Class 6 completion

Neocortex introduced
Neocortex and its elaboration in mammals

Topics

• "Shmoo 2": the mammalian brain
• Major ascending and descending connections
• General view of functions

In this introduction, we skip over the evolution of neocortex, but we will return to this major topic later.
Shmoo brain with neocortex indicated
“Shmoo 2”–side view.

Top view, embryonic brain (with spinothalamic tract)
Two major long pathways associated with neocortex of present-day mammals:

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

2) Corticospinal tract.
1) The dorsal column – medial lemniscus pathway.
2) The corticospinal tract.
1) The dorsal column – medial lemniscus pathway.  
2) The corticospinal tract.

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.
1) The dorsal column – medial lemniscus pathway.

2) The corticospinal tract.

One example neuron in each hemisphere.

(Remember: These pathways are)

decussation of medial lemniscus axons ("internal arcuate fibers") and of pyramidal tract.
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 both the triggering and execution of FAPs.
  - Separation of objects from background stimuli became better.

- 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. Imaging depends on posterior neocortex.
  - Planning abilities use the internal model, and depend on anterior (frontal) areas.
Review of a few basic points
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 hypersensitivitiy 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).
Taking stock of where we are in learning the anatomy of the CNS

Where do we go from here?

• We have a rudimentary outline.
• How do we 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.
A sketch of the central nervous system and its origins

G. E. Schneider 2005
Part 4: Development and differentiation, spinal level

MIT 9.14 Class 7
Neurulation, proliferation, migration & differentiation, spinal level
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 structure and the autonomic nervous system

topics

• Some embryology: a look at neurulation and the developing spinal cord
• Survey of adult spinal cord
• Autonomic nervous system
Developmental steps leading to a nervous system

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

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

According to Wolpert (1992, ch. 2):

- Contractions
- Changes in adhesion (*via* expression of CAMs)
- Cell movement
- Growth

These activities are how cells accomplish developmental changes.
From blastula to gastrula: Note the role of filopodia in gastrulation
Precursors of skeleton find their way along the inner wall of the embryo
Development of the CNS:
4 major events

1. Neurulation, formation of neural tube
2. Proliferation
3. Migration
4. Differentiation, with growth of axons and dendrites
Focus on the developing spinal cord

- Formation of the **neural tube** from the embryonic ectoderm (neurulation)
- **Alar and basal plates**; sulcus limitans (can be followed up to midbrain)
- **Neural crest cells**: 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

Neural plate

Neural groove

Neural tube and neural crest

Ectoderm
Notochord

Roof plate
Alar plate
Basal plate
Floor plate

BMP proteins

SHH protein (see below)
“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. They come from the “neural crest”.

• We will look at what happens using several different pictures and animations.
Neurulation and formation of neural tube

• Discovery of induction of CNS by notochord region

• 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).
Neural tube Closing

Figure by MIT OCW.
Neurulation: animation

Screenshots from neurulation videos removed due to copyright reasons.
Neurulation in *Xenopus*, movie

Screenshots from neurulation videos removed due to copyright reasons.
Neural Tube Formation

Screenshots from neurulation videos removed due to copyright reasons.
Neural Tube formation, 18-day human

Figure by MIT OCW.
Neural Tube formation, 22-day human

Figure by MIT OCW.
Closure of neural tube with **formation of sympathetic ganglia:**
learn the terms!

- Neural plate
- Neural groove
- Neural tube
  - and **neural crest**
  - **neural crest**
- Ectoderm
- Notochord
- Roof plate
- Alar plate
- Floor plate
Fate of the neural crest cells along the rostro-caudal axis of the embryonic CNS

We will mention some of these cells after we review the developing spinal cord.

Figure by MIT OCW.
**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 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)
    - During migration by the post-mitotic cell
Neurogenesis: Cell proliferation (by mitosis)
Neuroepithelial Cells (Cajal)

Figure removed due to copyright reasons.
Please see:
Cajal, S., and Ramón Y. *Histology of the Nervous System of Man and Vertebrates.*
Neuroepithelium,
chick spinal cord, day 3 (Cajal)

Figure removed due to copyright reasons.

Please see:
Cajal, S., and Ramón Y. *Histology of the Nervous System of Man and Vertebrates*.
Migration: 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 the controversy about the mechanism of cell migration in the developing CNS.

• Other mechanisms of cell migration in the CNS will be considered later.
• After – or even during -- neuronal migration in the spinal cord, the neurons are starting to differentiate.
Figure removed due to copyright reasons.
Please see:
Cajal, S., and Ramón Y. *Histology of the Nervous System of Man and Vertebrates.*
Chick spinal cord, day 3 (Cajal), showing early differentiation.
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, mantle layer, marginal layer
- modes of migration,
- radial glia (radial astrocytes),
- ependyma,
- sulcus limitans, alar and basal plates,
- neural crest,
- dorsal and ventral roots and rootlets.

From Nauta & Feirtag, ch.10, and other texts
Survey of adult human spinal cord

- Different levels, illustrated
- The sensory channels (reflex, spinocerebellar and spinothalamic tracts, origin of dorsal column axons)
- Major descending pathways (cortico-, rubro-, reticulo-, and vestibulo-spinal)
- “Propriospinal” fibers.
**Left:**
Internal structure of spinal cord

**Right:**
Levels, rostral to caudal

Figure by MIT OCW.
Different levels, illustrated:

Note the following things

- Gray vs. white matter. Gray matter: dorsal and ventral horns
- Changes in amount of white matter, rostral to caudal
  - More and more descending axons leave the white matter
  - More and more ascending axons join the white matter
- Cervical and lumbar enlargements
  - See p.222 of Striedter for picture of Brontosaurus
- Presence of “lateral horn” in thoracic and upper lumbar cord
Comparisons, speculations

• Role of myelin
  – “A crucial vertebrate innovation” (Allman p. 78): Why?
  – Not found in any invertebrate or in the jawless vertebrates (hagfish, lampreys)

• How does spinal cord of humans differ from spinal cords of other mammals?
Spinal cord cross section
Lumbar level

Figure by MIT OCW.

Note the laminae of Rexed.

Drawing based on cell - body stain
Survey of adult human spinal cord

- **Different levels**, illustrated
- **The sensory channels** (reflex, spinoreticular & spinothalamic, and spinocerebellar tracts; origin of dorsal column axons)
- **Major descending pathways** (reticulo-, vestibulo-, rubro-, and corticospinal)
- “Propriospinal” fibers
Selected References
