PSYCH 260/BBH 203

Development

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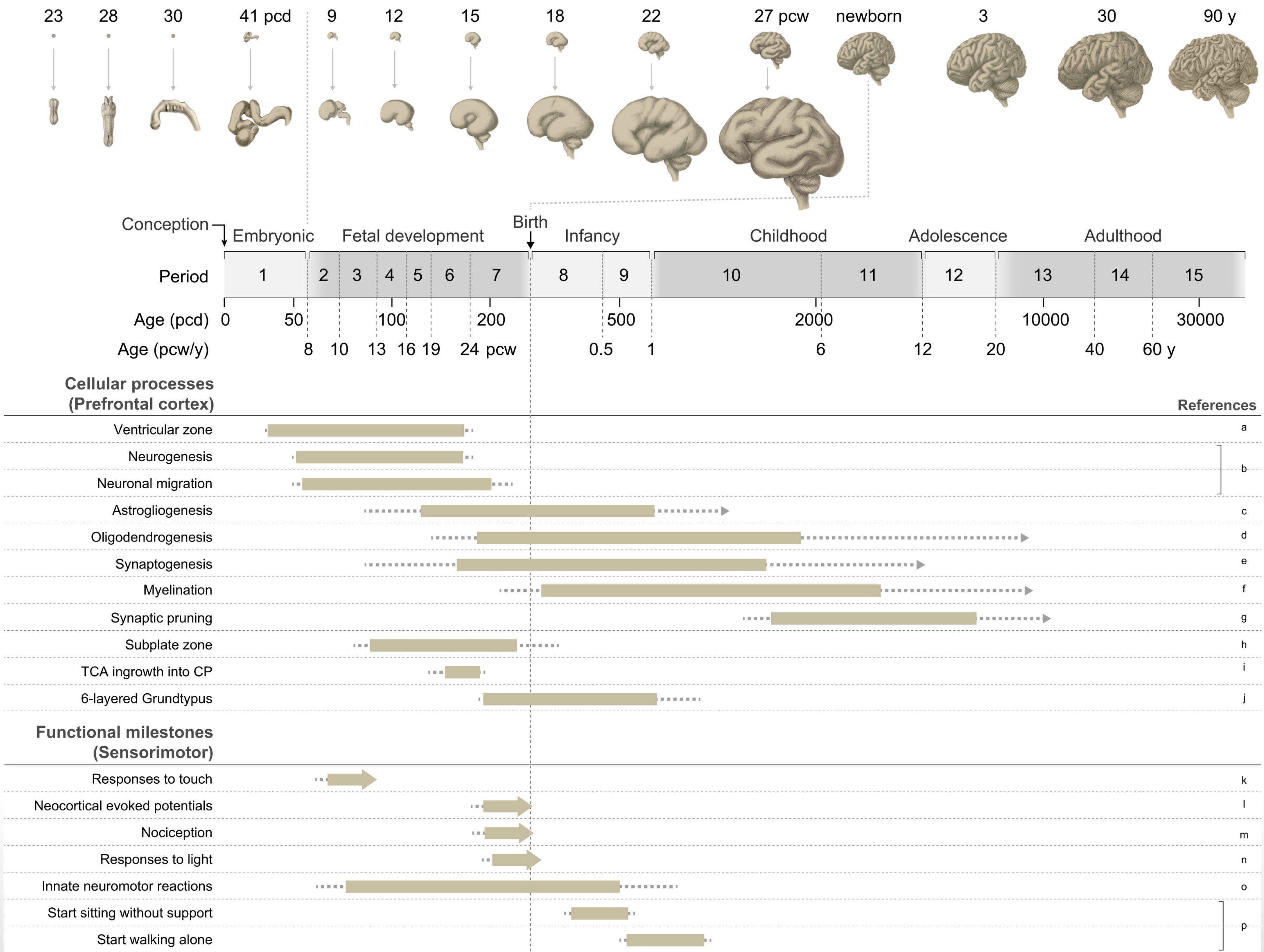
Prelude 8:01

(carlsagandotcom, 2009)

Today’s topic

- How the human brain develops

Timeline of milestones



- Brain ~ 2.5% of body mass
    - consumes 18% of O_2 at rest, (Kety & Schmidt, 1948)
    - about 20 W
- CNS among earliest-developing, last to finish organ systems
    - Prolonged developmental period (==childhood) makes CNS especially vulnerable

Neurons

- ~ 86 billion neurons in adult CNS
  - similar # of glia
- In cortex, about 16 (14-32) billion
  - 80/20% Glu/GABA
- Development generates millions neurons/hr

Synapses

- 7-80K synapses/cortical neuron
- $\sim 10^{15}$ (quadrillion) synapses in CNS
- 164 trillion synapses in cerebral cortex, (DeFelipe, Alonso-Nanclares, & Arellano, 2002)

Axons

- 145-175 km (90-109 mi) of myelinated axons, (Marner, Nyengaard, Tang, & Pakkenberg, 2003)

Prenatal period

- 38 weeks from conception/fertilization on average
- Embryonic period (weeks 1-8), fetal period (weeks 9+)
- Divided into 3 12-13 week trimesters

Insemination

- Can occur 3-4 days before or up to 1-2 days after… ovulation
- Some animals signal ovulation; humans do not

Fertilization

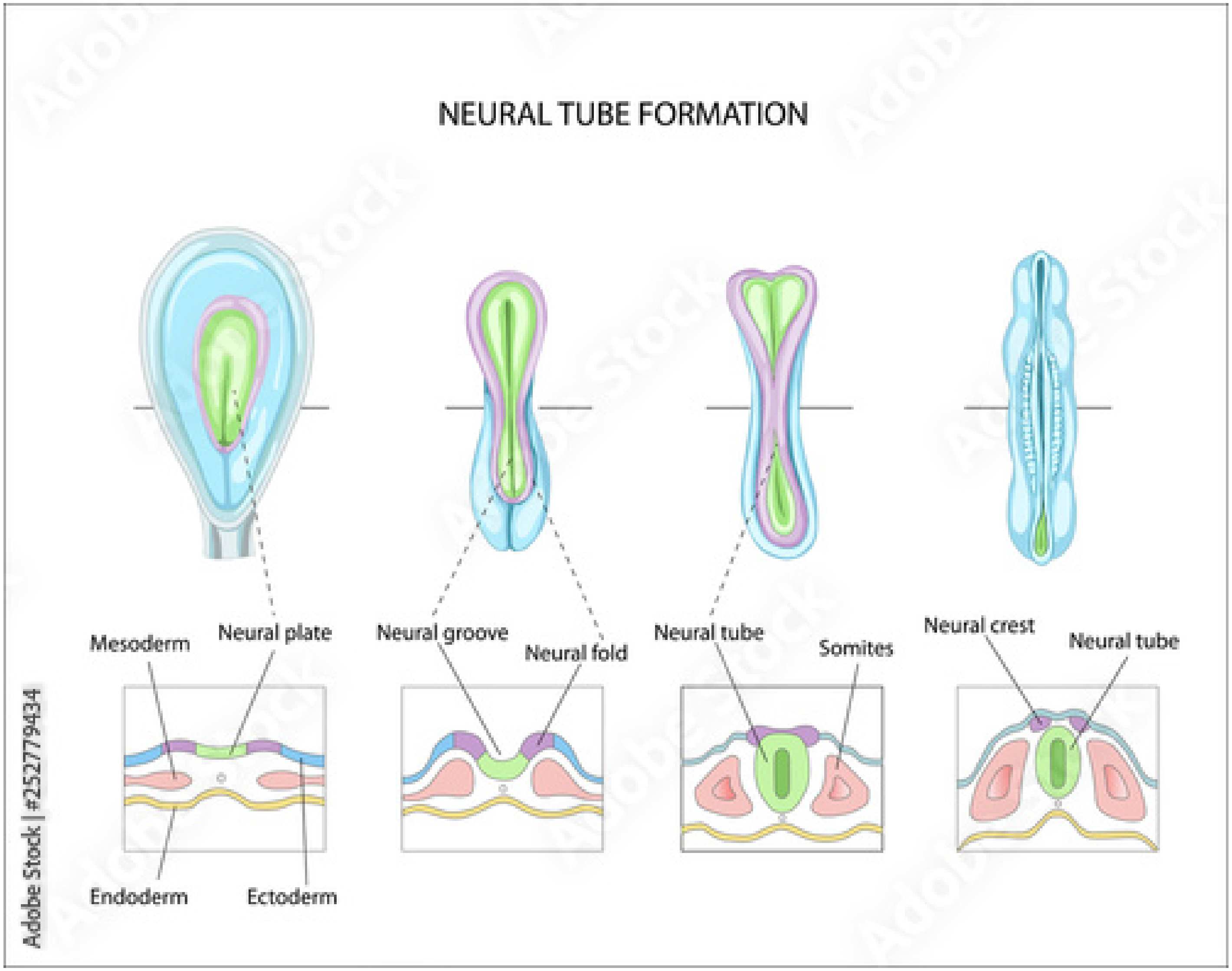
- Within ~ 24 hrs of ovulation

Implantation

- Fertilized ovum implants in wall of uterus
- ~ 6 days after fertilization

Early embryogenesis

Formation of *neural tube* (neurulation)

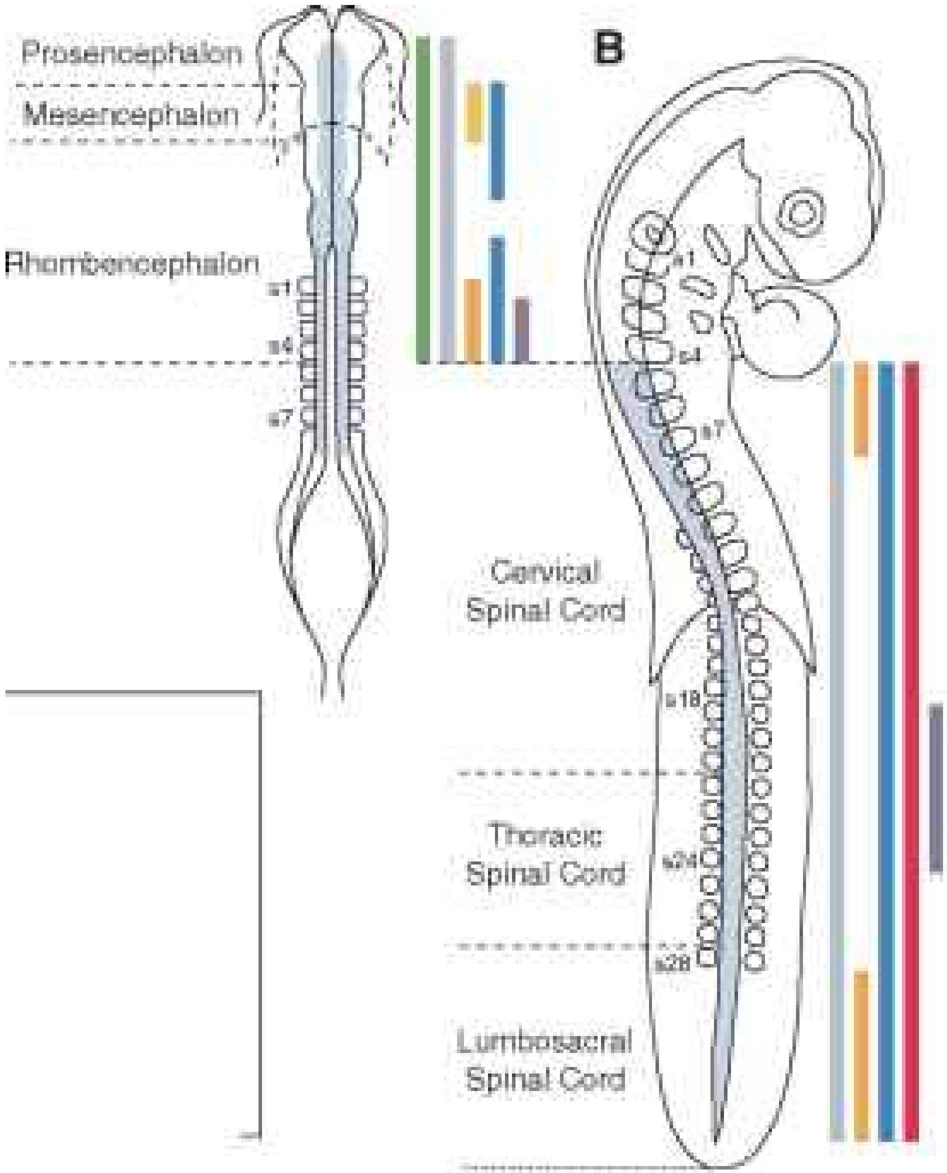


- Embryonic layers: ectoderm, mesoderm, endoderm
    - Neural tube forms ~ 23 pcd (postconceptual days)
- Neural tube closes in middle, moves toward rostral & caudal ends, closing by 29 - 30 pcd.
- Failures of neural tube closure
    - Anencephaly (rostral neuraxis)
    - Spina bifida (caudal neuraxis)

Spina bifida

Neural tube becomes…

- Ventricles & cerebral aqueduct
- Central canal of spinal cord



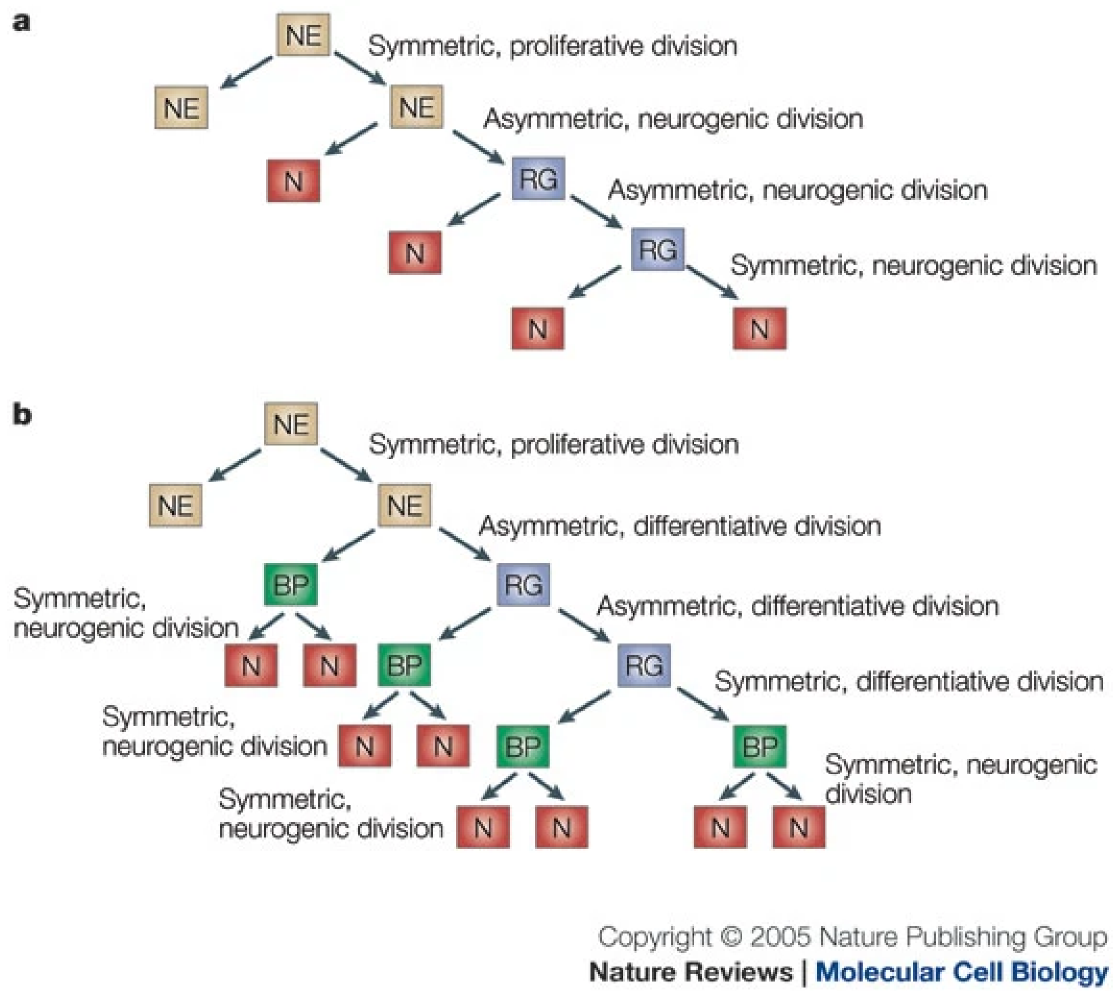
B
Prosencephalon
Mesencephalon
Rhombencephalon
s1
s4
s7
s1
s4
s7
Cervical Spinal Cord
s18
Thoracic Spinal Cord
s24
s28
Lumbosacral Spinal Cord

Differential growth of vesicles

- Rostro-caudal patterning via differential growth into vesicles
  - Forebrain (prosencephalon)
  - Midbrain (mesencephalon)
  - Hindbrain (rhombencephalon)

Neurogenesis and gliogenesis

- Neuroepithelium cell layer adjacent to neural tube
    - creating ventricular zone (VZ) and subventricular zone (SVZ)
- Pluripotent stem and progenitor cells divide, produce new neurons & glia



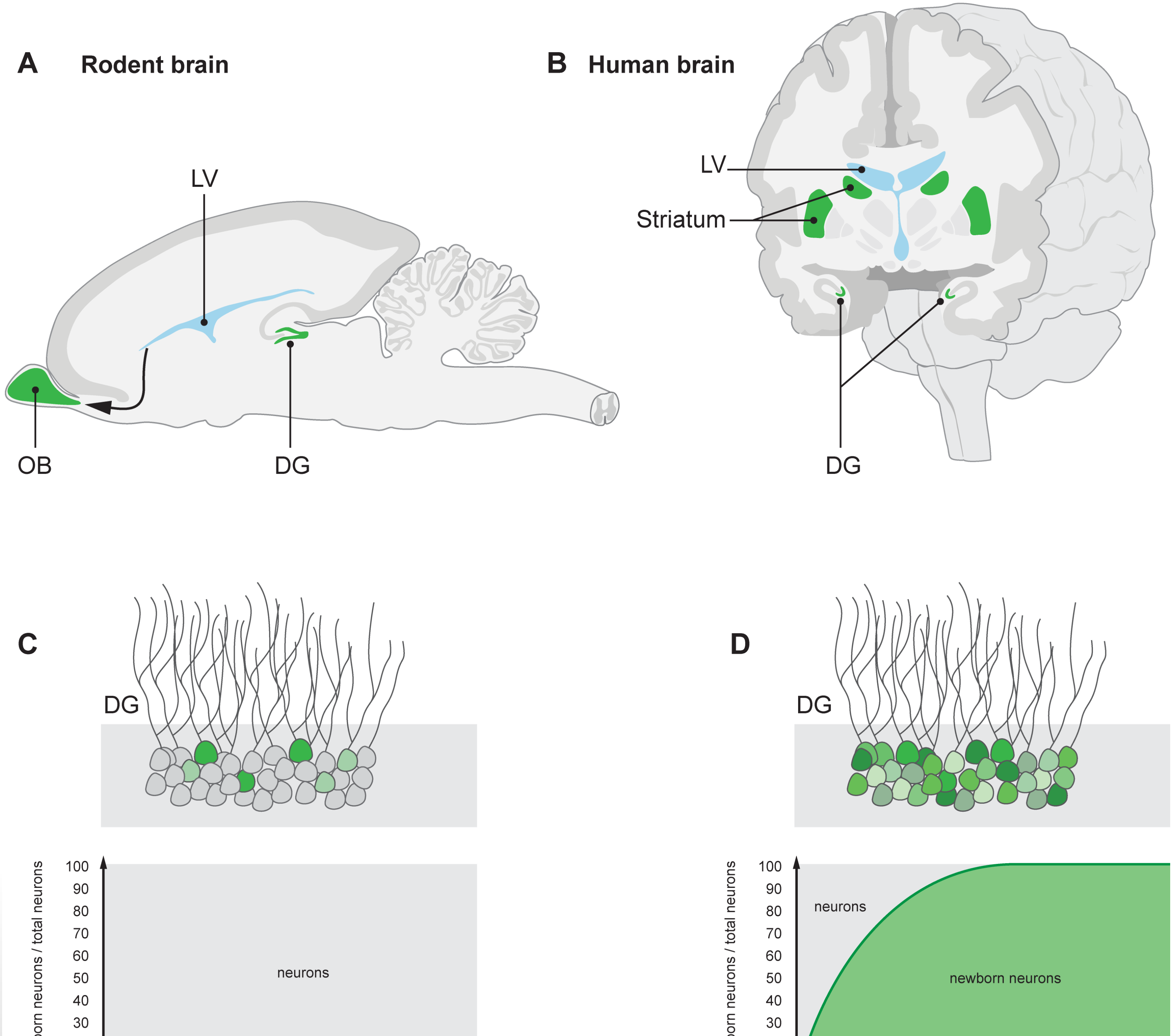
(Götz & Huttner, 2005)

Neurogenesis

- Neurogenesis (of excitatory Glu neurons) observed by 27 pcd (7 pcw; post-conceptual week)
    - complete by 191 pcd (27 pcw), (Silbereis et al., 2016)
- Most cortical and striatal neurons generated prenatally, but
    - Cerebellum continues neurogenesis ~ 18 mos postnatal mos

Old (adult) brains new neurons?

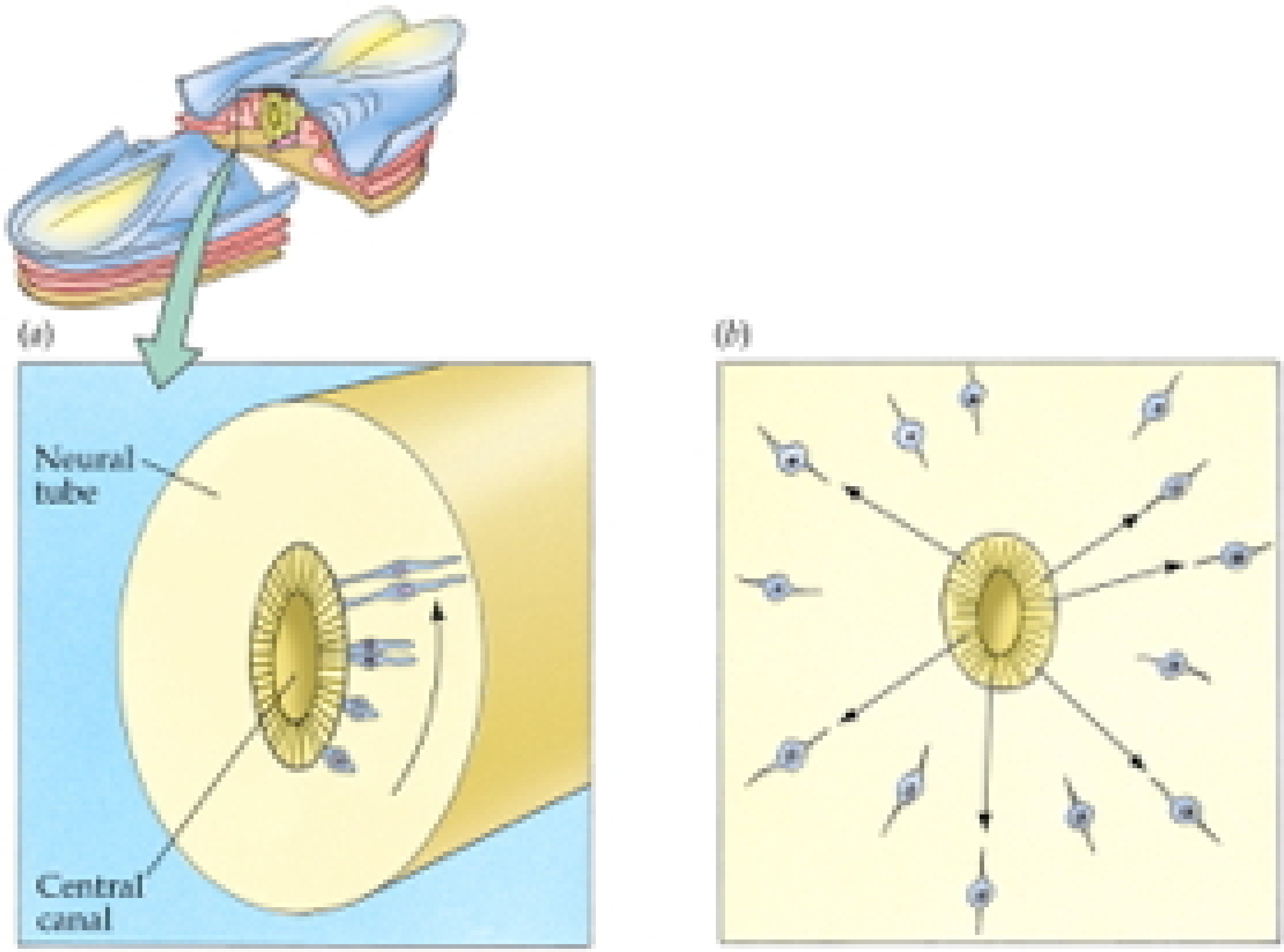
- Some animals, yes == songbirds, birds that store food caches
- Humans, on much more limited scale
    - hippocampus
    - striatum
    - olfactory bulb (minimally)
    - not much, if any, in cerebral cortex
- Most neurogenesis occurs near ventricles


A
Rodent brain
LV
OB
DG
B
Human brain
LV
Striatum
DG
C
DG
100
90
80
70
60
50
40
30
neurons
D
DG
100
90
80
70
60
50
40
30
neurons
newborn neurons

Neural progenitor/stem cells

- Undergo *symmetric* & *asymmetric* cell division
- Generate glia, neurons, and basal progenitor cells

Radial glia and cell migration



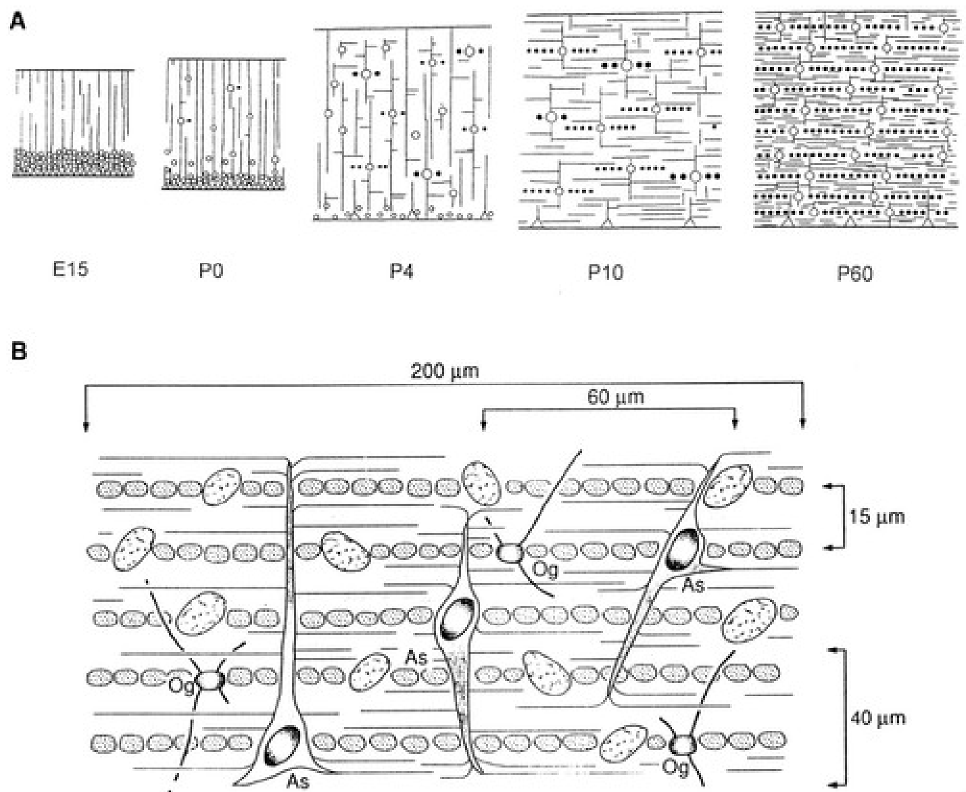
(a)
Neural tube
Central canal
(b)

Axon growth cone

Growth cones guided by

- Chemoattractants
  - e.g., Nerve Growth Factor (NGF)
- Chemorepellents
- Receptors in growth cone detect chemical gradients

Glia migrate, too



(Baumann & Pham-Dinh, 2001)

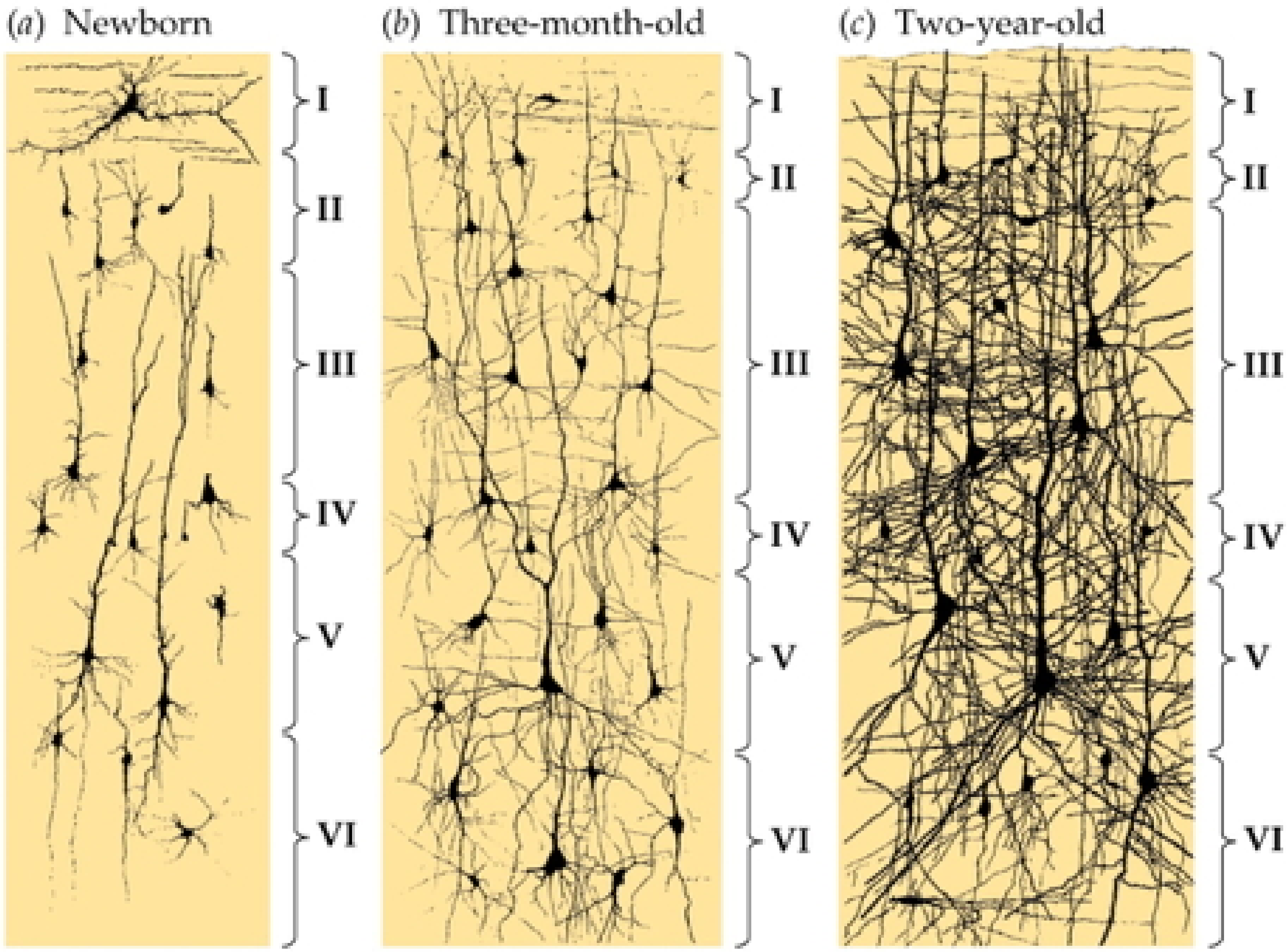
Differentiation

- Neuron vs. glial cell
- Cell type
    - myelin-producing vs. astrocyte vs. microglia
    - pyramidal cell vs. stellate vs. Purkinje vs. …
- NTs released
- Where to connect

Infancy & Early Childhood

Synaptogenesis

- Begins prenatally (~ 18 pcw)
- Peak density ~ 15 mos postnatal
- Spine density in prefrontal cortex ~ 7 yrs postnatal
- 700K synapses/s on average


(a) Newborn
(b) Three-month-old
(c) Two-year-old
I
II
III
IV
V
VI
I
II
III
IV
V
VI
I
II
III
IV
V
VI

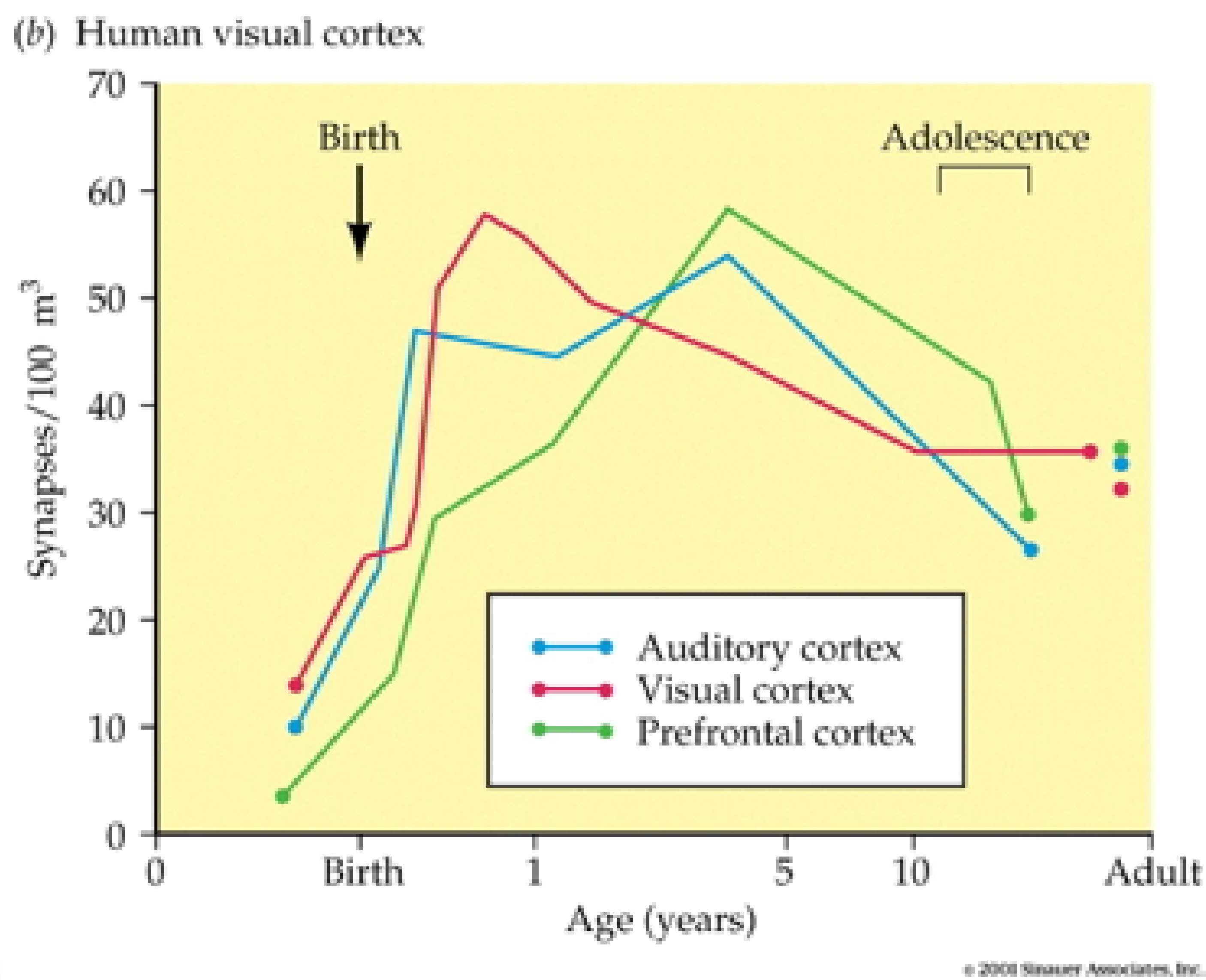
Proliferation, pruning

- Early proliferation (make many synapses)
- Later pruning
- Rates, peaks differ by area

Apoptosis (programmed cell death)

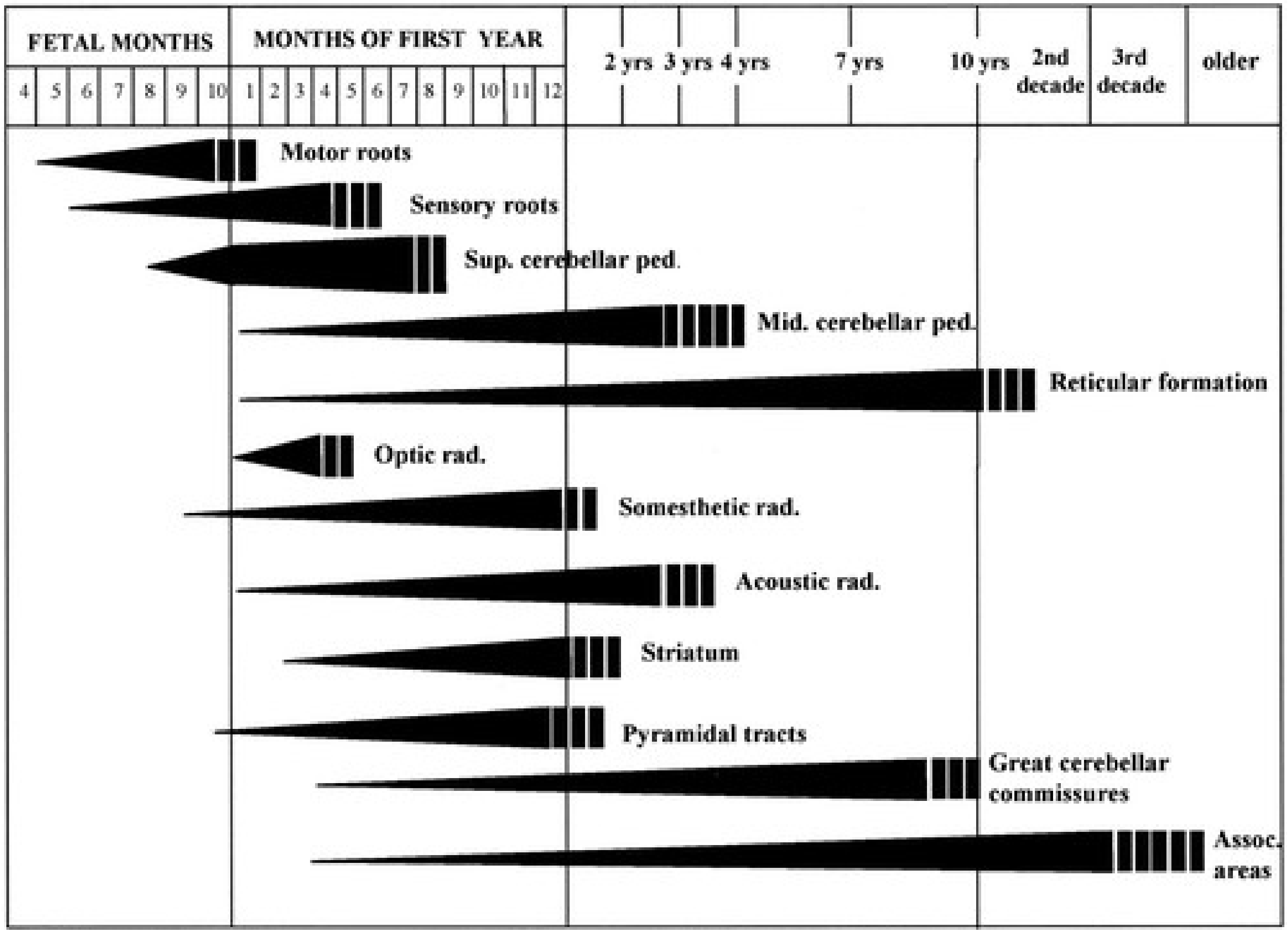
- 20-80%, varies by area
- Spinal cord >> cortex
- Quantity of nerve growth factors (NGF) influences

Synaptic rearrangement



- Progressive phase: growth rate >> loss rate
- Regressive phase: growth rate << loss rate

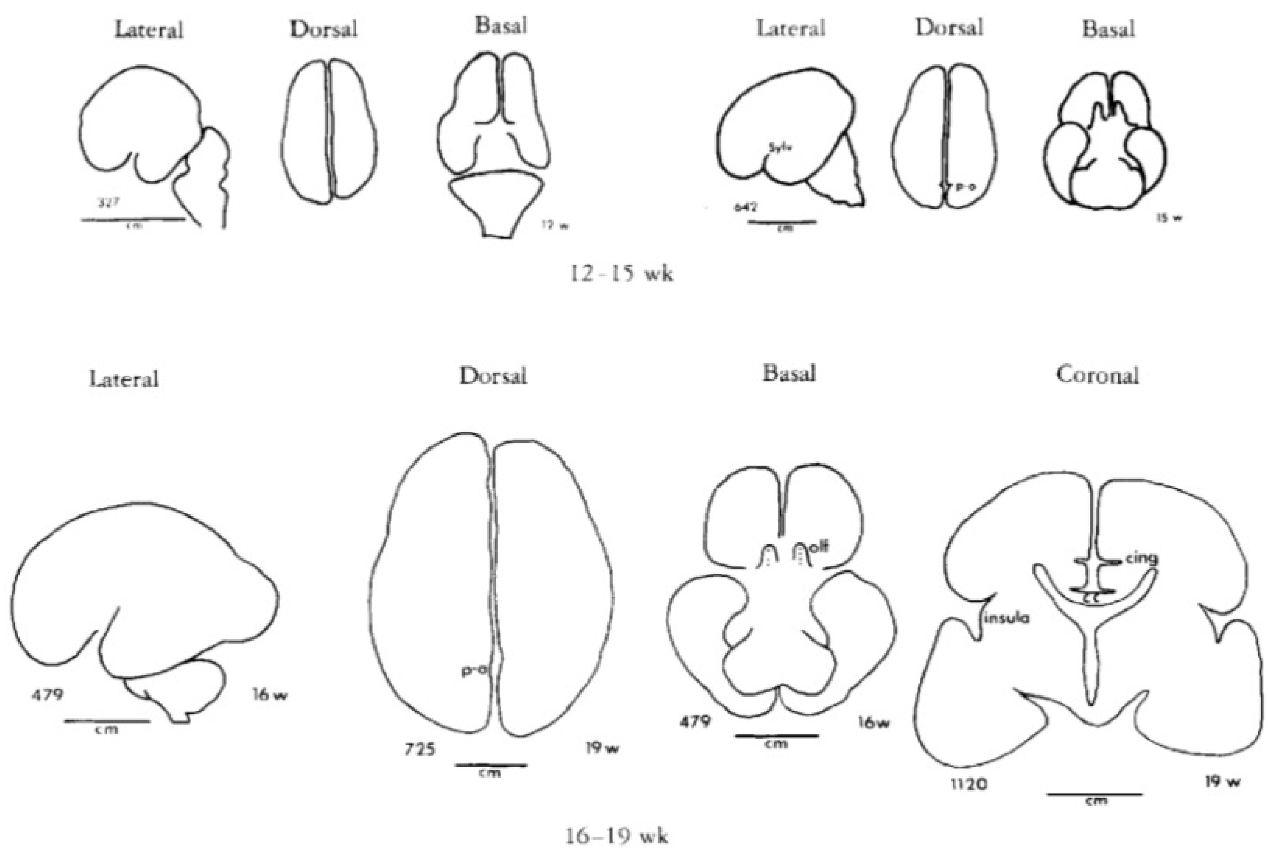
Myelination



(Baumann & Pham-Dinh, 2001)

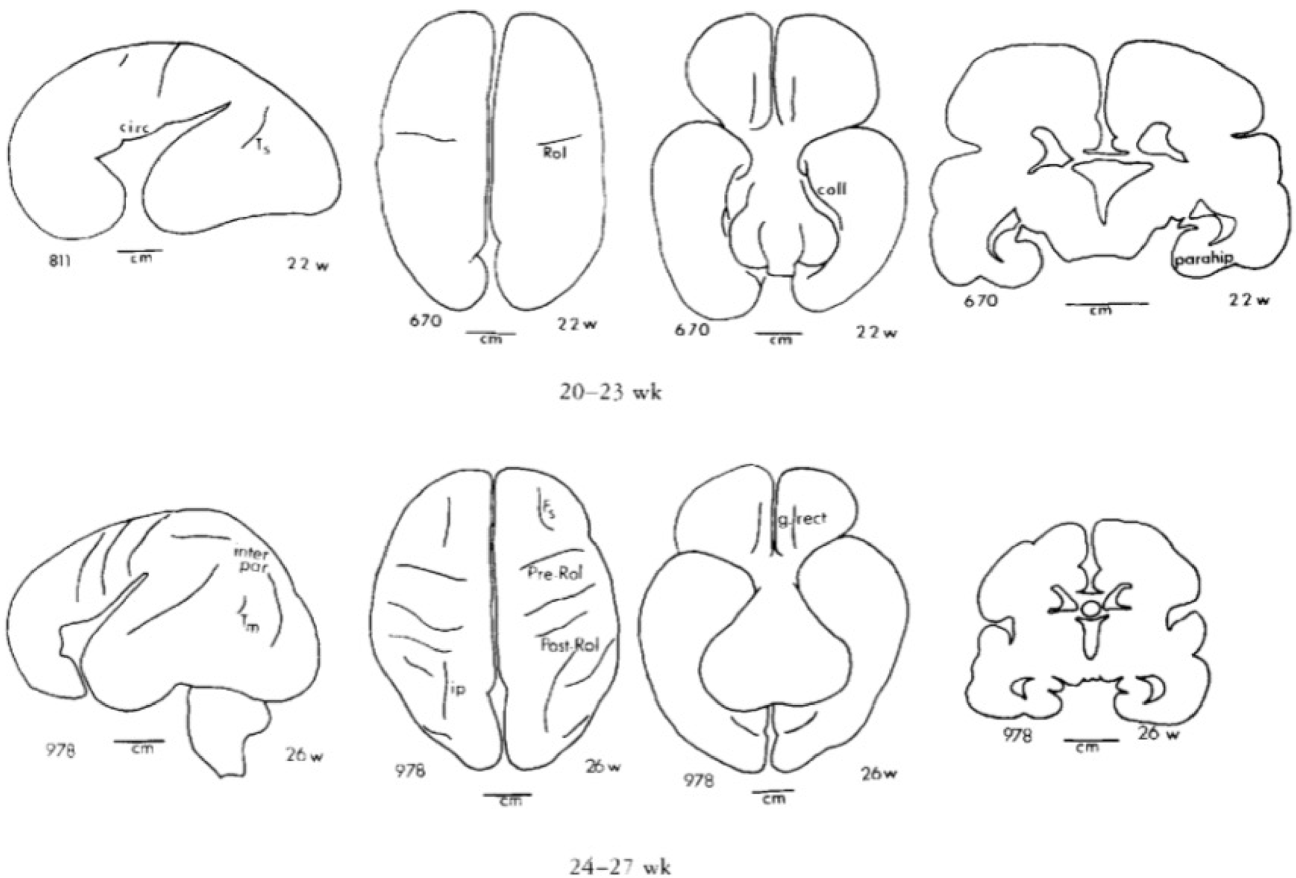
- Neonatal brain largely unmyelinated
- Gradual myelination, peaks in mid-20s
- Non-uniform pattern
    - Spinal cord before brain
    - Sensory before motor

Gyral development (12-19 pcw)



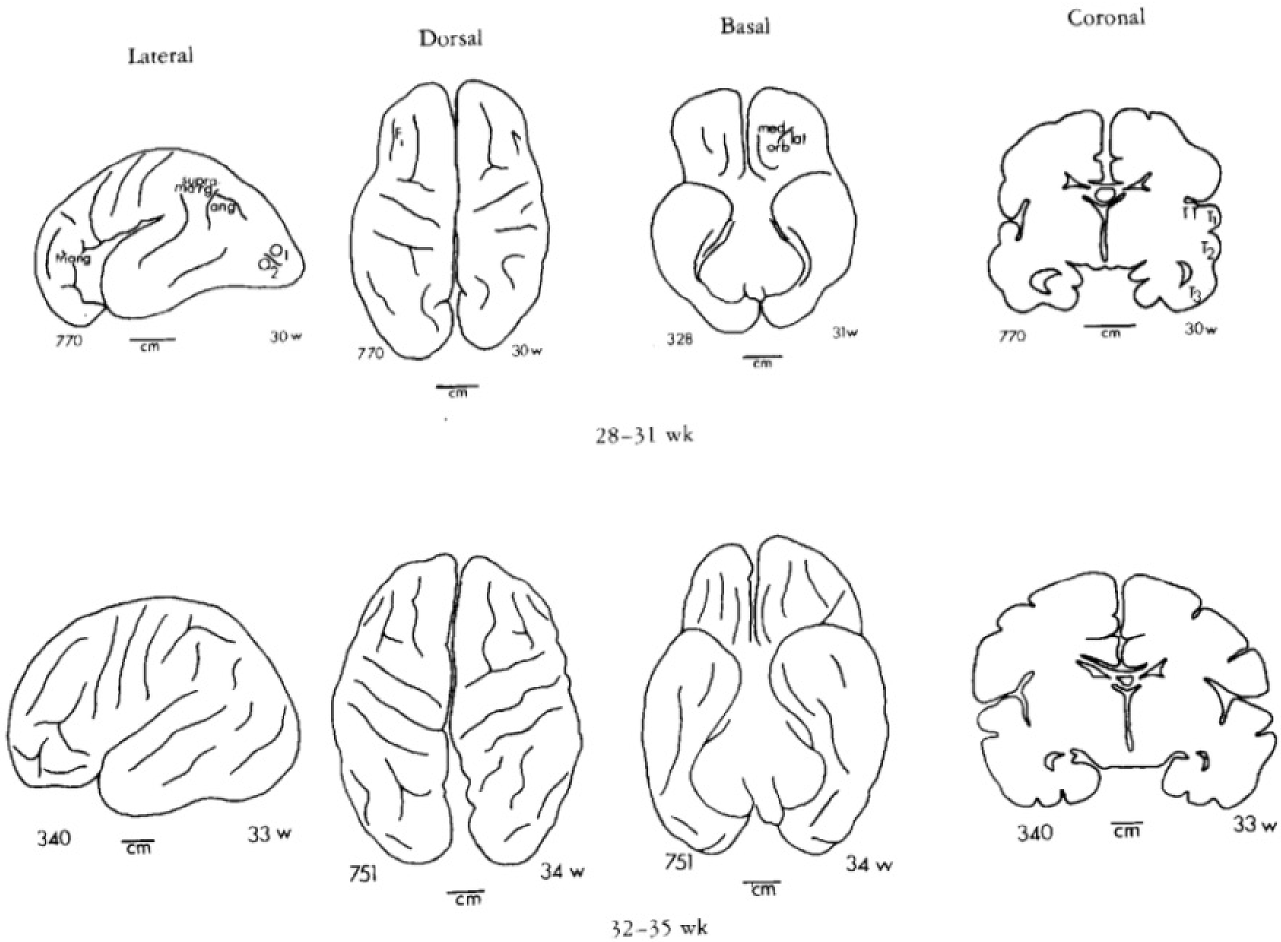
(Chi, Dooling, & Gilles, 1977)

20-27 pcw



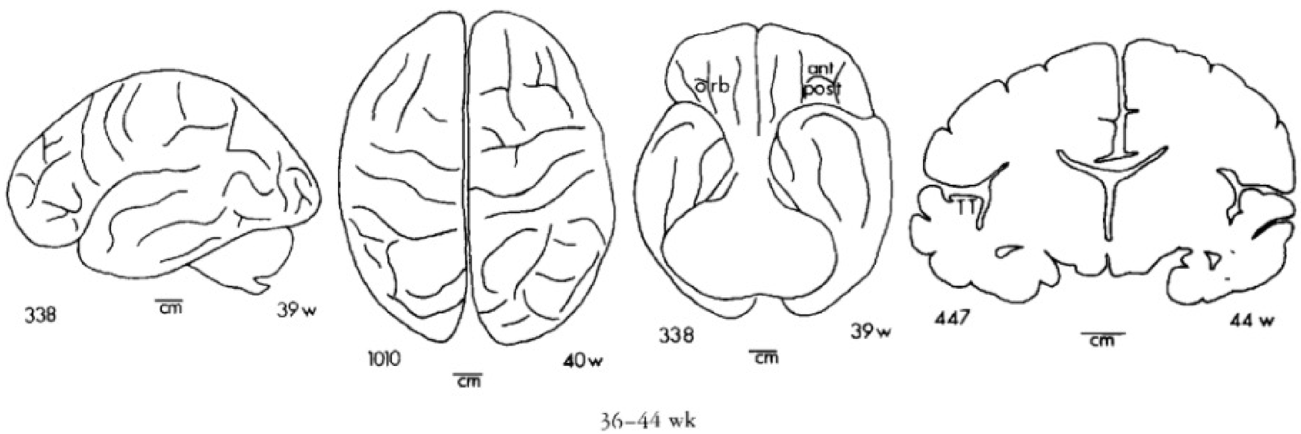
(Chi et al., 1977)

28-35 pcw



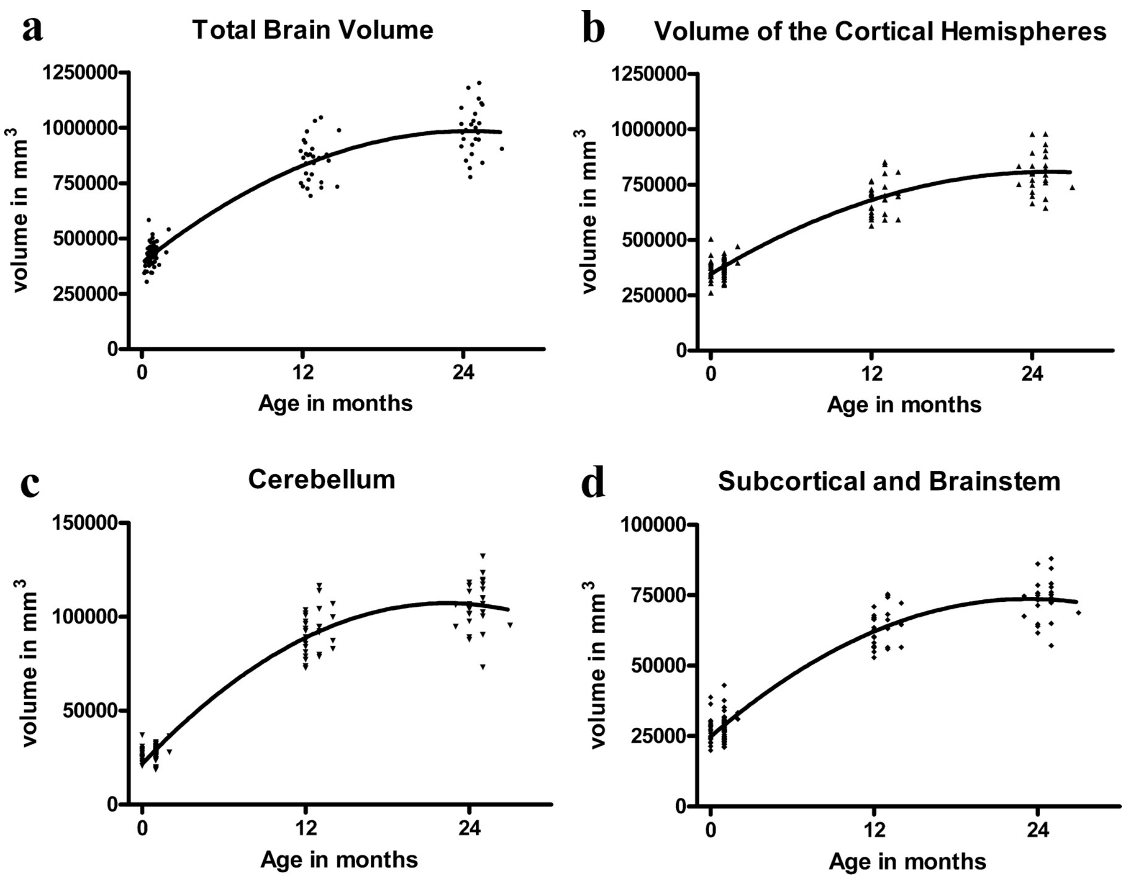
(Chi et al., 1977)

36-44 pcw



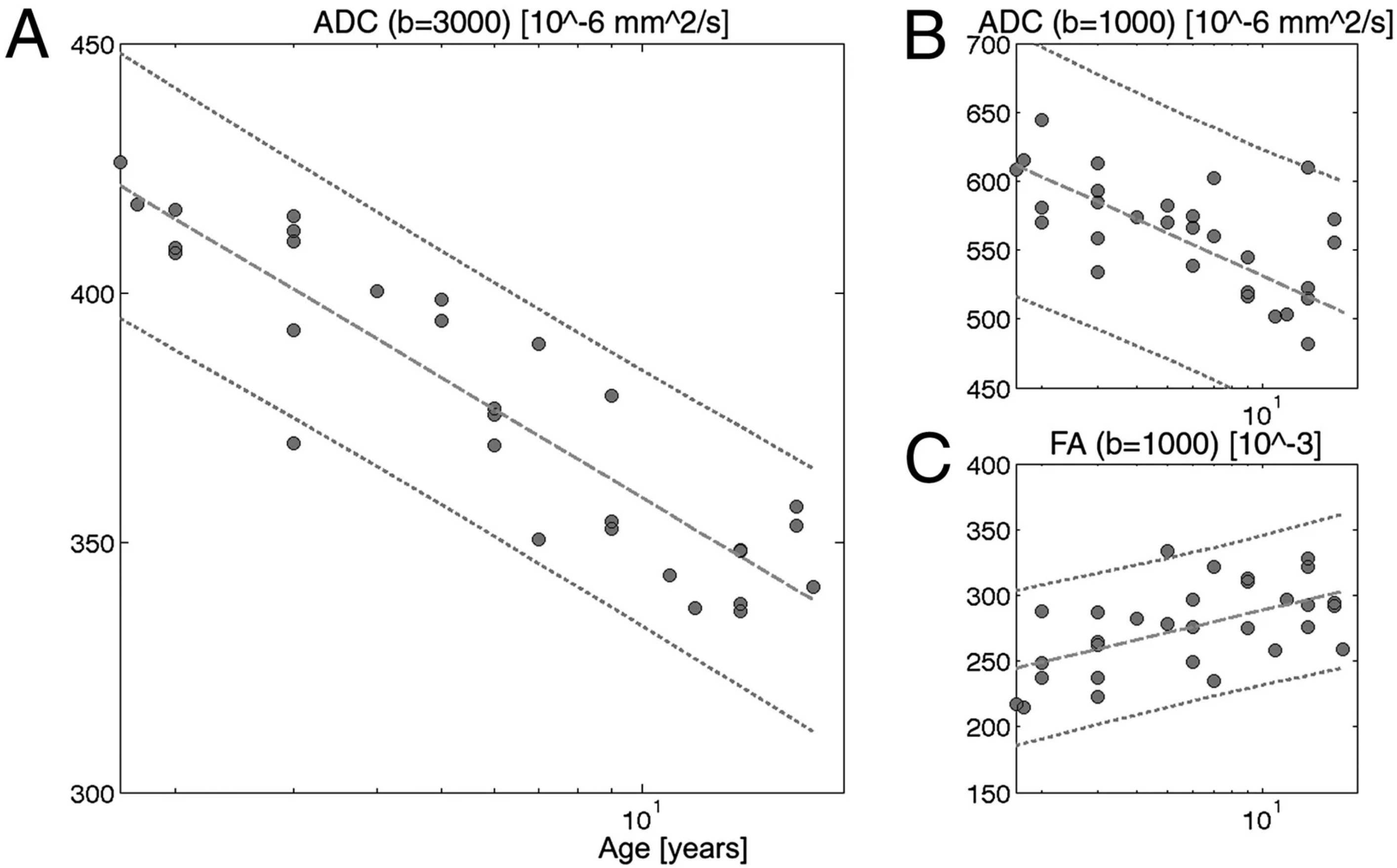
(Chi et al., 1977)

Structural/morphometric development



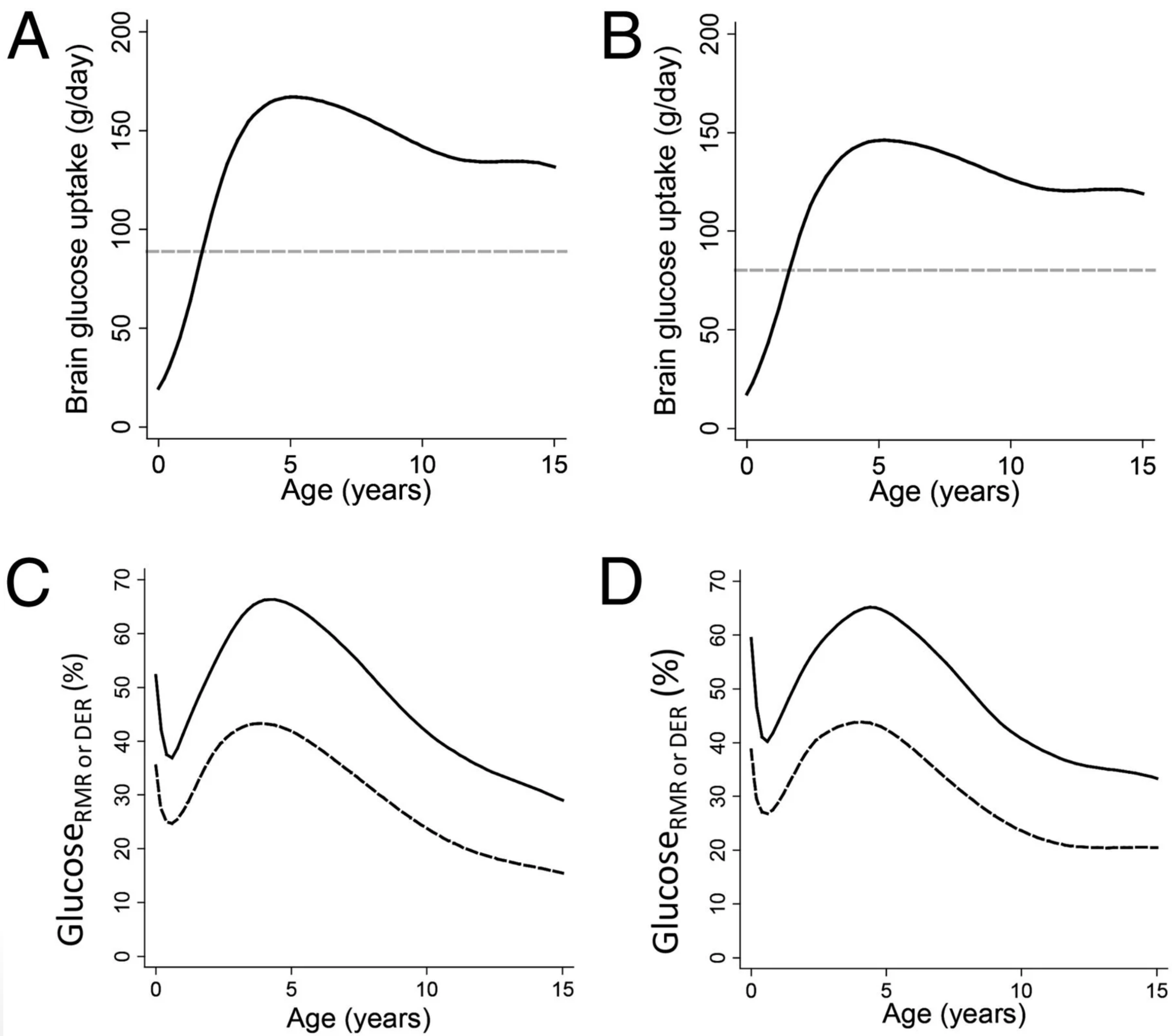
(Knickmeyer et al., 2008)

Myelination across human development



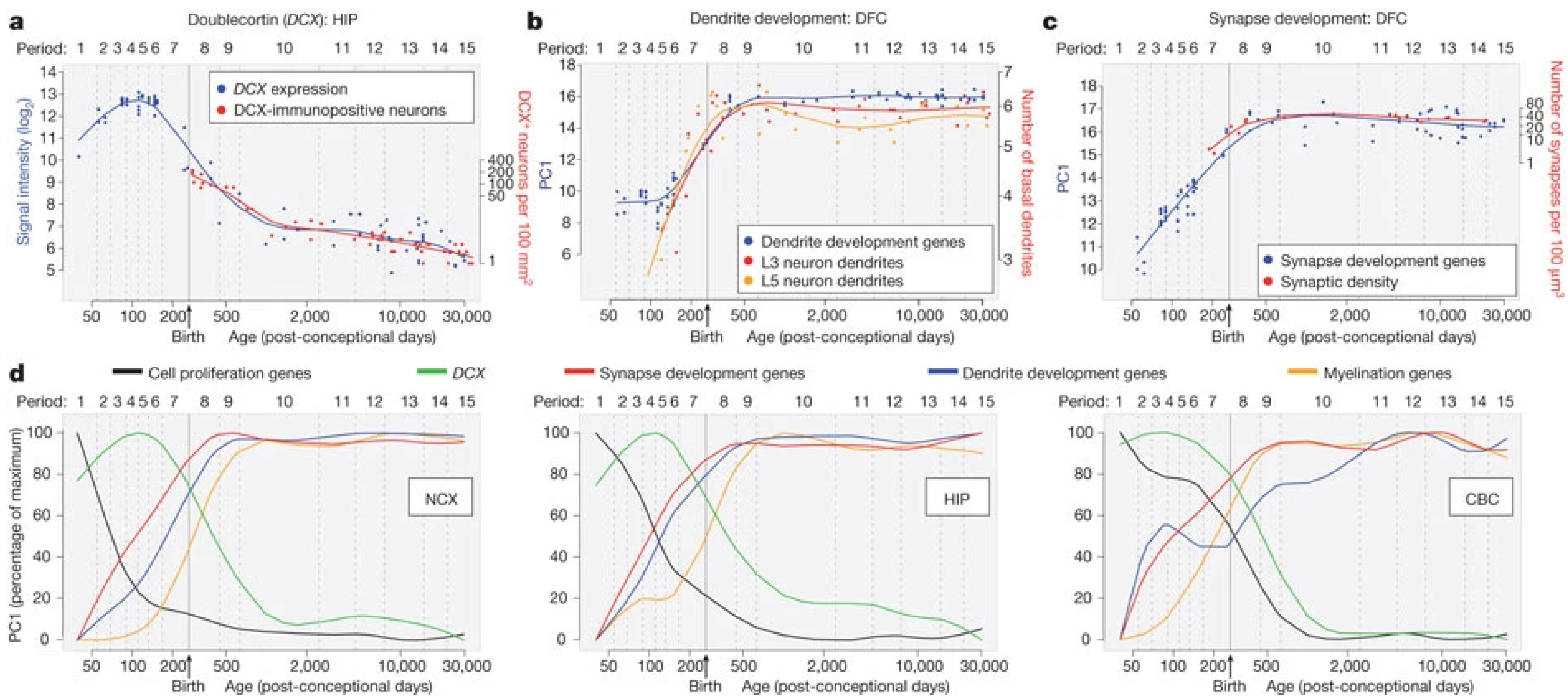
(Hagmann et al., 2010)

Changes in brain glucose use



(Kuzawa et al., 2014)

Gene expression across development



(Kang et al., 2011)

Summary of developmental milestones

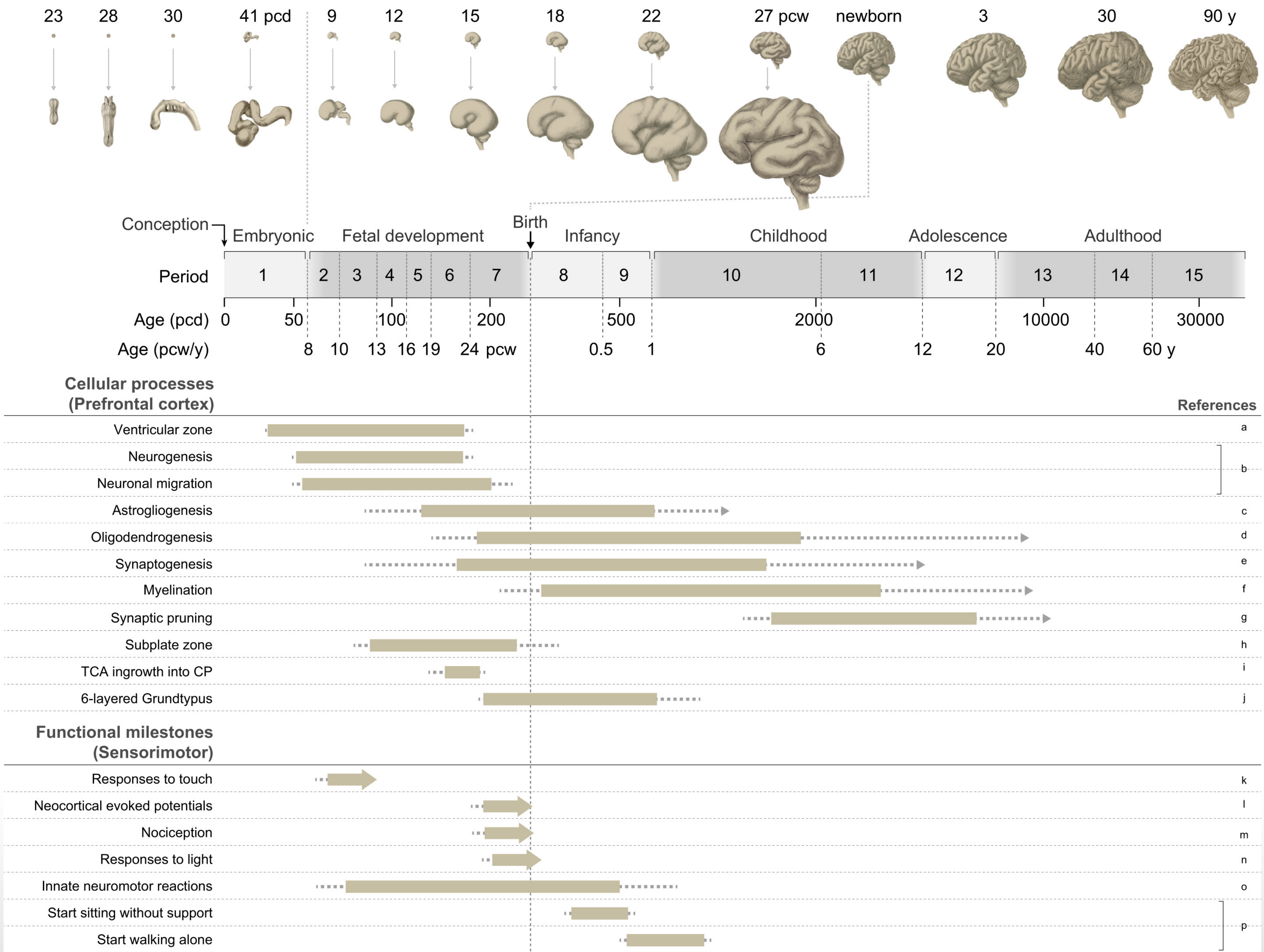
Prenatal

- Neuro- and gliogenesis
- Migration
- Synaptogenesis begins
- Differentiation
- Apoptosis
- Myelination begins

Postnatal

- Synaptogenesis
- Cortical expansion, activity-dependent change
- Then cubic, quadratic, or linear declines in cortical thickness
- Myelination
- Prolonged period of postnatal/pre-reproductive development (Konner, 2011)

Timeline of milestones



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