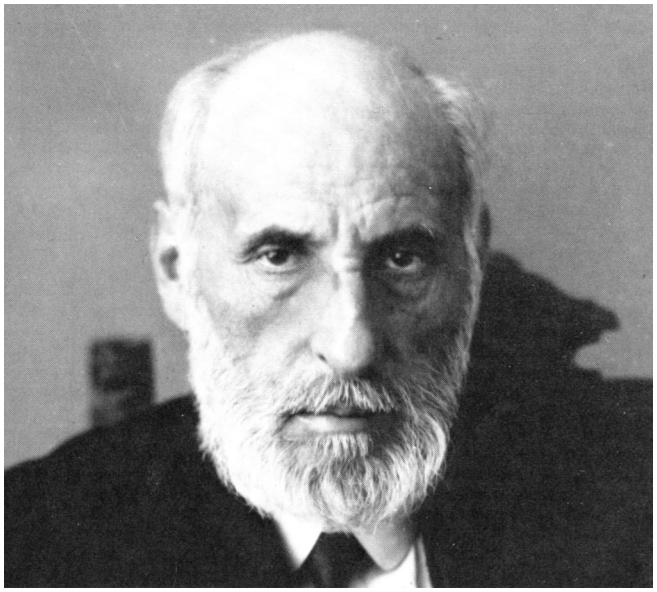
Emilio Golgi

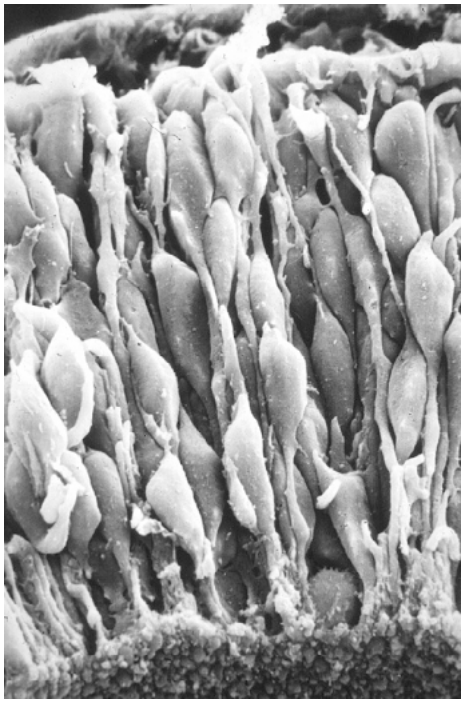
Santiago Ramon y Cajal



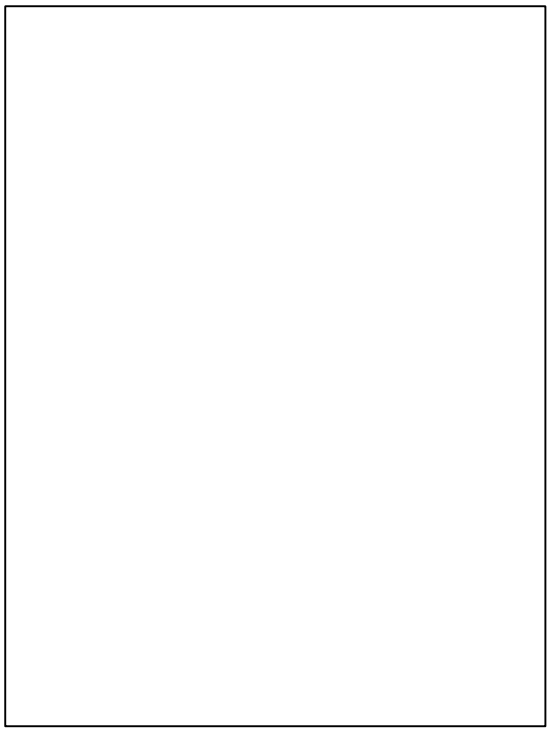
How to build a nervous system.

1. Cellular commitment to neural lineage.
2. Cell proliferation of neuroblasts and glioblasts.
3. Cellular migration.
4. Differentiation – neurons, astroglia (radial glia), oligodendroglia (myelination).
5. axonal outgrowth and synapse formation.
6. Cell death = apotosis.

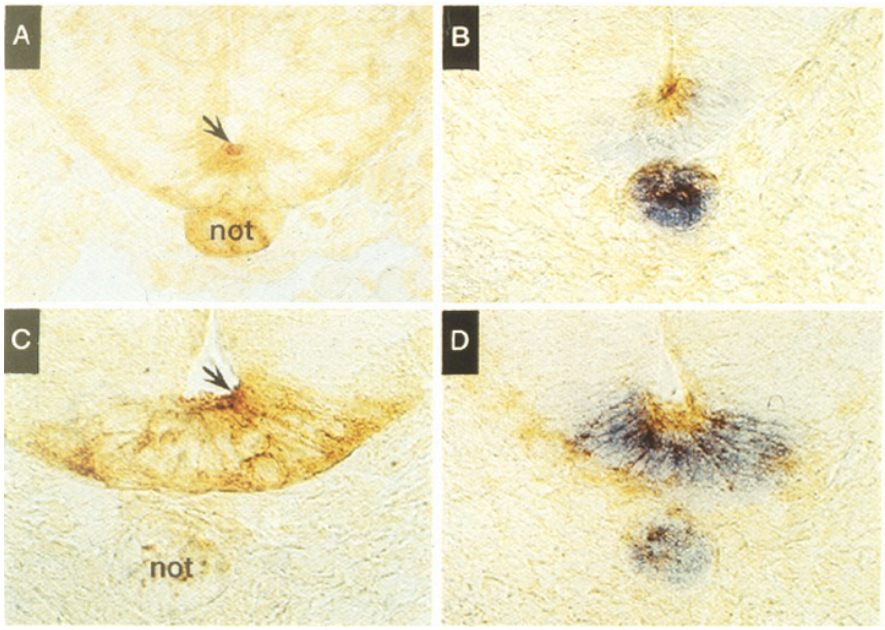
Cell Proliferation

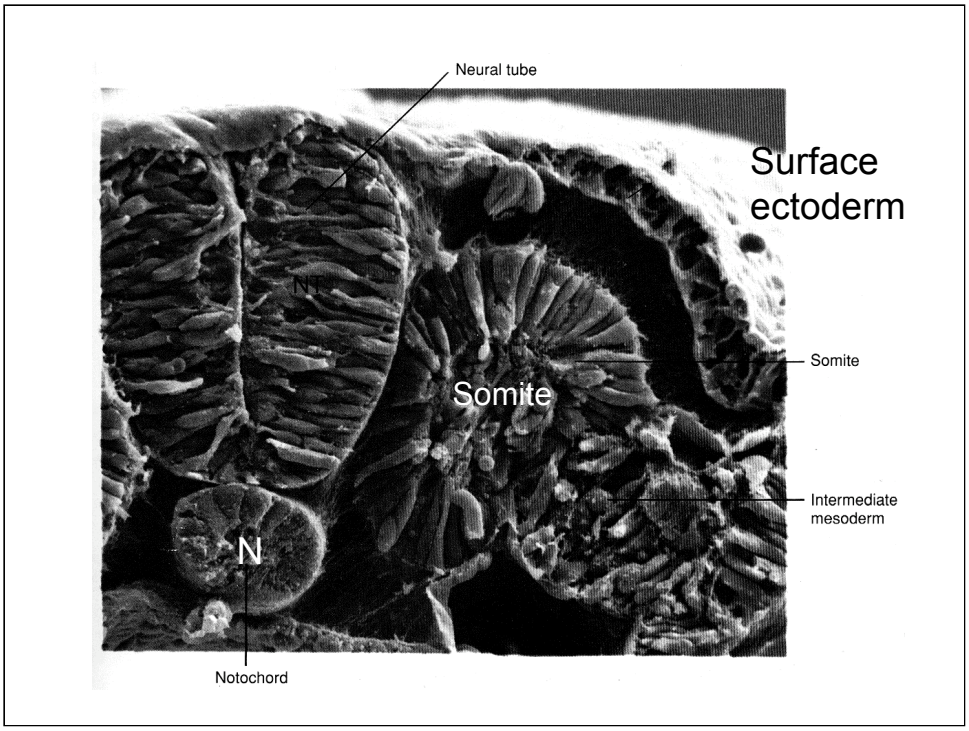


Neural tissue is generated by the columnar epithelium of the neural plate.

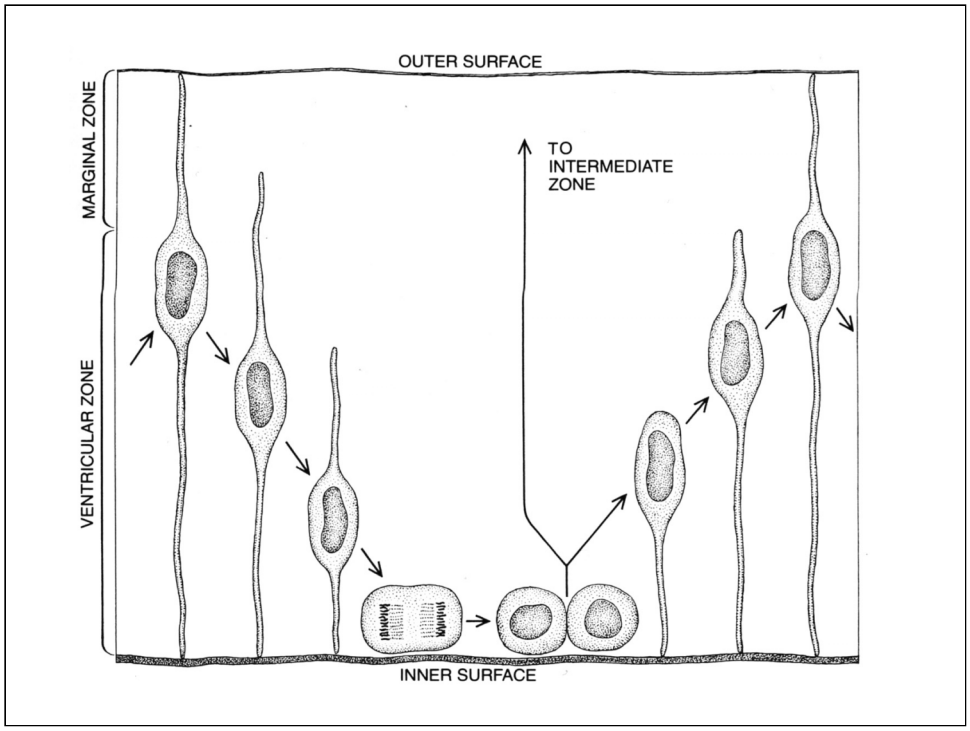


Different stages of neural plate induction. Generated from columnar epithelium (red) which
f plate (red). The ventralizing signal (sonic hedgehog, shh) is first secreted by the notochor
s established as indicated by red arrows. Exposure to these molecules induces neuronal g

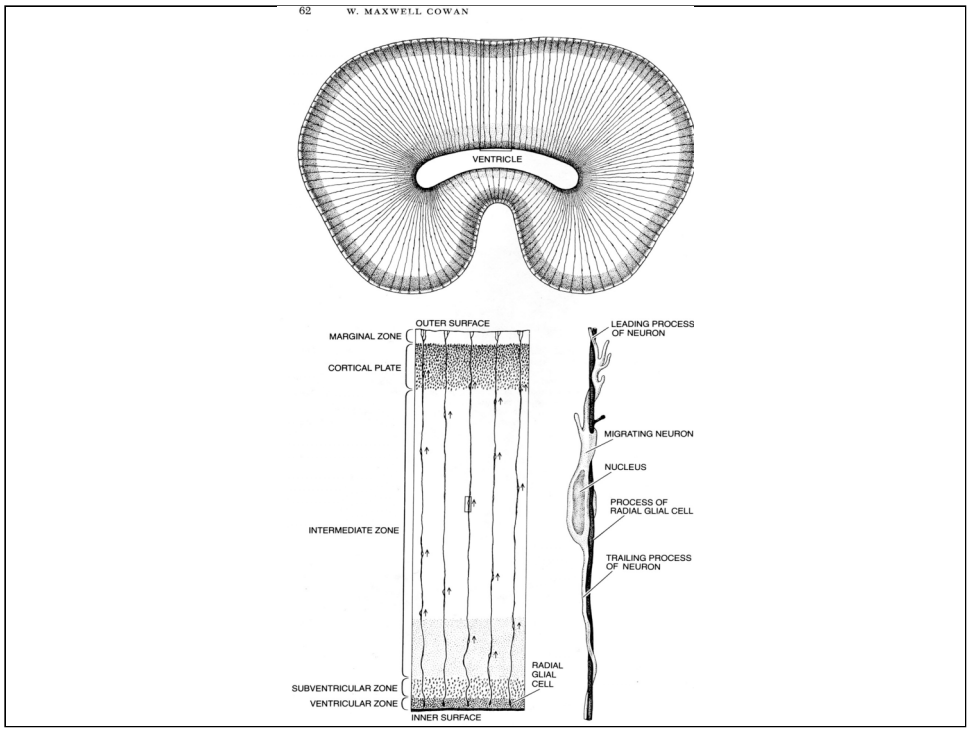

A
not
B
C
not
D



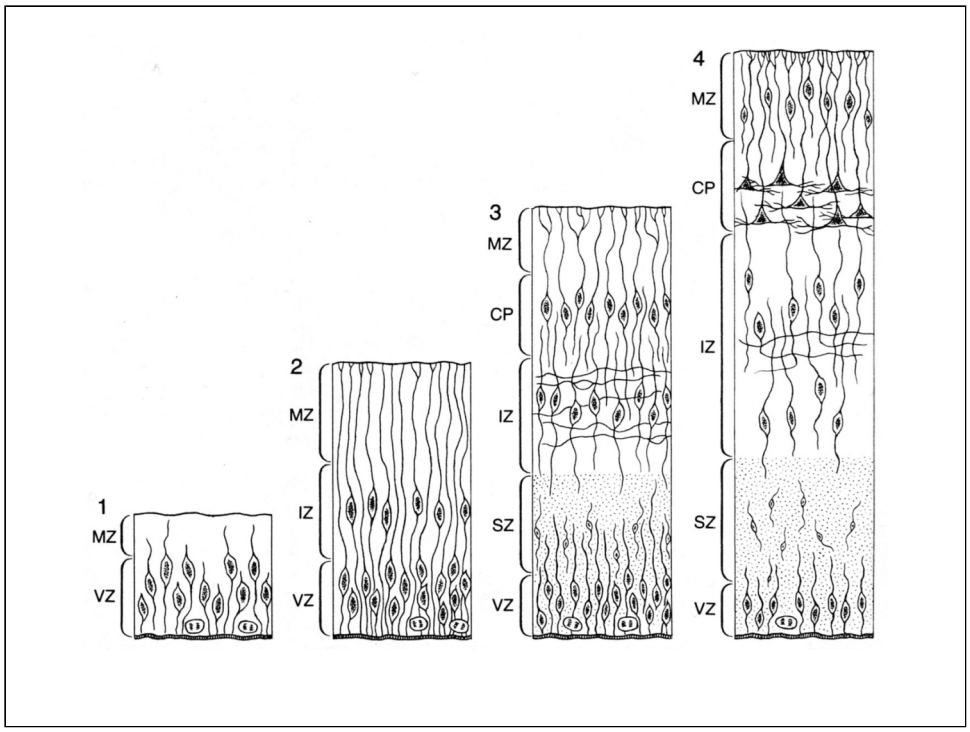
Closure of neuroepithelium to form neural tube. Notochord acts signaling center.



Schematic of cell division in the ventricular zone. Mitosis occurs on inner most surface/ventricular surface. After cell division is completed the new cells generate an apical and basal process and the nucleus of the cell translocates. The apical processes form the marginal zone.

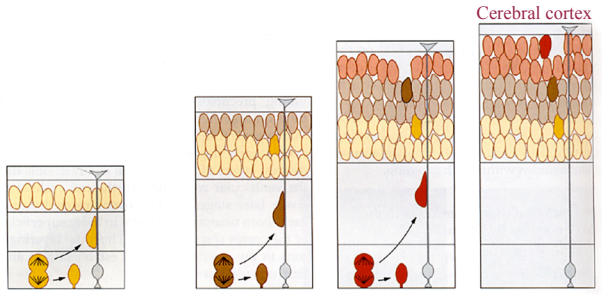


After cells are generated, they migrate to their final destination. Illustrated here is the columnar migration of cerebral cortical neurons. These cells migrate predominately along radial glia cells (also derived from neuroepithelium). The migratory cell has a dynamic leading process that interacts with the surface of the radial glia. The migratory cells form a subventricular zone, intermediate zone and the cortical plate. The marginal zone is comprised of processes of both the new neurons.

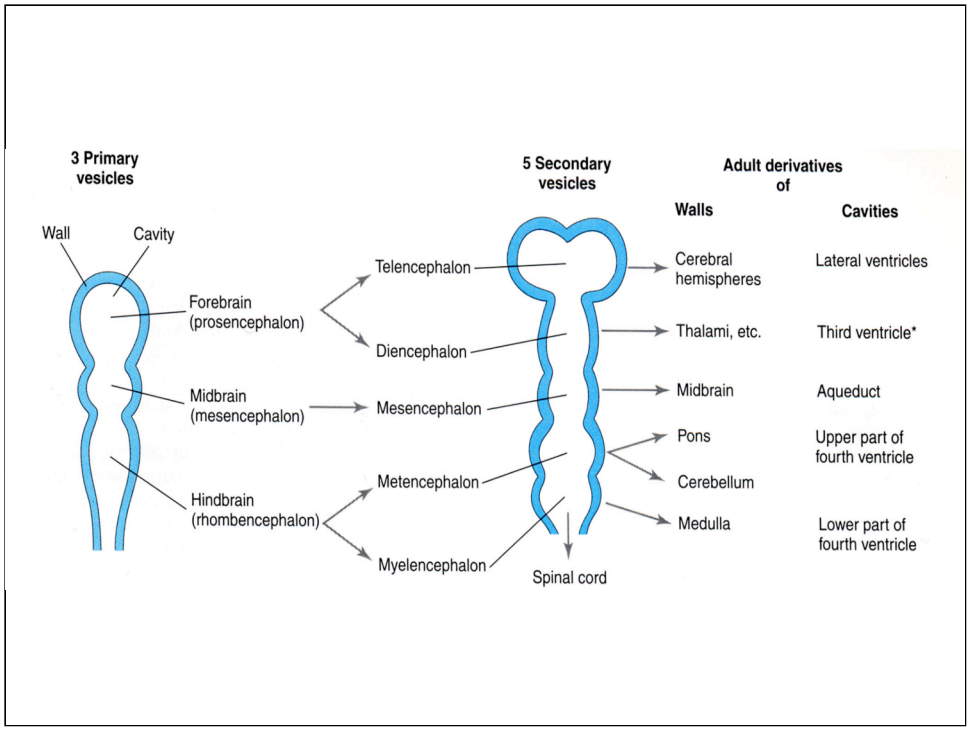


Higher magnification of cortical neuron migration. Of interest are: the subventricular zone from which glia are generated. This is also the zone of stem cells which potential to produce new neurons and glia. The production of new neurons in short lived animals, such as rats, is well documented. The production of new cells in adulthood in primates is highly controversial. Also of note is that the first generated cells stop migrating, for example at the intermediate zone. The next wave of cells migrates through the old ones so that the cortical plate is built inside to outside. Each wave or layer then differentiates into layer specific types.

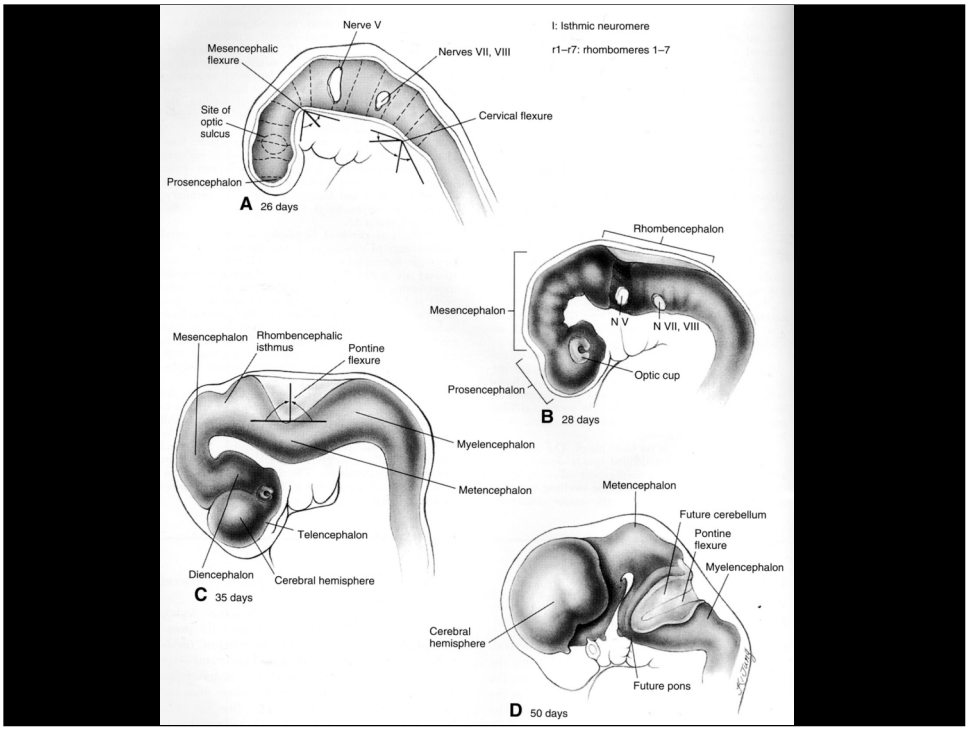
NEUROGENESIS IN THE CEREBRAL CORTEX



Neurons born at early stages migrate to the deepest layers of the cortical plate
Neurons born at later stages migrate form the more superficial layers of the cortex

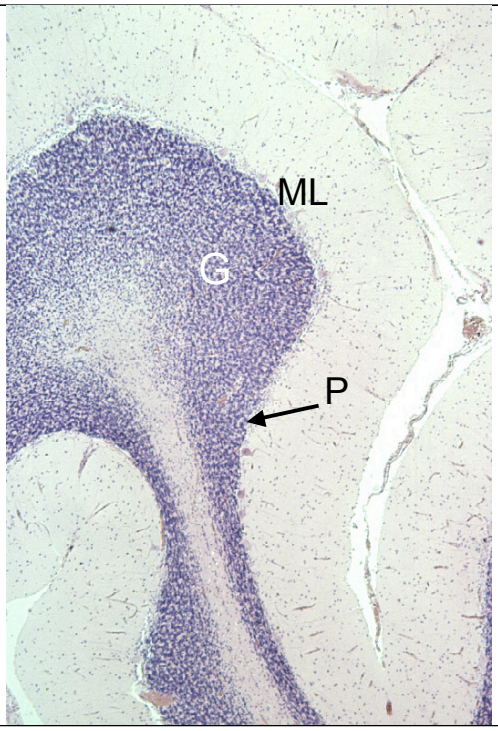


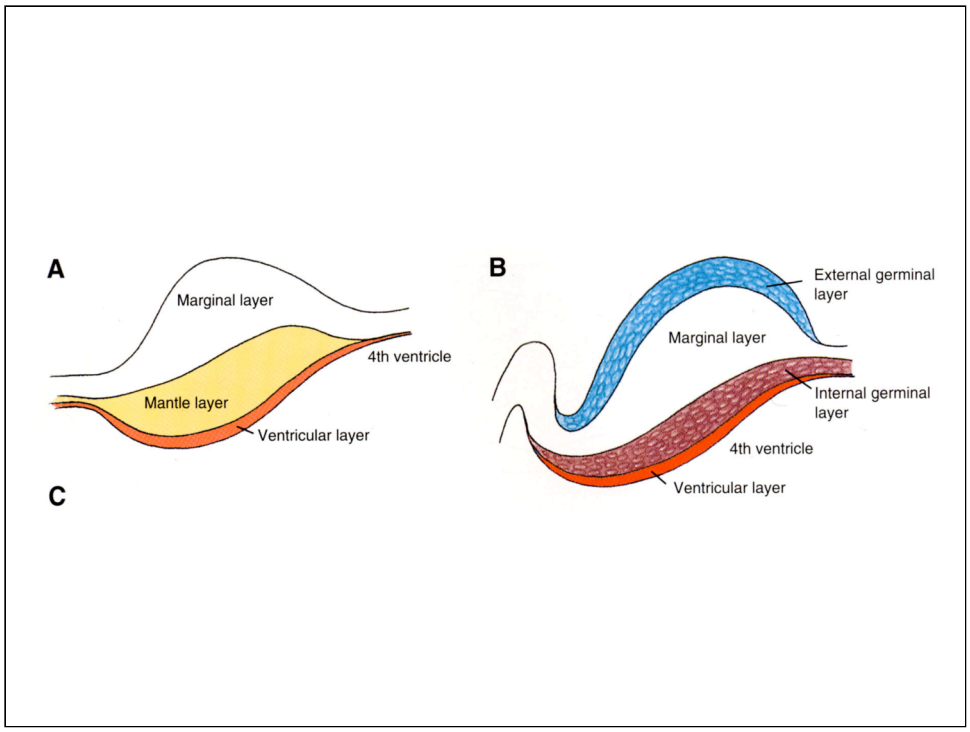
As neural plate expands, even before neurulation is complete, the 3 primary vesicles are demarcated. The slide illustrates that derivates of the three primary vesicles and the central cavity/ventricle associated with each.

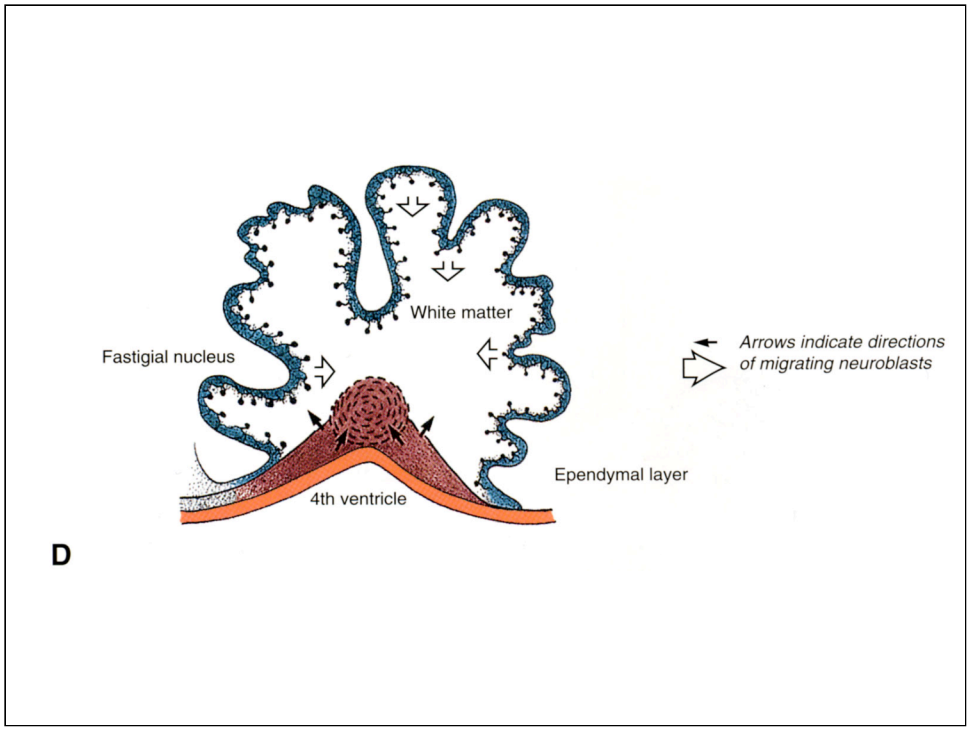


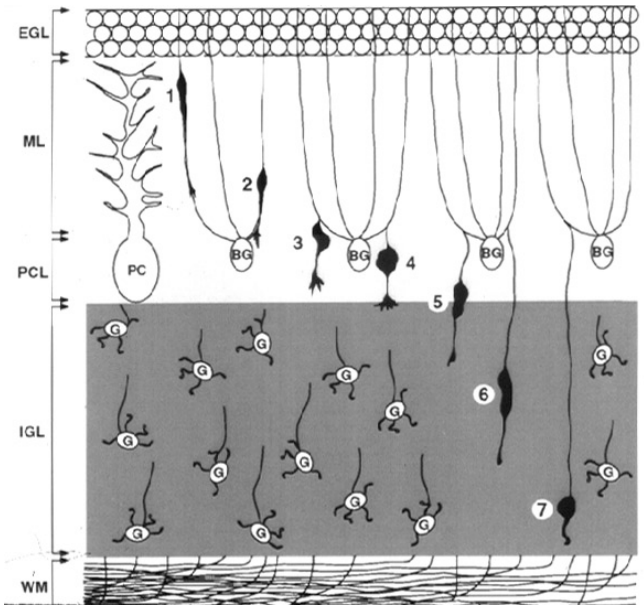
As mentioned in the introductory lectures, the rapid growth of the CNS and relative stiffness of notocord, results in bending of the tube. The flexures are demarcated on this slide. Of importance at this point is to noted that in fact the CNS is segmented and this can be seen most clearly in the rhobencephalon. Sites of exit of cranial nerves are indicated in B. In C the pontine flexure is the future site of the cerebellum as shown in D.

Cerebellum is generated by two regions of mitotic cells

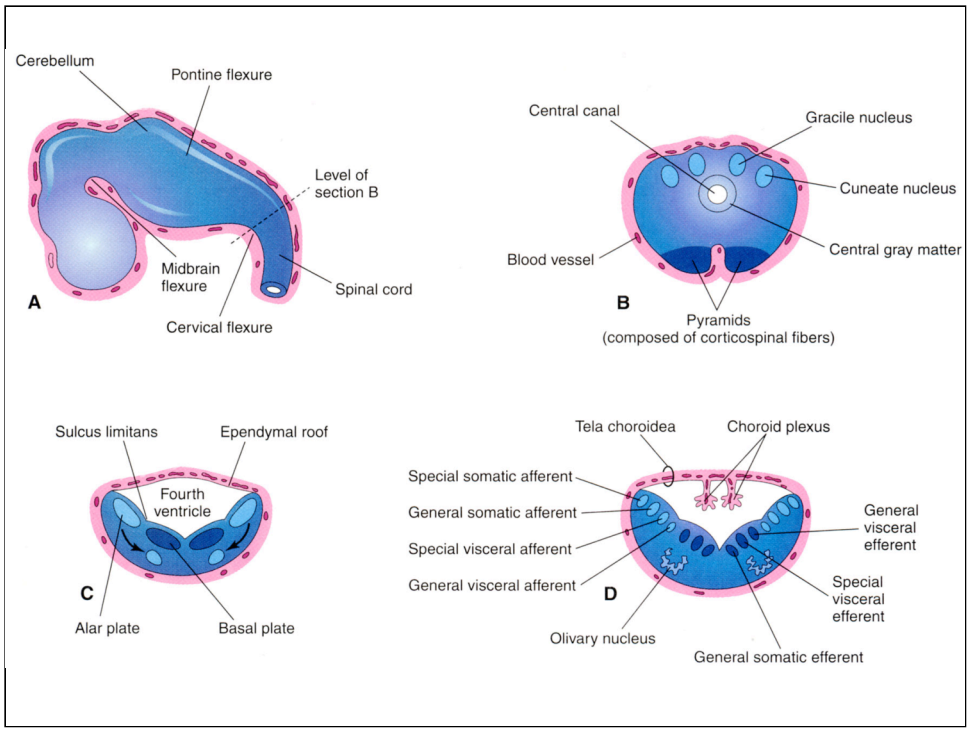

ML
G
P


A
Marginal layer
4th ventricle
Mantle layer
Ventricular layer
B
External germinal layer
Marginal layer
Internal germinal layer
4th ventricle
Ventricular layer
C


White matter
Fastigial nucleus
Arrows indicate directions
of migrating neuroblasts
Ependymal layer
4th ventricle
D


EGL
ML
PCL
IGL
WM
PC
BG
BG
BG
BG
1
2
3
4
5
6
7
G

Organization of rhomobencephalon



This and the following slide does the flexures in color!

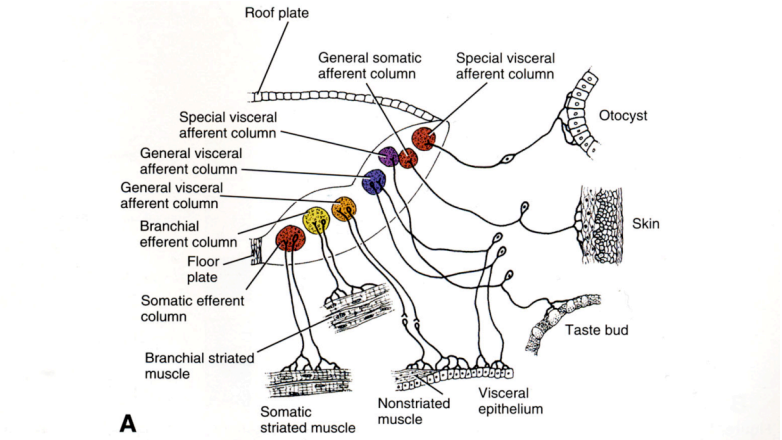


Figure 13–3. Organization of the brain stem cranial nerve nuclei. The basal columns give rise to motor (efferent) cranial nerve nuclei and the alar columns to associational (afferent) cranial nerve nuclei. These nuclei can be grouped into seven discontinuous columns, each subserving a specific type of function. *A,* Idealized organization of the brain stem cranial nerve nuclei into seven columns.

The alar (association/sensory input) and basal (motor/efferent) organization of the cranial nerve nuclei.

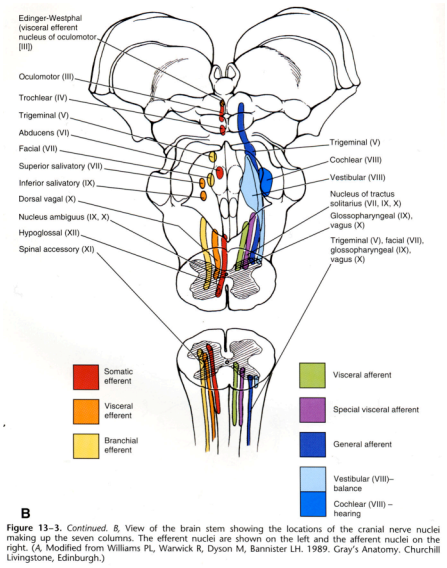


Figure 13–3. *Continued. B,* View of the brain stem showing the locations of the cranial nerve nuclei making up the seven columns. The efferent nuclei are shown on the left and the afferent nuclei on the right. (*A,* Modified from Williams PL, Warwick R, Dyson M, Bannister LH. 1989. Gray's Anatomy. Churchill Livingstone, Edinburgh.)

Organization of the discontinuous columns of cranial nerve nuclei. Covered in gross anatomy.

Table 13–1
Location of the Cranial Nerve Nuclei

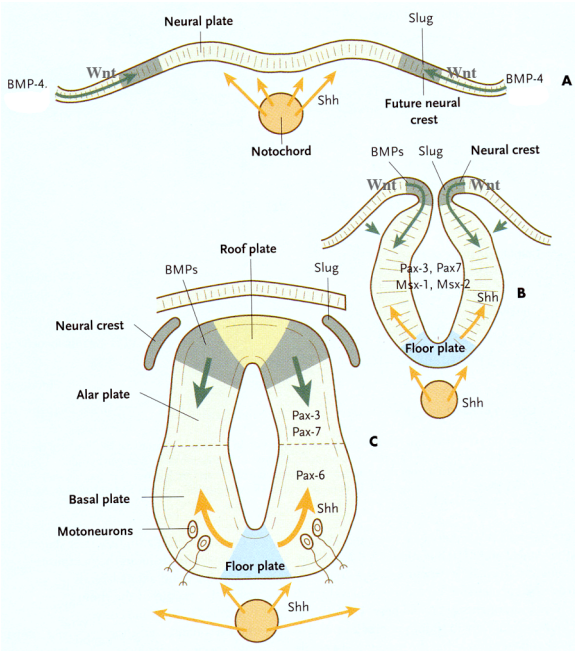
BRAIN REGION	ASSOCIATED CRANIAL NERVES
Telencephalon	Olfactory (I)
Diencephalon	Optic (II)
Mesencephalon	Oculomotor (III)
Metencephalon	Trochlear (IV) (Arises in the metencephalon but is later displaced into the mesencephalon)
	Trigeminal (V) (The trigeminal sensory nuclei arise in the metencephalon and myelencephalon but are later displaced partly into the mesencephalon. The trigeminal motor nucleus arises in the metencephalon and remains there.)
	Abducens (VI)
	Facial (VII)
	Vestibulocochlear (VIII)
Myelencephalon	Glossopharyngeal (IX)
	Vagus (X)
	Accessory (XI)
	Hypoglossal (XII)

Table 13–2
Origins of the Neurons in the Cranial Nerve Ganglia

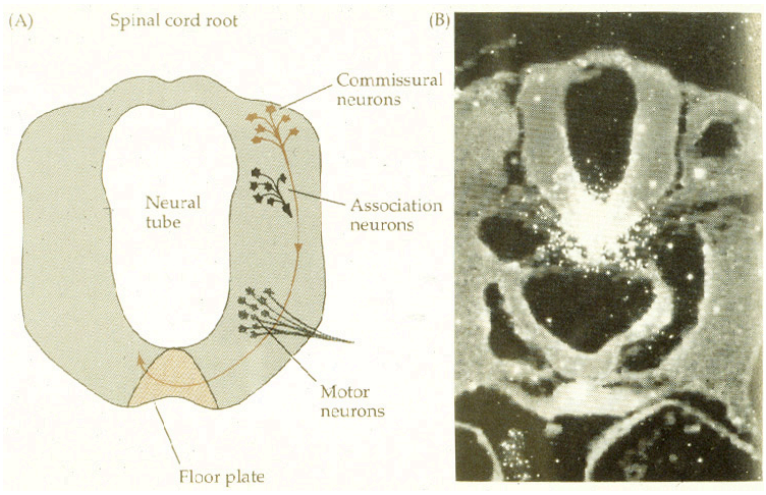
CRANIAL NERVE	GANGLION AND TYPE	ORIGIN OF NEURONS
Olfactory (I)	Olfactory epithelium (primary neurons of the olfactory pathway) (special afferent)	Nasal placode
Oculomotor (III)	Ciliary ganglion (visceral efferent)	Neural crest of the caudal diencephalon and cranial mesencephalon
Trigeminal (V)	Trigeminal ganglion (general afferent)	Neural crest of the caudal diencephalon and cranial mesencephalon; trigeminal placode
Facial (VII)	Superior ganglion of nerve VII (general and special afferent)	Rhombencephalic neural crest; 1st epibranchial placode
	Inferior (geniculate) ganglion of nerve VII (general and special afferent)	1st epibranchial placode
	Sphenopalatine ganglion (visceral efferent)	Rhombencephalic neural crest
	Submandibular ganglion (visceral efferent)	Rhombencephalic neural crest
Vestibulocochlear (VIII)	Acoustic (cochlear) ganglion (special afferent)	Otic placode
	Vestibular ganglion (special afferent)	Otic placode plus some contribution from neural crest
Glossopharyngeal (IX)	Superior ganglion (general and special afferent)	Rhombencephalic neural crest
	Inferior (petrosal) ganglion (general and special afferent)	2nd epibranchial placodes
	Otic ganglion (visceral efferent)	Rhombencephalic neural crest
Vagus (X)	Superior ganglion (general afferent)	Rhombencephalic neural crest
	Inferior (nodose) ganglion (general and special afferent)	3rd and 4th epibranchial placodes
	Vagal parasympathetic (enteric) ganglia (visceral efferent)	Rhombencephalic neural crest

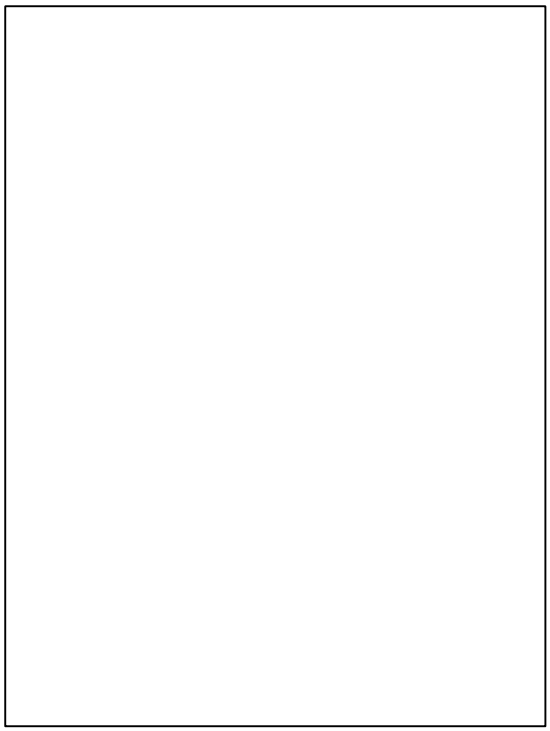
Neuronal differentiation:
Example – spinal cord.

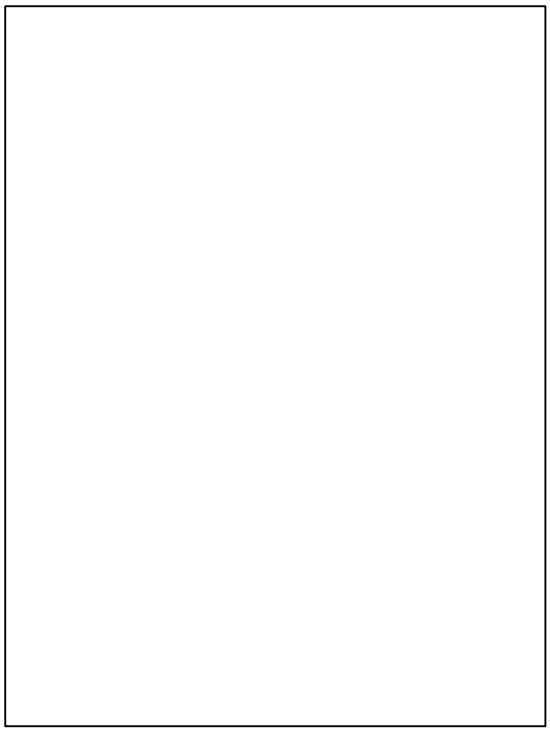
As noted for the rhombencephalon neurons closest to the floor plate became motor neurons and those closer to the roof plate became associational/ sensory. We will now look at the molecular signals underlying these choices in the spinal cord.



The generation of different classes of neurons in the spinal cord is dependent on BMP and SHH exposure which results in the expression of different PAX family transcription factors. For example, when the developing neurons see higher concentrations of SHH they express PAX6 and differentiate into motor neurons.

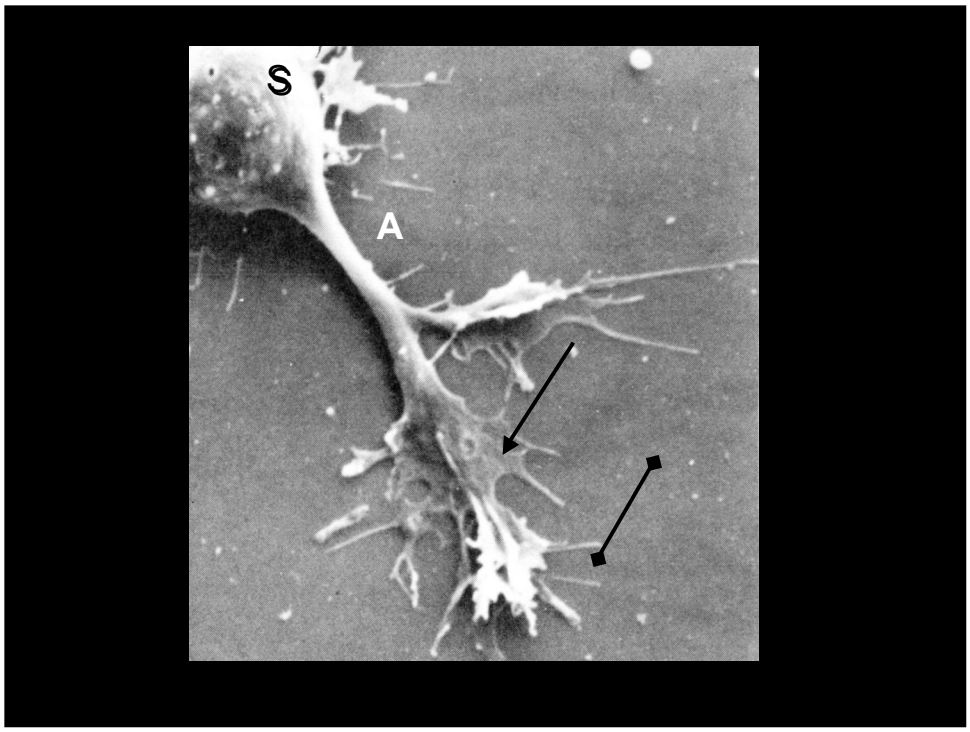

(A)
Spinal cord root
(B)
Commissural neurons
Neural tube
Association neurons
Motor neurons
Floor plate



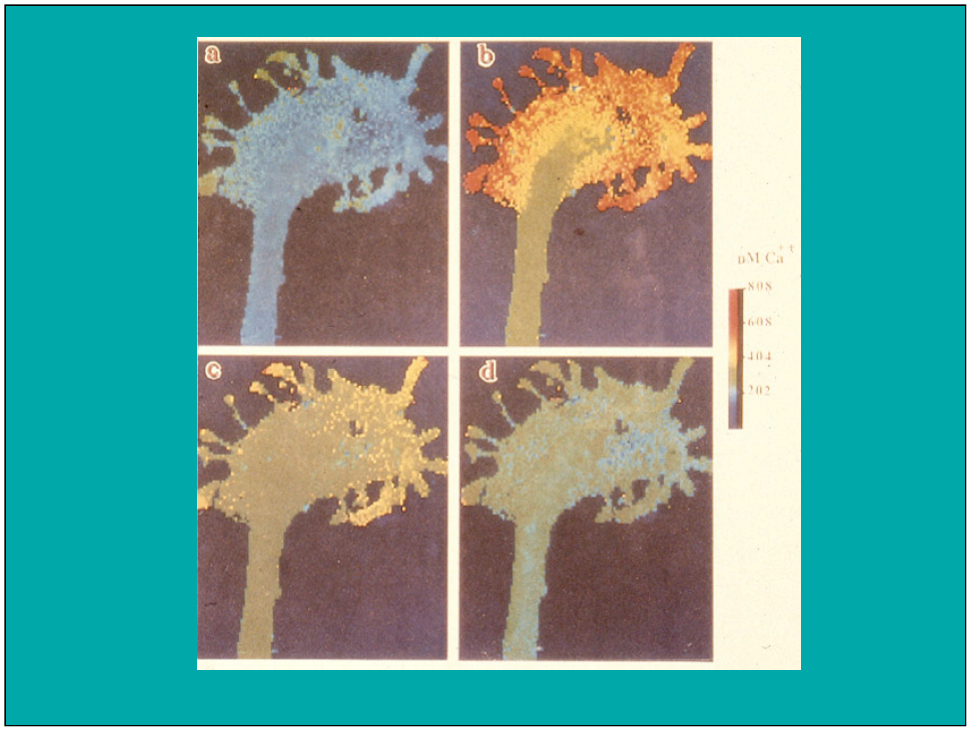


Motor neurons in spinal cord can be subdivided by their location of their cell bodies and ax
ain protein expression in motor columns in the chick spinal cord. The temporal sequence o
Differential expression of LIM homeodomain proteins occurs at around the time of axon ex
ated in different motor columns to their peripheral targets. The medial division of the media
MC) in red (LMCm); the lateral division of the LMC in green (LMCl) ; and the column of Te

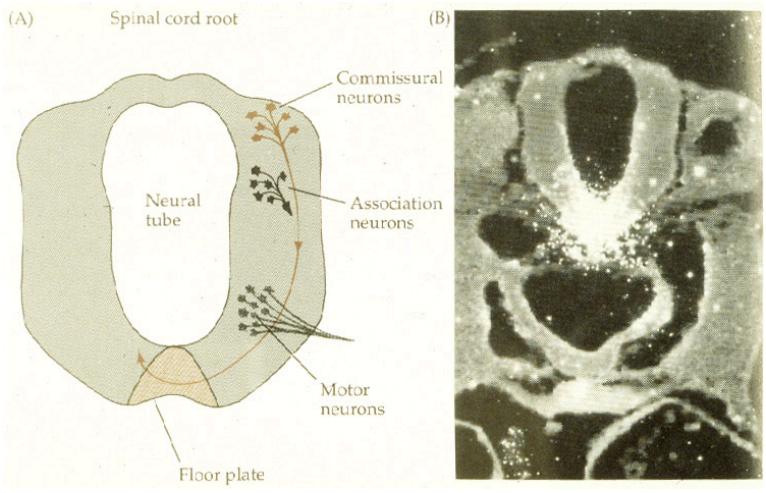
Neuronal polarity & axonal outgrowth



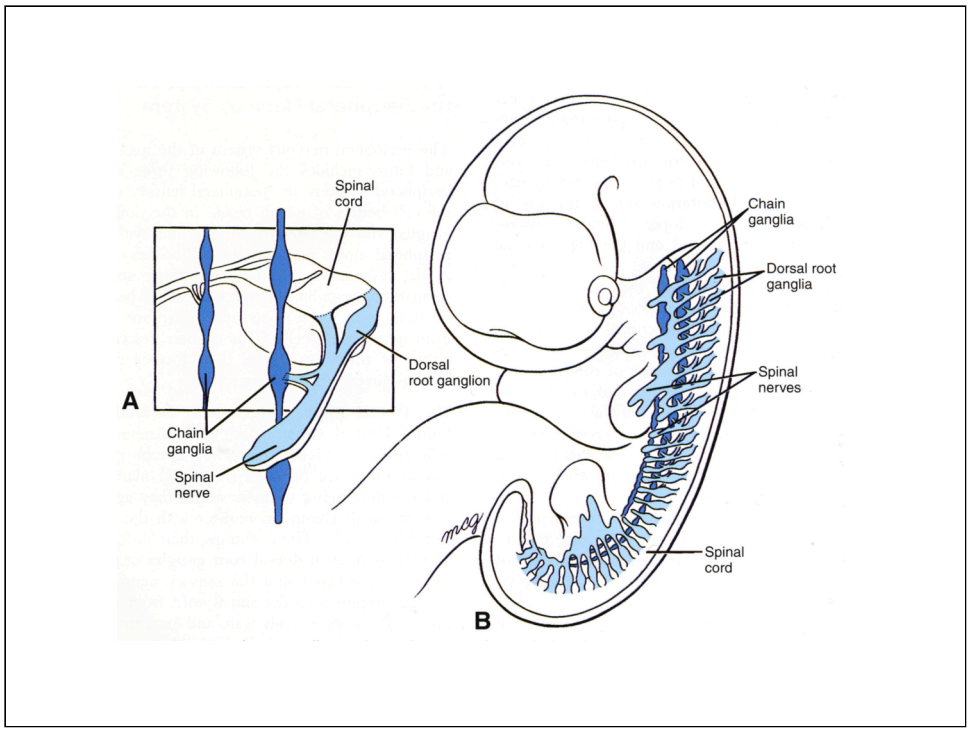
Neurons are polarized and processes are committed to becoming dendrites (not shown) or axons. Illustrated here is a neuron in culture with the axon (A) extending from the cell soma (S). The growing tip, growth cone, is characterized by flattened regions (upper arrow) or lammellopodia and spikes or filiopodia (lower arrow).



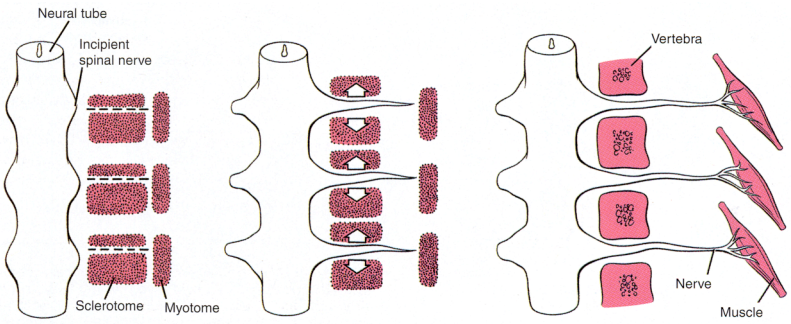
Growth is an active process. Illustration shows Ca++ in flux during active extension (compare A to B) and efflux (compare B to C to D) when growth cone at rest.



Floor plate and chemoattraction/repulsion guides axonal growth of commissural and motor axons.



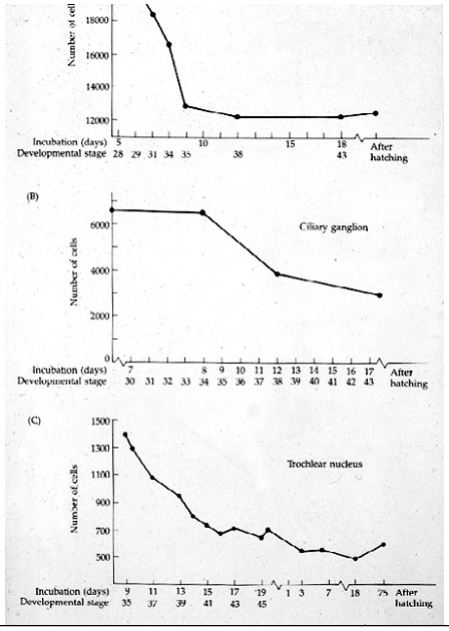
The spinal nerves of the peripheral nervous system (mixed motor and sensory) are segmented. Segmentation of DRG, chain ganglia and motor axons depends on segmentation of mesoderm.



Motor axons can only traverse mesodermal segment through its cranial ½ due to chemorepulsive molecules in the caudal ½.

Neuronal death

Programmed cell death by apoptosis



Neuronal loss is a normal aspect of the developing nervous system. It is usually associated with access to growth factors generated by the target. Timing of loss is region specific.