The Amazing Brain Webinar Series:

Select Topics in Neuroscience and Child Development for the Clinician

Part VI – What a Baby Can and Can't Do:

Early Brain Development

Hanna Stevens, MD, PhD

Jointly sponsored by the Association of University Centers on Disabilities, the Maternal and Child Health Bureau/Health Resources and Services Administration and Yale School of Medicine, Section of Developmental-Behavioral Pediatrics

Webinar Overview

- Webinar Recording
  - Visit www.aucd.org/webinars
- Q & A
  - Please submit your questions throughout the webinar via the “question box” on your webinar dashboard. Questions will be answered following the presentation.
- Survey
  - Please complete the short survey at the end of the webinar!

Introductions

Carol Weitzman, MD, Professor of Pediatrics and the Child Study Center, Yale School of Medicine

Hanna Stevens, MD, PhD, Assistant Professor, Child Study Center, Associate Director, Albert J. Solnit Integrated Training Program, Yale School of Medicine

Prenatal and Early Life Factors in Brain Development

What a Baby Can and Can't Do

Hanna Stevens M.D. Ph.D.
Yale Child Study Center

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childstudycenter.yale.edu

Yale SCHOOL OF MEDICINE

Present at Birth	Absent at Birth
"Sensing"	Fine tuned sensing
Being soothed	Awareness of and regulating moods
Having moods	Having complex moods
Sleeping	Providing for own care (feeding, toileting, etc)
Eating	Patterned behaviors
Reflexes	Complex Learning & preferring
Learning & preferring	Complex Social Interaction
Social Connecting	Complex gross and fine motor movement
Orienting & Unformed Movements	

“Neonatal Necessities”

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“Sensing”

Being soothed

Having moods

Sleeping

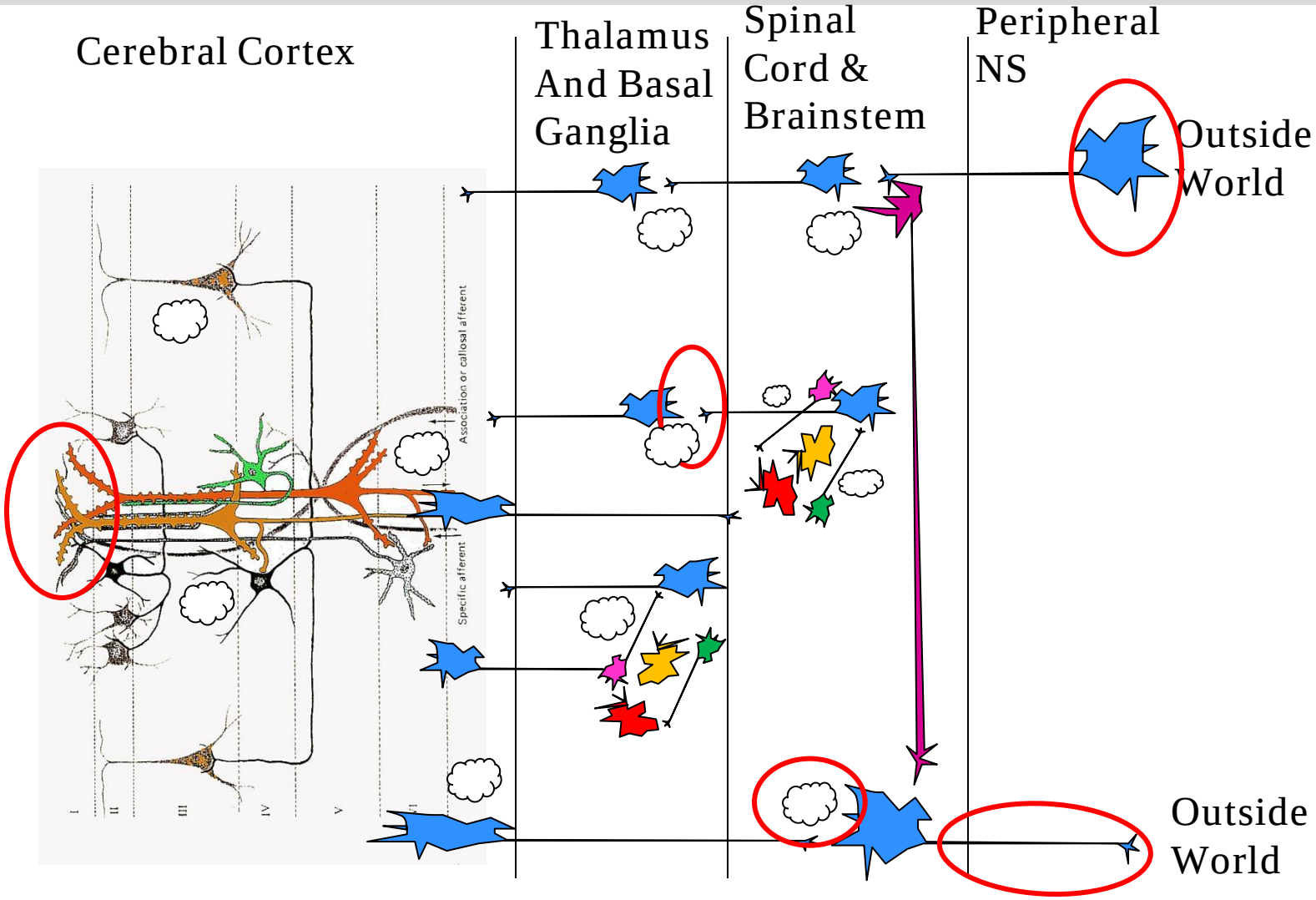
Eating

Reflexes

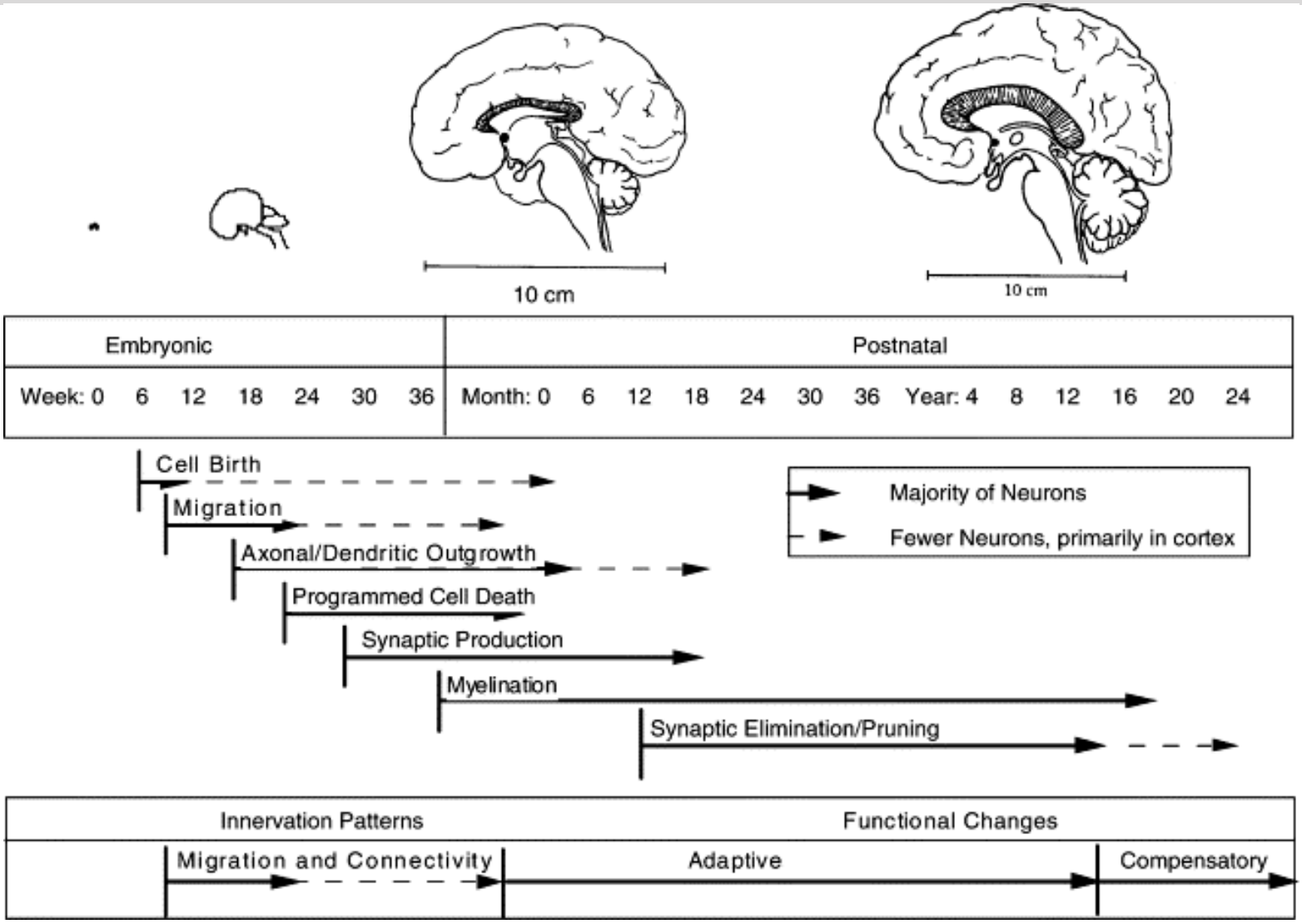
Learning& preferring

Social Connecting

Orienting & Unformed Movements



Developmental Processes



Andersen (Neurosci and Biobehav Rev; 2003)

Patterning the Nervous System

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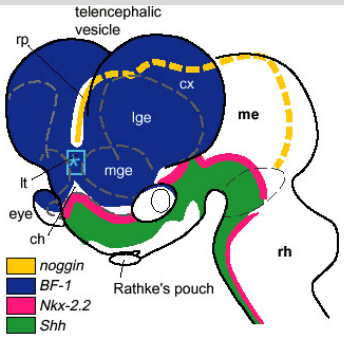
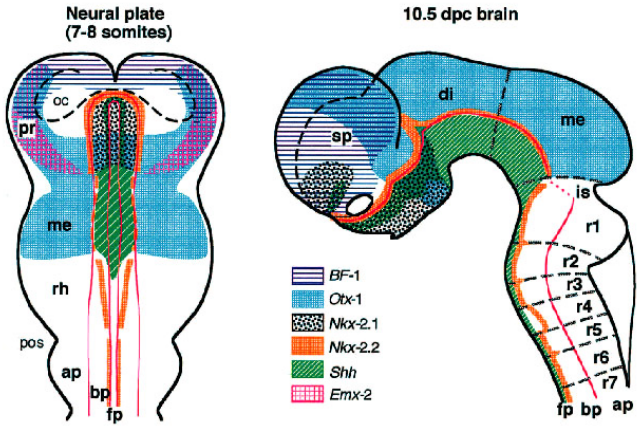
Regions defined by unique combinations of factors

Cellular fate determined by activation of one or more transcription factors





Development 121, 3923-3933 (1995)
Printed in Great Britain © The Company of Biologists Limited 1995
DEV9406

Longitudinal organization of the anterior neural plate and neural tube

Kenji Shimamura[1], Dennis J. Hartigan[1], Salvador Martinez[2], Luis Puelles[2] and John L. R. Rubenstein[1,*]

[1]Nina Ireland Laboratory of Developmental Neurobiology, Programs in Developmental Biology and Neuroscience, Center for Neurobiology and Psychiatry, Department of Psychiatry and Langley Porter Psychiatric Institute, University of California, San Francisco, 401 Parnassus Avenue, San Francisco, California 94143-0984, USA
[2]Department of Morphological Sciences, Faculty of Medicine, University of Murcia, 30100 Murcia, Spain

Patterning is not Temporary

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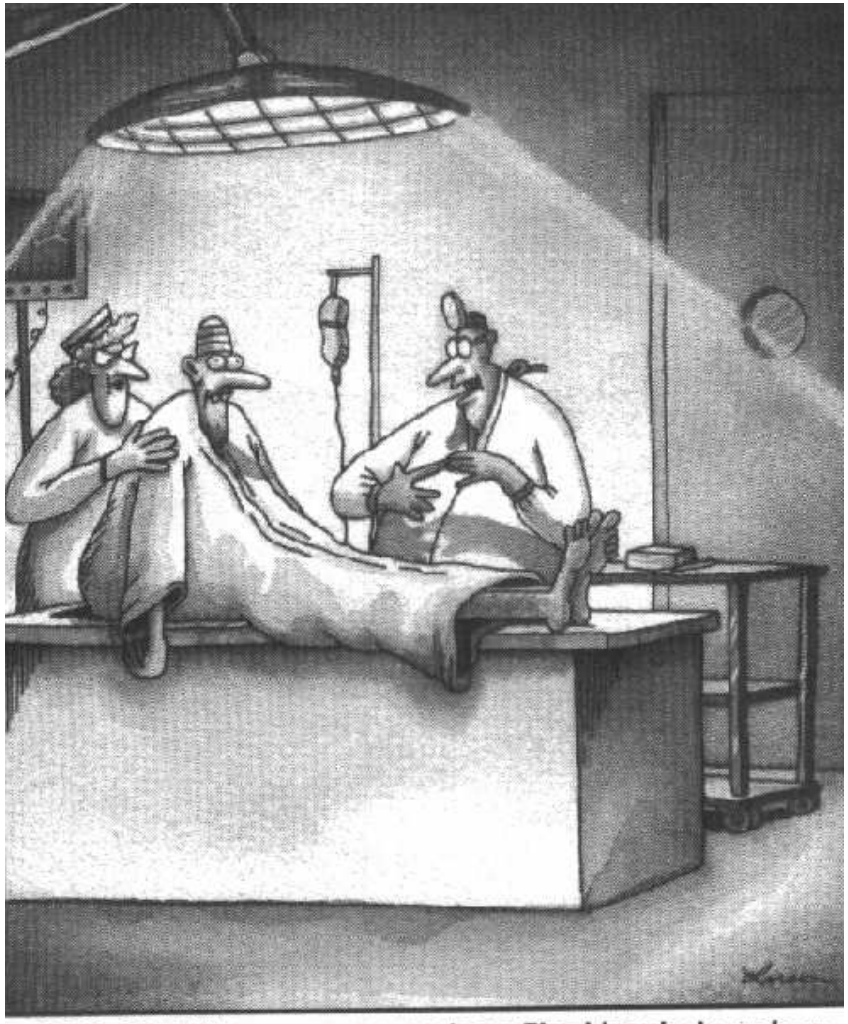

"OK, Mr. Dittmars, remember: That brain is only a temporary, so don't think too hard with it."

The Complete Cartoons of the The New Yorker, 2006

Patterning and Adult Brain

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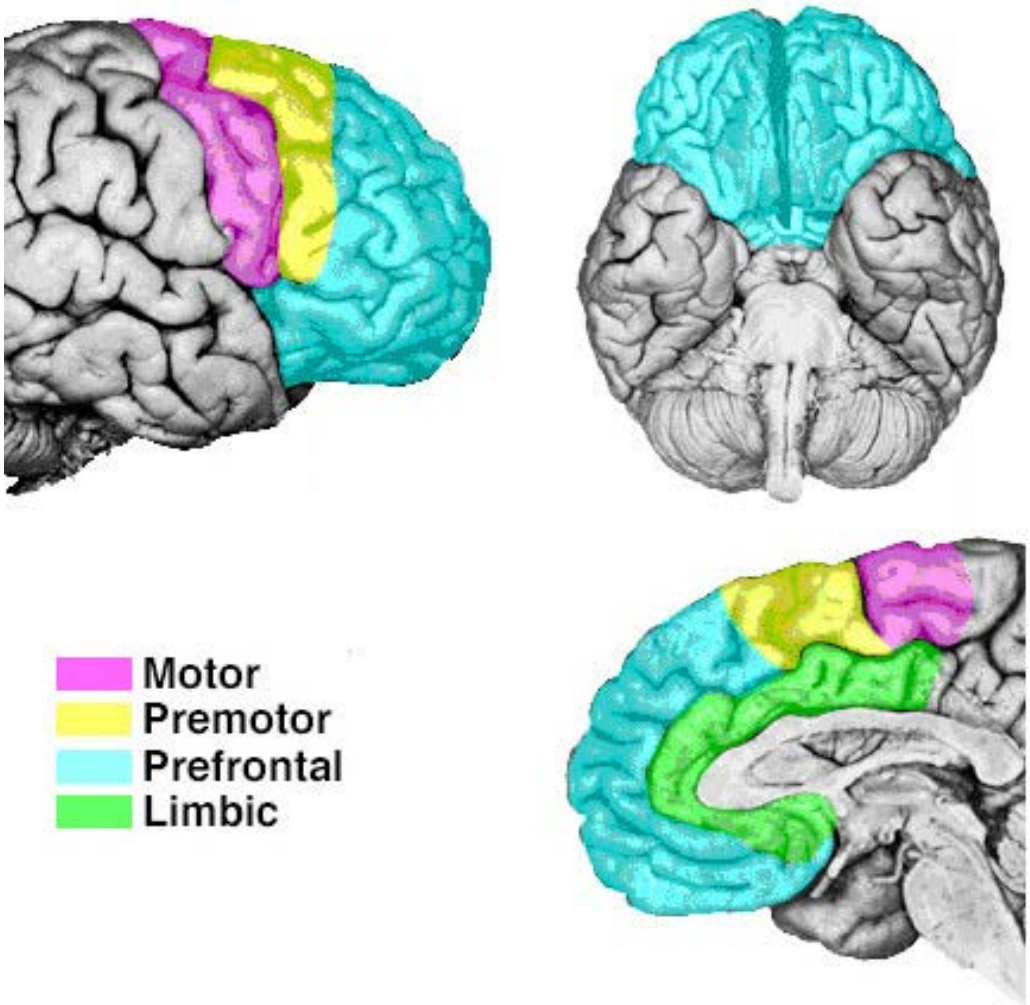
Cortex becomes defined by these early patterning signals to be the place where complex sensory, motor, emotional, executive and integrated processing occurs.



Development of the Nervous System
Sanes, Reh and Harris, Copyright 2006.

Human Cortical Expansion

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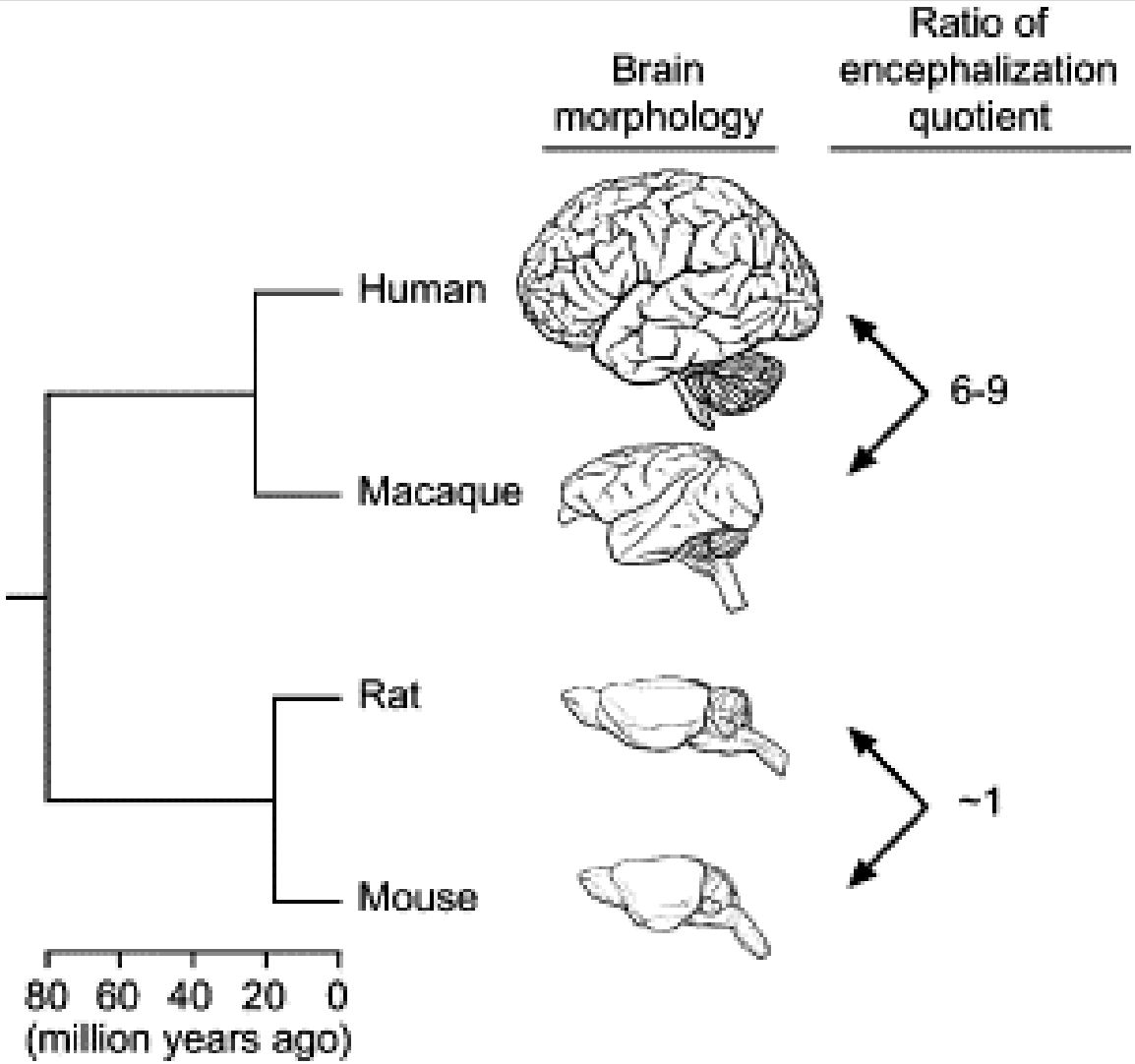
- PFC is implicated in many complex functions relevant to mental illness
  - Social functioning
  - Emotional regulation
  - Executive functioning
  - Stress regulation
- Prefrontal cortex (PFC) is most expanded region in primate brain



Dorus et al. *Cell*, Vol 119, 2004

Cortical Structure

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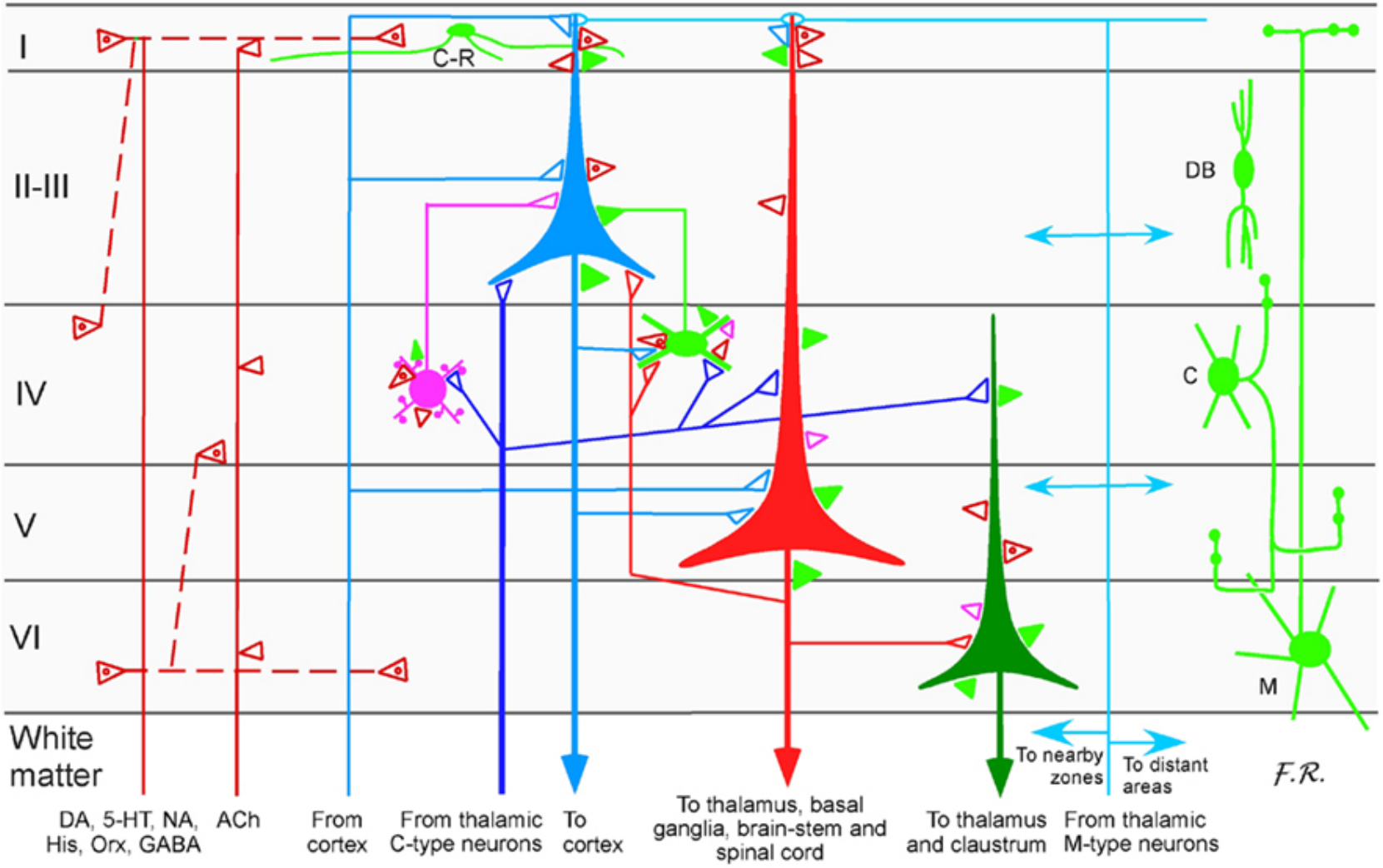
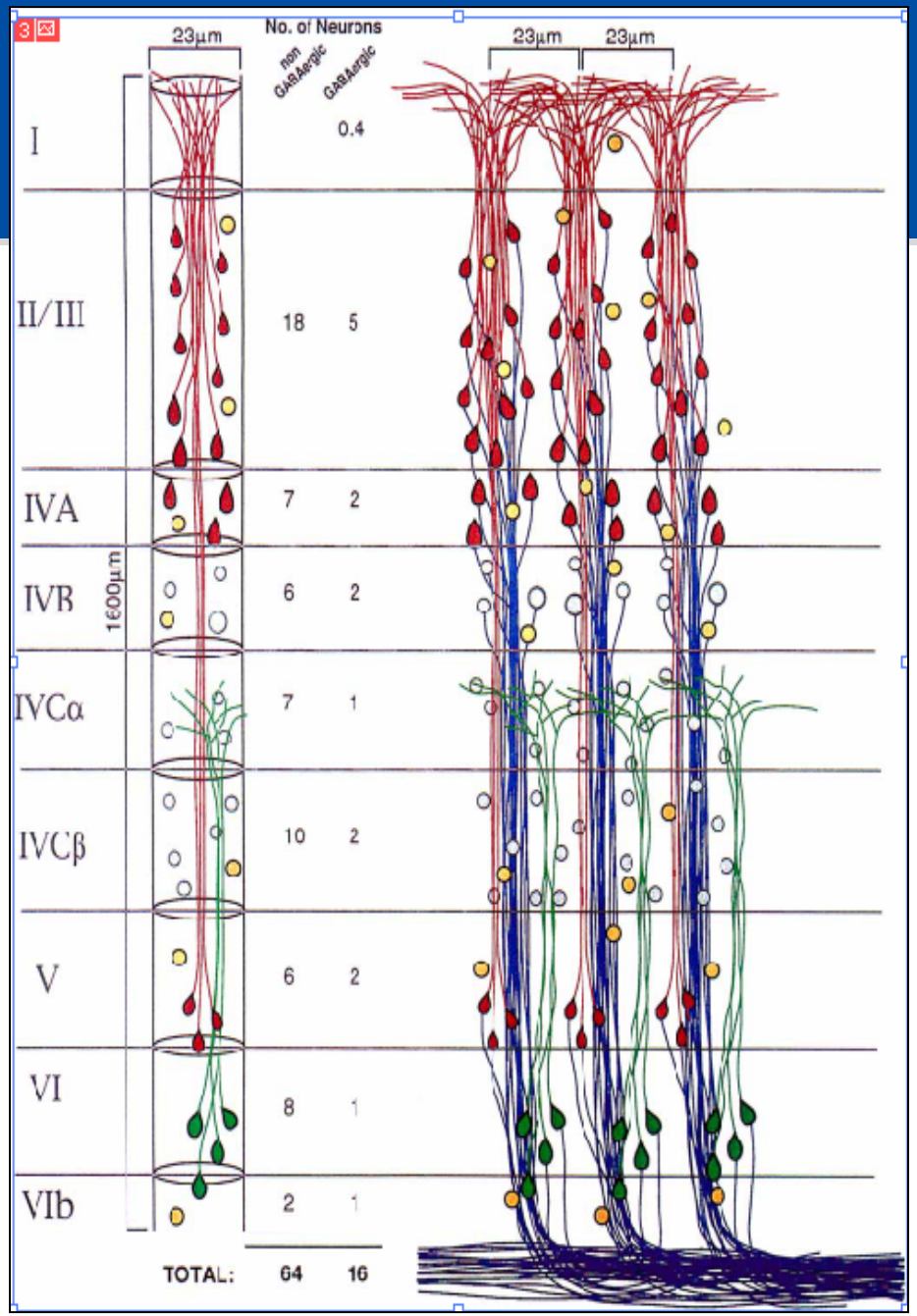
Pial Surface



de Andres et al, 2011 Frontiers in Neurology



Cortical Minicolumn Structure

Peters and Yilmaz, 1993

Expanding Cortex

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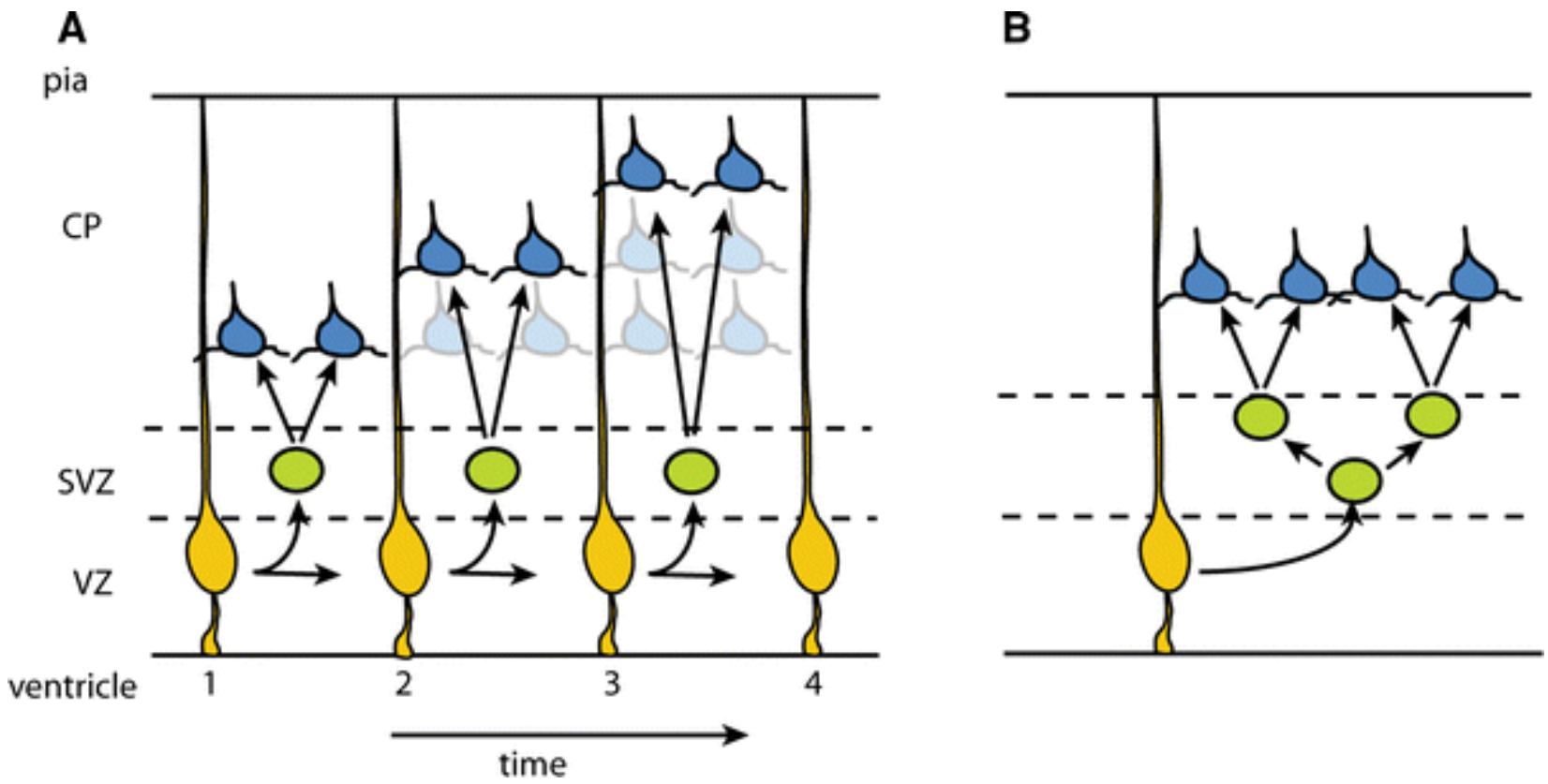

Vaccarino et al. *J. Autism Dev. Dis*, 2009

Processes for Cortex Formation

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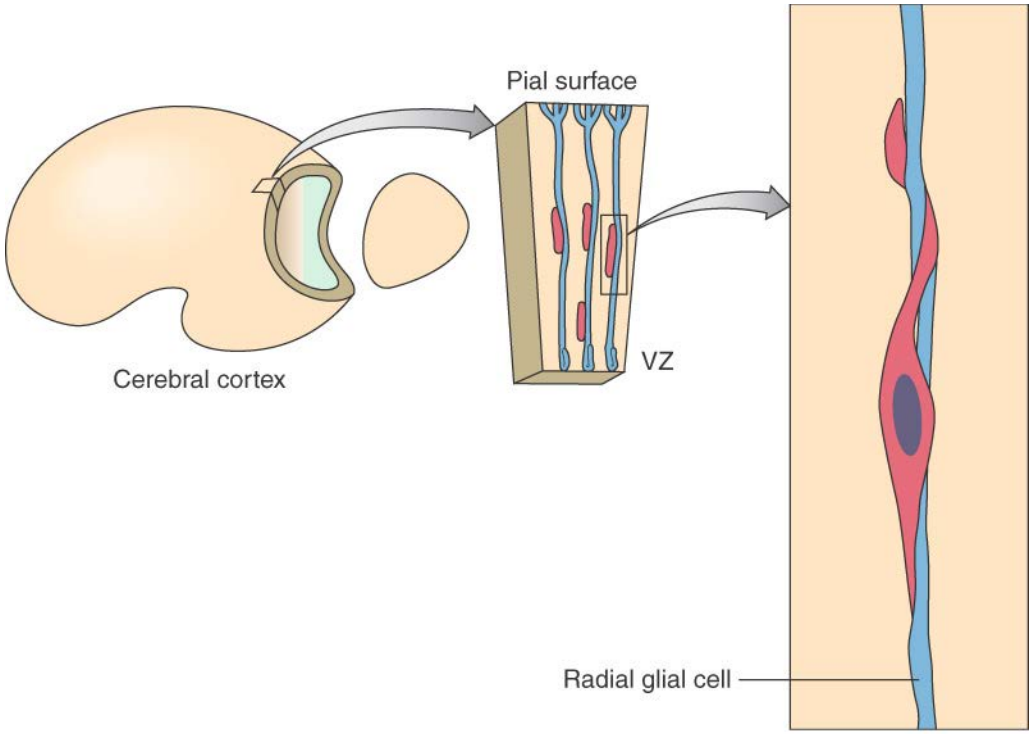
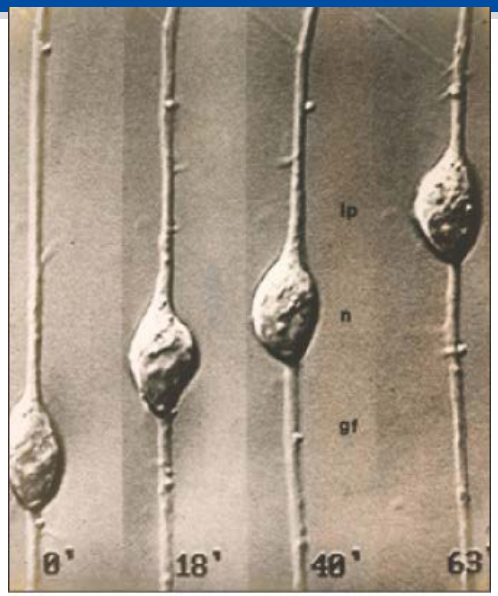
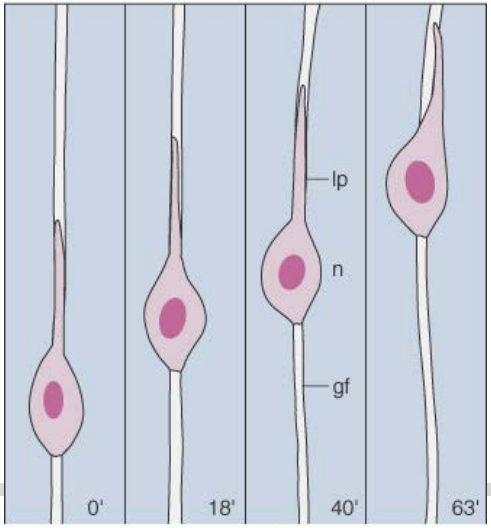
- Neuronal Migration:
  - newer cells migrate along processes of older, parent cell



(Modified from Rakic, 1972.)





(Courtesy of M.E. Hatten.)

Development of the Nervous System
Sanes, Reh and Harris, Copyright 2006.

Processes for Cortex Formation

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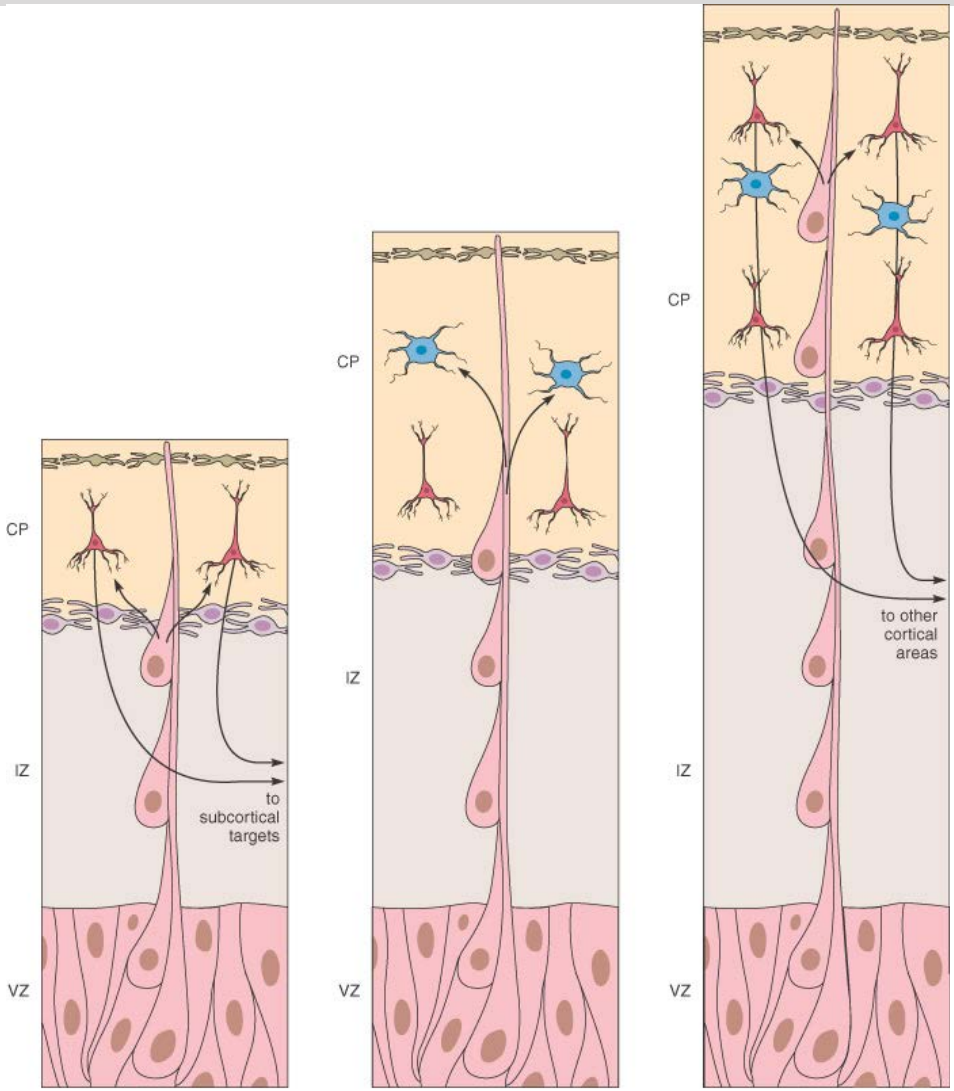
- Cortex populated in an inside-out manner
- Cells in different layers send axons to different locations
  - Other cortical regions
  - Thalamus and basal ganglia
  - Midbrain and spinal cord



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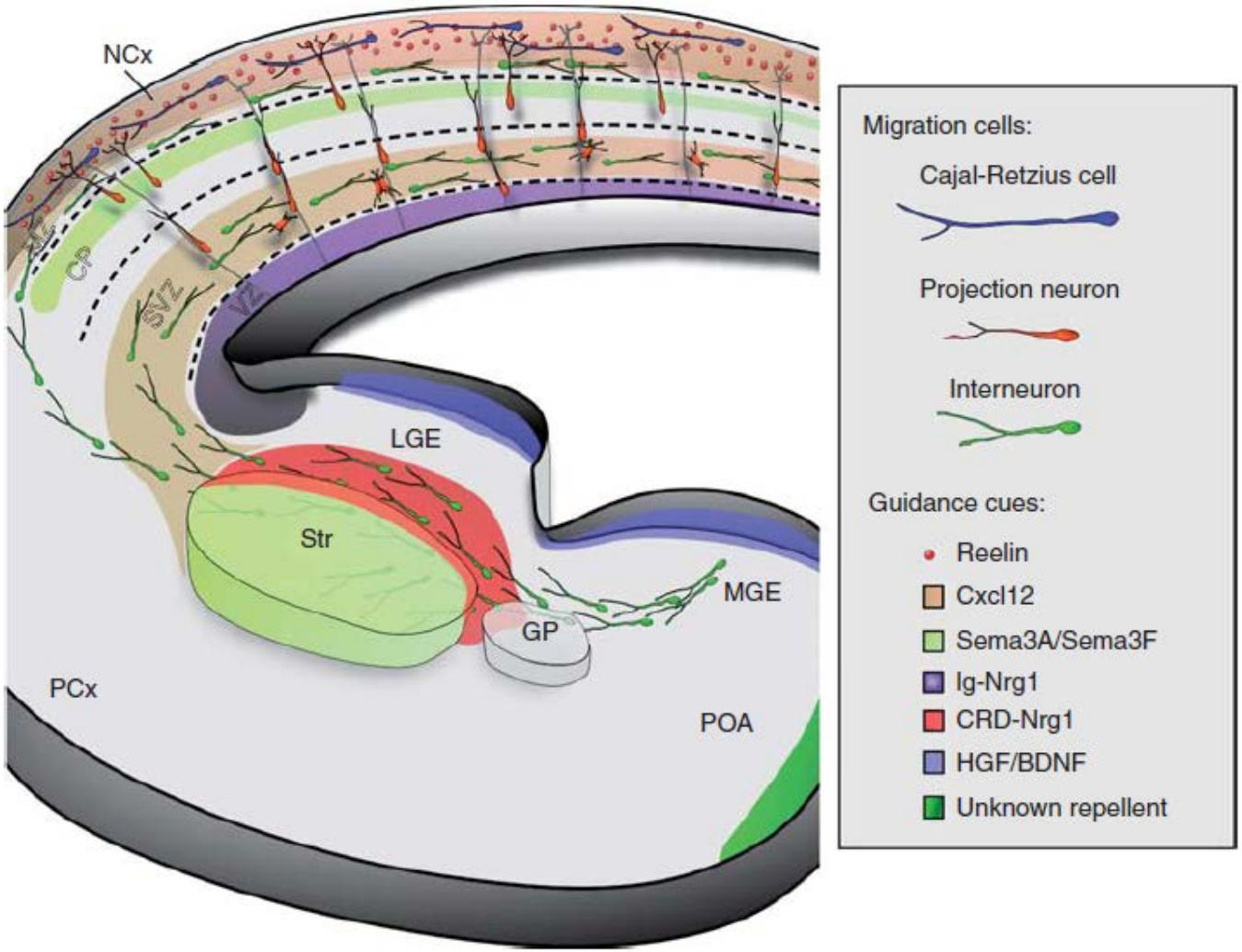
Development of the Nervous System
Sanes, Reh and Harris, Copyright 2006.

Inhibitory Neurons



Marin et al (CSH Perspectives; 2010)

Programmed Cell Death

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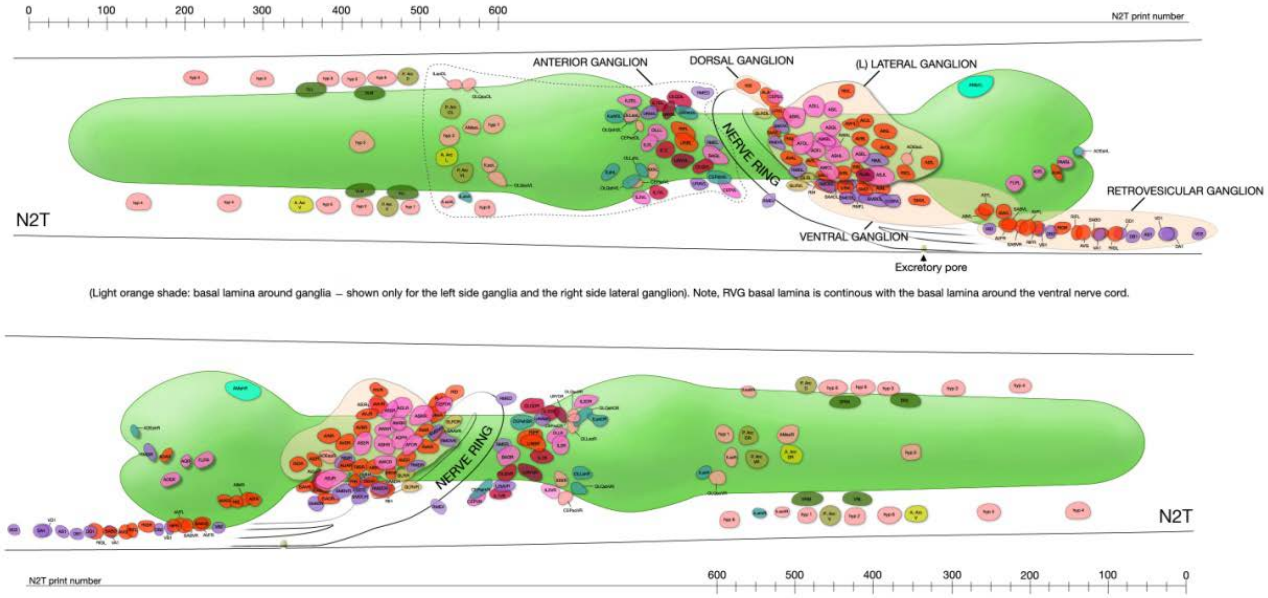
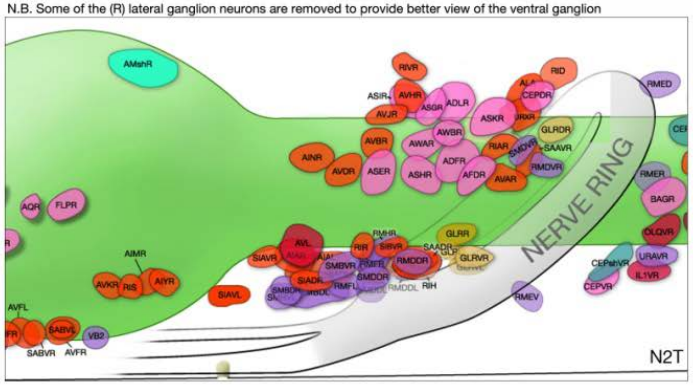
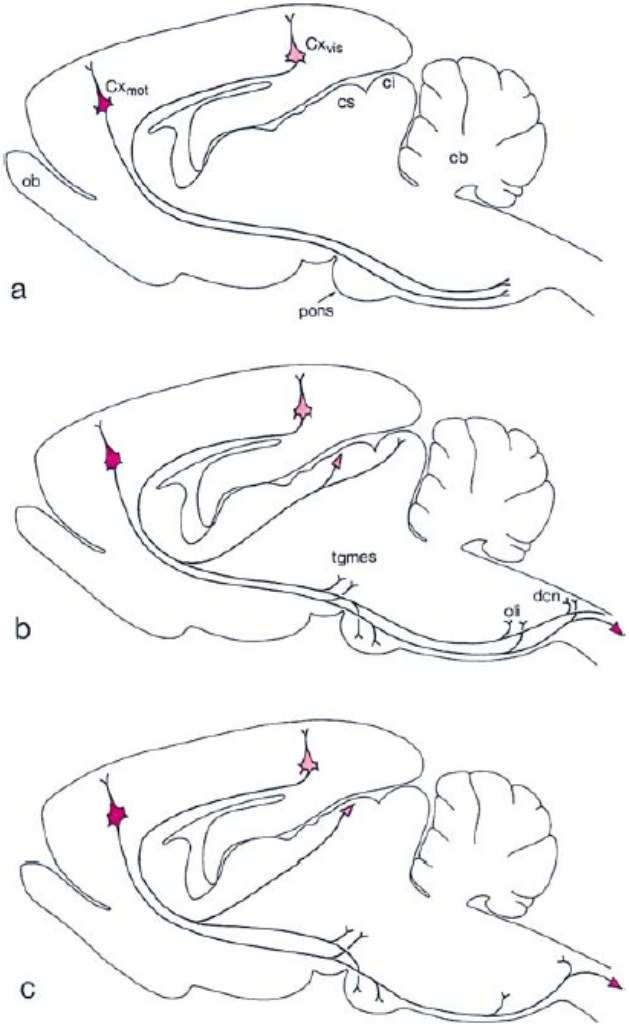
In worms, all neurons have a name and their eventual function/fate is known

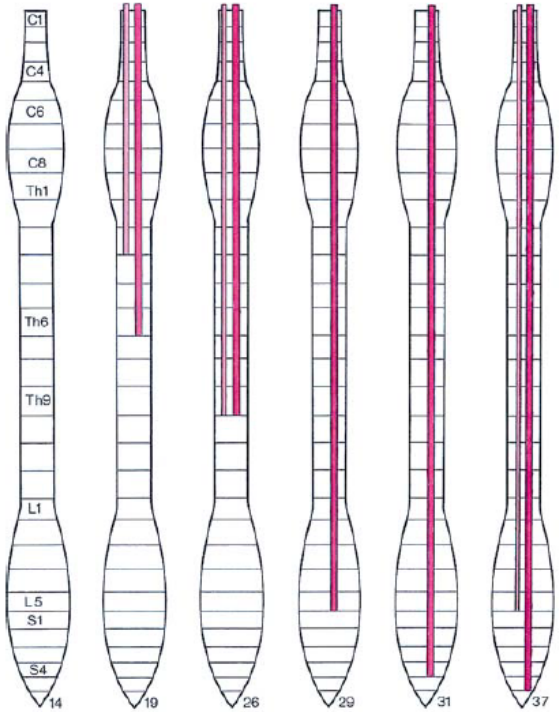
Death of some cells appears necessary for appropriate fate specification of other cells





Axonal Outgrowth





Axons grow as cells populate cortex

Axons respond to regional cues (as in patterning)

Distal growth established before proximal branching made

Connections made before function begins

Donkelaar et al (2004) J Neurology

Glial Development

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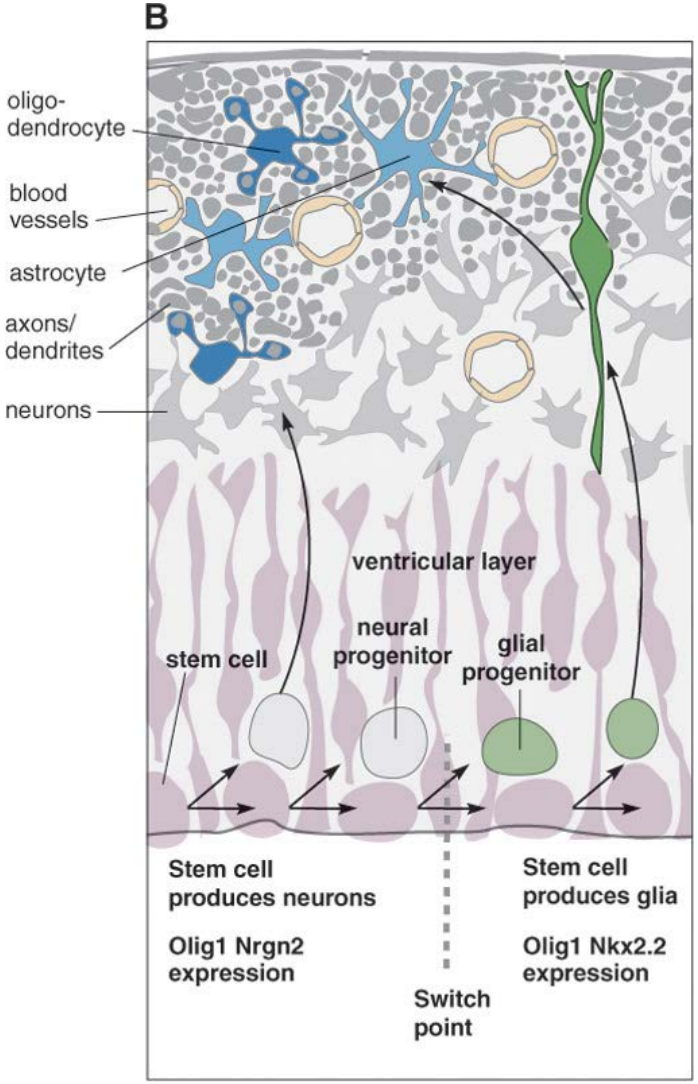
- Begins embryonically following the production of neurons
- Different types (astrocytes or oligodendrocytes) develop from different regions
- Continues throughout life, particularly in response to damage and injury



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Development of the Nervous System
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Orienting & Unformed Movements	

Sensitive Periods of Postnatal Development

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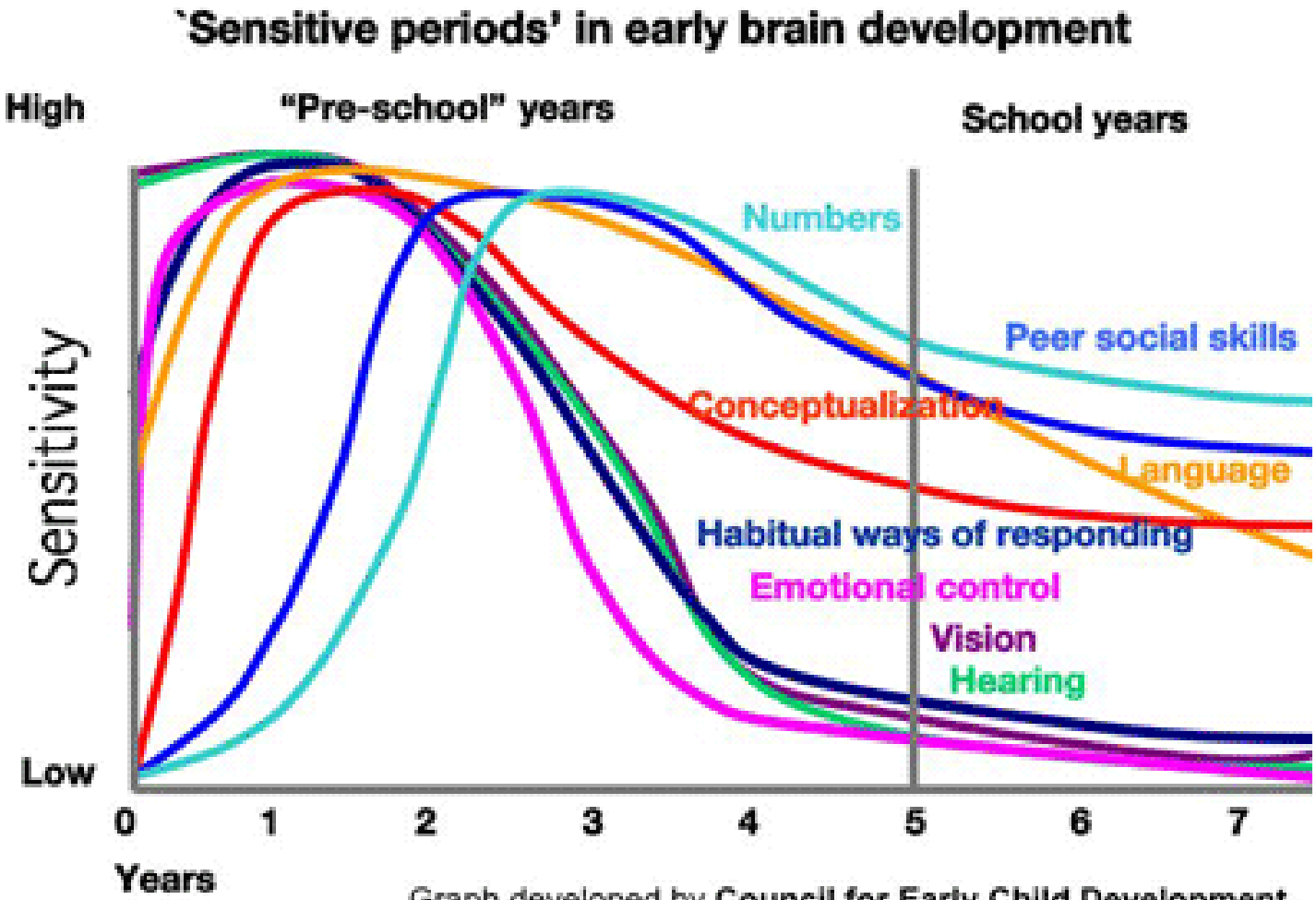

Graph developed by **Council for Early Child Development**
(ref: Nash, 1997; *Early Years Study*, 1999; Shonkoff, 2000.)

Sensitive Periods Simplified

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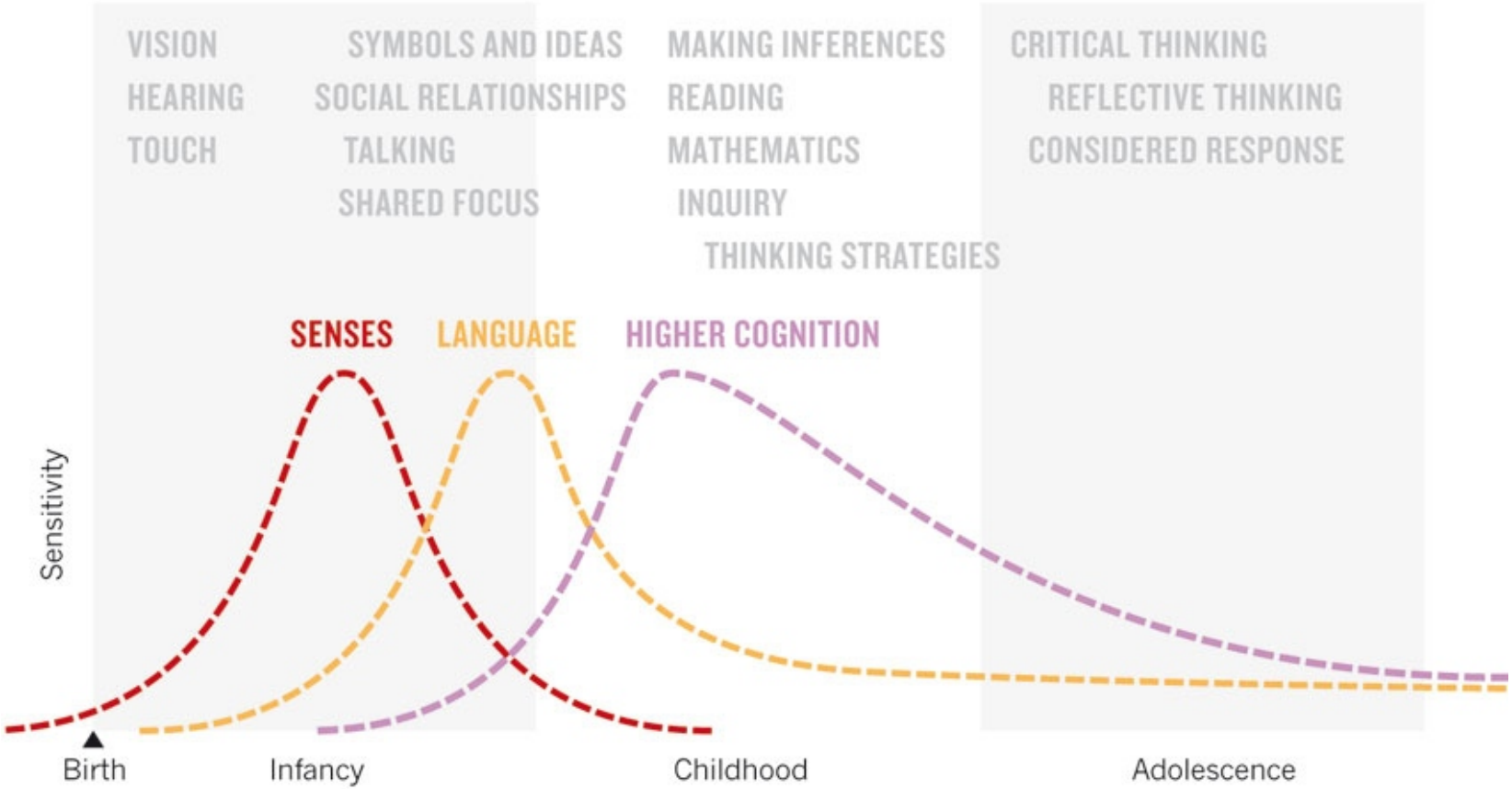
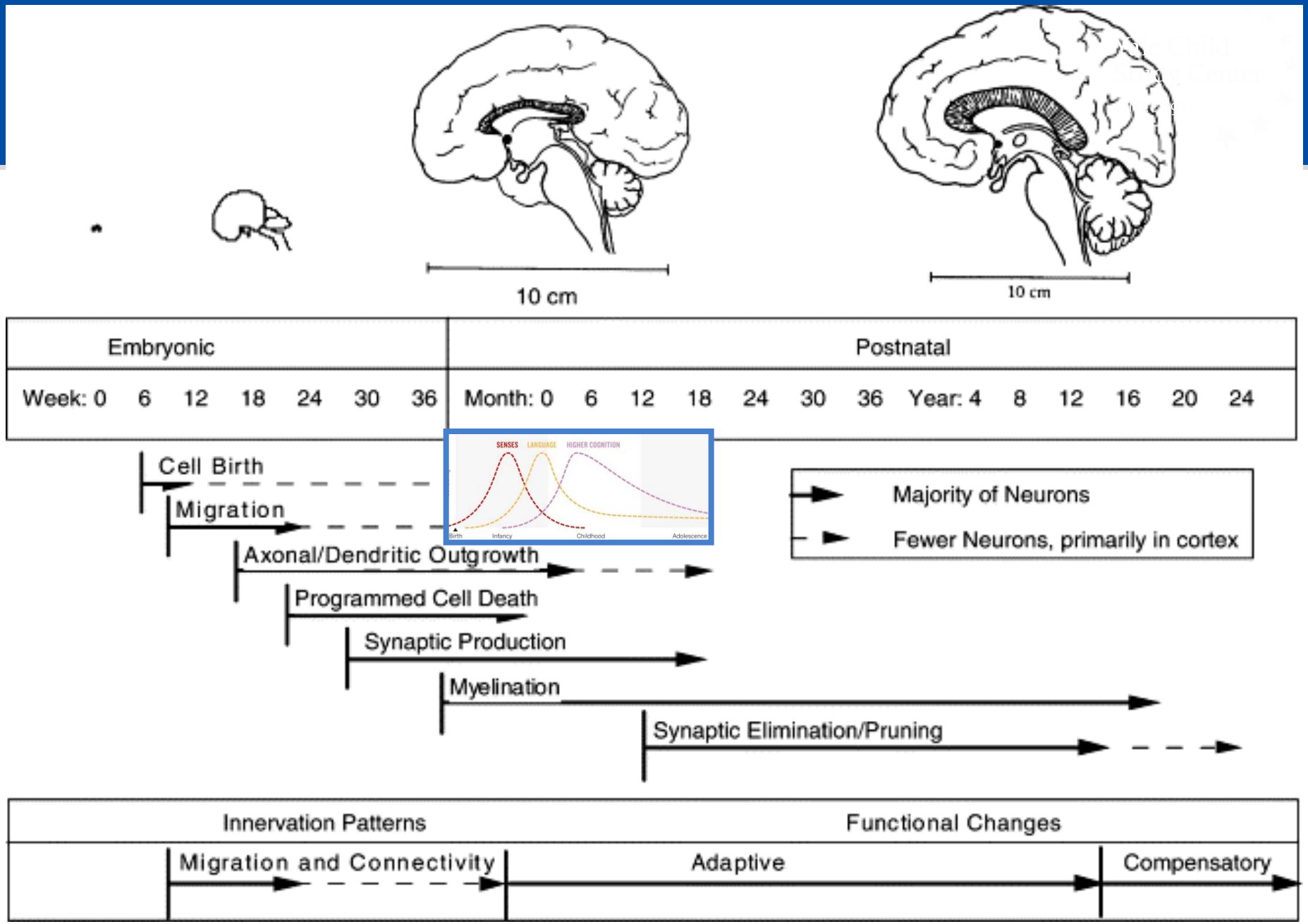
OPEN AND SHUT

The human brain's sensitivity to learning seems to crest in three broad waves. The critical periods for cortical regions devoted to vision and other senses (red) open in infancy, then close tightly. Those for language (yellow) and higher cognition (purple) open later, and never close entirely. The successive waves allow a child to acquire increasingly complex skills (grey text).



Hensch et al, (2011) EARLY YEARS STUDY 3 CH. 2



Andersen (Neurosci and Biobehav Rev; 2003)

Connections and Myelination

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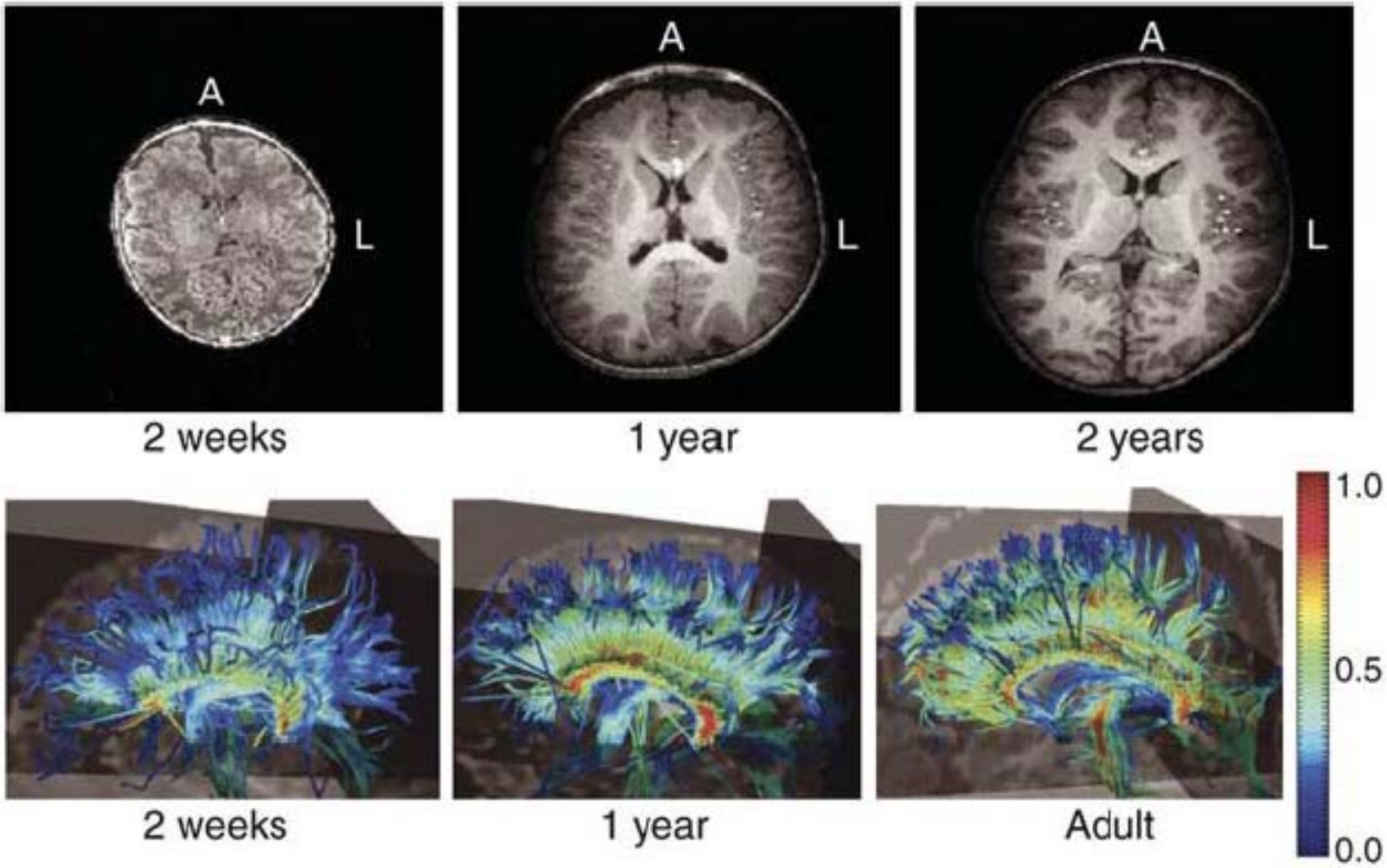

Gilmore et al Am J Psychiatry 2006

Connections and Performance: Reaction time

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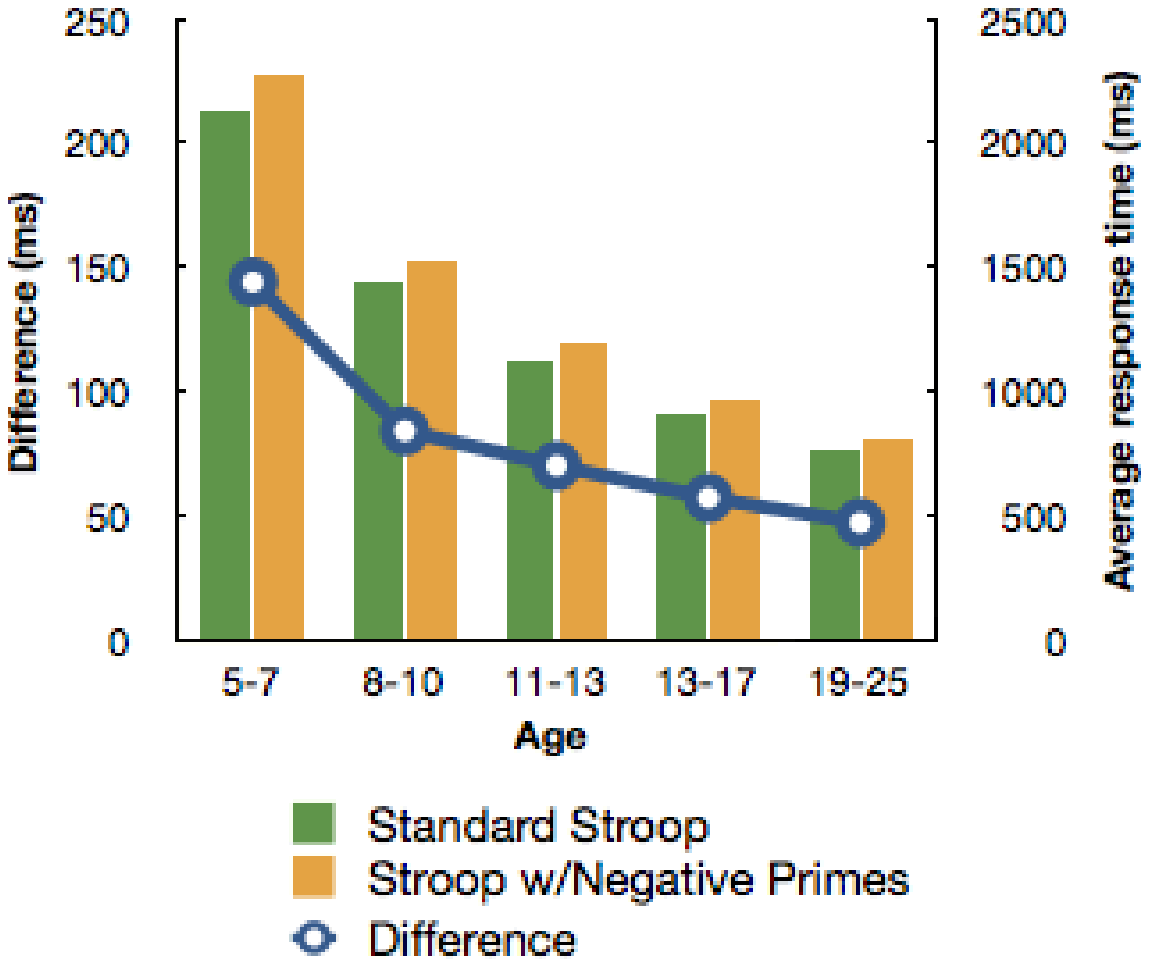

Pritchard and Neumann *Dev Psych*, 2009.

Connections and Performance: Critical Periods

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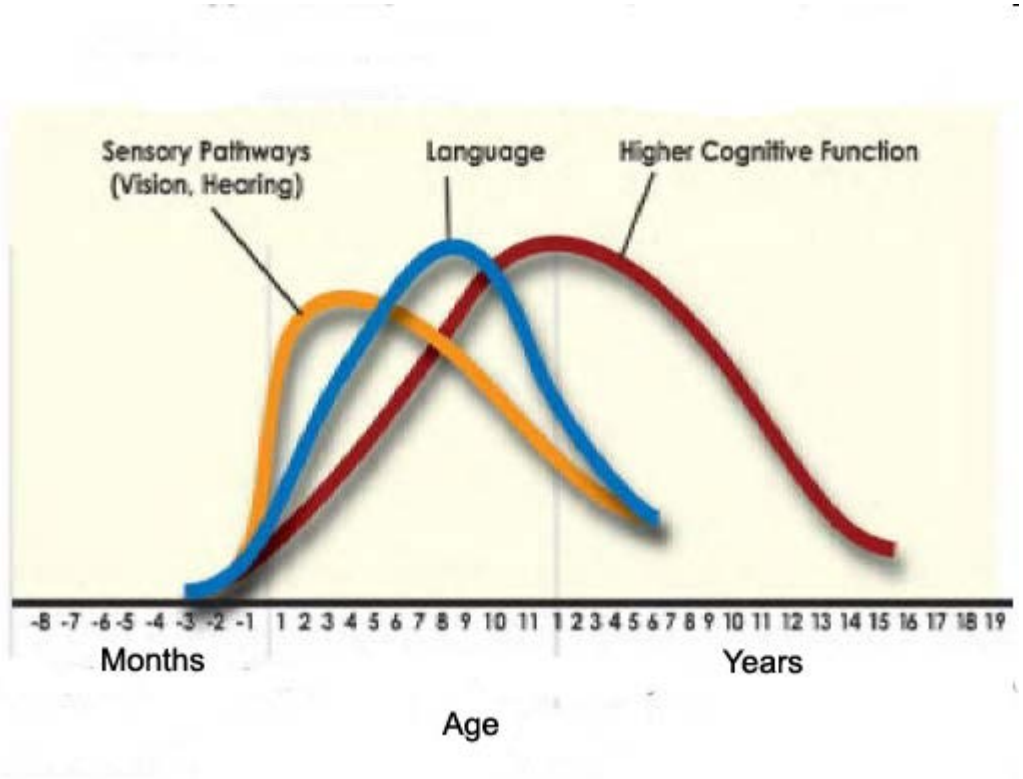

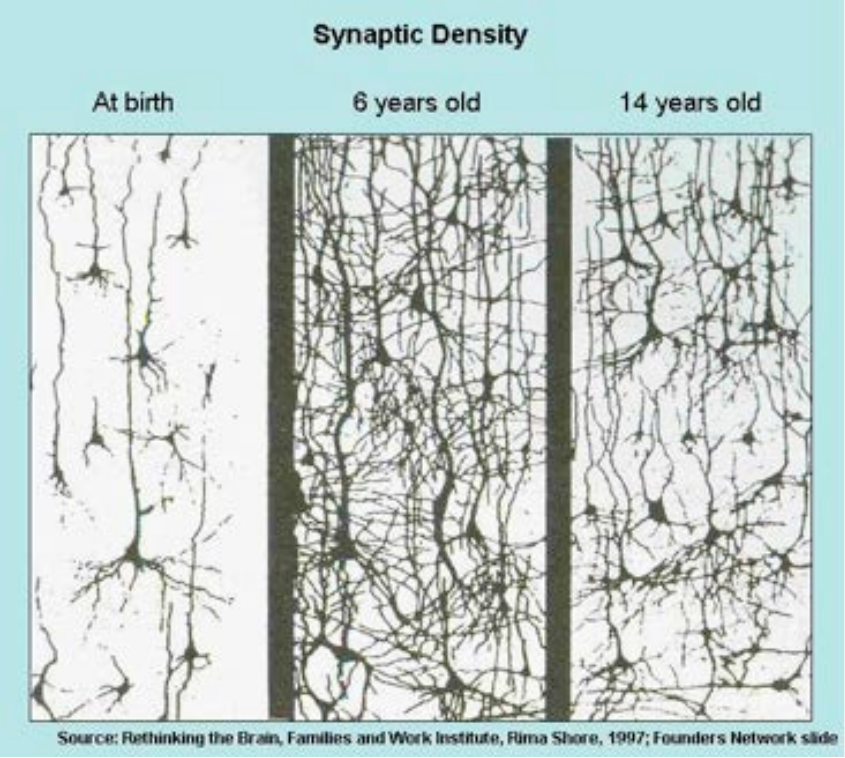

Development of the Nervous System
Sanes, Reh and Harris, Copyright 2006.

Connections and Performance: Receptive Fields

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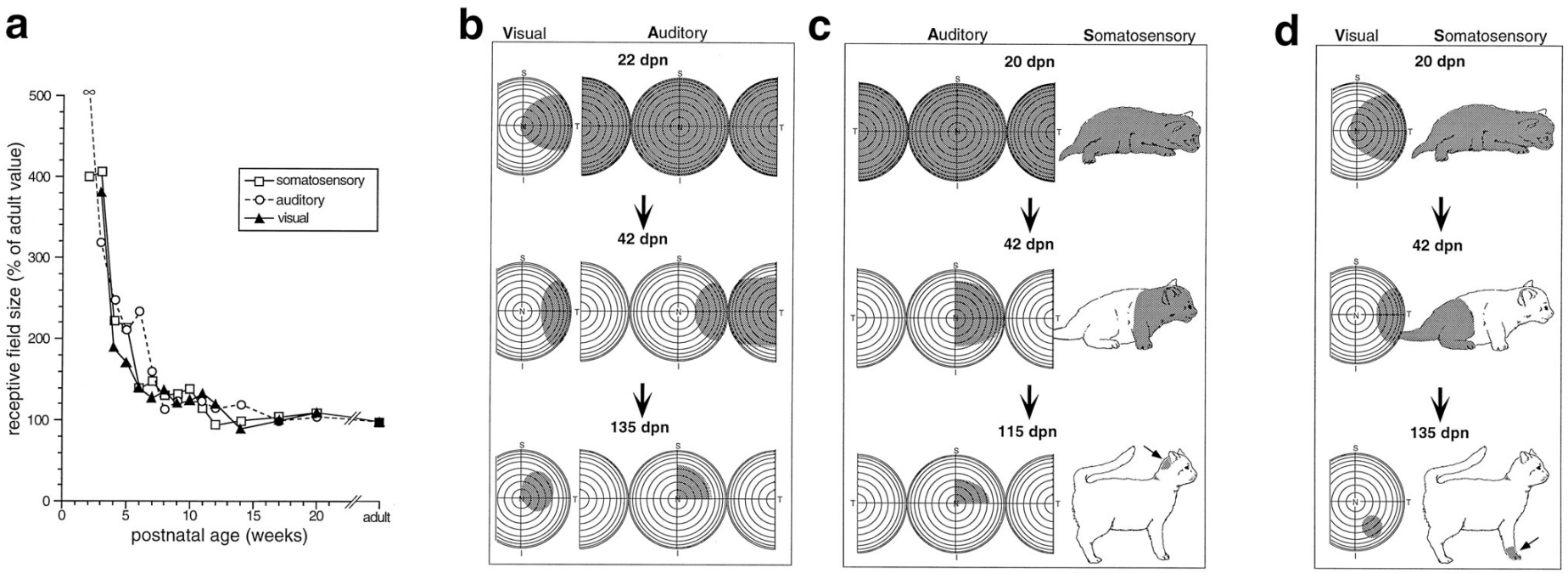
The receptive fields of multisensory neurons decline substantially in size during development.

a) Receptive field size (as a percentage of the mean adult value) is plotted as a function of postnatal age.



Wallace M T , Stein B E J. Neurosci. 1997

Recommended Reading

Yale Child Study Center
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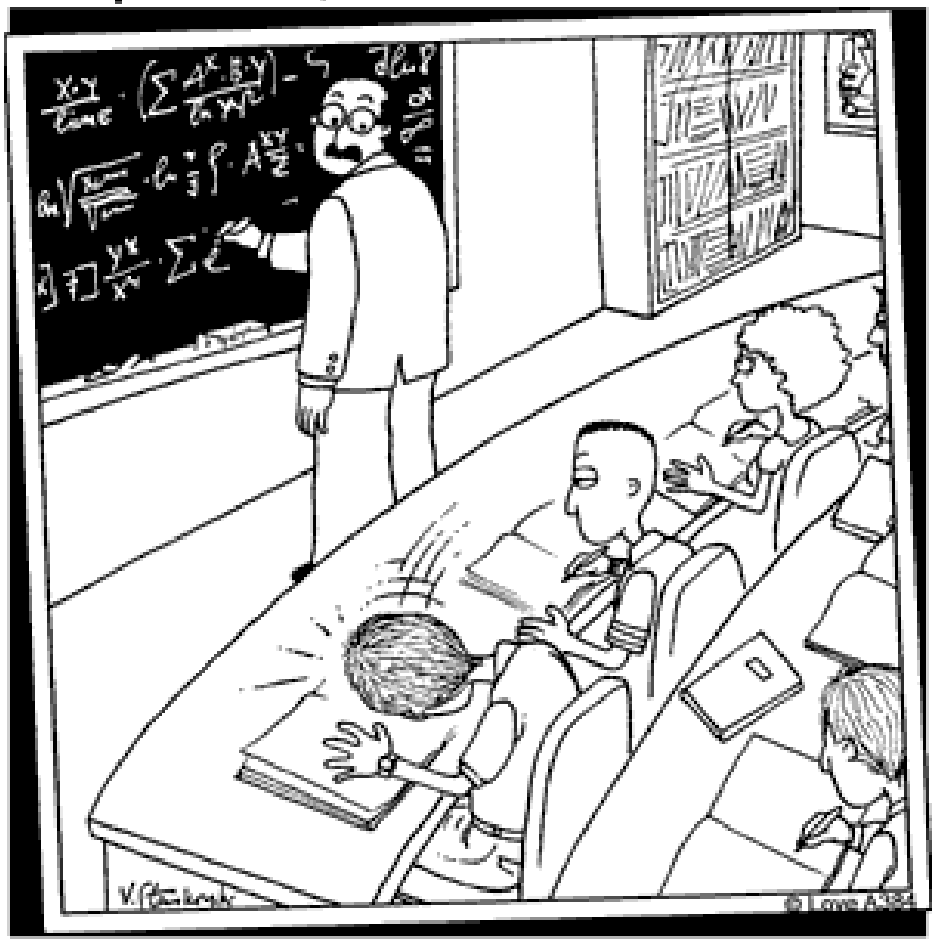
Snapshots at jasonlove.com



Professor Herman stopped when he heard that unmistakable thud – another brain had imploded.

Development of the Nervous System Sanes, Reh and Harris, Copyright 2006.

Tau and Peterson (2010) Neuropsychopharmacology Reviews

Stevens et al (2010) Frontiers in Neurogenesis

Rubenstein (2010) J Child Psychol and Psychiatry

Giedd and Rapoport (2010) Neuron

Fox et al (2010) Child Development