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

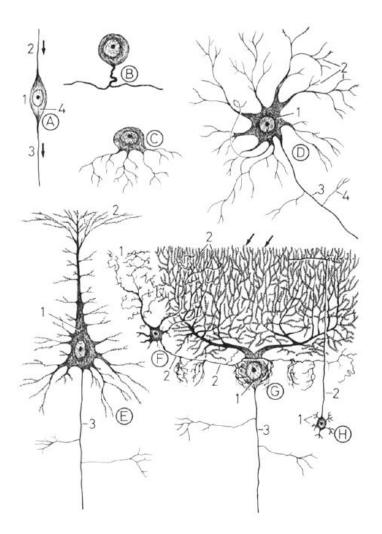
The connective tissue

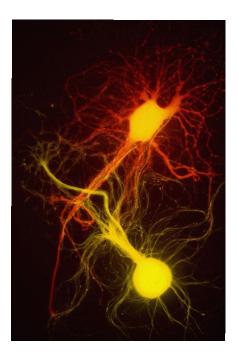
- provides protection of both previous components is organized into:
- meninges envelope the brain and spinal medulla
- epi-, peri- and endoneurium connective tissue within nerves or on their surfaces
- thin capsules surround the cerebrospinal and autonomic ganglia

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)

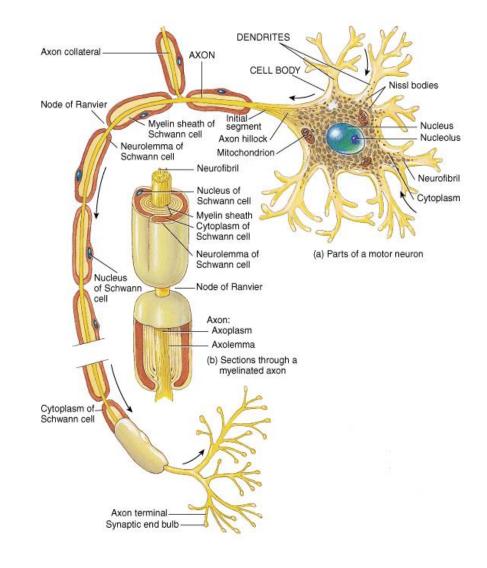
- axon

(always only one; centrifugal conduction)

- dendrit(es)

(centripetal conduction)

Neuron



Position:

CNS – grey matter PNS – ganglia

Shape:

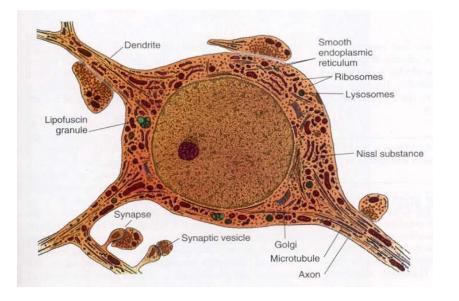
pyramidal, shpherical, ovoid, peer-shaped

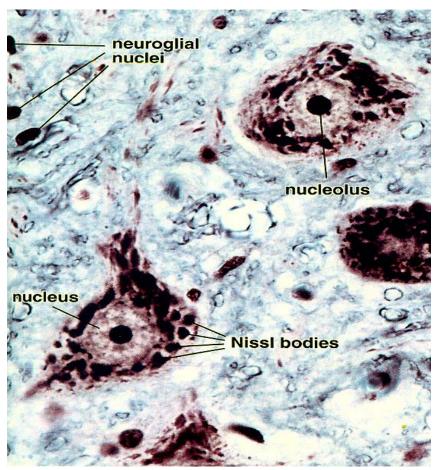
Size:

5 to 150 μm

Organelles:

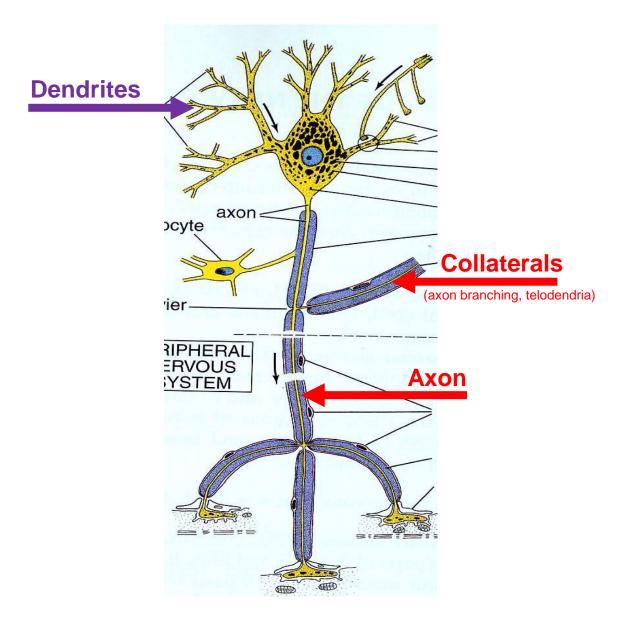
- Nuclues large + pale + prominent nucleoli
- Nissl substance rough ER
- Neurofibrils (neurofilaments + neurotubules + actin)
- Lipofuscin pigment clumps





Neuron - Perikaryon

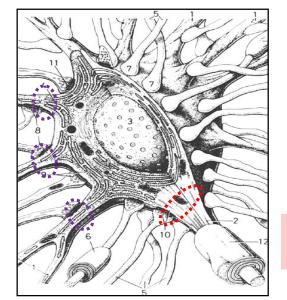
Neuron – Neurites / Processes



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

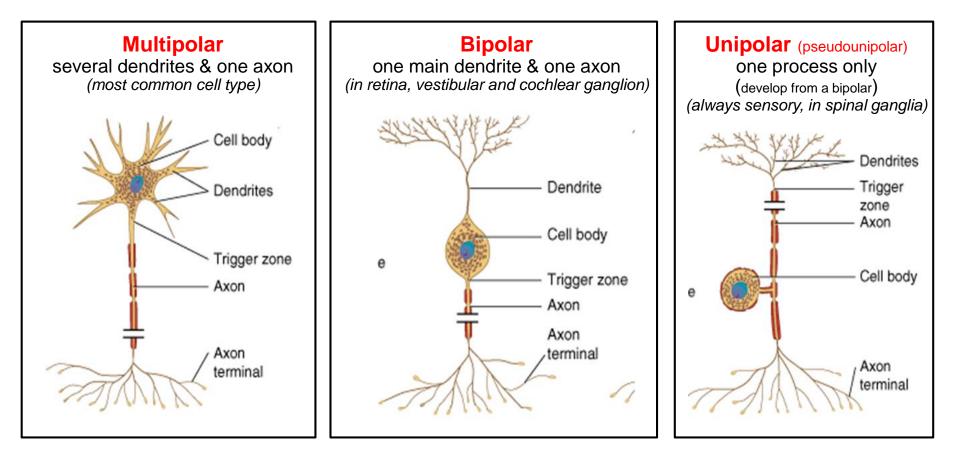


Axon (nerve fiber)

- 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

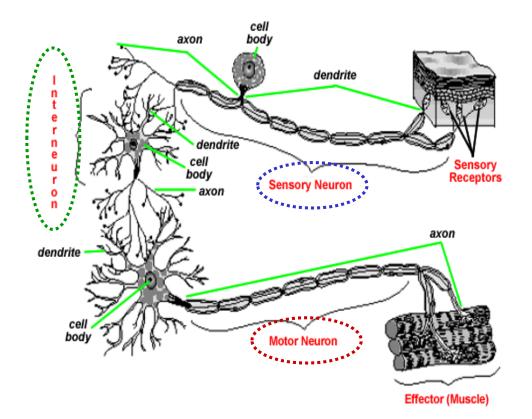
White matter: areas of myelinated axons Gray matter: areas of unmyelinated axons, cell bodies, and dendrites **Neuron – Classification 1**

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

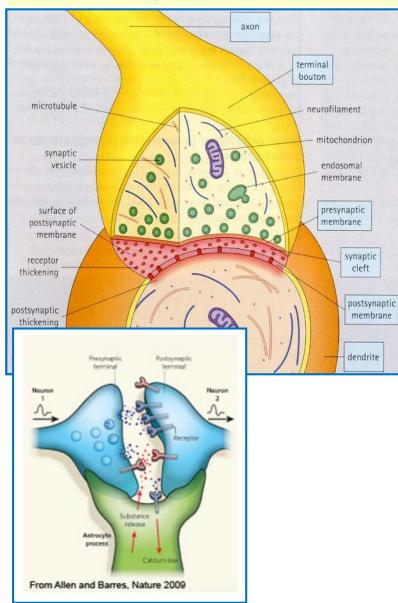
Interneurons:

local circuit neurons



Definition

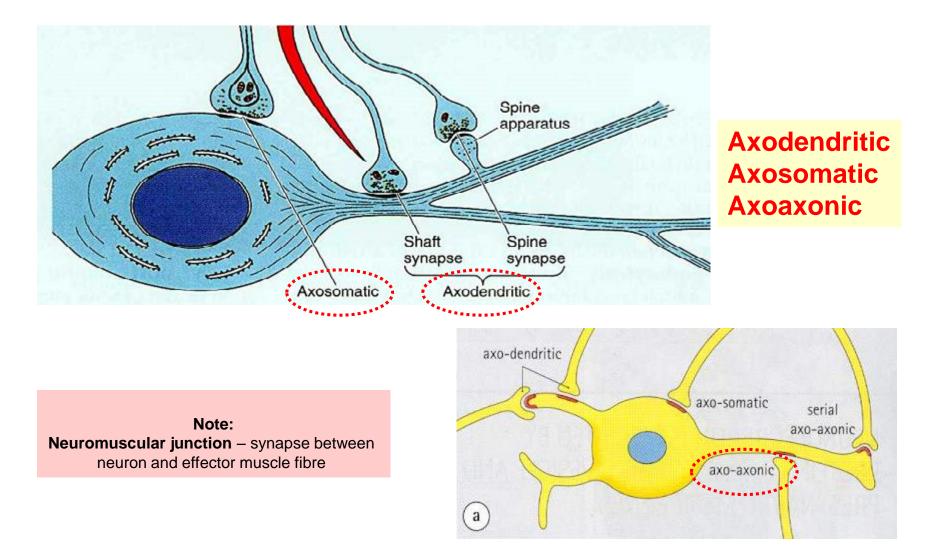
Synapses are highly specialized intercellular junctions, which link the neurons of each nervous pathway



- · 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

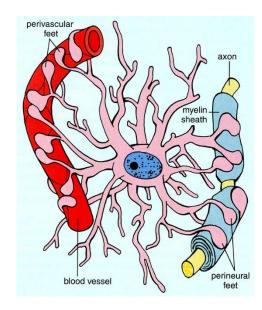
- Schwann cels
- Satellite cells

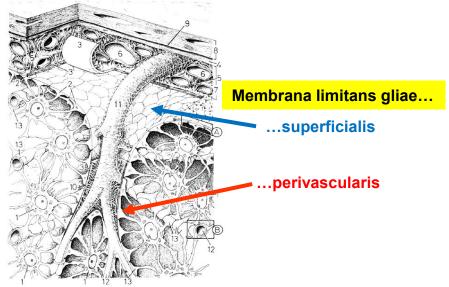
Neuroglia - Astrocytes

- 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:

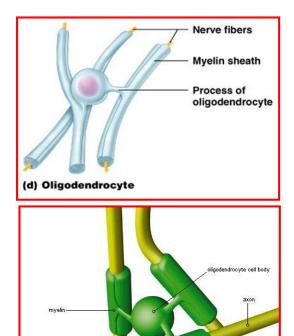
- ✓ form a supportive framework of nervous tissue
- have extensions (perivascular feet) that contact blood capillaries that stimulate them to form a tight seal called the blood-brain barrier
- convert blood glucose to lactate and supply this to the neurons for nourishment
- nerve growth factors secreted 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

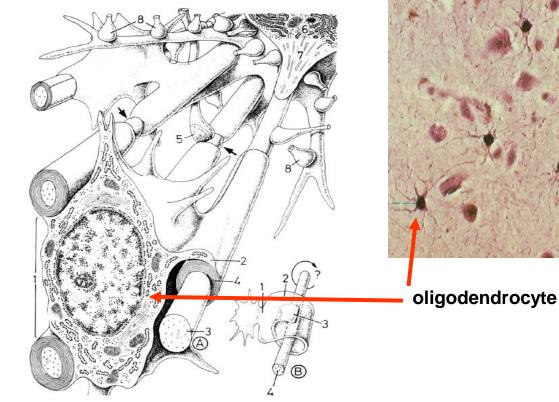




Neuroglia - Oligodendrocytes

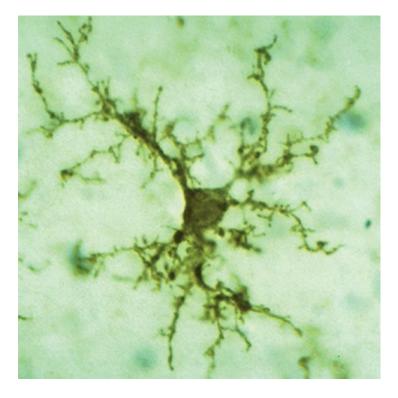
- ✓ smaller than astrocytes; darker, round nucleus, abundant RER, well developed golgi apparatus
- ✓ form myelin sheaths in CNS
- \checkmark one cell serves more then one axon
- cannot migrate around axons (unlike Schwann cells) must push newer layers of myelin under the older ones so myelination spirals 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

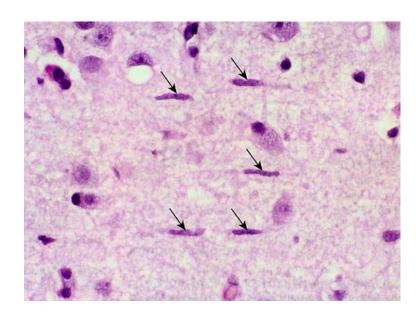




Neuroglia - Microglia

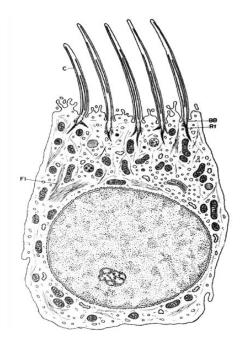
- ✓ smallest neuroglial cell
- ✓ small, dark, elongated nuclei
- ✓ possess **phagocytotic** properties
- ✓ when activated antigen presenting cell
- ✓ originate in bone marrow (**mesodermal** origin)

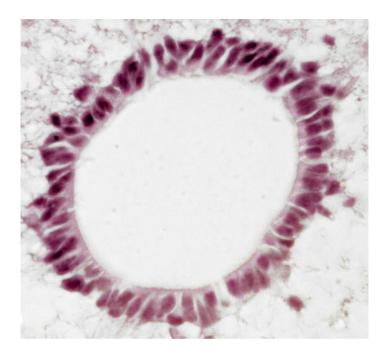




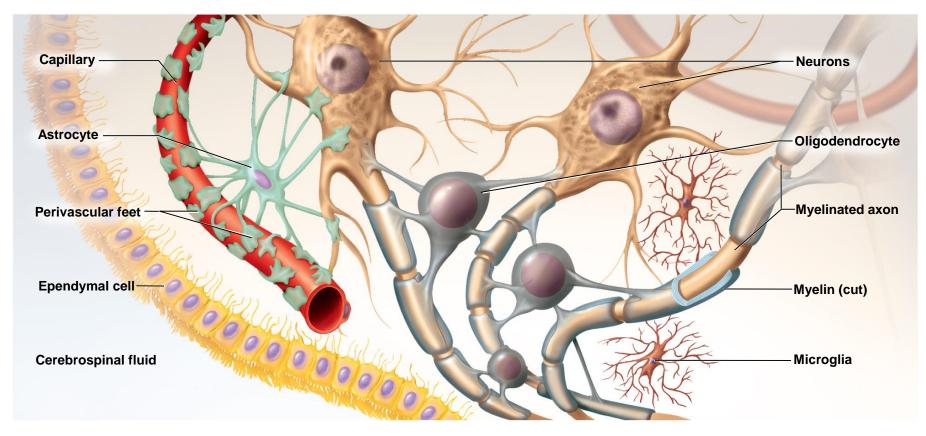
Neuroglia – Ependymal cells

- ✓ 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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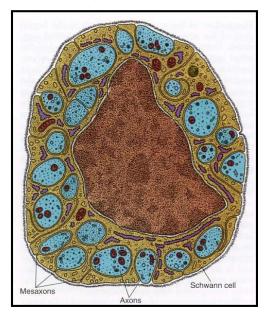
Neuroglia in PNS – Schwann cells

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

X

Small diameter axons

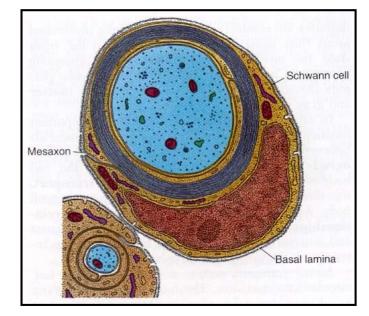
Enveloping by only cytoplasm



only Schwann sheath – gray nerve fiber

Large diameter axons

Wrapping by myelin sheaths

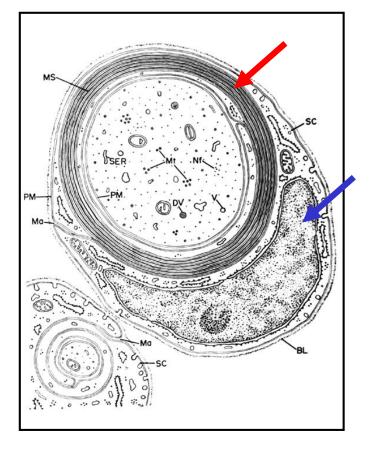


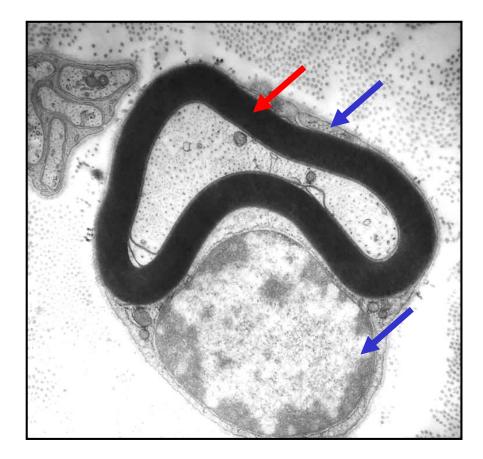
Schwann + myelin sheath – double contoured nerve fiber

Neuroglia in PNS – Schwann cells

Double contoured nerve fiber

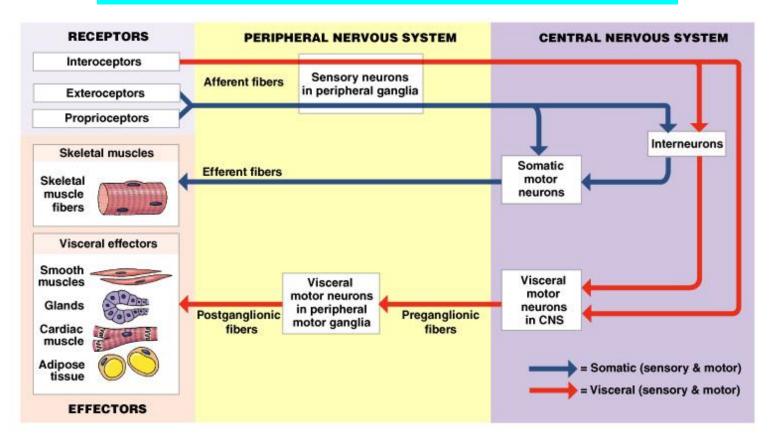




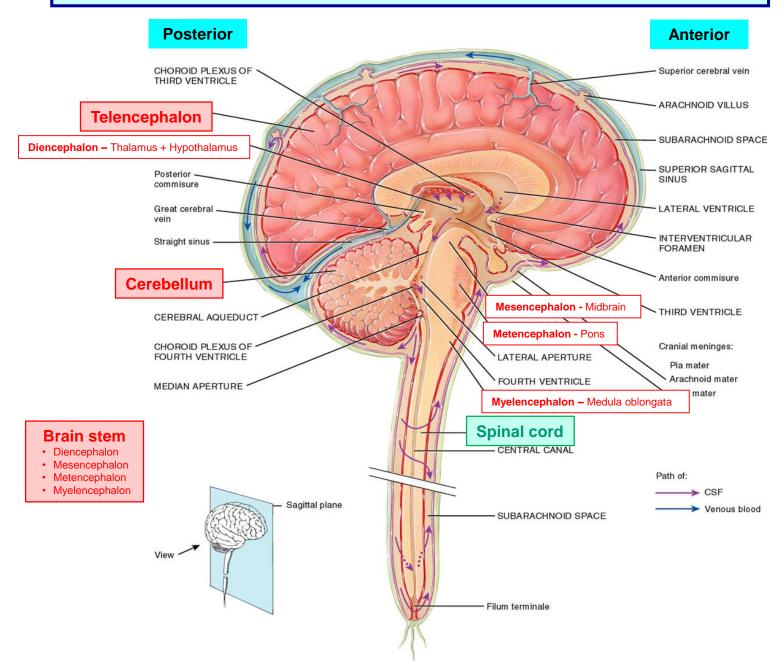


Nervous system – Peripheral x Central

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

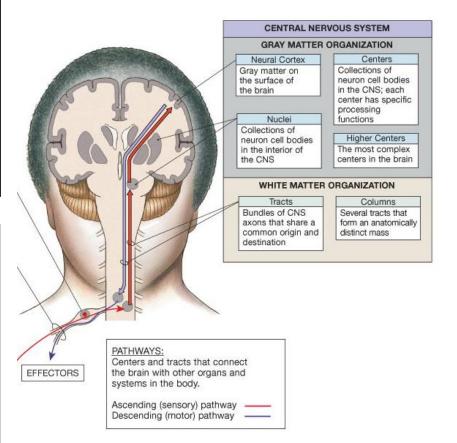
- Myelinated axons of nerve cells
- Neuroglia (oligodendrocytes, fibrilar astrocytes)
- Blood capillaries (lesser density than in the gray matter)

Brain

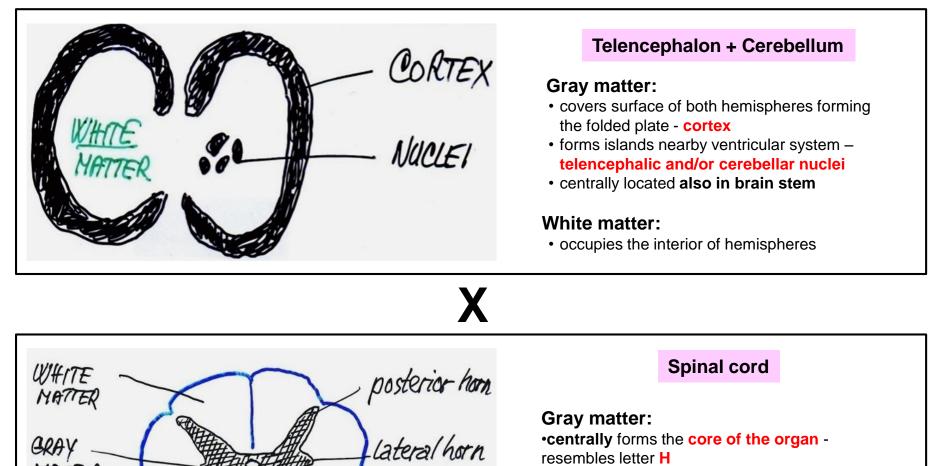
axons are bundled together to form white matter tracts
conduct nerve impulses from gray region to gray region
three types of tracts (commisural, association, projection)

Spinal cord

- sensory and motor tracts (ascending and descending)



Central nervous system – Distribution of grey/white matter



anterior

hom

GRAY

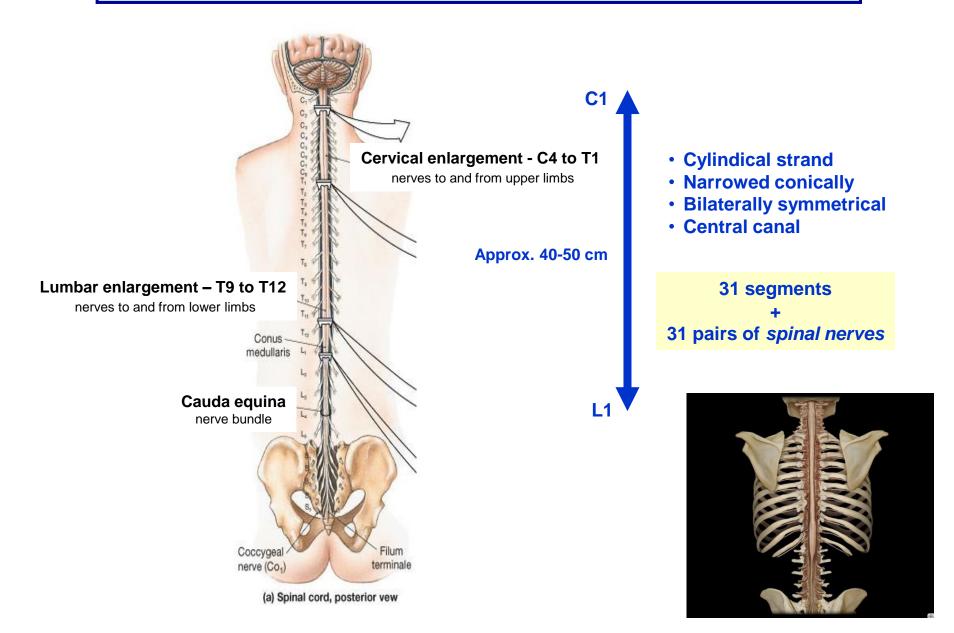
NATTER

Gray matter:

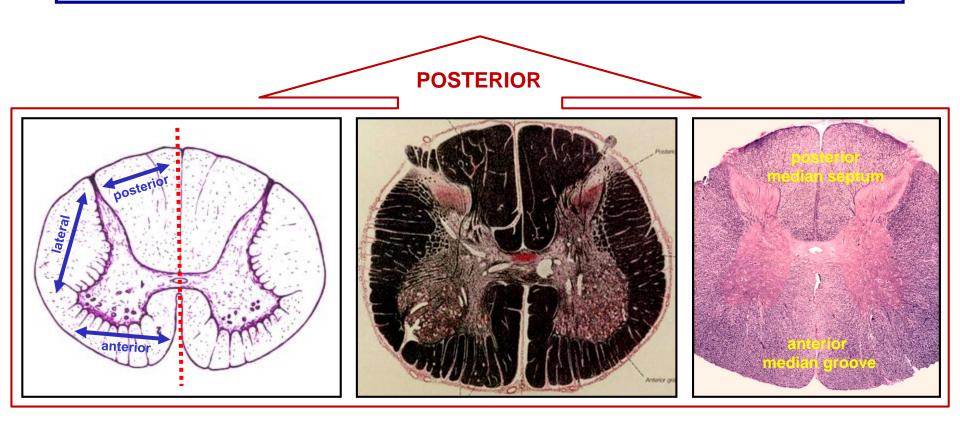
•centrally forms the core of the organ resembles letter H •at the periphery it is surrounded by funiculi of

the white matter

Central nervous system – Spinal cord - Anatomy



Central nervous system – Spinal cord – White matter



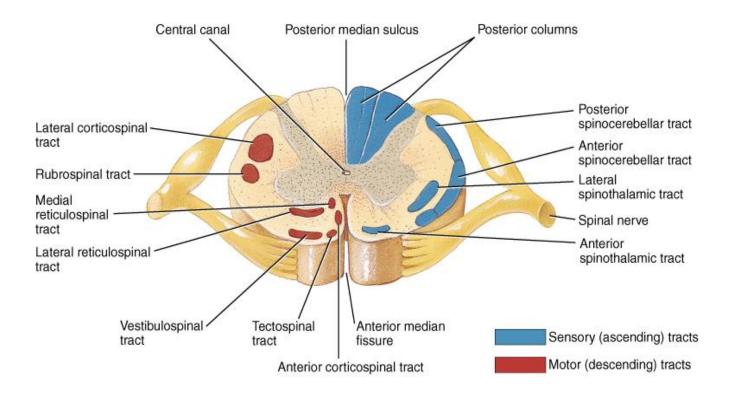
Fasciculi = Funiculi (= Collumns)

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

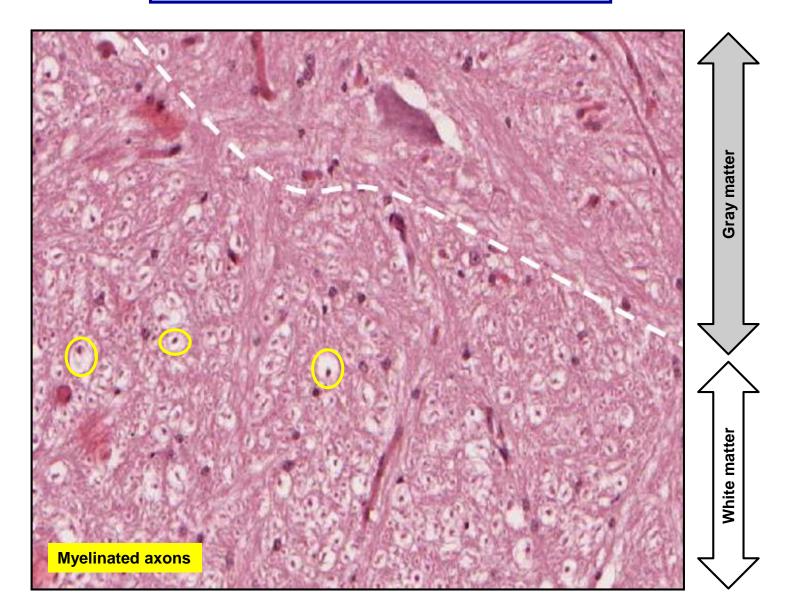
Sensitive = Ascending Motoric = Descending

Spinal cord – White matter - Tracts

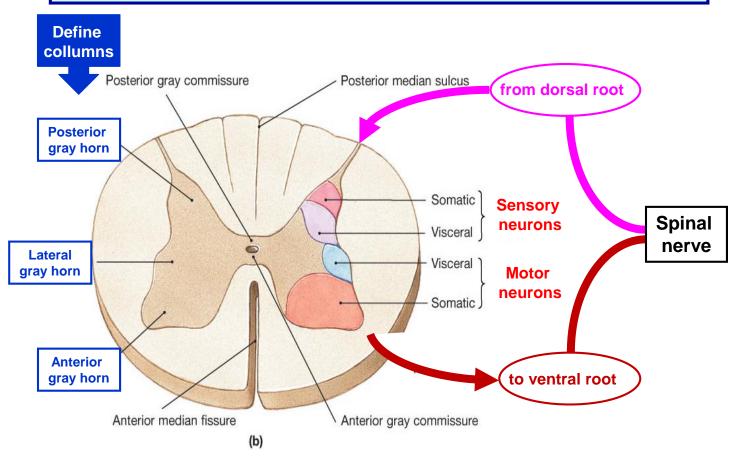
Only for demonstration purpose – no need of memorizing !!!



Spinal cord – White matter

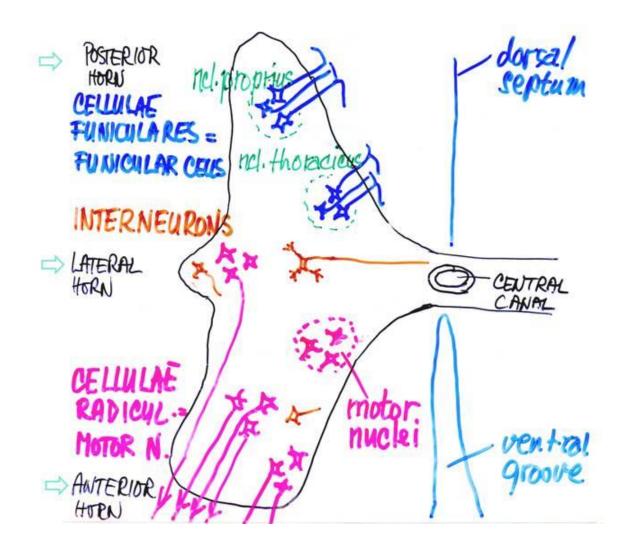


Spinal cord – Gray matter – Organization

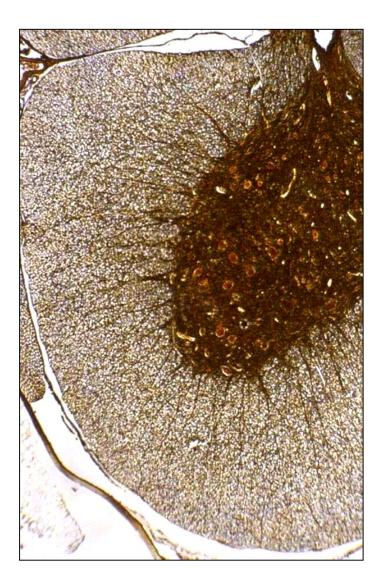


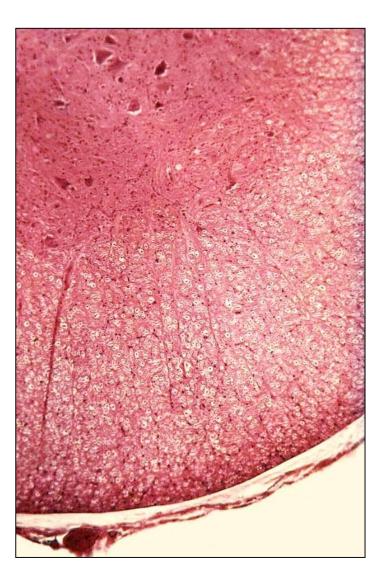
Neurons in gray matter – all are multipolar		
 Motor neurons (radicular) in the anterior (ventral) horns stellate shape, 150 μm in diameter send off long myelinated axons ending on muscle fibres 	 Funicular cells mainly in the posterior horns their axons enter the white matter and connect to other segments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

Spinal cord – Gray matter – Organization

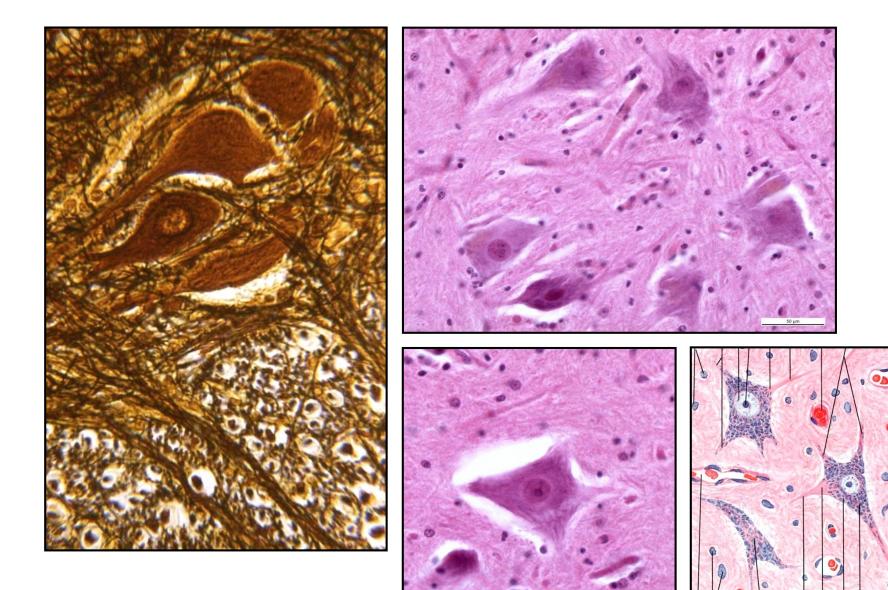


Spinal cord – Gray matter

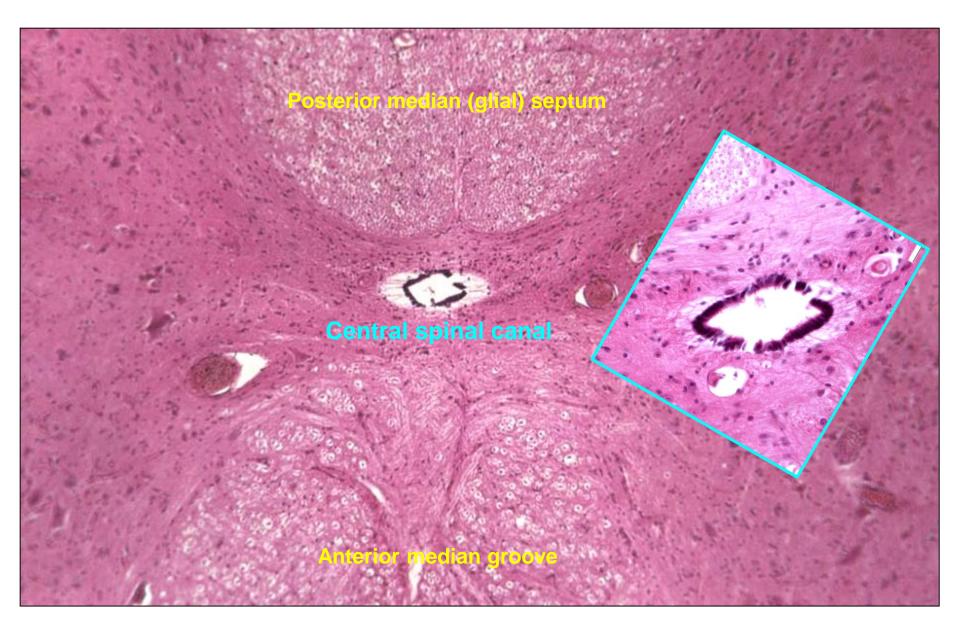




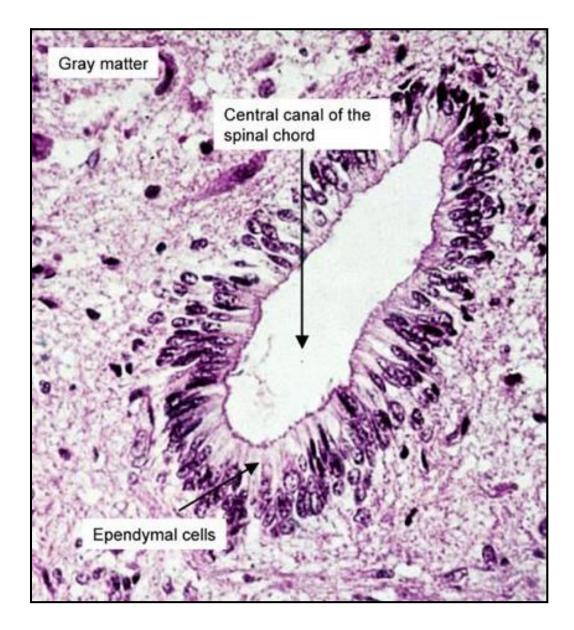
Spinal cord – Gray matter – Motor neurons



Spinal cord – Central spinal canal



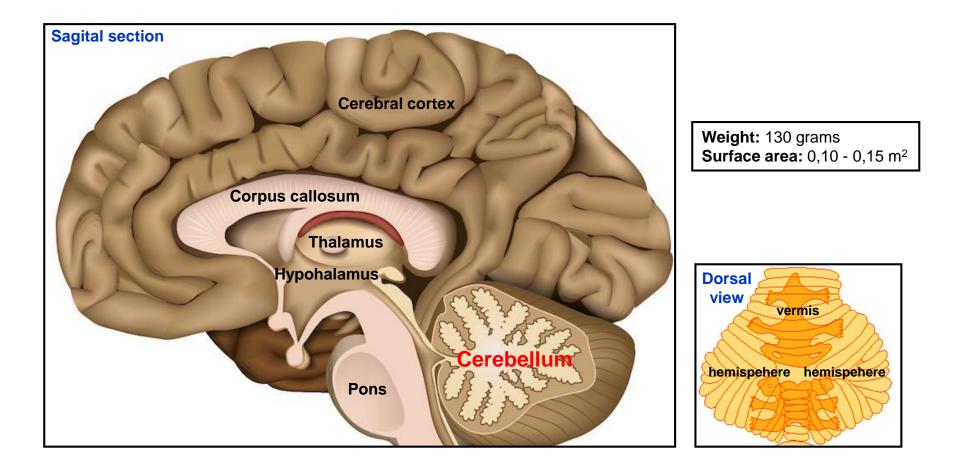
Spinal cord – Central spinal canal



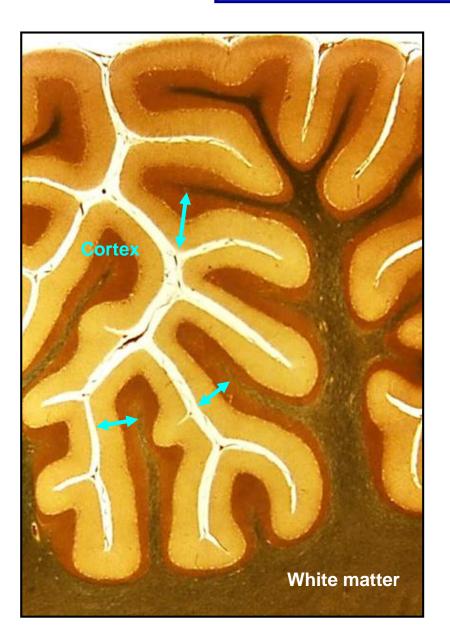


Function

•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

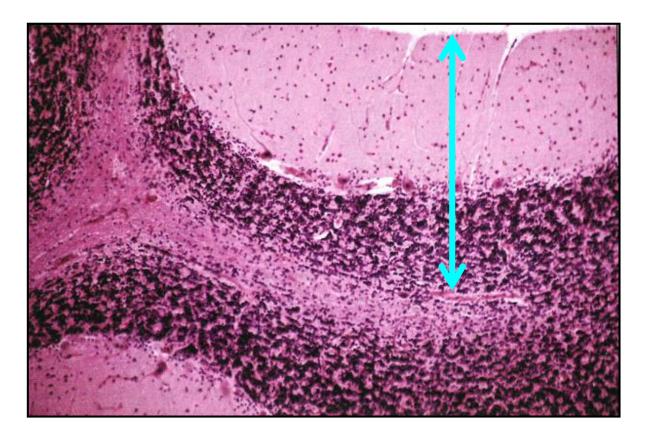
- Cortex at the surface (1 mm thick)
- Nuclei in white matter (nucleus dentatus, emboliformis, globusus, and fastigii)

Cerebellum – White matter



"Arbor vitae" – white matter

Cerebellum – Cortex



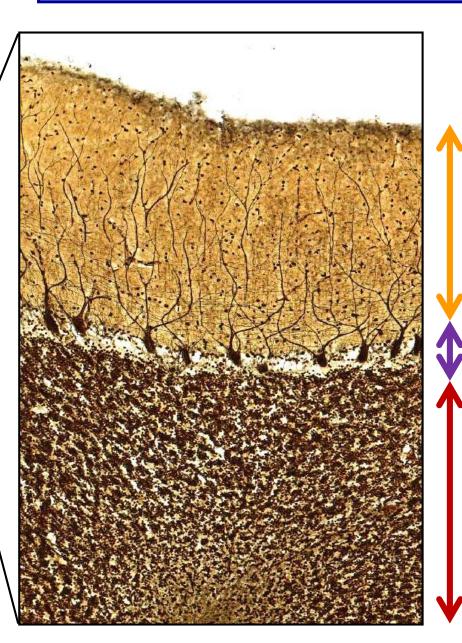
Molecular layer (stratum moleculare)

Purkinje cell layer (stratum gangliosum)

Granule cell layer (stratum granulosum)

Cerebellum – Cortex - Cells





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

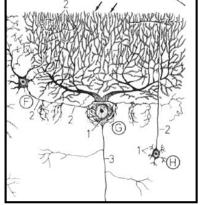
Purkinje cell layer (stratum gangliosum)

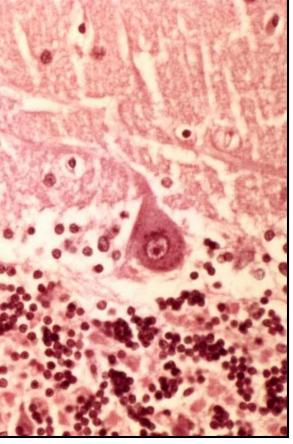
- Perikaryons of Purkinje cells
- Golgi (Bergman) glial cells

Granule cell layer (stratum granulosum)

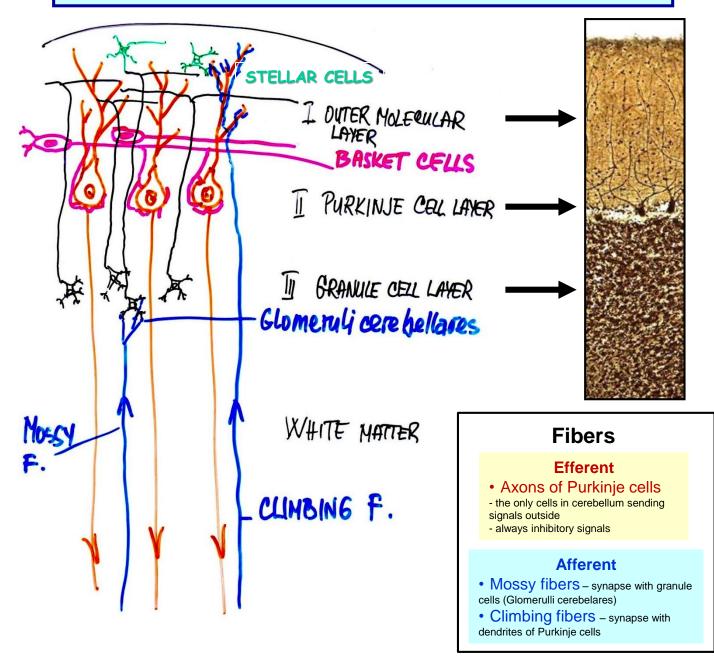
- Granule cells
- Golgi (Bergman) glial cells

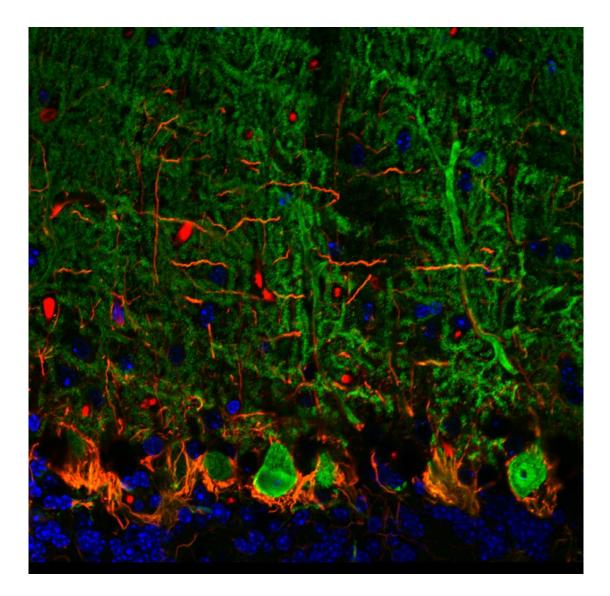


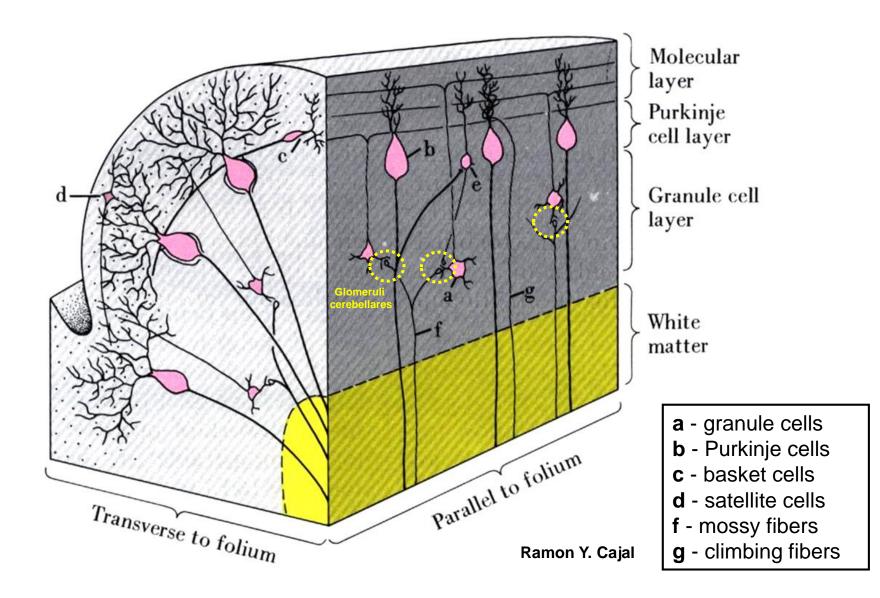


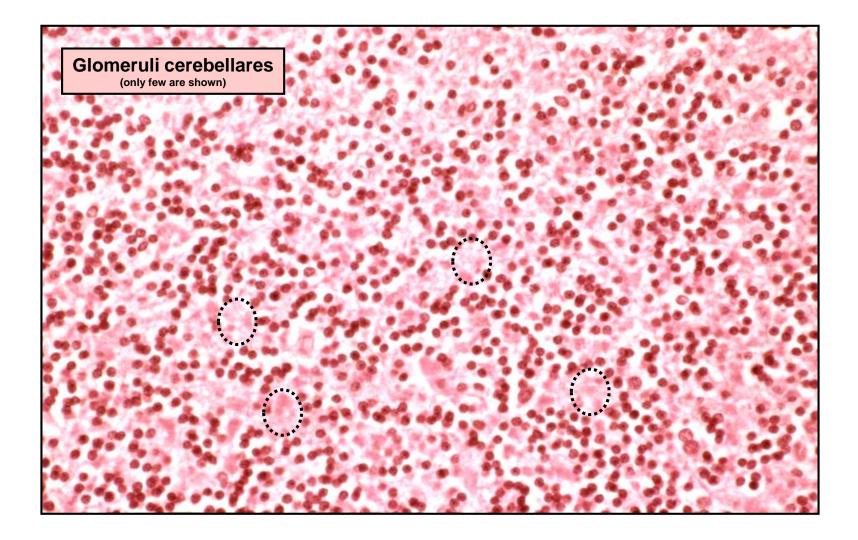




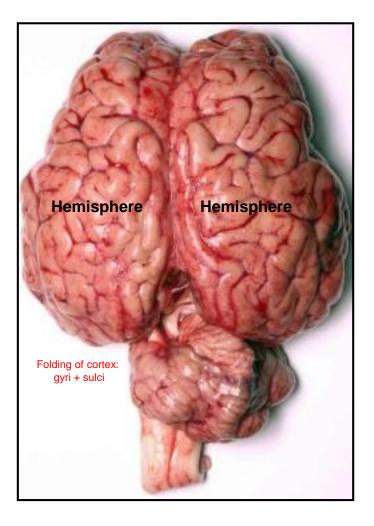








Telencephalon



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

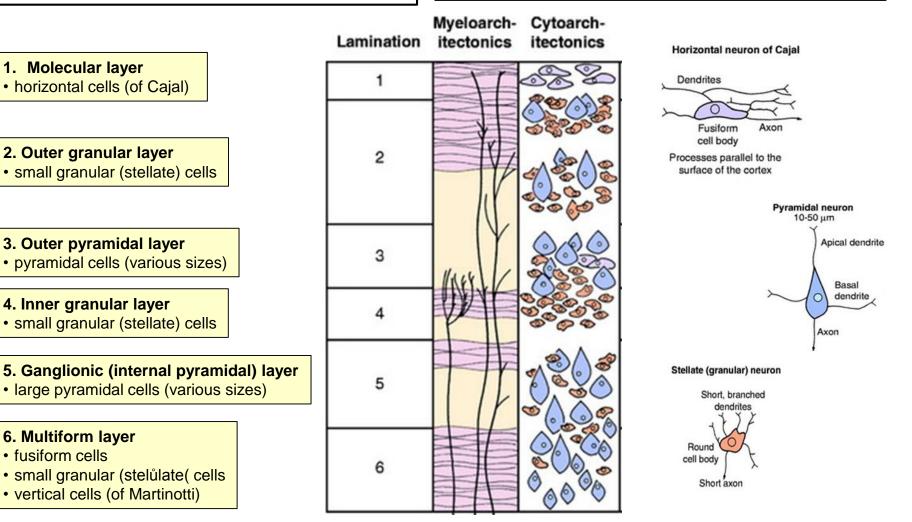
- efferent projecting neurons
- triangular perikaryon (different size)
- · axons with mvelin sheets

fusiform cells

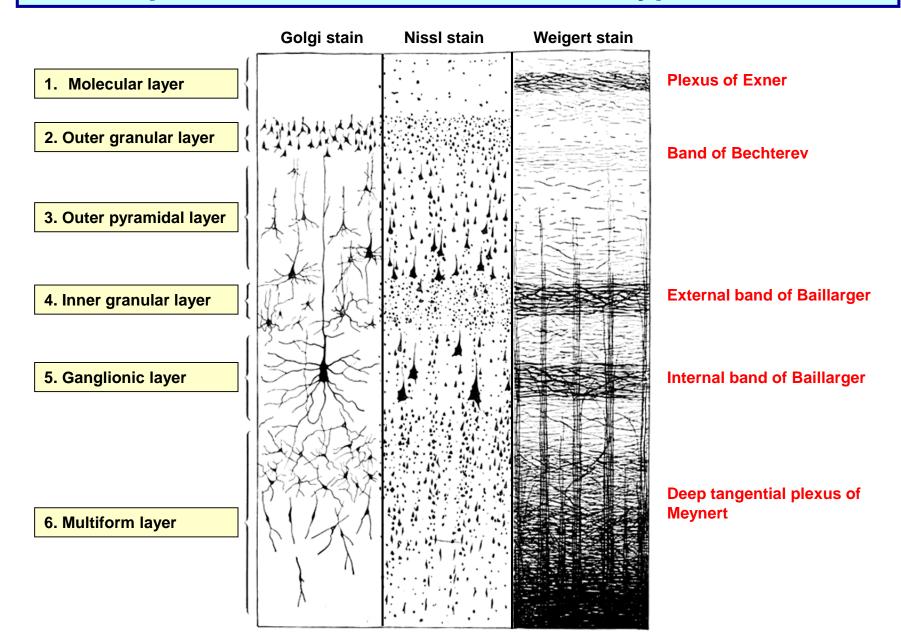
axons travel to different cortical layers and to subcortical areas

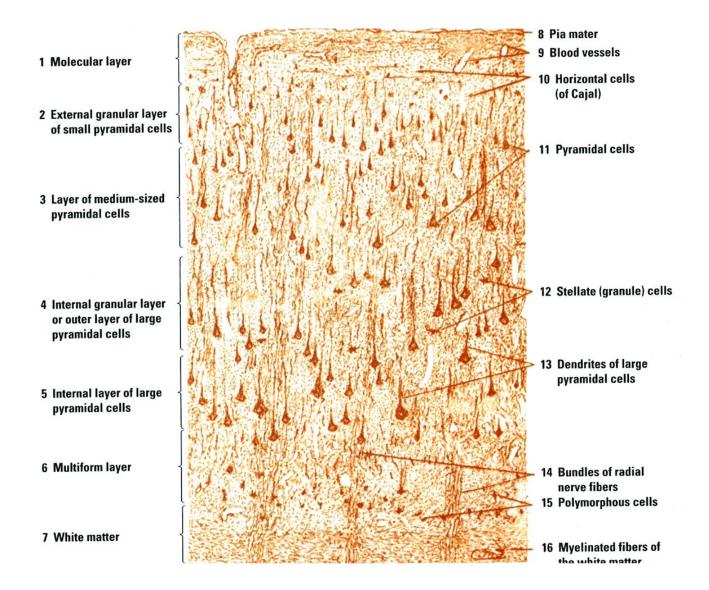
Non-pyramidal

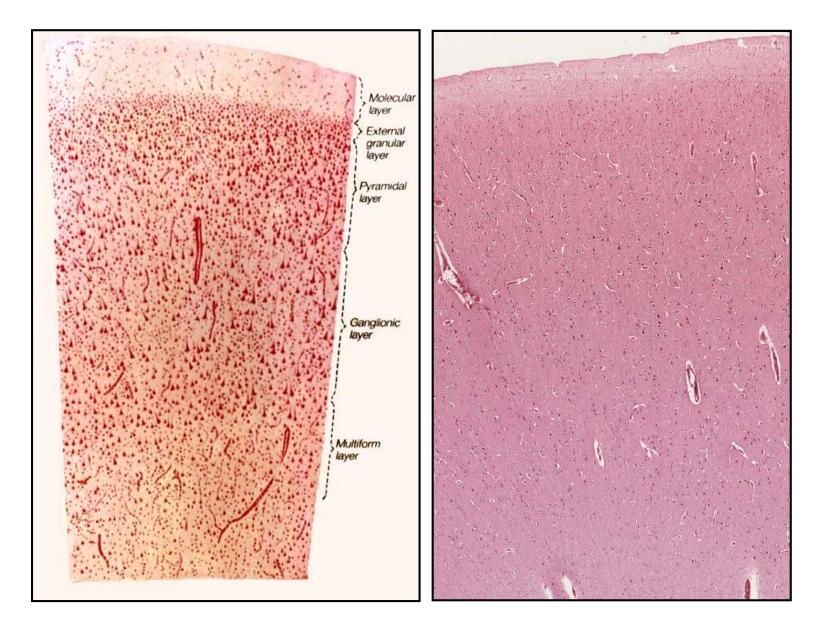
- · variety of different cells
- act as interneurons
- axons stay in the layer with their perikayons
- (e.g. fusiform cells, granule (stellate) cells, horizontal cells (Cajal), vertical cells (Matinotti)

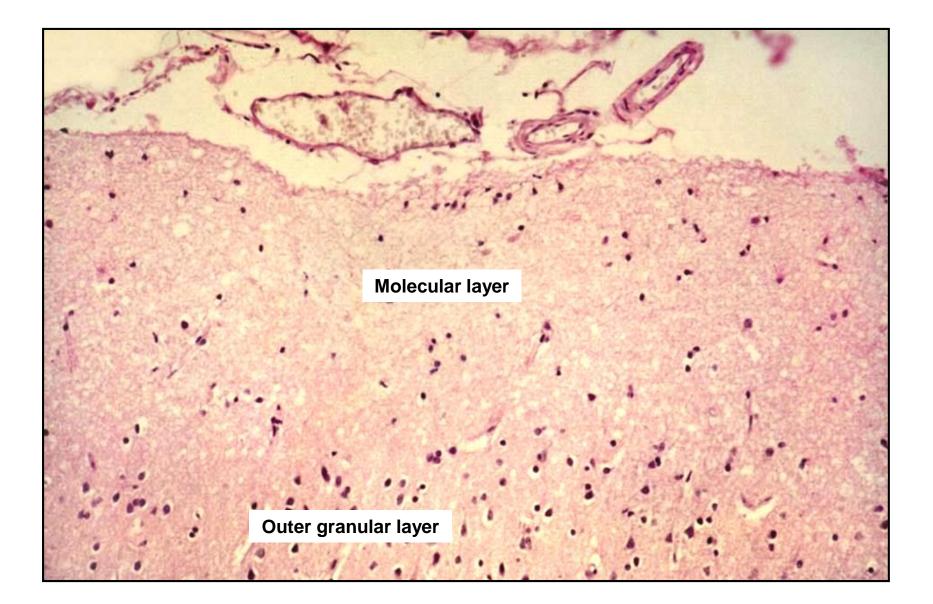


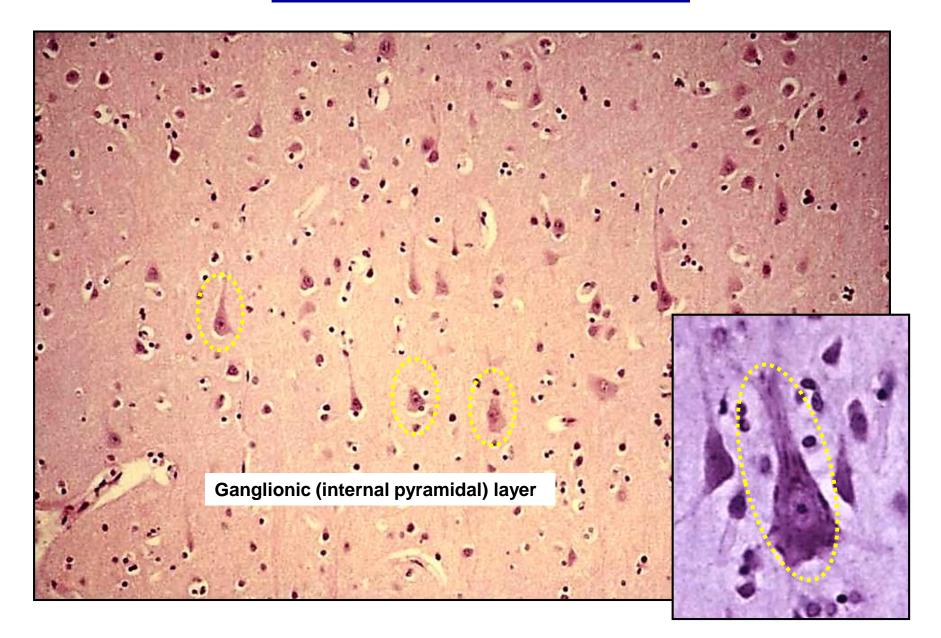
Telencephalon – Cerebral cortex – Cell types + Plexuses

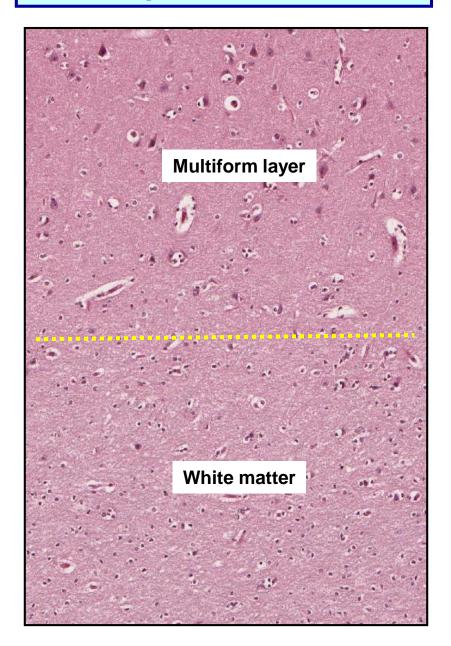


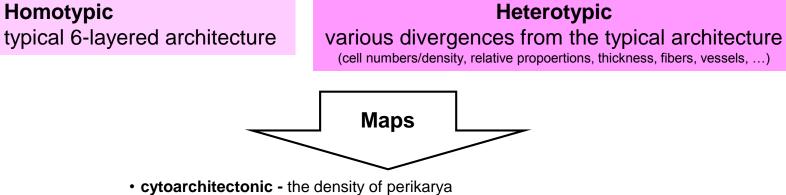




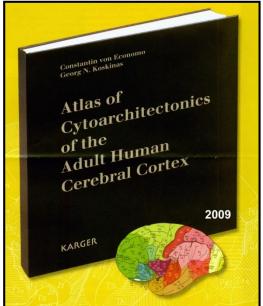


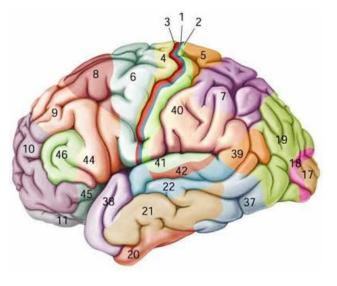






- myeloarchitectonic the density of myelinated fibers
- · glioarchitectonic the type and density of glial cells
- angioarchitectonic the density of blood capillaries or vascularization
- synaptoarchitectonic the density synapses in the isocortex

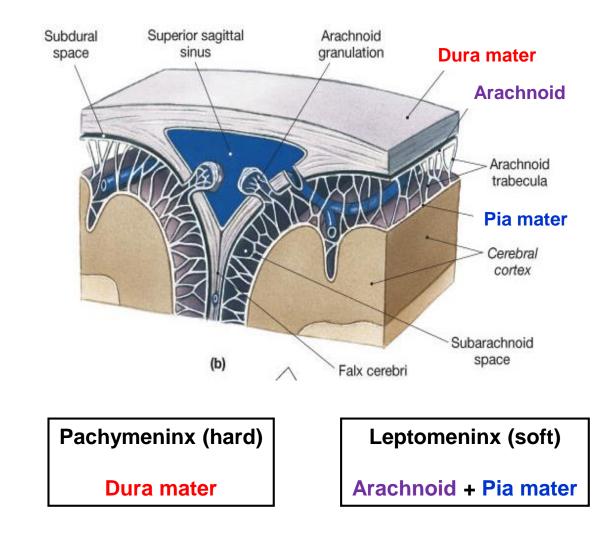




1909 - K. Brodman 11 regions and 52 areas

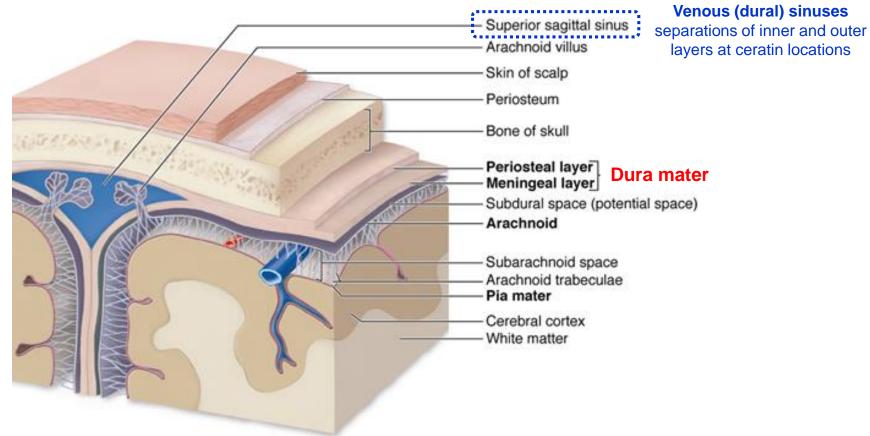


- membranes
- protect CNS + contribute to distribution of liquor
- cover both brain and spinal cord (are continuos)



Meninges – Dura mater

the outermost + robust (fibrous)



Cranial dura

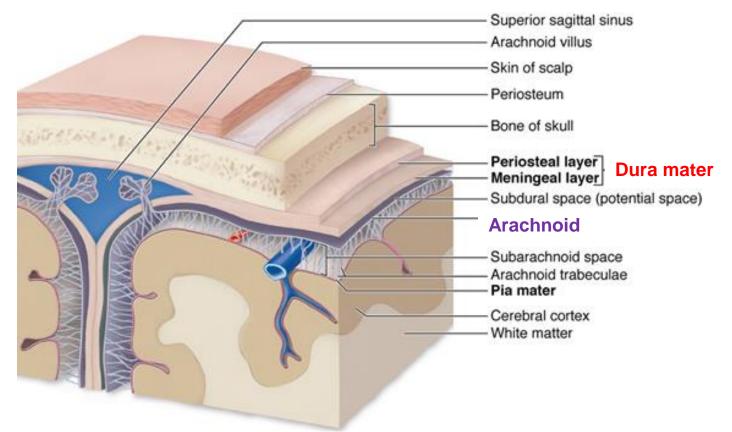
- Endosteal layer (periosteal; outer) adhering to the inner surface of the bones of the skull
- Meningeal layer (inner) thinner fibrous tissue membrane, inner surface covered by mesothelial cells

Spinal dura

- continuation of the inner layer of cranial dura

Meninges – Arachnoid

middle + spider web-like + avascular



Arachnoid

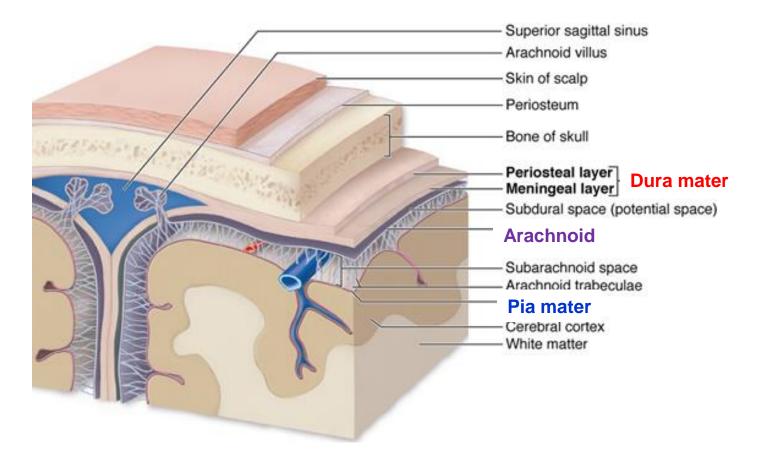
- Neurothel (*lamina neurothelialis*) adhering to the inner layer of dura mater, tight junctions barrier between CSF and blood in dura mater
- **Trabaculas** deligate fibere severed by flat (maningsel) cells
- Trabeculae delicate fibers covered by flat (meningeal) cells

Subarachnoid space

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

Meninges – Pia mater

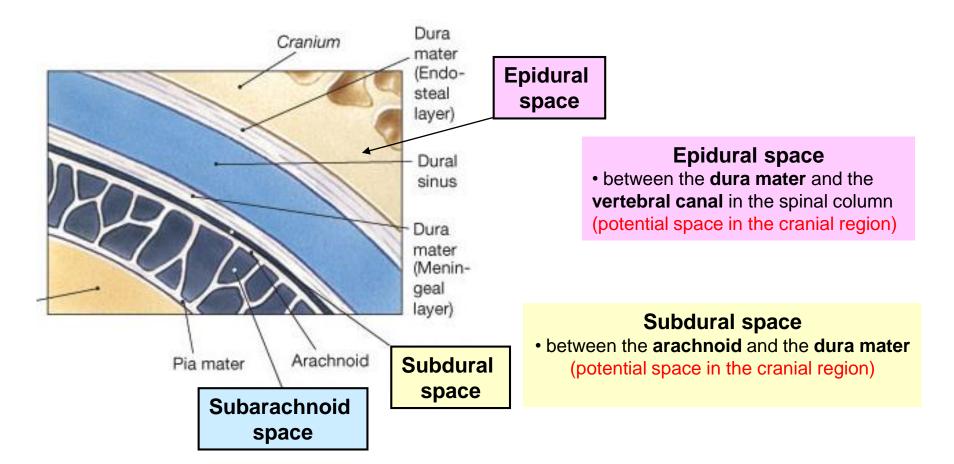
the innermost + delicate + vascular + adheres to and follows the surface of brain



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

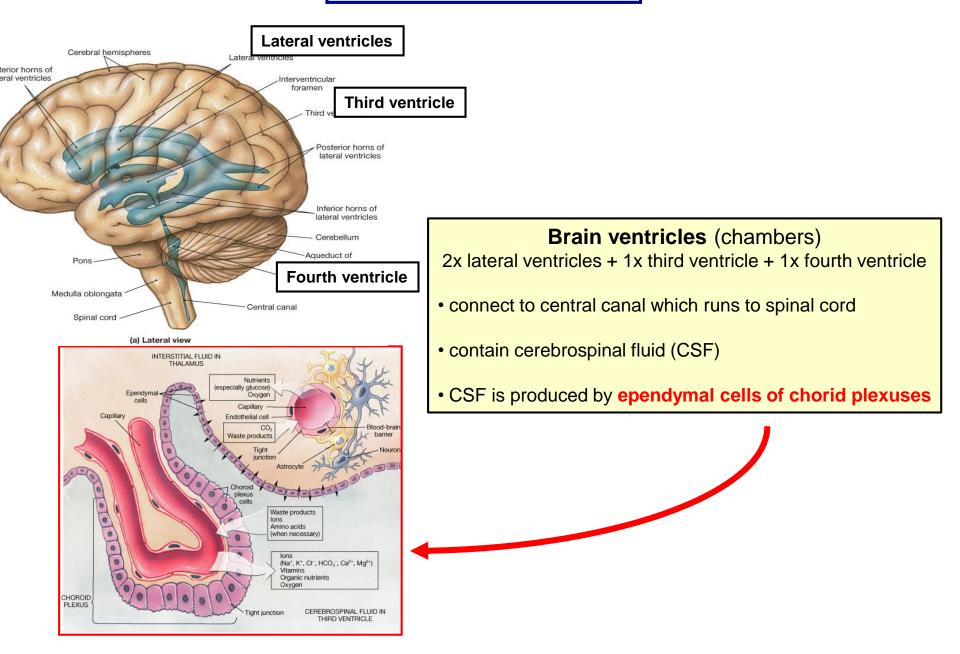


Subarachnoid space

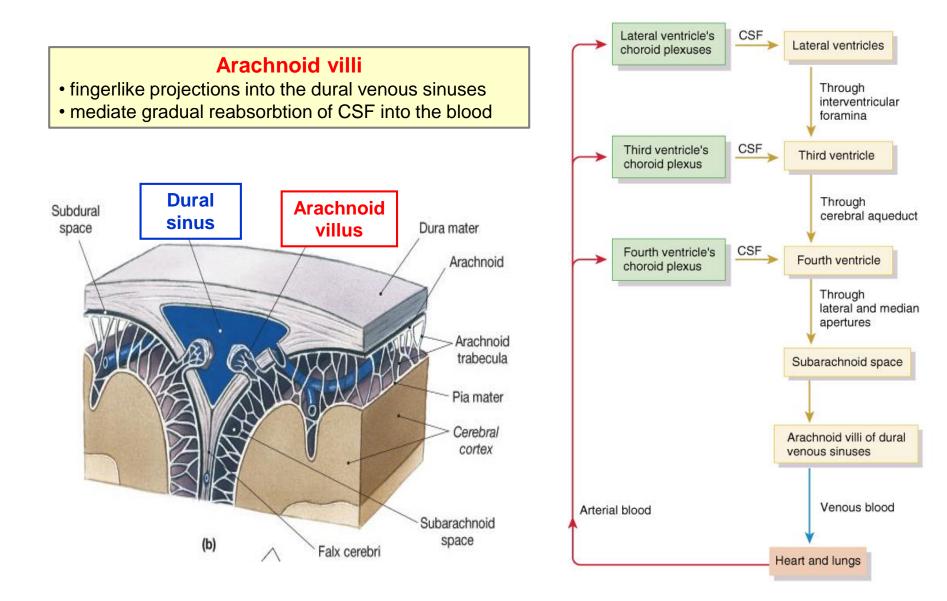
• between the arachnoid and pia mater

(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:

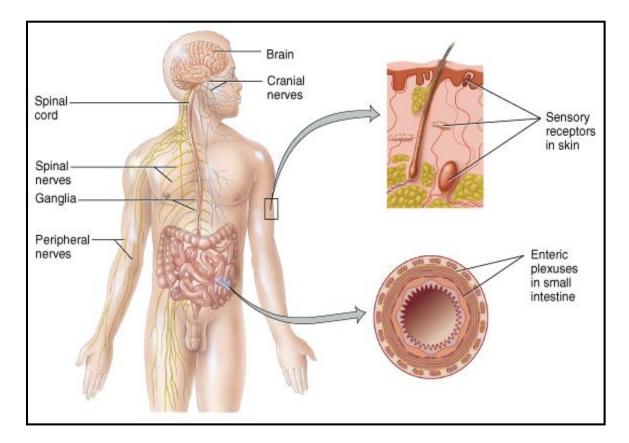
Carry information to the CNS.

Efferent (motor) pathways:

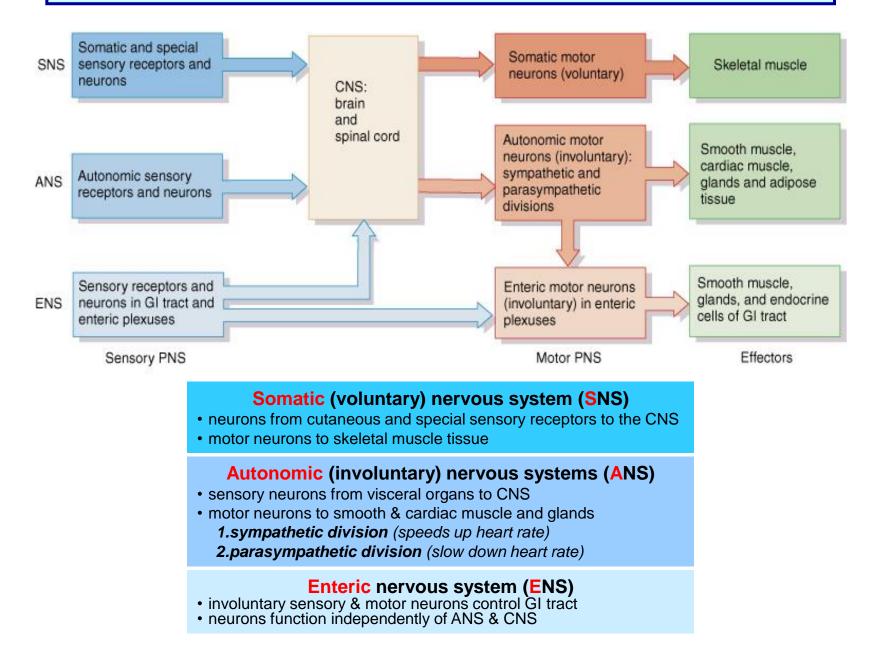
Carry information from the CNS.

Includes:

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

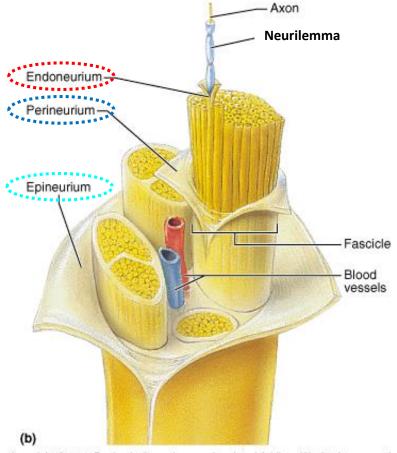


Peripheral nervous system – Overall organization



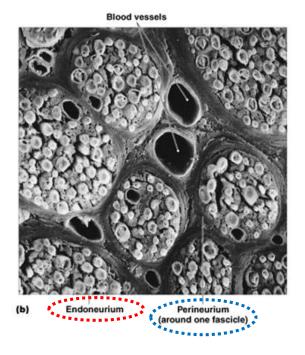
Peripheral nervous system - Nerves

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



Connective tissue layers composing nerves:

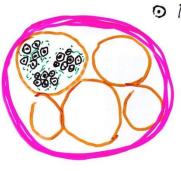
- Endoneurium surrounds axons primary nerve bundles
- Perineurium surrounds fascicles secondary n. bundles
- Epineurium surrounds the entire nerve



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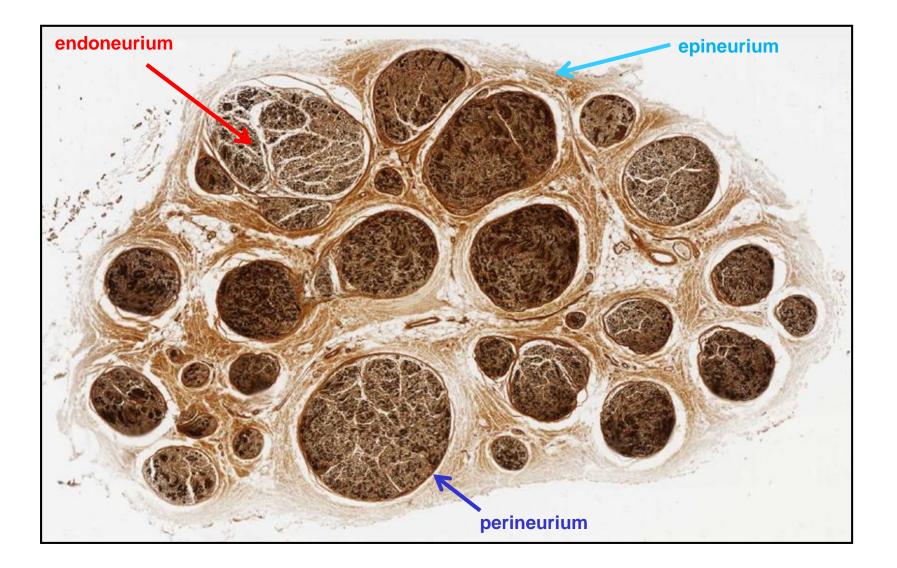
Peripheral nervous system - Nerves



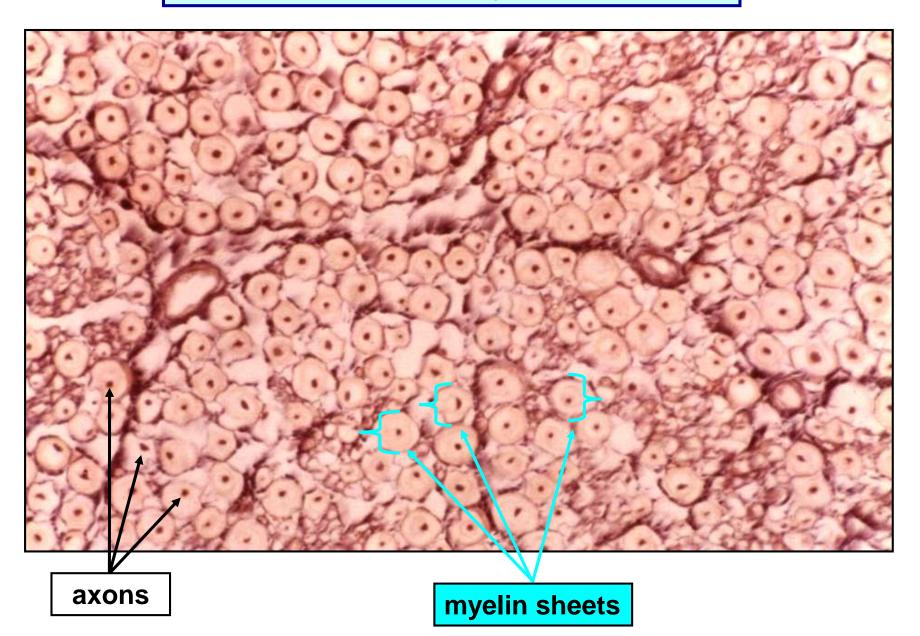
NYELINATED FIBER
 PRIMARY N.B.
 ENDONEURIUM
 SECONDARY N.B
 PERINEURIUM
 EPINEURIUM



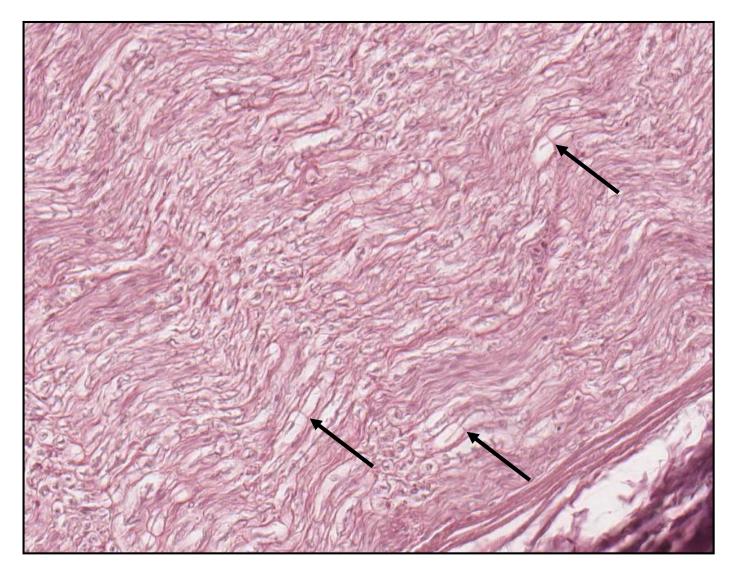
Peripheral nervous system – Nerves



Peripheral nervous system – Nerves



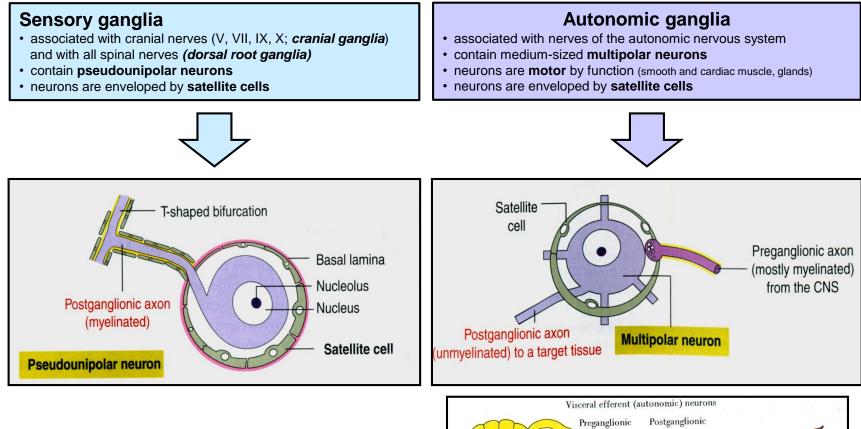
Peripheral nervous system – Nerves

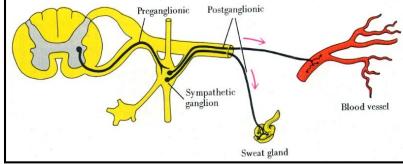


Nodes of Ranvier

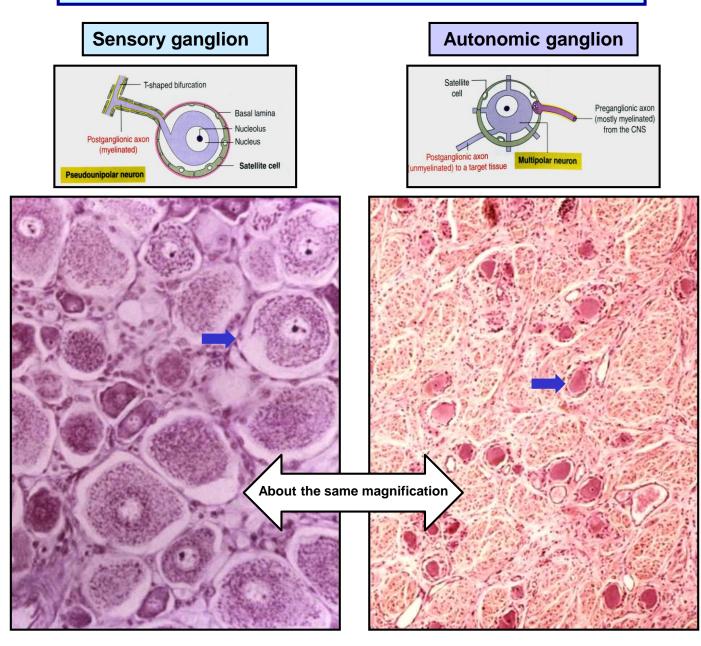
Peripheral nervous system – Ganglia

= aggregations of cell bodies of neurons located outside of CNS

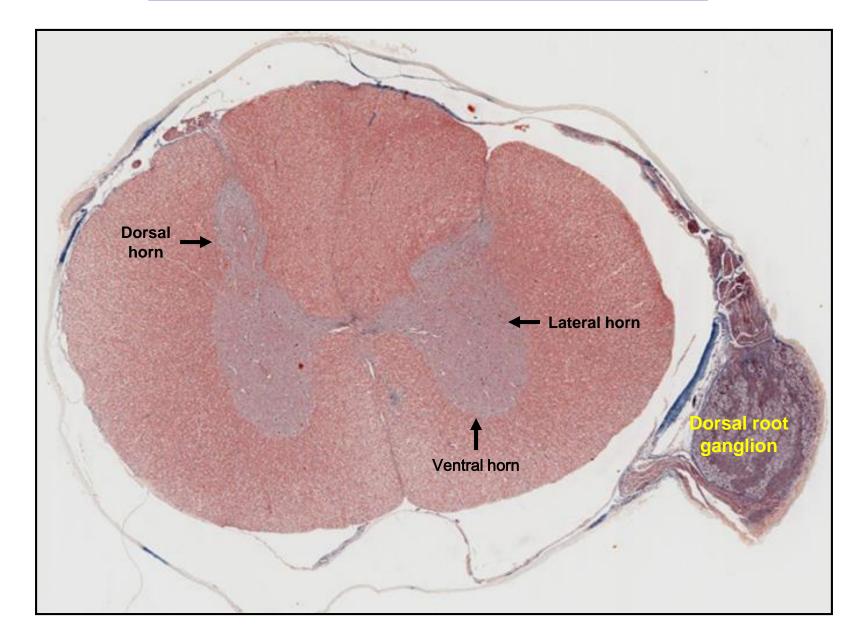




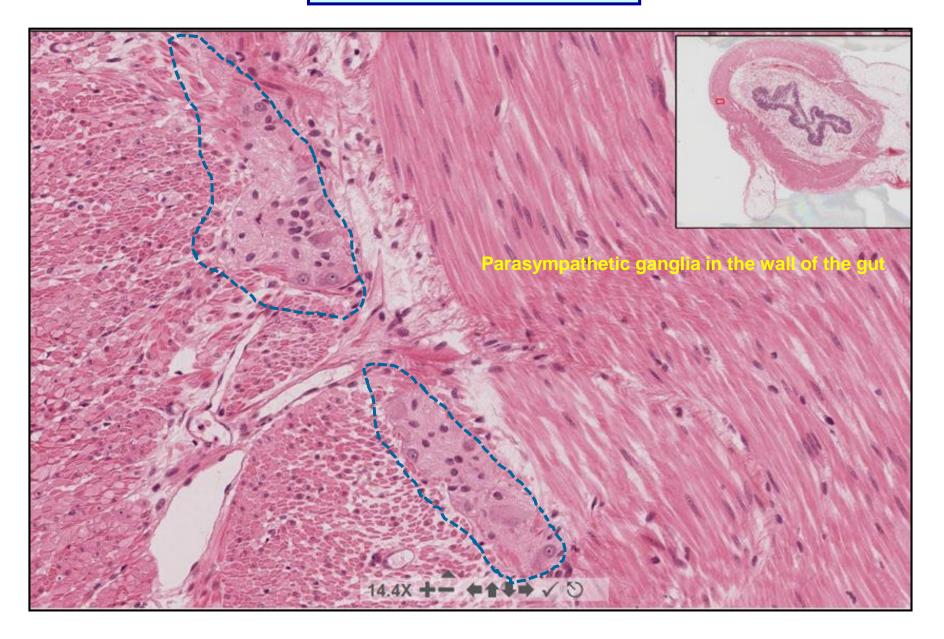
Peripheral nervous system – Ganglia



Spinal cord + Dorsal root ganglion



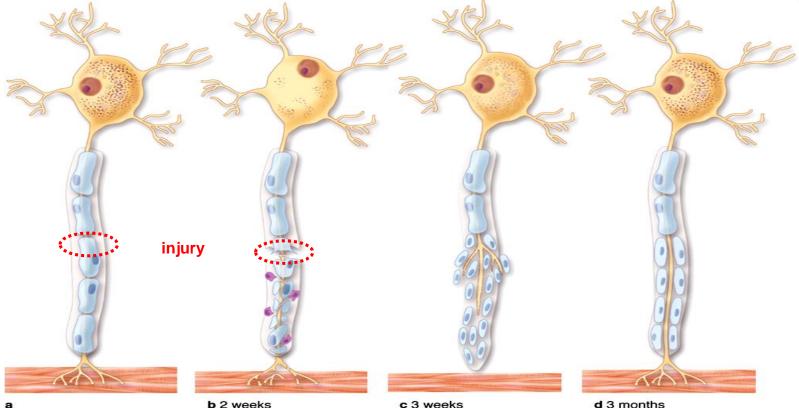
Autonomic ganglion



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

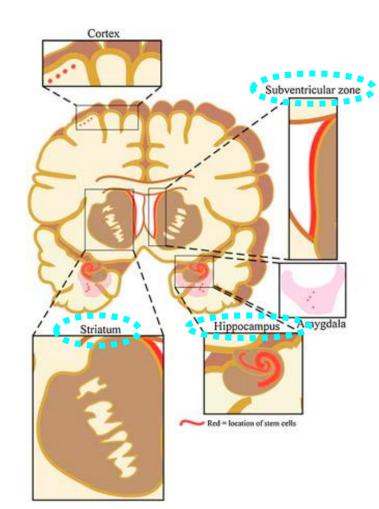
Schwann cells divide Axon begins to grow (1.5 mm/day) Navigaion by Schwann cells Collaterals will die

Nerve tissue regeneration - CNS

Stem / progenitor cells resiging in some areas of adult brain

Life-long plasticity of CNS

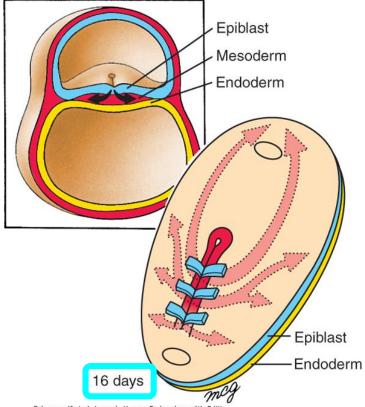
- Sprouting new dendrites
- Synthesis of new proteins
- Changes of synaptic contacts



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.**

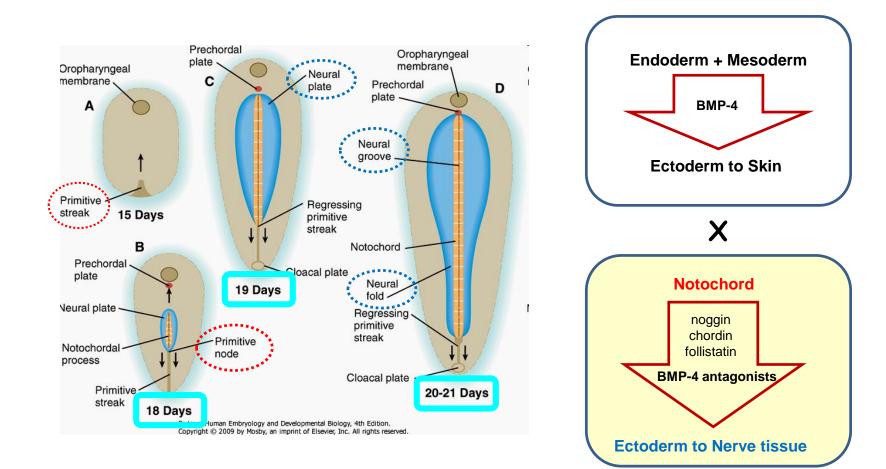
Schoenwolf et al: Larsen's Human Embryology, 4th Edition. Copyright \odot 2008 by Churchill Livingstone, an imprint of Elsevier, Inc. All rights reserved

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

Nerve tissue – Neural plate

Neural Induction

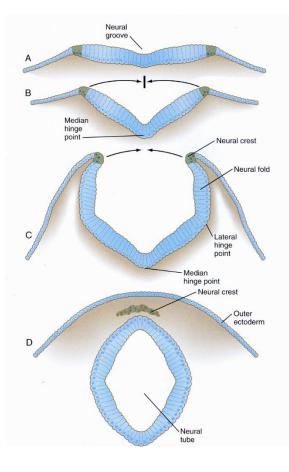
In addition to patterning the forming mesoderm, the primitive node also sets up the neural plate



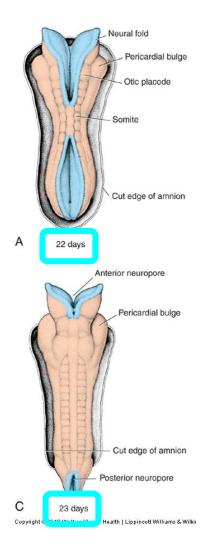
Nerve tissue – Neural tube

Neurulation

Folding and closure of the neural plate



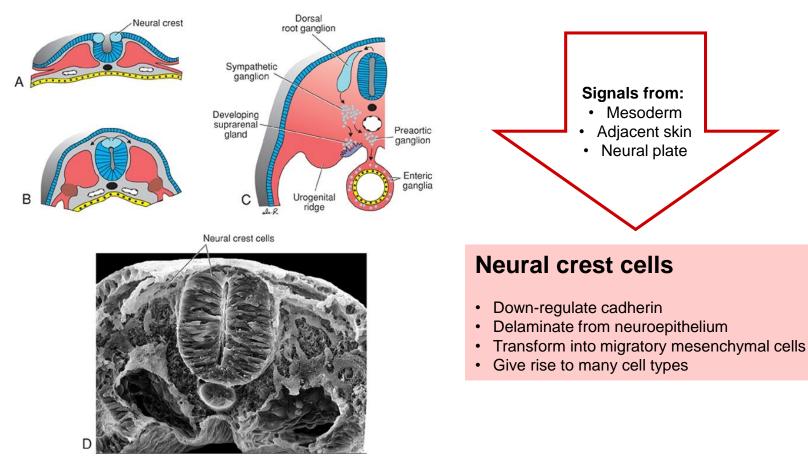
- neural folds close
- neural crest delaminates and migrates away
- closure happens first in middle of the tube and then zips rostrally and caudally
- anterior neuropore closes around day 25
- posterior neuropore closes around day 28



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

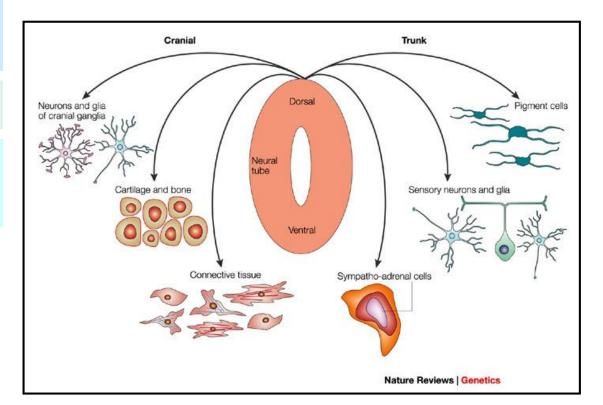
- Schwann cells
- satellite cells

Melanocytes

•migrate to the epidermis

Ectomesenchymocytes

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



hb

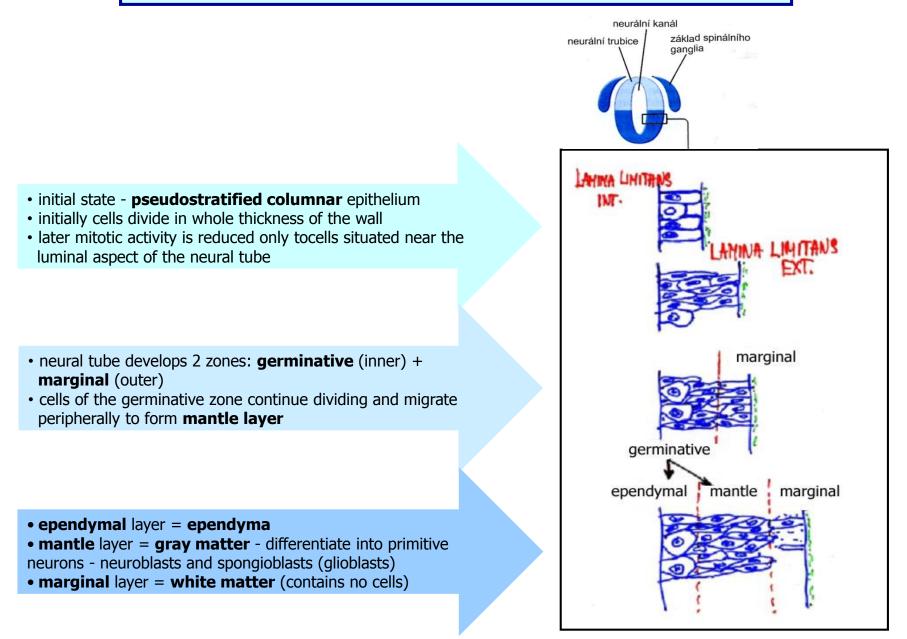
mb

fb

fnp

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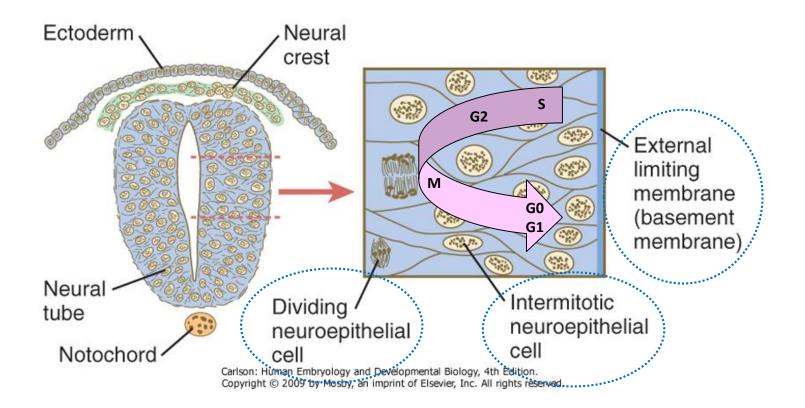
Nerve tissue – Histogenesis of neural tube



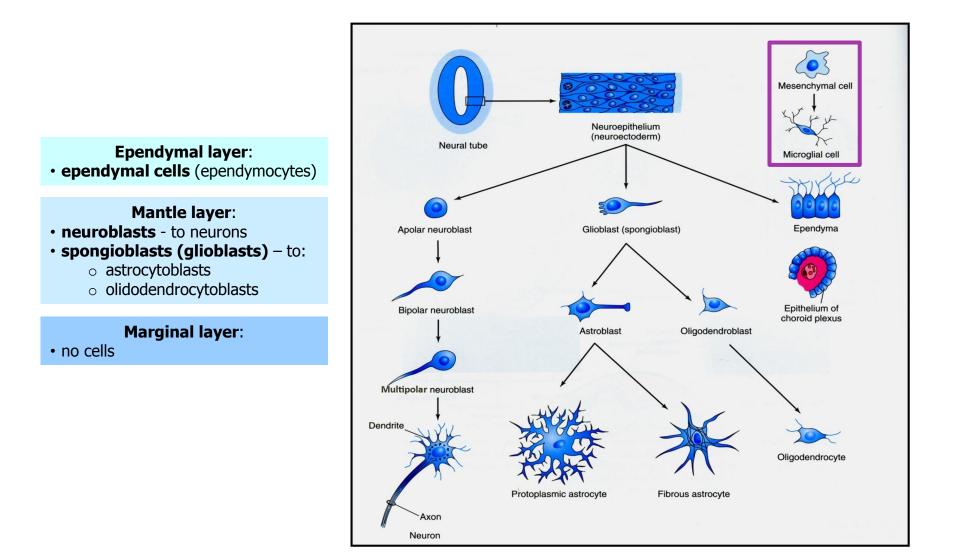
Nerve tissue – Neural tube

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.



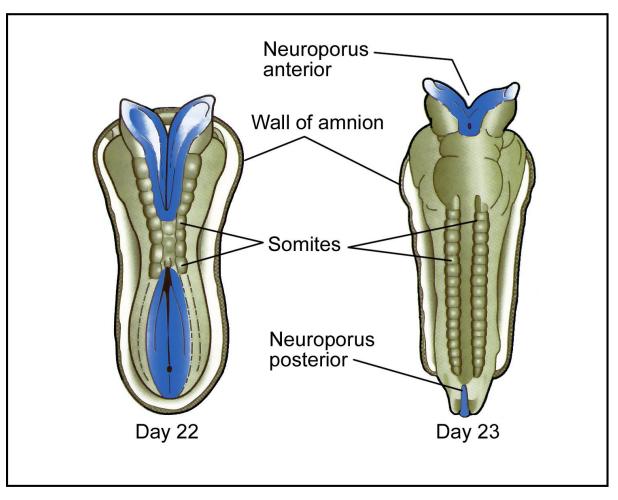
Nerve tissue – Neural tube – Cell differentiation



Nerve tissue – Morphogenesis

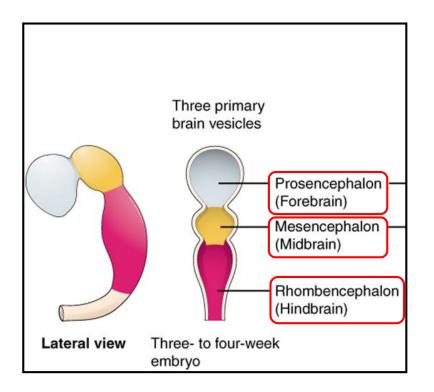
Brain – develops from the proximal segment of the neural tube that is broadened from the very beginning

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

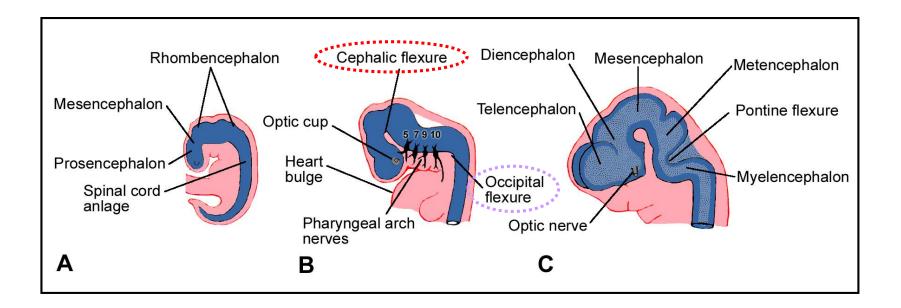
Forebrain - prosencephalon
Midbrain - mesencephalon
Hindbrain - rhombencephalon



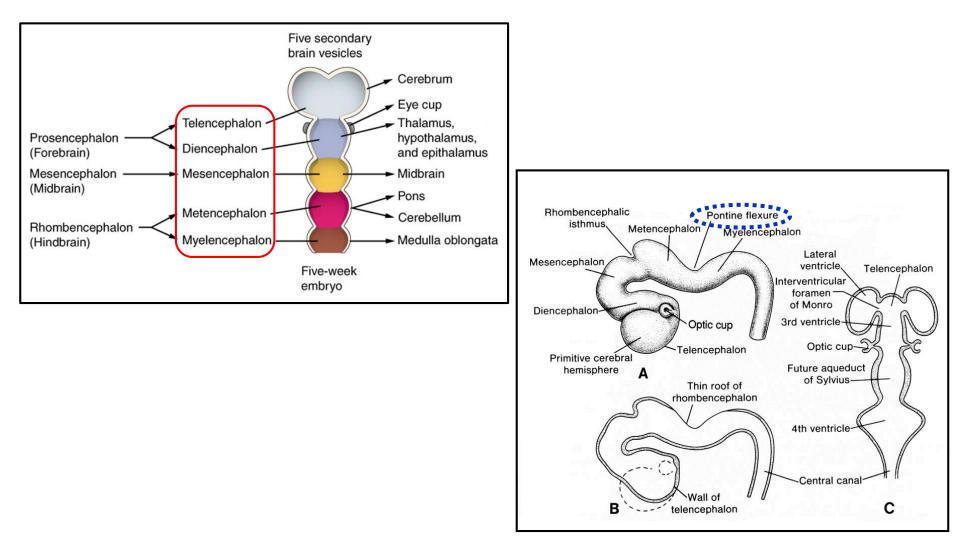
vesicles are not followed each to other linearly, but are bent in the sagittal plane

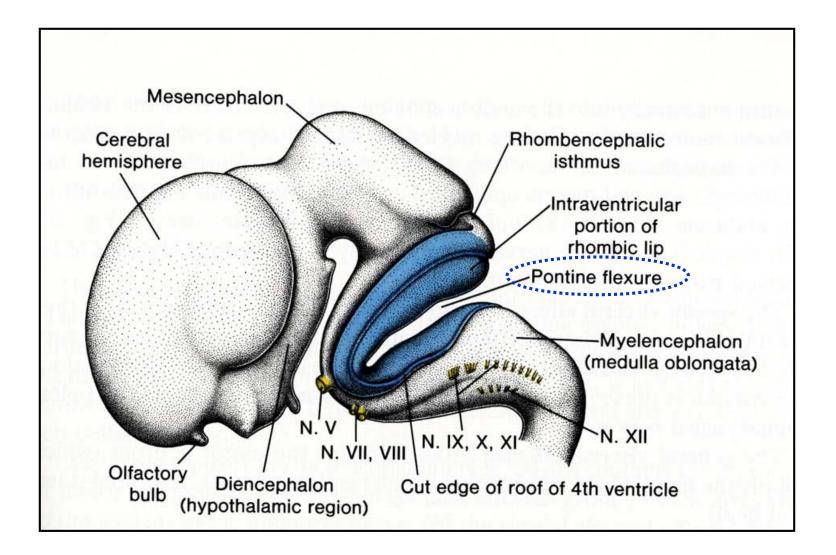
Cephalic flexure - permanent

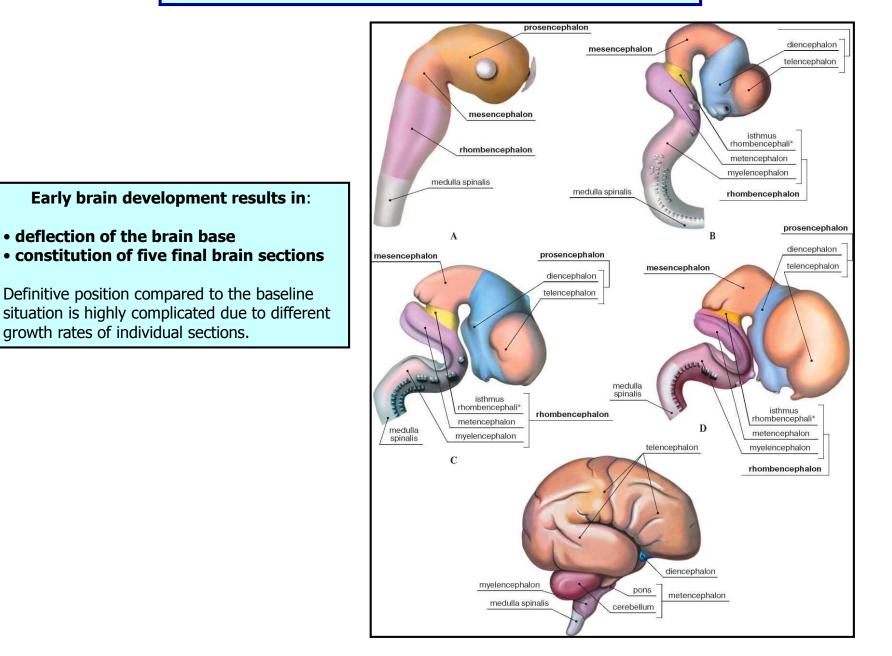
Occipital (cervical) flexure - after 2 months it is on straightening, so is not evident in the adulthood



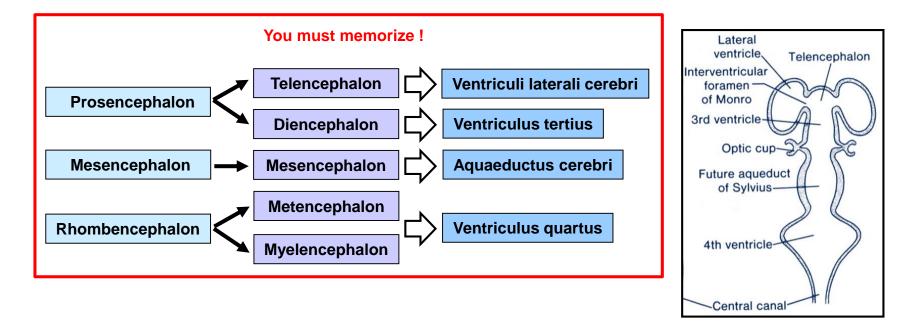
- 5th week
- 5 secondary vesicles
- · Pontine flexure remains to adulthood

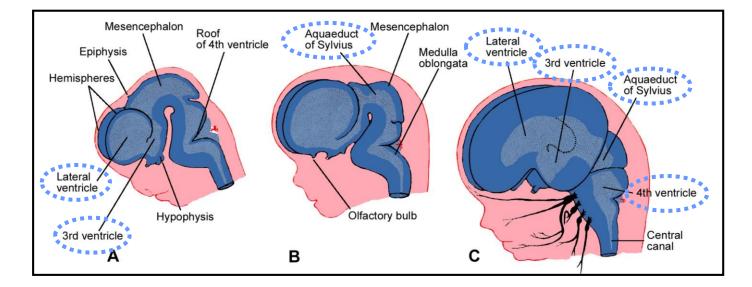






Nerve tissue – Brain development - Ventricles



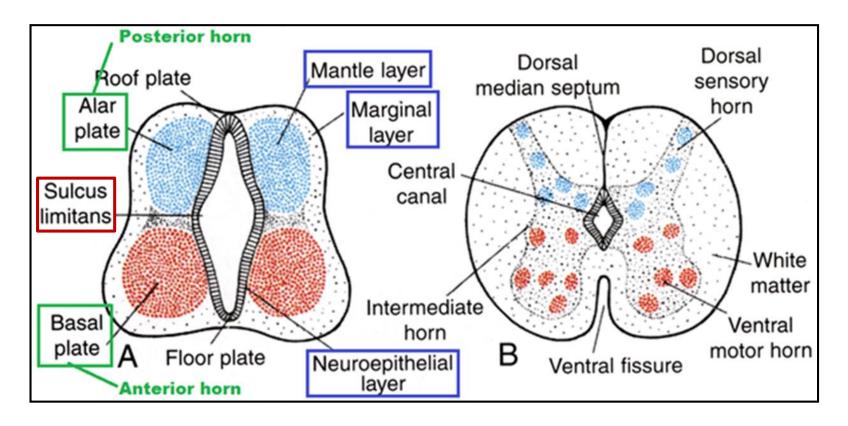


Nerve tissue – Spinal cord development

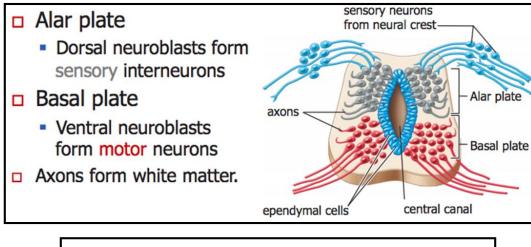
• it develops from the caudal part of neural tube

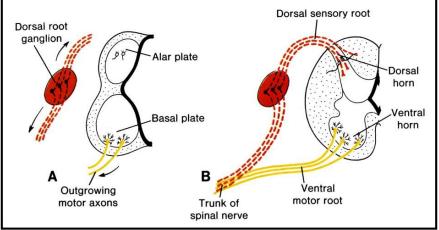
• cells of mantle layer proliferate and produce 2 sheets - the dorsal **alar plate** and ventral **basal plate**, which are separated by longitudinal groove called the **sulcus limitans**

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**.

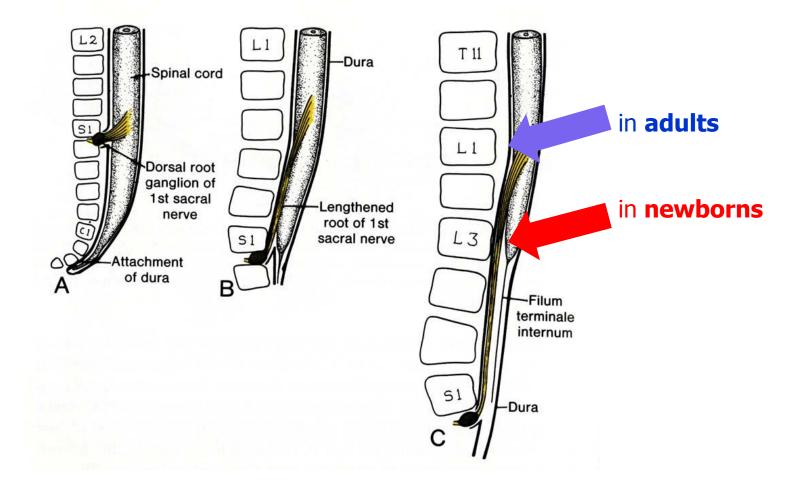
Nerve tissue – Spinal cord development

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