NEUR3905 – FUNCTIONAL NEUROANATOMY

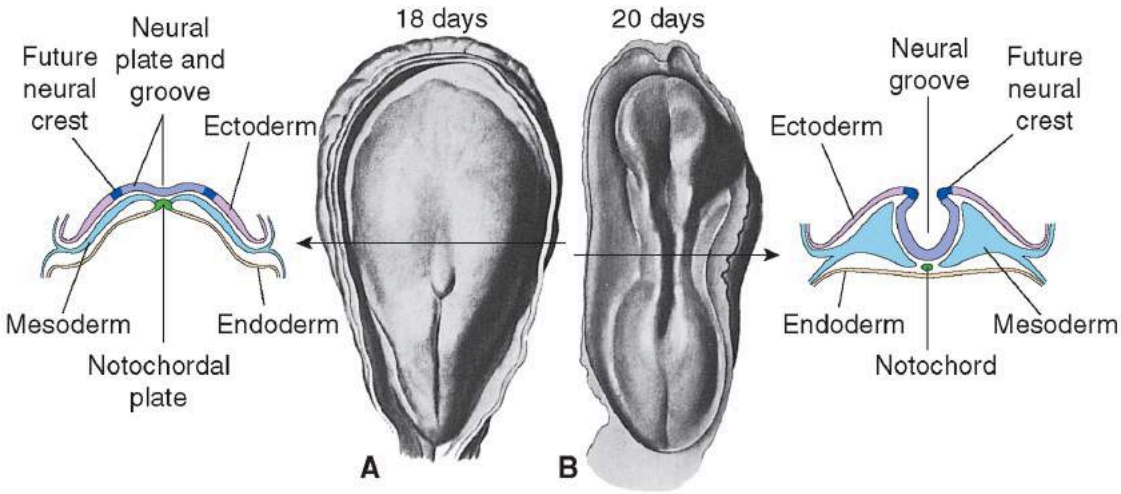
DEVELOPMENT OF BRAIN

CELLS OF CNS

- Neurons: Derived from neural stem cells
    - 100 bn, 10% of all cells in brain
    - Varying sizes, lengths of dendrites etc.
    - Development timeline:
        - 1-5 months: Neuronal proliferation
        - 5-9 months: Neuronal differentiation e.g. multipolar/bipolar
        - Post-natal: Formation of synapses
- Glial cells: All except microglia derived from neural stem cells
    - Astrocytes: Homeostasis of ECM for neurons – recycle glutamate released by neurons, structural support, contribute to BBB, activated in response to injury → inflammatory mediators, scar tissue
    - Oligodendrocytes: Myelination of axons post-natally → fast, salutatory conduction
    - Microglia: Immune cells – phagocytoses damaged neurons, releases inflammatory cytokines and mediators, searches for intruders
        - Becomes less ramified, more ameboid when activated
        - Derived from hematopoietic stem cells in bone marrow
    - Ependymal cells: Lines ventricles and choroid plexus to produce CSF
        - Specialised epithelial cells

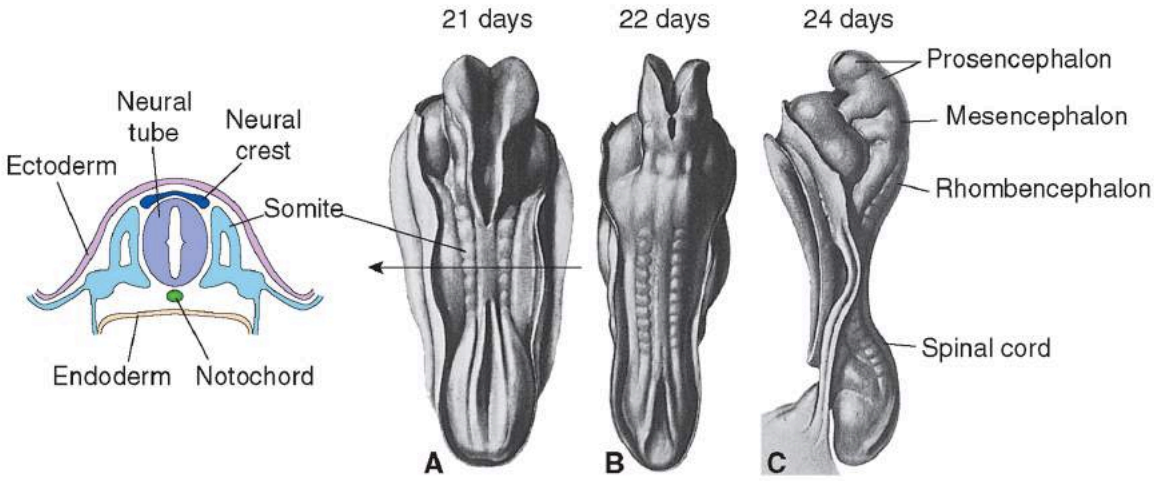
ANATOMICAL OVERVIEW OF BRAIN DEVELOPMENT

- Formation of neural groove (3rd week):

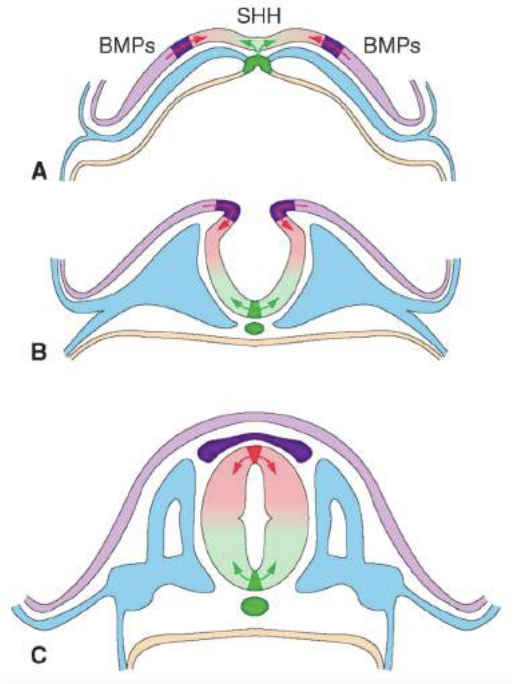


- Notochord (midline mesoderm) releases signaling molecules → thickening of ectoderm to form neural plate
- Neural plate folds → neural groove (beginning from middle)

- Primary neurulation (Week 4):

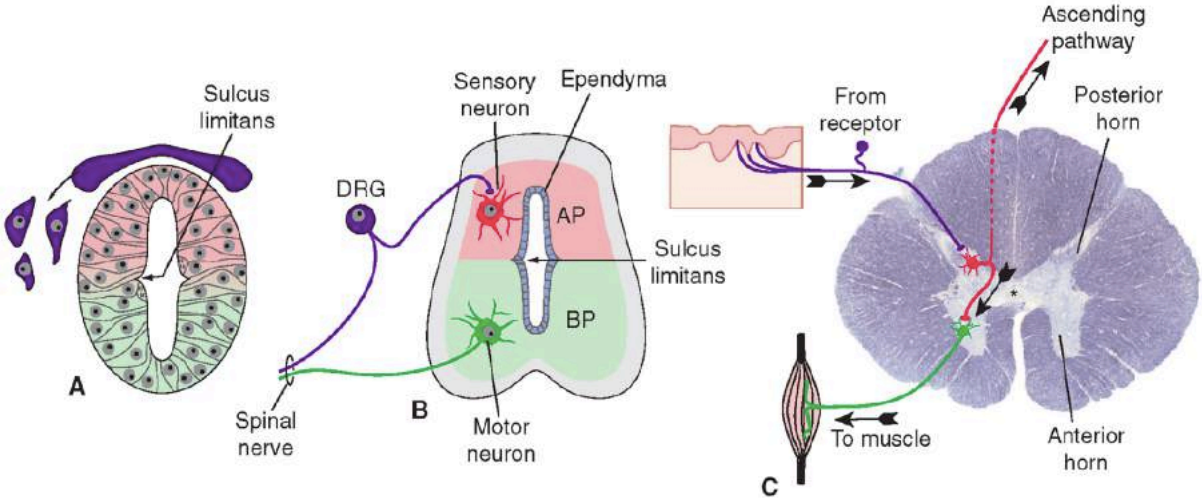


- Neurulation = folding of neural plate → neural tube
- Day 21-26: Neural tube closes and detaches from ectoderm, leaving neural crest cells
  - Closes in middle first (day 21) > rostral (day 24) > caudal (day 26)
- Defects:
  - Failure to close rostral end: Anencephaly - death
  - Failure to close caudal end: Spina bifida – does not hold spinal cord + nerves in place
    - Myelomeningocele: Vertebral bodies do not form around spinal cord → nerves exposed to outer environment
- Dorsal-ventral differentiation of neurons in neural tube:

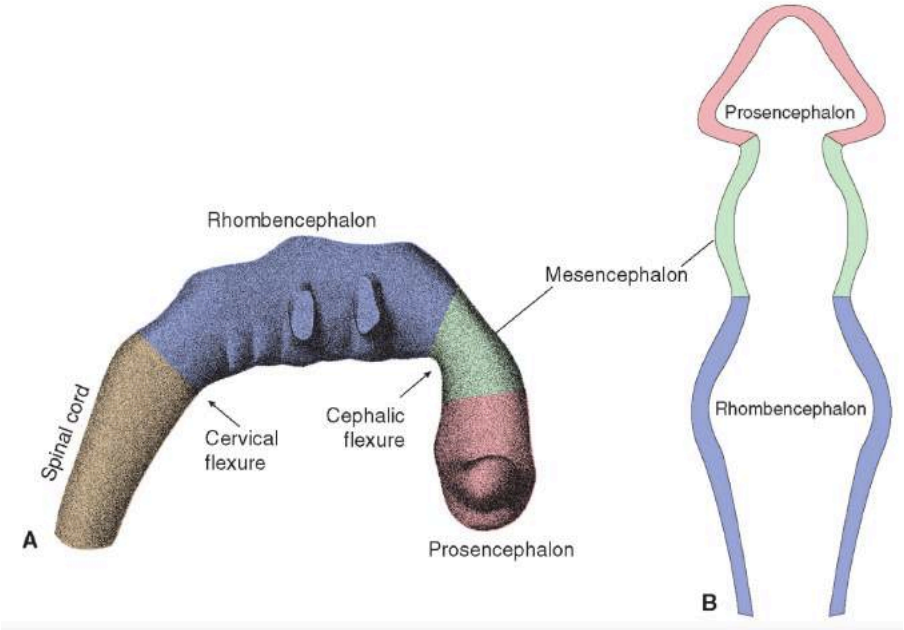


  - Signaling molecules → differentiation of neurons during neurulation (folding)
    - Notochord produces sonic hedgehog (SHH)

        - Ectoderm lateral to neural plate produces bone morphogenetic proteins (BMPs)
    - Neural tube folds ventral (basal) to dorsal (alar)
    - Different gradients of signaling molecules as neural tube forms → different organization of neurons
        - Alar (dorsal) plate derivatives → Sensory neurons
            - Due to BMPs
        - Basal (ventral) plate derivatives → Motor neurons
            - Due to SHH

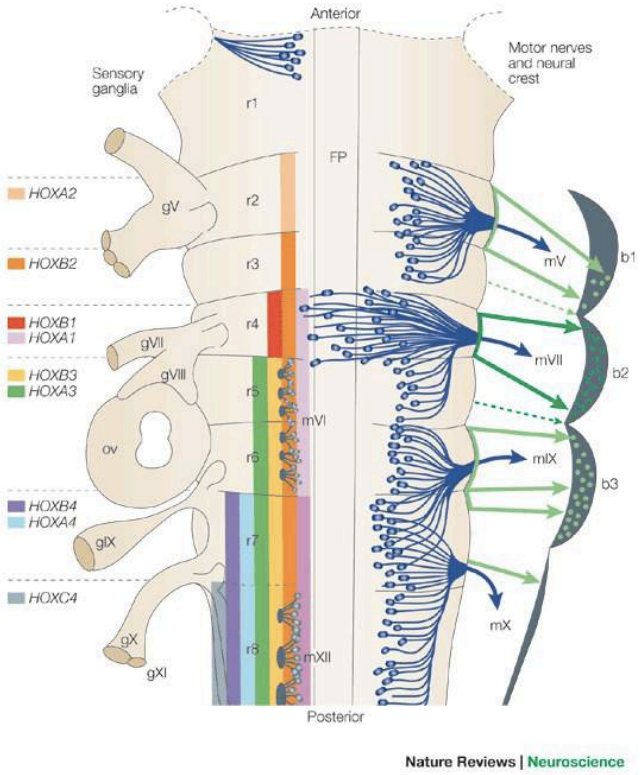


- Primary vesicles: Forms from cavity in neural tube (Week 4)



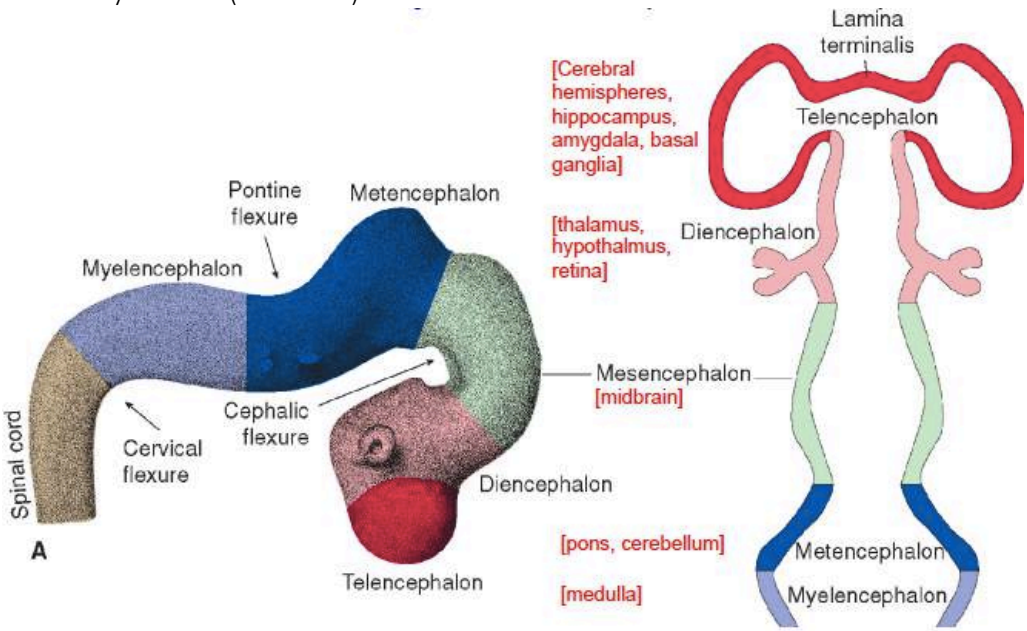
    - Prosencephalon (forebrain): Cerebrum
    - Mesencephalon (midbrain): Midbrain
    - Rhombencephalon (hindbrain): Pons, medulla, cerebellum
        - Rostrocaudal patterns of differentiation: Different gradients of FGF8 (rostral) and retinoic acid (RA) signaling molecules → different levels of each HOX gene expressed + transcribed in different rhombomeres (segments) → different cranial nerves

- Present by day 29



  - *Cephalic flexure still present in adult brain

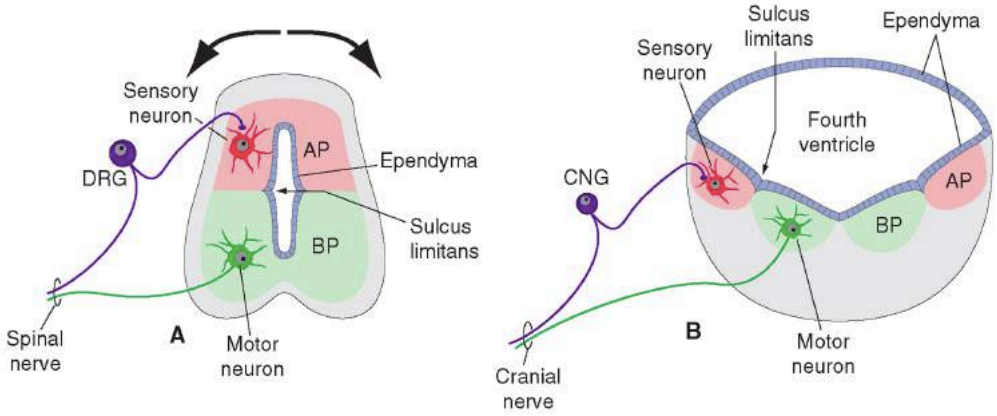
- Secondary vesicles (Week 5-6)



  - Differentiation into secondary vesicles
    - Prosencephalon → telencephalon (cerebrum, hippocampus, amygdala, basal ganglia) + diencephalon (thalamus, hypothalamus, retina)
    - Mesencephalon
    - Rhombencephalon → metencephalon (pons, cerebellum), myelencephalon (medulla)

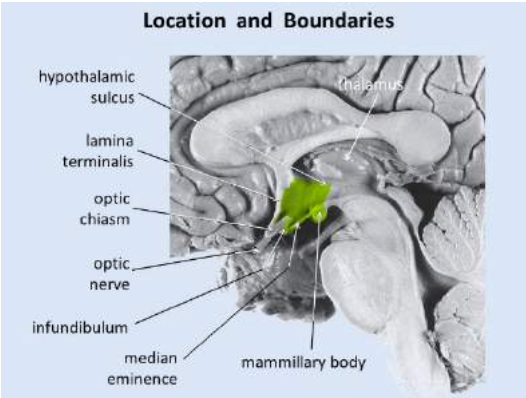
- Pontine flexure (4th ventricle)

- At the pontine flexure (junction of myelencephalon + metencephalon), the neural tube (metencephalon) widens to form 4th ventricle w/ diamond-shaped cavity in brainstem

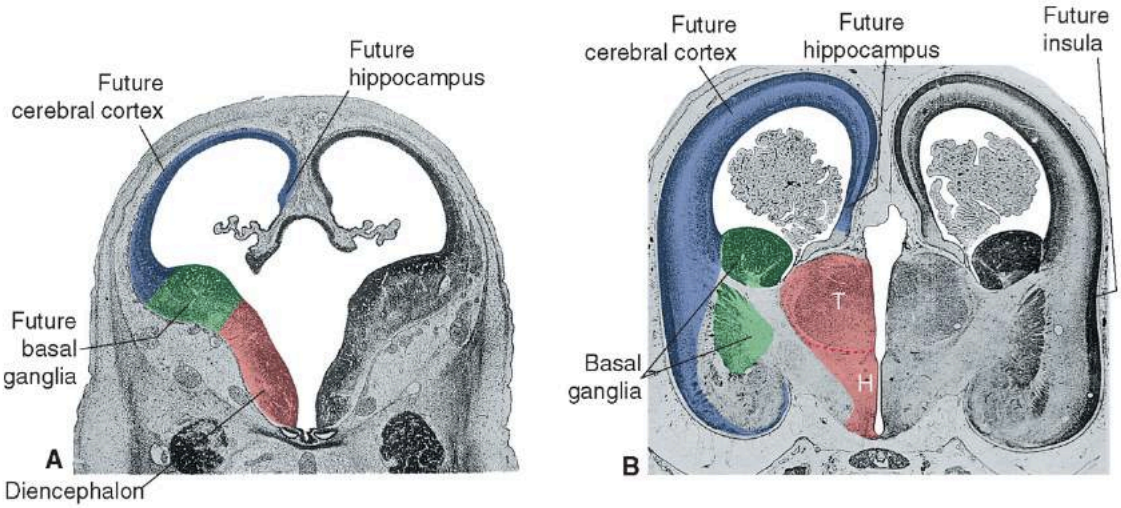


- Sensory neurons from AP move laterally
- Motor neurons from BP are medial
- Sulcus limitans: Landmark for junction between motor neurons (from BP) and sensory neurons (from AP)

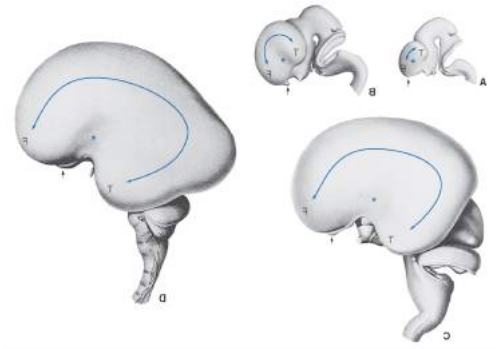
- Shaping telencephalon (week 6-12)
  - Telencephalon forms cerebral hemispheres + basal ganglia:
    - Lamina terminalis: Rostral tip - Origin of fibres connecting 2 hemispheres
    - Basal part thickens → basal ganglia



  - Diencephalon → thalamus + hypothalamus
  - 3rd month/Week 12: Fusing of diencephalon + telencephalon



- Frontal and temporal poles (w/ hippocampus) of telencephalon grow and wrap around insula → insula covered
  - Normally hippocampus more dorsal to insula in other mammals, but is pushed into temporal lobe (ventral to insula)



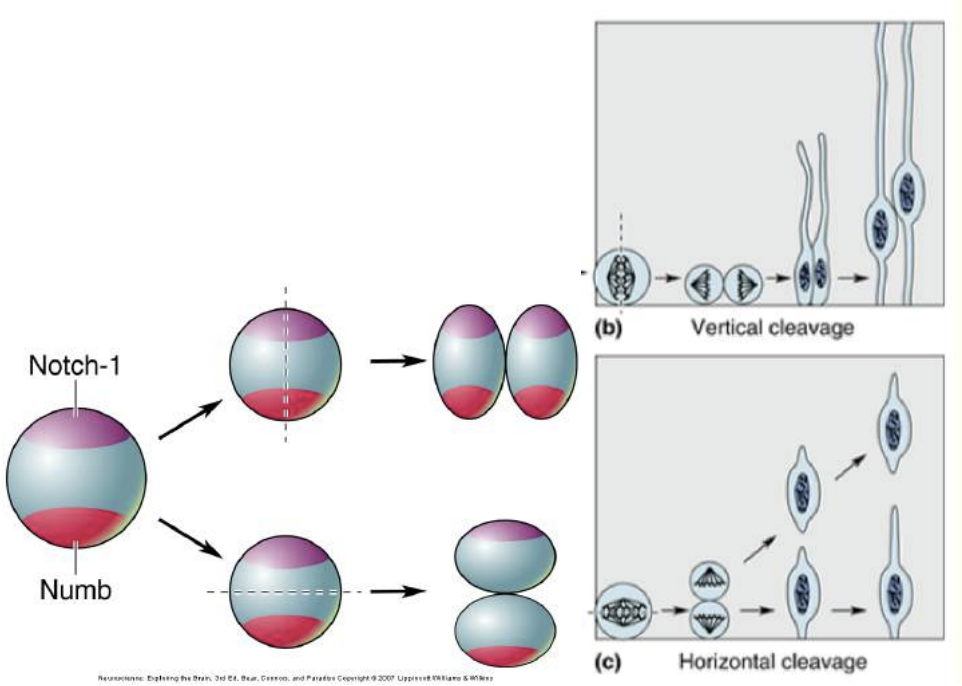
- Ventricular system: Form from cavity of neural tube
- Development of cortical convolutions w/ sulci and gyri post-natally

FATE OF EMBRYONIC LAYERS

- Ectoderm: Nervous system, skin, hair, nails
  - Neural tube: Neural stem cells → CNS
  - Neural crest:
    - PNS (Dorsal root ganglion cells, autonomic ganglia, cranial ganglia)
    - Glial cells of PNS (satellite cells, Schwann cells)
    - Epidermal pigment cells (skin)
    - Adrenal medulla
- Mesoderm: Bones, muscle e.g. gonads, kidneys
- Endoderm: Epithelial lining of organs + vessels e.g. gut/bladder, some organs e.g. liver/pancreas

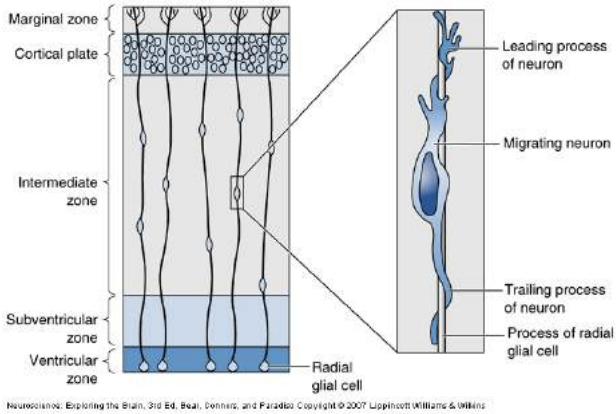
CELLULAR OVERVIEW OF BRAIN DEVELOPMENT

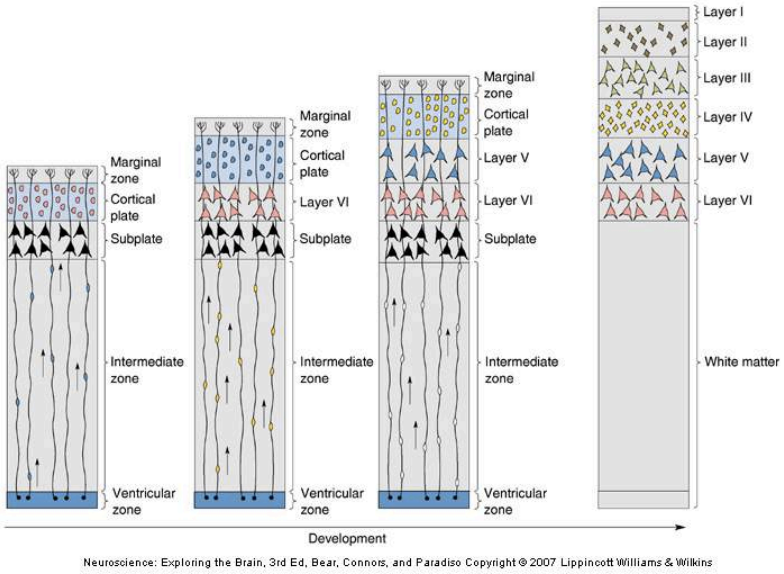
- Neuronal proliferation of neuroblasts (immature neurons) (5 weeks-5 months)



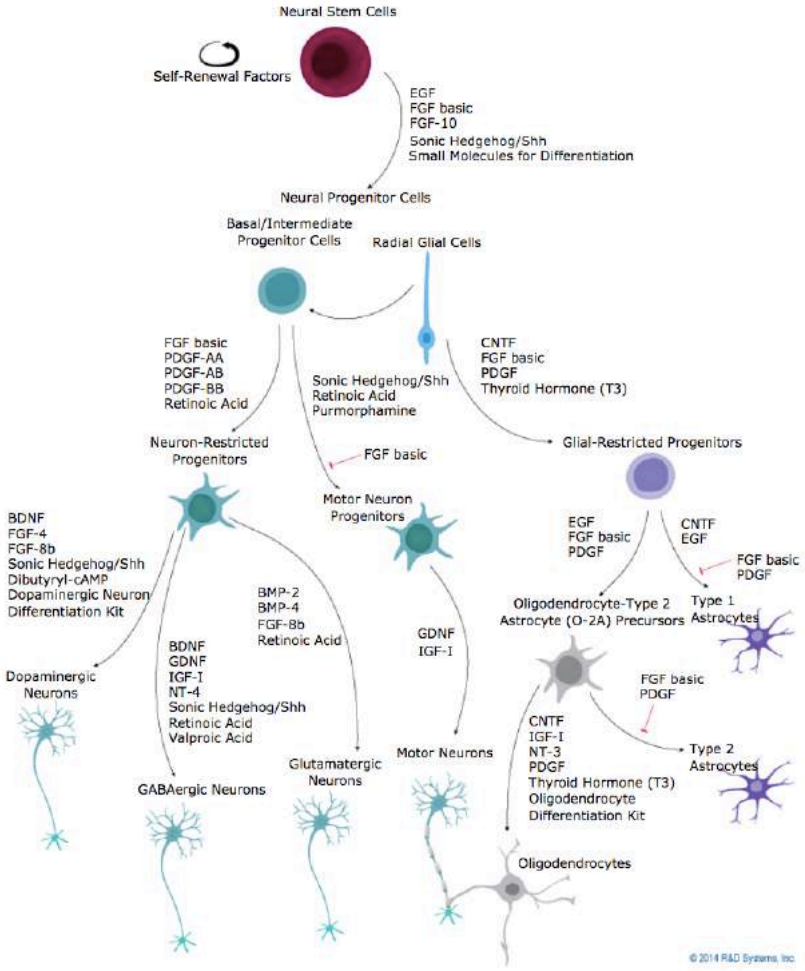
- Occur in ventricular zone – closest to cavity in neural tube
- Signalling molecules:
  - Notch-1: Closest to pial surface, causes migration
  - Numb: Inhibits Notch-1
- Early development (5 weeks – 3 months): Vertical cleavage
  - Daughter cells have both Notch-1 and Numb → can both proliferate (divide)
- Late development (3-5 months): Horizontal cleavage
  - Notch-1 cell migrates and stops dividing
    - As no Numb to inhibit it
  - Numb cell can further divide

- Neuronal migration:





    - Radial glial cells: Scaffold for neuroblasts to migrate
    - Inside-out development: Cortex develops from layer VI to I
        - Newer neuroblasts migrate past subplate and existing layers to cortical plate (forms layer VI to II)
        - Marginal zone becomes layer I
        - Subplate is removed
- Cellular differentiation (>5 months): Cells differentiate to specific type



- Glial cells + neurons from neural stem cells → neural progenitor cells
  - Neuroblasts/neuron-restricted progenitors: Neuronal fate
    - Further differentiation into dopaminergic/GABAergic/glutamatergic neurons…
  - Glial-restricted progenitors: Glia – Astrocytes/oligodendrocytes
    - Differentiation of astrocytes peak at birth
    - Oligodendrocytes differentiate post-natally
- Post-natal production of myelin w/ differentiation of oligodendrocytes
- Differentiation of cells based on diff combination of diff signaling molecules

BLOOD SUPPLY, MENINGES, VENTRICLES, CISTERNS

BLOOD SUPPLY