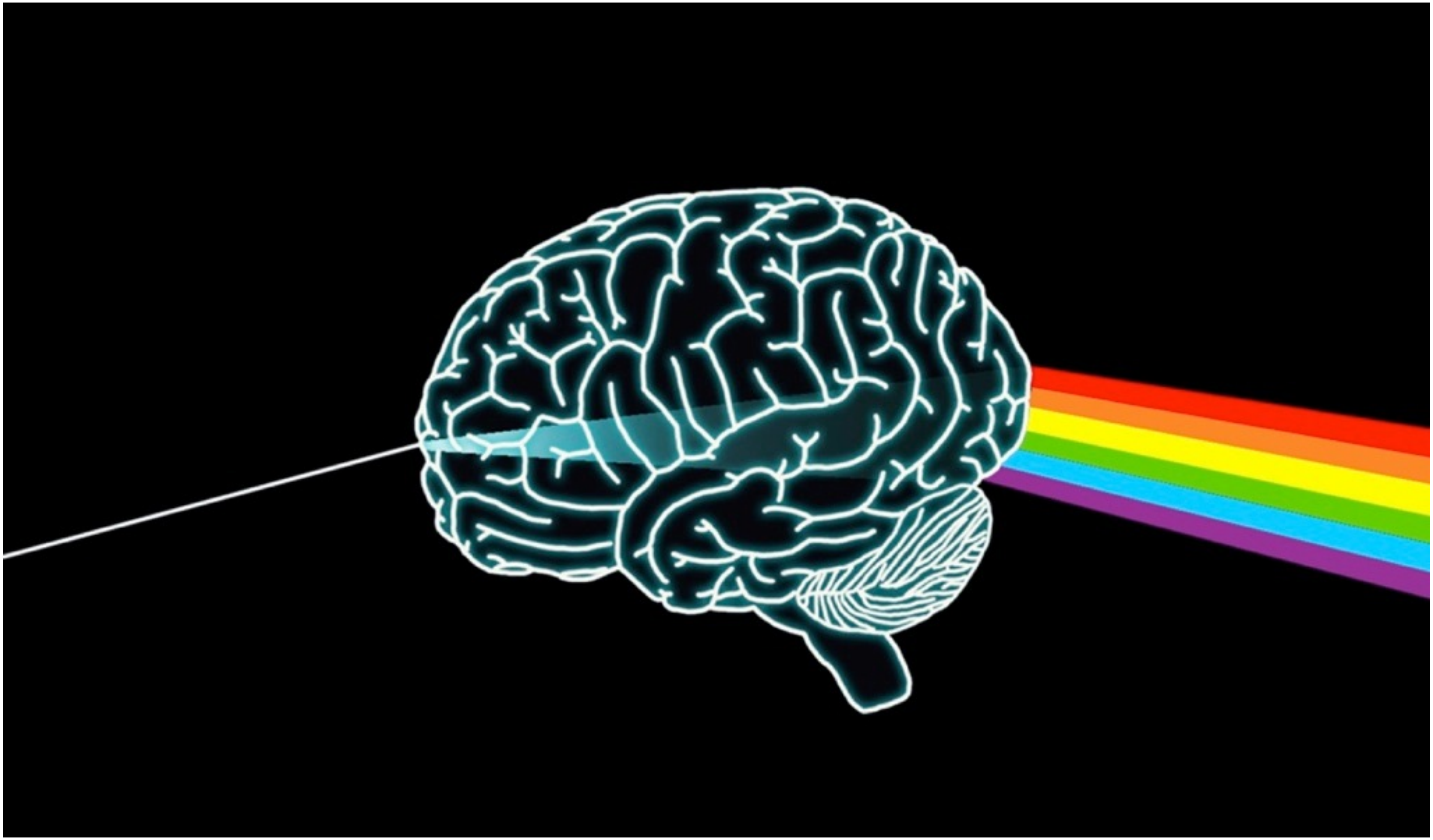
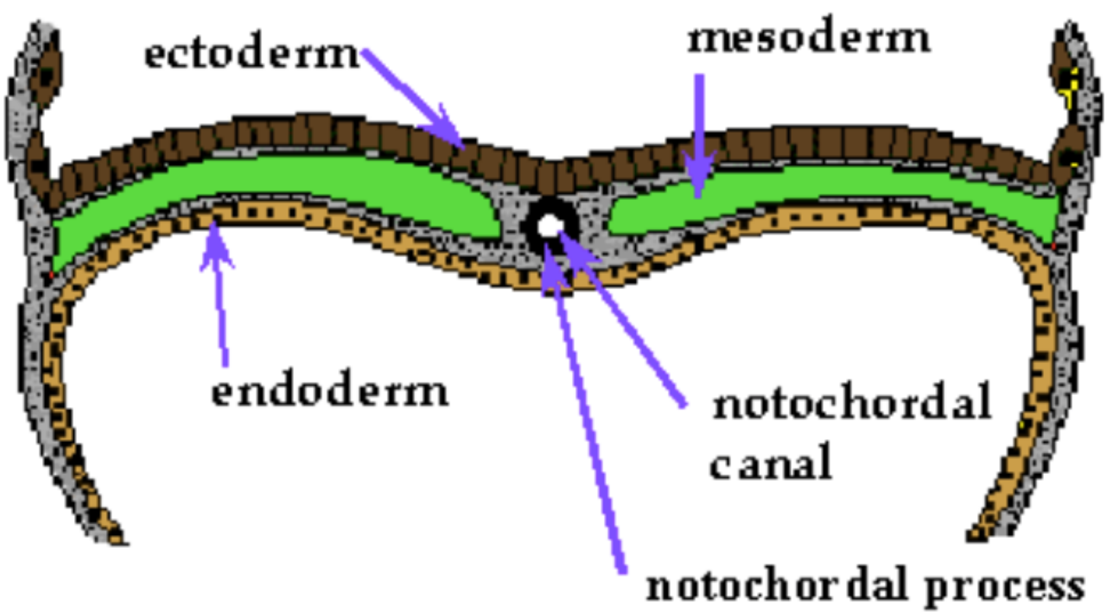
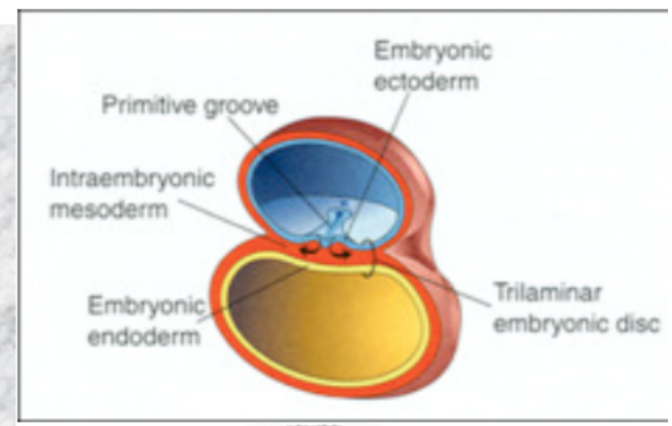
NEURODEVELOPMENT / SYNAPTIC PLASTICITY

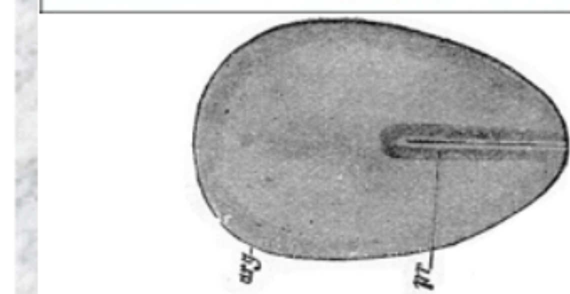


Development of the Nervous System – 1st month

- day 1 - fertilization of egg
- day 6 - uterine implantation
- day 18 - trilaminar (3-layered) disc (blastoderm, embryo) with a groove
    - medial-lateral, anterior-posterior, dorsal-ventral
  - ectoderm (outermost / dorsal) - nervous system and skin / hair / nails
  - mesoderm (middle) - connective tissue / muscle / vasculature
  - endoderm (ventral) - visceri (inner organs)

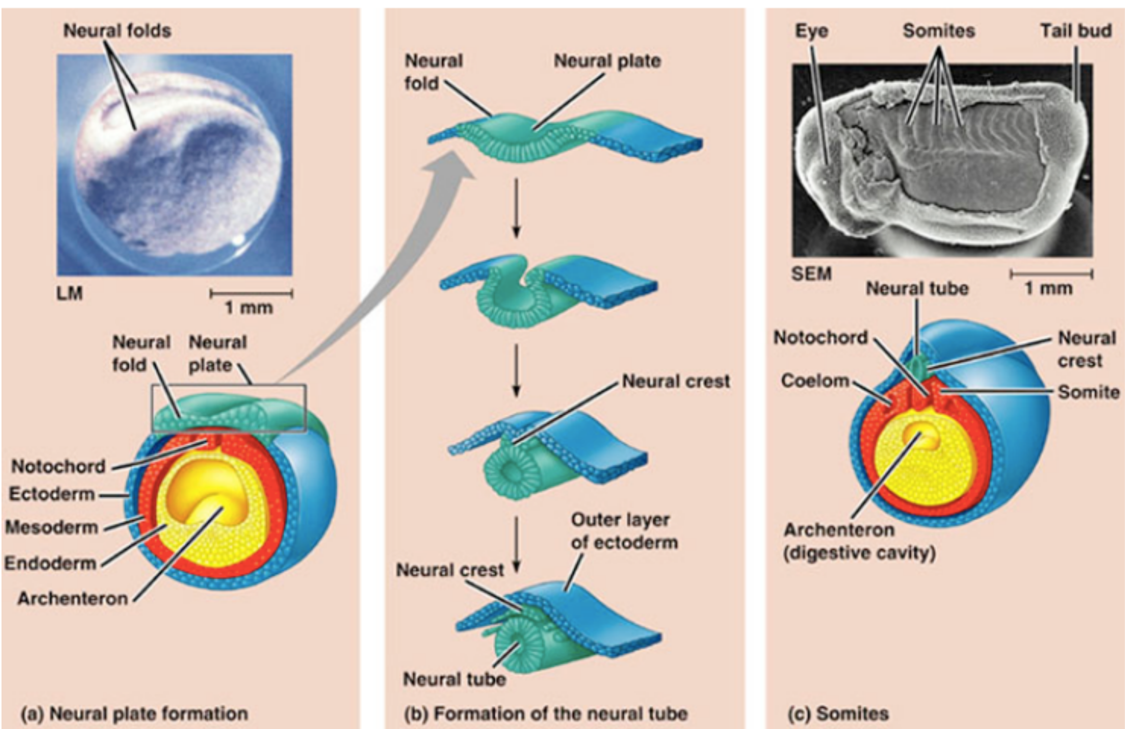


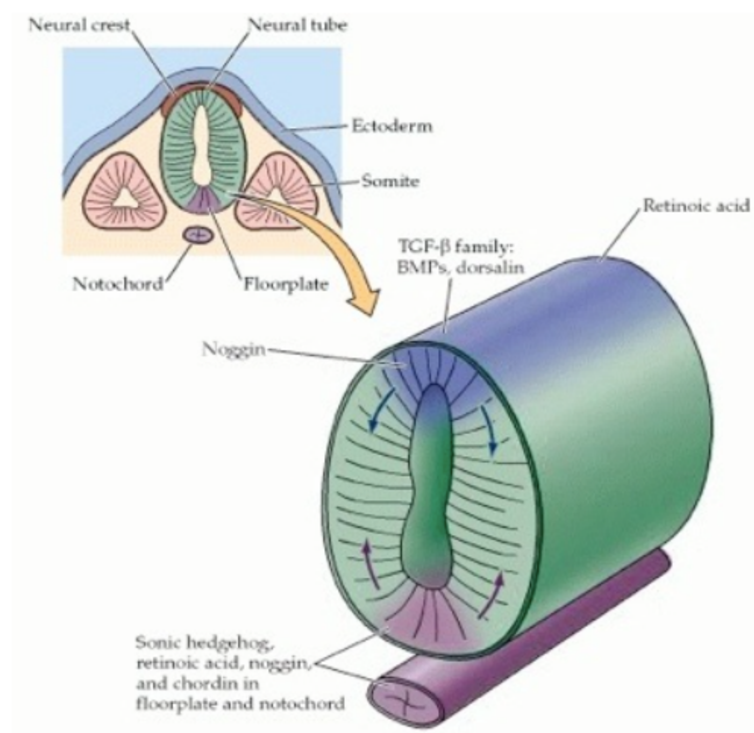




Development of the Nervous System – 1st 3 weeks

- day 18 - *neural induction*: midline of ectoderm differentiates into *neural plate* made of neuroepithelium cells (future CNS / PNS)
  - rest of ectoderm is *surface ectoderm*
    - CNS anomalies can often be assessed by certain severe birthmarks
- day 21 – *neurulation*: neural fold becomes neural tube (future CNS)
  - neural crest migrates away from tube (future PNS)

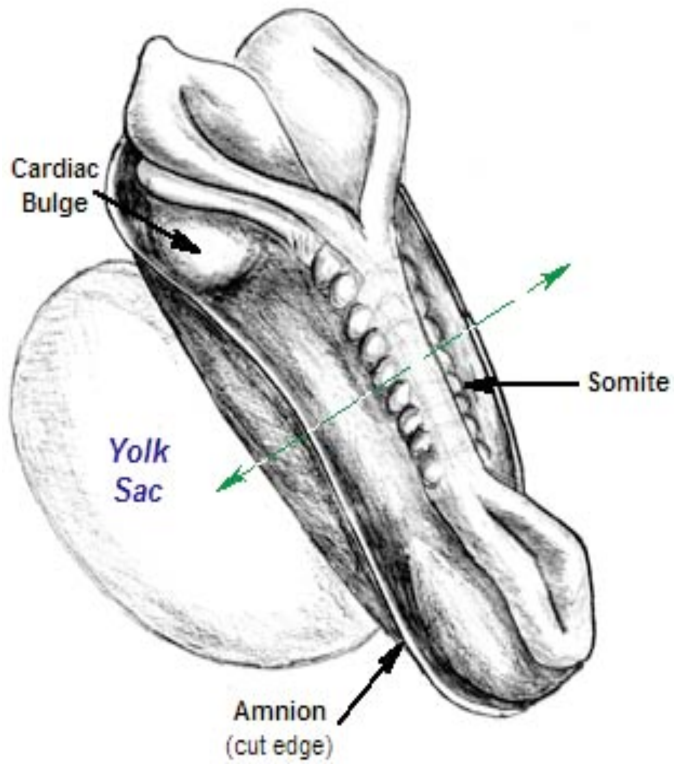


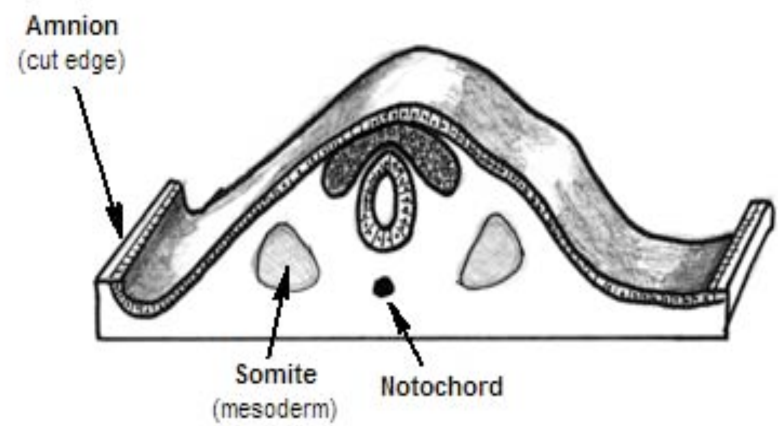


Development of the Nervous System – 1st 4 weeks

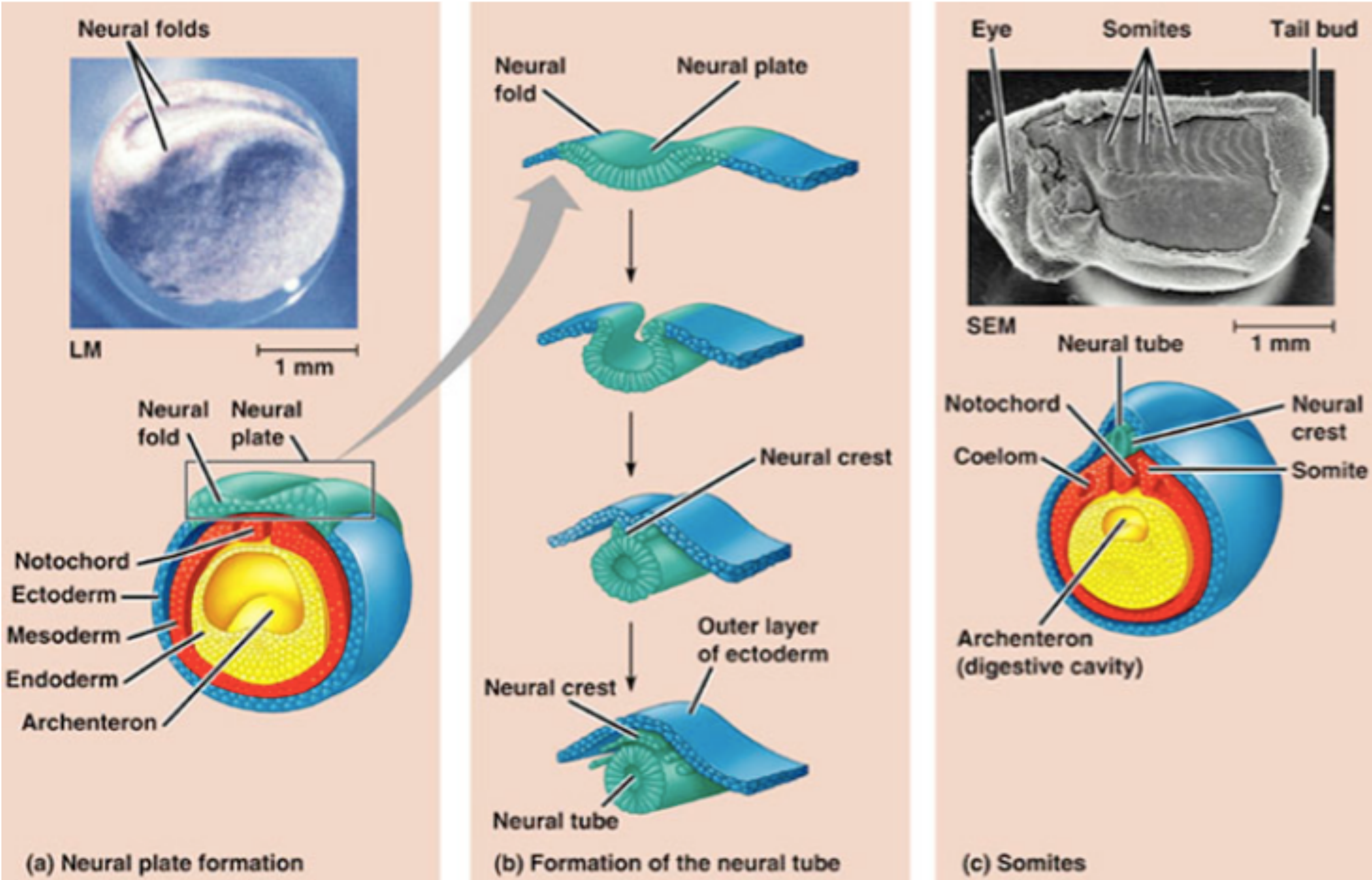
- day 22 - *cervical / medulla* neural tube closes (death)
- day 24 - *rostral* neural tube closes *(*brain / anencephaly)
- day 26 - *caudal* neural tube closes (spinal cord / spina bifida)
- day 28 - neural tube is completely closed
  - hollow part ("lumen") becomes ventricles and neural canal

22 days
Approx 3 mm



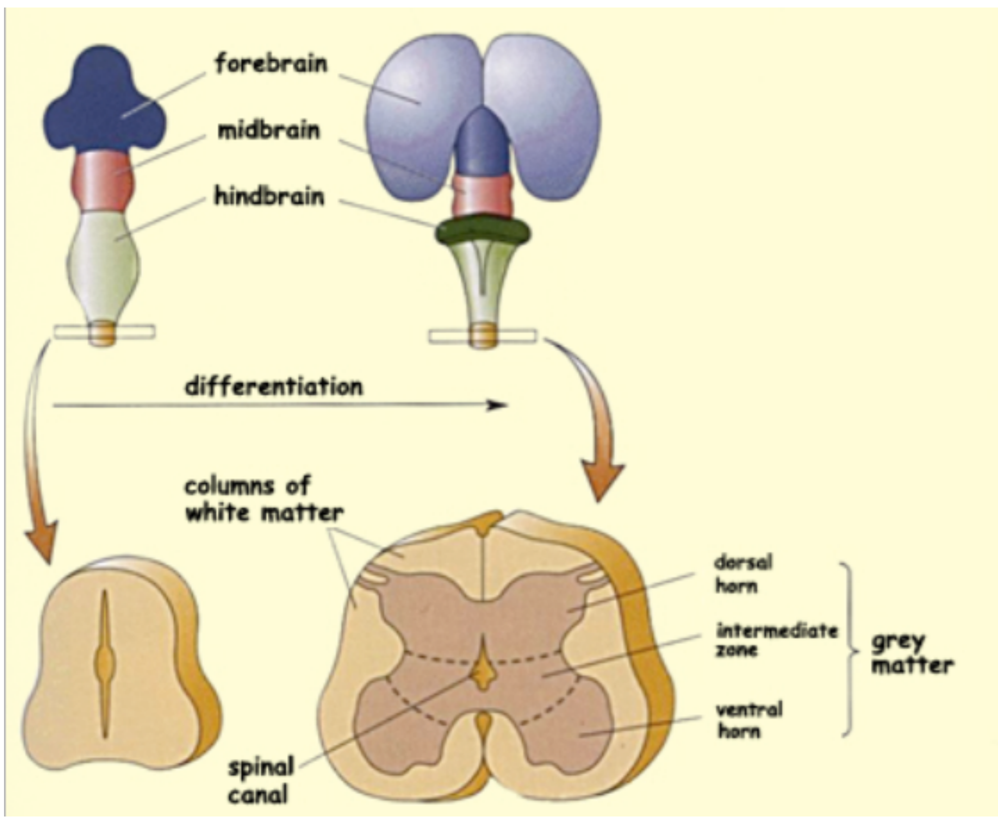


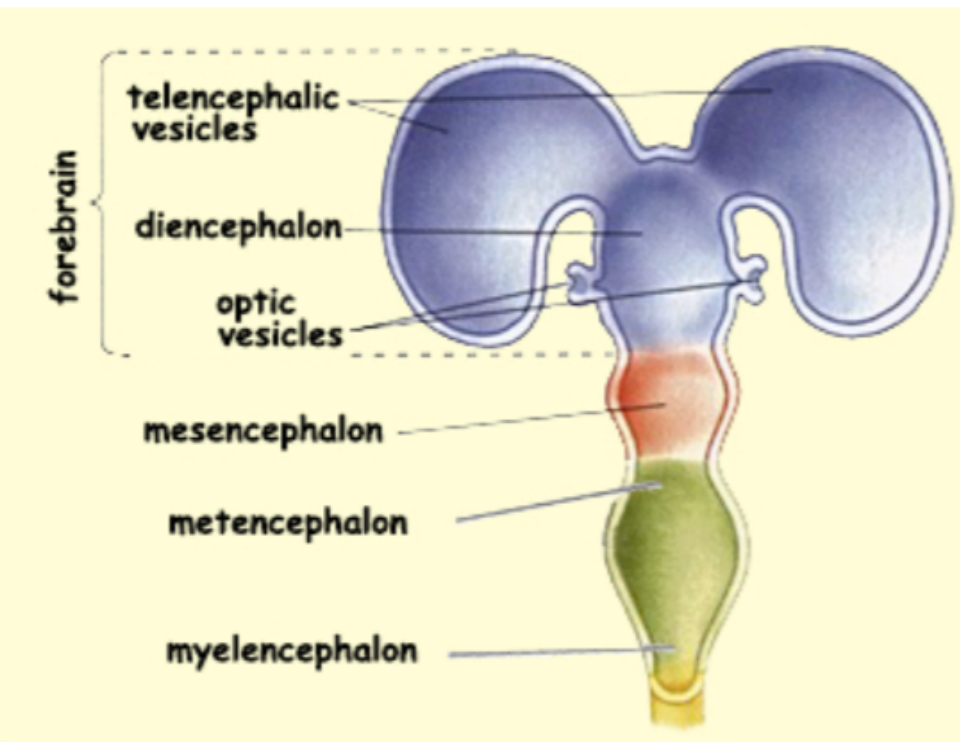
Development of the Nervous System – 1st 4 weeks



Development of the Nervous System – 1st 4 weeks

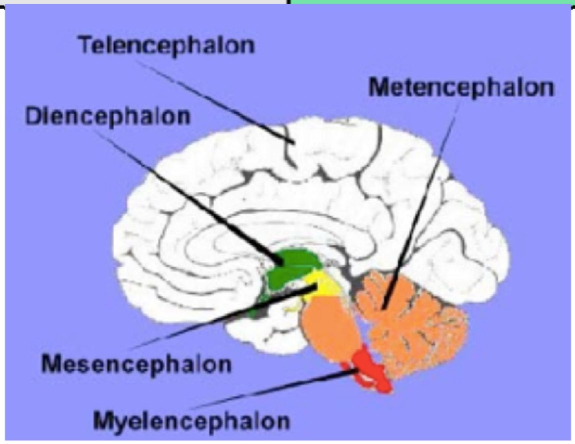
- Neural tube undergoes a series of folds & growth spurts (guided by gene expression)
  - rostral end of tube has 3 chambers (future *ventricles*)
    - surrounding tissue becomes
      - forebrain - telencephalon & diencephalon / lateral & 3rd ventricles
      - midbrain - mesencephalon / cerebral aqueduct
      - hindbrain - metencephalon & myelencephalon / 4th ventricle
  - caudal end of tube becomes spinal cord / central canal





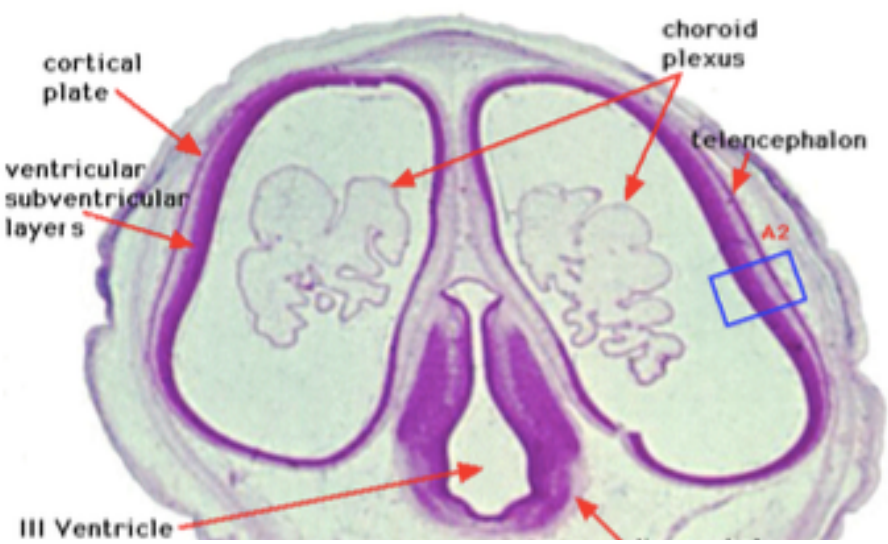
Development of the Nervous System

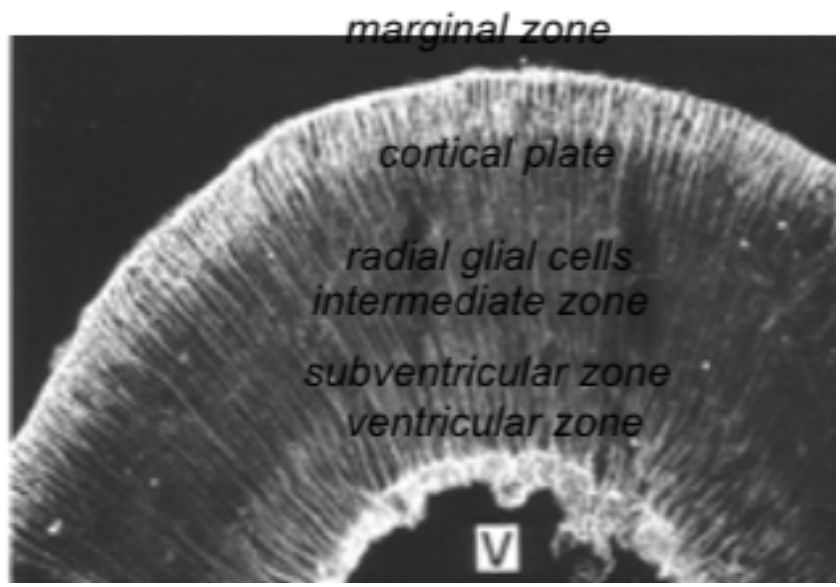
Forebrain	Lateral	Telencephalon	Cerebral cortex
			Basal ganglia
			Limbic system
	Third	Diencephalon	Thalamus
			Hypothalamus
Midbrain	Cerebral aqueduct	Mesencephalon	Tectum Tegmentum
Hindbrain	Fourth	Metencephalon	Cerebellum
			Pons
		Myelencephalon	Medulla oblongata



Development of the Nervous System

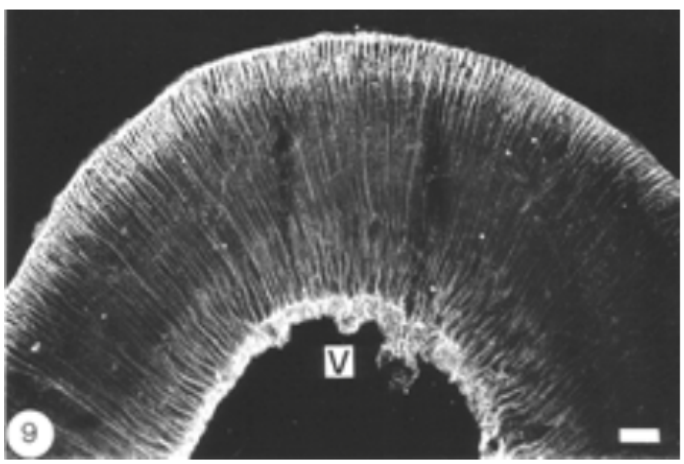
- Neurons not "born" until neural tube closes
  - ventricular zone - founder / neuroepithelial / germinal / stem cells
    - line the inside of the neural tube
    - become neurons (large projection) & glial cells
      - dorsal (sensory)
      - ventral (motor)
        - skeletal (alpha) motor neurons are among the 1st formed
          - we can ACT before we can REACT

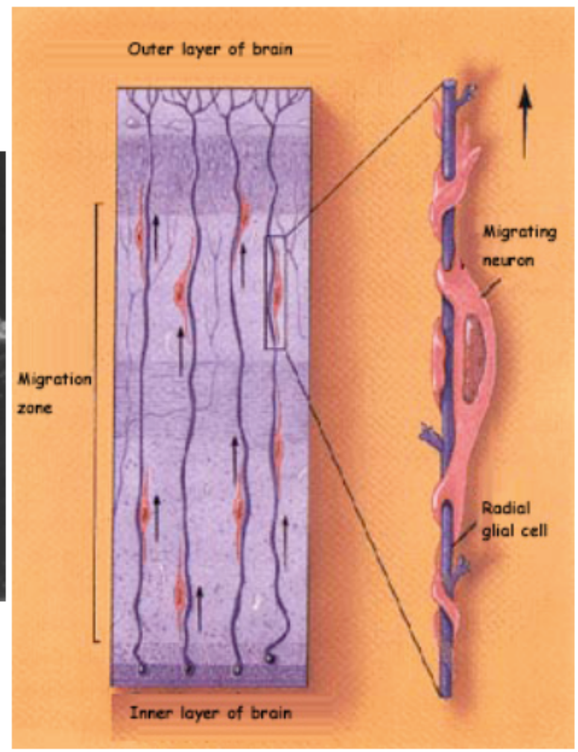


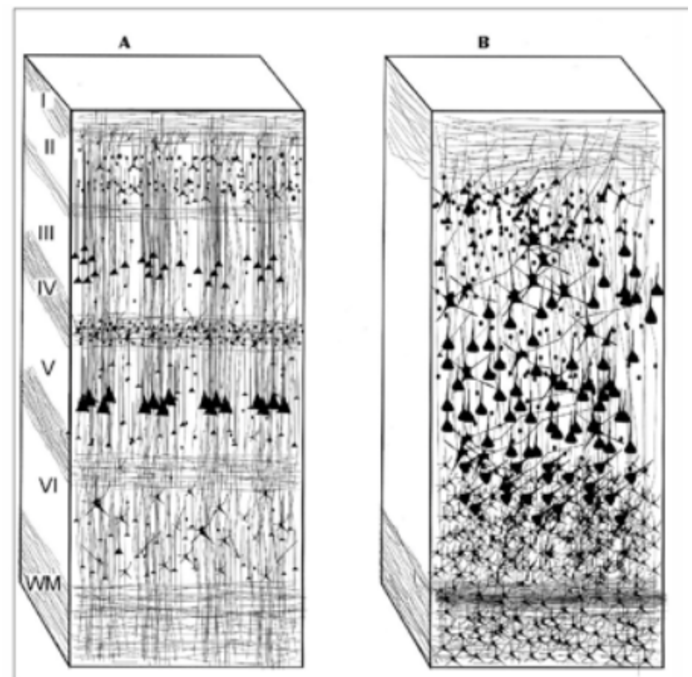


Neural Proliferation and Aggregation

- *radial glial cells* extend through intermediate zone (from ventricular to marginal zones)
- *founder* cells give rise to *neuroblasts* (baby neurons)
  - climb up the pole to form cortex and subcortical structures
- cortical layers form *inside to outside*
- neurons stop (*aggregate*) at layer 6 1st, layer 5 next, layer 4, etc
  - ~1 billion neurons migrating at any 1 time for ~ 3 months







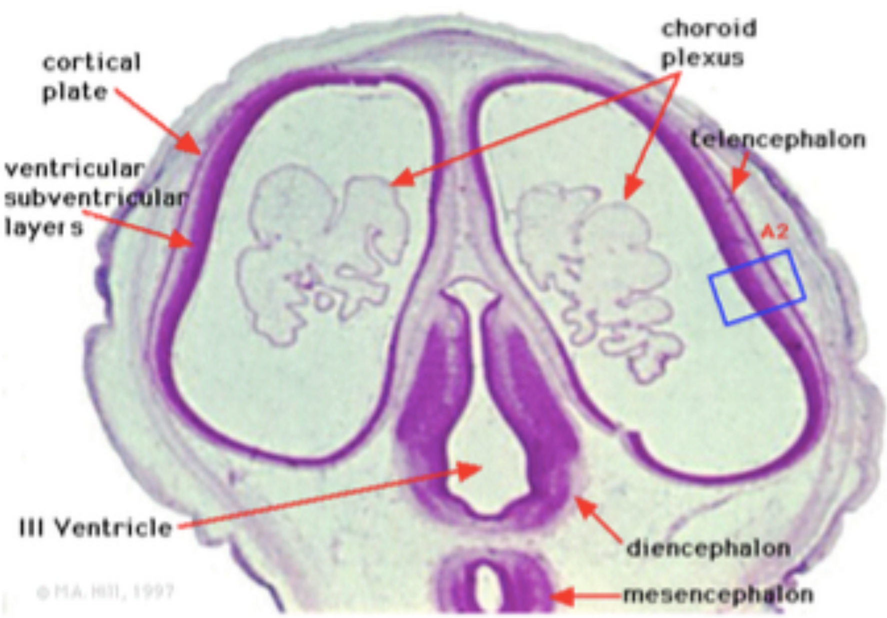
ectopic migration

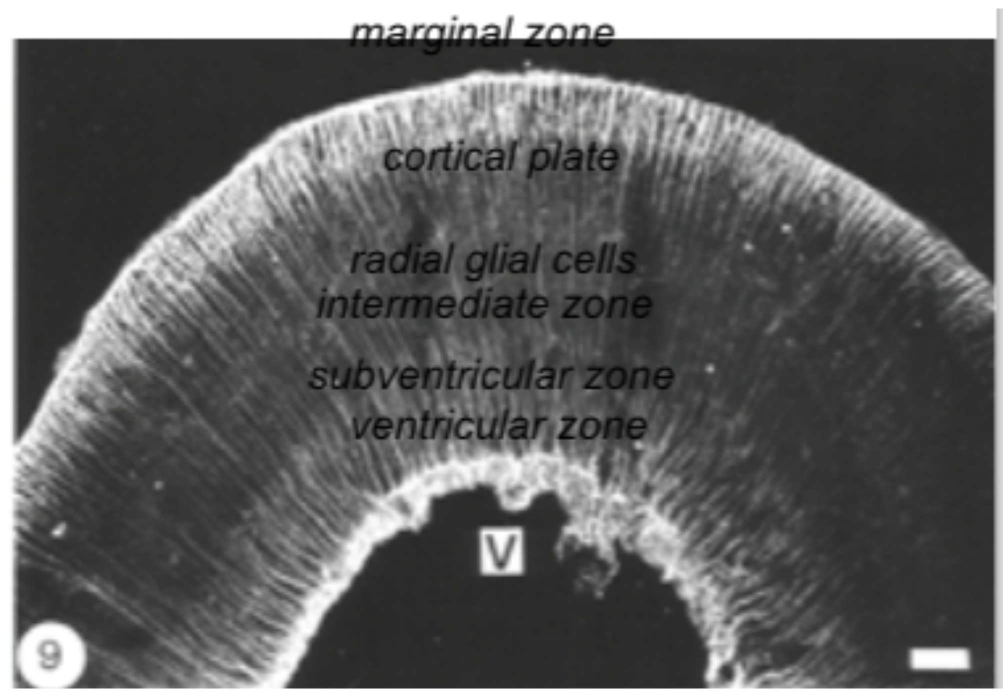
Neural Proliferation and Aggregation

- ventricular zone stops proliferating at about 4 months, turning into *ependymal* cells that line the ventricles

  - subventricular zone becomes the new germinal zone, forming small interneurons (and glial cells throughout life)

- marginal zone - outside of tube (next to pia mater)



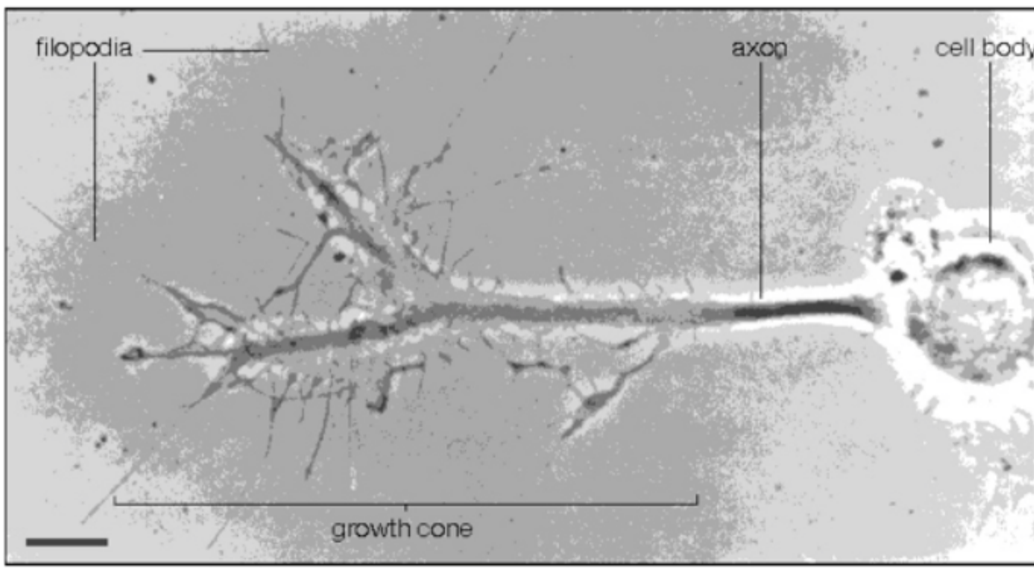


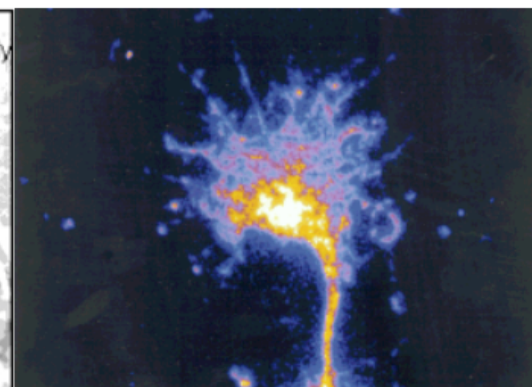
Neural Proliferation and Aggregation

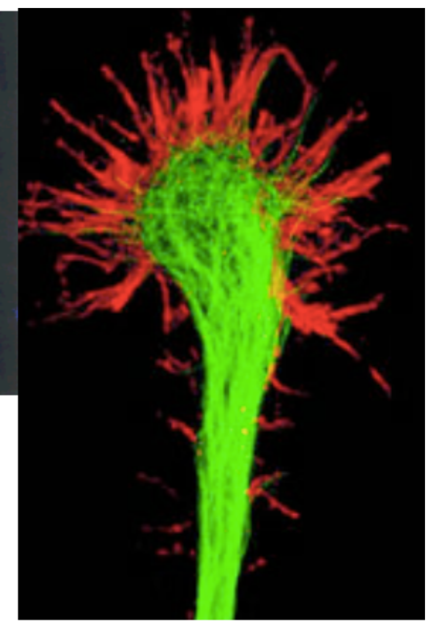
- *aggregation* determined by timing, genetics, and electrochemical signals
  - voltage pulsations (“activity dependence”)
  - neurotrophic factors (e.g., NGF / BDNF)
  - neurotransmitters
  - cell surface molecules (like with like)
  - “chaotic” self-organizing randomness
- radial glial cells later become astrocytes

Neural Growth

- after aggregation, neurons start to grow
- axons generally precede dendrites (act before react)
- axon's "growth cone" (initial growth of axon, ~1st 50μ) is under genetic control, then electrochemical factors







Synaptogenesis

- 3rd trimester through a couple of years
- at first, there is physical contact between pre- (former filopodia) & post-synaptic membranes
- contact initiates formation of postsynaptic receptors and presynaptic NT vesicles
- axon can retreat if trophic factors are not sufficient
- occurs throughout life
- microcircuitry (about 95% of synapses) develop through structure-function interactions rather than predetermined genetic unfolding

Pruning / Parcellation

- too many synapses are made at first
  - followed by withdrawal / elimination of inappropriate ones (up to 90%)
    - “pruning”
      - Like topiary for neural pathways
- groups of similar / close neuronal axons *cooperate* to *compete* with other groups of axons for limited trophic factors
- foundation of basic neural networks

Pruning / Parcellation

- *Parcellation* in development
  - early in development, there is a multiple, overlapping innervation pattern
  - stimulation of a young baby will result in a “mass action” type of response
  - as the nervous system develops, it becomes more compartmentalized, allowing for *fractionation* of responses

Apoptosis

- newborn's brain is ~25% of adult weight (.75 vs. 3 lbs)
  - but more neurons than adult brain
- neurons that don't form enough connections (~50-80%) die off via "programmed cell death" (*apoptosis*)
  - "selective" neuronal death
  - unable to attain trophic substances
- late fetal period - ~2 year postnatal
- depressant drugs can induce "turn off" neurons and induce apoptosis in early development

- in certain areas of the brain, neurogenesis continues throughout life
  - learning

Maturation / Myelination

- *myelination* - rough index of maturation (~parallels walking ability)
    - begins following proliferation (axon doesn't have to be fully developed for myelin to start growing)
    - starts at axon hillock
        - CNS - oligodendrocytes
        - PNS - Schwann cells
    - motor cells first
    - intracortical connections last

Critical Periods

- *critical periods* are irreversible “decision-points” when neurons become committed to one or another pathway of differentiation
    - e.g., language / perfect pitch before 6 years old
- monkeys raised in the dark for 3-6 months are deficient in form recognition
    - peak of visual critical period is 1st 6 weeks
    - 1 week of deprivation almost totally vetoes perceptual ability
        - cells in retina and LGN respond normally, but not cortical cells

Critical Periods

- so, normal development of "perception" generally requires early exposure to that stimulus
  - Similar for motor systems:
    - a monkey trained to use only its middle 3 fingers will eventually have modified topographic maps in the primary somatosensory AND primary motor homunculi
      - larger areas for the 3 fingers & less for the other 2
      - no more or less neurons, just different connections
- early experiences can have a major impact on adult behavior / capabilities

Critical Periods

- Gender development:
  - Gender differences in the adult brain
  - default pathway is “female”
    - spectrum, from very “masculinized” to very “feminized”
- effects of sexual hormones:
  - early - organizational
  - adolescence - activational

Neuroplasticity vs. neurostability

- neuroplasticity = nervous system’s ability to adapt
  - Changes in neural organization leading to short- or long-lasting / enduring behavior modification
    - From:
      - Maturation
      - Adaptation to environment
      - Learning
      - Compensatory adjustment to loss of function due to aging / injury

Neuroplasticity vs. neurostability

- Makes us adaptable - we are the most adaptable organism that we know of
  - As opposed to a very neurostable animal (e.g., turtle)
    - Born ready to go, but behavior is severely messed up by any small environmental change