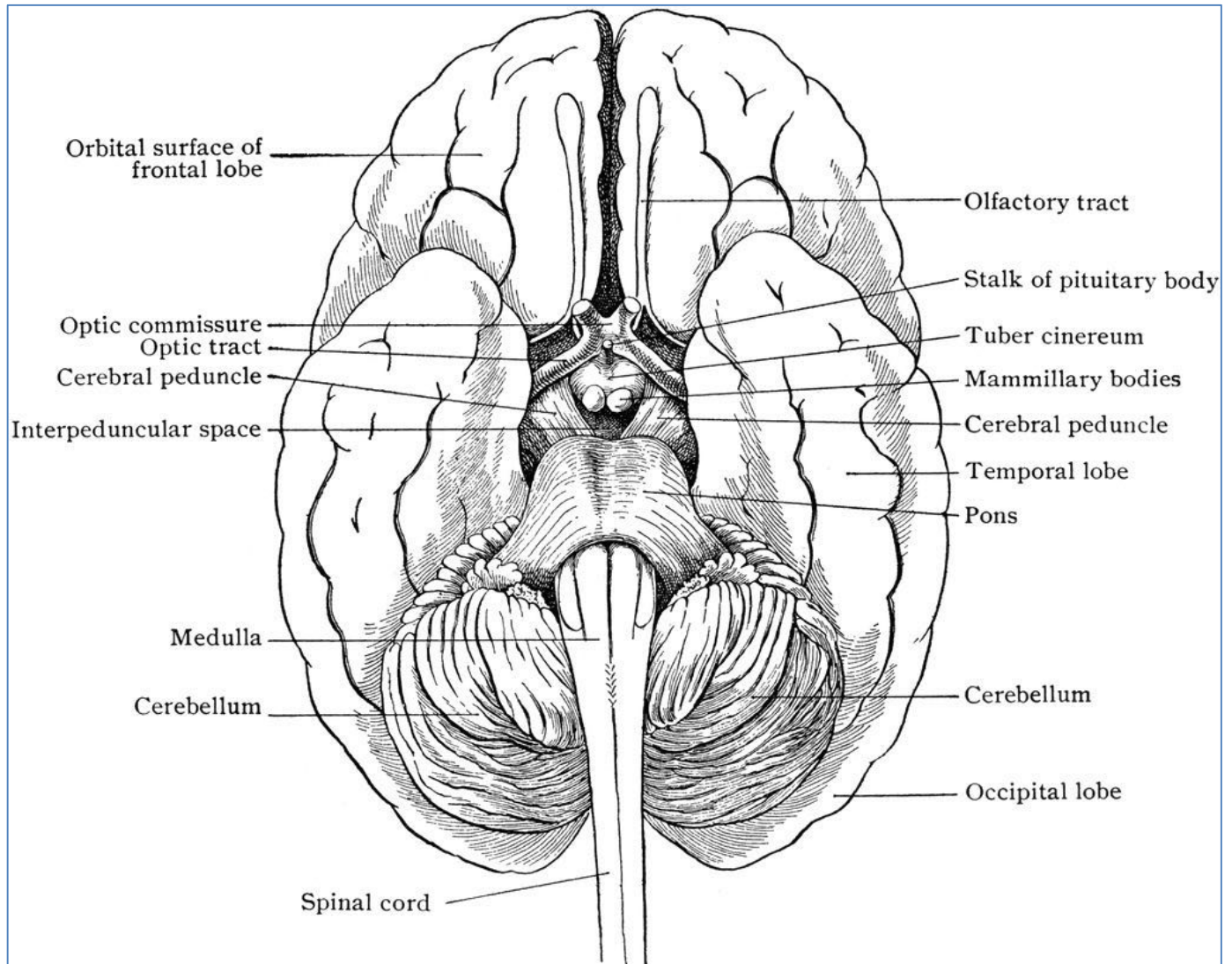
- **Fissures:**
 - **Longitudinal Fissure:** Separates Left & Right Hemispheres
 - **Transverse Cerebral Fissure:** Separates Occipital Lobe from Cerebellum
- **Sulci:**
 - **Central Sulcus:** Separates the Frontal & Parietal Lobes.
 - **Lateral Sulcus:** Separates the Temporal Lobe from the Other Lobes.
 - **Parieto-Occipital Sulcus:** Separates Parietal Lobe & Occipital Lobe
- **Lobes:**
 - **Occipital Lobe:** Most Caudal Lobe (Visual Cortex)
 - **Temporal Lobe:** Most Lateral Lobe
 - **Frontal Lobe:** Most Anterior Lobe



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- **Ventral Landmarks:**

- **Olfactory Bulbs:** Responsible for sense of smell
- **Optic Chiasm ("Optic Crossing"):** 'X'-shaped crossing-over of Optic Nerves.
- **Infundibulum:** Connection between Pituitary & Hypothalamus.
- **Hypothalamus:** Responsible for many autonomic homeostatic functions
- **Pituitary:** Important neuroendocrine organ.
- **Mammillary Bodies:** Form part of the Limbic System & are important for recollective memory.
- **Pyramids (Pyramidal Tracts):** Carry motor fibres from the cerebral cortex to the spinal cord.

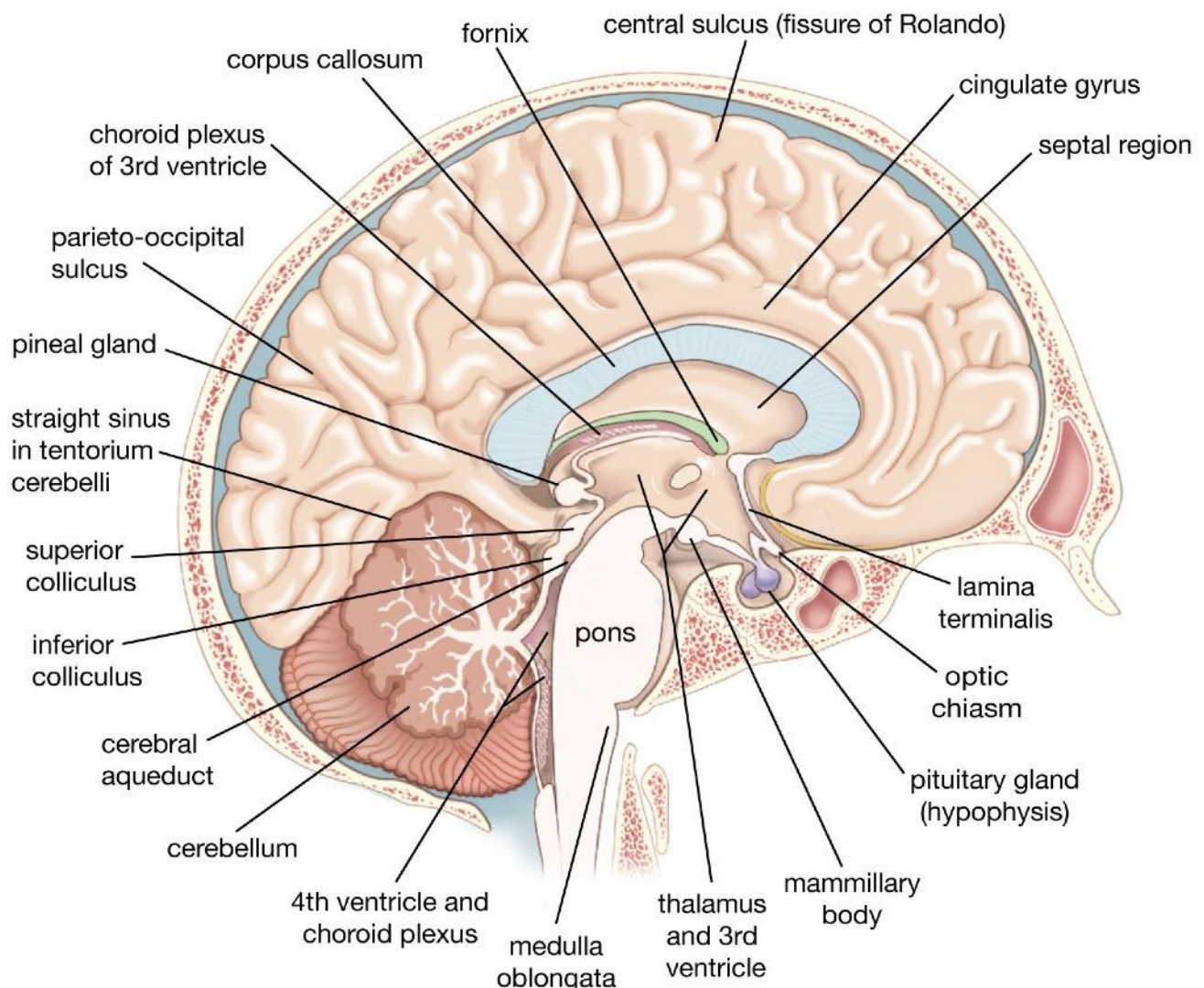


https://etc.usf.edu/clipart/53100/53182/53182_brain.htm

- **Medial Landmarks (Ie: On Sagittal Section):**

- **Cingulate Gyrus:** Part of the Limbic System. Involved in emotion and behaviour regulation.
- **Corpus Callosum:** Thick bundle of connecting nerve fibres connecting left and right hemispheres.
- **Lateral Ventricle:** Holds Cerebrospinal Fluid
- **Pineal Body:** Involved in Circadian Rhythm (night/day body clock)
- **Thalamus:** Multiple physiological roles including sensory, motor, & consciousness regulation.
- **Hypothalamus:** Regulates hunger, thirst, temperature control, memory & stress responses.
- **Pituitary Gland:** Controls metabolism, growth, sexual function, blood pressure & others.
- **Colliculi:** Nestled in between the Cerebrum & Cerebellum.
 - **2x Superior:** Controls eye movements
 - **2x Inferior:** Part of Auditory Pathway
- **Cerebellum:** Important for coordination, precision & timing of movements.
- **Pon:** Critical for respiratory rhythm & breathing.
- **Medulla Oblongata:** Relays messages between the brain and spinal cord. Also regulates cardiorespiratory functions.
- **Fourth Ventricle:** contains CSF.

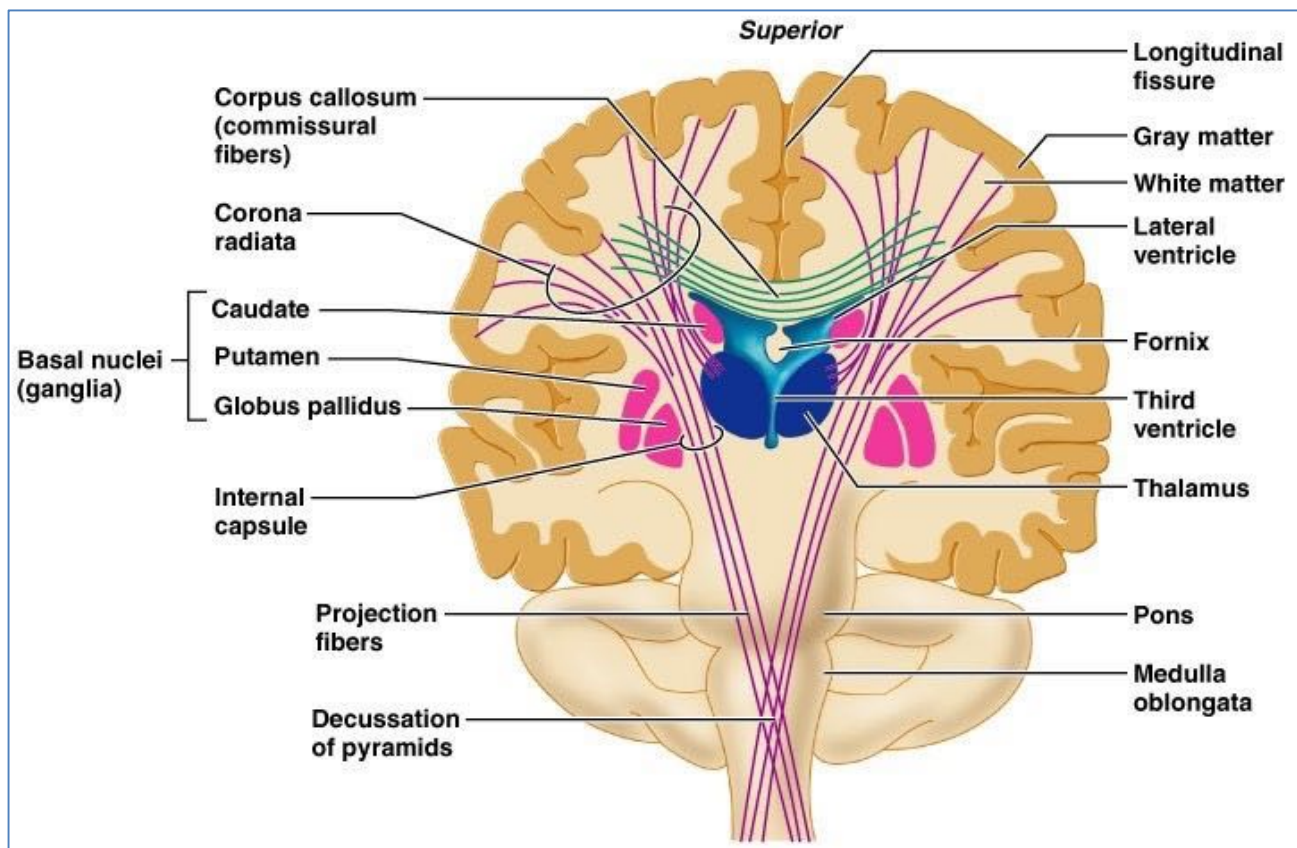
Human brain in cross section



Source: Encyclopaedia Britannica; <https://www.britannica.com/science/superior-colliculus#/media/1/574381/93859>

- **Coronal Section Landmarks:**

- **Cortex (Grey Matter):** Key roles in attention, perception, awareness, thought, memory, language, sensation, and motor functions.
- **White Matter:** Mostly axons & myelin – Relays action potentials to their destinations.
- **Lateral Ventricle:** Contains CSF
- **Caudate Nucleus:** Important in planning & executing movement. Also has learning, memory, reward, motivation & emotional functions.
- **Corpus Striatum:** Reinforcement circuit of the brain.
- **Thalamus:** Multiple physiological roles including sensory, motor, & consciousness regulation.
- **Massa Intermedia:** The Bridge between the Left & Right Thalamus.
- **Hippocampus:** Major role in learning and memory.



<https://anatomyinfo.com/corpus-callosum/>

BLOOD SUPPLY OF THE BRAIN

BLOOD SUPPLY OF THE BRAIN

Why Does the Brain Need Blood?

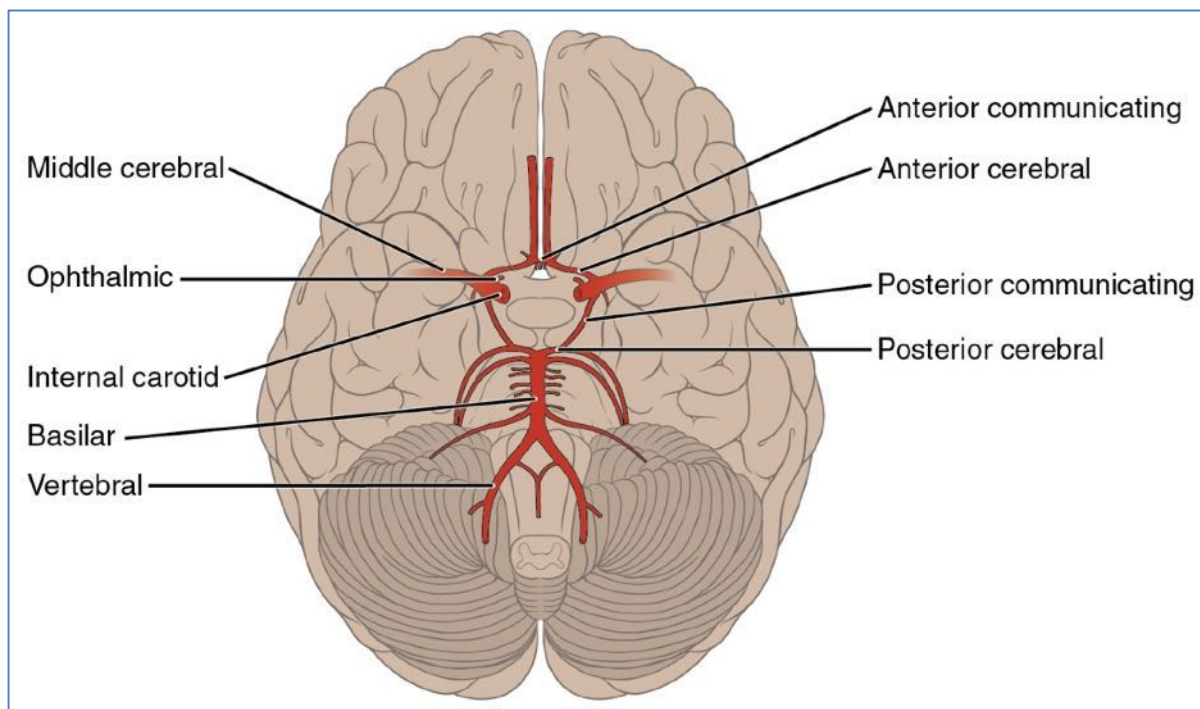
- Consumes **15-20% of the body's total energy needs**, (and receives 15% of Cardiac Output), despite being only **2% of total body mass**.
- **Neurons require high ATP to:**
 - o Maintain Ion Gradients across Plasma Membrane
 - o Regulate Neurotransmitter synthesis/re-uptake.
- **Neurons have NO ANAEROBIC CAPACITY** → Therefore the brain absolutely depends on Oxygenated Blood.
 - o Hence, any deficit in blood supply is detrimental ($\approx 30^+$ sec lack of blood/ O_2 to brain → unconscious)

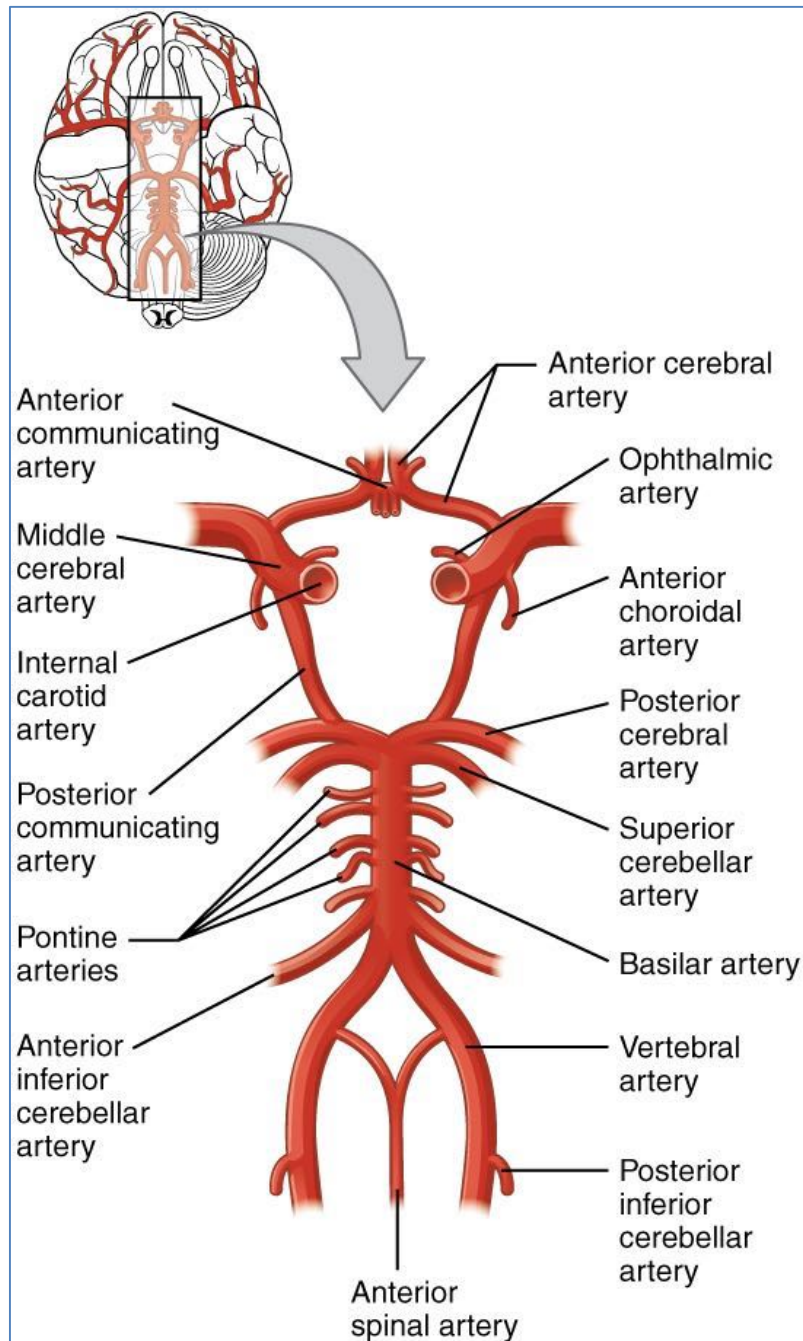
Blood Supply to the Brain is an ANASTOMOSIS:

- **Anastomosis:** Where *Multiple Arteries Supply the Same Region of Tissue*. **ie: A Dual Blood-Supply.**
- **The Advantage:** If one of the arteries becomes blocked/damaged, the other artery will compensate for it.

Arterial Supply of the Brain:

- **Brain is Supplied by 2 Arterial Systems:**
 - o 2x Vertebral Arteries → 1x Basilar Artery → Circle of Willis
 - o 2x Internal Carotid Arteries → Circle of Willis
- **'Circle of Willis', The Anastomosis of the Brain:**
 - o (The 'Roundabout' of Arteries on the underside of the Brain with multiple 'Roads' coming off it)
 - o (Encircles the Optic Chiasma, The Pituitary Gland & the Mammillary Bodies.)
 - o **The 'Roads': (Anterior → Posterior)**
 - 2x Anterior Cerebral Arteries
 - 1x Anterior Communicating Artery
 - **2x Internal Carotid Arteries**
 - 2x Middle Cerebral Arteries
 - 2x Posterior Communicating Arteries
 - 2x Posterior Cerebral Arteries
 - **1x Basilar Artery**
 - o **Note:** Communicating Arteries are always patent, but generally not functional (no blood flow) when blood flow from both Carotids & Basilar Arteries is normal. However, if blood flow from one of the major arteries is impeded, blood is shunted through the Communicating Arteries to compensate.



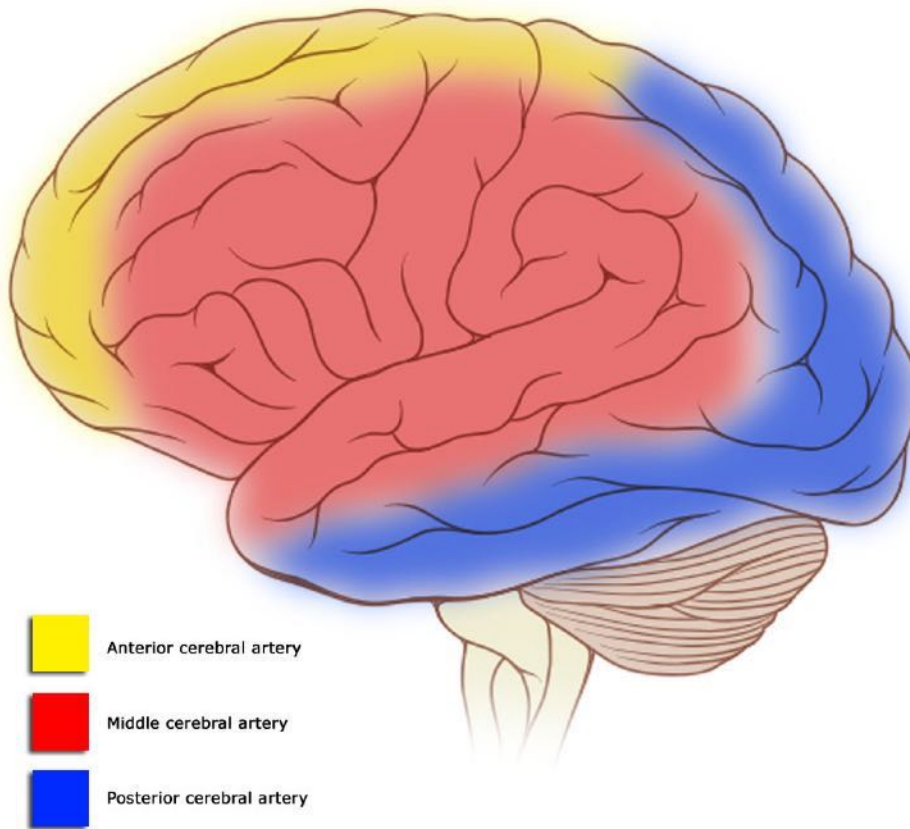


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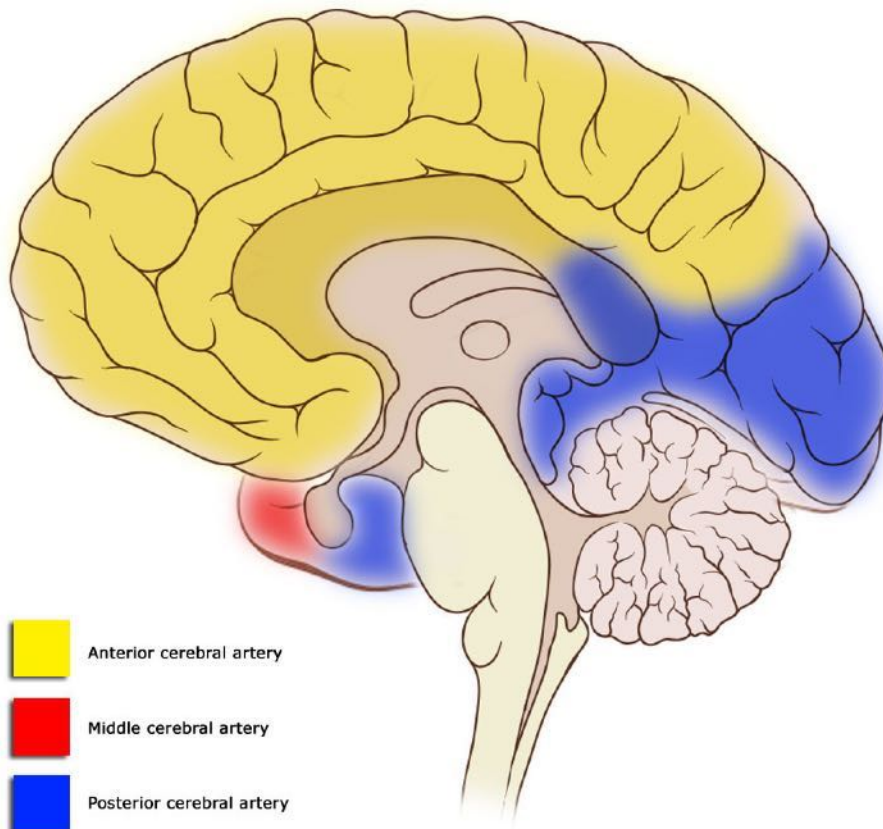
Distribution of Cerebral Arteries:

- **Anterior Cerebral Arteries:**
 - (Travels up and over the Corpus Callosum, sprouting branches outwards towards the cortex)
 - Medial Portion of Frontal Lobe (Incl. Cortex)
 - Medial Portion of Parietal Lobe (Incl. Cortex)
 - Corpus Callosum
- **Middle Cerebral Arteries:**
 - (Travels through the Lateral Fissure/Sulcus and emerges onto the Lateral Surface of the Brain)
 - Lateral Portion of the Frontal Lobe (Incl. Cortex)
 - Lateral Portion of the Parietal Lobe (Incl. Cortex)
 - Entire Temporal Lobe (Incl. Cortex)
- **Posterior Cerebral Arteries:**
 - (Travels along the Inferior brain surface between the Cortex and the Cerebellum)
 - Inferior Portion of Temporal Lobe (Incl. Cortex)
 - Postero-Medial Portion of Parietal Lobe (Incl. Cortex)
 - Entire Occipital Lobe (Incl. Cortex)

Cortical vascular territories

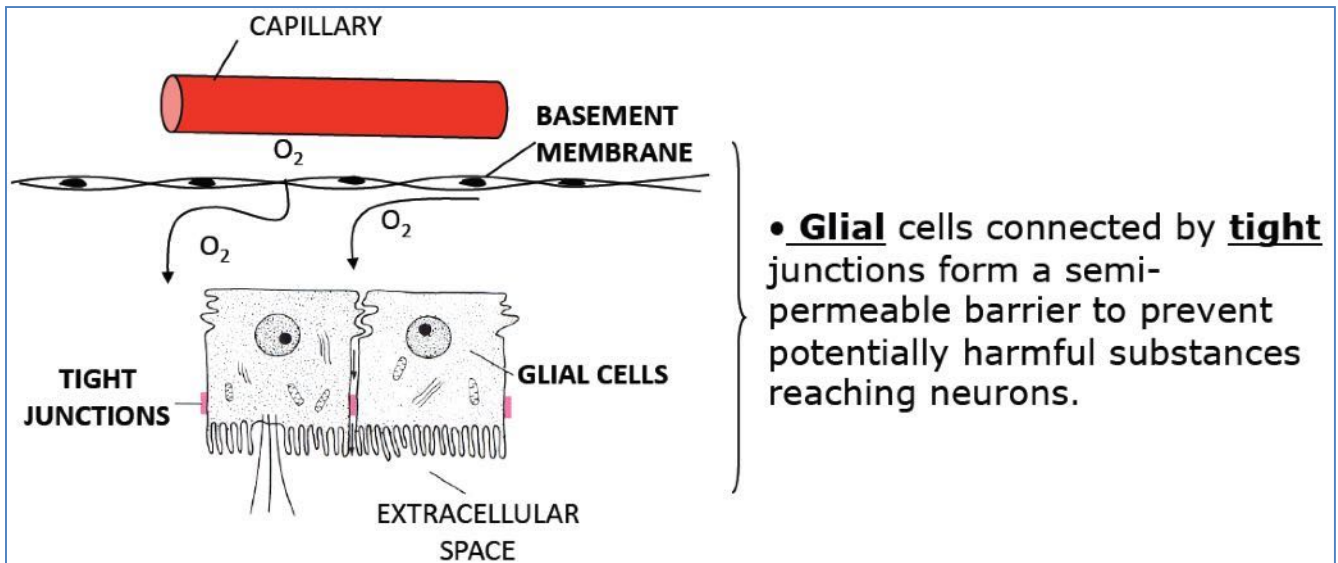


Cortical vascular territories



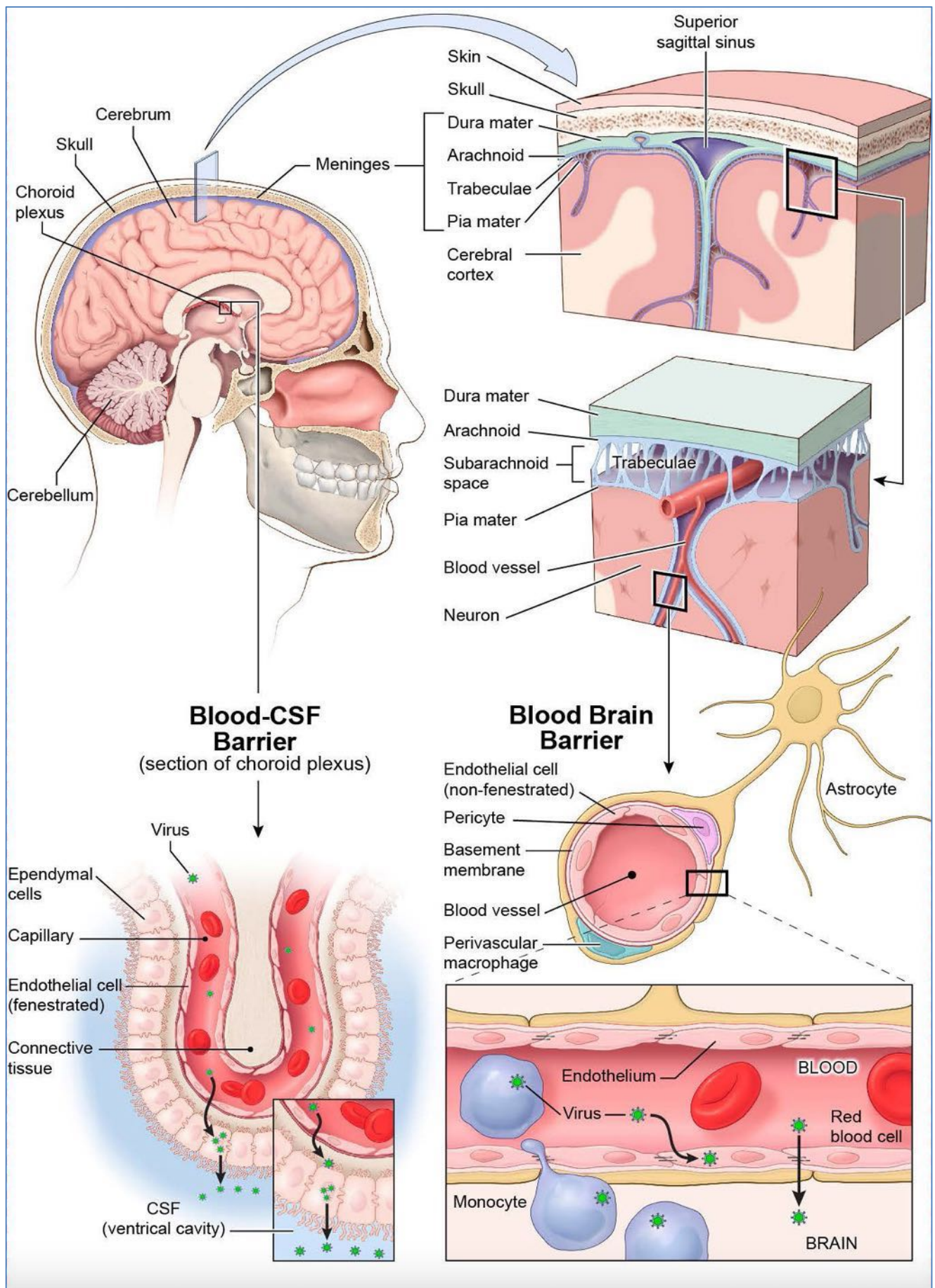
The Blood-Brain Barrier:

- Isolates Brain from Blood to provide a **Stable Environment**, necessary for control & function of CNS Neurons.
- **How?:**
 - 1. The **Endothelial Cells** of the CNS Capillaries are seamlessly joined by **Tight Junctions**.
 - This prevents diffusion of most materials except dissolved gasses & lipid-soluble compounds.
 - Therefore, any required water-soluble compound must be transported across the BBB.
 - 2. **Thick Basement Membrane of Capillary**



- **Note:** In the **2 Choroid Plexuses**, the BBB is formed by **Tight Junctions between Glial (Ependymal) Cells** as the capillaries in this region are Fenestrated & highly leaky.
- **The BBB exists everywhere except:**
 - Hypothalamus – (Monitors chemical composition of blood. Ie: Hormone levels, water balance, etc)
 - Vomiting Centre - (Monitors poisonous substances in blood)

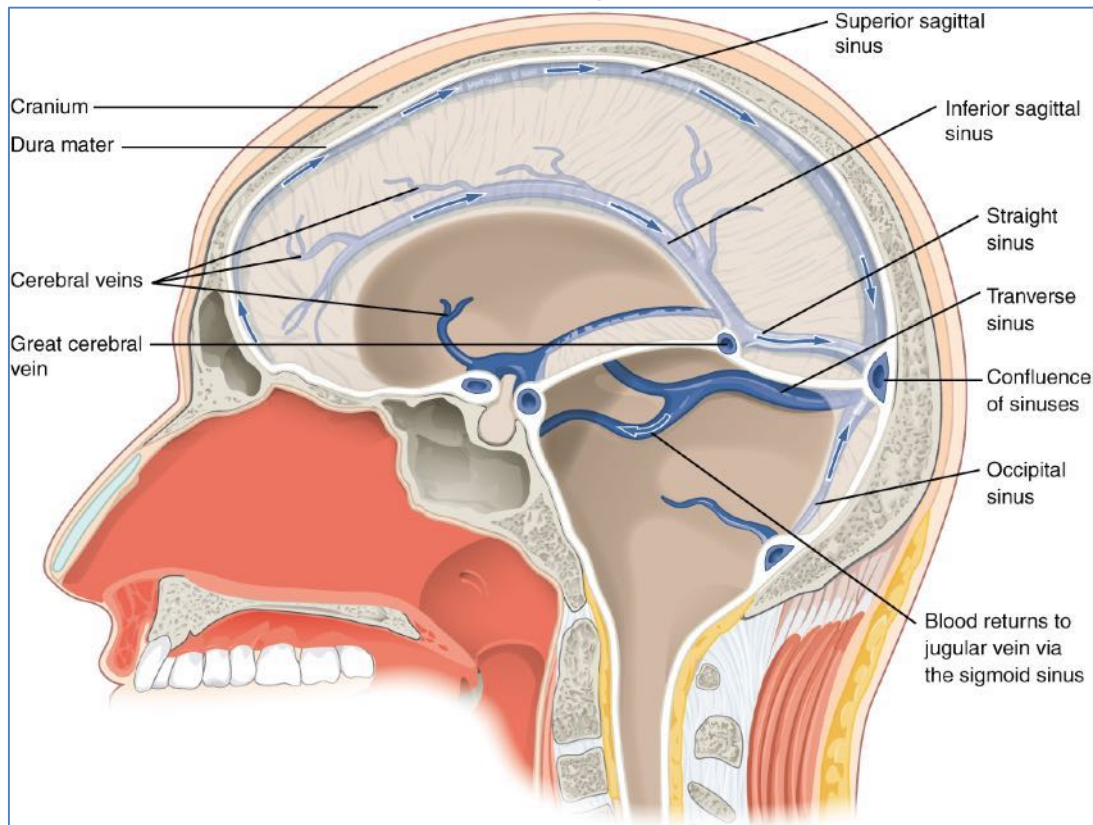
(Diagram over page)



Credit: NIH Medical Arts; <https://www.ncbi.nlm.nih.gov/>

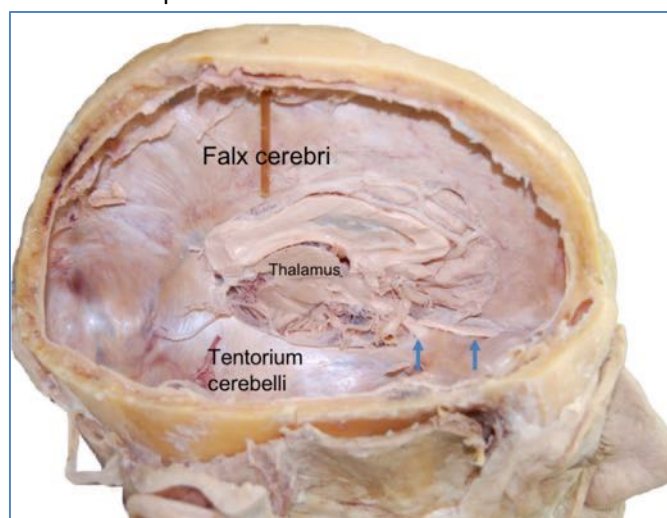
Venous Drainage of the Brain – Via “Dural Sinuses”:

- Venous Drainage begins with venous blood collecting in small venous channels known as “Dural Sinuses”.
- **Sinuses Sit Within The Dura-Mater:**
 - o The Dura-Mater is the thickest & outermost of the 3 Meninges of the brain. It extends deep into the brain in **2 locations**, the **Falx Cerebri** & the **Tentorium Cerebelli**:
 - **1. Falx Cerebri:**
 - The Dura Mater folds deep into the Longitudinal Fissure (Falx Cerebri) of the brain, where it forms 2 Sinuses:
 - o 1. A Triangular ‘**Superior Sagittal Sinus**’ at the top of the dural fold.
 - o 2. A lower ‘**Inferior Sagittal Sinus**’ at the bottom of the dural fold.



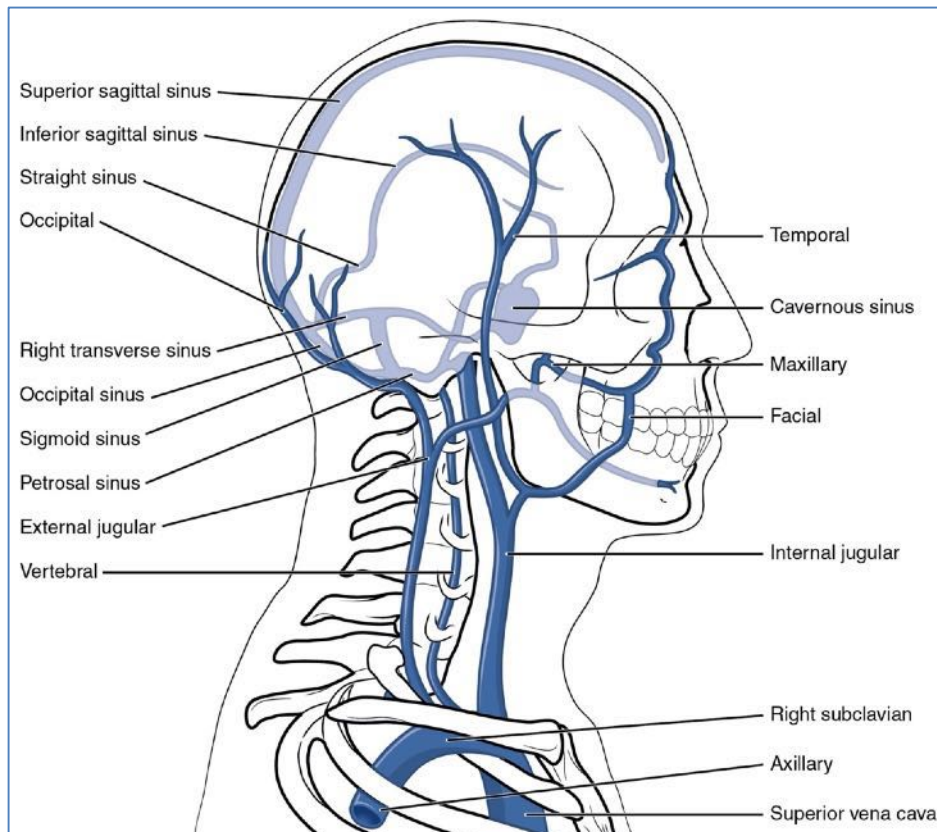
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- **2. Tentorium Cerebelli:**
 - The Dura Mater folds deep into the Transverse Cerebral Fissure (Tentorium Cerebelli) of the brain, where it forms a pair of sinuses:
 - o **The R.&L. “Transverse Sinuses”.**
 - o Note: All blood from Sup. & Inf. Sagittal Sinuses and the Straight Sinus empties into these Transverse Sinuses.



Rabjot Rai, Joe Iwanaga , Gaffar Shokouhi, Rod J. Oskouian, R. Shane Tubbs, CC BY 3.0
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- The L.&R. Transverse Sinuses then become the L.&R. **Sigmoid Sinuses** (Respectively).
- These **Sigmoid Sinuses** turn Inferiorly and become the **Internal Jugular Veins**.



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Regulation of Blood Flow to the Brain:

- Blood Flow to the Brain is **AUTOREGULATED**:

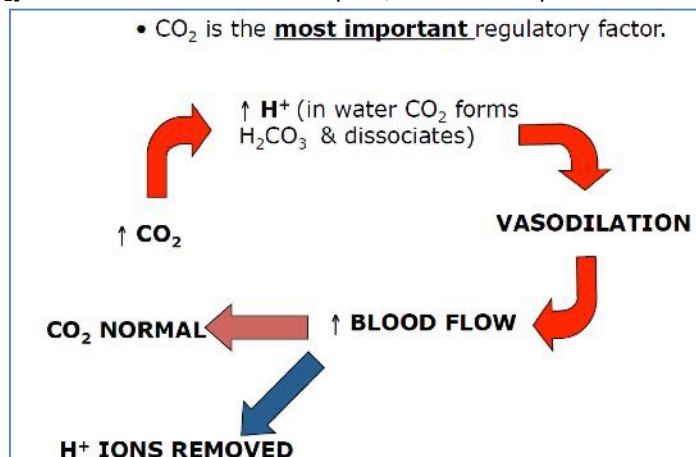
- I.e: BP in the Brain is kept constant, despite systemic BP fluctuations.
- It also means different areas of the brain control their blood flow depending on metabolic activity.

- The **Myogenic Autoregulation of Blood Flow to the Brain**:

- When Mean Arterial Pressure rises, the SNS constricts the larger arteries of the brain to prevent damaging high pressures in the smaller, more delicate vessels. (Important for preventing Stroke)

- The **3 Metabolic Autoregulatory Factors Affect Blood Flow to the Brain**:

- ****1. Blood [CO₂]:**
 - $\uparrow[\text{CO}_2] \rightarrow \text{Vasodilation}$ (to \uparrow Blood Flow)
 - $\downarrow[\text{CO}_2] \rightarrow \text{Vasoconstriction}$ (to \downarrow Blood Flow)
- **2. Blood/CSF pH:**
 - $\uparrow[\text{CO}_2] \rightarrow \uparrow[\text{H}^+] \text{ via carbonic anhydrase} \rightarrow \downarrow\text{pH} \rightarrow \text{Vasodilation}$ (to \uparrow Blood Flow)
 - $\downarrow[\text{CO}_2] \rightarrow \downarrow[\text{H}^+] \text{ via carbonic anhydrase} \rightarrow \uparrow\text{pH} \rightarrow \text{Vasoconstriction}$ (to \downarrow Blood Flow)
- **3. Blood/CSF [O₂]:**
 - $\downarrow[\text{O}_2] \rightarrow \text{Vasodilation}$ (to \uparrow Blood Flow)
 - $\uparrow[\text{O}_2] \rightarrow \text{Vasoconstriction}$ (to \downarrow Blood Flow)

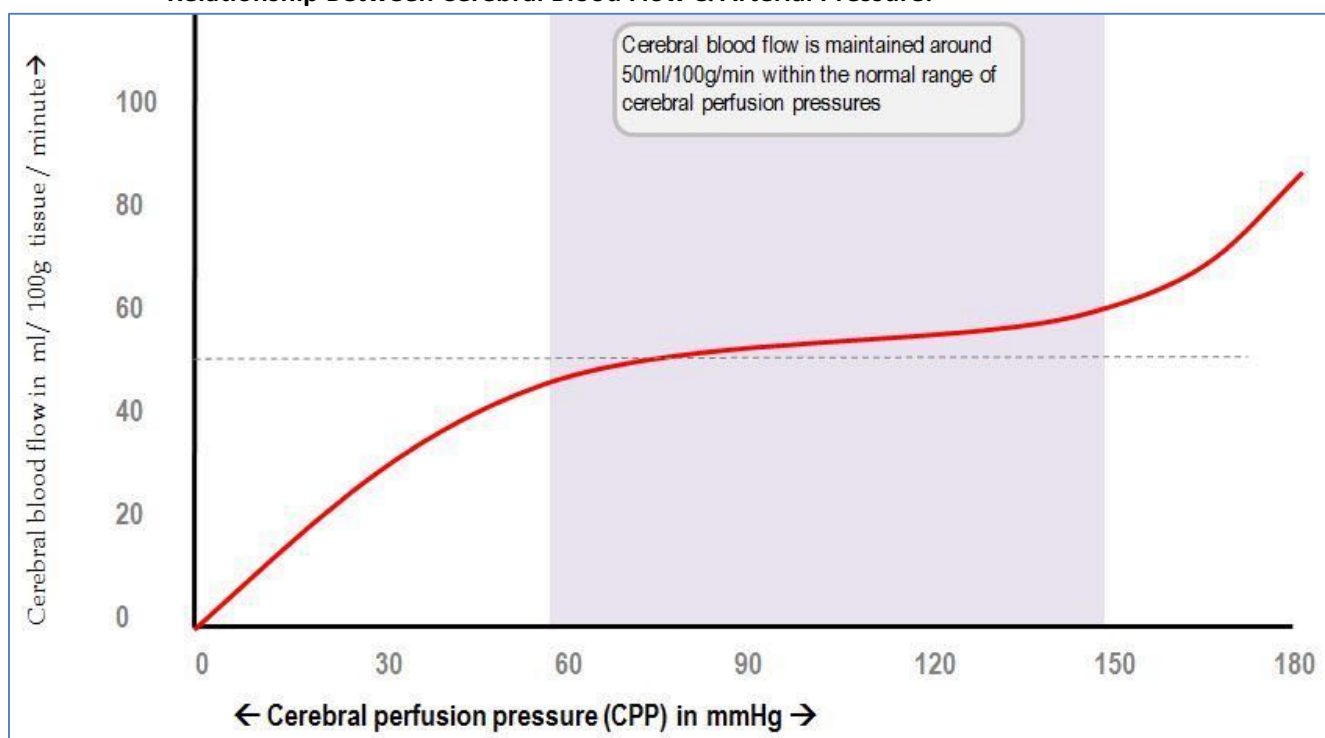


Intracranial Pressure:

- **What is it?**
 - o The pressure within the cranium created by the cerebrospinal fluid (CSF), and exerted on the brain tissue & the brain's blood circulation vessels.
- **Determinants:**
 - o CSF Production/Resorption (Eg: ↑Production + ↓Resorption)
 - o Brain Tissue (Eg: Tumour / Inflammation)
 - o Blood (Eg: Haemorrhage)
- **High Intracranial Pressure:**
 - o Compresses the Cerebral Arteries → Decreased Blood Supply → Brain Damage
 - o Can also displace the brain.
- **Symptoms of High ICP:**
 - o Altered Consciousness
 - o Changes in BP & HR
 - o Changes in Eye Responses
 - o Changes in Motor Function

Cerebral Blood Flow And Intracranial Pressure:

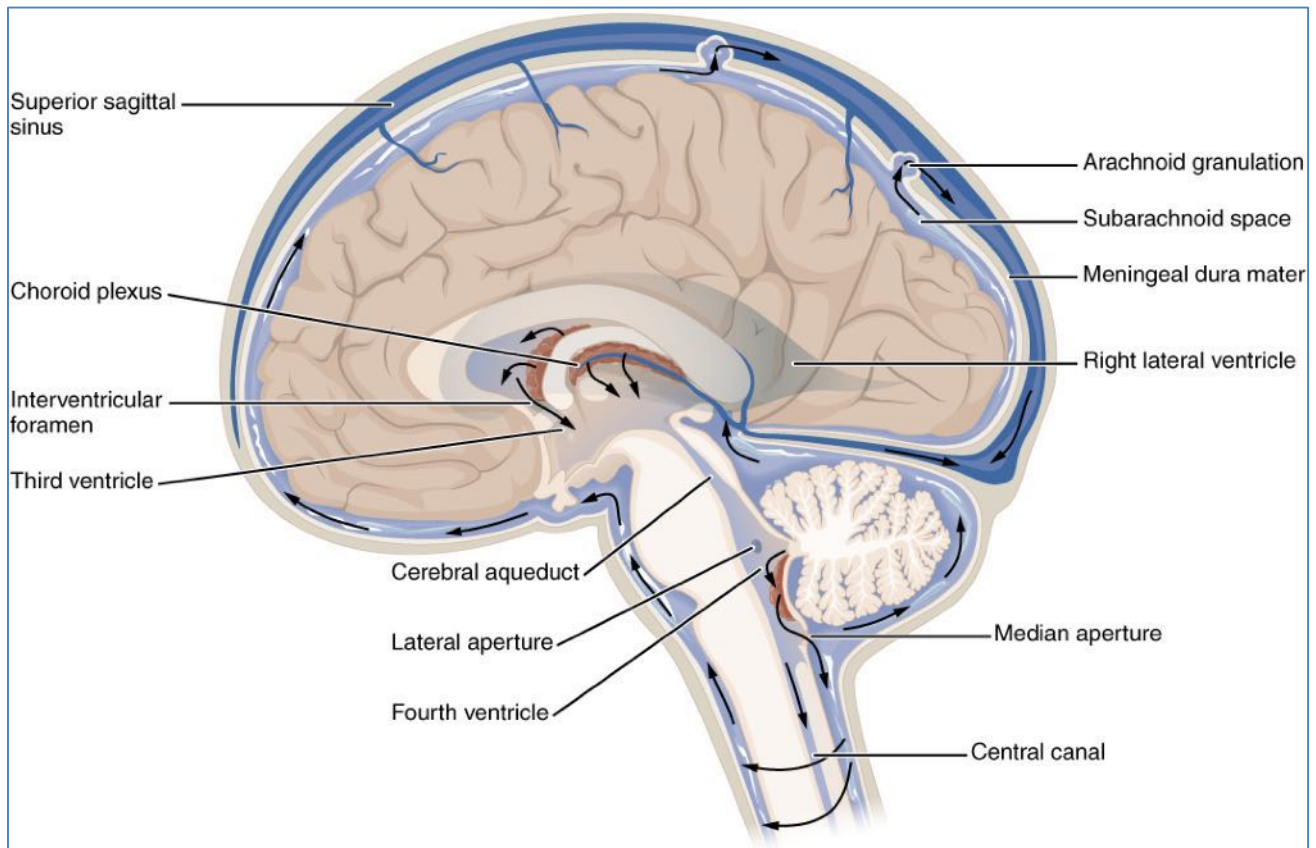
- Cerebral blood flow is carefully regulated under normal conditions.
- **Cerebral Blood Flow:**
 - **What percentage of cardiac output goes to the cerebral circulation *at rest*?**
 - 750ml/min (15% of cardiac output)
 - **Relationship Between Cerebral Blood Flow & Arterial Pressure:**



<https://derangedphysiology.com/cicm-primary-exam/required-reading/cardiovascular-system/Chapter%20474/cerebral-blood-flow-autoregulation>

- **Kelly-Monroe Doctrine:**
 - States that the Cranial Compartment is Incompressible, and the Volume is Fixed.
 - The Cranial Constituents (Blood, CSF, and Brain Matter) create a state of Volume Equilibrium:
 - Any increase in Volume of one of the constituents must be compensated by a decrease in volume of another.
 - **Volume Buffers:**
 - Both **CSF and**, to a lesser extent, **Blood Volume**
 - (Eg: In Extradural Haematoma → CSF & Venous Blood Volumes are Decreased)
 - → Maintain normal ICP
 - Buffer Capacity ≈ 100-120mL

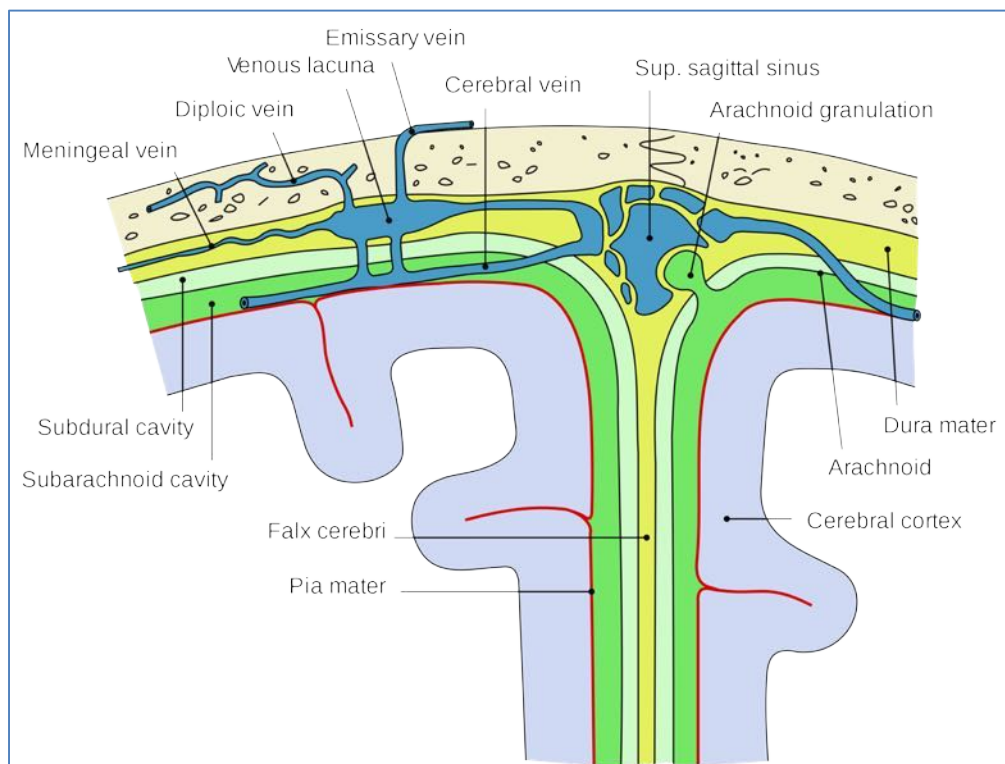
Flow & Production of CSF



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Reabsorption of CSF into the Dural Sinuses:

- Note: CSF is constantly being produced, and therefore must also be constantly drained to prevent a rise in intracranial pressure. Therefore:
- **CSF is Reabsorbed** into the **Venous System** via diffusion through **Arachnoid Villi (Arachnoid Granulation)**.
 - **Arachnoid Villi** are invaginations of Arachnoid Mater **through the Dura Mater** and **into the Superior Sagittal Sinus**.



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Cerebral Oedema:

- **What is it?**
 - An excess accumulation of water in the intracellular and/or extracellular spaces of the brain.
- **Types of Cerebral Oedema:**
 - **Vasogenic:**
 - (Extracellular Oedema)
 - Due to a breakdown of tight endothelial junctions which form the BBB.
 - Eg: Hydrostatic Cerebral Oedema – where acutely high cerebral capillary pressure results in fluid moving from Capillary to ECF.
 - **Cytotoxic:**
 - (Intracellular Oedema)
 - Due to a defect in cellular metabolism → inadequate functioning of the Na/K-ATPase in the cell membrane → cellular retention of H₂O
 - **Osmotic:**
 - (Extracellular Oedema)
 - Where a drop in Plasma Osmolality (compared to CSF Osmolality) causes water to flow from the Venous Sinuses back into the Sub-Arachnoid Space.

Migraines:

- **What are They?**
 - Incapacitating Neurovascular disorder characterized by unilateral, throbbing headaches, photophobia, phonophobia, nausea & vomiting.
- **What Causes Them?**
 - Decrease in **Serotonin** Levels → ↑Sensitivity to Migraine Triggers + Cerebral Vasoconstriction → ↓cerebral blood flow → Raphe Nuclei in Brain-Stem release Serotonin → Cerebral Vasodilation + Release of Proinflammatory Mediators from **Trigeminal Nerve** & Spinal Nerves → Perivascular Cerebral Inflammation → Pain.
- **Classic Vs. Common:**
 - **Classic:**
 - Associated with '**Aura**'. (A visual symptom, such as an arc of sparkling (scintillating) zig-zag lines or a blotting out of vision or both)
 - **Common:**
 - Migraine without 'Aura' (Only 20% of sufferers experience aura. Most bypass the aura phase)
- **Migraines as a Risk Factor:**
 - ↑ Risk of Silent Post. Cerebral Infarcts.
 - ↑ Risk of Stroke & CVD (Women)
 - ↑ Risk of MI (Men)

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