# Lecture 11

# **Nervous system**

- Reminder on composition of nerve tissue
- Structure of gray matter of spinal cord, cerebellum, and telencephalon (iso- and allocortex)
- Peripheral nervous system ganglia and peripheral nerves
- Earliest phases of development of nervous system
- Histogenesis of neural tube
- Development of brain and spinal cord

Brno, November 2019

**Nervous system - Histologically** 

Made of 3 structurally different components:

The nerve tissue

### **Blood vessels**

capillaries, arterioles and venules that densely penetrate the nerve tissue

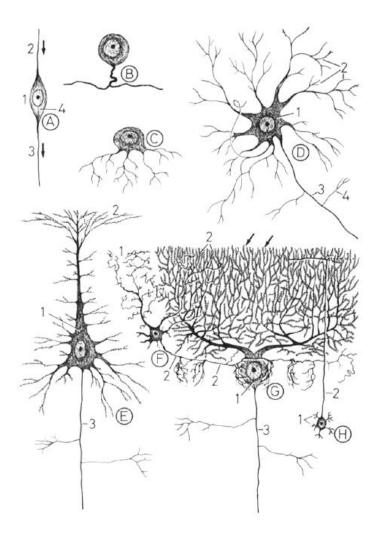
### The connective tissue

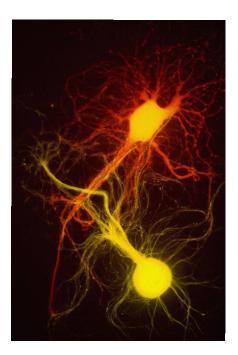
- provides protection of both previous components is organized into:
- meninges envelope the brain and spinal medulla
- epi-, peri- and endoneurium connective tissue within nerves or on their surfaces
- thin capsules surround the cerebrospinal and autonomic ganglia

### **Nerve tissue – General features**

Nervous tissue is made up of just 2 types of cells:

- <u>Neurons</u>
- Neuroglia glial cells (supporting cells)
- Neurons are the basic functional units of nervous tissue.
- They are highly specialized to transmit nerve impulses.





1. Perikaryon (neurocyte)

### 2. Processes:

(one-way signal conduction)

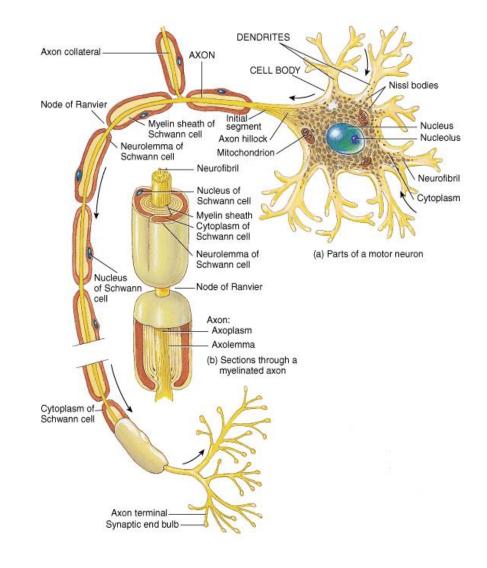
#### - axon

(always only one; centrifugal conduction)

### - dendrit(es)

(centripetal conduction)

# Neuron



#### **Position:**

CNS – grey matter PNS – ganglia

#### Shape:

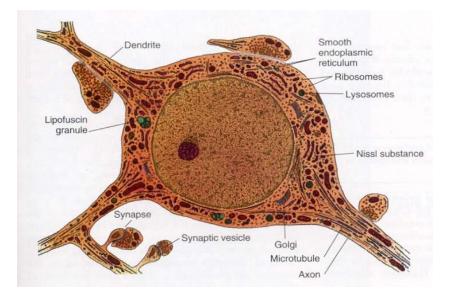
pyramidal, shpherical, ovoid, peer-shaped

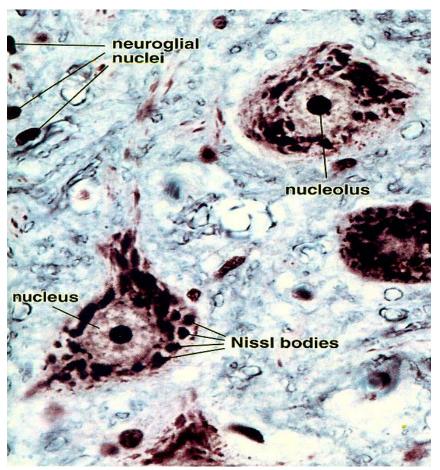
#### Size:

5 to 150  $\mu m$ 

#### **Organelles:**

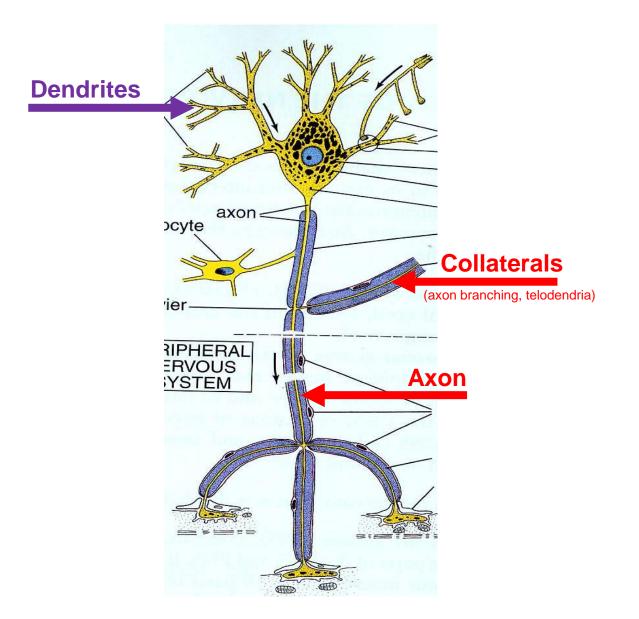
- Nuclues large + pale + prominent nucleoli
- Nissl substance rough ER
- Neurofibrils (neurofilaments + neurotubules + actin)
- Lipofuscin pigment clumps





## **Neuron - Perikaryon**

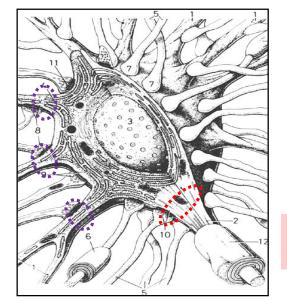
### **Neuron – Neurites / Processes**



### **Neuron – Neurites / Processes**

### **Dendrites**

- Conducts impulses towards the cell body
- Typically short, highly branched & unmyelinated
- Surfaces specialized for contact with other neurons
- Contains neurofibrils & Nissl bodies
- Receptive surface for synaptic junctions
- Contain MAP-2 (distinction from axon)
- Tens of thousands of synapses on large dendrites
- Dendritic spines located on surface of some dendrites
- Spines diminish with age and poor nutrition

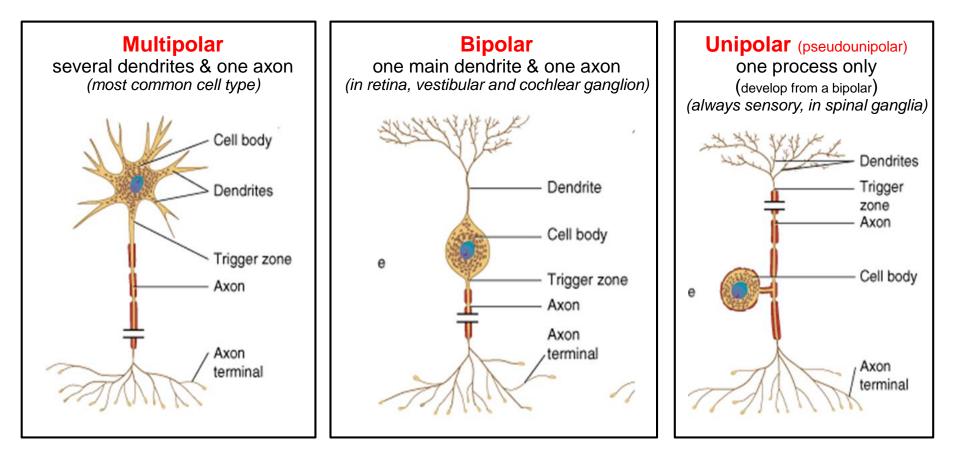


### Axon (nerve fiber)

- 1 axon projects from cell body at axon hillock
- <u>Axon hillock</u> pyramid shaped region of the soma that is devoid of RER
- Some axons are up to 100 cm
- Initial segment = Spike trigger zone (a portion of axon from its origin to the beginning of myelin sheath)
- At spike trigger zone trigger zone summation of excitatory and inhibitory impulses occurred
- Collateral branches, Terminal arbor
- Myelinated or Unmyelinated
- Conduct impulses away from cell body
- Swollen tips called <u>synaptic knob (terminal button)</u> contain synaptic vesicles filled with neurotransmitters
- Cell membrane = axolemma
- Cytoplasm = axoplasm

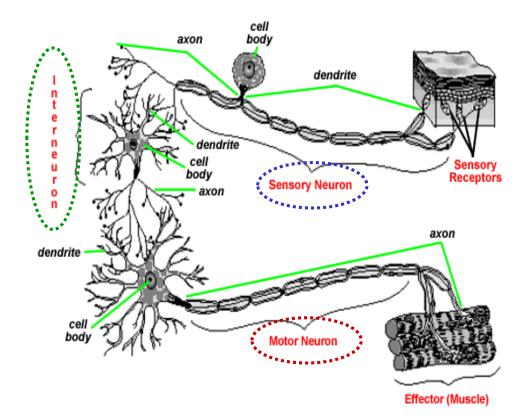
White matter: areas of myelinated axons Gray matter: areas of unmyelinated axons, cell bodies, and dendrites **Neuron – Classification 1** 

### According to the number of the processes



### **Neuron – Classification 2**

### According to the function



#### Motor (efferent) neurons:

conduct impulses to muscles, neurons, glands

#### Sensory (afferent) neurons:

receive sensation

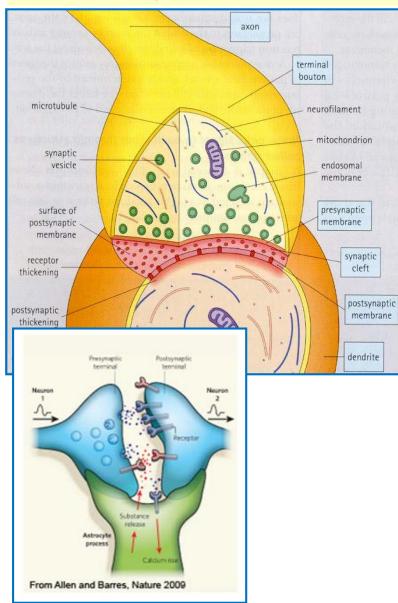
#### Interneurons:

local circuit neurons



#### Definition

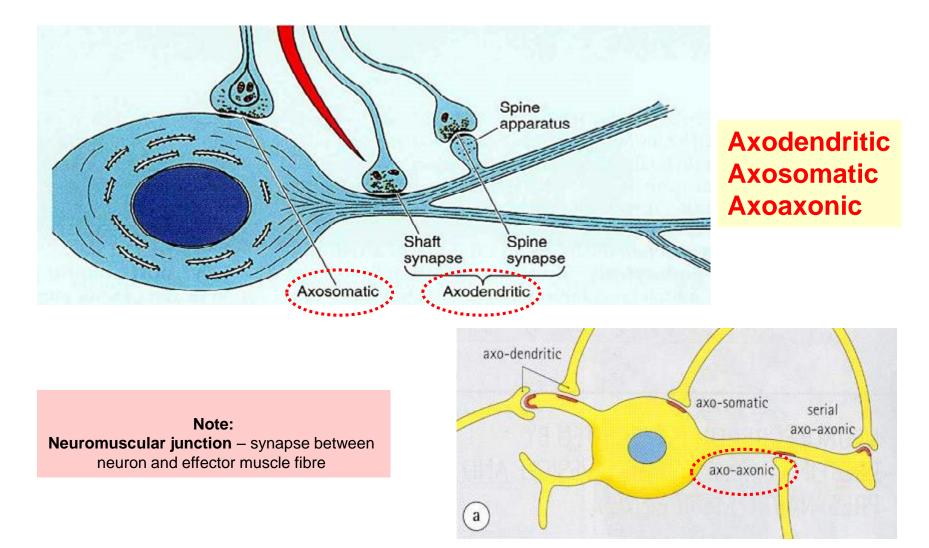
Synapses are highly specialized intercellular junctions, which link the neurons of each nervous pathway



- · Axon terminal forms bouton terminal
- Presynaptic membrane contains mitochondria, and an abundance of synaptic vesicles with neurotransmitter
- **Presynaptic dense projections -** are associated with synaptic vesicles form active sites of synapse
- Synaptic vesicles (smaller + larger storage)
- Postsynaptic membrane contains receptors and some dense materials
- Synaptic cleft 20-30 nm width, occupied by fine filaments
- Glial cells increase synaptic efficacy
- Asymmetric synapses are excitatory (a thick postsynaptic membrane and a 30 nm synaptic cleft)
- **Symmetric synapses are inhibitory** (thin postsynaptic membrane and a 20 nm synaptic cleft)
- Need special staining to see by light microscopy



### **Classification according to the constitution**





#### **General features**

- non-neuronal cells of several types
- · support and protect the neurons
- bind neurons together and form framework for nervous tissue
- in fetus, guide migrating neurons to their destination
- if mature neuron is not in synaptic contact with another neuron, it is covered by glial cells
- · prevents neurons from touching each other
- gives precision to conduction pathways
- · only nuclei visible by light microscopy without special staining
- · there are several glial cells for each neuron

Number of **neurons**: about **100 billions to 1 trillion** Number of **glial cells: 50x more** then neurons



- Astrocytes
- Oligodendrocytes
- Microglia
- Ependymal cells



#### **Peripheral neuroglia**

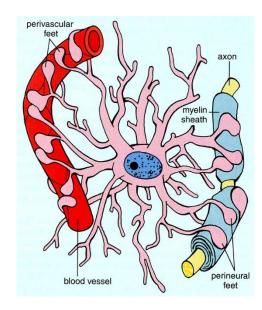
- Schwann cels
- Satellite cells

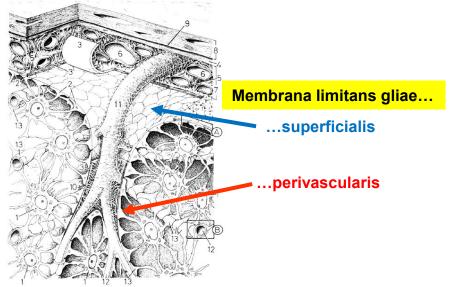
## **Neuroglia - Astrocytes**

- most abundant glial cell in CNS
- covers entire brain surface and most non-synaptic regions of the neurons in the gray matter of the CNS

#### diverse functions:

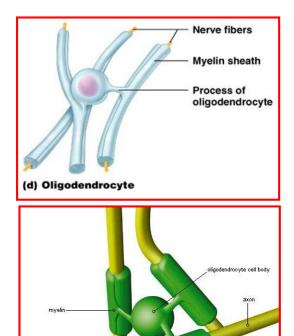
- ✓ form a supportive framework of nervous tissue
- have extensions (perivascular feet) that contact blood capillaries that stimulate them to form a tight seal called the blood-brain barrier
- convert blood glucose to lactate and supply this to the neurons for nourishment
- nerve growth factors secreted by astrocytes promote neuron growth and synapse formation
- communicate electrically with neurons and may influence synaptic signaling
- regulate chemical composition of tissue fluid by absorbing excess neurotransmitters and ions
- astrocytosis or sclerosis when neuron is damaged, astrocytes form hardened scar tissue and fill space formerly occupied by the neuron
- ✓ contains GFAP

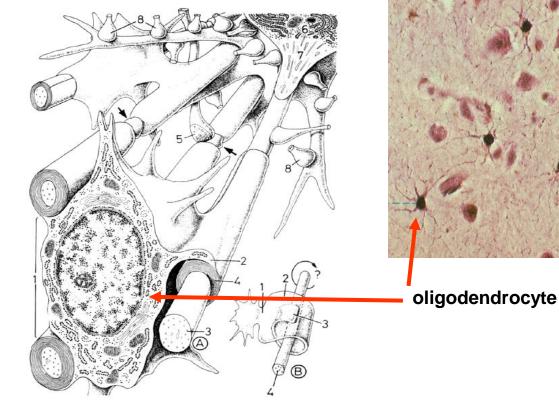




## Neuroglia - Oligodendrocytes

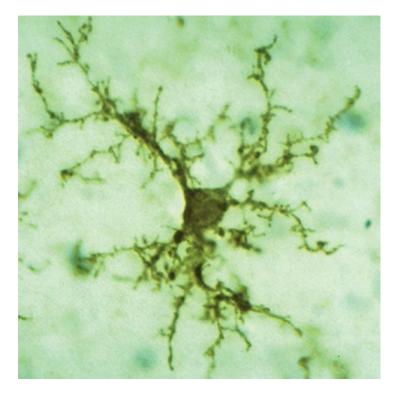
- ✓ smaller than astrocytes; darker, round nucleus, abundant RER, well developed golgi apparatus
- ✓ form myelin sheaths in CNS
- $\checkmark$  one cell serves more then one axon
- cannot migrate around axons (unlike Schwann cells) must push newer layers of myelin under the older ones so myelination spirals inward toward nerve fiber
- ✓ nerve fibers in CNS have no Schwann sheath (neurilemma) or endoneurium
- each arm-like process wraps around a nerve fiber forming an **insulating** layer that speeds up signal conduction
- ✓ damaged in multiple sclerosis

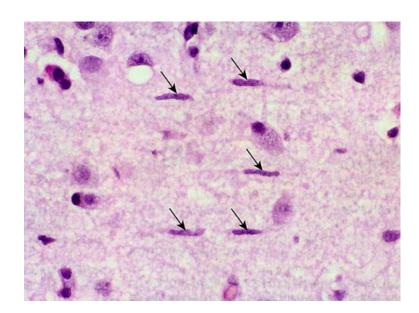




## Neuroglia - Microglia

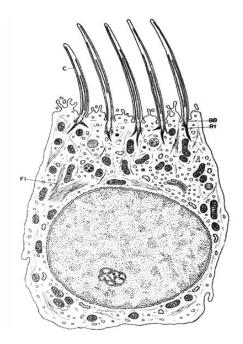
- ✓ smallest neuroglial cell
- ✓ small, dark, elongated nuclei
- ✓ possess **phagocytotic** properties
- ✓ when activated antigen presenting cell
- ✓ originate in bone marrow (**mesodermal** origin)

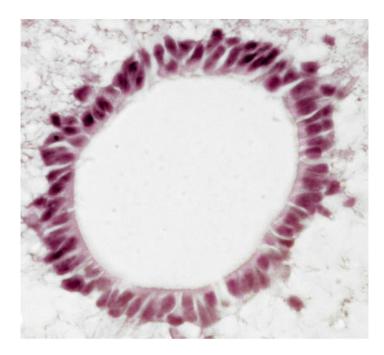




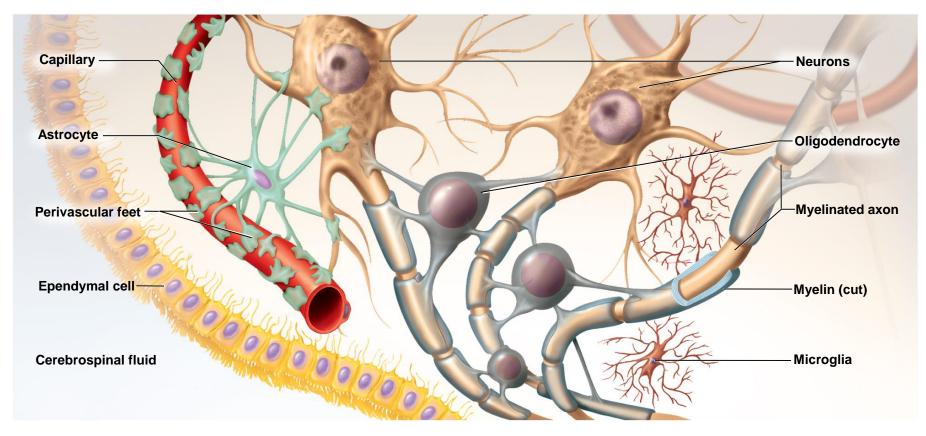
### **Neuroglia – Ependymal cells**

- ✓ line ventricles of CNS and central canal of spinal cord
- ✓ cuboidal or low columnar shape
- ✓ no basal lamina
- ✓ secrete cerebrospinal fluid (CSF)
- ✓ some are **ciliated**, facilitate movement of CSF
- ✓ participate in formation of Choroid plexus





### **Neuroglia – Central - Summary**



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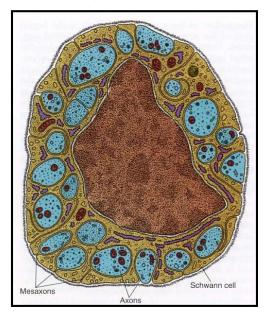
### **Neuroglia in PNS – Schwann cells**

- cells that encircle all axons in PNS
- provide structural and metabolic support to axons
- provide guidance for axonal growth

X

### Small diameter axons

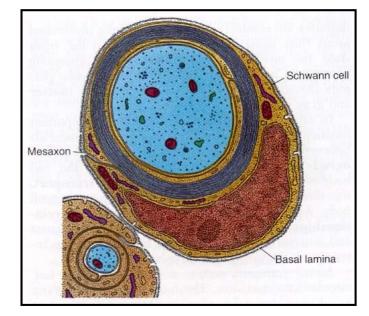
#### Enveloping by only cytoplasm



only Schwann sheath – gray nerve fiber

#### Large diameter axons

Wrapping by myelin sheaths

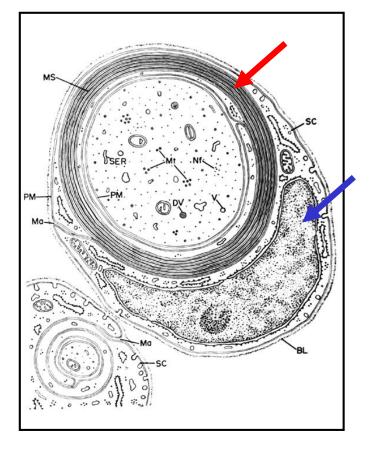


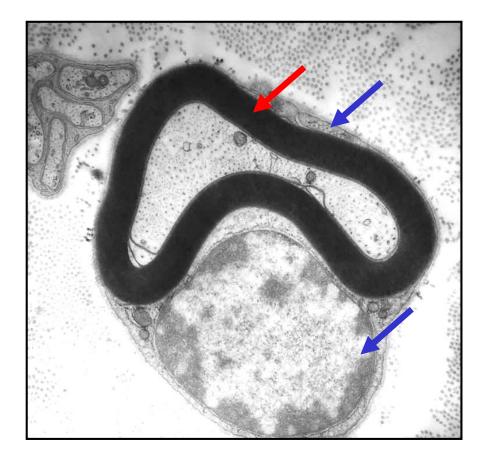
Schwann + myelin sheath – double contoured nerve fiber

## **Neuroglia in PNS – Schwann cells**

Double contoured nerve fiber

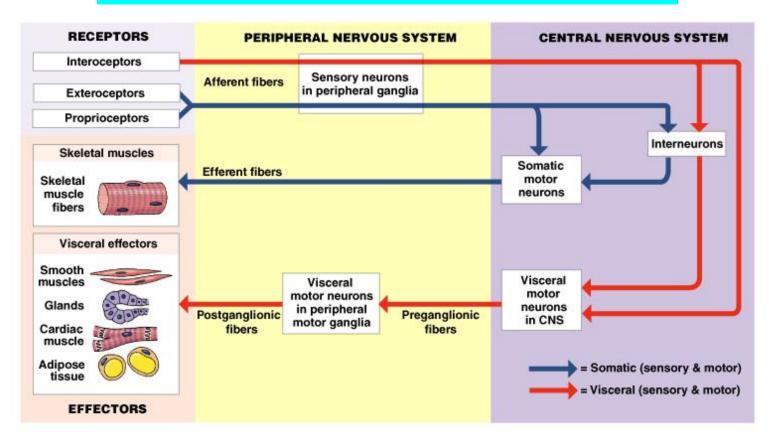




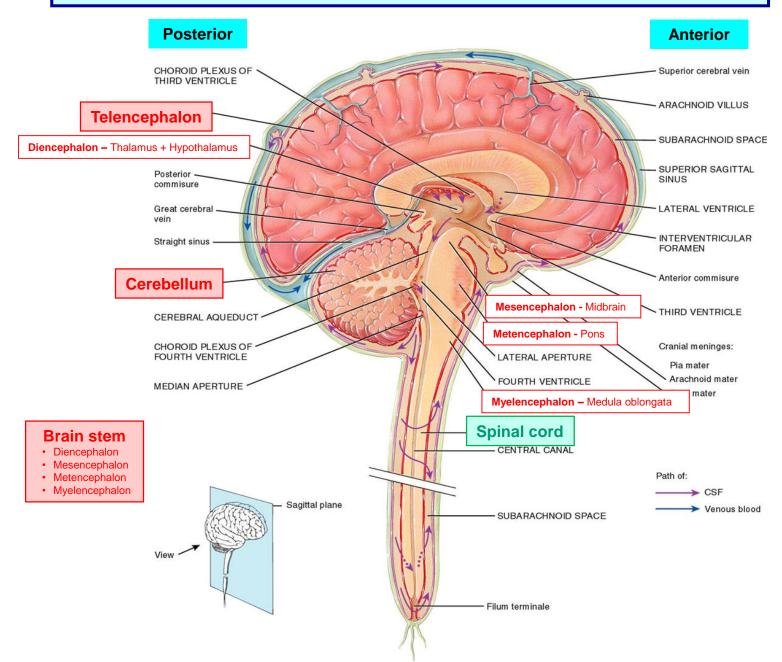


### **Nervous system – Peripheral x Central**

#### **CNS is Brain and Spinal cord + PNS is everything else**



### **Central nervous system – Brain + Spinal cord**



### **Central nervous system – Neuronal organization**

#### **Gray matter**

- Cell bodies
- Nonmyelinated neurons (dendrites, proximal + distal ends of axons)
- Neuroglia (plasmatic astrocytes, microglia)
- Capillaries (Blood-Brain barrier)
- forms the outer layer of the cerebrum cerebral cortex
- also forms nuclei deep in the brain = clusters of neuronal cell bodies in CNS

- collections of nuclei can form a centers (higher brain function)

#### White matter

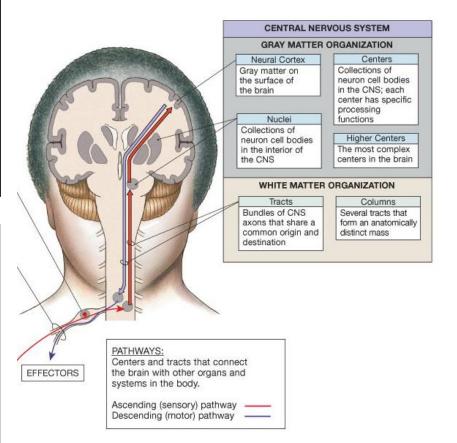
- Myelinated axons of nerve cells
- Neuroglia (oligodendrocytes, fibrilar astrocytes)
- Blood capillaries (lesser density than in the gray matter)

#### Brain

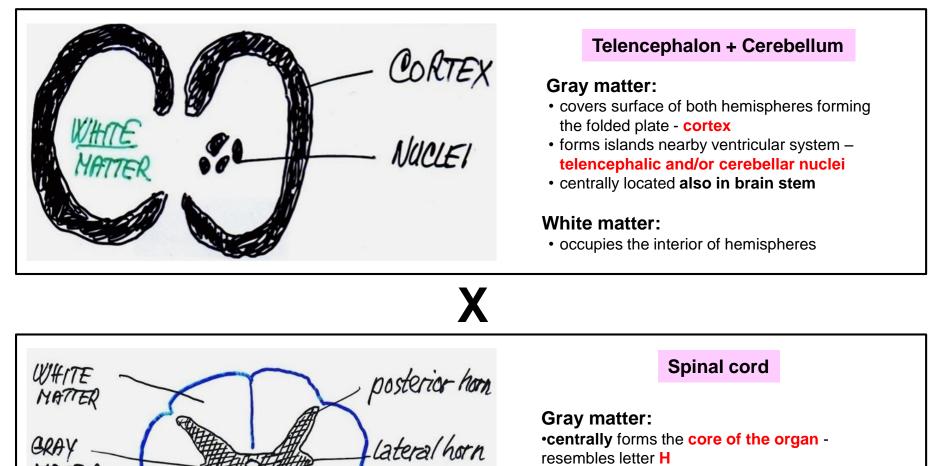
axons are bundled together to form white matter tracts
conduct nerve impulses from gray region to gray region
three types of tracts (commisural, association, projection)

#### Spinal cord

- sensory and motor tracts (ascending and descending)



### **Central nervous system – Distribution of grey/white matter**



anterior

hom

GRAY

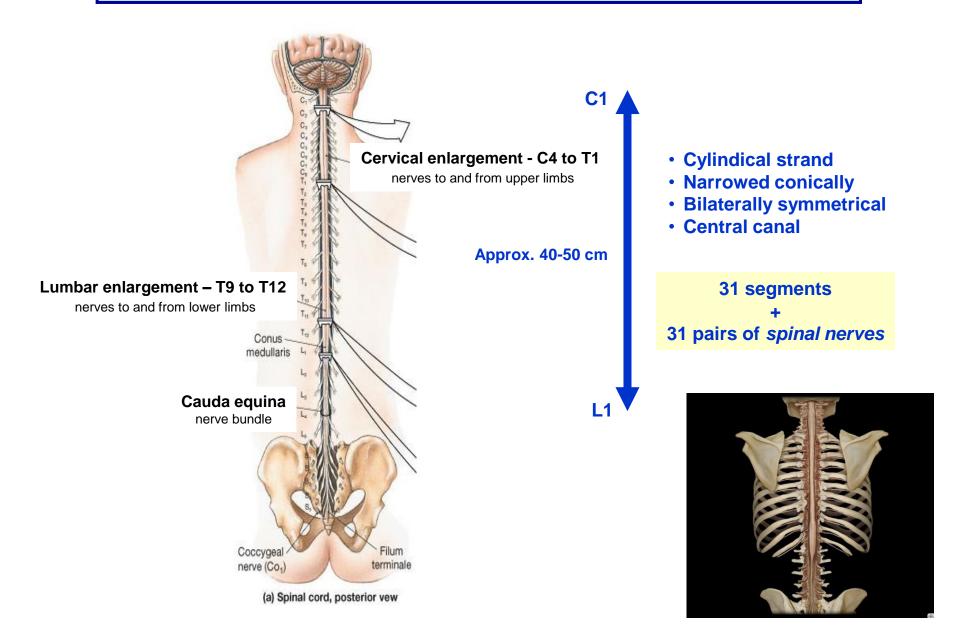
NATTER

### Gray matter:

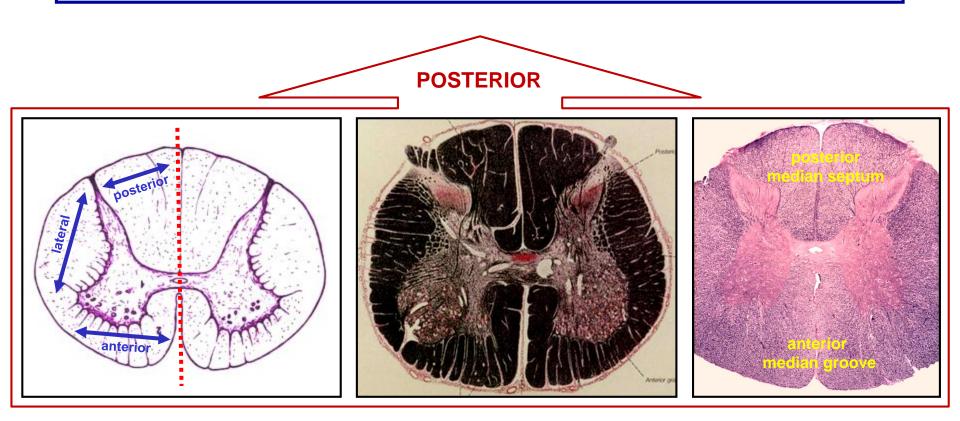
•centrally forms the core of the organ resembles letter H •at the periphery it is surrounded by funiculi of

the white matter

### **Central nervous system – Spinal cord - Anatomy**



### **Central nervous system – Spinal cord – White matter**



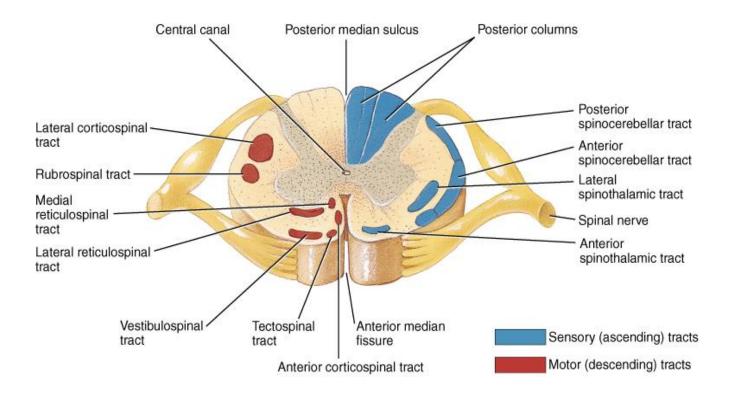
### Fasciculi = Funiculi (= Collumns)

- Anterior sensitive tracts + motoric tracts
- Lateral sensitive tracts + motoric tracts
- Posterior sensitive tracts

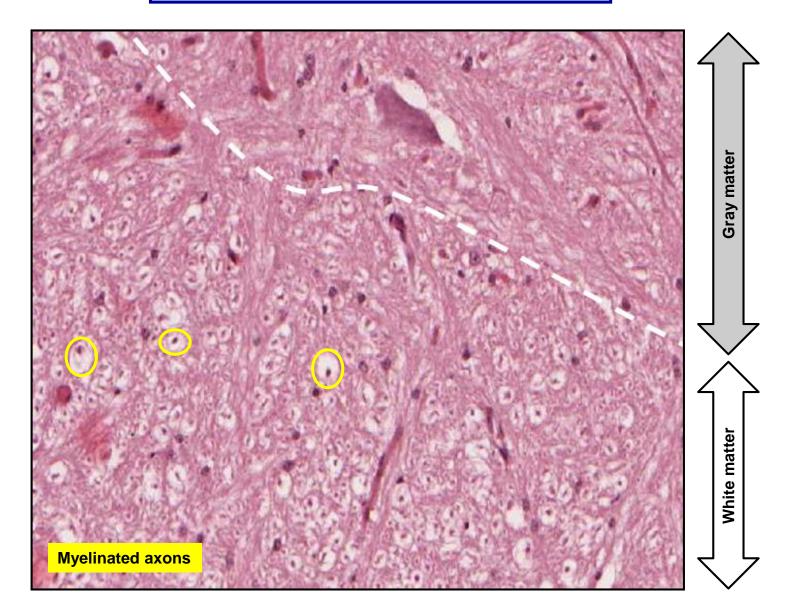
Sensitive = Ascending Motoric = Descending

### **Spinal cord – White matter - Tracts**

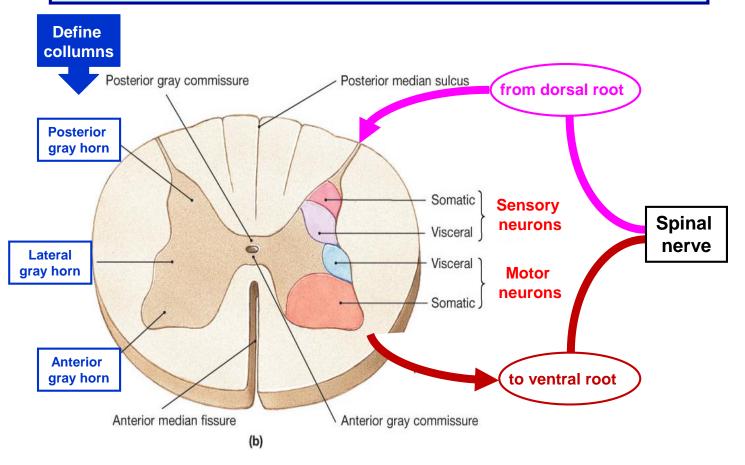
#### Only for demonstration purpose – no need of memorizing !!!



### **Spinal cord – White matter**

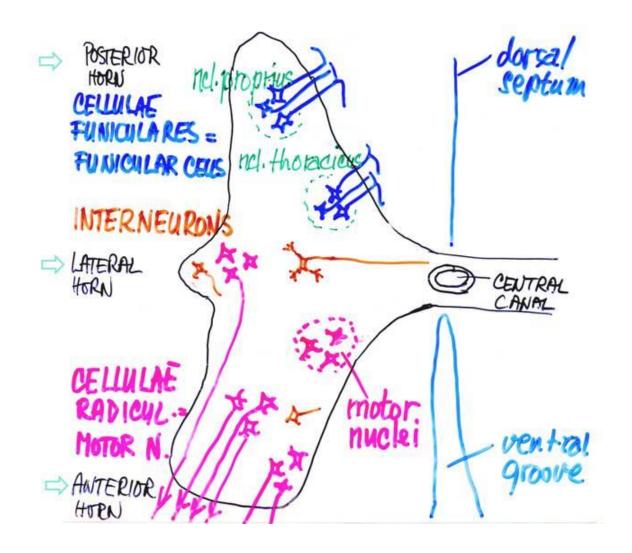


## **Spinal cord – Gray matter – Organization**

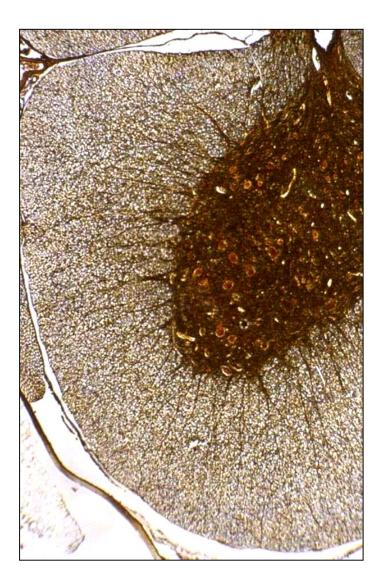


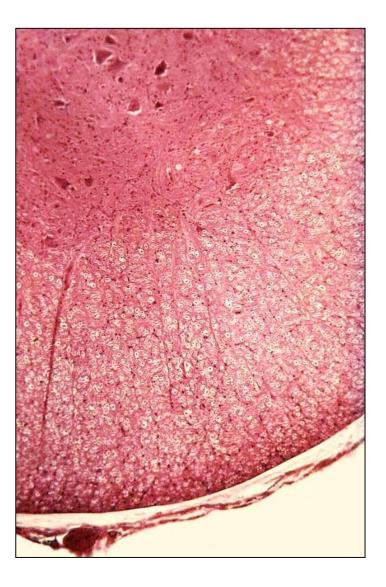
Neurons in gray matter – all are multipolar		
<ul> <li>Motor neurons (radicular)</li> <li>in the anterior (ventral) horns</li> <li>stellate shape, 150 μm in diameter</li> <li>send off long myelinated axons ending on muscle fibres</li> </ul>	<ul> <li>Funicular cells</li> <li>mainly in the posterior horns</li> <li>their axons enter the white matter and connect to other segments of SC and to brain stem</li> </ul>	Interneurons <ul> <li>small neurons</li> <li>diffusely distributed among motor and funicular cells</li> </ul>

### **Spinal cord – Gray matter – Organization**

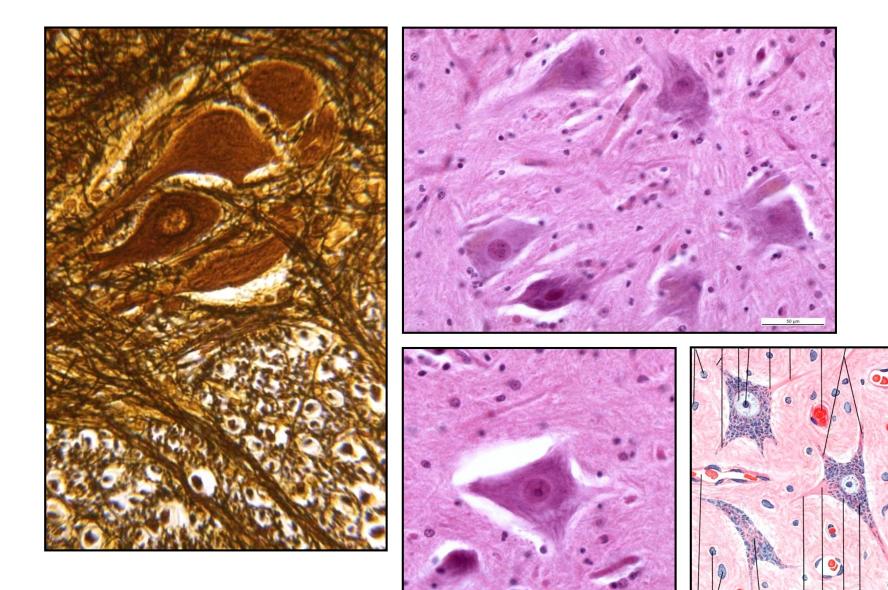


## Spinal cord – Gray matter

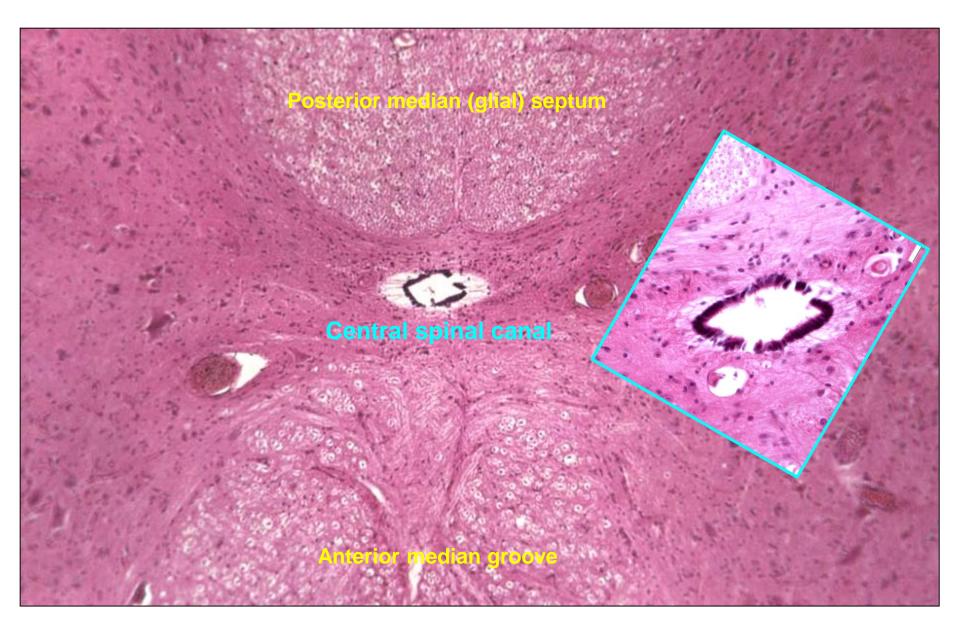




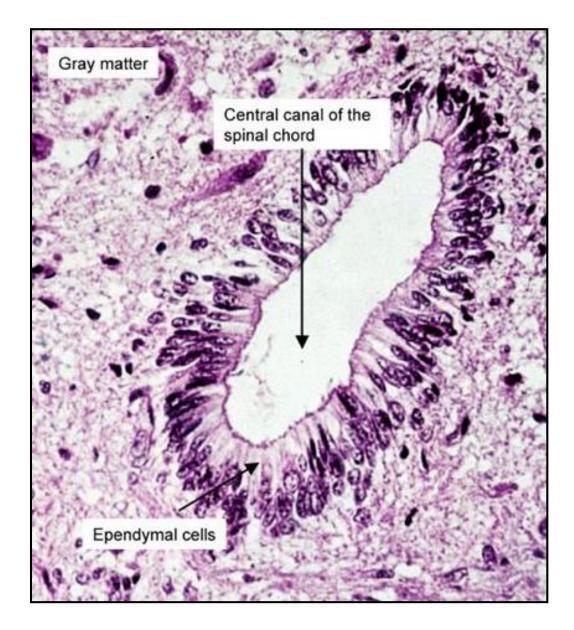
### **Spinal cord – Gray matter – Motor neurons**



## **Spinal cord – Central spinal canal**



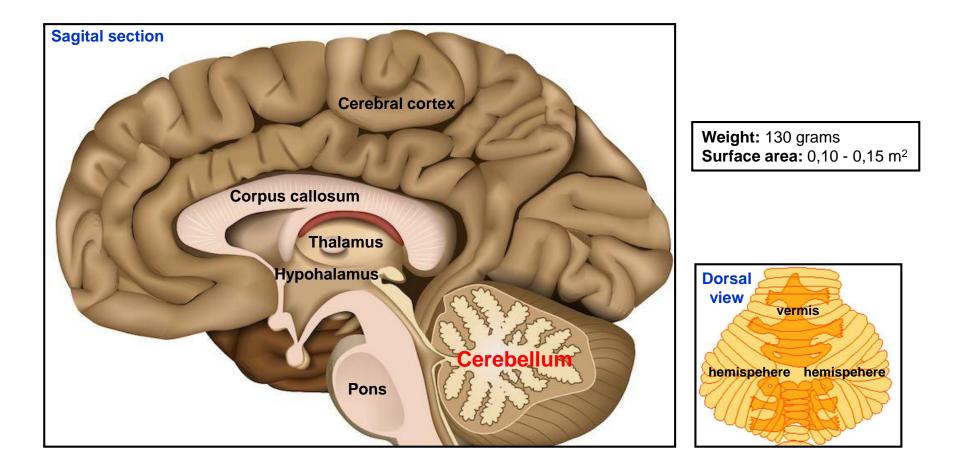
### **Spinal cord – Central spinal canal**



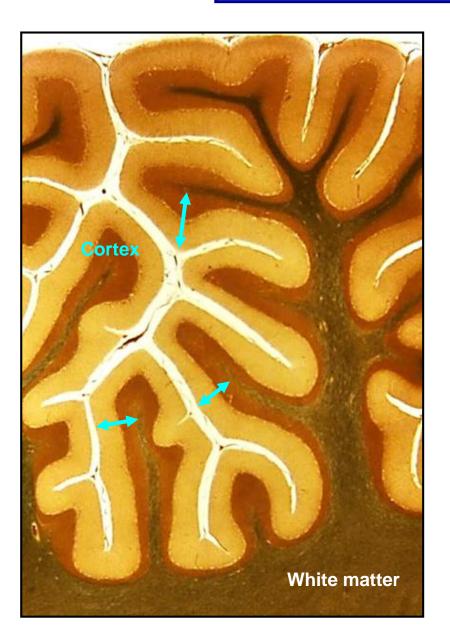


#### Function

•co-ordination of voluntary movements and helping to maintain balance
•allows for smooth, co-ordinated movements by constantly adjusting muscle tone and posture



### **Cerebellum – Gray matter**



#### **Gray matter**

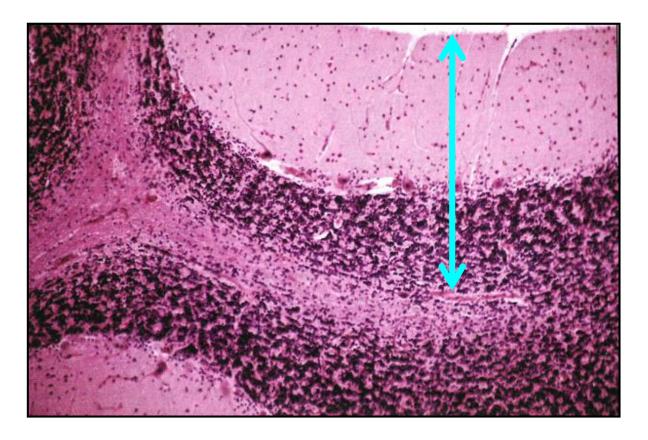
- Cortex at the surface (1 mm thick)
- Nuclei in white matter (nucleus dentatus, emboliformis, globusus, and fastigii)

## **Cerebellum – White matter**



"Arbor vitae" – white matter

# **Cerebellum – Cortex**

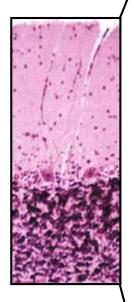


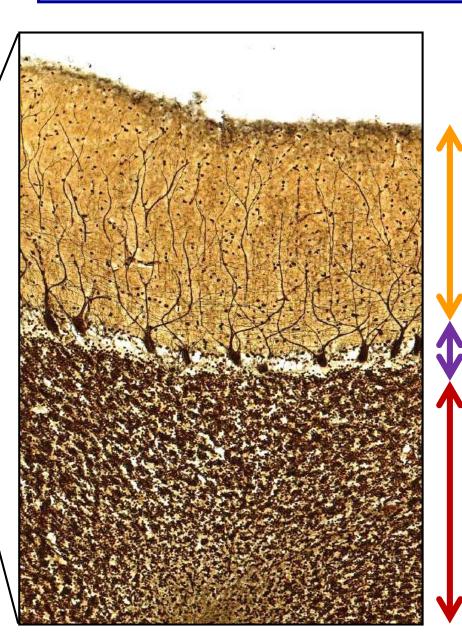
Molecular layer (stratum moleculare)

Purkinje cell layer (stratum gangliosum)

Granule cell layer (stratum granulosum)

# **Cerebellum – Cortex - Cells**





Molecular layer (stratum moleculare) •Basket cells •Stellate cells

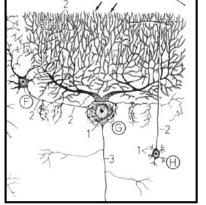
#### Purkinje cell layer (stratum gangliosum)

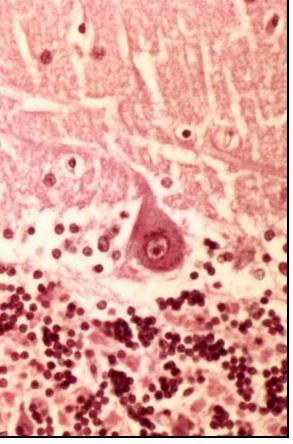
- Perikaryons of Purkinje cells
- Golgi (Bergman) glial cells

# **Granule cell layer** (stratum granulosum)

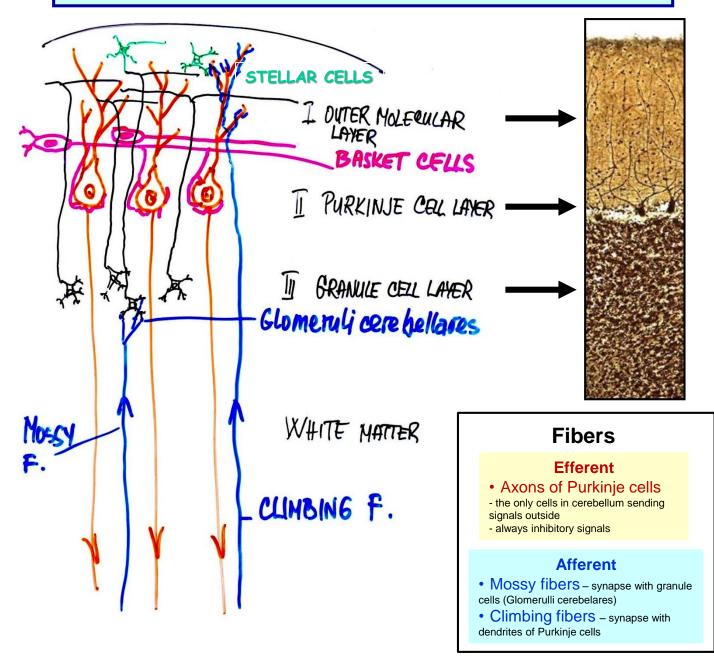
- Granule cells
- Golgi (Bergman) glial cells

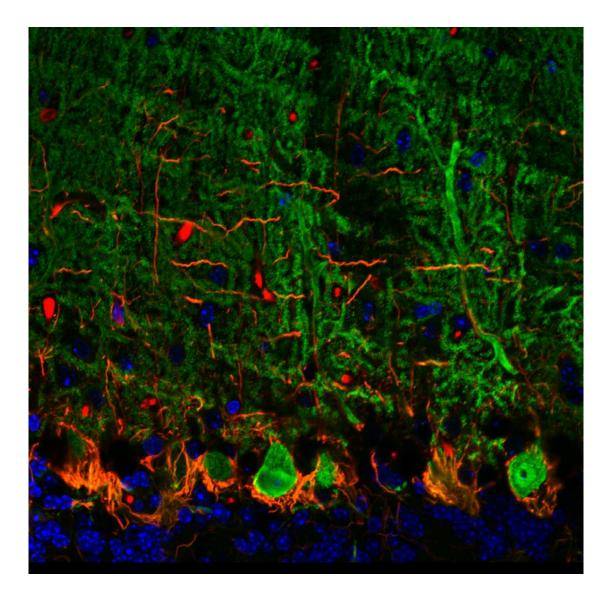


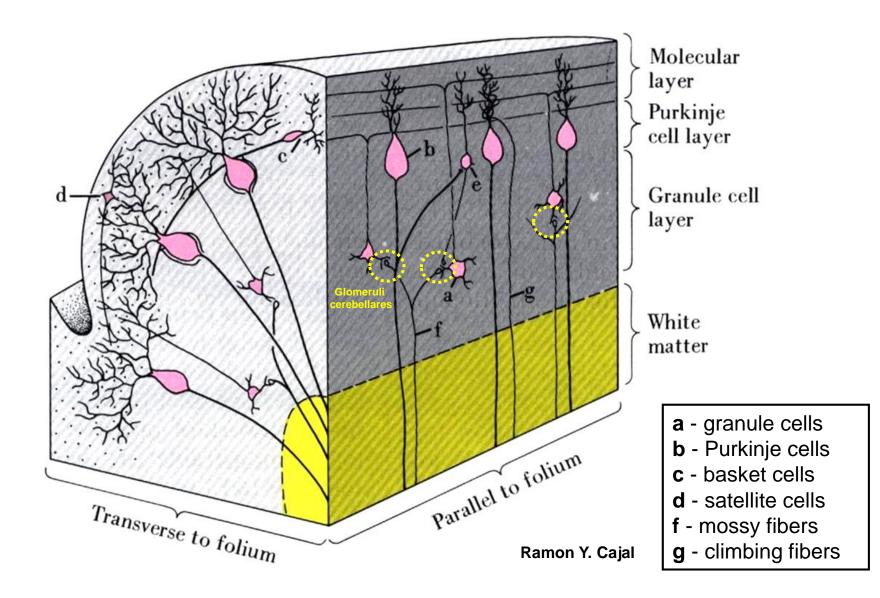


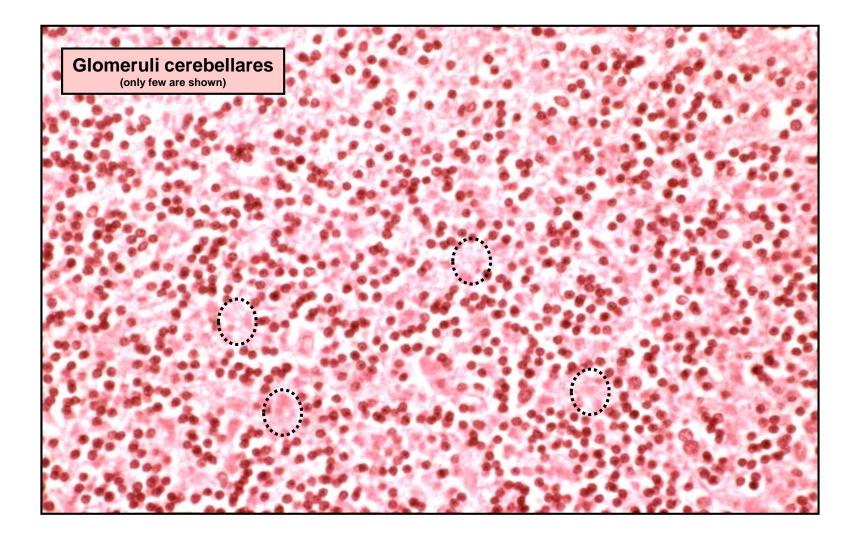




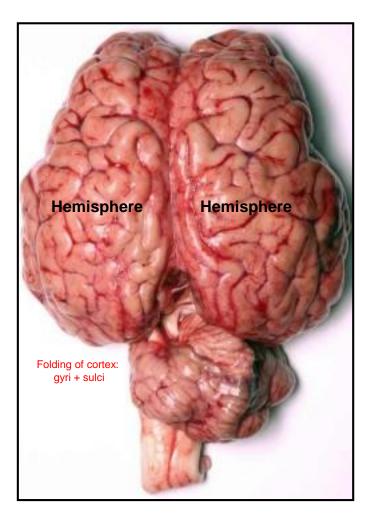








Telencephalon



### **Gray matter**

- Cortex at the surface
- Nuclei in white matter

### White matter

• Among the cortex and nuclei

### **Telencephalon – Cerebral cortex**

#### **Functions:**

- · perception and conscious understanding of all sensations
- · integration of different sensory modalities
- higher cognitive and advanced intellectual functions
- responsible for features such as emotion, personality and intellect
- · involved in planning and executing complex motor activities

### **Overall characteristics:**

- about 80% of the mass of the brain
- surface area about 0.20 0.25  $m^2$
- thickness about 2 5 mm
- contains about 10 billion neurons

#### Isocortex:

- = **neocortex** (phylogenetically youngest)
- only in mammals
- 90% of the cortex in humans
- 6 distinguishable layers of cells

#### Allocortex:

- = archicortex + paleocortex
- less layers of cells
- (e.g. olfactory cortex 3 layers, hipocampus 1 layer)

### **Telencephalon – Cerebral cortex – Neuron types + layers**

### **Pyramidal**

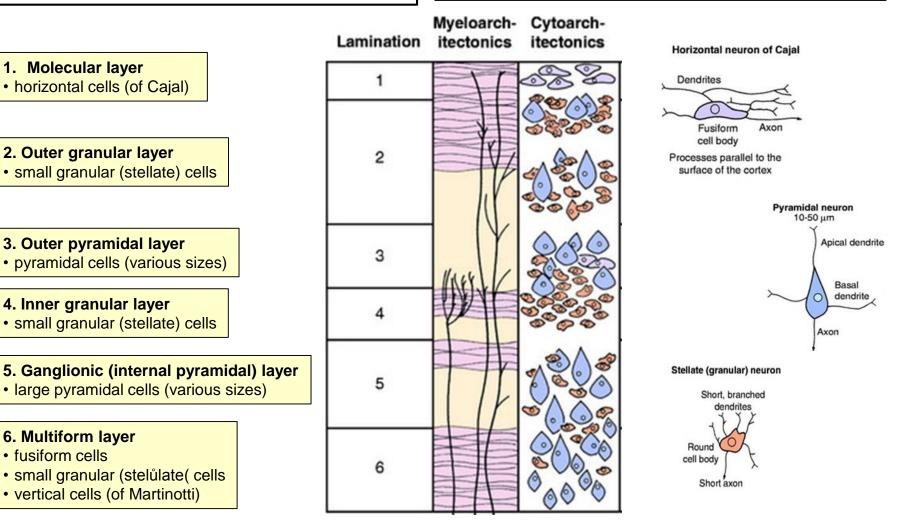
- efferent projecting neurons
- triangular perikaryon (different size)
- · axons with mvelin sheets

fusiform cells

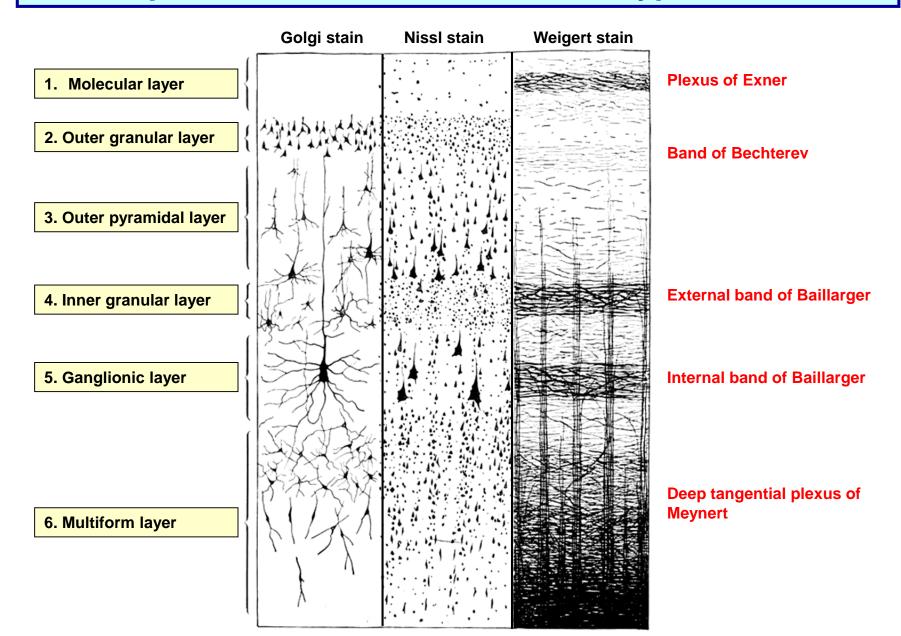
axons travel to different cortical layers and to subcortical areas

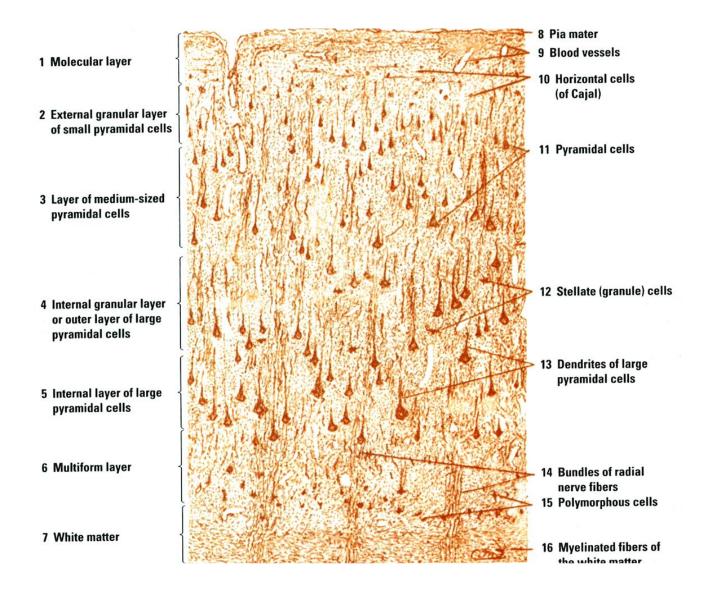
### Non-pyramidal

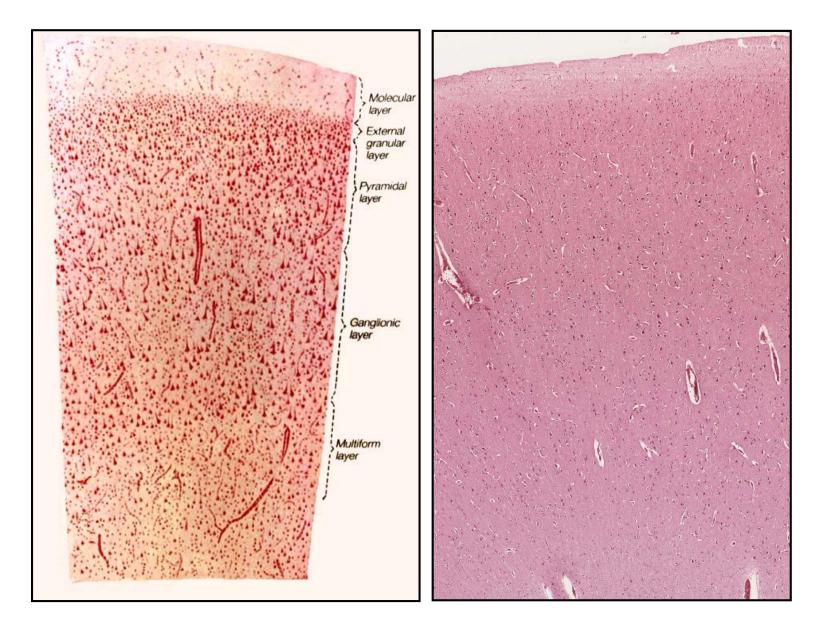
- · variety of different cells
- act as interneurons
- axons stay in the layer with their perikayons
- (e.g. fusiform cells, granule (stellate) cells, horizontal cells (Cajal), vertical cells (Matinotti)

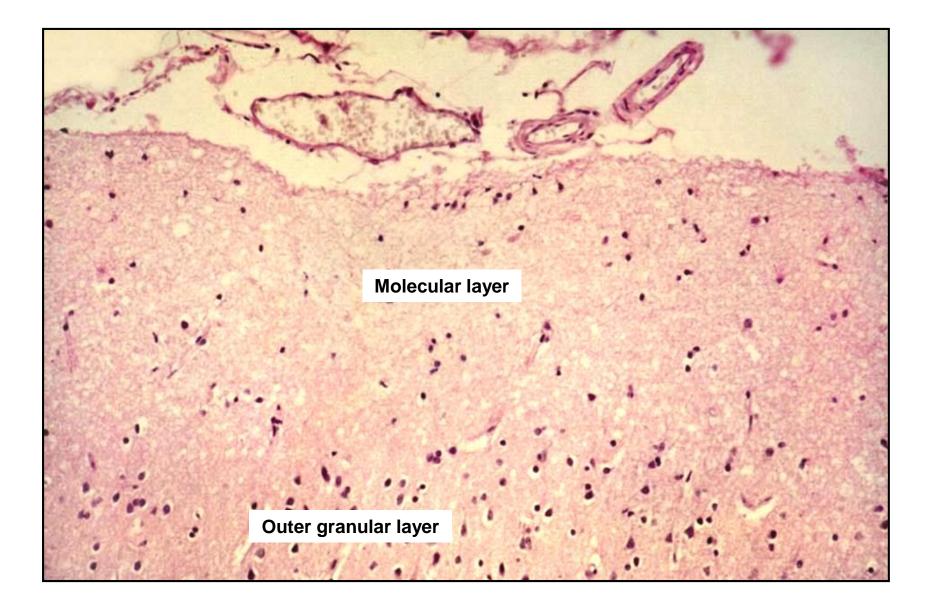


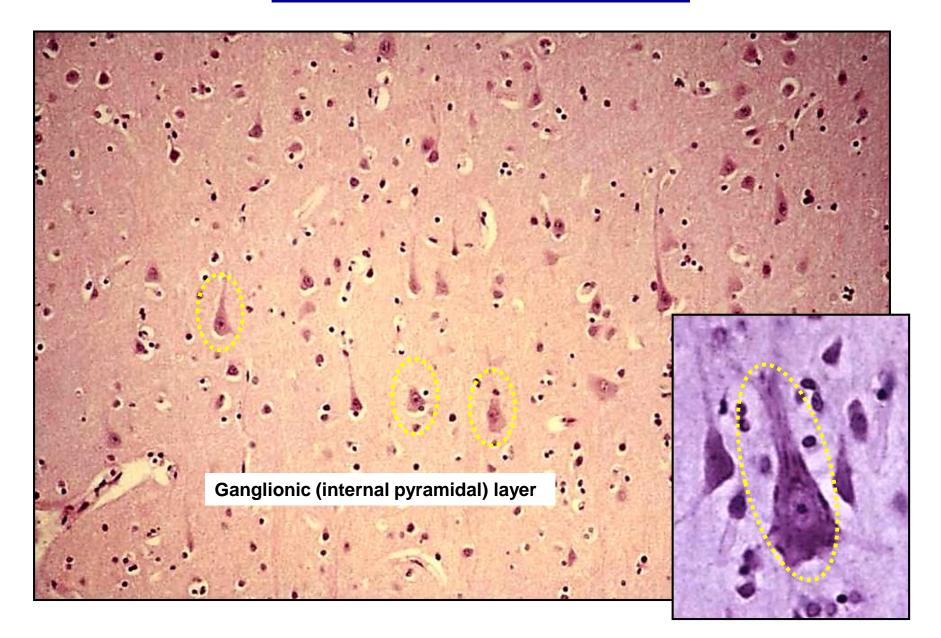
### **Telencephalon – Cerebral cortex – Cell types + Plexuses**

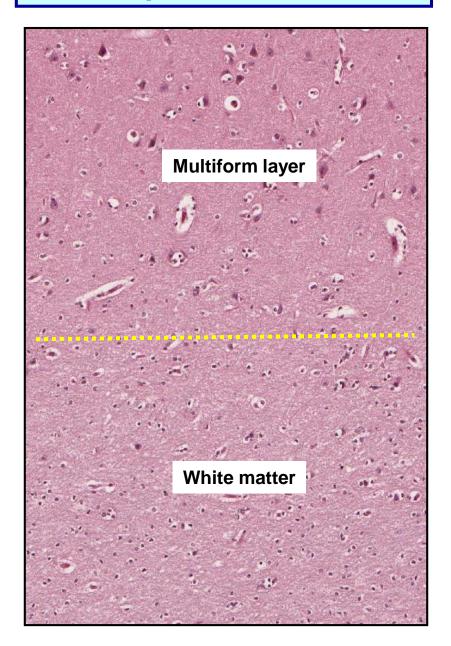


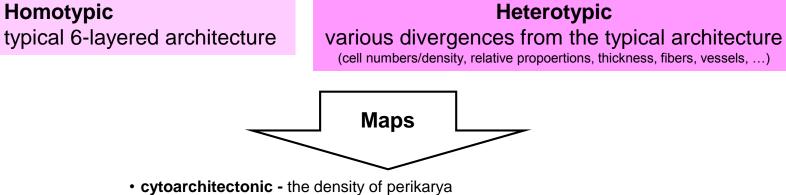




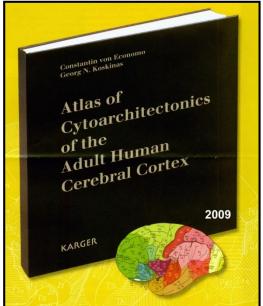


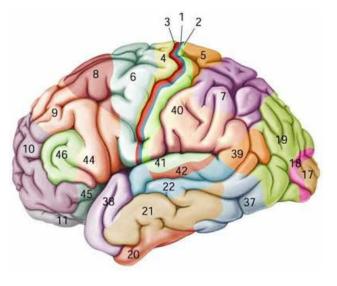






- myeloarchitectonic the density of myelinated fibers
- · glioarchitectonic the type and density of glial cells
- angioarchitectonic the density of blood capillaries or vascularization
- synaptoarchitectonic the density synapses in the isocortex

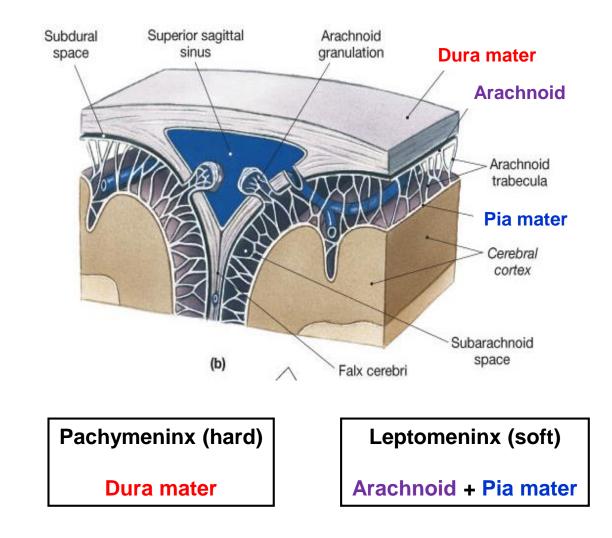




**1909 - K. Brodman** 11 regions and 52 areas

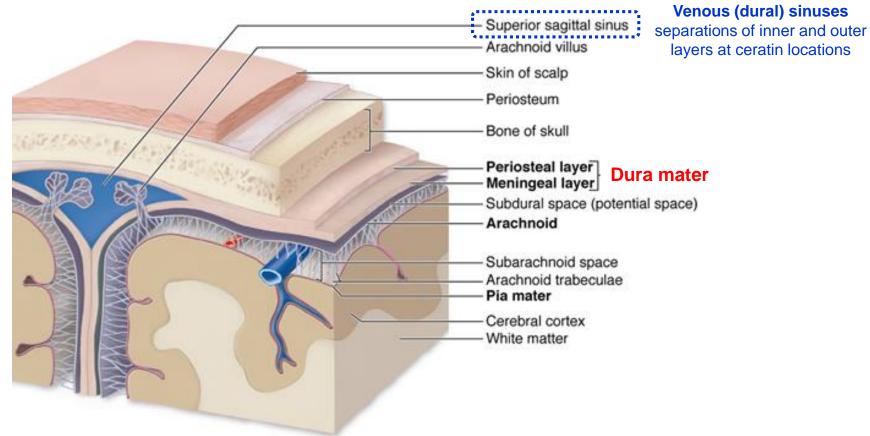


- membranes
- protect CNS + contribute to distribution of liquor
- cover both brain and spinal cord (are continuos)



### **Meninges – Dura mater**

### the outermost + robust (fibrous)



#### **Cranial dura**

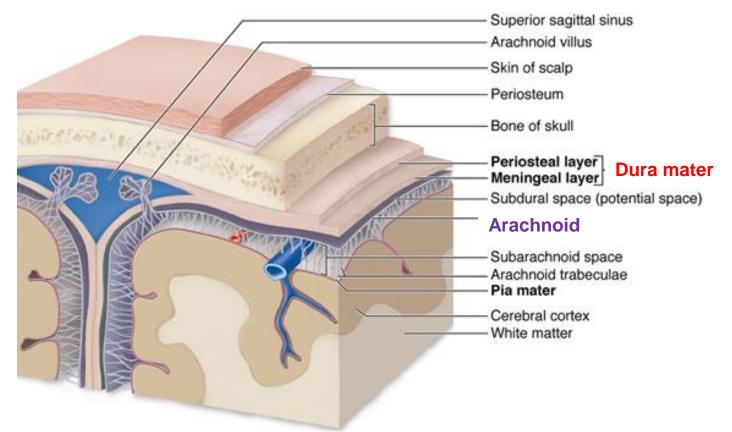
- Endosteal layer (periosteal; outer) adhering to the inner surface of the bones of the skull
- Meningeal layer (inner) thinner fibrous tissue membrane, inner surface covered by mesothelial cells

#### **Spinal dura**

- continuation of the inner layer of cranial dura

# **Meninges – Arachnoid**

### middle + spider web-like + avascular



#### Arachnoid

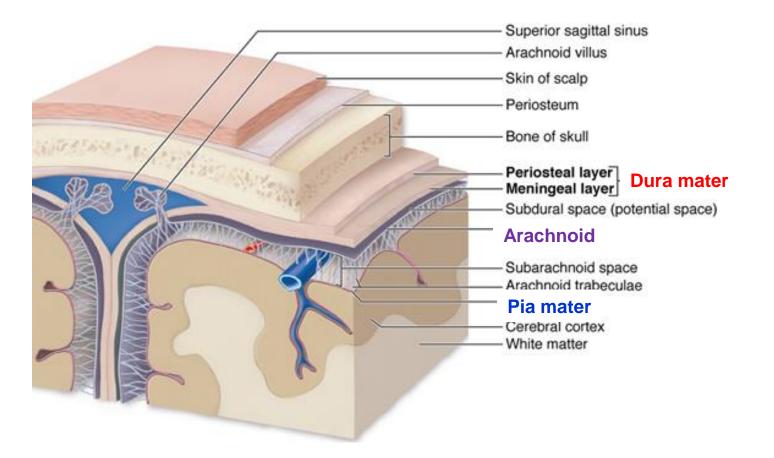
- Neurothel (*lamina neurothelialis*) adhering to the inner layer of dura mater, tight junctions barrier between CSF and blood in dura mater
- **Trabaculas** deligate fibere severed by flat (maningsel) cells
- Trabeculae delicate fibers covered by flat (meningeal) cells

#### Subarachnoid space

- enclosed between the arachnoid and pia mater
- filled by cerebrospinal fluid (CSF)

## Meninges – Pia mater

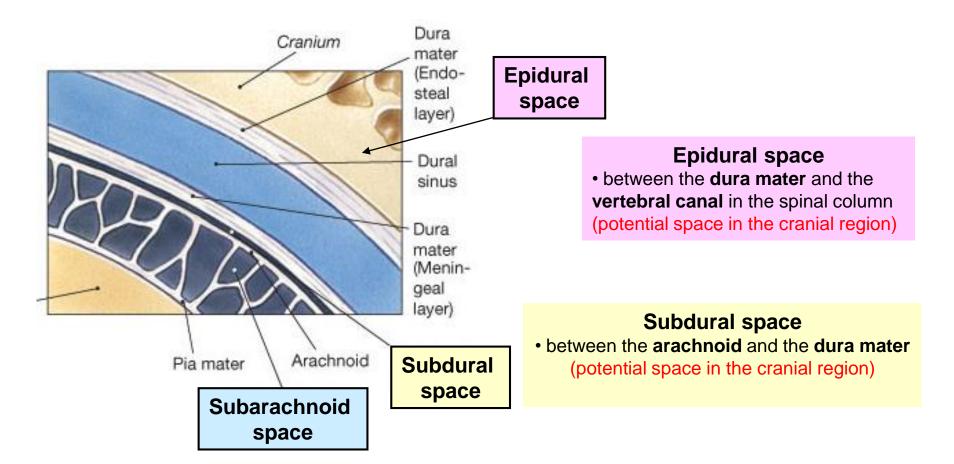
### the innermost + delicate + vascular + adheres to and follows the surface of brain



#### Pia mater

- · Superficial layer- receives trabeculae of the arachnoid
- **Inner layer** elastic and reticular fibers, firmly attached to the under-lying nervous tissue, covered from outside with simple squamous cells of mesodermal origin

# **Meninges – Spaces between the membranes**

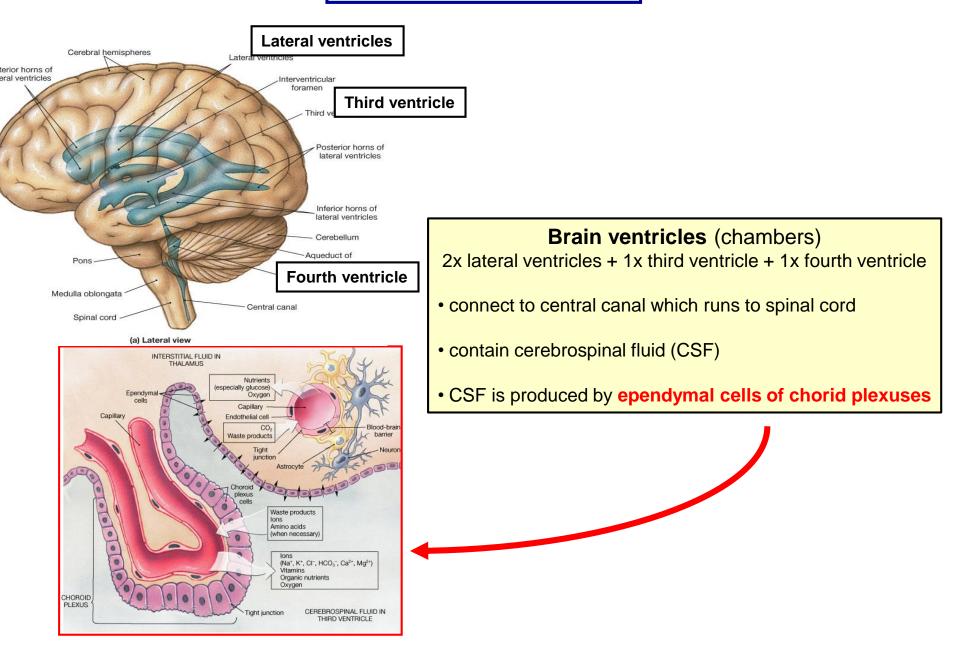


#### Subarachnoid space

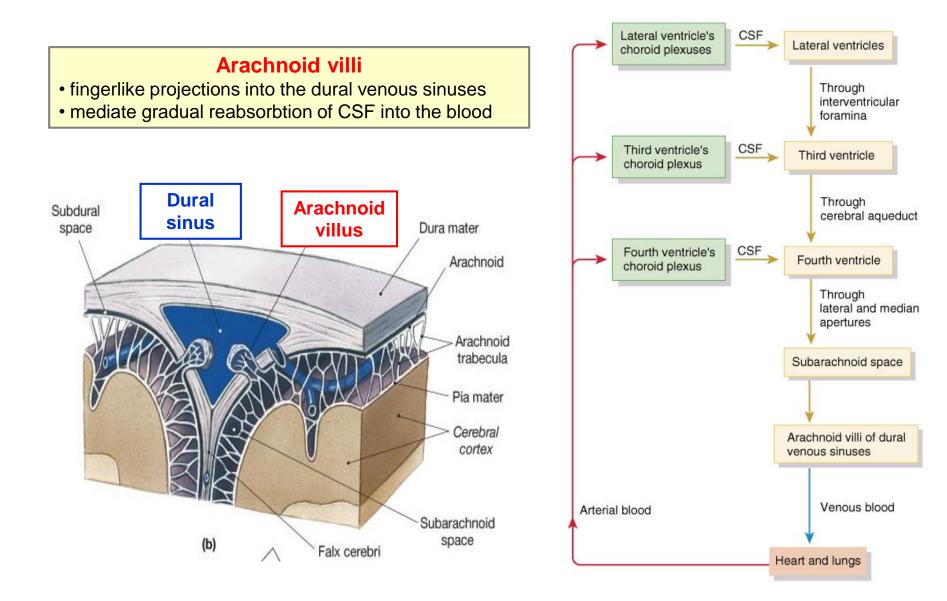
• between the arachnoid and pia mater

(large veins run through the subarachnoid space - e.g. cerebral veins)

# **Cerebrospinal fluid**



## **Cerebrospinal fluid - Circulation**



# **Peripheral nervous system - Components**

#### **Definition:**

Made up of transmission pathways carrying information between the CNS and external/internal environments.

#### Afferent (sensory) pathways:

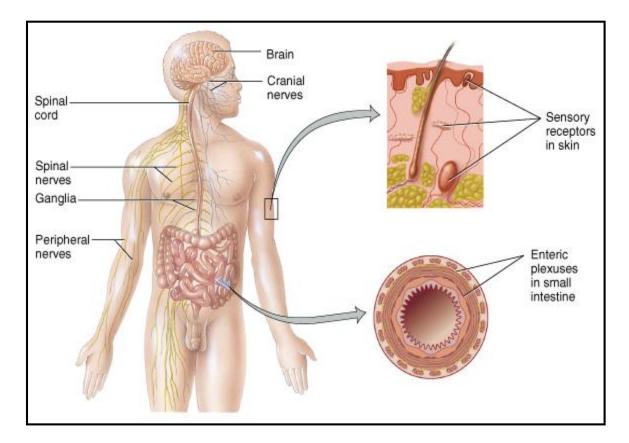
Carry information to the CNS.

#### Efferent (motor) pathways:

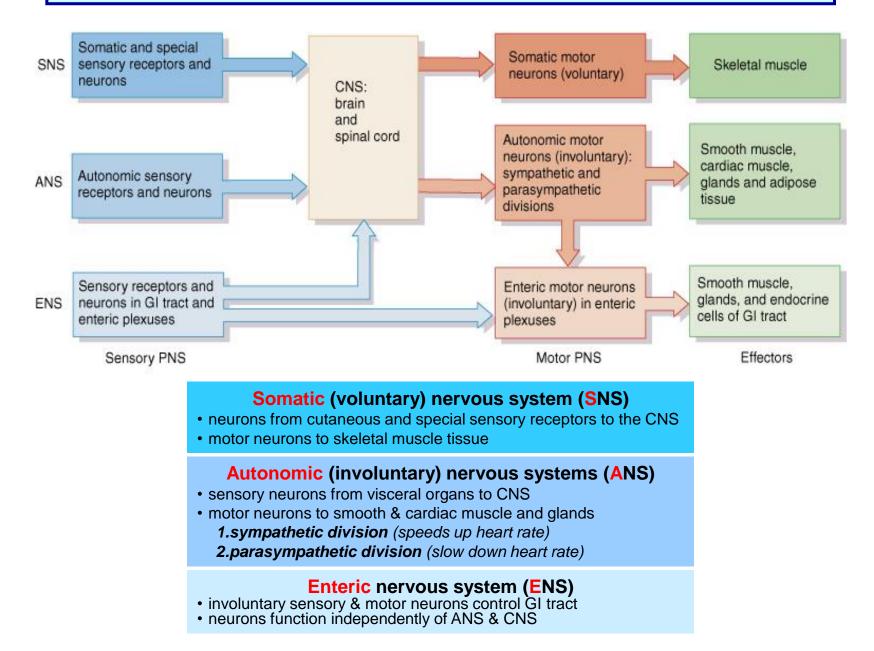
Carry information from the CNS.

#### Includes:

- Cranial nerves (12 pairs)
- Spinal nerves (31 pairs)
- Peripheral nerves
- Ganglia
- Sensory receptors

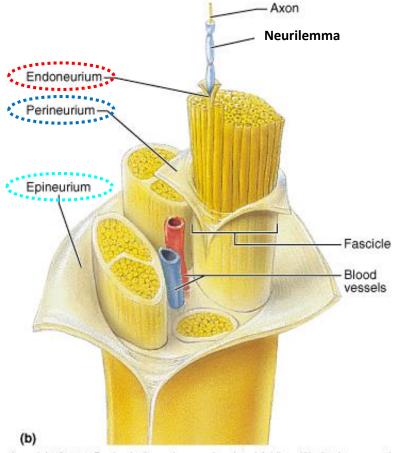


## **Peripheral nervous system – Overall organization**



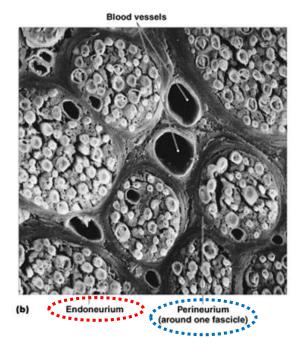
## **Peripheral nervous system - Nerves**

Consists of 100's to 100,000's of myelinated and unmyelinated axons (nerve fibers).



#### Connective tissue layers composing nerves:

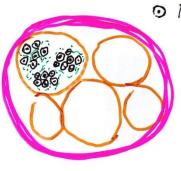
- Endoneurium surrounds axons primary nerve bundles
- Perineurium surrounds fascicles secondary n. bundles
- Epineurium surrounds the entire nerve



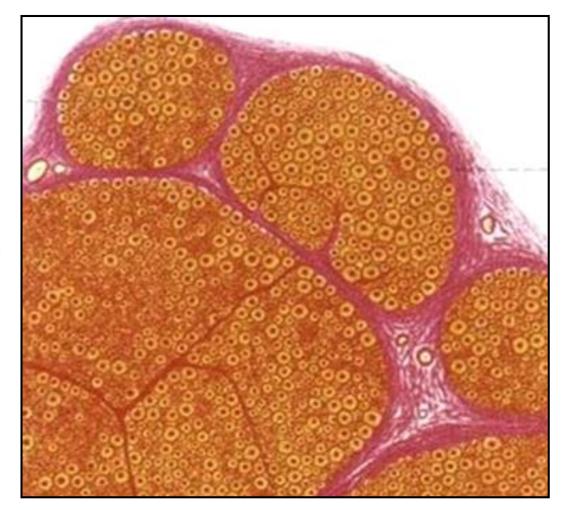
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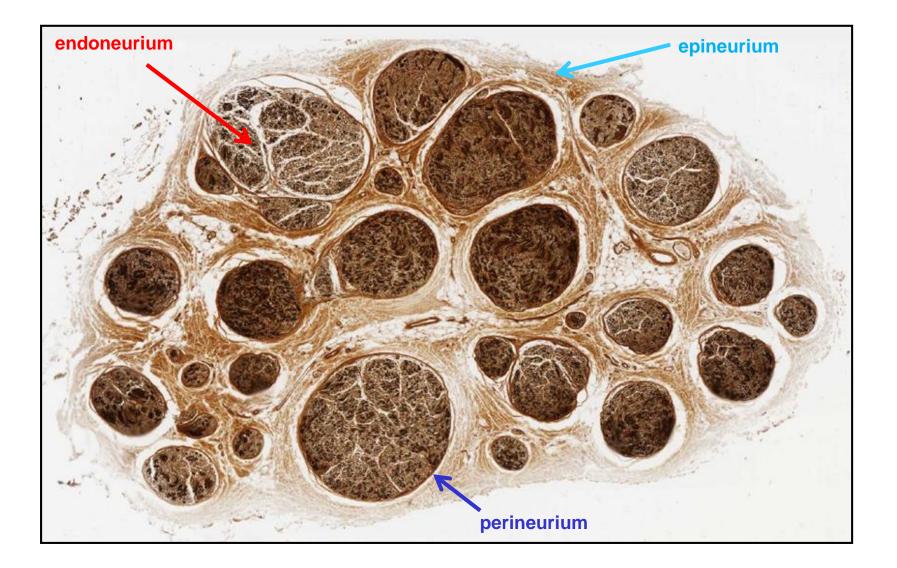
## **Peripheral nervous system - Nerves**



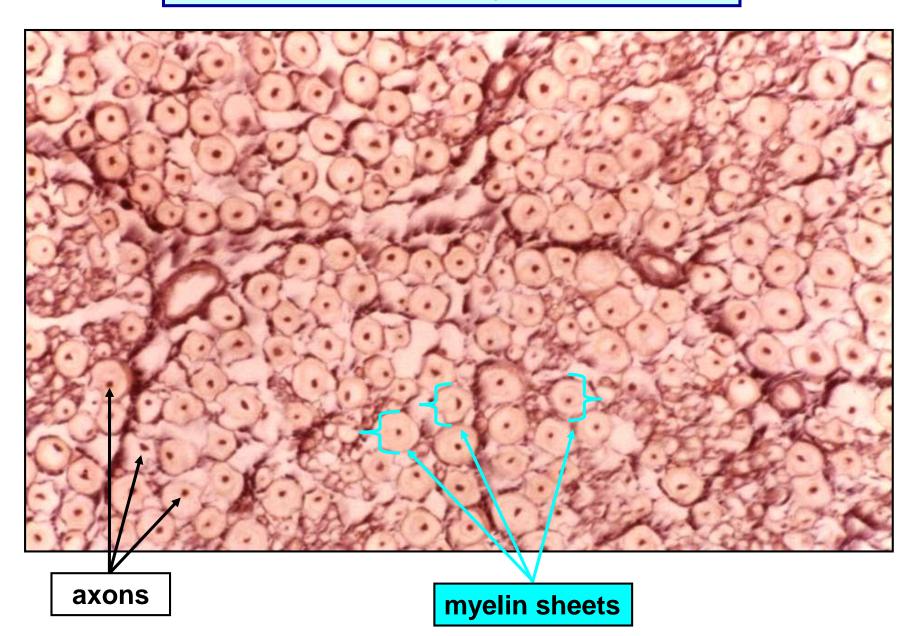
NYELINATED FIBER
 PRIMARY N.B.
 ENDONEURIUM
 SECONDARY N.B
 PERINEURIUM
 EPINEURIUM



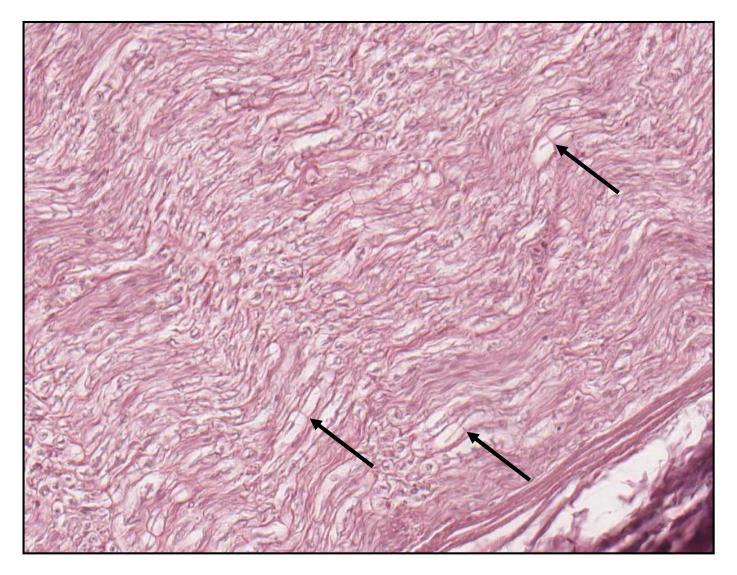
# **Peripheral nervous system – Nerves**



# **Peripheral nervous system – Nerves**



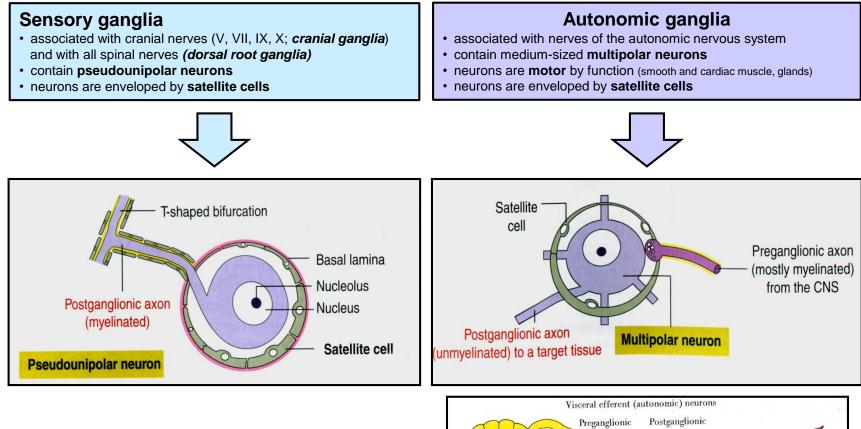
## **Peripheral nervous system – Nerves**

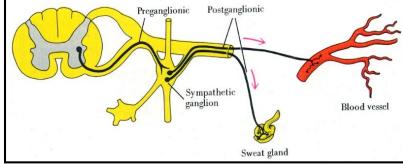


**Nodes of Ranvier** 

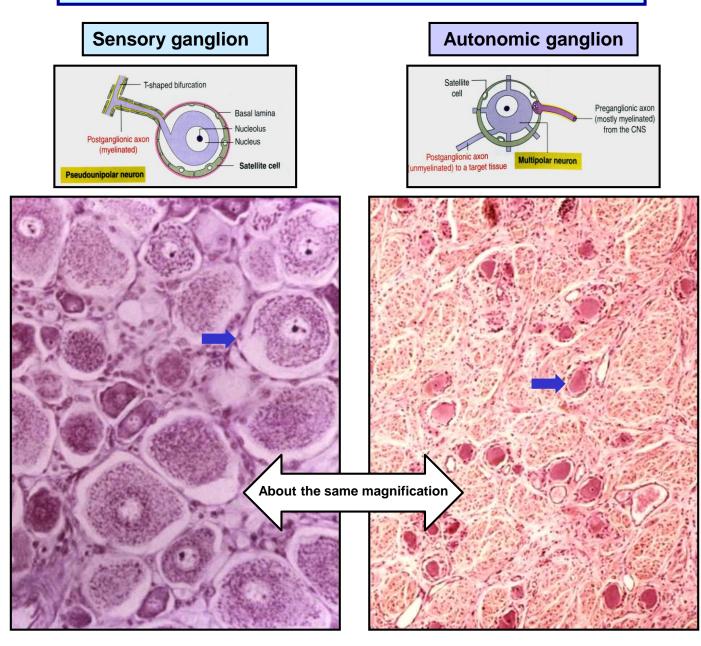
**Peripheral nervous system – Ganglia** 

= aggregations of cell bodies of neurons located outside of CNS

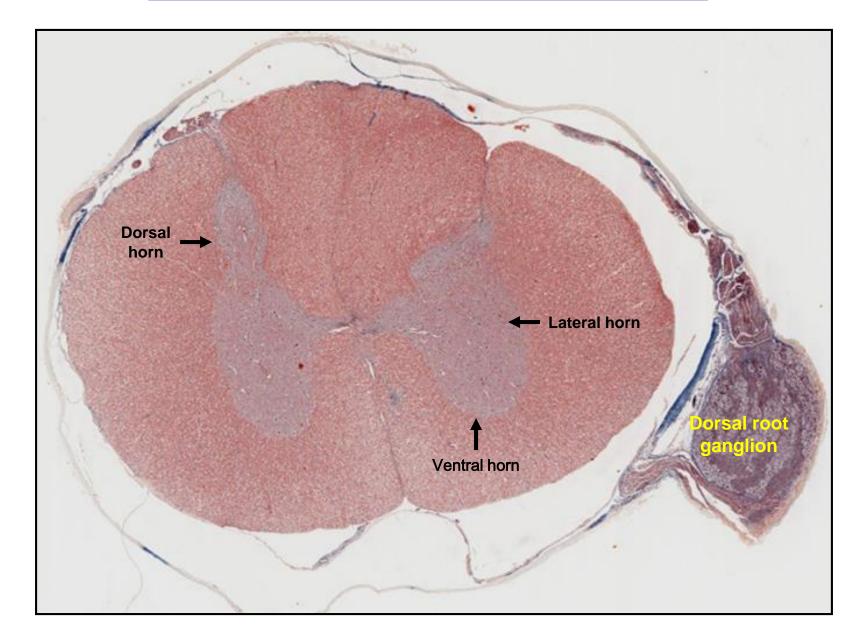




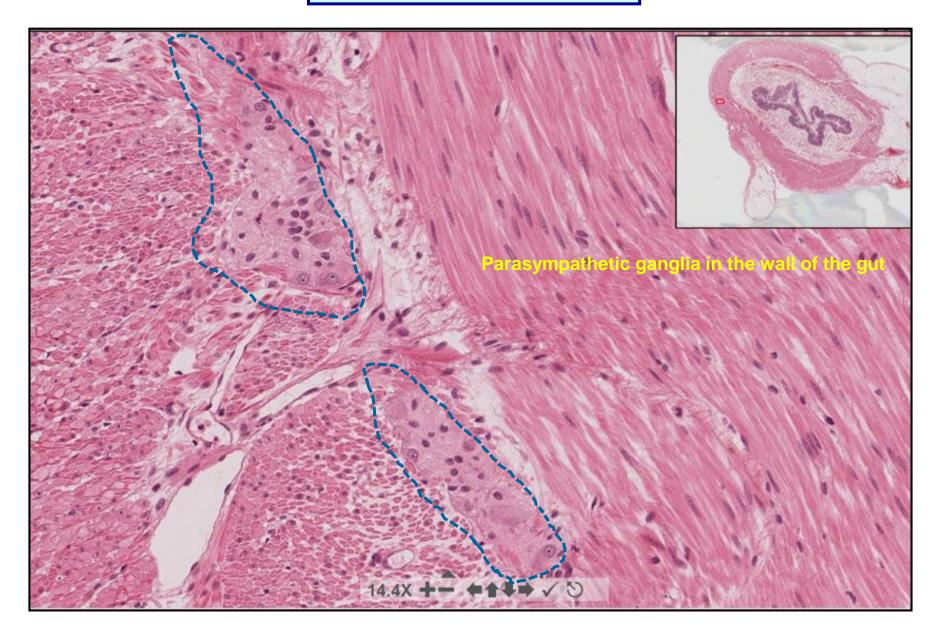
# **Peripheral nervous system – Ganglia**



# Spinal cord + Dorsal root ganglion



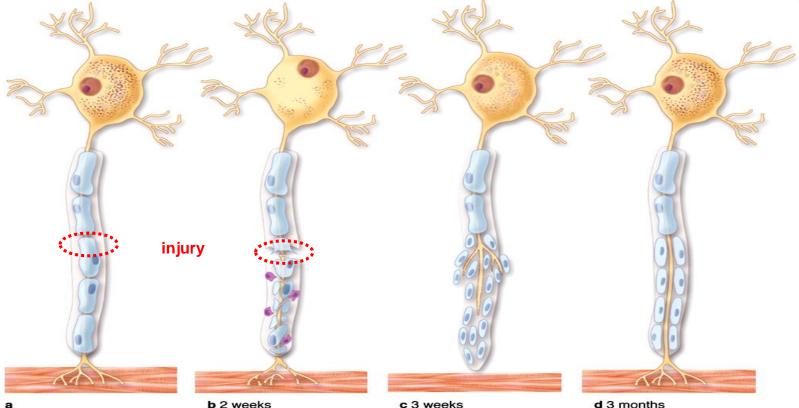
# Autonomic ganglion



## **Nerve tissue regeneration - PNS**

#### Axons and dendrites may be repaired if:

- Neuron cell body remains intact
- Schwann cels remains active and form tube •
- Scar tissue does not form too rapidly •



b 2 weeks

Breakdown of axon Breakdown of myelin sheath c 3 weeks

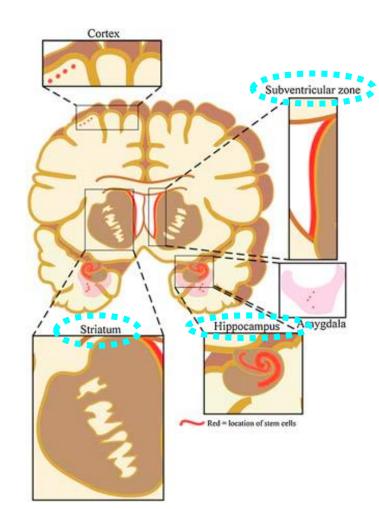
Schwann cells divide Axon begins to grow (1.5 mm/day) Navigaion by Schwann cells Collaterals will die

## **Nerve tissue regeneration - CNS**

Stem / progenitor cells resiging in some areas of adult brain

#### Life-long plasticity of CNS

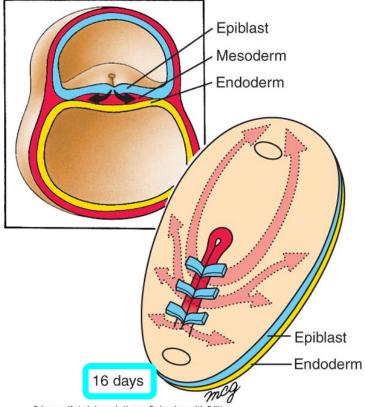
- Sprouting new dendrites
- Synthesis of new proteins
- Changes of synaptic contacts



#### **Nerve tissue – Ectoderm**

#### Gastrulation

Formation of the three germ layers



- <u>Mesoderm</u>: middle layer, generates most of the **muscle, blood** and **connective tissues** of the body and placenta.
- Endoderm: eventually most interior of embryo, generates the **epithelial lining** and associated **glands** of the **gut**, **lung**, and **urogenital tracts.**

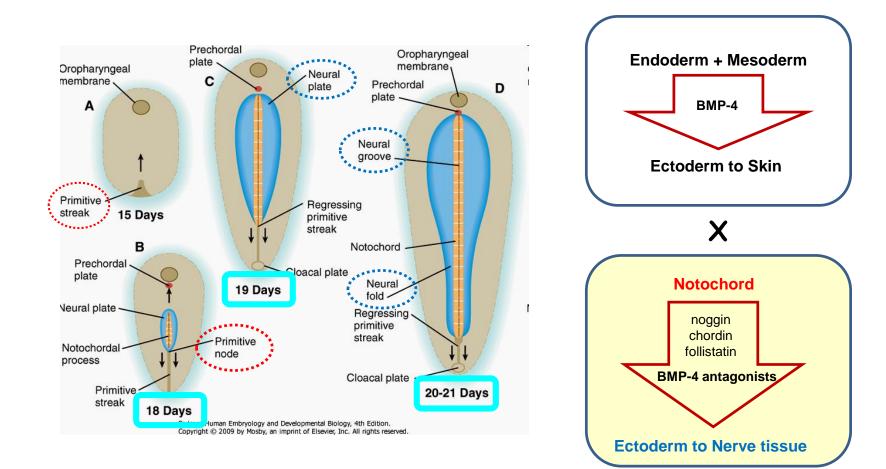
Schoenwolf et al: Larsen's Human Embryology, 4th Edition. Copyright  $\odot$  2008 by Churchill Livingstone, an imprint of Elsevier, Inc. All rights reserved

Ectoderm: outside, surrounds other layers later in development, generates skin and nervous tissue.

### **Nerve tissue – Neural plate**

#### **Neural Induction**

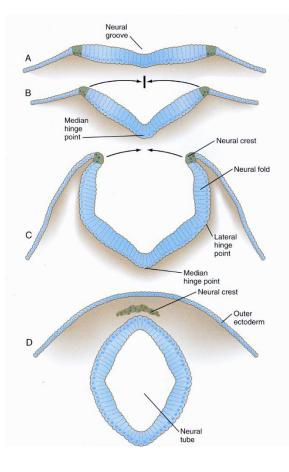
In addition to patterning the forming mesoderm, the primitive node also sets up the neural plate



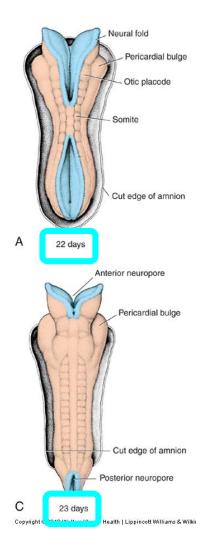
### **Nerve tissue – Neural tube**

#### Neurulation

Folding and closure of the neural plate



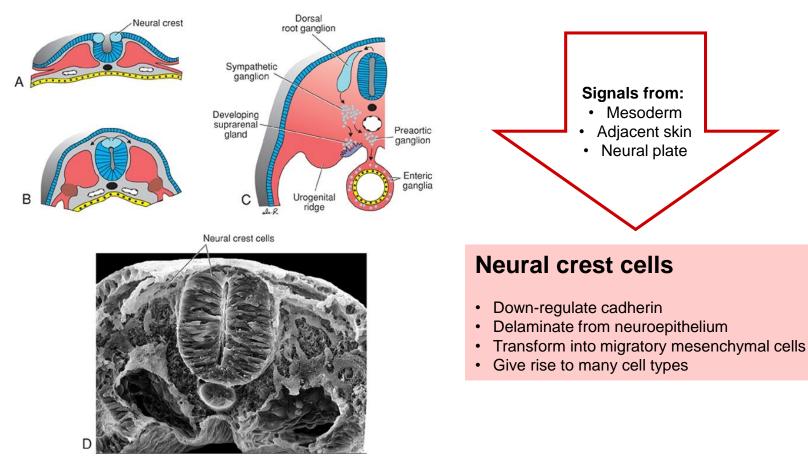
- neural folds close
- neural crest delaminates and migrates away
- closure happens first in middle of the tube and then zips rostrally and caudally
- anterior neuropore closes around day 25
- posterior neuropore closes around day 28



#### **Nerve tissue – Neural crest**

#### **Neural crest**

the "4th germ layer"



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### **Nerve tissue – Neural crest derivates**

#### **Neuroblasts**

- **psedounipolar** neurons of spinal ganglia
- multipolar neurons of autonomic ganglia
- chromaffin cells of the adrenal medulla

#### **Spongioblasts**

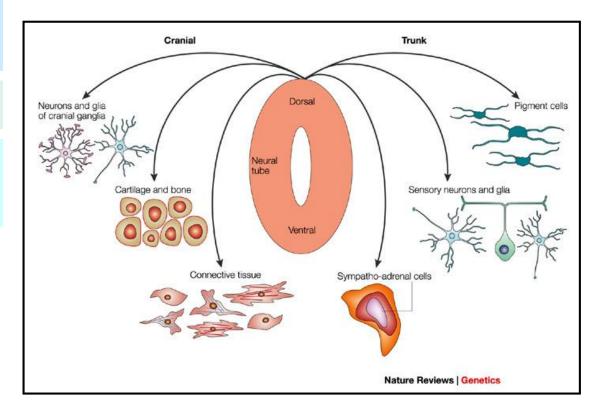
- Schwann cells
- satellite cells

#### **Melanocytes**

•migrate to the epidermis

#### Ectomesenchymocytes

- migrate into the branchial arches
- replace the mesenchyme of mesodermal origin



hb

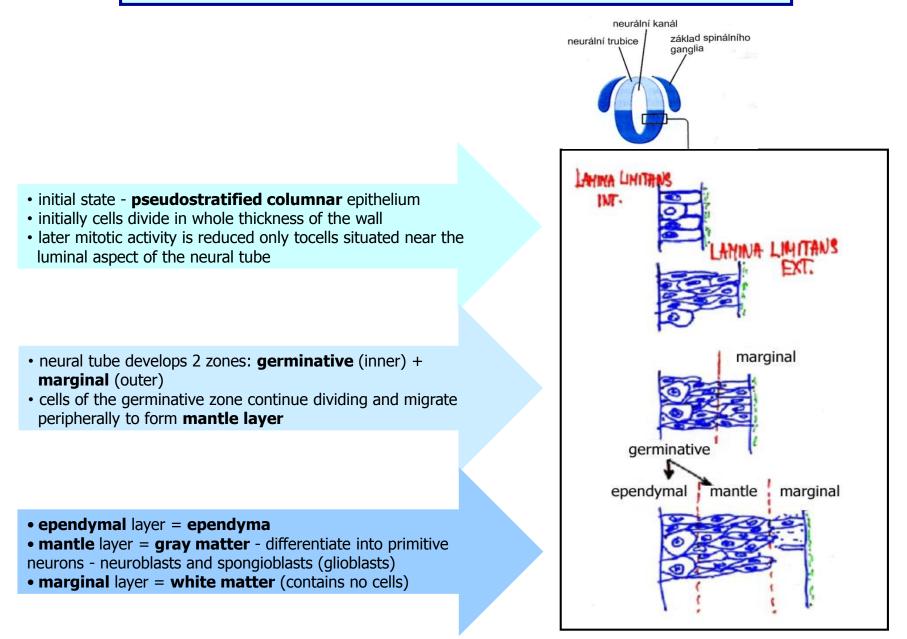
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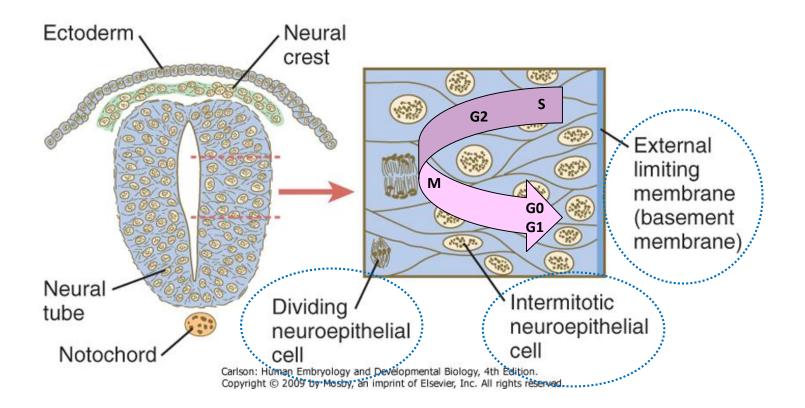
## **Nerve tissue – Histogenesis of neural tube**



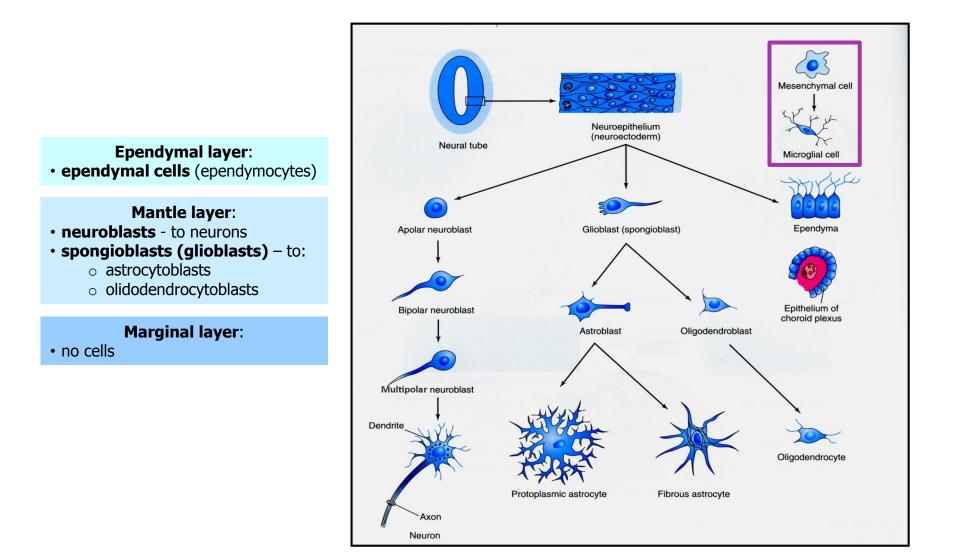
#### **Nerve tissue – Neural tube**

The early neural tube is a pseudostratified epithelium

- The "apical" portion abuts the central canal
- The **"basal" portion** abuts the **surrounding tissue** (e.g. somites, notochord, etc.).
- Cell division occurs in the apical portion.



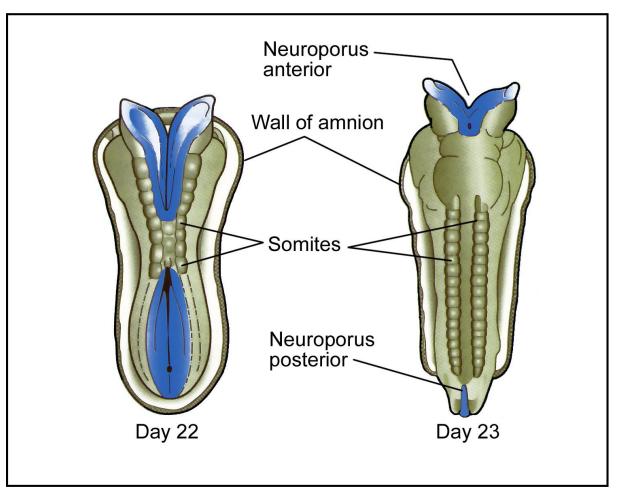
### **Nerve tissue – Neural tube – Cell differentiation**



## **Nerve tissue – Morphogenesis**

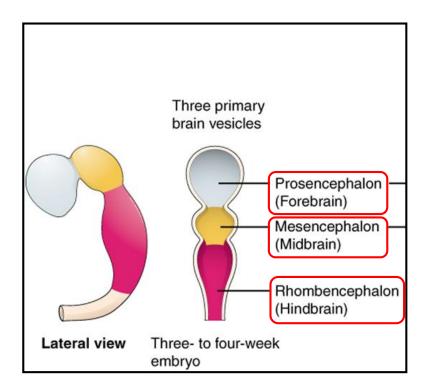
**Brain** – develops from the proximal segment of the neural tube that is broadened from the very beginning

**Spinal cord** – develops from the narrower caudal segment of the neural tube



Brain develops from the cranial part of the neural tube at 4th week - 3 primary brain vesicles

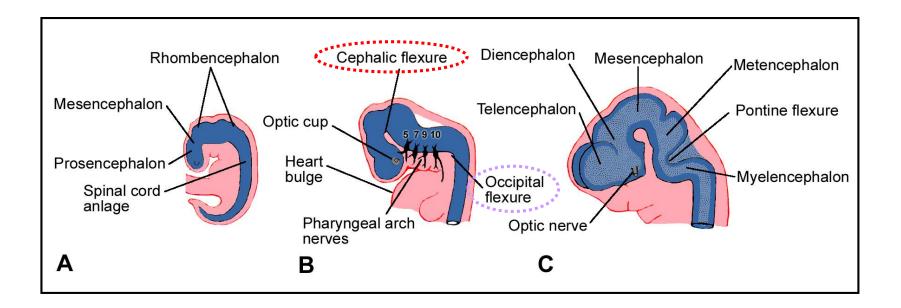
Forebrain - prosencephalon
Midbrain - mesencephalon
Hindbrain - rhombencephalon



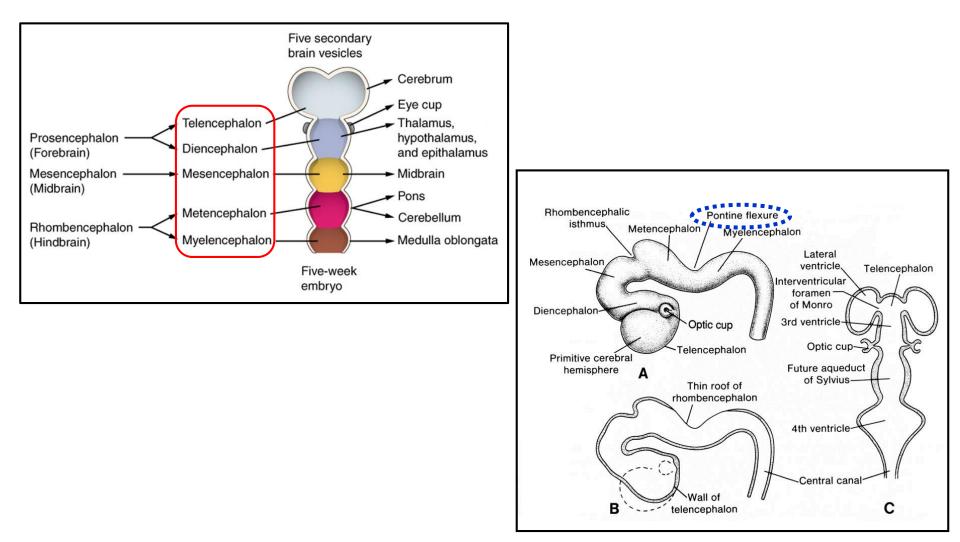
#### vesicles are not followed each to other linearly, but are bent in the sagittal plane

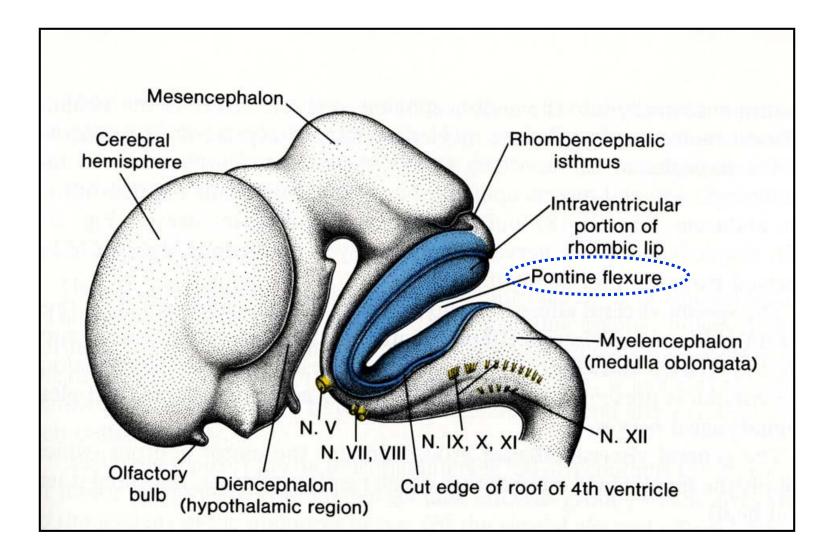
#### **Cephalic flexure** - permanent

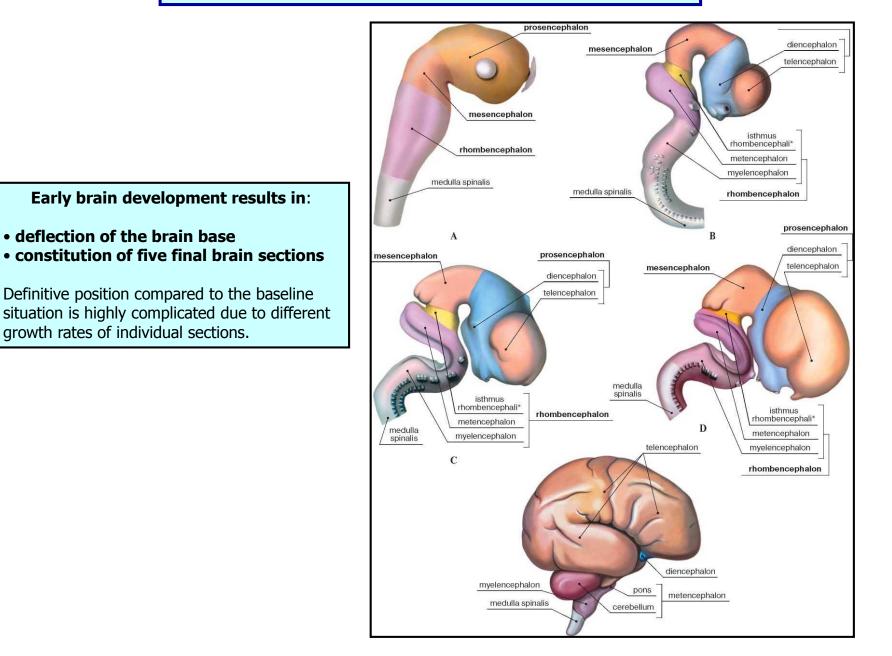
Occipital (cervical) flexure - after 2 months it is on straightening, so is not evident in the adulthood



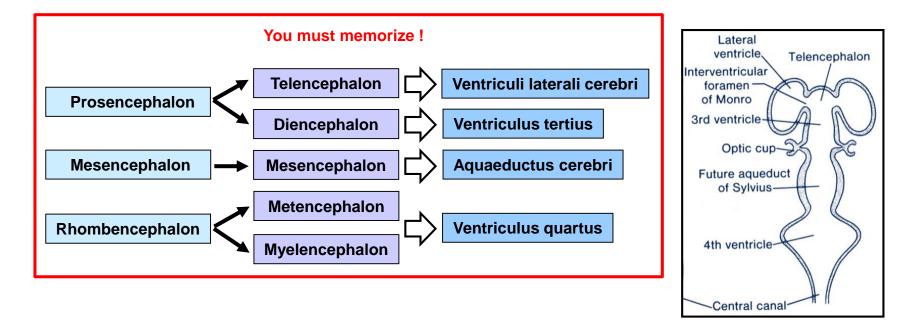
- 5th week
- 5 secondary vesicles
- · Pontine flexure remains to adulthood

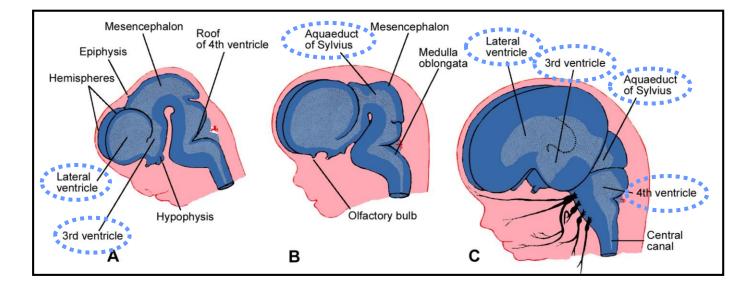






### **Nerve tissue – Brain development - Ventricles**



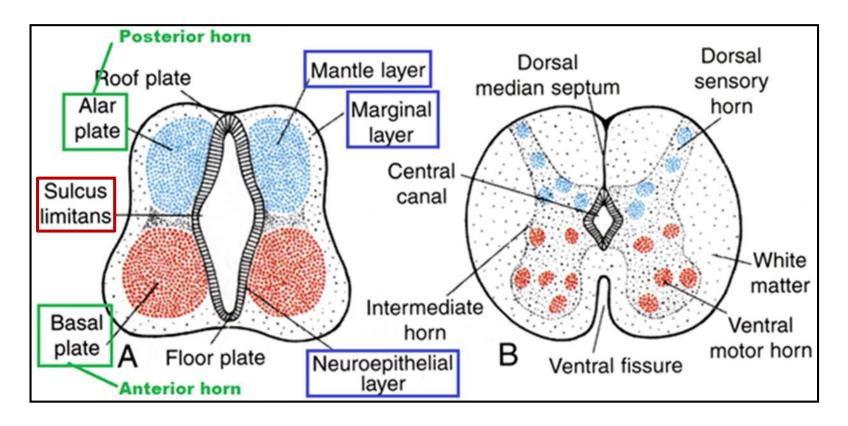


## **Nerve tissue – Spinal cord development**

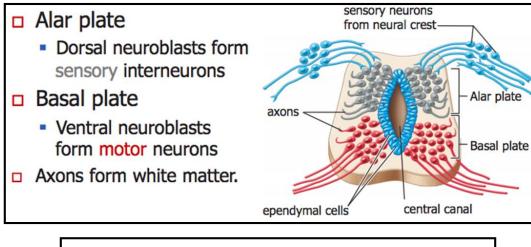
• it develops from the caudal part of neural tube

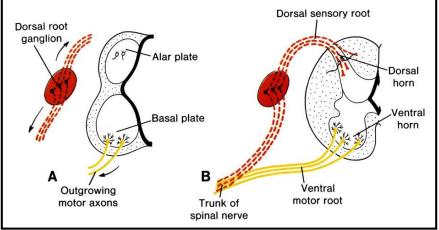
• cells of mantle layer proliferate and produce 2 sheets - the dorsal **alar plate** and ventral **basal plate**, which are separated by longitudinal groove called the **sulcus limitans** 

To remember:
alar plate - gives rise to dorsal horn
basal plate - gives rise to ventral horn



### **Nerve tissue – Spinal cord development**





Axons of neuroblasts of anterior horns unite with peripheral processes of corresponding spinal ganglia neuroblasts and together leave the spinal canal as a trunk of **spinal nerve**.

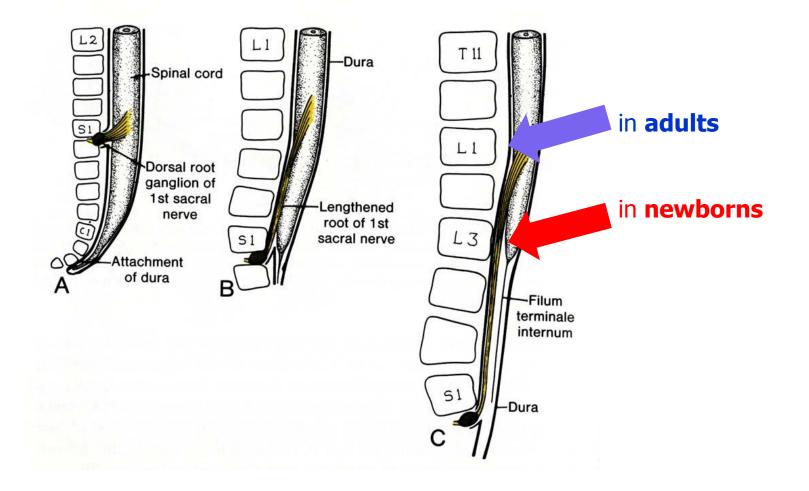
## **Nerve tissue – Spinal cord development**

#### Positional changes of the spinal cord

•initially, length of spinal cord correlates with length of the vertebral canal

•during further development, the vertebral canal grows more rapidly than spinal cord so that its caudal end gradually comes to lie at relatively higher levels of the canal

•in adults, it usually terminates at the inferior border of the first lumbar vertebra



# Thank you for your attention !

Questions and comments at: ahampl@med.muni.cz