Brain development: from an egg to a brain

3 phases of prenatal development

Germinal Period – **(Period of the zygote)**

conception ➔ implantation

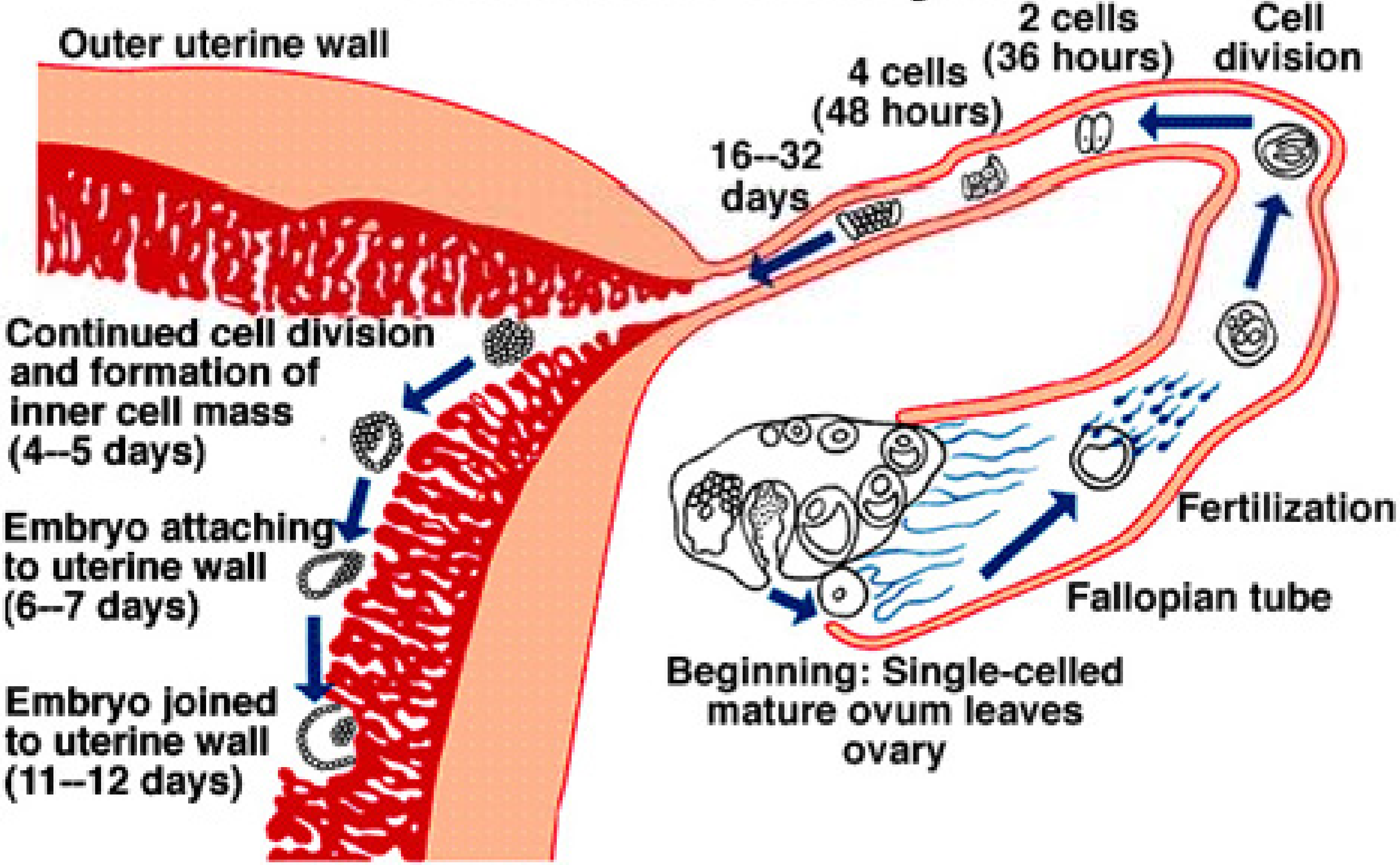
Period of the Embryo

beginning of 3rd week ➔ end of 8th

Period of the fetus

9th week ➔ child is born

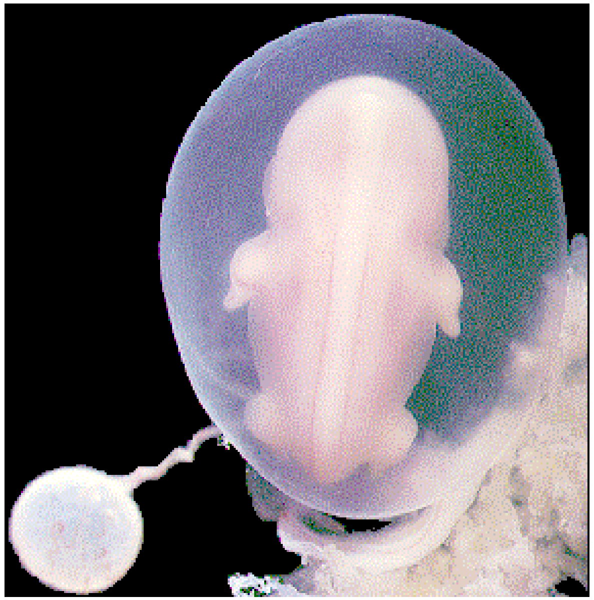
Early Development of a Human Embryo



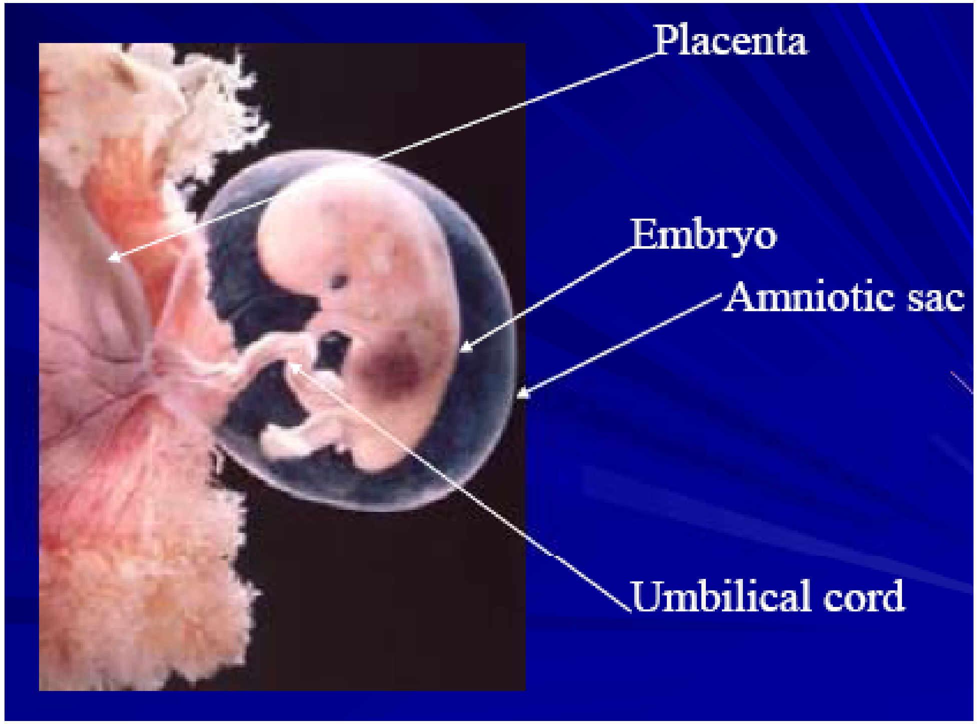
Embryonic Period
Week 3 & 4

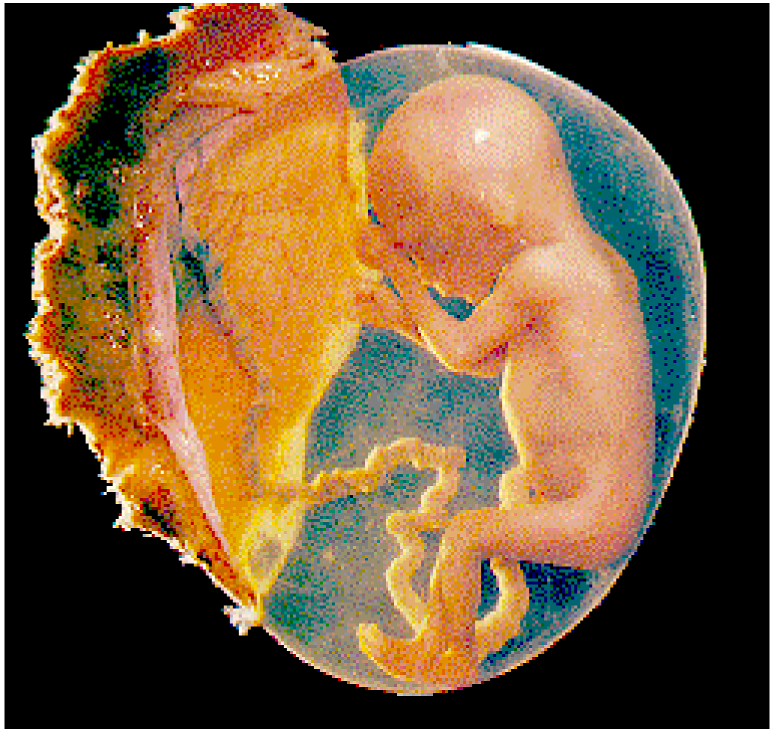
Embryonic Development
Week 5

Embryonic Development
Week 6 - 8

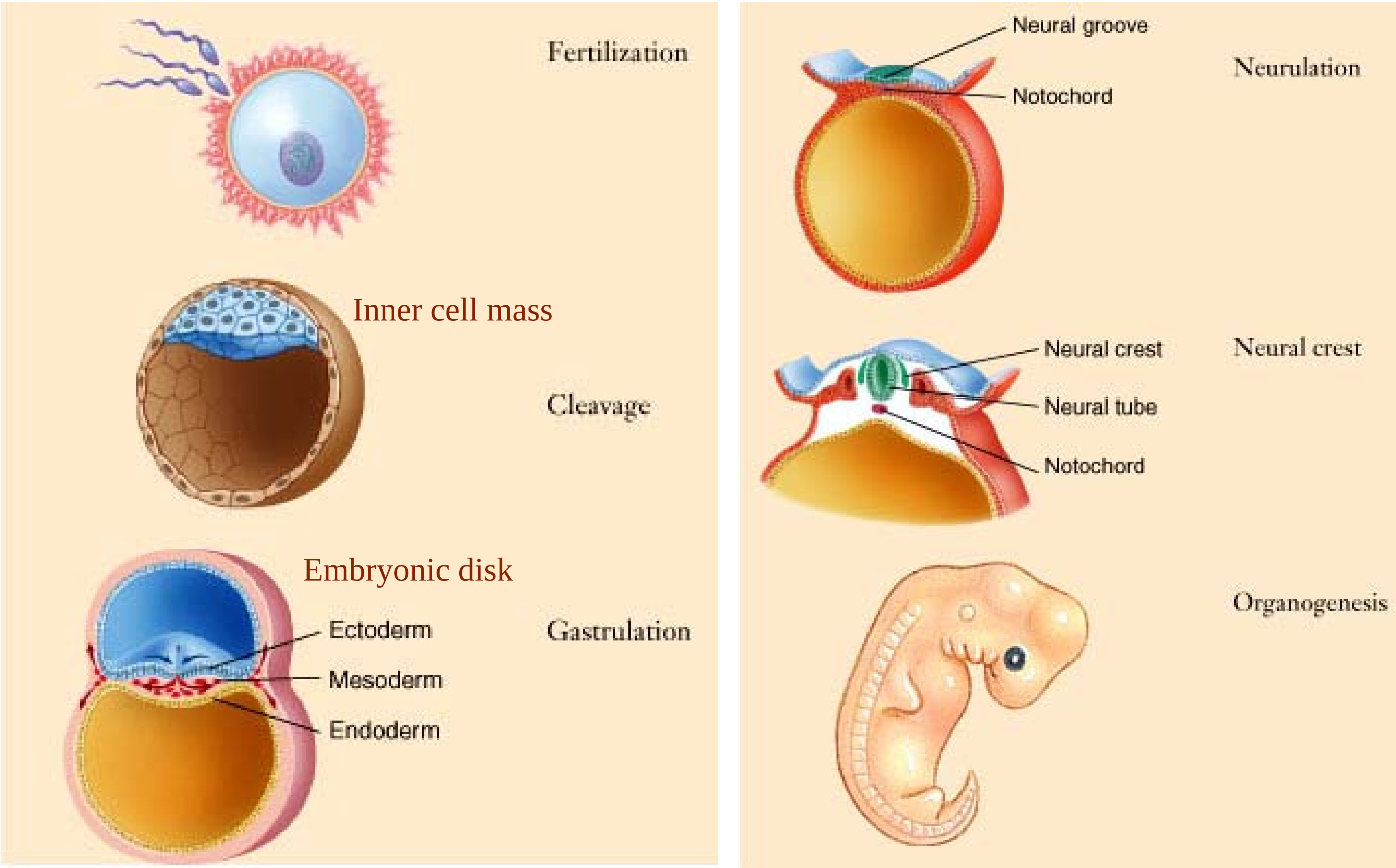


The Fetus
Week 16



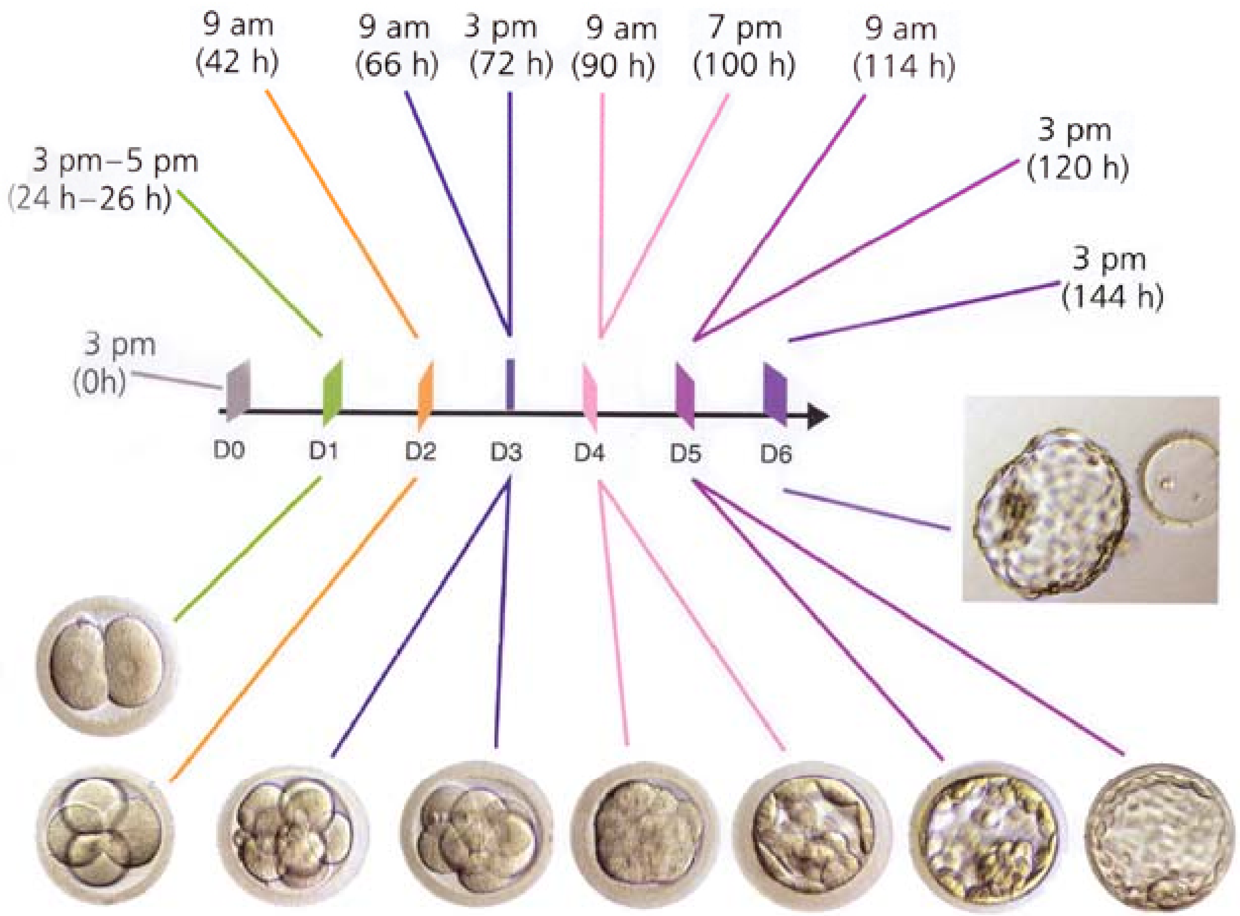


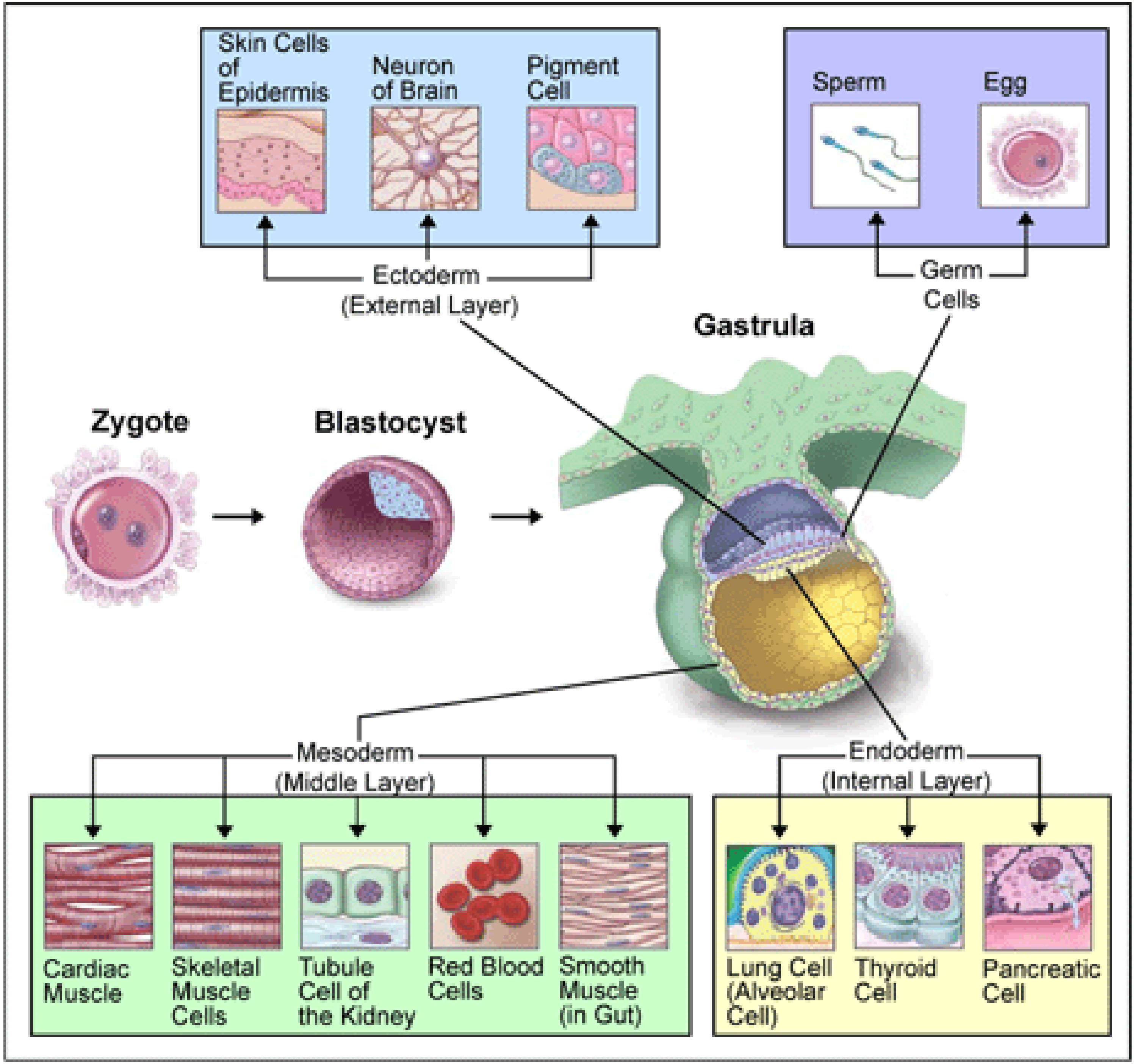
Stages of Development

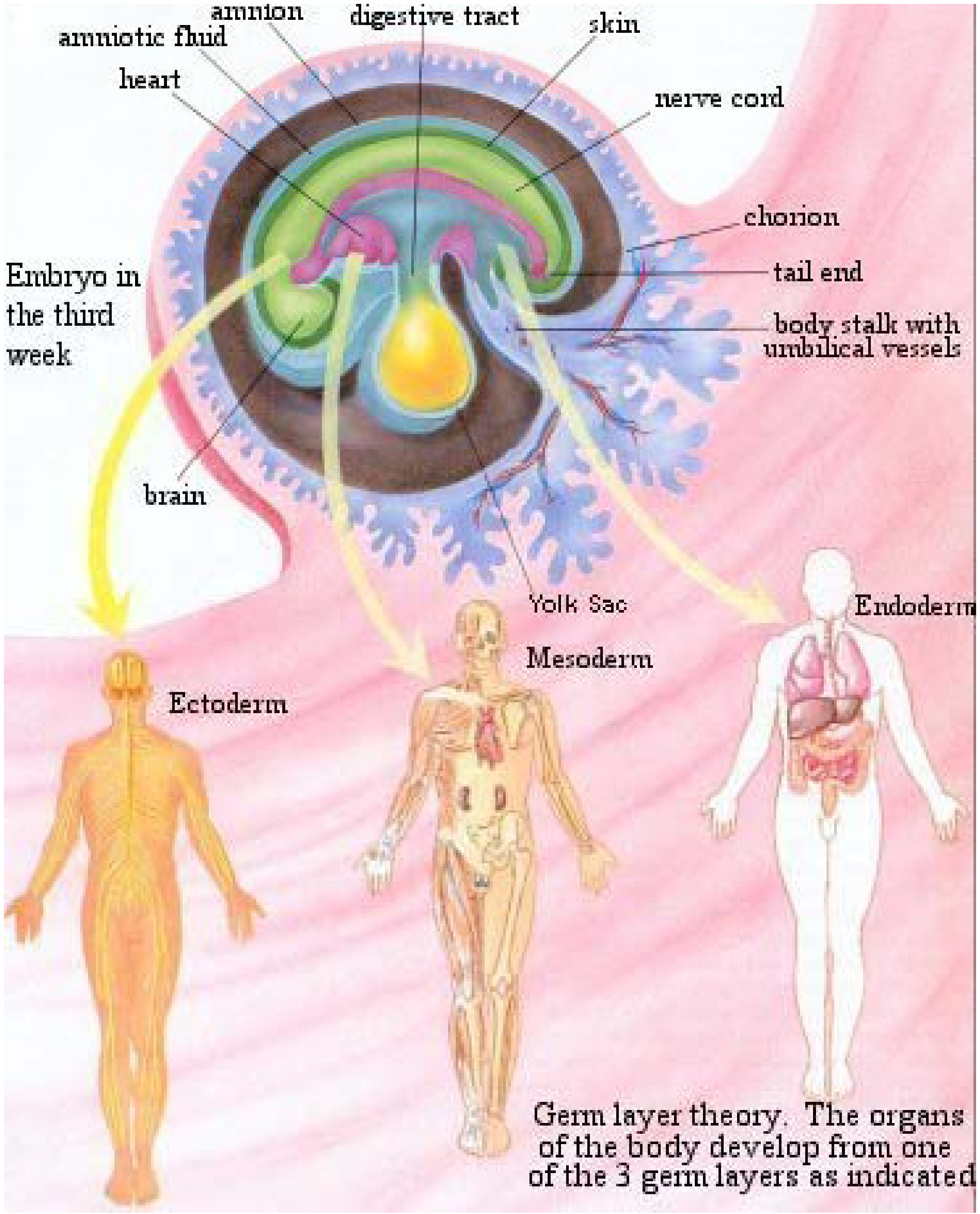


http://embryology.med.unsw.edu.au/embryo.htm

Development of stage 2 (morula) and stage 3 (blastocyst) embryos




Skin Cells of Epidermis
Neuron of Brain
Pigment Cell
Sperm
Egg
Ectoderm (External Layer)
Germ Cells
Gastrula
Zygote
Blastocyst
Mesoderm (Middle Layer)
Endoderm (Internal Layer)
Cardiac Muscle
Skeletal Muscle Cells
Tubule Cell of the Kidney
Red Blood Cells
Smooth Muscle (in Gut)
Lung Cell (Alveolar Cell)
Thyroid Cell
Pancreatic Cell


amnion
digestive tract
skin
amniotic fluid
heart
nerve cord
chorion
tail end
body stalk with umbilical vessels
Embryo in the third week
brain
Yolk Sac
Endoderm
Mesoderm
Ectoderm
Germ layer theory. The organs of the body develop from one of the 3 germ layers as indicated

Neurulation

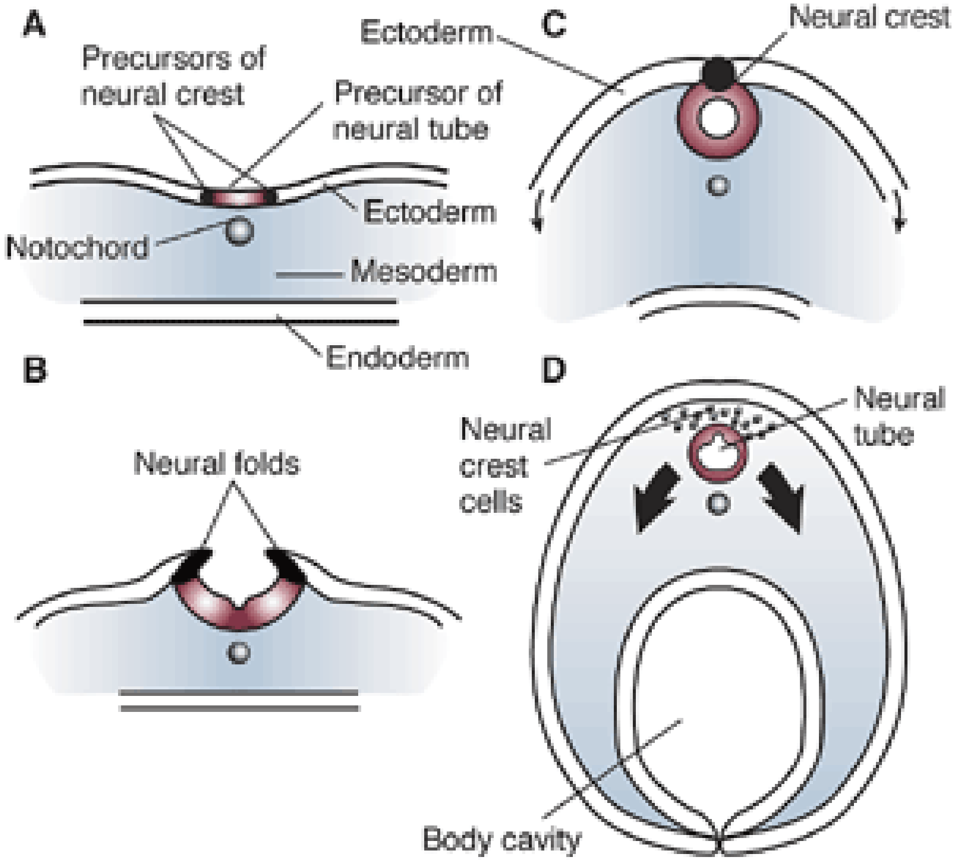
Neurulation includes the ***formation*** of the ***neural*** plate (day 18-19), ***neural*** folds (day 20-21), and the ***neural tube*** (day 22-26)

The ectoderm layer (outermost layer) of the fertilized egg folds and fuses to form the neural tube surrounding a fluid-filled cavity

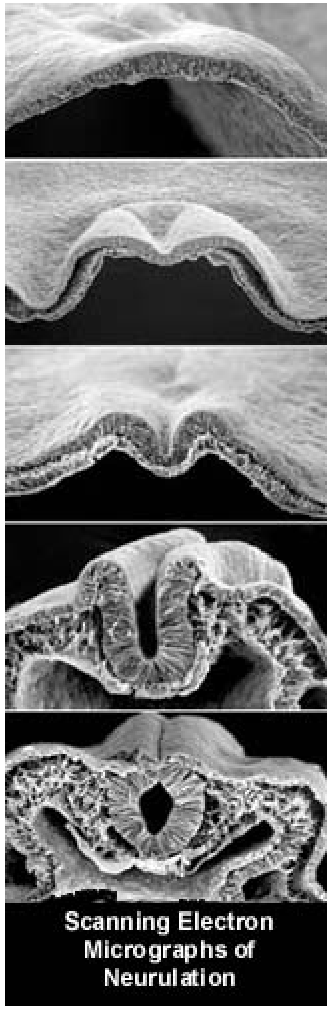
The open ends of the neural tube close around 25 days, with anterior regions giving rise to the brain, and posterior the spinal cord.

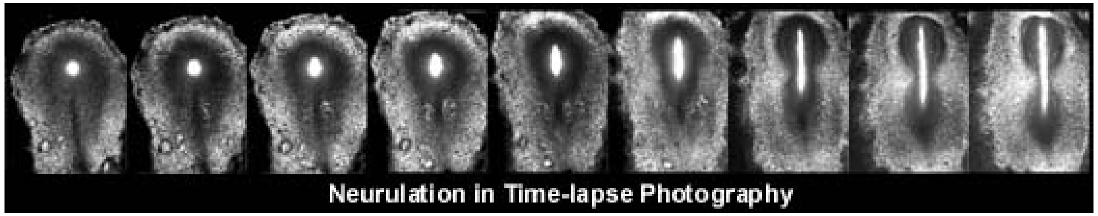
The cavity gives rise to the ventricular system, and the cells lining the cavity create the neurons and glia.

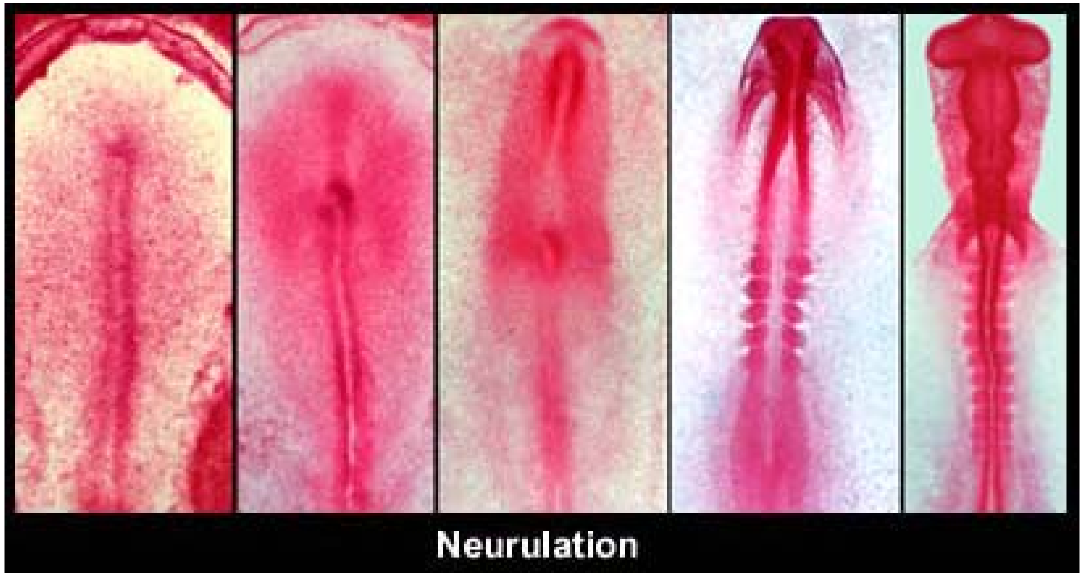
Formation of the neural tube (cross view).



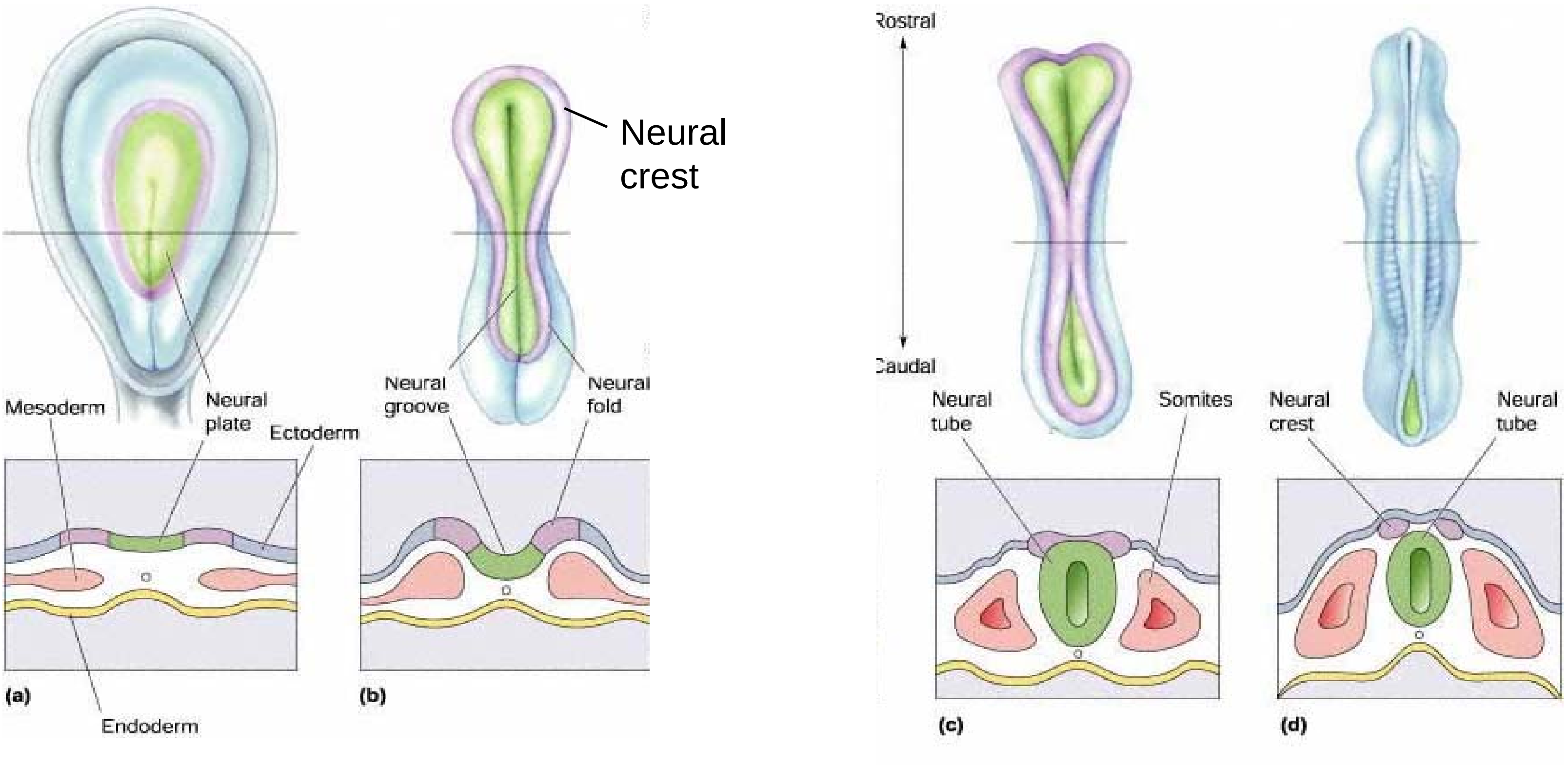
■ A strip of specialized cells called the notochord (A) induces the cells of the ectoderm directly above it to become the primitive nervous system (i.e., neuroepithelium).
■ The neuroepithelium then wrinkles and folds over (B).
■ As the tips of the folds fuse together, a hollow tube (i.e., the neural tube) forms (C).
■ Meanwhile, the ectoderm and endoderm continue to curve around and fuse beneath the embryo to create the body cavity, completing the transformation of the embryo from a flattened disk to a three–dimensional body.
■ Cells originating from the fused tips of the neuroectoderm (i.e., neural crest cells) migrate to various locations throughout the embryo, where they will initiate the development of diverse body structures (D).





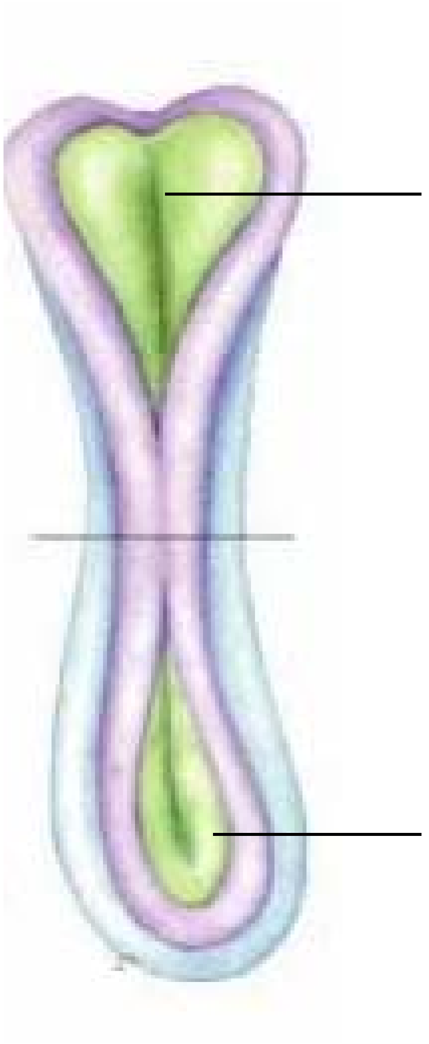


http://teratology.org/jfs/Schoenwolf.html



Neural crest becomes peripheral nervous system (PNS)
Neural tube becomes central nervous system (CNS)
Somites become spinal vertebrae.

Neural Tube Related Birth Defects



failure to close = anencephaly

failure to close = spina bifida

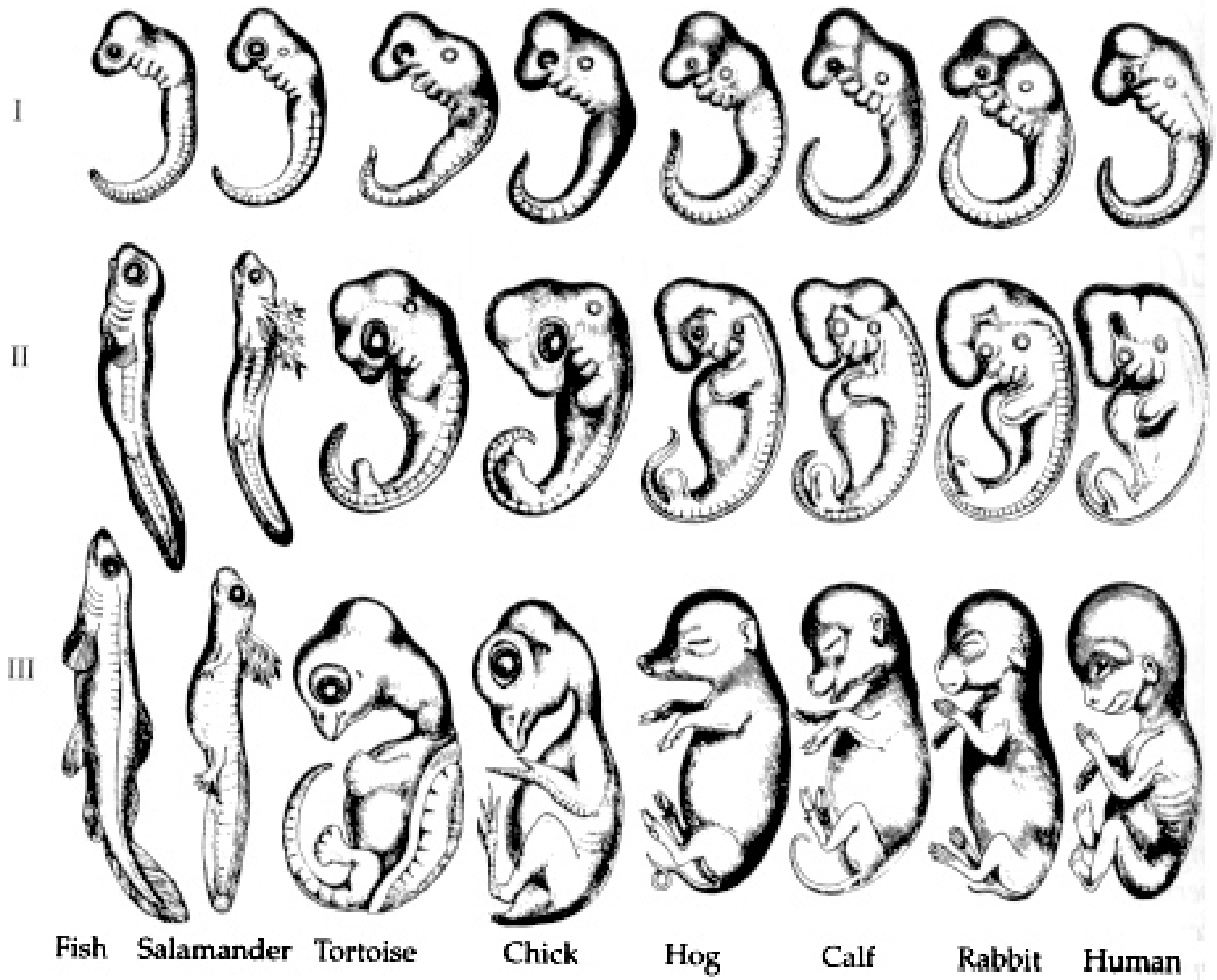
Human brain development reflects evolution?

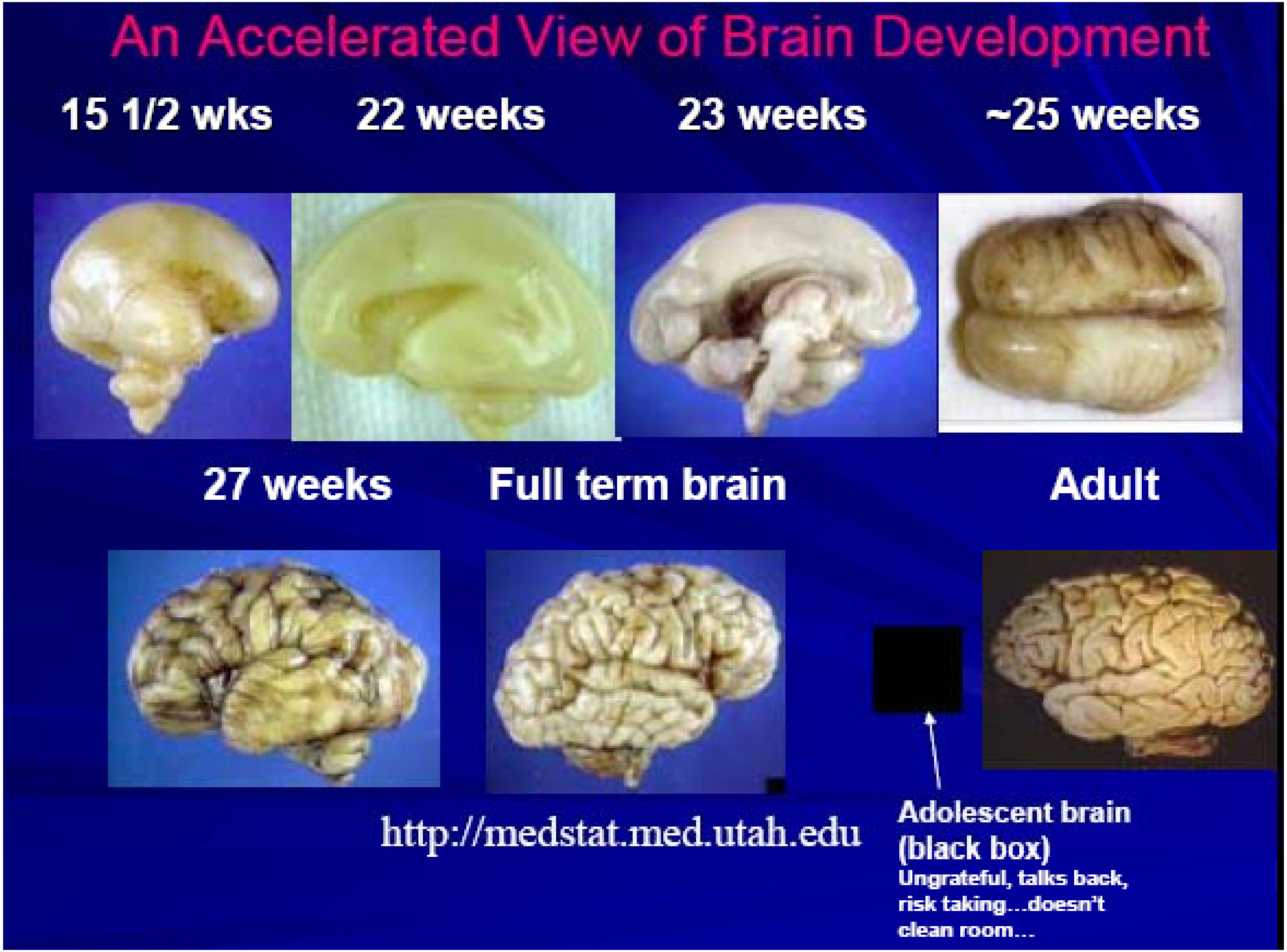
brains of reptile, fish, bird, rat, cat, higher animals,
primates, and finally human
(ontogeny reflects phylogeny)

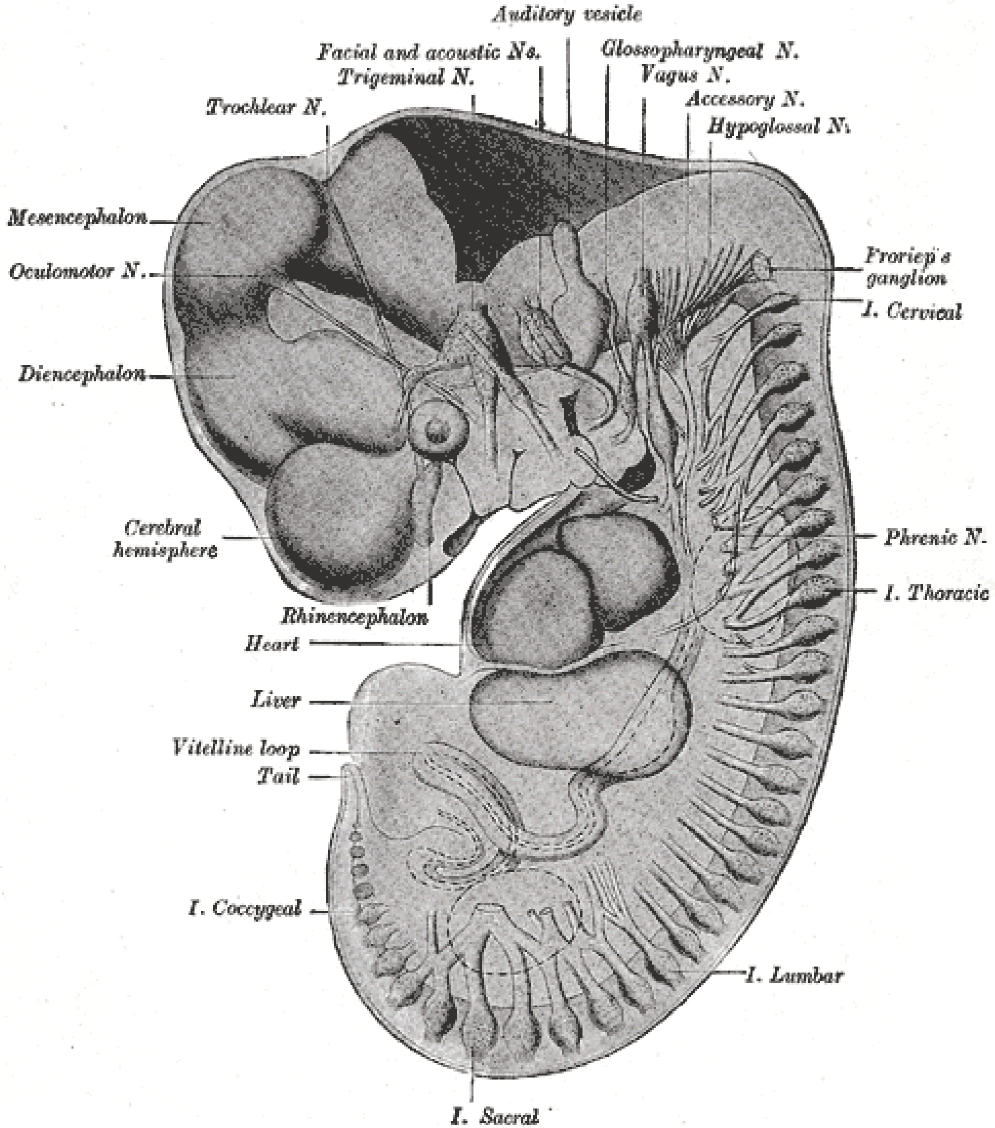
immature cortex at different stages resemble
that of other species

development of a wrinkled cortex

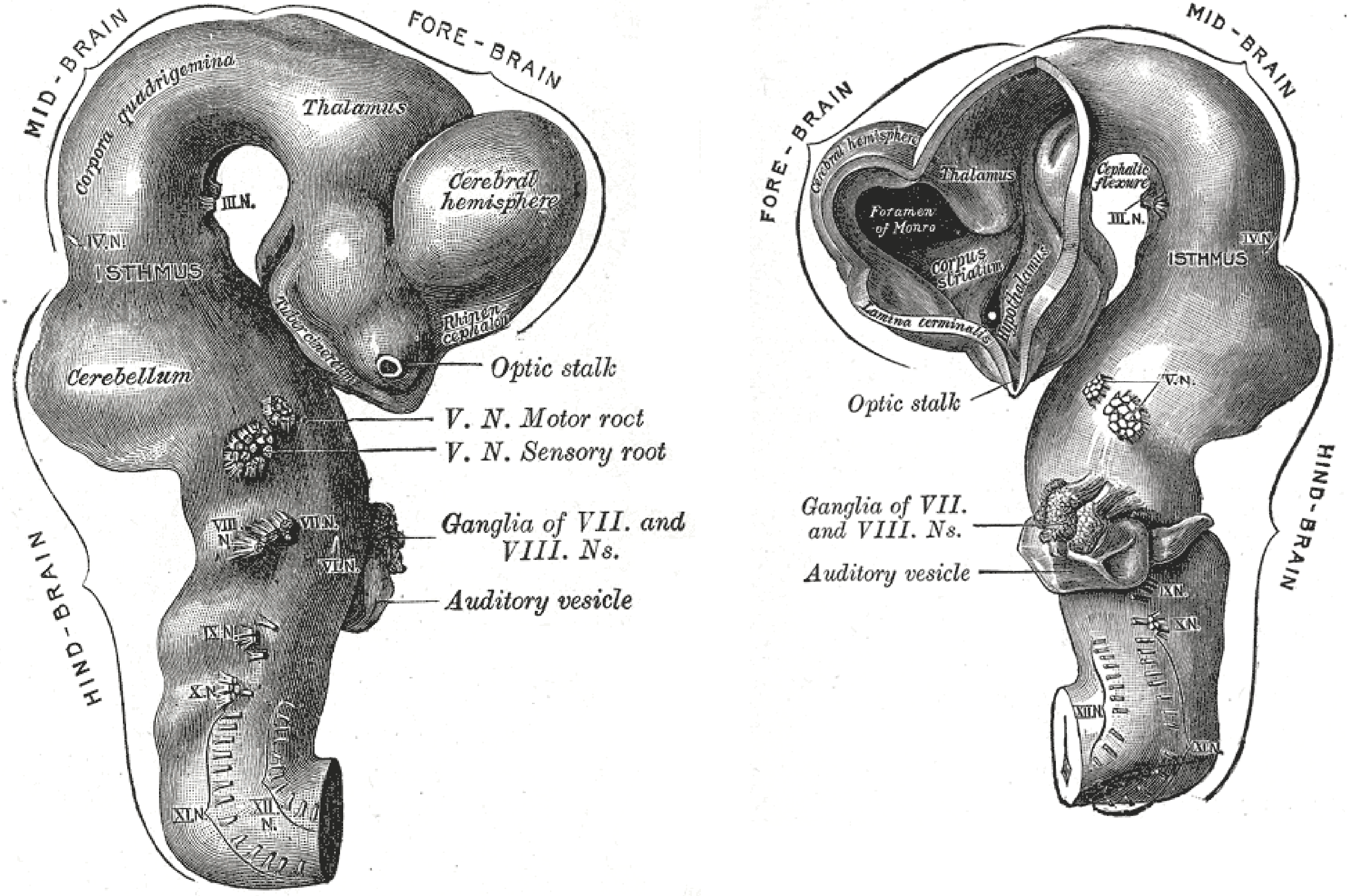
are convolutions enough?
dolphin has more convolutions but intelligent as dogs
thinner than that of human
less organized


I
II
III
Fish
Salamander
Tortoise
Chick
Hog
Calf
Rabbit
Human

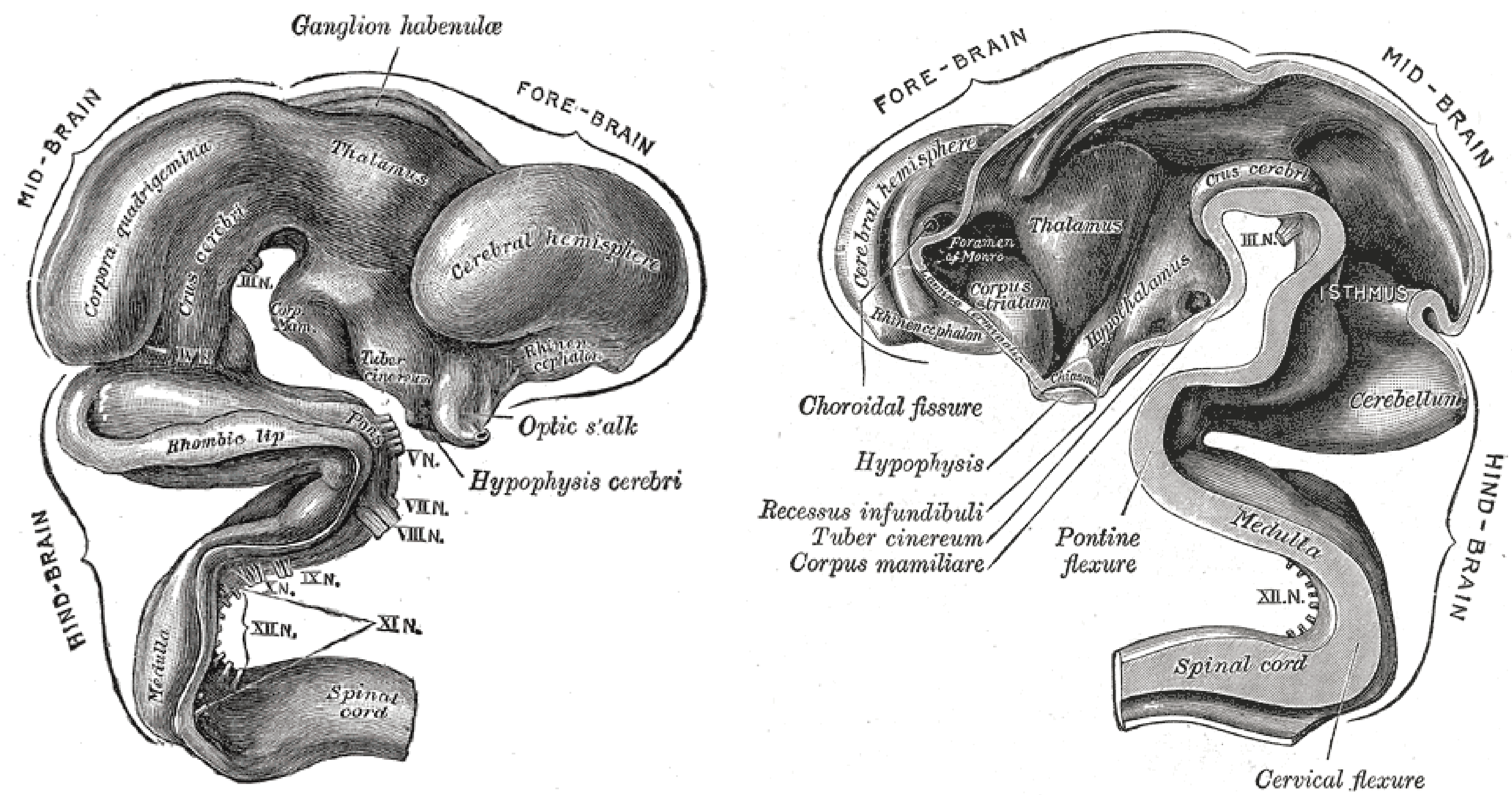

An Accelerated View of Brain Development
15 1/2 wks
22 weeks
23 weeks
~25 weeks
27 weeks
Full term brain
Adult
http://medstat.med.utah.edu
Adolescent brain (black box)
Ungrateful, talks back, risk taking…doesn't clean room…



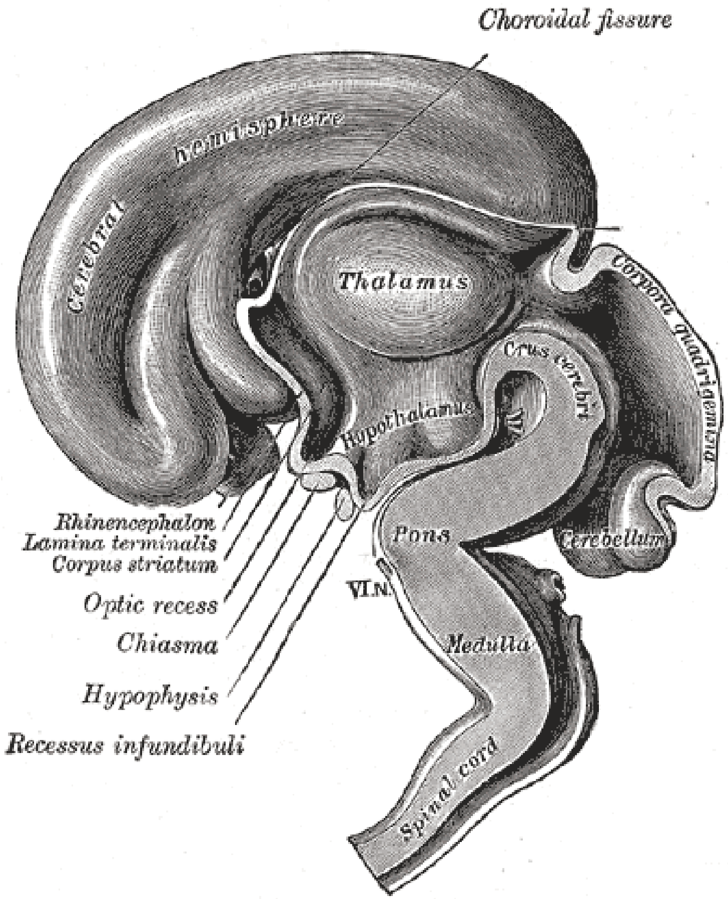
Reconstruction of periphera nerves of a human embryo of 10.2 mm. (After His.) The abducent nerve is not labelled, but is seen passing forward to the eye under the mandibular and maxillary nerves

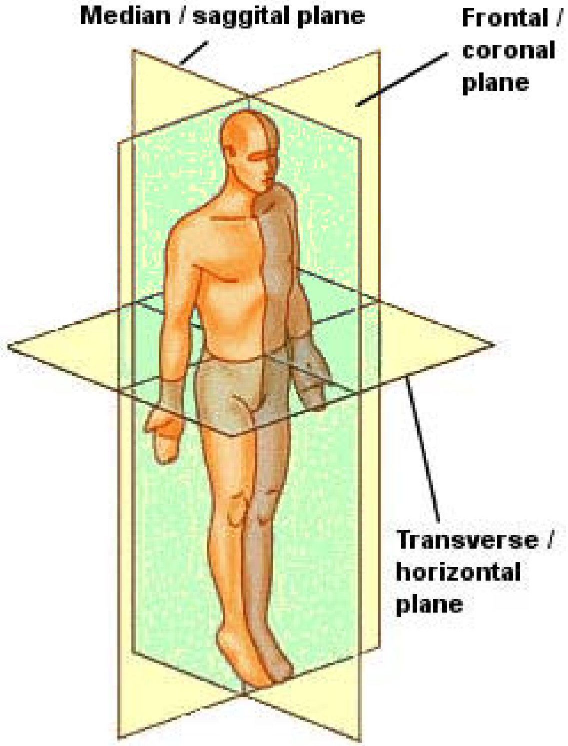


Exterior and interior of brain of human embryo of four and a half weeks

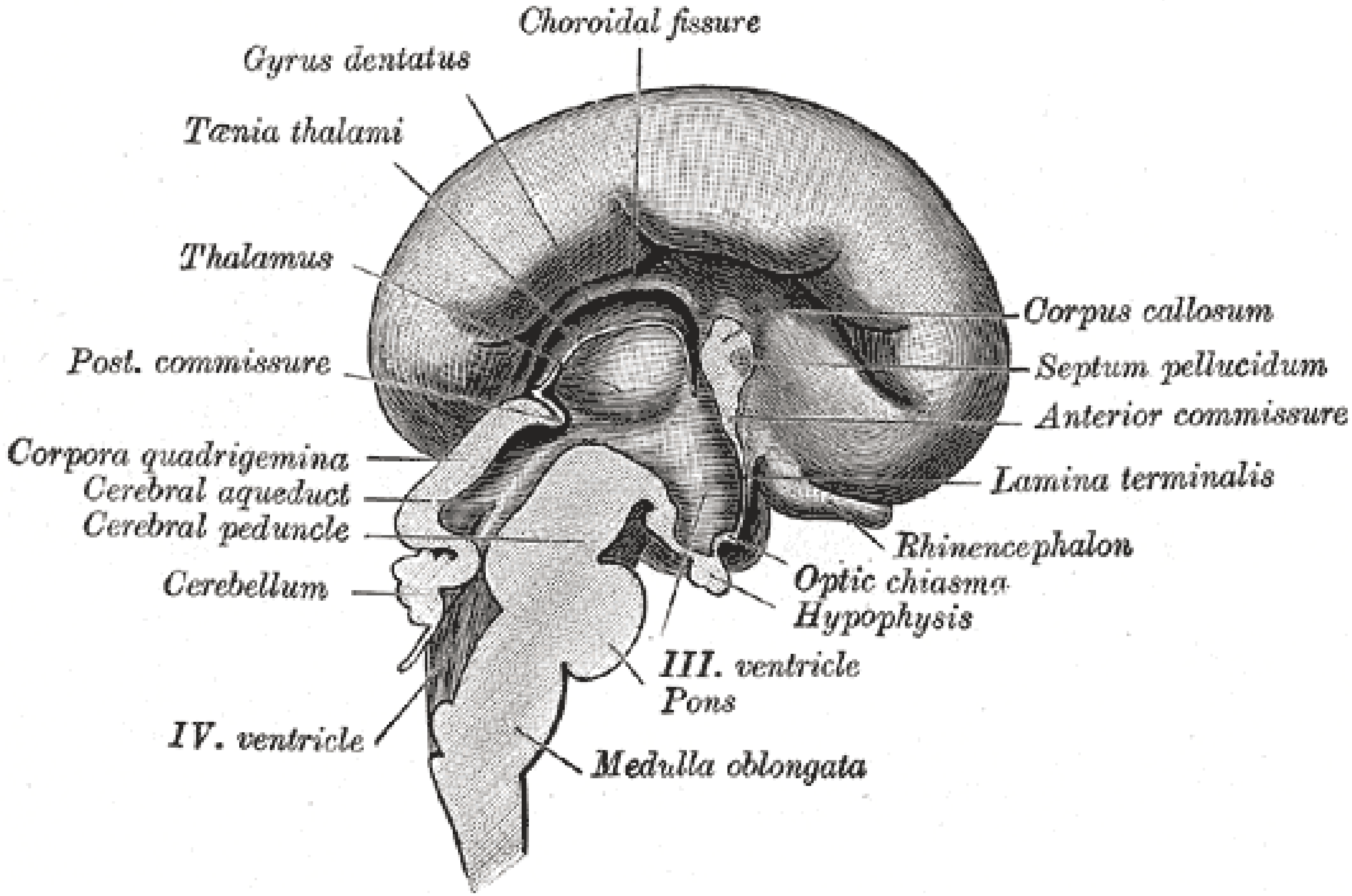


Exterior of brain of human embryo of five weeks

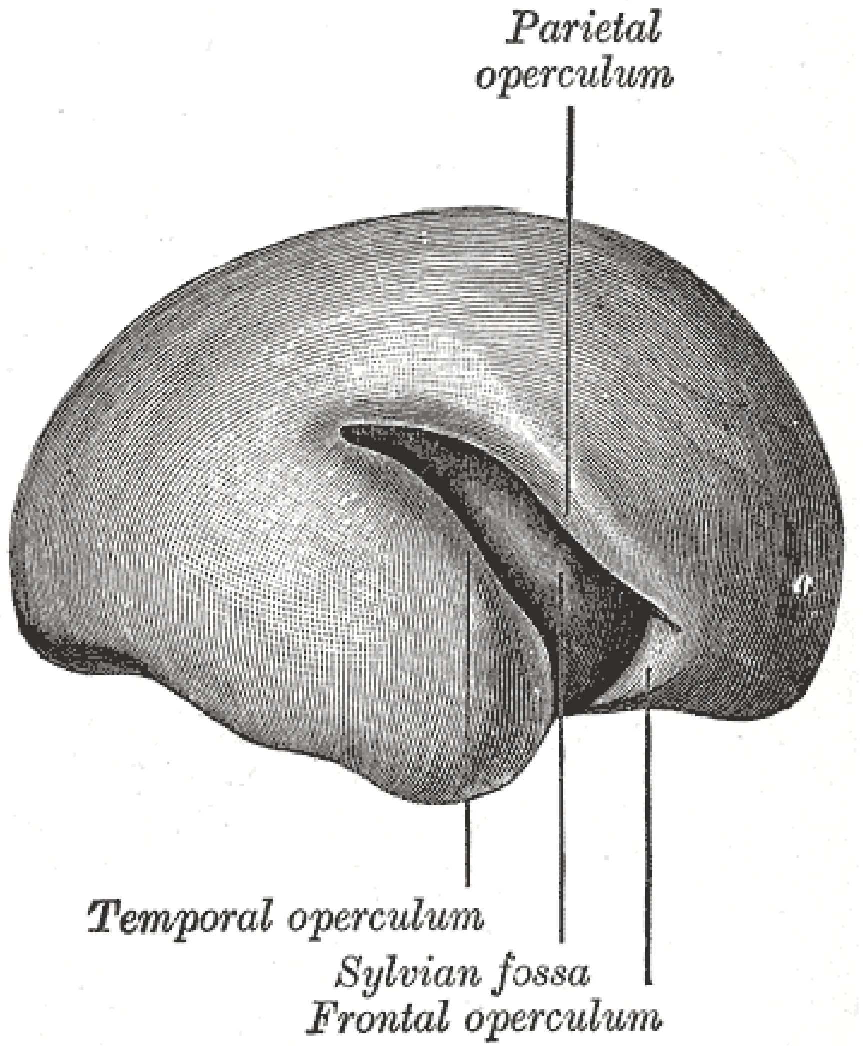




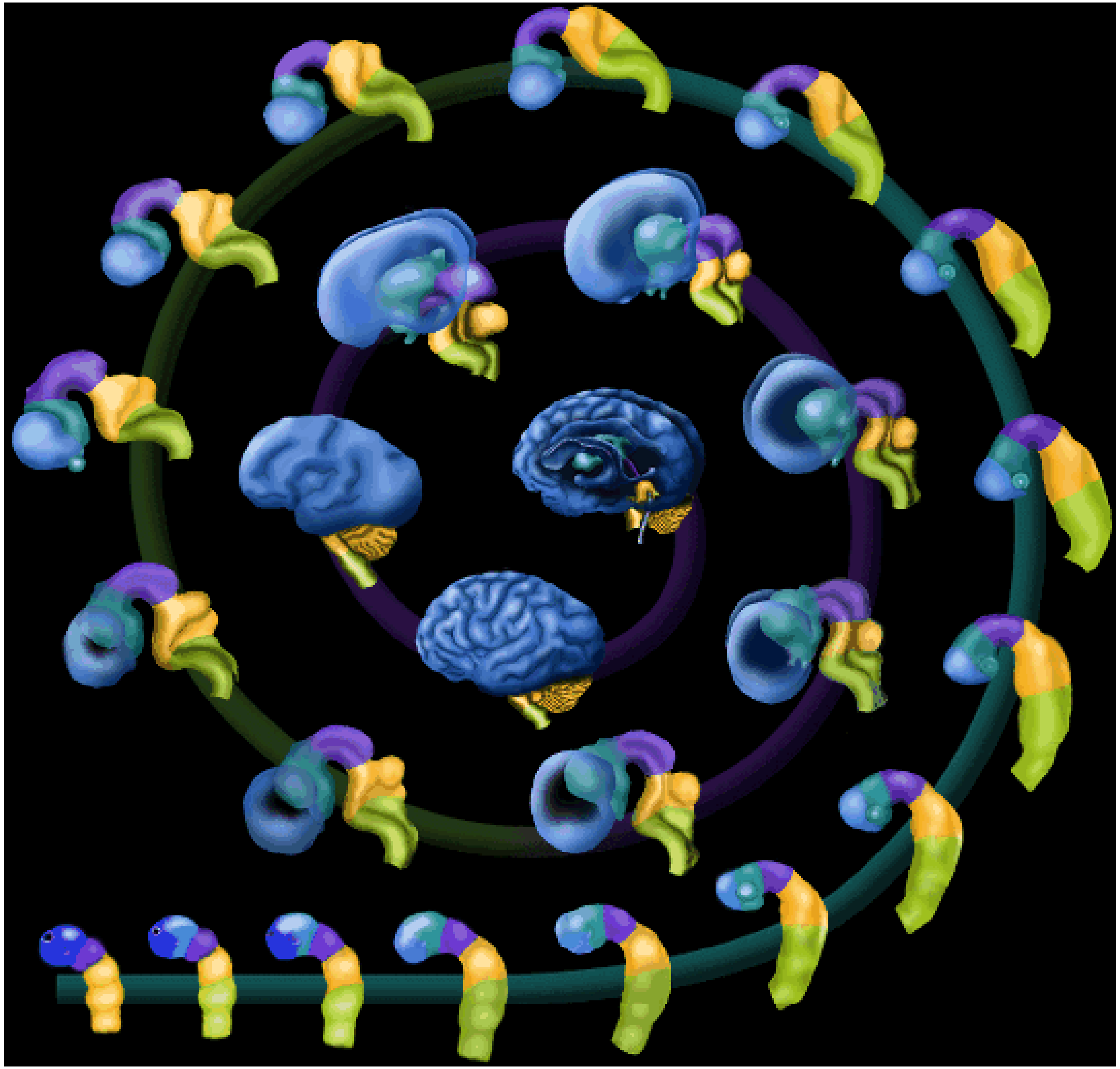
Median sagittal section of brain of human embryo of three months



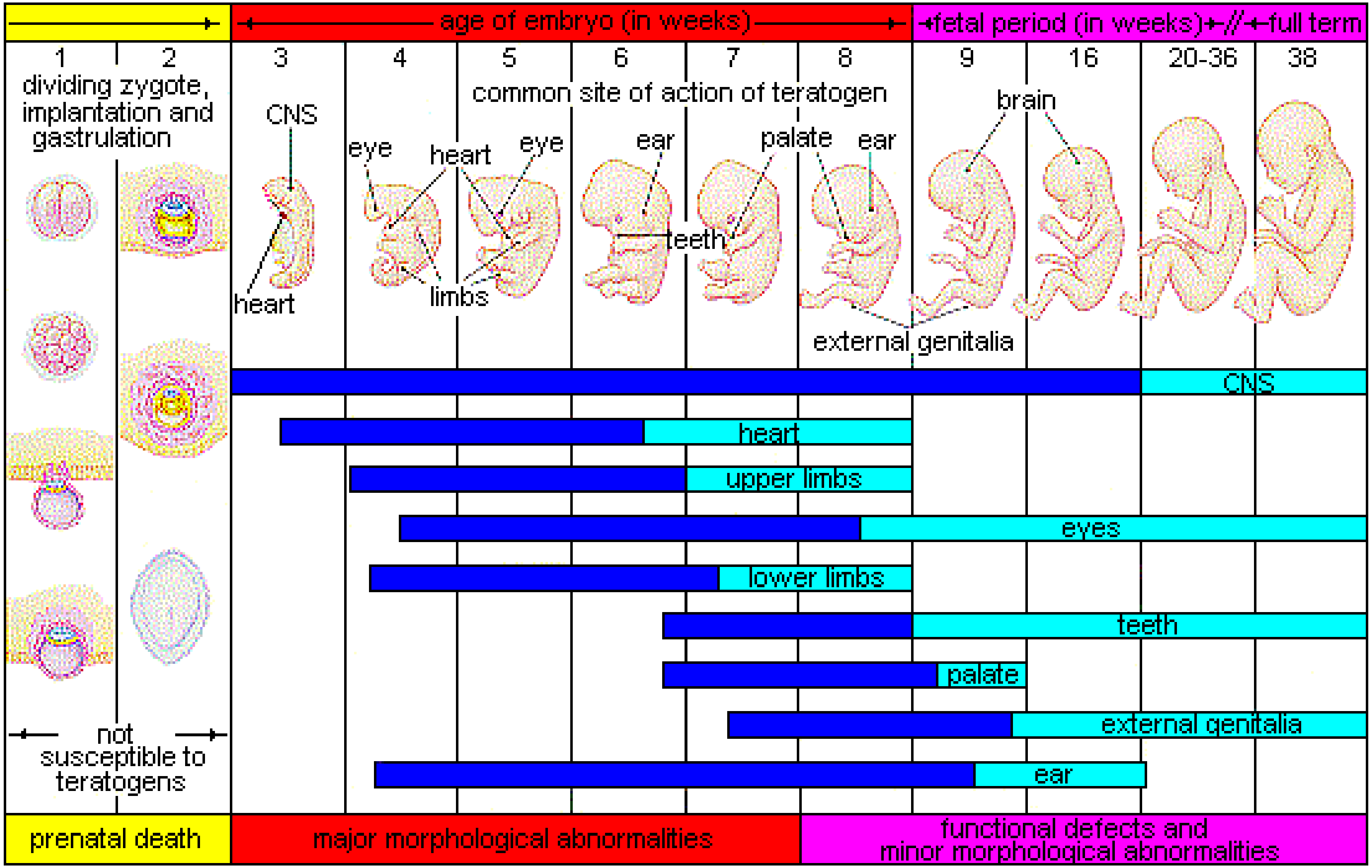
Median sagittal section of brain of human embryo of four months



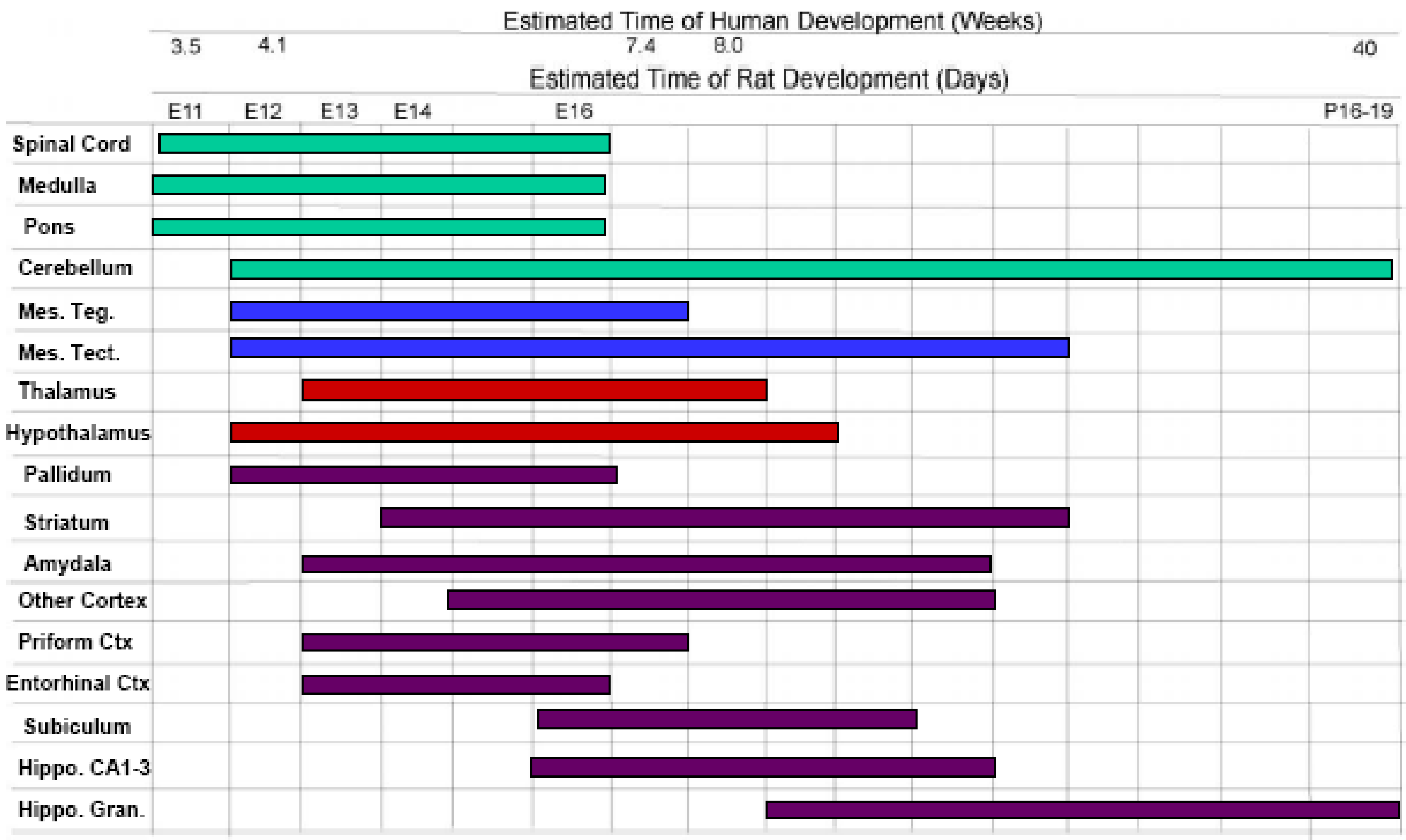
Outer surface of cerebral hemisphere of human embryo of about five months



Critical Periods of Human Development



Estimated timelines of regional neurogenesis in rats and humans

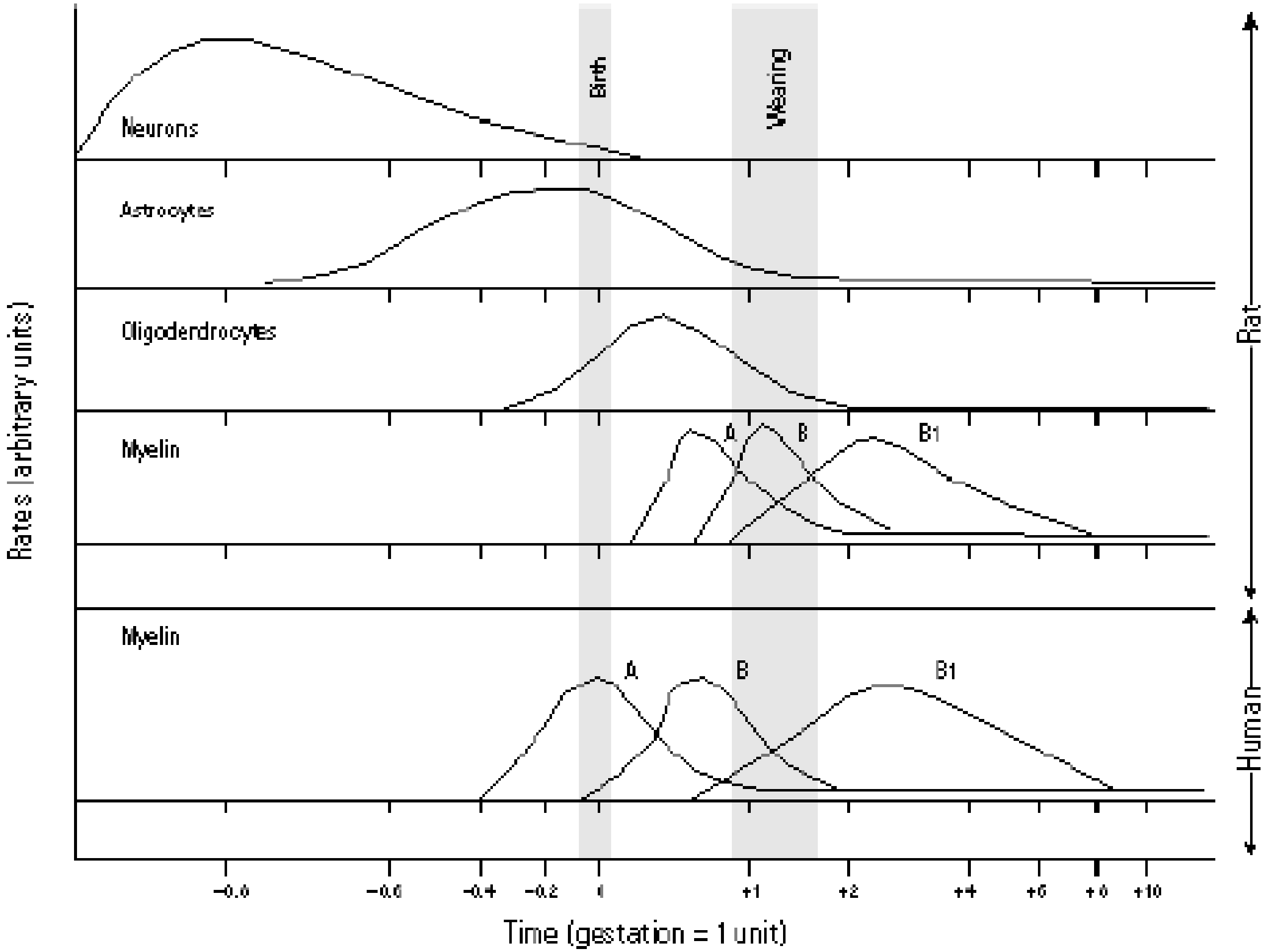


Brain development at the cellular level (neuron)

Stages of Development

- Six stages of Development
  - Neurogenisis - produces neurons
    - May also have new neurons during adulthood
  - Cell migration - development of distinct populations
    - Radila glial cells provide a map
  - Differentiation- different neuron types
  - Synaptogenesis - connections between cells
    - Probably a function of chemotropic guidance of axons
  - Neuronal Cell Death - killing off the extras
    - Competition for targets, and trophic factors (NGF)
  - Synapse Rearrangement - Use it or loose it

NEURONOGENESIS AND GLIOGENESIS



Proliferation of neurons and glia are depicted with the temporal and regional pattern of myelination which occurs later in development. Abbreviations: A, sciatic nerve; B, whole brain; B1, corpus callosum. The schedule of brain development for rats and humans is in arbitrary units (*x*-axis).

Neurogenesis

The earliest stage of brain development involving the proliferation of neurons of the neural tube and the migration of these cells to predetermined locations.

The CNS and PNS begin to develop approximately 18 days after conception.

Neurogenesis & Cellular Migration

<u>Corticogenesis</u>: the development of the cortex; <u>begins at 6 weeks</u>

The rapidly proliferating cells along the wall of the neural tube migrate (“neural migration”) outward at different predetermined times.

The neurons migrate in sheets, which ultimately create the 6 laminated layers of the cortex.

By week 18, nearly all cortical neurons have reached their designated locations.

neural migration

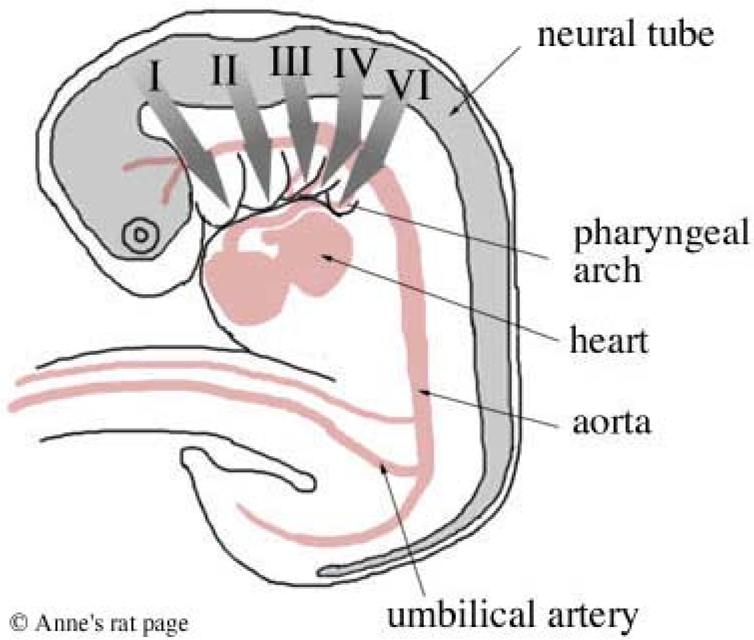
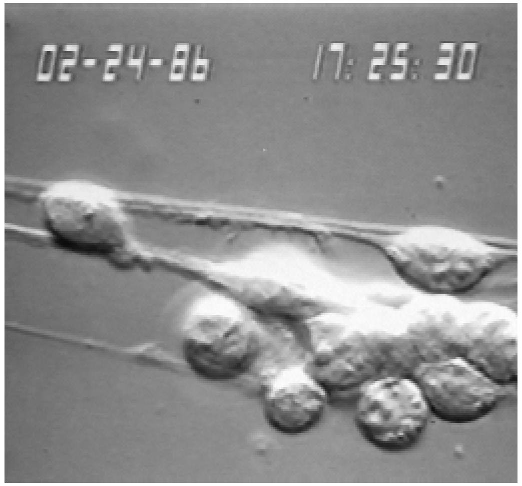


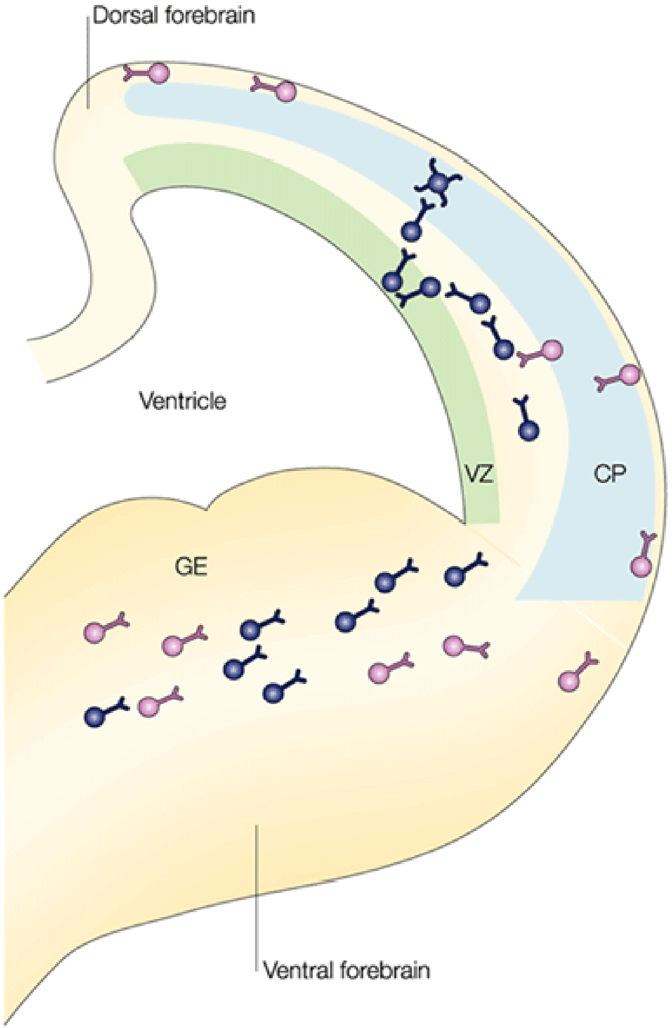
Diagram of the migration of neural crest cells (thick grey arrows) from the neural crest to the five pharyngeal arches (I, II, III, IV, and VI. Arch V degenerates). (Adapted from Gilbert 1994, p. 284.)
http://www.ratbehavior.org/DumboRatMutation.htm

Glial-Guided Neuronal Migration



http://www.rockefeller.edu/labheads/hatten/mechanism.html

Movement of cortical interneurons in the developing cerebral cortex



Interneurons that arise in the ganglionic eminence (GE) migrate into the neocortex through the intermediate zone (blue cells) and the marginal zone (pink cells). We propose that a subset of interneurons (blue cells) that migrate through the intermediate zone avoid the repellent signals that might be present in the cortical plate (CP; blue band), but are attracted by chemoattractants that are secreted in the ventricular zone (VZ; green band). While in the VZ, in addition to losing responsiveness to the repellent signals expressed in the CP, these interneurons might also acquire positional information that is required for their subsequent migration to the correct layers of the developing cortex.

***Nature Reviews Neuroscience* 3, 423-432 (June 2002)**

Nature Reviews | Neuroscience

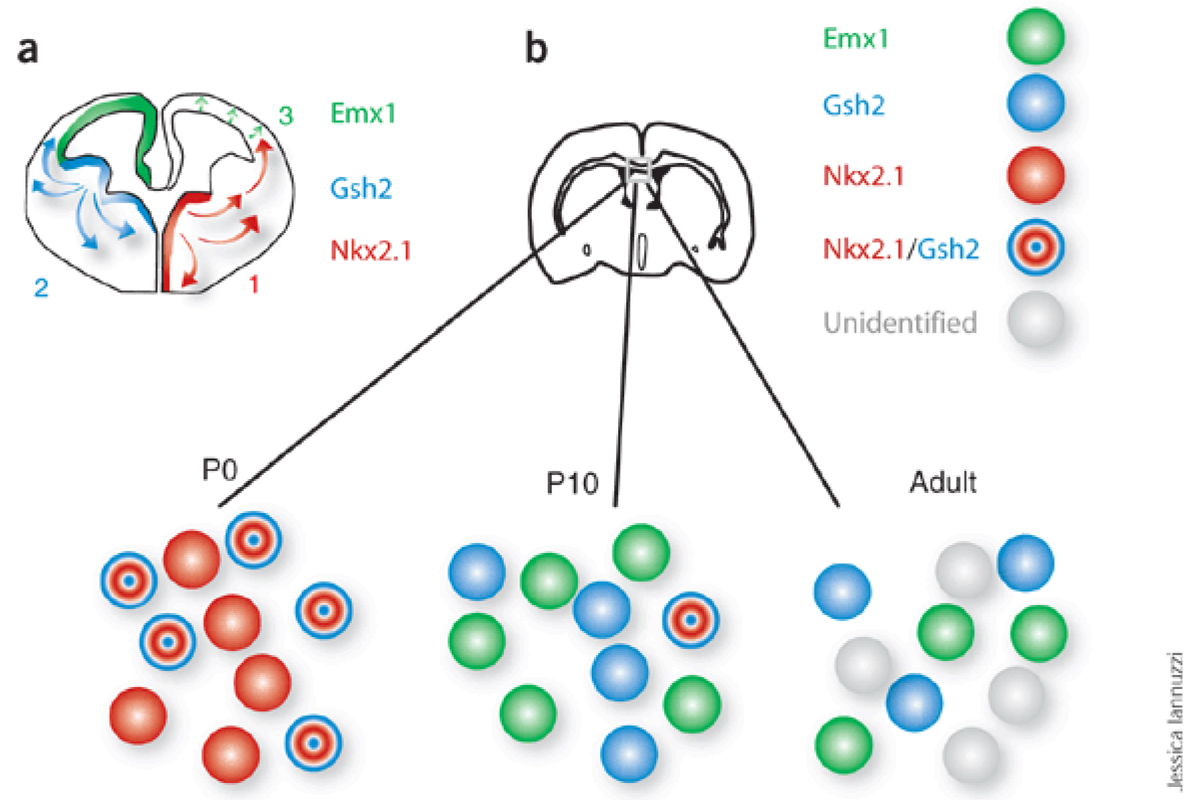
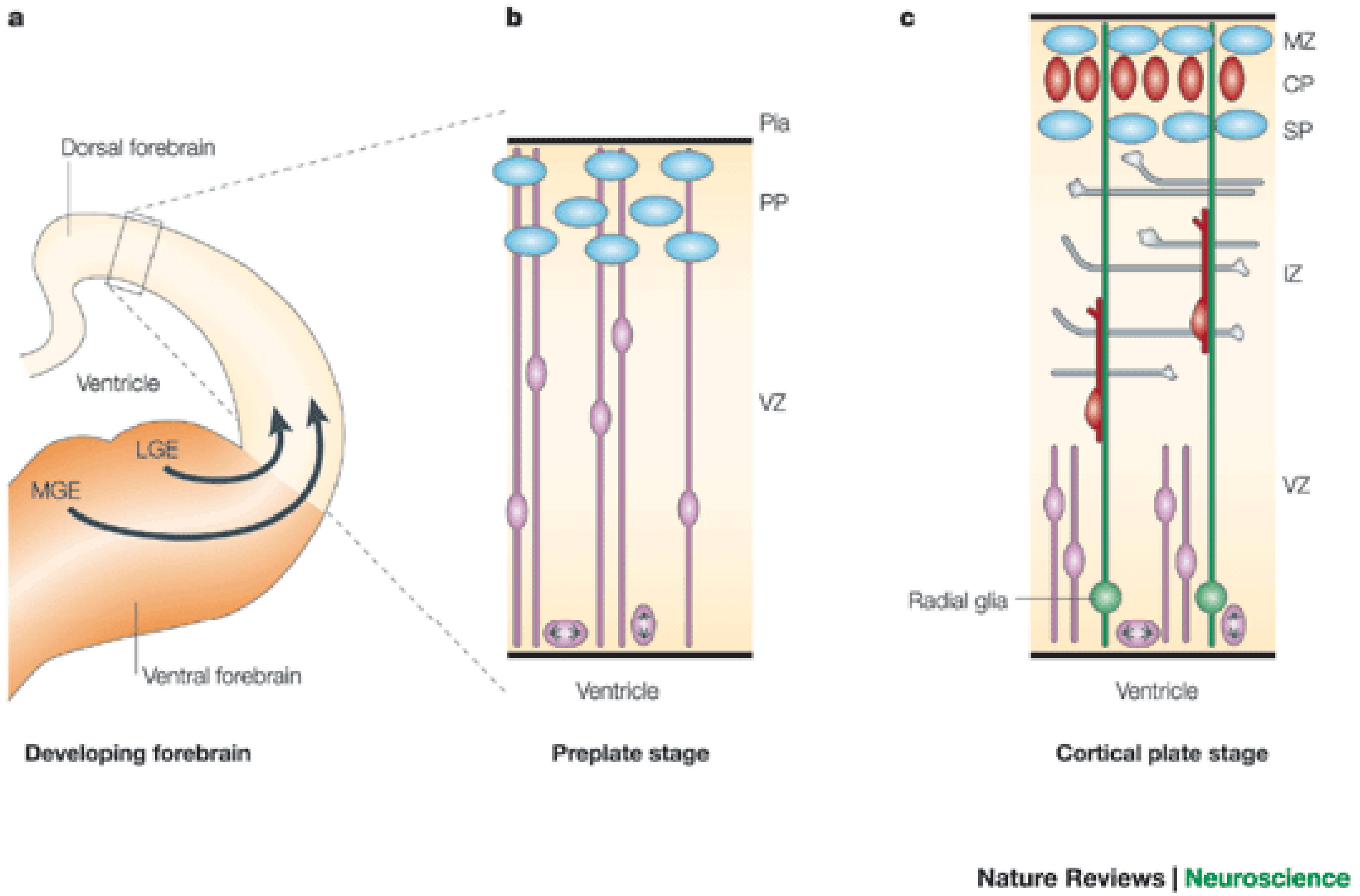
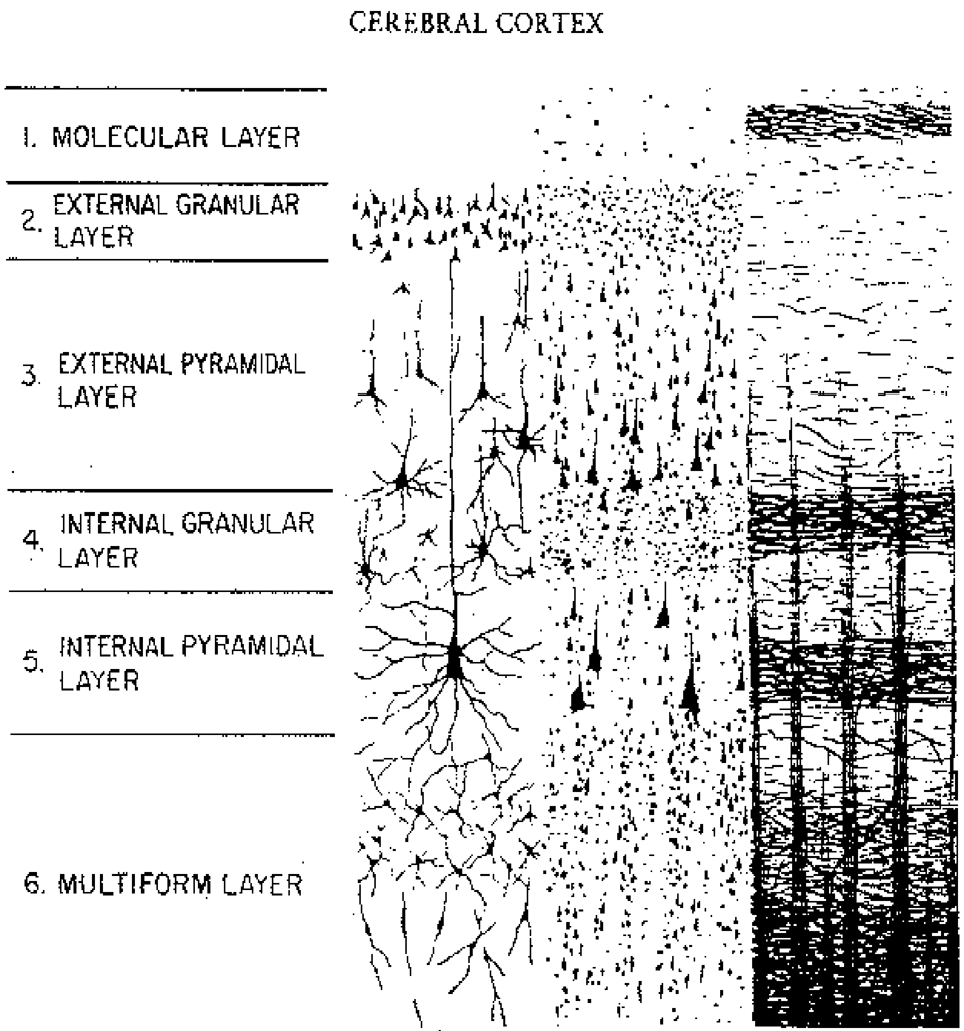


Figure 1. Sources of oligodendrocytes in the developing brain.
(**a**) Three waves of oligodendrocytes generated from different lineages in the telencephalic ventricular zone. Cells from the Nkx2.1 population begin to migrate around E12.5, those from the Gsh2 population around E15.5, and those from the Emx1 population around P0. Nkx2.1 and Gsh2 expressions overlap in the ventricular zone overlying the medial ganglionic eminence. Also shown are presumed migratory pathways of oligodendrocyte precursors from each of these areas. (**b**) Sources of oligodendrocytes in the corpus callosum (square) at three time points. At P0, most of the cells arise from the ventral, Nkx2.1 and Gsh2 domains. By P10, cells from the Nkx2.1 lineage have mostly disappeared, replaced by a mix of Emx1 and Gsh2 cells. In the adult, the Emx1 and Gsh2 lineages make up most of the oligodendrocytes, but an unlabeled population is also present.

Neocortical development



a | Schematic diagram of a section through the developing rodent forebrain. **b**,**c** | Illustrations of the different stages of neocortical development. The dorsal forebrain gives rise to the cerebral cortex. The lateral ganglionic eminence (LGE) and medial ganglionic eminence (MGE) of the ventral forebrain generate the neurons of the basal ganglia and the cortical interneurons; the latter follow tangential migratory routes to the cortex (**a**; arrows). In the dorsal forebrain (**a**; boxed area), neuronal migration begins when the first cohort of postmitotic neurons moves out of the ventricular zone (VZ) to form the preplate (PP) (**b**). Subsequent cohorts of neurons (pyramidal cells) migrate, aided by radial glia, through the intermediate zone (IZ) to split the PP into the outer marginal zone (MZ) and inner subplate (SP) (**c**). CP, cortical plate



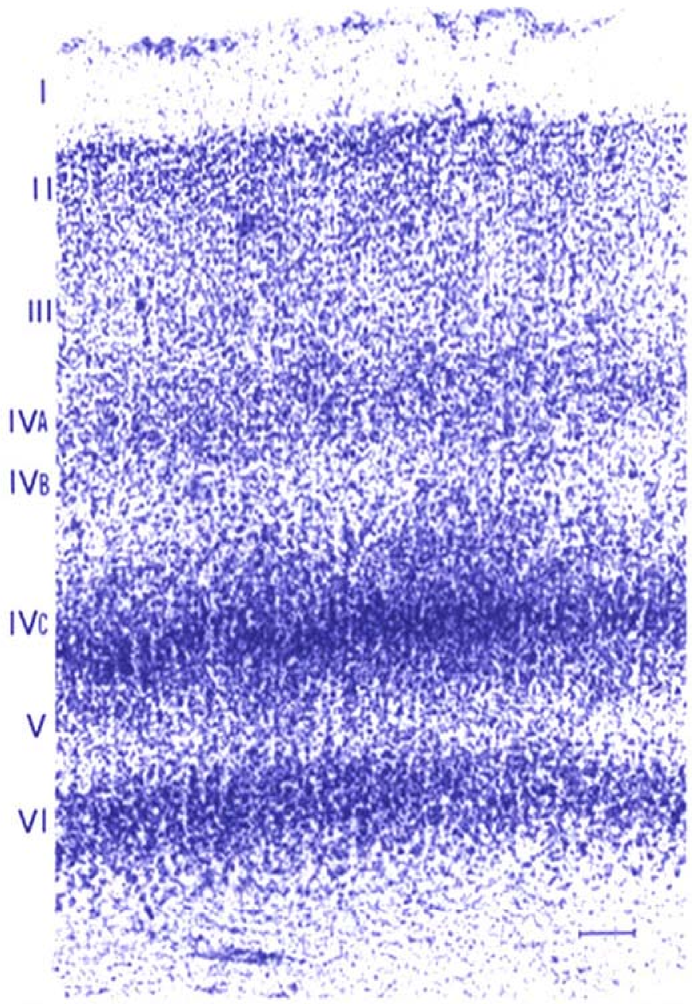


Figure 13. Nissl stain of the visual cortex reveals the different layers I through VI quite clearly.

http://www.benbest.com/science/anatmind/anatmd5.html

Axon & Dendrite Development

Axons

As the neurons migrate, axons form making cortical-cortical, cortical-subcortical, and interhemispheric connections.

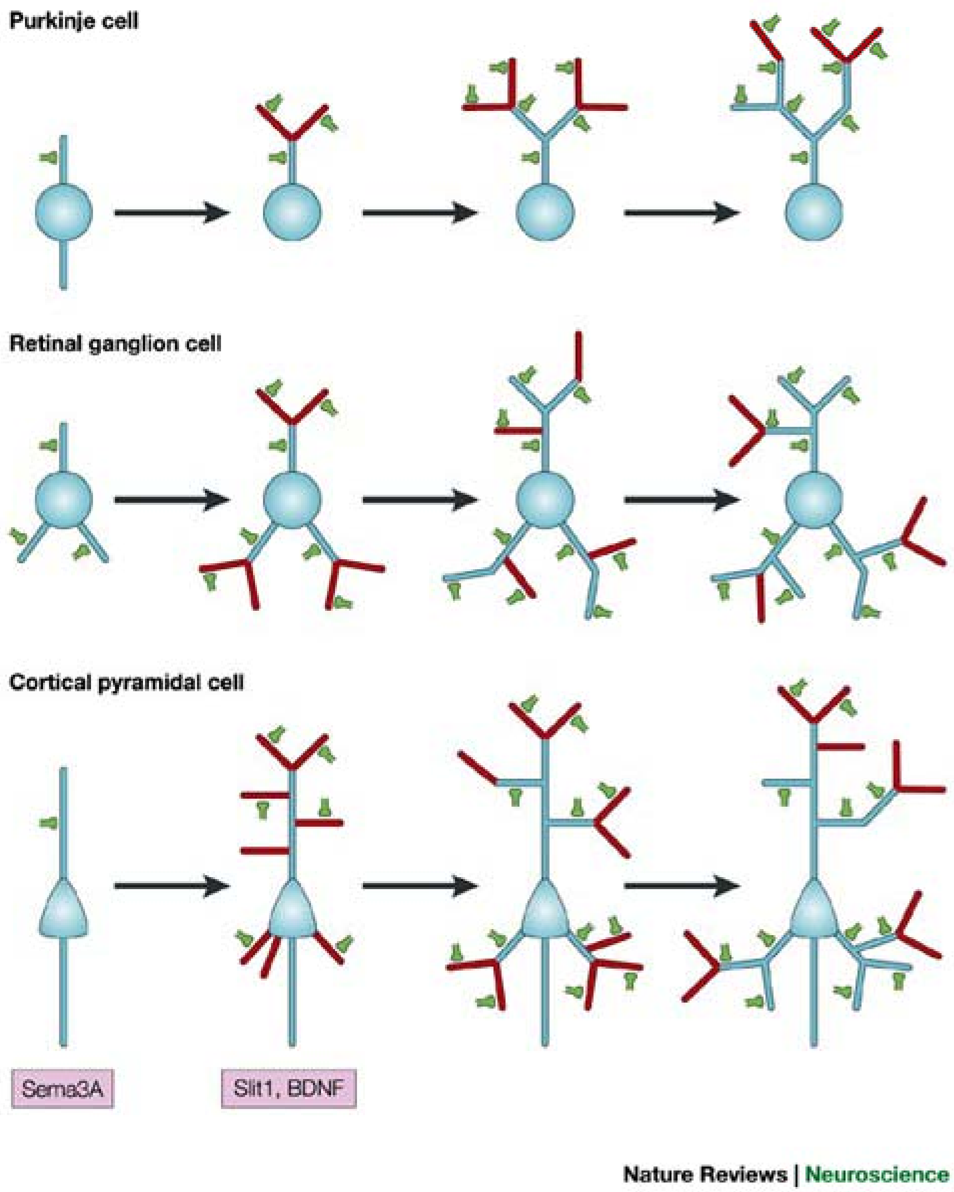
Dendrites

As the migrating neuronal cells reach their designated positions, dendrites being to sprout ("*arborization*").

Dendrites then form synapses for gathering information.

This begins prenatally, but the most intensive dendrite growth period is from birth to 18 months.

Dendritic growth and patterning during development



These stick diagrams of dendrites show the development of three cell types.
Nature Reviews Neuroscience 3, 803-812 (October 2002)

Synaptogenesis

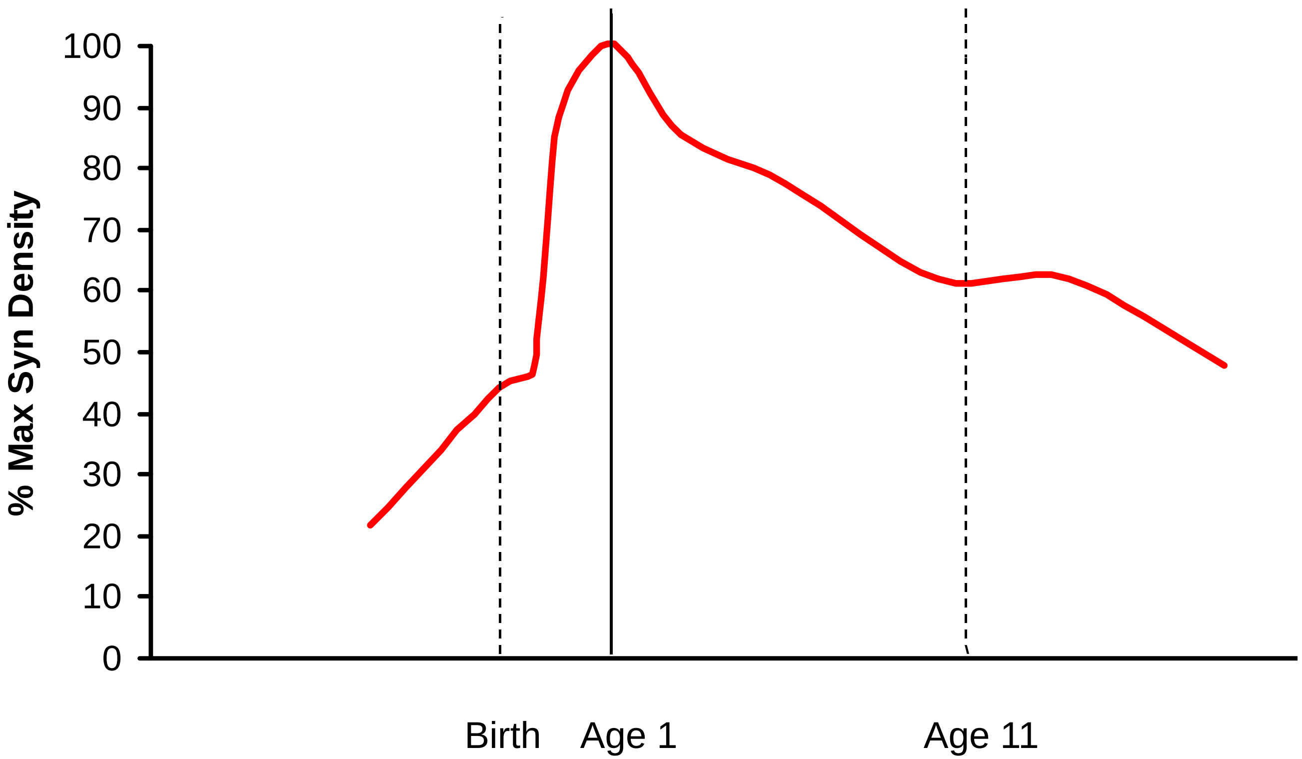
Synapses form as dendrites and axons grow.

Function emerges secondary to synaptic formation in specific regions.

Synapses grow at different rates in different parts of the brain

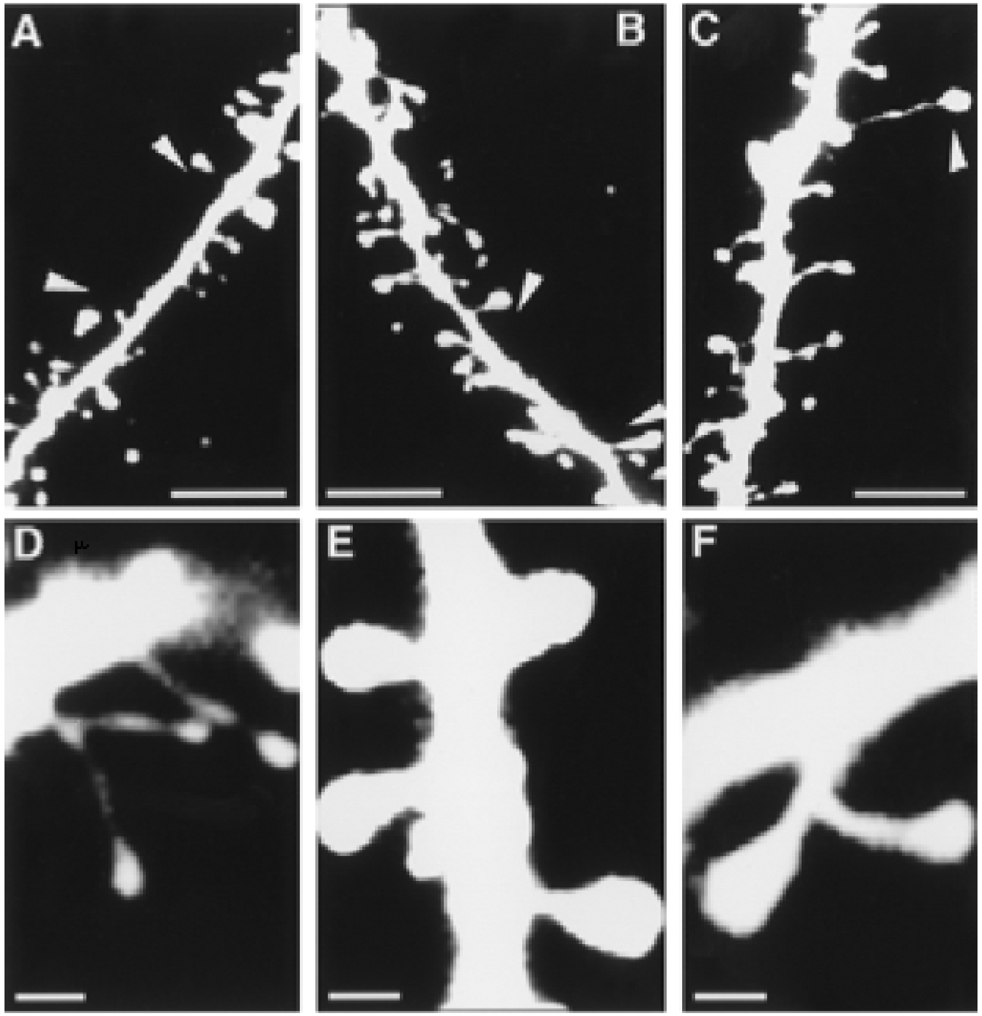
- Occipital lobe – begins prenatally and achieves near adult-level synaptic density between ages of 2 to 4 years
- Prefrontal cortex – does not reach adult levels until late adolescence/adulthood

Synaptic Density over the Lifespan
(human visual cortex)



Redrawn from P. Huttenlocher 1987

Neuronal Plasticity and Dendritic Spines: Effect of Environmental Enrichment on Intact and Postischemic Rat Brain



Morphologic features of dendritic spines in the somatosensory cortex of adult rats housed in standard or enriched environments. "Naked" sections of dendrites (arrowheads) in rats housed in standard environment **(A** and **B)**. Note the spine with a very long neck (arrowhead) in a rat housed in an enriched environment **(C)**. "Inactive" thin spines on the oblique apical dendrite in standard-environment specimens **(D)**. In enriched-environment specimens, many spines had big heads **(E)** or double heads **(F)**. All illustrations are from pyramidal layer III except **A** (layer II). Scale bars = 5 m **(A–C)** or 1 m **(D–F)**.

http://www.nature.com/jcbfm/journal/v22/n1/full/9591196a.html

Myelination

Near the end of neural migration, glial cells begin to encircle the axons, forming the myelin sheath.

Myelination begins with the spinal cord, then subcortical structures, then the cortex.

Within the cortex, myelination begins in posterior region and moves anteriorly, ending with the parietal and frontal lobes

The significant increase in brain weight postnatally is primarily due to myelination.

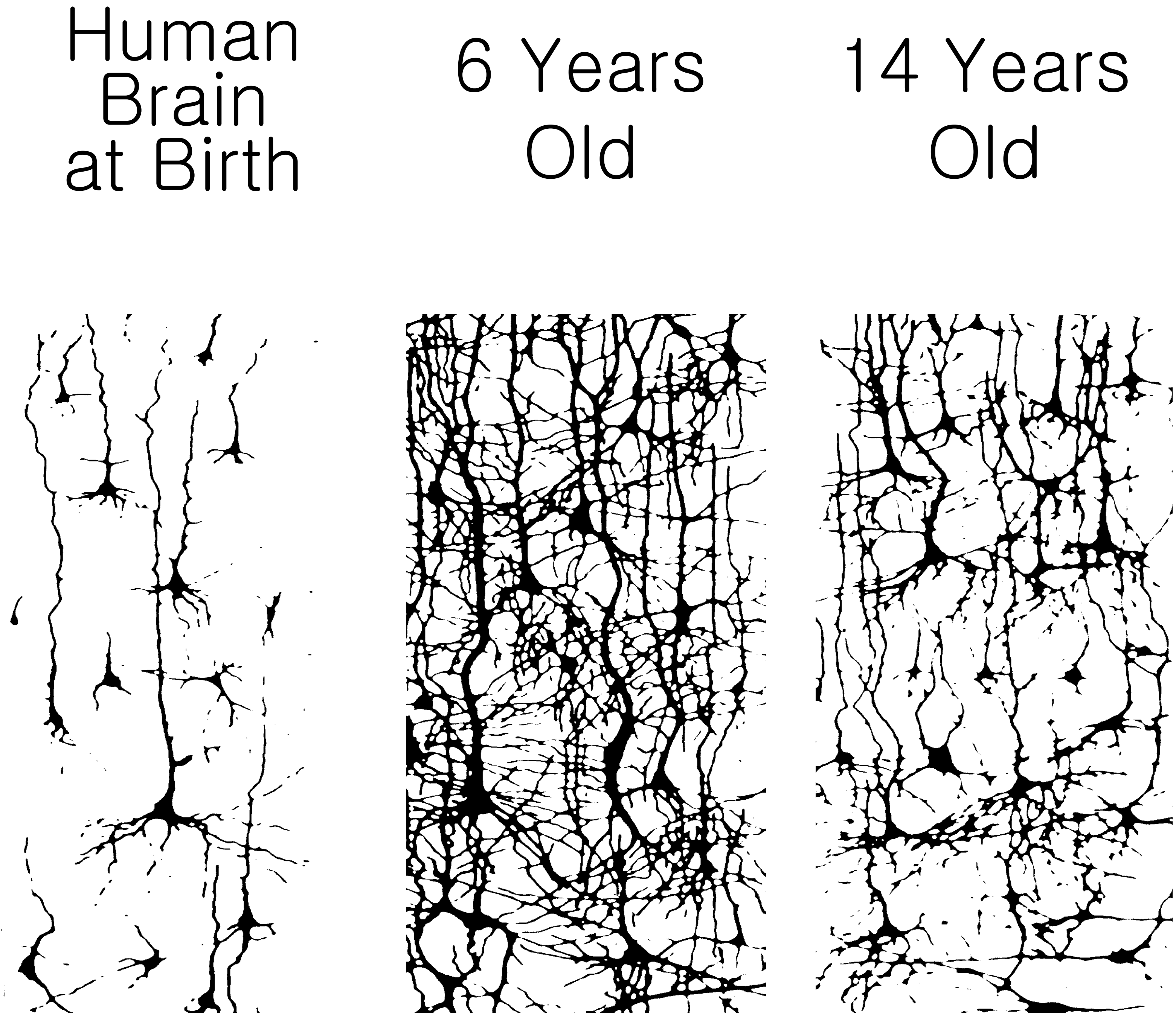
Pruning

During early development, neurons and synapses are overproduced.

Early synapses are thought to be random, in part, thus resulting in some inappropriate connections.

Pruning is not random; it is the purposeful sculpting of the brain. Connections, which are used, are spared.

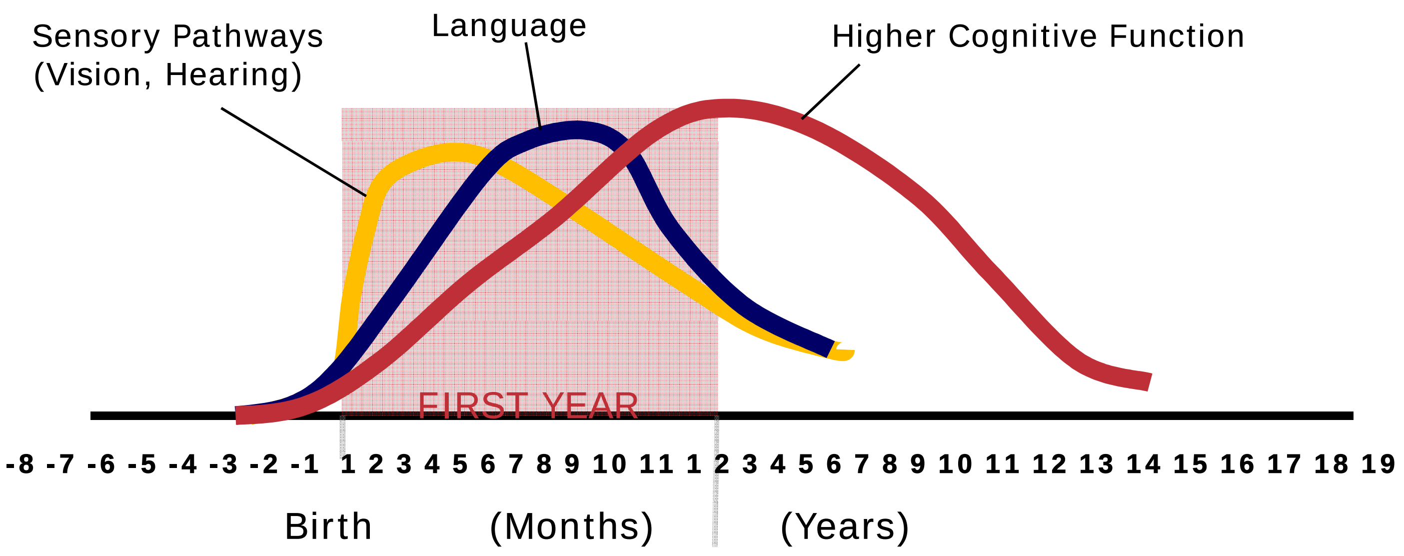
Pruning is primarily postnatal, eliminating 40% of the brain's cortical neurons during childhood.



Human Brain at Birth
6 Years Old
14 Years Old

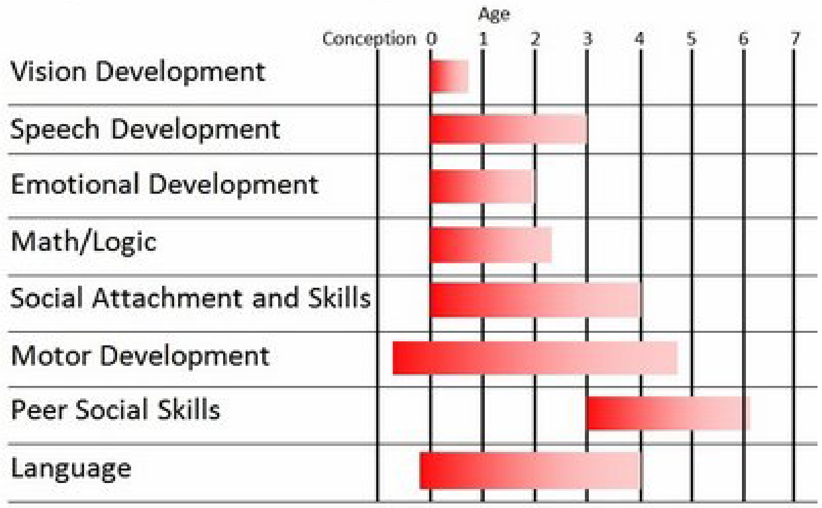
Human Brain Development

Synapse Formation Dependent on Early Experiences



Source: C. Nelson (2000)

Stages of Brain Development in an Infant



Postnatal Development

At birth, the brain weighs ¼ of its final adult weight of approximately 1300 - 1500 g.

By age 2, it has achieved ¾ of its final weight.

During the first 2 years of life, the cortex doubles and reaches adult dimensions.

During this period, synapses, dendrites, and myelin form.

Development of voluntary function

Development of involuntary function

Development of consciousness

Connections: use it or lose it

Aging

Video of neuronal cells

http://www.ipmc.cnrs.fr/~duprat/neurophysiology/video.htm