NEUR3905: Functional Neuroanatomy & Brain Development

Cells of the CNS

Neurons – derived from neural stem cells

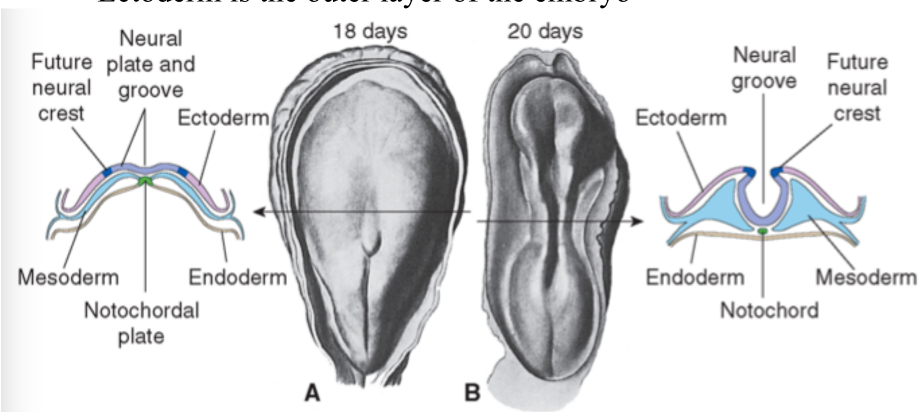
- 100 billion in total, but only 10% of all brain cells
- Most neuronal proliferation in first 5 months
- Most neuronal differentiation 4-9 months
- Neuronal connections continue to form postnatally
- Axon and cell body can vary in length and size dramatically

Glial cells ("glue")

- **Astrocytes –** homeostatic functions, structural support, contribute to blood brain barrier, response to injury
    - Can form scar tissue in the brain
- **Oligodendrocytes –** myelination of axons, occurs postnatally
    - Wraps its processes around the axons → faster conduction
- **Microglia –** resident immune cells of CNS, phagocytosis, and response to injury
    - Arose from the mesoderm
    - Can release inflammatory mediators e.g. cytokines
- **Ependymal cells –** line ventricles and choroid plexus, produce CSF
    - Choroid plexus is the structure that produces the CSF
- Glia (except microglia) are also derived from neural stem cells but differentiate later than neurons

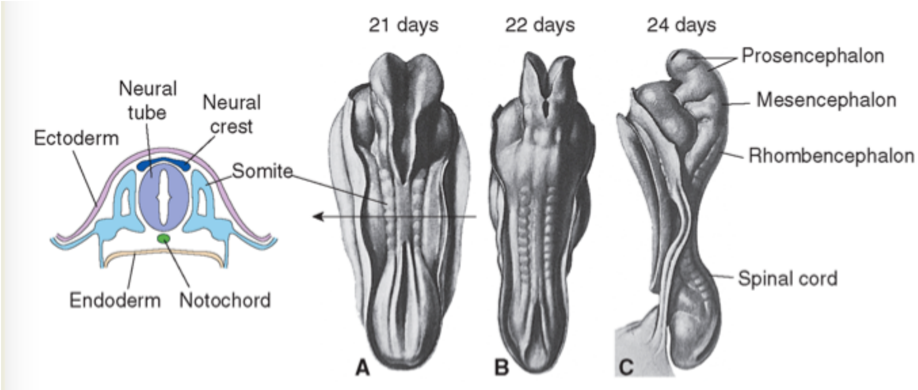
Formation of the neural groove (3rd week)

- Midline mesoderm releases signalling molecules which lead to thickening of the overlying ectoderm to form the neural plate
- Neural plate then folds inwards to form the neural groove
- Ectoderm is the outer layer of the embryo



Primary neurulation and formation of the primary vesicles (4th week)

- Neural tube closes (days 21-26) and detaches from the ectodermal surface (the skin)
- Groups of cells from the crest of the neural fold are left behind
- *Neural crest cells go on to form peripheral nerves*



Neural tube defects

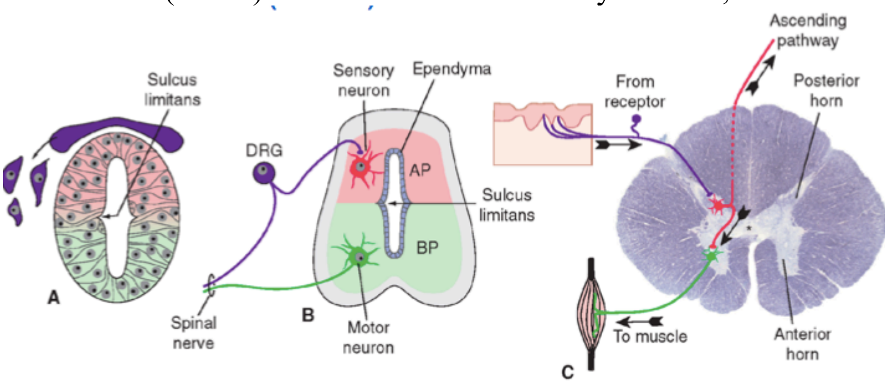
- Failure of the rostral end of the neural tube to close is a catastrophic developmental defect
- Failure of the caudal end of the neural tube to close results in spina bifida
- End up with a cystic fluid filled sack
- Consequences for motor function and sensation of the lower limbs

Dorsal-ventral patterns of differentiation

- Midline mesoderm (and later the notochord) produces a signalling molecule called sonic hedgehog (SHH)
- Ectoderm next to the neural plate produces an opposing signalling molecule bone morphogenetic proteins (BMPs)
- Sonic hedgehog → causes differentiation of the cells that form the ventral pod of spinal cord (where the motor neurons are formed)
- BMPS → get released from the ectoderm, just lateral to the neural groove, cause formation of the sensory neurons

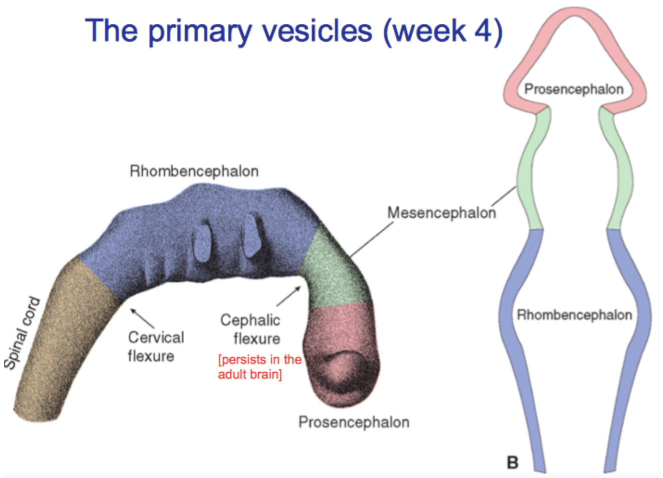
Alar versus basal plate derivatives

- Different gradients of signalling molecules establish a functional organisation, which persists in the adult spinal cord
- Alar (dorsal) derivative become sensory neurons, whilst basal (ventral) derivatives become motor



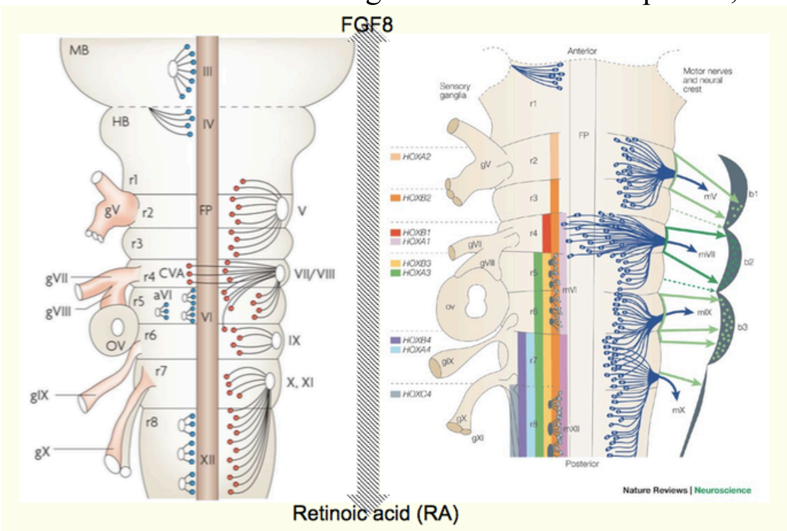
Primary vesicles (week 4)

- Prosencephalon → cerebrum, thalamus
- Mesen → part of the brain stem
- Rhomben → pons, medulla and cerebellum

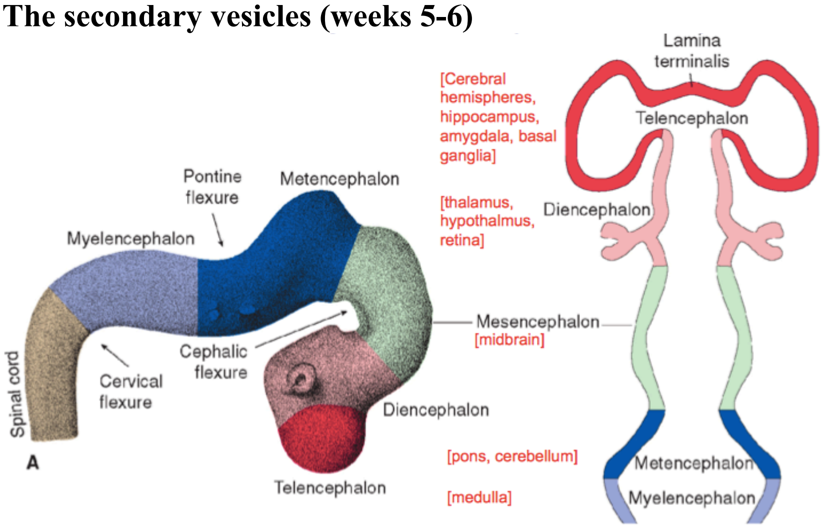


Rostrocaudal patterns of differentiation in rhombencephalon

- Depending on concentration of FGF8 and retinoic acid, it causes difference in transcription of HOX genes
- Rhombomeres are segments of rhombencephalon, each drive by different set of HOX genes

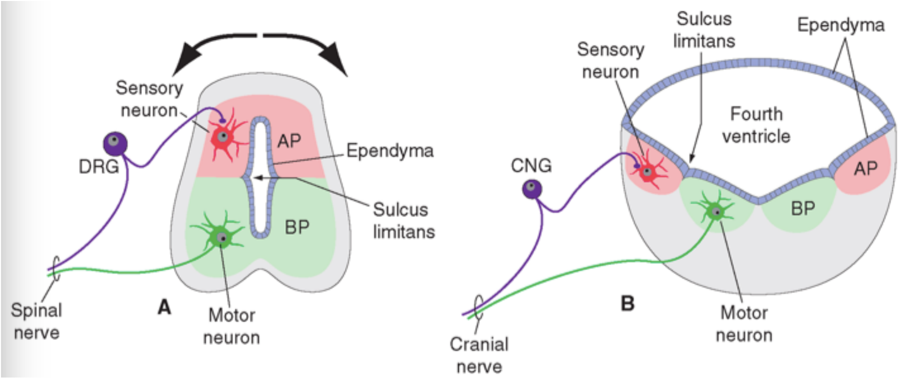


The secondary vesicles (weeks 5-6)



Pontine flexure (formation of the 4th ventricle)

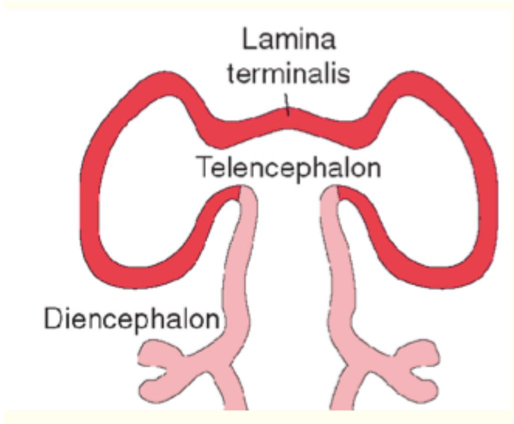
- The neural tube spreads apart to form a diamond-shaped cavity, with a thin membrane roof
- Dorsal/ventral orientation in the spinal cord becomes medial/lateral in the brain stem
- Sulcus limitans persists as an important boundary

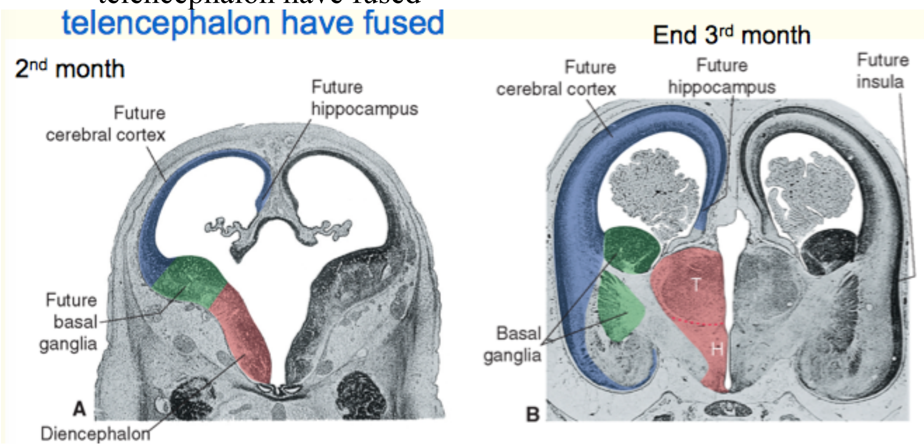


- Important for development of the 4th ventricle
- Ventral parts are now in medial position → motor neurons are now medial
- Dorsal are now in lateral position → sensory are now lateral

Shaping the telencephalon (wks 6-12)

- Rostral tip of the neural tube forms a thin membrane called "lamina terminalis"
- Lamina terminalis is the origin of the bridge between the two hemispheres where bundles of interconnecting fibres begin to grow
- The basal part of the telencephalon thickens to form the pre-cursor of the basal ganglia
- The diencephalon thickens for form the thalamus and hypothalamus, separated by a sulcus
- By the end of the 3rd month the diencephalon and telencephalon have fused

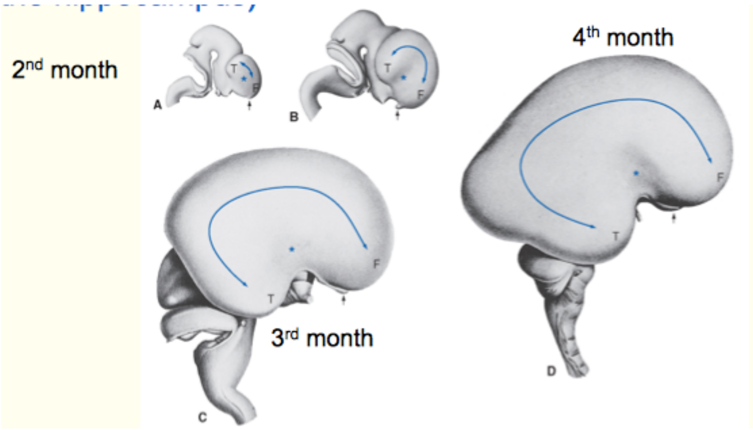




- Starts to develop 2 different hemispheres
- Connected by the lamina terminalis → still exists in the adult, except as a minute structure
    - Where the fibres of the corpus callosum originated

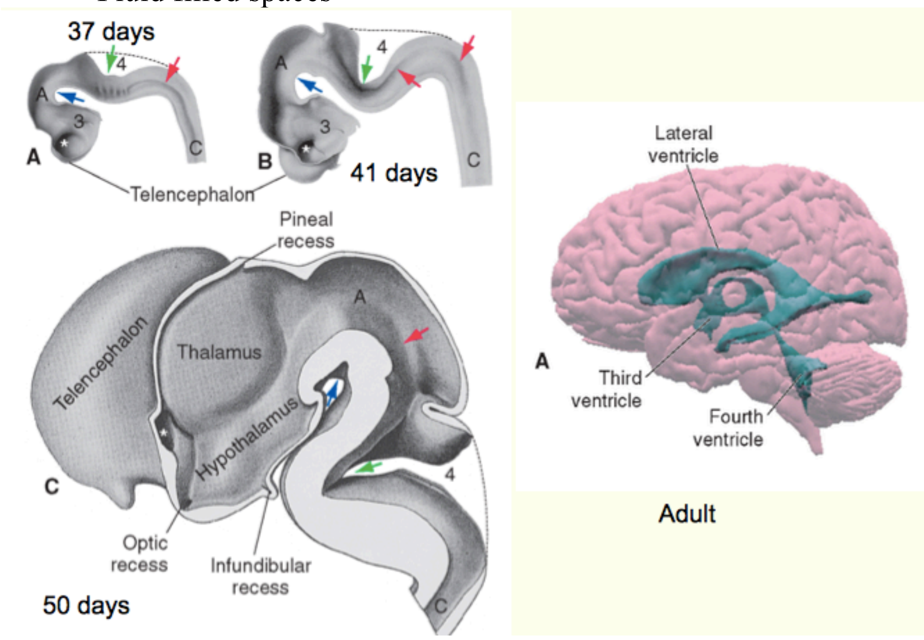
Formation of temporal and frontal lobes

- * is the insula cortex
    - Hidden from external view
- T → temporal pole, F → frontal pole
- Each cerebral hemisphere assumes the shape of a great arc around the insula
- Parts of the hemisphere originally dorsal to the insula get pushed around into the temporal lobe (i.e. the hippocampus)



Cavity of the neural tube becomes the ventricular system

- Fluid filled spaces

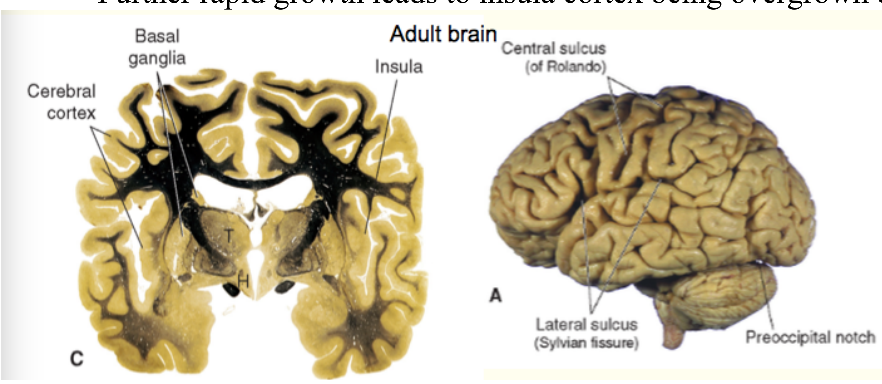


Progressive development of cortical convolutions (ages in weeks)

- See development of sulci and gyri as brain increases in surface area

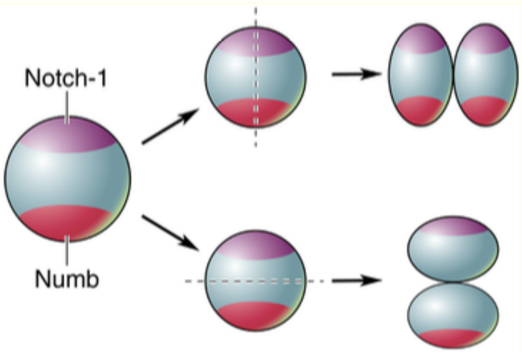
Continued growth of the telencephalon

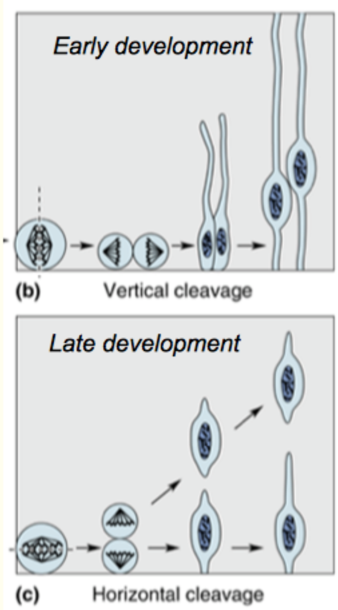
- Further rapid growth leads to insula cortex being overgrown by frontal, parietal and temporal lobes



Neuronal proliferation (peak 5 weeks – 5 months)

- Proliferation of neuroblasts (immature neurons derived from neural stem cells)
- Occurs in ventricular zone
- Cleavage plane during cell division determines their fate
- Top → peal surface
- Bottom → ventricular zone
- Notch-1 cell migrates away and stops division
- Numb cell continues to divide

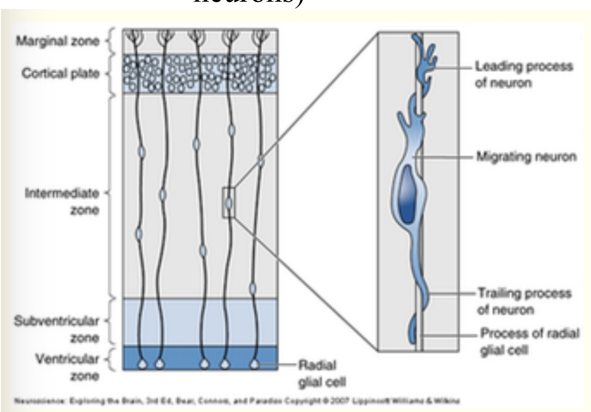


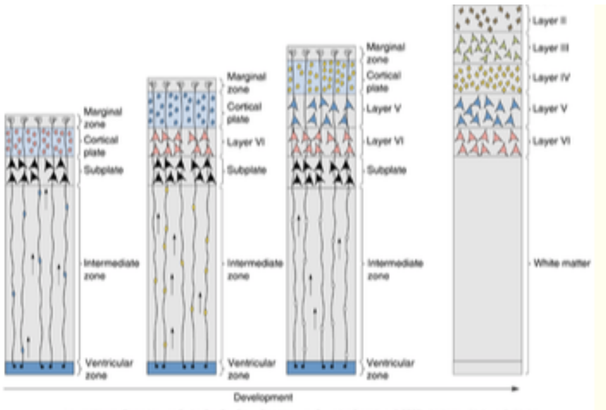


- Vertical cleavage in early stages of development → splits along vertical axis and produces two daughter cells
- Horizontal cleavage during later development → split along horizontal axis and only one of the daughter cells can continue to proliferate (remains on ventricular surface) and other migrates up to peal surface → lose half of capacity for future cleavage
- There is a surface receptor called notch 1→ sits on peal surface
- Numb sits on ventricular surface
- Daughter cells have this in vertical cleavage, in horizontal, will only express one or the other
- Numb inhibits Notch (which normally causes migration up to peal surface)

Migration

- Cerebral cortex is formed of 6 layers of neurons
- Develop in inside out fashion
- Scaffolding radial glial cells stretch from ventricular surface to peal surface → surface on which neuroblasts can migrate upwards
- First cell layer to develop is layer 6 (innermost layer)
- Inside out development of the cortex
    - Radial glial cells: provide scaffold on which cortex is built and guide migration of neurblasts along their thin fibres
    - Neuroblasts cross the subplate to arrive in the cortical plate (first cells become layer VI neurons)



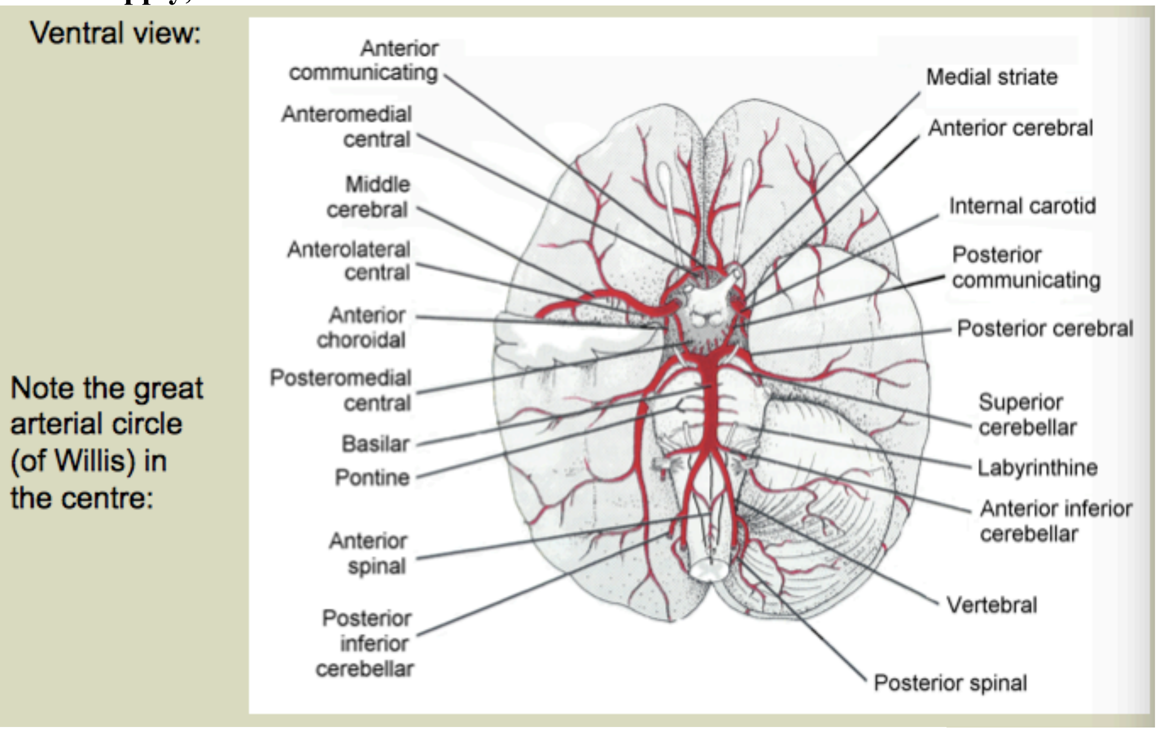


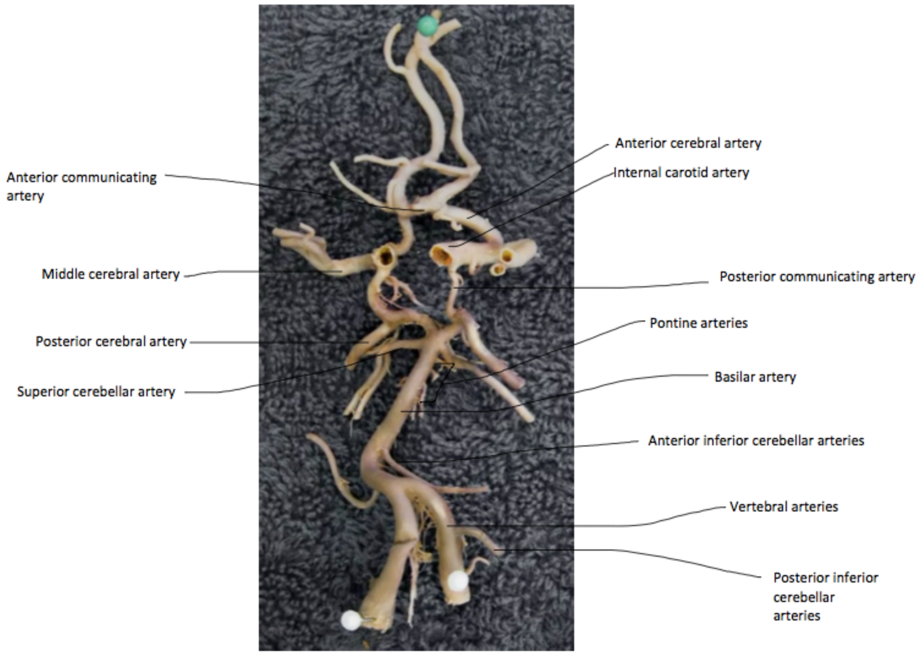
Differentiation

- Neuroblast is already committed to a neuronal fate
- Microglia are not derived from neural stem cells

- Neuroblasts get created at ventricular surface and then migrate and differentiate based to differing chemical concentrations at different places
- Neuroblasts differentiate into a neuron of a specific phenotype
- Differentiation of astrocytes peaks at birth
- Differentiation of oligodendrocytes postnatal
- Most myelination occurs postnatally

Blood Supply, Ventricles and Blood Brain Barrier





- Brain blood supply comes from internal carotid artery (2/3) and vertebral arteries (1/3)
- Often irregularities/things missing in this system of blood vessels