A sketch of the central nervous system and its origins

G. E. Schneider 2014

Part 3: Specialization in the evolving CNS; introduction to connection patterns

&

Part 4: Development and differentiation, spinal level

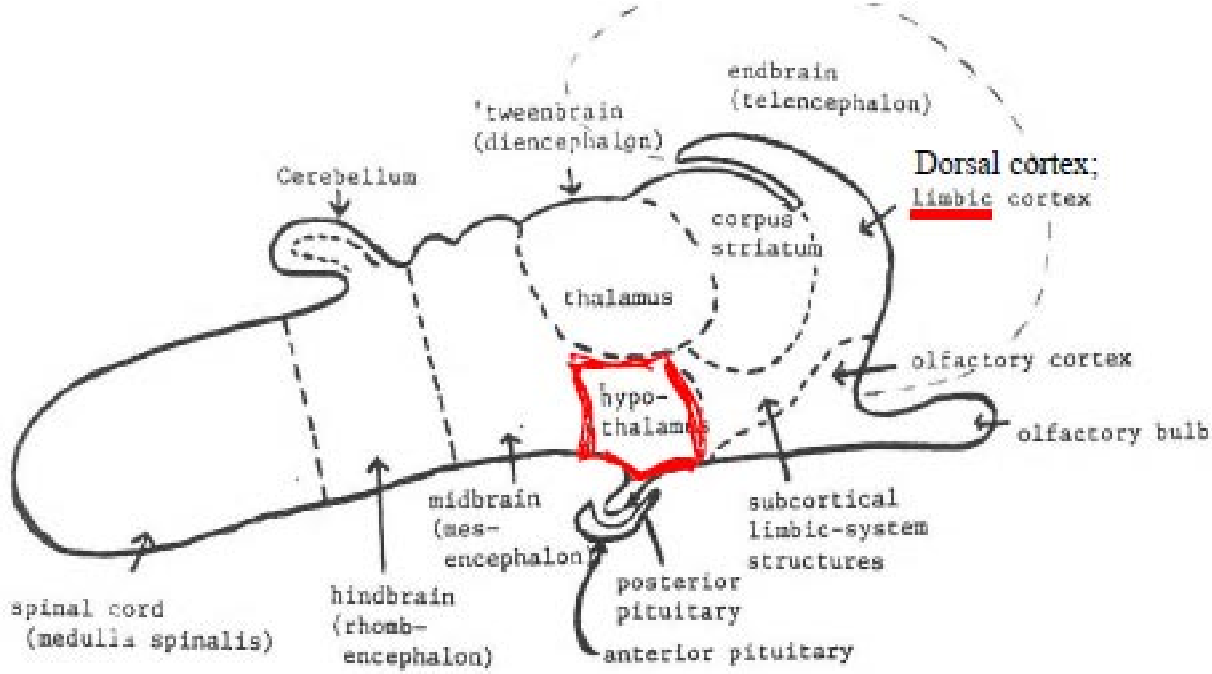
MIT 9.14 Class 7

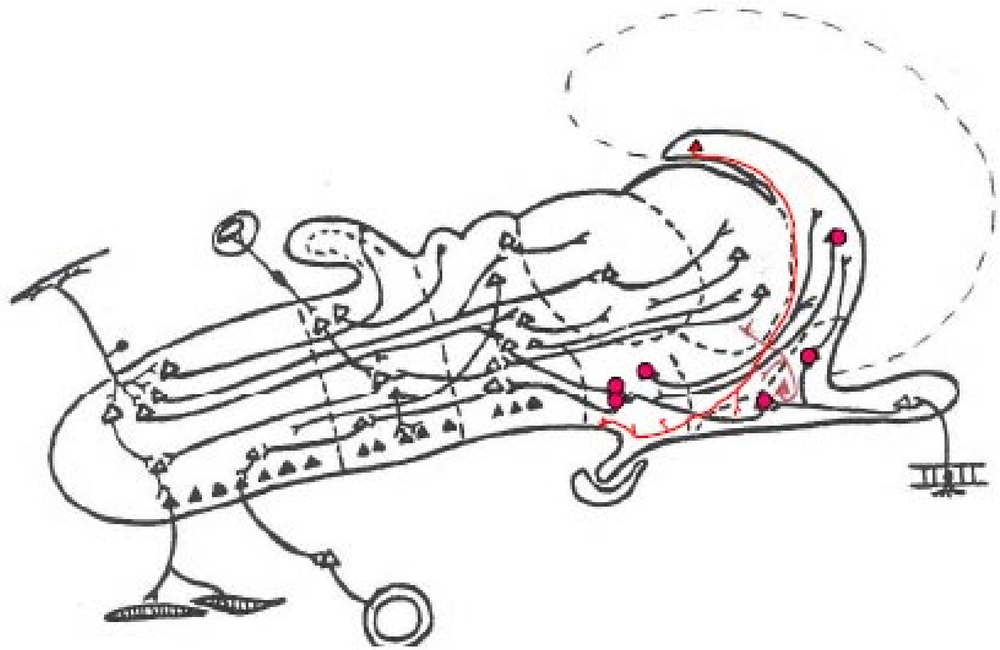
Completion of overview of forebrain structures in vertebrates and introduction to the neocortex (**Questions on chapter 7 of book**)

&

The neural tube forms in the embryo, and CNS development begins at the spinal level (**Questions on chapter 8 of book**)

Some "Limbic" connections





(Note definition of limbic system)

Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

Questions, chapter 7

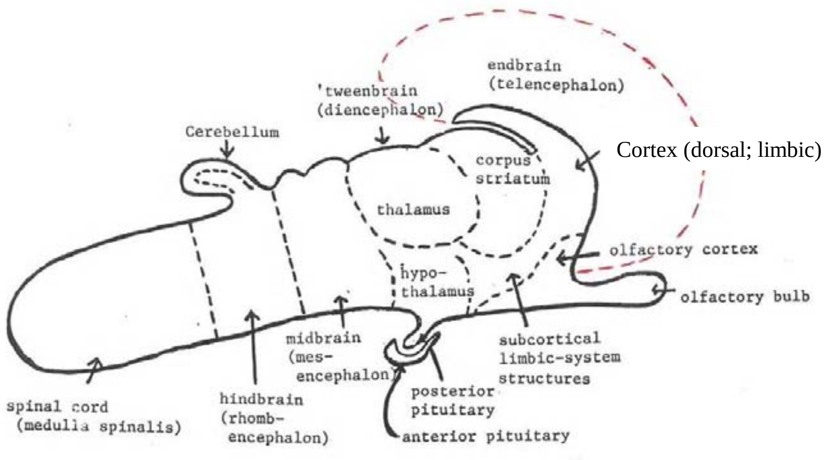
11. Olfactory input dominated the ancient chordate endbrain, the predecessors of the limbic endbrain structures of mammals. This input was most likely important for two different types of learning, that later in evolution have come to depend just as much or more on inputs of other sensory modalities. Describe the two types of learning.

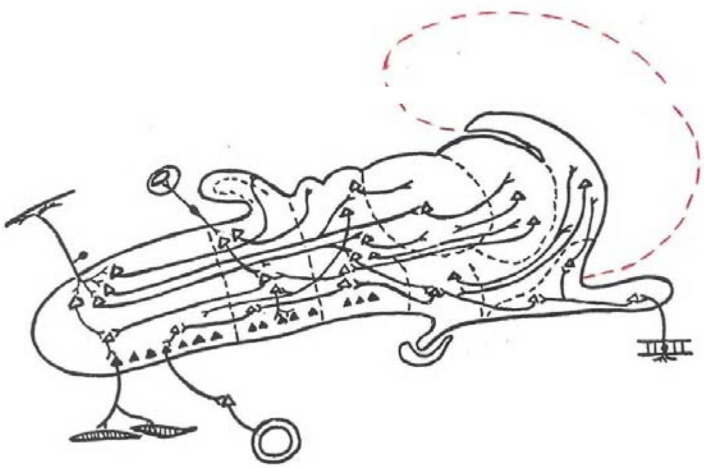
There was an amazing evolution of major functions dependent originally on olfactory inputs and their projections to the endbrain:

- Learned object preferences; identification of desired (good) and abhored (bad) things
- Place learning: Identification and memory of good places and bad places

Questions, chapter 7

12. Within the endbrain of the first mammals or in their immediate predecessors, within the pallial structures, the neocortex evolved. With this evolution there was an expansion of a rapidly conducting pathway from the spinal cord carrying somatosensory information. It is sometimes called the neolemniscus. Describe or draw this pathway, indicating the location of the cell groups where synapses occur, and the location of a decussation.





M.I.T. 9.01

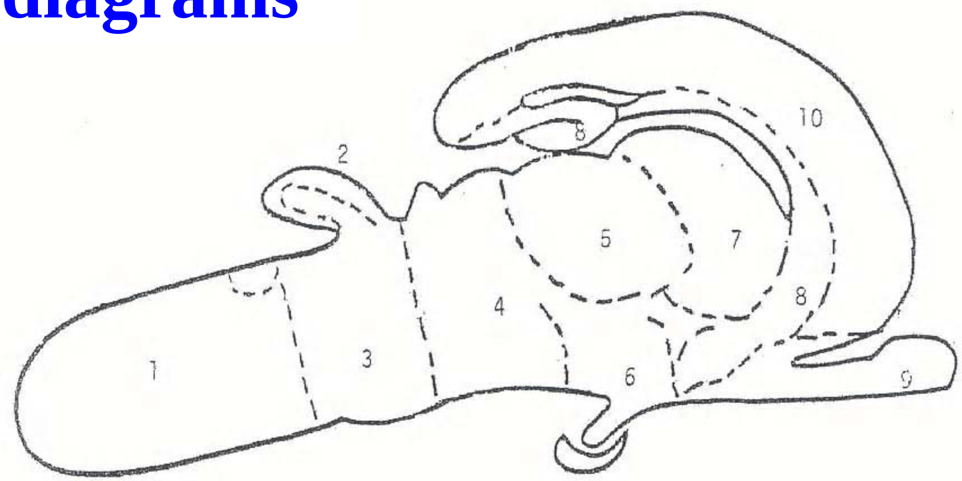
G.E. Schneider

Addition of neocortex to the ancestral premammalian brain

Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

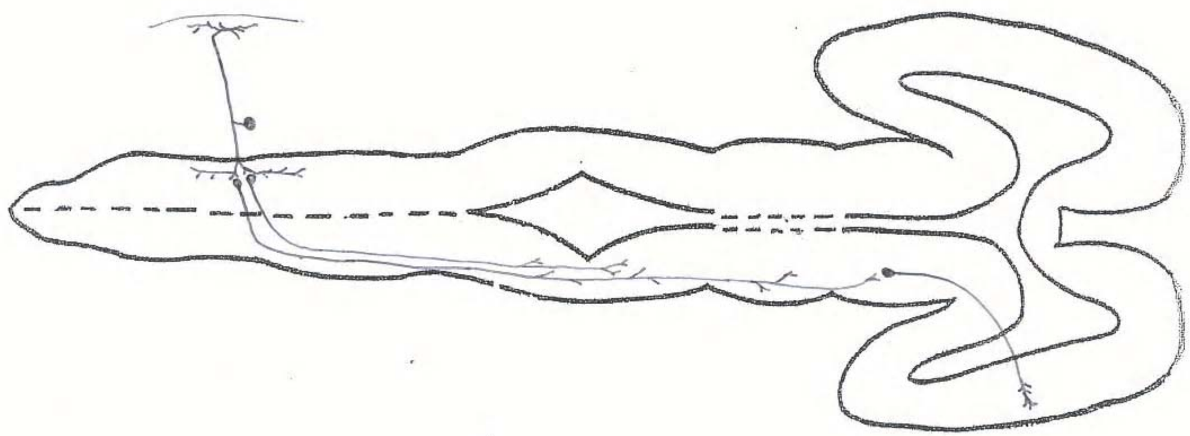
Mammalian brain diagrams

Schematic side view



Identify each part

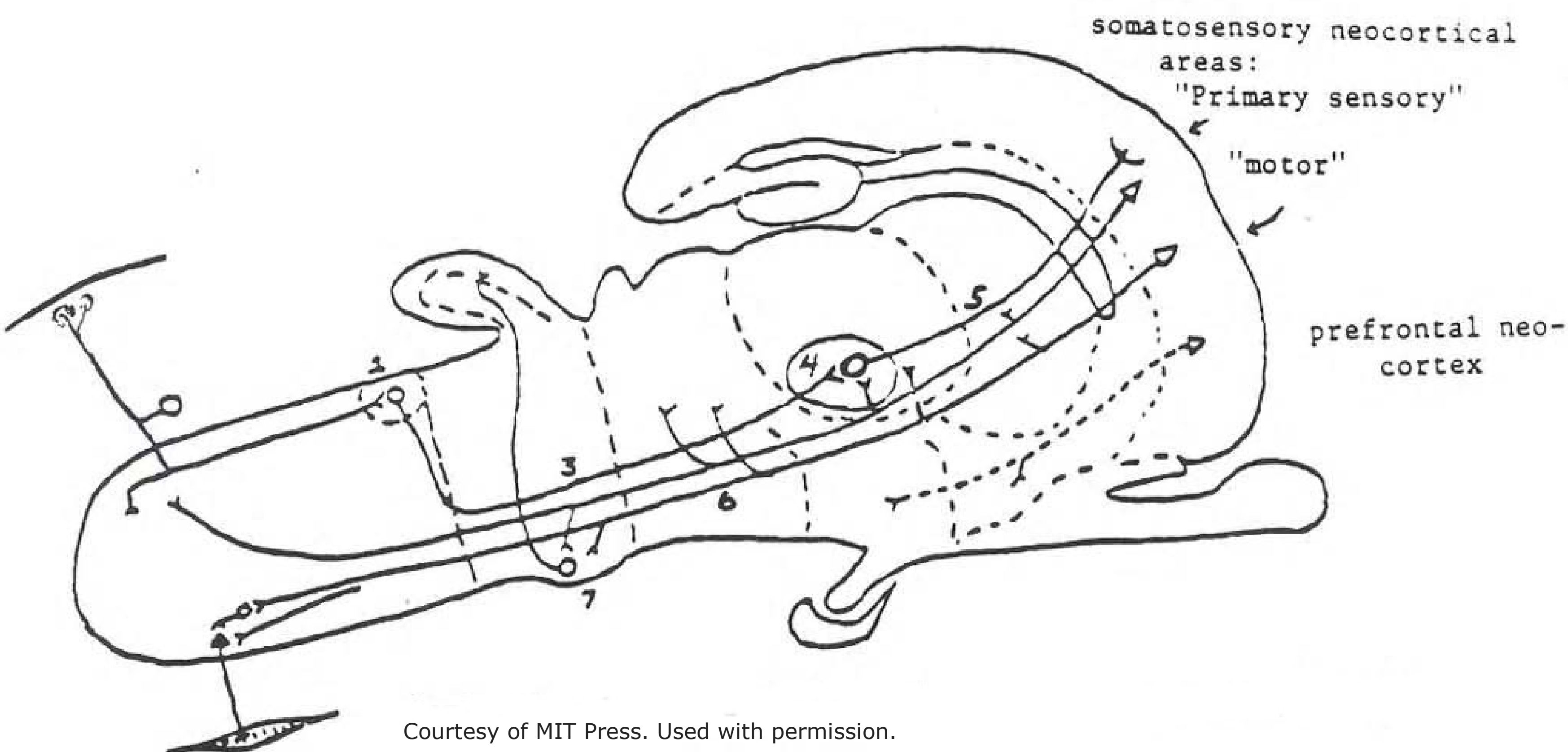
Top view, embryonic brain (with spinothalamic tract)



Courtesy of MIT Press. Used with permission.
Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

1) The dorsal column – medial lemniscus pathway.

2) The corticospinal tract.



Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

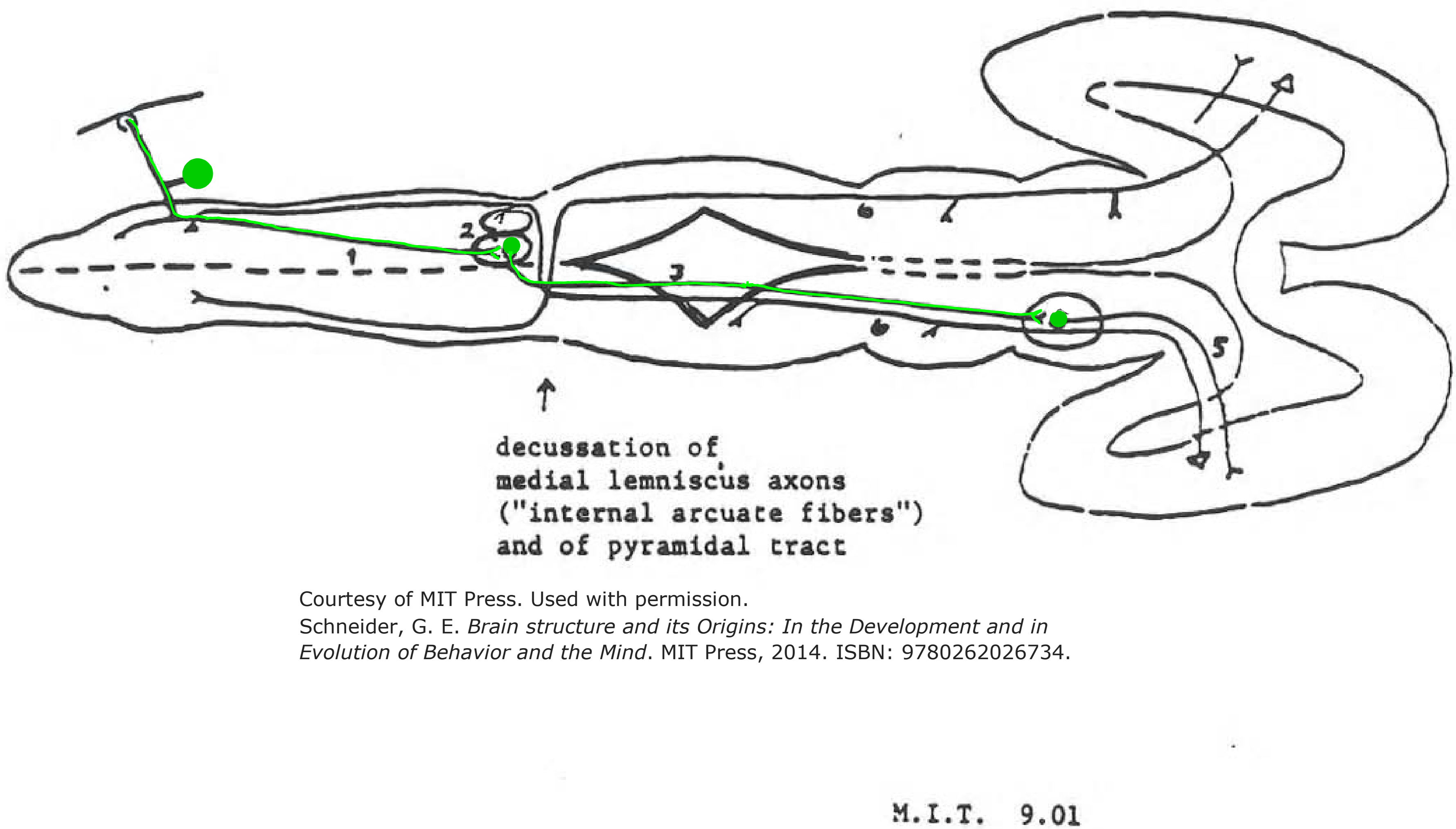
Some major long connections of the somatosensory system of mammals.

Terms:

1. **Dorsal columns**
2. **Nuclei of the dorsal columns**
3. **Medial lemniscus**
4. **Ventrobasal nucleus of thalamus (n. ventralis posterior)**
5. **Thalamocortical axon in the "internal capsule"**
6. **Corticofugal axons, including corticospinal components. Called "pyramidal tract" in hindbrain below pons.**
7. **Pons**

1) The dorsal column – medial lemniscus pathway

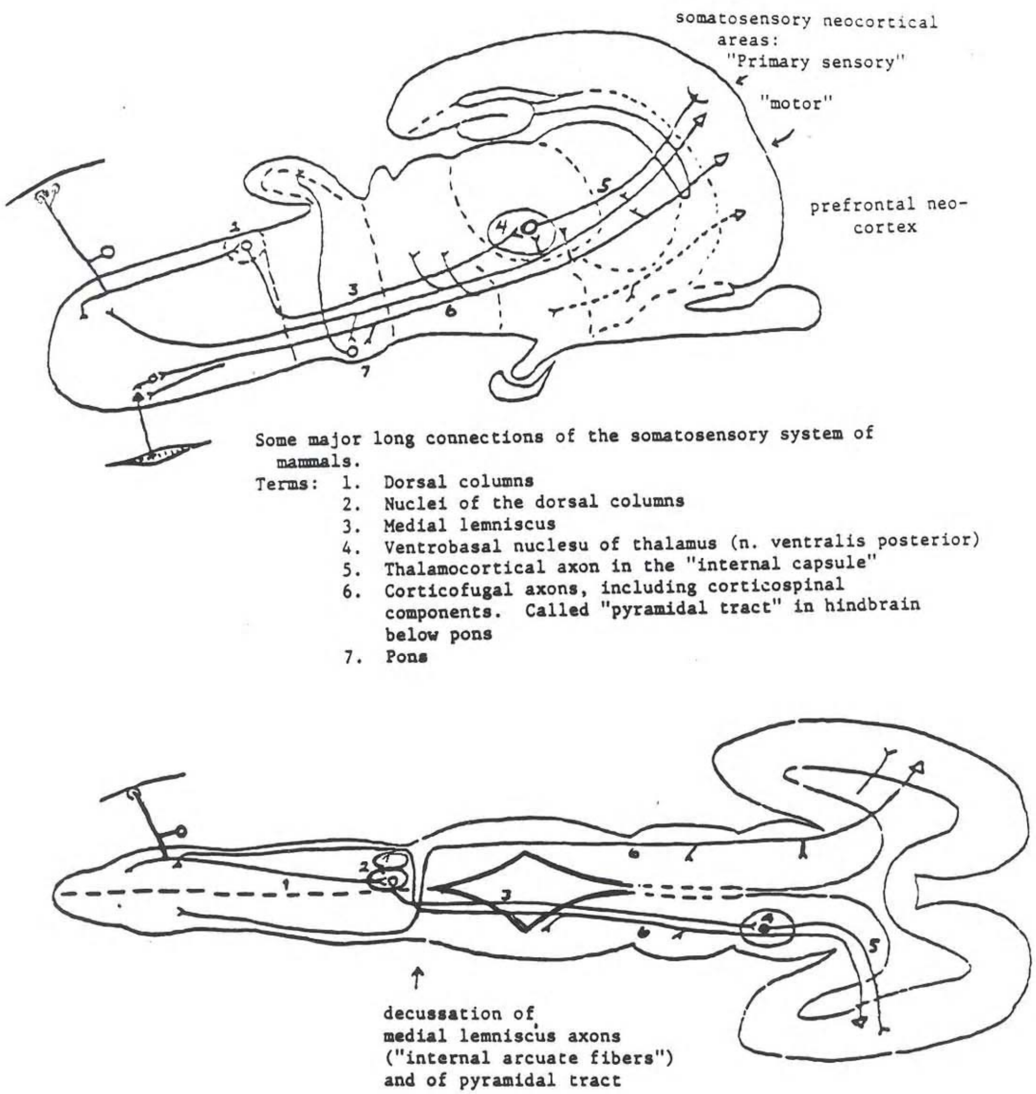
2) The corticospinal tract



Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

Questions, chapter 7

13. With neocortex, there also evolved long descending connections from somatosensory areas, one of which evolved into the motor cortex. Describe or draw the pathway of corticospinal axons, indicating where it decussates.



Two major long pathways* **associated with neocortex of present-day mammals:**

1) "Neolemniscus": the dorsal column–medial lemniscus pathway.

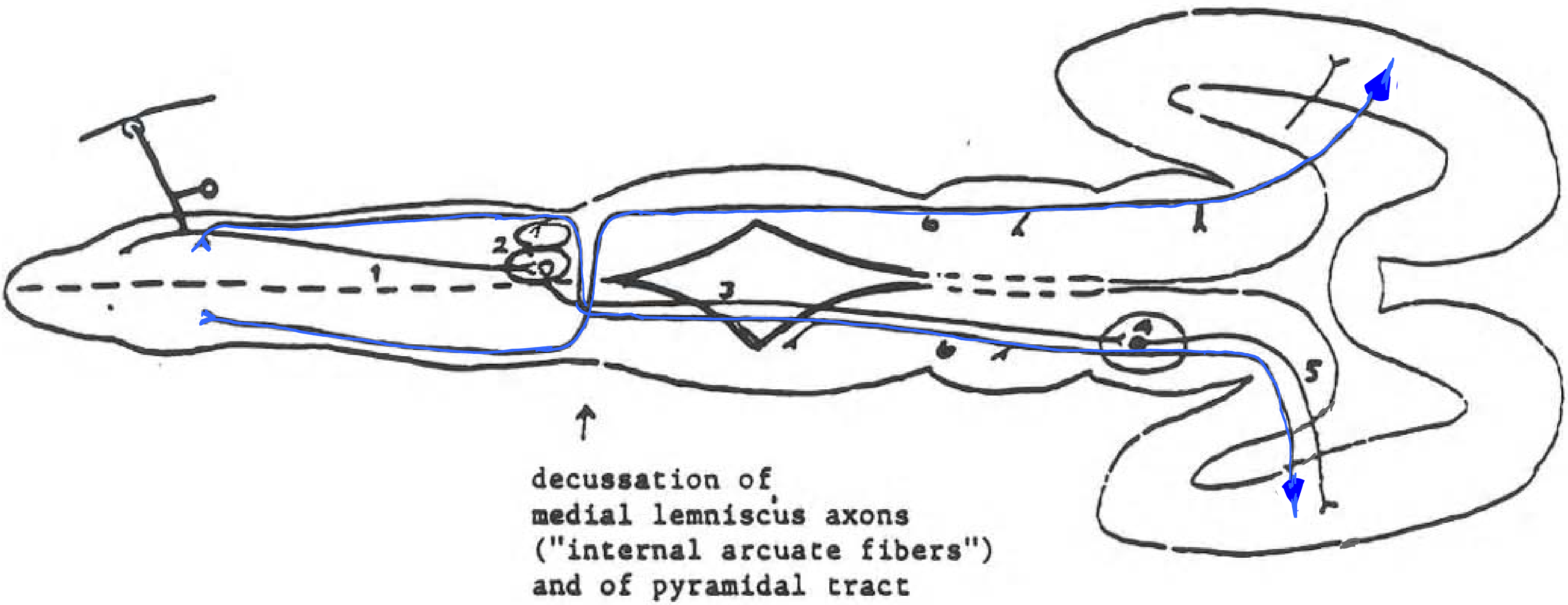
2) Corticospinal tract.

* *There are many others*

Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

1) **The dorsal column – medial lemniscus pathway.**

2) **The corticospinal tract.**

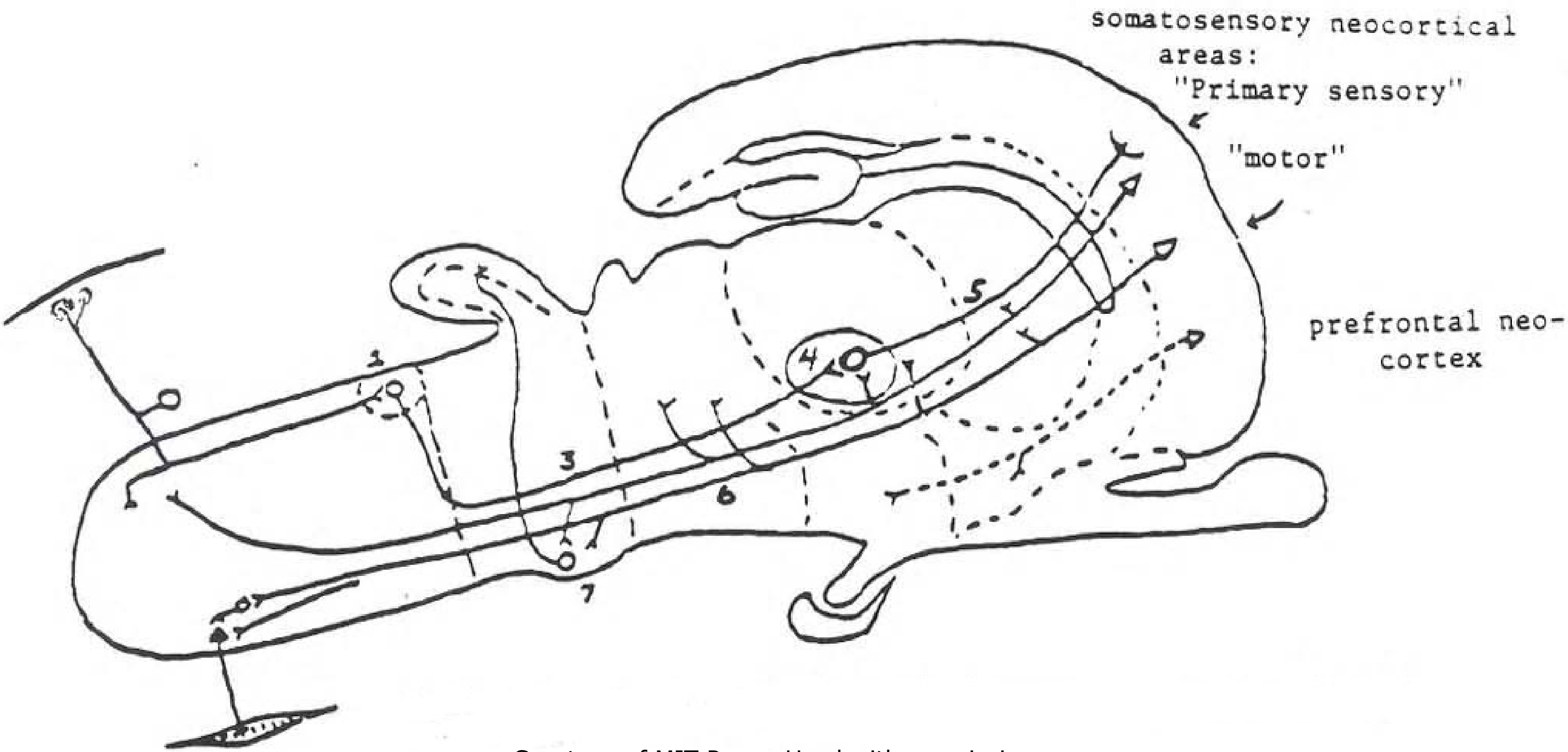


Courtesy of MIT Press. Used with permission.
Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

M.I.T. 9.01

1) The dorsal column – medial lemniscus pathway

2) The corticospinal tract



Courtesy of MIT Press. Used with permission.
Schneider, G. E. *Brain Structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN:9780262026734.

Some major long connections of the somatosensory system of mammals.
Terms:

1. **Dorsal columns**
2. **Nuclei of the dorsal columns**
3. **Medial lemniscus**
4. **Ventrobasal nucleus of thalamus (n. ventralis posterior)**
5. **Thalamocortical axon in the "internal capsule"**
6. **Corticofugal axons, including corticospinal components. Called "pyramidal tract" in hindbrain below pons.**
7. **Pons**

Questions, chapter 7

14. What characterizes the sensory and motor functions of the neocortex?

15. In general, what other type of functions depend on the neocortex?

But **what** does neocortex do? (i.e., **why** did it evolve?)

- In evolution there was an **increasing specialization of thalamic and corresponding neocortical areas**.
  - These specialized areas added greater sensory and motor **acuity**.
  - Such acuities affected not only learning abilities but also both the triggering and execution of FAPs.
  - **Object** perception: Separation of objects from background stimuli became better.

But **what** does neocortex do? --More on why it evolved--

- More uniquely, neocortical expansion is associated with an increasing ability to **anticipate stimuli,** and an increasing ability to **plan actions** in advance.
  - Anticipation depends on imaging abilities, using an internal model of the external world—a simulation of scenes and objects. Imaging depends on posterior neocortex.
  - Planning abilities use the internal model, and depend on anterior (frontal) areas.

Review of a few basic points

REVIEW with addendum:

Behavioral recovery from diaschisis effects

- “Recovery” implies a return to normal.
- However, this is not generally true for recovery from deafferentation depression.
- After depression of spinal reflexes caused by a loss of descending connections to the spinal cord, the changes can go too far, resulting in hypersensitvity of spinal reflexes: “reflex spasticity”.

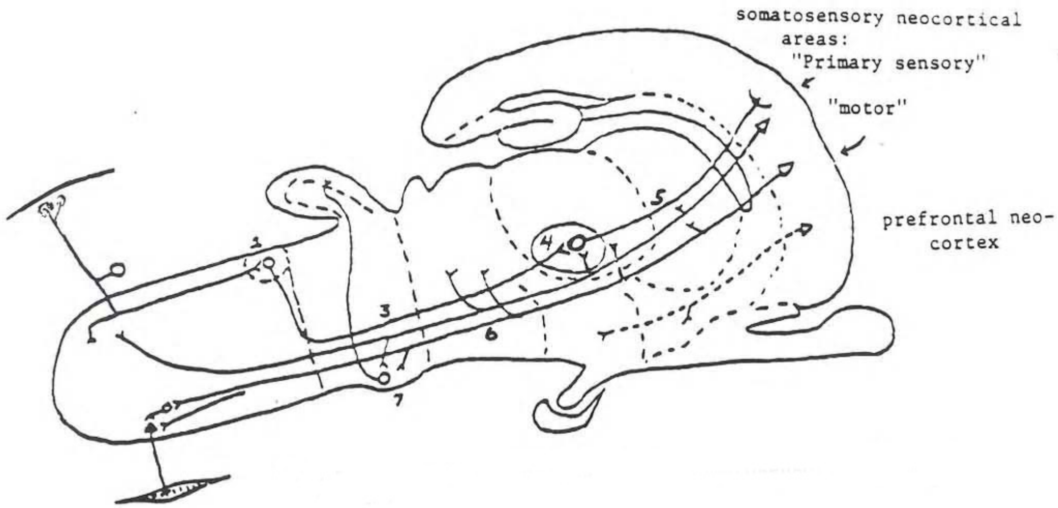
REVIEW:

The long pathways which evolved with the neocortex:

- **Rapid inputs to the neocortical mantle** of the endbrain, *via* a synaptic connection in the diencephalon: We depicted a major one for somatosensory information.
- **More direct outputs to the spinal motor mechanisms**, bypassing the intervening structures: We depicted projections from somatosensory and motor areas of neocortex.
- STUDY THE FIGURES!

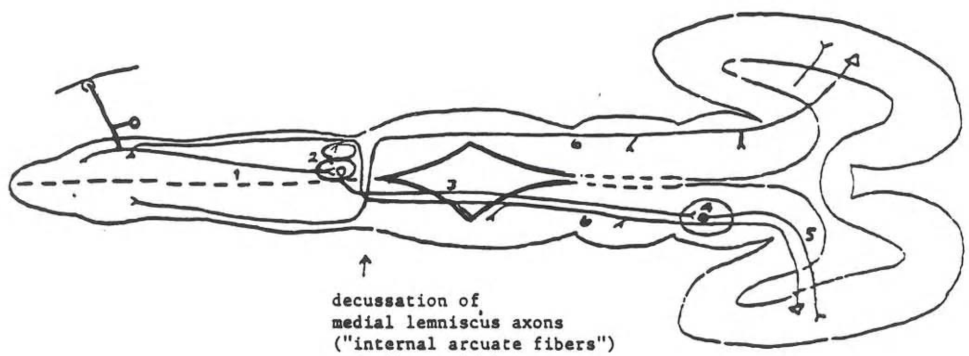
Terms:

- “Projection”: the output pathway from a group of neurons *via* their long axons.
- Examples:
  - The projection from motor cortex to the spinal cord is called the corticospinal tract (or pyramidal tract).
  - The spinotectal projection, or spinotectal pathway: axons from the spinal cord, *via* the spinothalamic tract, to the midbrain tectum (roof of the midbrain).



Some major long connections of the somatosensory system of mammals.
Terms:

Dorsal columns



Courtesy of MIT Press. Used with permission.
Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

Two major long pathways* associated with neocortex of present-day mammals:

1) "Neolemniscus": the dorsal column–medial lemniscus pathway.

2) Corticospinal tract.

* *There are many others*

Taking stock of where we are in learning the anatomy of the CNS:

Where do we go from here?

- We have a rudimentary outline.
- Now we will get more involved in learning about these basic structural divisions.
- We will be aided by studies of CNS evolution and by studies of development in mammals, including humans.

Note on evolution:

- **We will study spinal cord first. But remember:**
  - The brain did not evolve only after the evolution of spinal cord. It – most obviously the hindbrain – evolved **along with** the primitive spinal cord.
  - This is supported by data on the little non-vertebrate chordate *Amphioxus*.

Spinal cord development and structure
topics

- Some embryology: neurulation and the developing spinal cord (this class)
- Survey of adult spinal cord (class 8)
- Autonomic nervous system (classes 8b-9)

Developmental steps leading to a nervous system

1) Fertilized egg
2) Morula
3) Blastula
4) Gastrula
5) Neurula

Chapter 8 questions

1) What are the four basic cellular events that result in transformation of the very early embryo from fertilized cell to morula to blastula to gastrula? (These were summarized by Lewis Wolpert in his book, *Triumph of the Embryo*.) Give examples of what is meant by each event.

As the basic form of the embryo is moulded in these early stages of development, what are the **basic cellular activities**?

- Contractions
- Changes in adhesion (*via* expression of CAMs—cell adhesion molecules)
- Cell movement (using contractile proteins and membrane adhesion)
- Growth/proliferation

These activities are how cells accomplish developmental changes. Examples follow

As summarized by Lewis Wolpert (*The triumph of the embryo, 1991,* ch. 2)

From egg to gastrula: Note the role of filopodia in gastrulation.

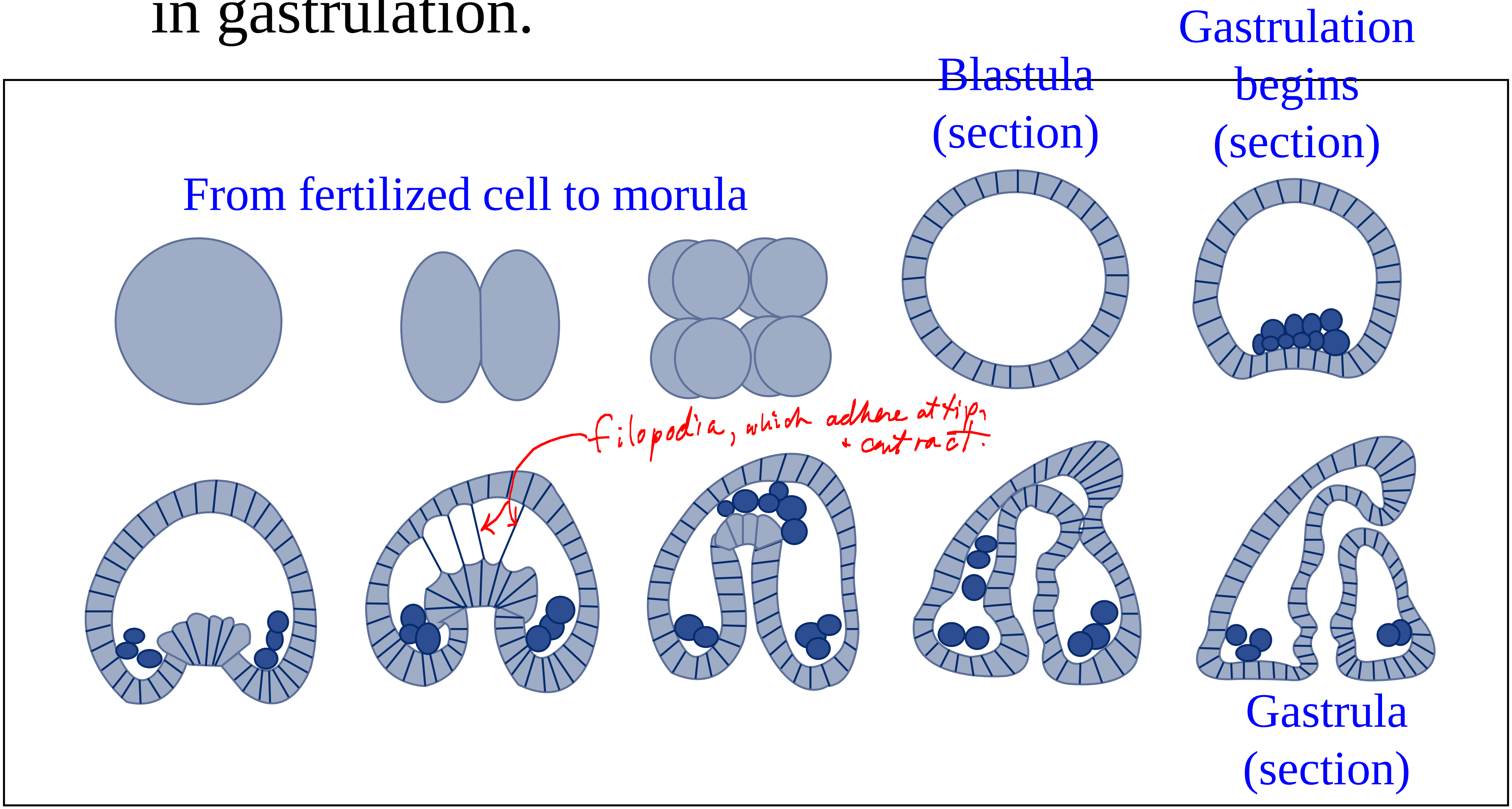


Image by MIT OpenCourseWare.

Precursers of skeleton find their way along the inner wall of the embryo.

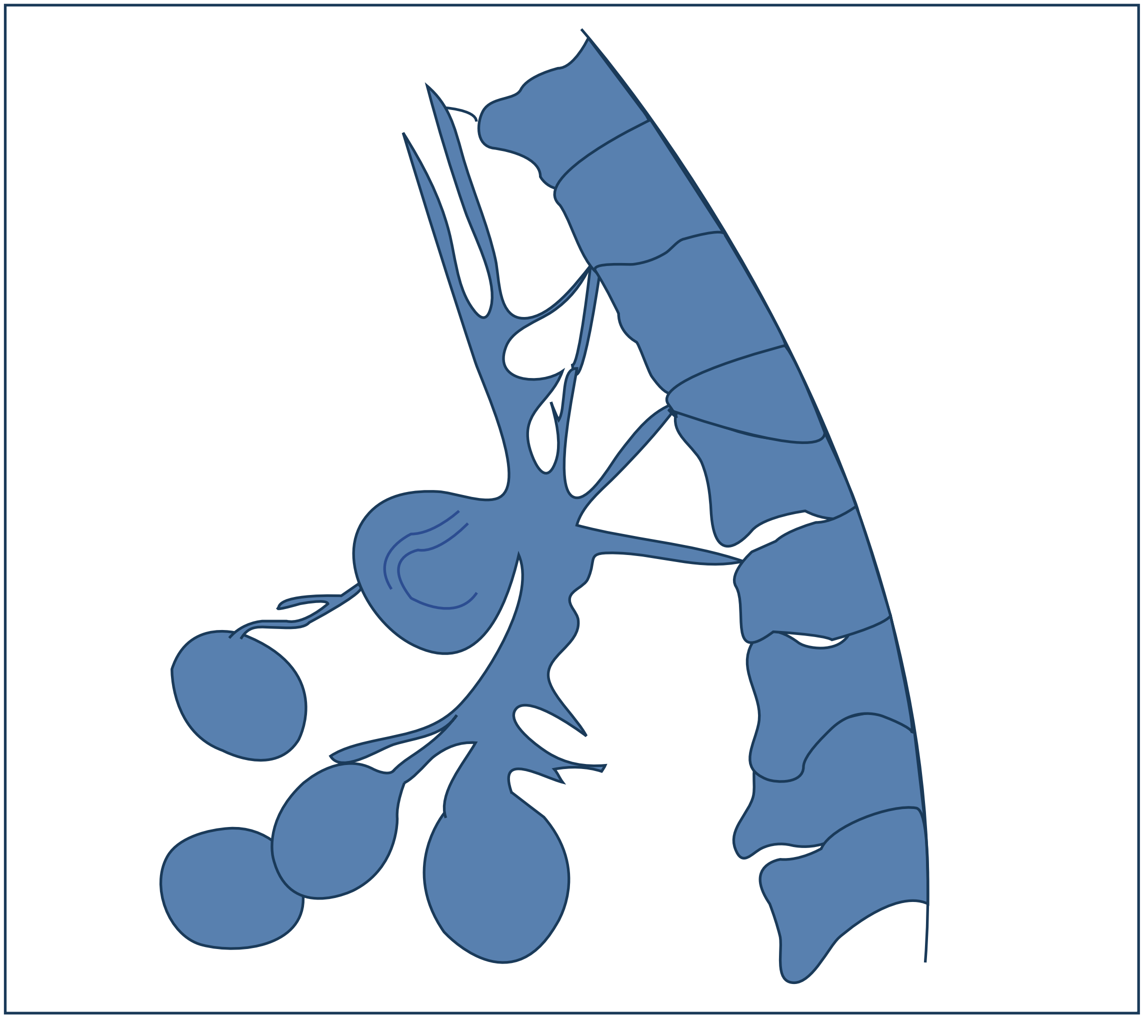


Image by MIT OpenCourseWare.

Development of the CNS: 4 major events following gastrulation

1. **Neurulation** & **formation of neural tube**
2. **Proliferation** of CNS cells
3. **Migration** of CNS cells
4. **Differentiation** of these cells, with growth of axons and dendrites

Chapter 8 questions

2) What is the notochord, and what is its role in neurulation? Describe the process of neurulation.

3) Who discovered the phenomenon of induction of CNS formation? (One of them received most of the recognition. Why?)

4) What are neural crest cells, and what do they become?

Focus on neurulation and the developing spinal cord

terms:

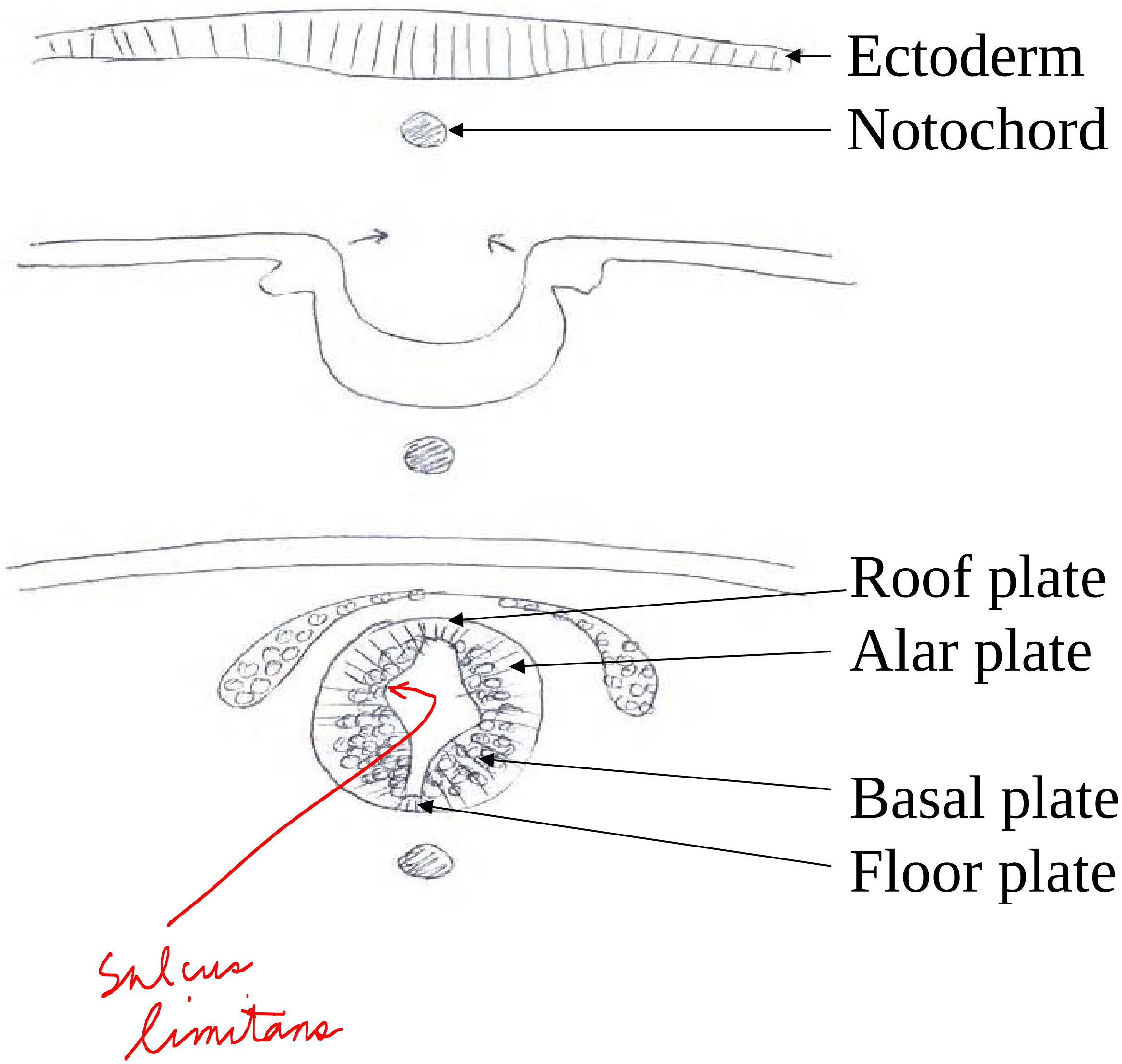
- Formation of the **neural tube** from the embryonic ectoderm (neurulation)
- **Alar and basal plates** separated by the sulcus limitans (can be followed rostrally into the midbrain)
- **Neural crest cells**, which form the dorsal root ganglia, and the ganglia of the autonomic nervous system plus adrenal gland cells (as well as some other cells)

Closure of neural tube:
Note the various terms

Neural plate

Neural groove

Neural tube
and
neural crest



Courtesy of MIT Press. Used with permission.

Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

“Neurulation”

- Separation of neuronal cells from the ectoderm and formation of the neural tube is called neurulation.
- When this occurs, the cells of the peripheral nervous system separate from those of the central nervous system. The PNS comes from the “neural crest”.
- We will look at what happens using several different pictures and animations.

Neurulation and formation of neural tube

- Discovery of <u>induction</u> of CNS by notochord region came out of work by Hans Spemann & Hilde Mangold (1924). [Mangold's original name was Hilde Proescholdt; she died in a kitchen accident at age 26.]

Chapter 8 questions

5) Where does closure of the neural tube begin? What are the last regions to close?

6) Define the terms: neural plate, neural groove, alar plate, basal plate, roof plate and floor plate, sulcus limitans. (seen in pictures)

Neural tube Closing

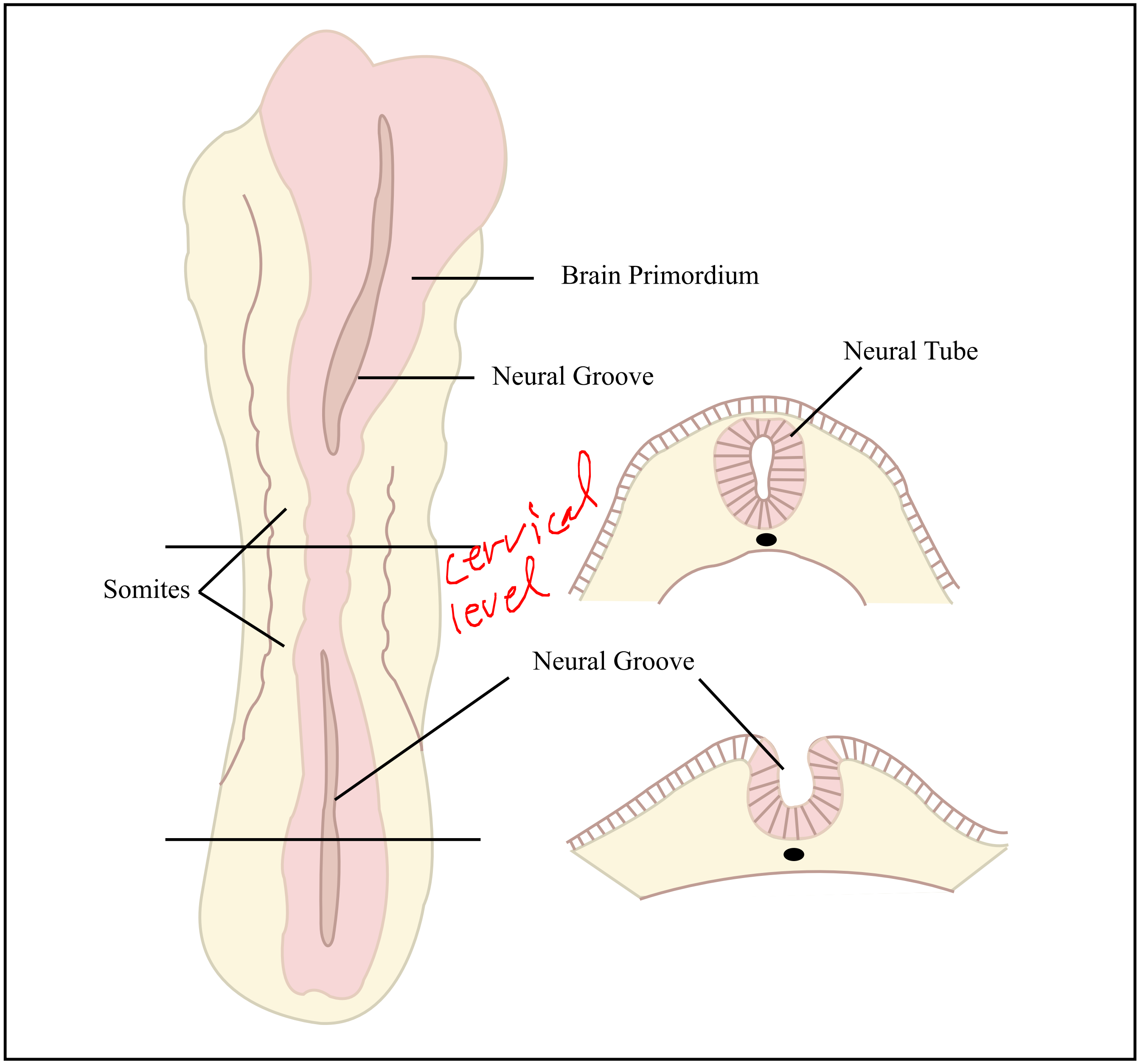


Image by MIT OpenCourseWare.

Neurulation: animation

can be found online

Video removed due to copyright restrictions.

Neurulation in *Xenopus*, movie

Video removed due to copyright restrictions.

Neural Tube Formation

e.m. of freeze-fractured surface

Image removed due to copyright restrictions.

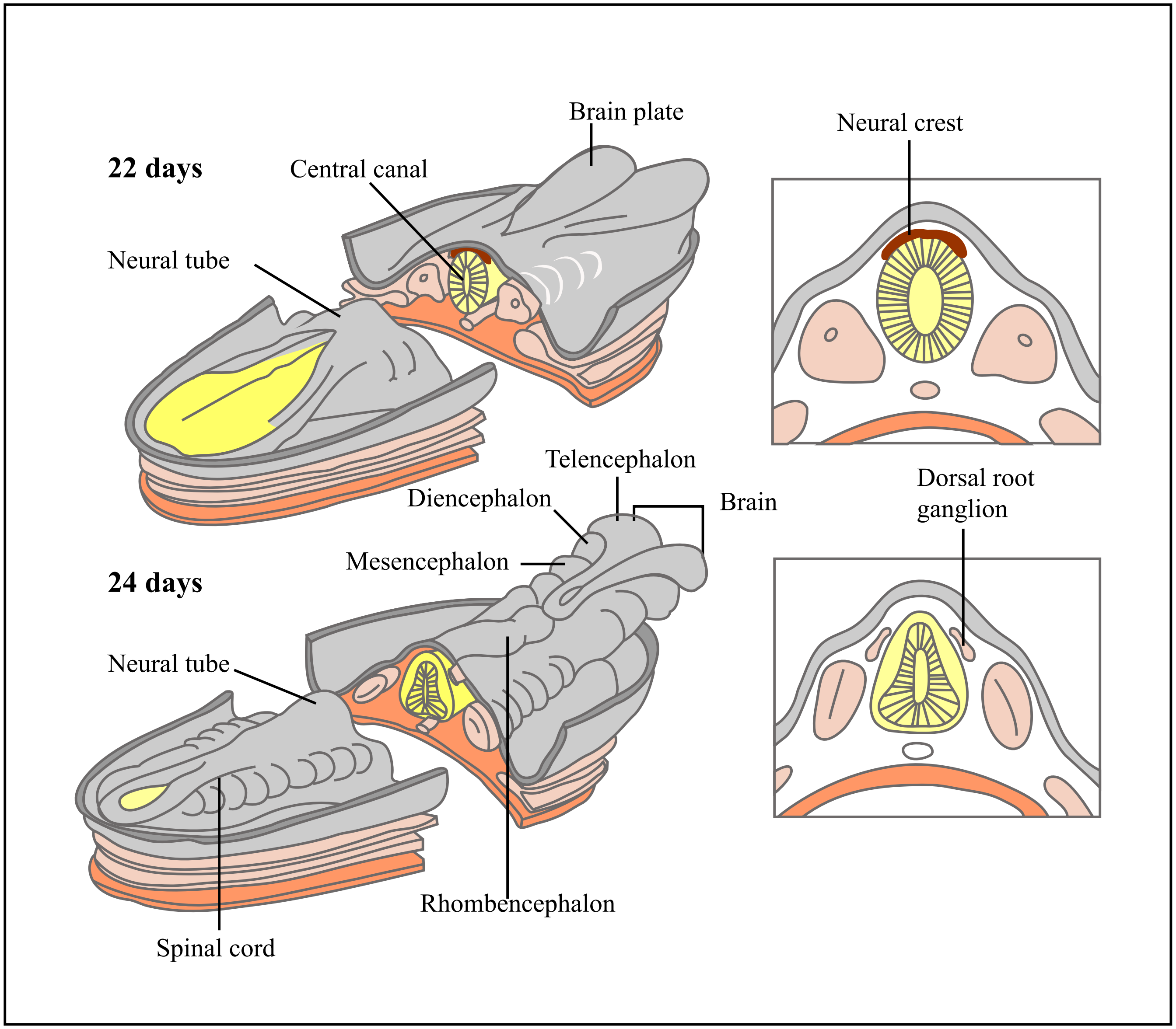


Image by MIT OpenCourseWare.

Neural Tube formation, human at 22 and 24 days

Chapter 8 questions

7) What is sonic hedgehog, and what are two major roles it plays in spinal cord development?

Neurulation and formation of neural tube

- Discovery of inducing molecules
  - SHH (sonic hedgehog protein) diffuses from notochord
  - SHH functions also as a "ventralizing factor" influencing the differentiation of basal plate cells

- Discovery of "dorsalizing factors" secreted by ectoderm adjacent to neural plate
  - BMP-4 & 7 (BMP=bone morphogenetic protein).

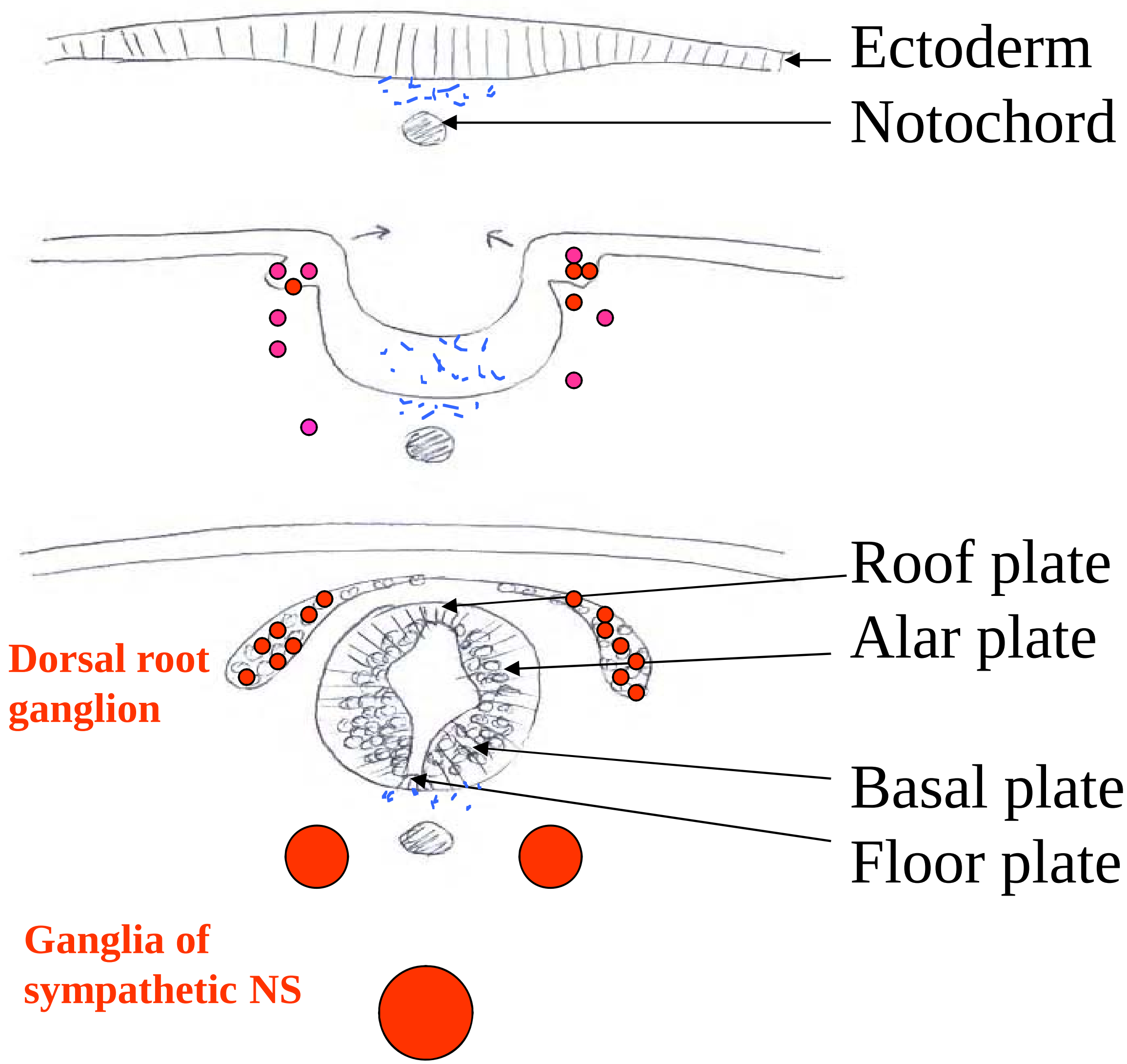
Closure of neural tube with formation of sympathetic ganglia: !

Learn the terms!

Neural plate

Neural groove

Neural tube
and
neural crest



Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

Chapter 8 questions

8) Describe the two types of cell division that occur adjacent to the ventricular surface of the neural tube.

Proliferation in the early neural tube

- Mitoses adjacent to the ventricle
  - Symmetric cell division:
    - two daughter cells remain in proliferative state.
  - Asymmetric cell division:
    - one daughter cell becomes post-mitotic and migrates away from ventricular layer.
- Ventricular layer is called the “matrix layer” of the developing spinal cord [the mother layer]
  - The neural tube is a one-cell thick "pseudostratified epithelium".
  - Cell nucleus moves within the elongated cell:
    - During the steps of cell division (proliferation by mitoses) the cell cycle
    - During migration by the post-mitotic cell

Neurogenesis: Cell proliferation (by mitosis)

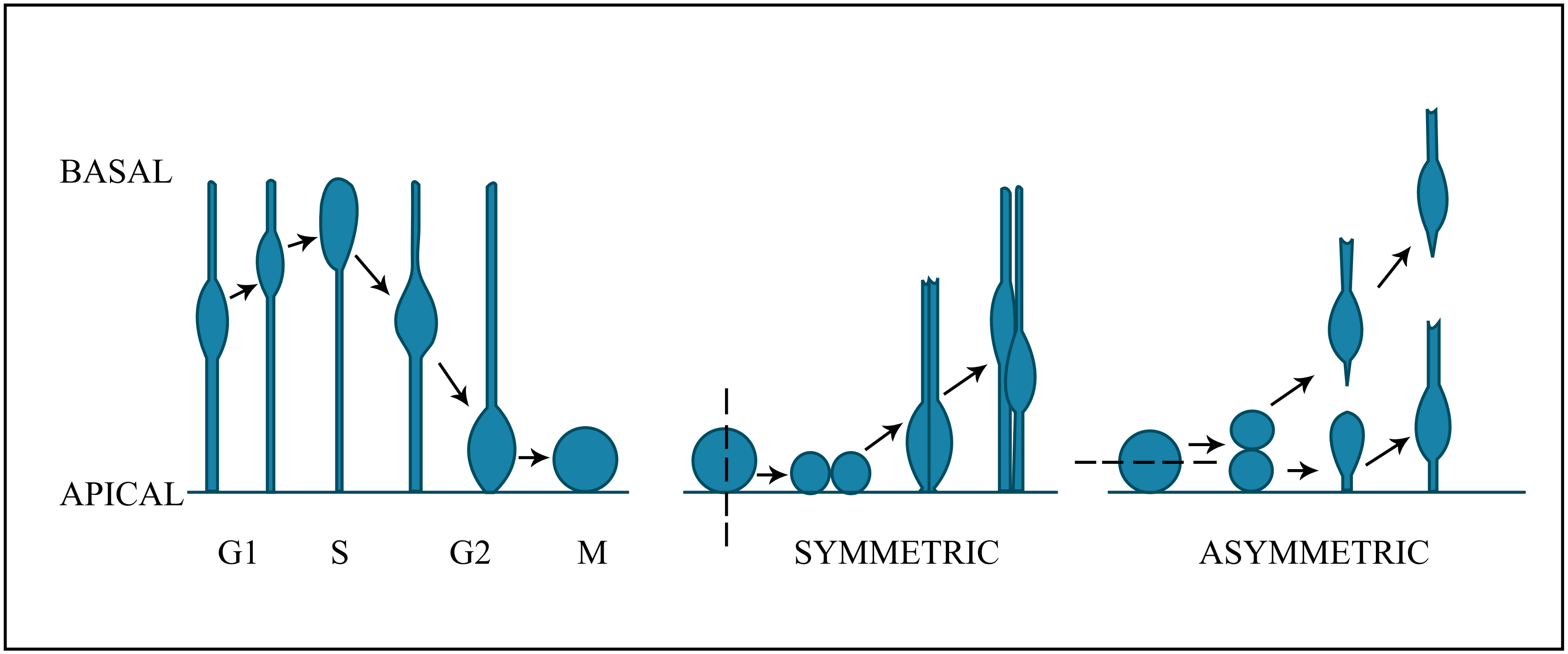
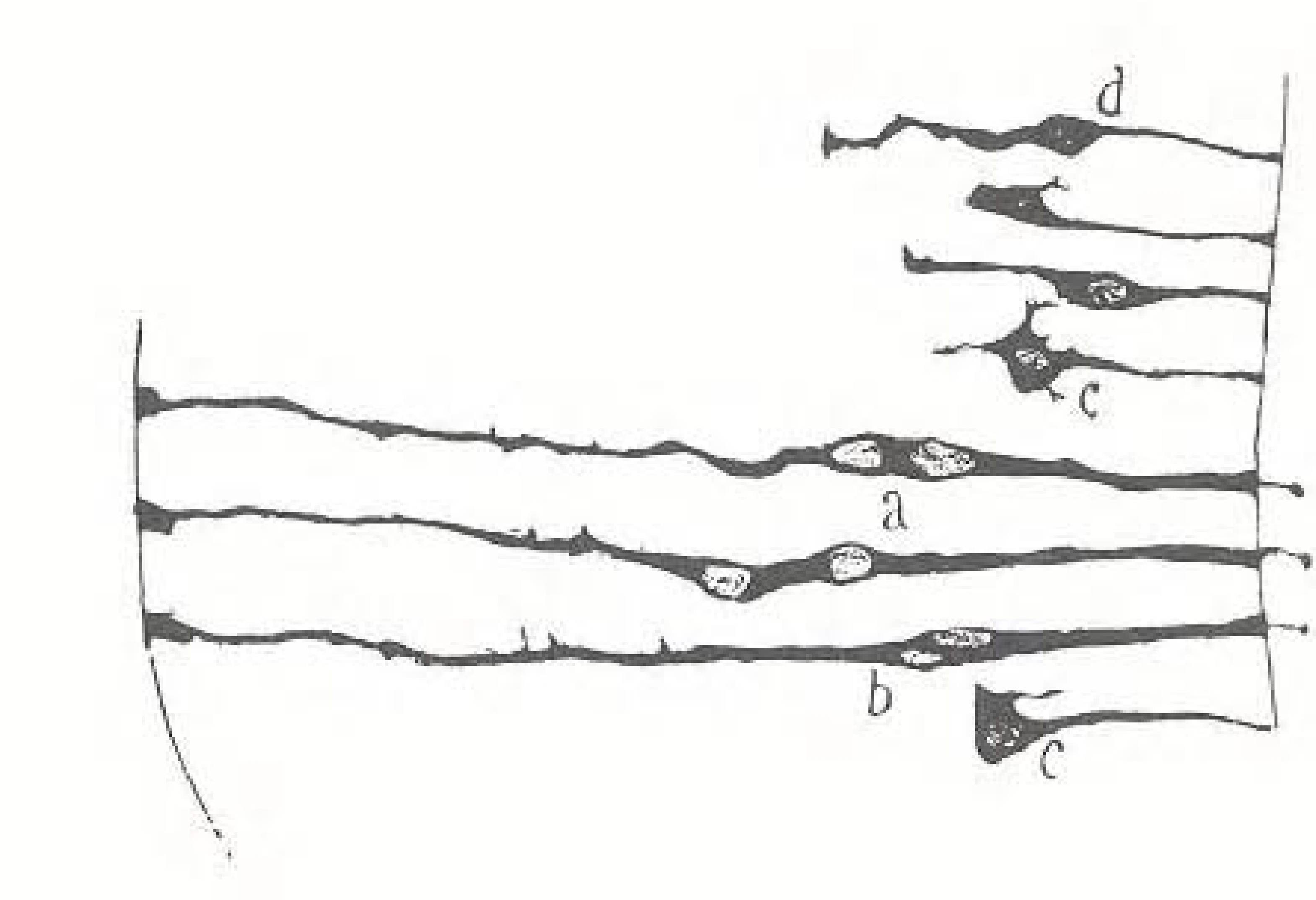


Image by MIT OpenCourseWare.

Cell cycle **Two types of cell division**

Neuroepithelial Cells (Cajal)



Neuroepithelium, chick spinal cord, day 3 (Cajal)

Other, more differentiated cells at this stage are not shown in the drawing.

Reticular appearance of its outer half.

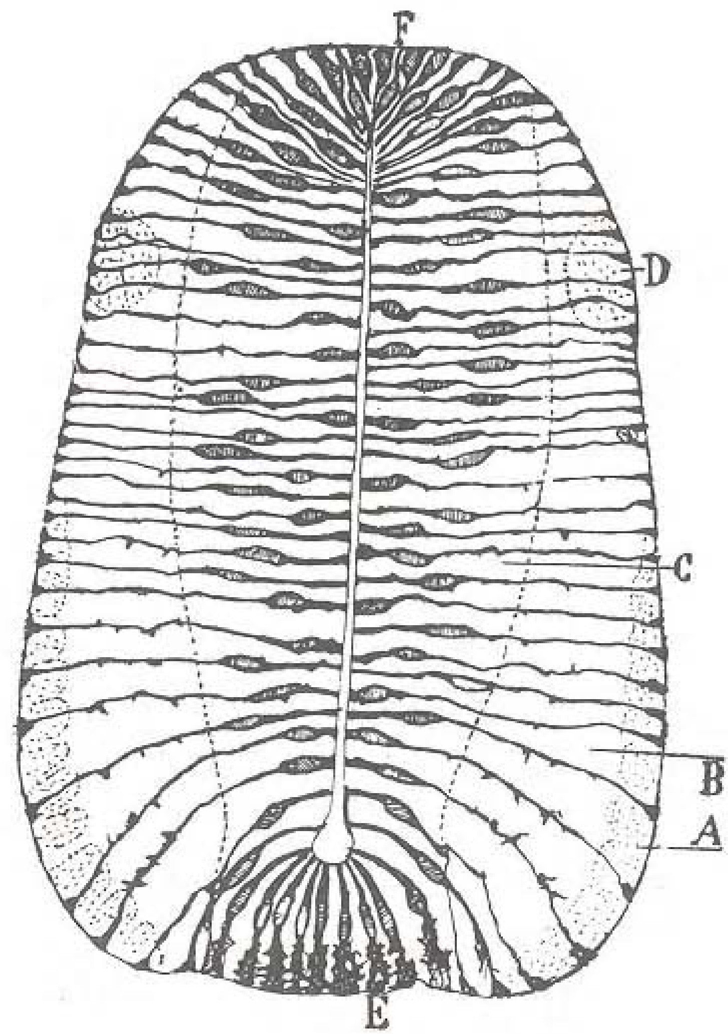


Image is in public domain.

Chapter 8 questions

9) How did neuroscientists come to know that there are at least two major modes of cell migration in the embryonic central nervous system? Describe the two modes.

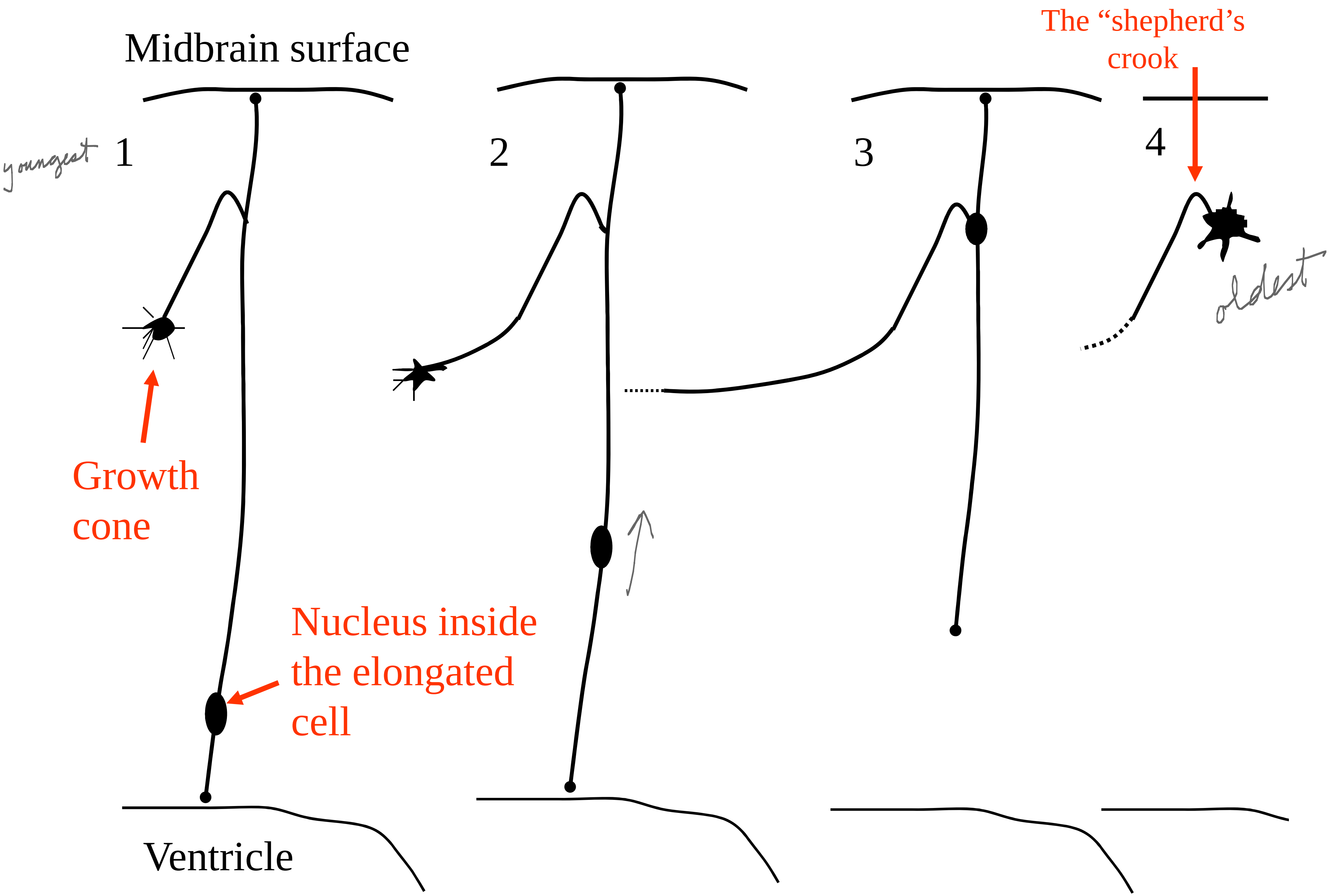
Migration: There are actually three types

- **Nuclear translocation**
- Guidance of cell movement by radial glia cells
- Guidance of cell movement by other substrate factors

A definitive demonstration of nuclear translocation as a mechanism of cell "migration" in the CNS

- Development of the Shepherd's Crook Cell in Chick Optic Tectum
- Why was this important? Think about the techniques being used, and the nature of a controversy about the mechanism of cell migration in the developing CNS.
- Investigators tried to assume that there was only one way for cells to migrate.

Domesick V.B. and Morest D.K. (1977) Migration and differentiation of shepherd's crook cells in the optic tectum of the chick embryo. Neuroscience 2: 477-492



Midbrain surface
The "shepherd's crook
youngest
1
2
3
4
oldest
Growth cone
Nucleus inside the elongated cell
Ventricle

- Other types of cell migration in the CNS will be discussed later.
- After – or even during – neuronal migration in the spinal cord, the neurons are starting to **differentiate**. — they form axons + dendrites, synapses.

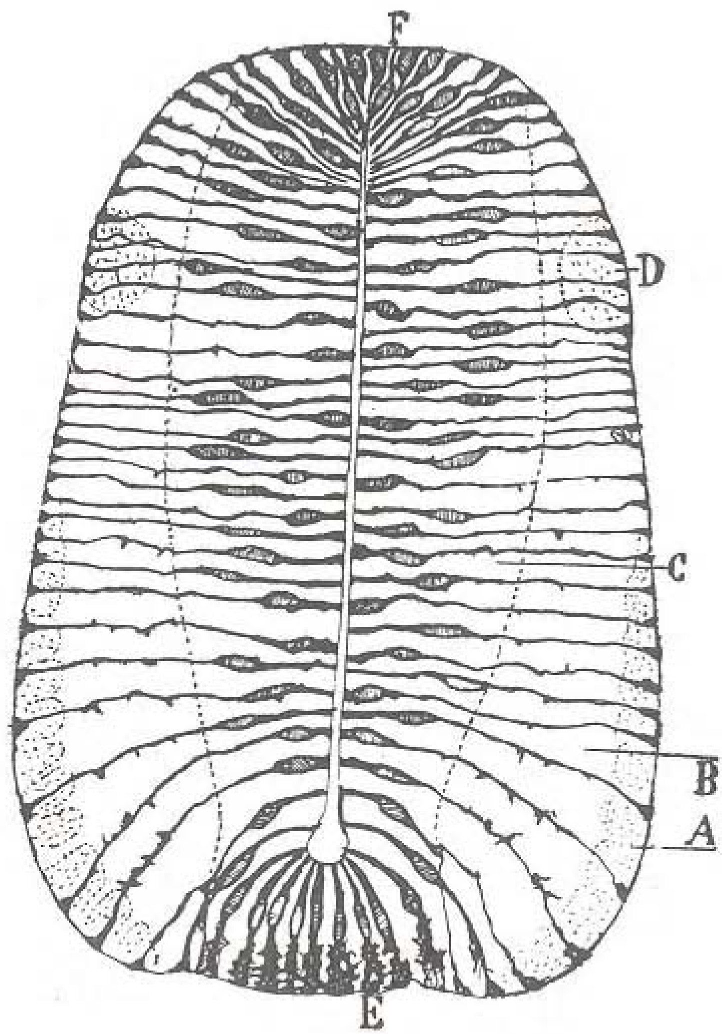
Chapter 8 questions

10) In his studies of development of the embryonic chick CNS, how did Ramon y Cajal recognize the initial stages of dorsal and ventral root development?

He correctly identified "growth cones" of developing axons

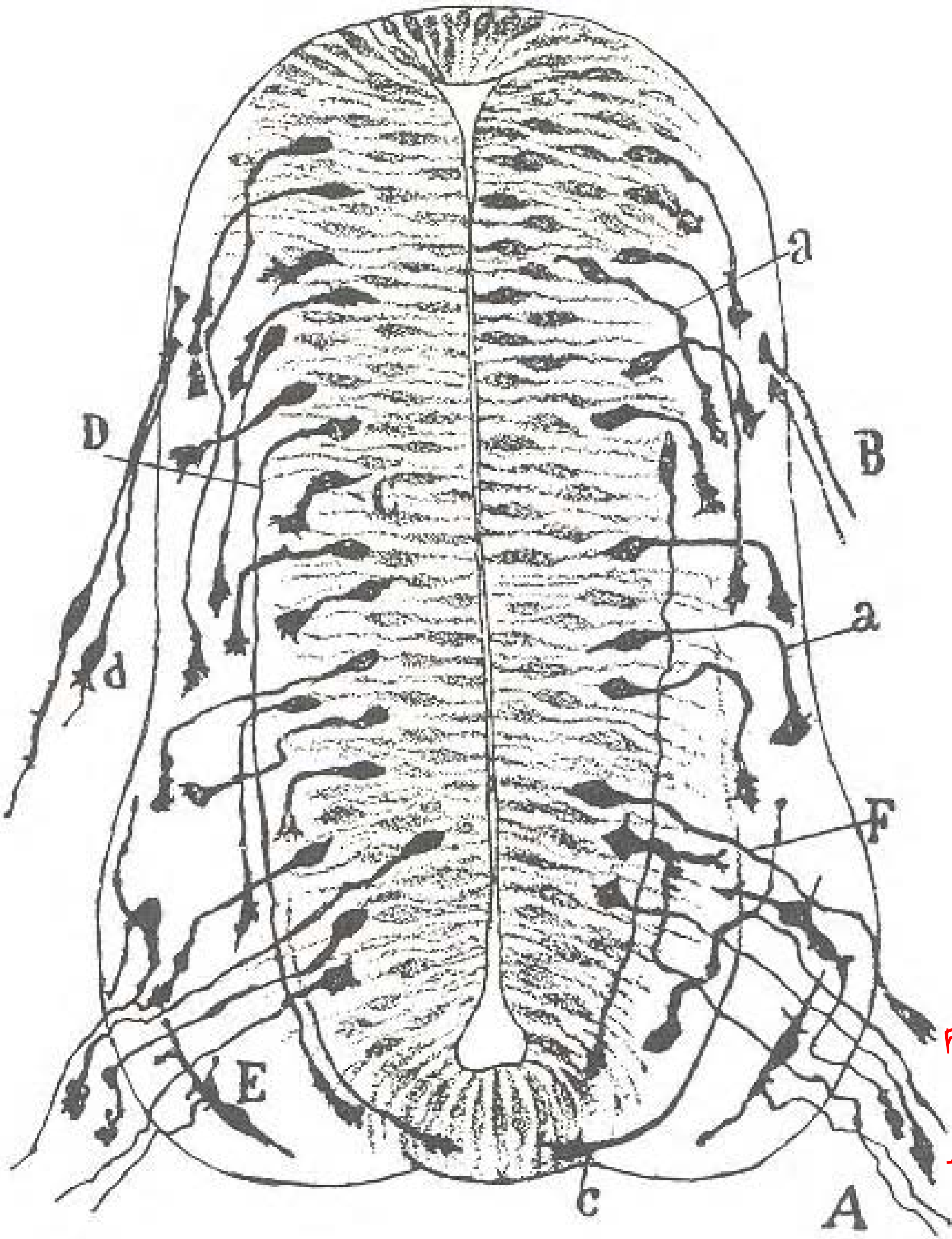
Neuroepithelium, chick spinal cord, day 3 (Cajal)

SHOWN EARLIER



Reticular appearance of its outer half.

Image is in public domain.

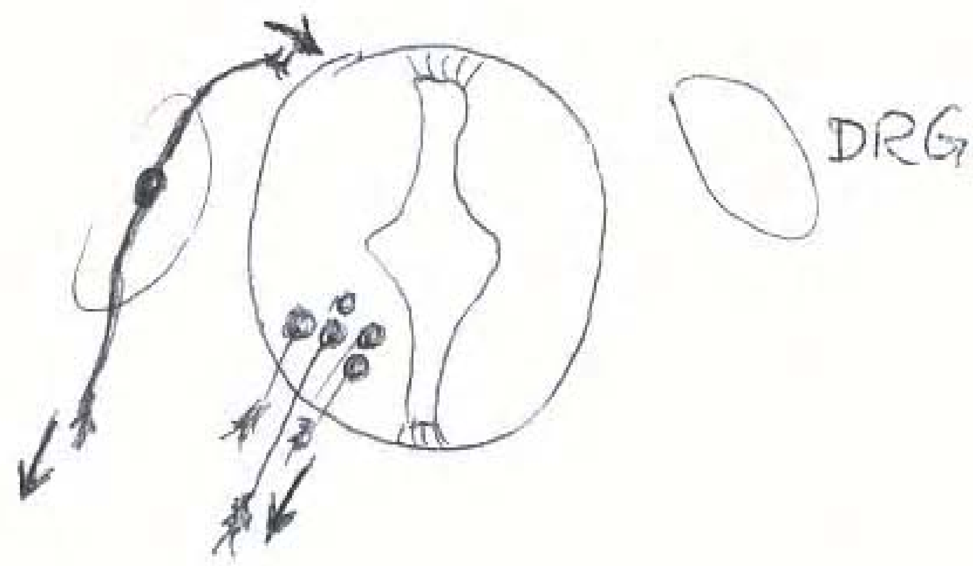


Same age, same species:

Chick spinal cord, day 3 (Cajal), showing early differentiation

growth cones

Differentiation:
Growth of dorsal and ventral roots



We will return to axonal growth later.
First, a look at the adult spinal cord and brain.

REVIEW

Some neurodevelopment terms to be familiar with

- ectoderm (*vs*. mesoderm and endoderm),
- ventricular layer, intermediate layer, marginal layer (= matrix layer, mantle layer, zonal layer)
- modes of migration,
- radial glia (radial astrocytes),
- ependyma, cells that line the ventricle of CNS.
- sulcus limitans, separating alar and basal plates,
- neural crest,
- dorsal and ventral roots and rootlets.

See Nauta & Feirtag, ch.10, and other texts

9.14 Brain Structure and Its Origins
Spring 2014